DIABETES MELLITUS: TREND, RISK FACTORS AND HYPERGLYCEMIC CRISIS AMONG ADULTS IN SELECTED PUBLIC HOSPITALS IN TIGRAI REGION: - A MULTI-FACILITY STUDY

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Declaration

I, the undersigned, declare that this is my original work, which has never been presented at this university or any other university, and that all the resources and materials used for the dissertation have been fully acknowledged.

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This dissertation has been submitted for examination with my approval as University supervisor.

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Dedication

This dissertation is dedicated to the memory of those individuals with diabetes who tragically lost their lives due to diabetes medication inaccessibility and my esteemed supervisor, the late Professor Fikre Enquesilasie (Ph.D).

List of Original Papers

This dissertation work is based on the following three original papers listed below.

I. **Paper I:** Getachew Gebremedhin, Fikre Enqueselassie, Negussie Deyessa, Helen Yifter: Urban-rural differences in the trends of type 1 and type 2 diabetes among adults who received medical treatment from public hospitals in resource-poor community Tigray, Ethiopia: Hospital-based retrospective study. Dove Medical Press; Diabetes Metab Syndr Obes. 2020 Mar 23:13:859-868. doi: 10.2147/DMSO.S238275.

II. **Paper-II:** Getachew Gebremedhin; Fikre Enqueselassie[2] Helen Yifter[3] Negussie Deyessa[2:] Risk factors for type 2 diabetes mellitus among middle-aged adults' out-patients in Ayder comprehensive specialized hospital, Tigrai: Matched Case-Control study. (Ref: Submission ID ce55d25a-aa9b-47fb-b306-a48f6ed8b38f) BMC Public Health: On Review

III. **Paper III:** Getachew Gebremedhin, Fikre Enqueselassie. Helen Yifter, Negussie Deyessa: Hyperglycemic Crisis Characteristics and Outcome of Care in Adult Patients without and with a History of Diabetes in Tigrai, Ethiopia: A Comparative Study. Dove Medical Press: Diabetes Metab Syndr Obes. 2021; 14:547–556. doi: 10.2147/DMSO.S275552.

Abbreviations/Acronyms

2Hpg:	2-hour Plasma Glucose
AAU:	Addis Ababa University
ACSM	American College of Sports Medicine
ACSH	Ayder Comprehensive Specialized Hospital
ADA:	American Diabetes Association
ASDRs:	Age-standardized Death Rates
ASIRs:	Age-standardized Incidence Rates
CSA	Central Statistical Agency
CI:	Confidence Interval
BRICS	Brazil, Russia, India, China, and South Africa
BMI:	Body mass index
CKD:	Chronic Kidney Disease
COBAS	Comprehensive Biochemical Analysis System
CVD	Cardio Vascular Diseases
CHS:	College of Health Sciences
DKA:	Diabetic Ketoacidosis
DKD:	Diabetic Kidney Disease
DM:	Diabetes Mellitus
DBP:	Diastolic blood pressure
DKA:	Diabetic Ketoacidosis
DSME:	Diabetes Self-Management Education
DALYs:	Disability Adjusted Life Years
ED	Emergency department
ESRD:	End Stage Renal Diseases
EOPD:	Emergency Out Patient Department
ETB:	Ethiopian Birr
FHD	Family History of Diabetes
FFAs	Free Fatty Acids
FPG:	Fasting plasma glucose
GDM:	Gestational Diabetes Mellitus
GLP-1:	Glucagon-Like Peptide-1
GI	Glycemic Index
HbA1c:	Haemoglobin A1C
HeRAMS	Health Resources and Services Availability Monitoring System
HDL-C:	High-Density Lipoproteins Cholesterol
HC:	Hyperglycemic Crisis
HEW:	Health Extension Workers
HHS:	Hyperglycaemic Hyperosmolar State
HMIS:	Health Management information system

IDDM	Insulin Dependent Diabetes Mellitus
ICU:	Intensive Care Unit
IDF:	International Diabetes Federation
IFG:	Impaired Fasting Glucose
IGT:	Impaired glucose tolerance
IQR	Inter Quartile Range
IRB:	Institutional Review Board
LPA:	Leisure Physical Activity
LDL:	Low-Density Lipoprotein
MH-OR:	Mantel-Haenszel- Odds Ratio
MNT	Medical Nutritional Therapy
MODY:	Maturity Onset Diabetes of Young
MVPA	Moderate to Vigorous Physical Activity
NCDs:	Non-communicable diseases
NIDDM	Non-Insulin Dependent Diabetes Mellitus
N/A:	Not Applicable
OR	Odds Ratio
OGTT:	Oral Glucose Tolerance Test
OHAs:	Oral Hypoglycemic Agents
OPD:	Out Patient Department
PA	Physical Activity
SBP:	Systolic blood pressure
SBGM:	Self-blood glucose monitoring
SD	Standard Deviation
SOP	Standard of Operating Procedure
SSA:	Sub-Saharan Africa
TC:	Total Cholesterol
T1D:	Type 1 Diabetes
T2D:	Type 2 Diabetes
TG:	Triglyceride level
UAE	United Arabe Emirates
UK:	United Kingdom
UN:	United Nations
USA:	United State of America
US:	United States
WC:	Waist circumference
WHA:	World Health Assembly
WHR:	Waist-to-hip ratio
WHtR:	Waist Height Ratio
WHO:	World Health Organization

Table of Contents

List of Tables

List of Figures

Abstract

Background: Diabetes mellitus is a pressing global health crisis, profoundly impacting mortality rates, morbidity, and economic stability. Type 1 and Type 2 diabetes are particularly severe public health challenges in low- and middle-income countries like Ethiopia, where urban diabetes incidence is alarmingly on the rise. The disease triggers serious acute and chronic complications, diminishing quality of life and inflating healthcare costs. Hyperglycemic crises, rampant in low-income settings such as Ethiopia, further exacerbate the burden, leading to disability, reduced life expectancy, and escalated healthcare expenses. Despite being a leading cause of hospital admissions and deaths, comprehensive data on diabetes trends, Type 2 diabetes risk factors among middle-aged adults, and treatment outcomes for hyperglycemic crises remain scarce in Ethiopia and other sub-Saharan African nations.

Objective: This study aimed to assess time trends in proportions of people with type 1 and type 2 diabetes and risk factors for type 2 diabetes among people attending adult medical outpatient departments, and treatment outcomes of patients with hyperglycemic crises admitted in adult medical wards in selected public hospitals in Tigrai Region.

Methods: A comprehensive study conducted across seven public hospitals in the Tigrai Region aimed to investigate time trends in the proportion of type 1 and type 2 diabetes cases alongside hyperglycemic crises. This retrospective cross-sectional hospital-based research spanned from September 2018 to June 2019. It involved the extensive review of 299,806 adult patient records from registry logbooks, 3056 medical charts focusing on diabetes trends, and 589 cases of hyperglycemic crises using a data abstraction checklist. Additionally, a matched case-control study at Ayder Comprehensive Specialized Hospital explored factors associated with type 2 diabetes among middle-aged adults. The study employed rigorous methods, including lottery-based sampling, to select 120 confirmed type 2 diabetes patients and 240 non-diabetic controls aged 45 to 64 years consecutively. Data collection utilized the WHO STEPS protocol customized for the local context to comprehensively assess the case-control study's socio-demographic, lifestyle, physical, and biomarker measurements. For the trend analysis of type 1 and type 2 diabetes, an Extended Mantel-Haenszel chi-square test of the linear trend was used. Associations between exposure and outcome variables in the case-control study were determined using bivariate and multivariable conditional logistic regression. The study employed descriptive

statistics and a logistic regression model to determine the relationship between exposure and outcome variables for hyperglycemic crises related to in-hospital mortality using SPSS version 25. The significance level was set at $p < 0.05$ (two-tailed) for all statistical tests. The overall findings were presented using figures, tables, and text. Ethical approval and permissions were secured, ensuring compliance with ethical standards and participant confidentiality throughout the study.

Results: From September 1, 2013, to August 31, 2018, among 299,806 adult patients receiving care at outpatient departments, the proportion of people with confirmed diabetes was 10.2 per 1000 adult patients (95% CI: 9.8-10.6). The proportion of people with diabetes significantly rose from 6.8 to 14.3 per 1000 adult patients during this period. Specifically, the proportion of type 1 diabetes increased from 1.0 to 2.2 per 1000 adult urban residents (Ptrend=0.002) and from 1.2 to 2.6 per 1000 adult rural residents (Ptrend=0.001). Similarly, the proportion of type 2 diabetes increased from 6.9 to 14.0 per 1000 adult urban residents (P trend=0.001) and from 4.0 to 9.5 per 1000 adult rural residents (Ptrend=0.001). Notably, this increase was more pronounced among women for both type 1 and type 2 diabetes.

The mean ages of cases and controls were similar at 55.9±5.0 years and 55.7±4.8 years, respectively. The odds of Type 2 diabetes were significantly higher among urban residents (AOR=5.1, 95% CI [2.0, 13.2]), widowhood individuals (AOR=3.3, 95% CI [1.3, 8.6]), divorced individuals (AOR=2.8, 95% CI[1.1,7.3]), a positive family history of diabetes (AOR=5.4, 95% CI [2.4, 12.5]), daily alcohol consumption (AOR=3.5, 95% CI [1.2, 10.2]), consumption of white rice as a favorite food (AOR=3.8, 95%CI [1.2,11.6]), elevated waist circumference (AOR=2.4, 95% CI [1.1,5.0]), and elevated waist-to-height ratio (AOR=4.4, 95% CI [1.7, 11.2]), hypertension (AOR=3.0, 95% CI [1.7,5.5]), dyslipidemia (AOR=2.8, 95% CI [1.5, 5.4]), Conversely, engaging in moderate to vigorous intensity leisure physical activity was associated with lower odds of Type 2 diabetes (AOR=0.27, 95% CI [0.1, 0.72]).

The mean age of patients with diabetic ketoacidosis and hyperosmolar hyperglycemic state was 42.9(±13.6) and 59.3(±11.2) years, respectively. About 24.2% of diabetic ketoacidosis and 42% of hyperosmolar hyperglycemic state patients were precipitated by infection, and also 163(37.6%) diabetes ketoacidosis and 33(21.2%) hyperosmolar hyperglycemic state were newly diagnosed diabetes patients. The in-hospital mortality was 78(13.2%), of which 43(7.3%) deaths were in patients with hyperosmolar hyperglycemic states. Rural residents had a higher proportion

of in-hospital mortality (17.9%) compared to urban residents (10.4%). Patients without a history of diabetes were younger (mean age 43.9±12.6 vs. 48.4±14.9), more likely to reside in rural areas (53.1% vs. 30.3%), and had a lower proportion of Type 2 diabetes (38.3% vs. 53.7%), hyperosmolar hyperglycemic state (15.8% vs. 31.8%), and lower proportion of in-hospital mortality (8.7% vs. 15.5%) compared to those with known diabetes. Rural residence (AOR 3.1, 95% CI 1.8-5.4), history of stroke (AOR 2.7, 95% CI 1.3-5.6), Type 2 diabetes (AOR 2.3, 95% CI 1.1-4.7), hyperosmolar hyperglycemic state (AOR 2.4, 95% CI 1.1-5.4), and prior diabetes history (AOR 2.0, 95% CI 1.04-3.8) were significantly associated with increased mortality risk. Conversely, presentation with excessive thirst was associated with lower in-hospital mortality risk (AOR 0.47, 95% CI 0.27-0.81).

Conclusions: The proportion of people with type 1 and type 2 diabetes has increased among urban and rural residents over time during the study period. Factors such as urban residency, widowhood/divorce, family history of diabetes, daily alcohol consumption, white rice, elevated waist circumference, hypertension, and dyslipidemia were associated with a higher risk of type 2 diabetes. In contrast, engagement in moderate to vigorous physical activity was protective. Rural residents and patients with hyperosmolar hyperglycemic states had higher in-mortality, with a history of stroke, type 2 diabetes, hyperosmolar hyperglycemic state, and history of diabetes being significant predictors, while polydipsia was protective. Health education is crucial for raising awareness about substance misuse, physical activity, and healthy eating habits at workplaces, schools, and community and family levels. Targeted screening programs for patients with existing diabetes may reduce morbidity and mortality if cost-effective interventions (for example education on healthy eating, regular physical activity, medication, and self-monitoring of blood glucose) are available. A feasible option might be to implement diabetes screening for patients aged 45 and above and those with known diabetes risk factors attending hospital adult medical outpatient departments for co-existing illnesses(patients with malaria, tuberculosis, hypertension, and so on). Furthermore, decentralizing diabetes care services to lower-level health facilities, enhancing the efficiency of bidirectional referral systems and ensuring the quality, availability, and affordability of insulin and other diabetes commodities are imperative to improve outcomes for people with diabetes in Ethiopia and similar settings.

Keywords: trend, type 1 diabetes, type 2 diabetes, middle age adults, hyperglycemic crisis,

I. Introduction

1.1. Background

Diabetes mellitus (DM) is a chronic progressive group of metabolic disorders characterized by hyperglycemia, resulting from defects in insulin-producing beta cells in the pancreas, insulin action, or both, manifested by carbohydrates, fat, protein metabolism, fluid, and electrolyte abnormalities(1). Chronic hyperglycemia, characterized by the occurrence of an FPG value greater than 126mg/dl, or A1C ≥ 6.5%, or 2-hour post-load plasma glucose (2-hPG) ≥ (200 mg/dl), leads to organ damage, dysfunction, causing symptoms, like excessive thirst, urination, vision blurring, and weight loss(2,3).

Diabetes risk factors are shaped by genetic and environmental influences, resulting in complex pathogenesis and presentations. Diabetes is classified based on physiological conditions and disease etiology into four main types: type 1 diabetes (T1D), type 2 diabetes (T2D), gestational diabetes mellitus (GDM), and other specific types due to various causes. T1D and T2D are heterogeneous, differing in pathogenesis, clinical features, and progression. While classification is crucial for appropriate therapy, some individuals cannot be distinctly classified as T1D or T2D at diagnosis(1–4).

Type 2 diabetes contributes significantly to diabetes incidence and prevalence, accounting for 90-95% of all cases. Factors in the development of T2D include physical inactivity, unhealthy diet, cigarette smoking, alcohol use, and obesity(2,5,6). Gender differences in health are linked to health-protective behaviors, with men's health significantly influenced by health behaviors, while structural determinants influence women's health. Urbanization leads to health changes, with sedentary lifestyles increasing obesity and potentially T2D rates(7).

Diabetes is a global public health issue. Almost one-in-two adults with diabetes in the age of 2079-year-olds are estimated to be unaware of their status, with nearly 90% of undiagnosed individuals living in low and middle-income countries (LMICs) in 2021. Diabetes is estimated to be among the top 10 causes of death globally, among adults 20-79 years old, with sub-Saharan Africa(SSA) experiencing the highest morbidity and mortality rates(3). The International Diabetes Federation(IDF) reported an estimated 4.6% of people with diabetes in 2000(8),

increasing to 10.5% in 2021(3) for adults 20-79 years old, with prevalence varying by age, gender, and residence. Diabetes incidence rates have decreased or remained stable in high-income countries like the US, Sweden, Italy, and Switzerland(3,9–12). but are increasing in LMICs like China, India, Pakistan, Indonesia, and Brazil, diabetes capitals of the world, since these countries are on rapid epidemiologic, economic, and societal transitions(3,13–15)**.** Eritrea has the highest documented incidence of T1D globally for 15-24-year-olds with 46.2/100,000 people affected(3,16).

Diabetes results in significant morbidity, mortality, and healthcare costs, with poorly controlled hyperglycemia leading to both long-term and acute complications. Hyperglycemic crises (HCs), including diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS), are severe acute complications requiring intensive treatment and hospitalization(17). In 2016, the U.S. reported 224,000 cases of HCs, with 203,000 for DKA(18). DKA is more common in young patients with type 1 diabetes, while HHS is more frequent in older patients with T2D. These conditions, characterized by varying levels of insulin deficiency, dehydration, ketosis, and metabolic acidosis, often coexist(17,19–22). Notably, the mortality rate for HHS is ten times higher than that for DKA(17).

Diabetes is a growing global health issue, with 27% of countries lacking an operational policy or action plan for diabetes(23). The United Nations (UN) and the WHO advise developing national diabetes strategies to address specific needs(24,25). The 75th World Health Assembly (WHA) recommended integrating diabetes prevention and treatment into primary healthcare services. The WHA adopted five global targets for 2030, including 80% diabetes diagnosis, 80% glycemic control, 80% blood pressure control, 60% cholesterol-lowering drug access, and 100% access to affordable insulin, blood glucose meters, and test strips(26). Ethiopia is implementing a strategic action plan for 2020-2025 to combat non-communicable diseases (NCDs), including diabetes, through improvements in healthcare infrastructure, public awareness, and provider training, focusing on community education and early detection(27).

In general, many studies on diabetes in high-income countries reveal varying trends, risk factors of T2D, and treatment outcomes for the hyperglycemic crisis, while hospital-based data on

diabetes and diabetes-related complications among adults is limited in low-income countries like Ethiopia.

1.2. Statement of the Problem

Diabetes is a global health concern with increasing morbidity and mortality rates, estimated to affect 537 million adults 20-79-year-olds and projected to reach 783 million by 2045 based on available data from 144 countries extrapolated to 71 countries with no data available from studies in countries of similar geographical location, IDF Region, World Bank income classification (low-, middle-, and high-income), ethnicity and language(3). Using the extremlely limited data available on relative risks of diabetes for mortality was estimated to be responsible for 6.7 million deaths in 2021, one death every five seconds, and 11.3% of all deaths among 20-79-year-olds, with higher rates among women and under 60 years old(3). Diabetes-related deaths account for 35.6% of NCD deaths and 2.7% of all causes worldwide(28), primarily caused by cardiovascular, kidney, DKA, infection, neuropathy, and foot ulcers(3). The global diabetes mortality rate varies significantly by region, with regions like Oceania, the Caribbean, and SSA experiencing rates 2 to 12 times higher than the global average(28). Diabetes imposes a significant economic burden, with global health expenditure on the condition reaching USD 966 billion in 2021, a 316% rise over the past 15 years(3).

Diabetes incidence has declined in high-income nations, but in LMICs, including Sub-Saharan Africa(SSA), it is currently a significant public health concern(3). The incidence of T2D in Brazil, Russia, India, China, and South Africa (BRICS) countries increased by 83.3% from 1990 to 2019, with diabetes-related mortality significantly differing due to disparities in healthcare infrastructure, economic development, and public health initiatives(29).

Diabetes affects 24 million adults 20-79-year-olds in SSA, increasing 134% by 2045. High mortality rates, especially among individuals under 60, with 76.4% of deaths occurring in this age group, represent the highest diabetes-related mortality rates globally. These outcomes are driven by inadequate healthcare, limited medication access, and socio-economic challenges (30). Diabetes-related morbidity and mortality in SSA vary significantly, with South Africa(28–30), Nigeria(3,31), Tanzania(30), Kenya (28), and Ethiopia(32) having the highest rates, with a

notable urban-rural disparity in morbidity and mortality, mainly due to urbanization, lifestyle changes, and inadequate healthcare(30,33).

Diabetes-related deaths in Ethiopia significantly contribute to the overall mortality from NCDs (34,35). NCDs are responsible for about 55% of total deaths in urban areas like Addis Ababa, 51% in Tigrai, and 29-43% in more rural regions. Diabetes is one of the top five leading causes of death due to NCDs in Ethiopia(35). The Global Burden of Disease(GBD) Study estimates for diabetes-related deaths in Ethiopia accounts 1.0% of all deaths in Ethiopia in 2010 and trended upward to 1.4% of all deaths in 2015 generated using Cause of Death Ensemble model (CODEm), highlighting a growing public health concern(34). Ethiopia is grappling with a significant burden of diabetes and other chronic diseases due to inadequate health literacy, resource-poor environments, and inadequate health systems(35,36). According to IDF estimates; Ethiopia's diabetes prevalence has significantly increased from 1.0% from extrapolated estimates in 2000(8) to 3.3% in 2021 generated from Animaw, W. and Seyoum, Y 2017 from locally representative 691 urban and 714 rural settings (3) among adults 20-79 years old, with 1.92 million cases, with 57% undiagnosed and 26,448 deaths in 2021, expected to rise due to lifestyle changes and urbanization (3).

A cross-sectional multistage stratified sampling National STEPS Survey in Ethiopia conducted in nine regions and two city administrations by Ethiopian Public Health Institute (EPHI) in 10260 people indicated gender disparities in the prevalence of diabetes. Diabetes prevalence is 3.2%, with 3.5% males and 3.0% females in 2016 in the age group of 15 to 69 years old(38). A hospital-based retrospective record review at the main referral hospital in northwest Ethiopia reported a 125% average increase in the proportion of both type 1 and T2D from 2000 to 2009(37). Similarly, in 2015, a three year retrospective record review study at Ayder Comprehensive Specialized Hospital in Tigrai revealed a diabetes proportion of 1.3%(39). A survey in Gondar revealed that men, poor rural farmers with low BMI, stunted, and undernutrition are more likely to be diagnosed with T1D, with an annual incidence of 2.75 per 100,000 people(40). Understanding diabetes incidence trends in Ethiopia is crucial for effective public health planning, disease management, economic planning, and global health equity, enabling more effective targeted interventions and policies(30,35,41).

Global research indicates that age over 45, gender, residence, marital status, income and education level, family history of diabetes, high blood pressure, cholesterol, smoking, alcohol consumption, physical inactivity, and unhealthy diets—all of which are made worse by sedentary lives and obesity are common risk factors for T 2D(42–47).

Nigerian studies revealed that hyperglycemic crises(36.1%), diabetic foot (19.6%), uncontrolled hypertension (16.9%), and stroke (8.7%) were the most common complications for T2D patients upon admission(48), with 18% and 35% fatalities for DKA and HHS, respectively(49).

Diabetes in Ethiopia leads to hospital admissions, complications, and economic losses, affecting individuals, families, healthcare structures, and national economies(50,51). A study at Tikur Anbesa Hospital in Ethiopia revealed a 6.5% diabetes-related hospitalization rate, with diabetic foot ulcers and cardiovascular disease being primary diagnoses for T2D admission. At the same time, DKA was the leading diagnosis for T1D patients, leading to a 21.0% in-hospital mortality rate(51). Studies in Ethiopia found that 34.6-45.4%, 13.2-59%, and 32.3-40.4% of hyperglycemic patients had no prior diabetes history, infection, and non-compliance on admission, respectively, with mortality rate ranges of 9.8-21%(50–55).

A study in Haramaya revealed that 16.5% of hyperglycemic crisis-related mortality occurs, with 21.4% for HHS and 11.1% for DKA(54). Diabetes-related morbidity and mortality in Ethiopia are primarily attributed to delayed diagnosis, limited healthcare access, lack of awareness, inadequate infrastructure, shortage of trained professionals, and inpatient facilities(50). Most studies on hyperglycemic crises in SSA focused on DKA, while HHS is linked to higher mortality rates compared to DKA (49,54). Understanding hyperglycemic crises in patients with and without a prior diabetes history is crucial for improving clinical outcomes, treatment protocols, patient education, self-management, and public health planning and resource allocation to better address diabetes challenges(56).

Ethiopia's diabetes prevalence has significantly increased in the past two to three decades, posing significant economic challenges for drug consumption and bed occupancy(50,51). Hospital-based evidence on trends, risk factors, and treatment outcomes is limited in SSA countries, including Ethiopia. This study assessed diabetes mellitus in Tigrai public hospitals, focusing on

time trends of type 1 and type 2 diabetes, risk factors of T2D, and hyperglycemic crisis characteristics.

1.3. The rationale of the study

Diabetes mellitus is a significant public health issue, causing hospital admissions, mortality, and economic loss in high-income and LMIC countries, with Ethiopia being the fourth with diabetes burden in SSA(3); faces a disproportionate burden of diabetes and other NCDs due to urbanization, economic changes, healthcare system limitations, socio-economic disparities, and policy inadequacies, necessitating multifaceted approach for addressing challenges(3). However, healthcare funding focuses on communicable diseases and neglects large populations experiencing excess morbidity and mortality from NCDs, including diabetes in SSA(36). The Ethiopian Federal Ministry of Health has developed and implemented national strategic action plans for 2020-2025 to combat NCDs, including diabetes, focusing on prevention, early detection, and management(27). However, little attention is given to diabetes, with all those burdens.

As per IDF and hospital reports, diabetes mellitus has been increasing in the last three decades in Ethiopia(3,8). Hospital-based data offers valuable insights into diabetes incidence, reflecting the disease burden among patients seeking medical care and aiding in resource planning, early detection, and timely intervention. It also helps to identify trends and patterns in outpatient settings, enabling timely management and intervention. However, hospital-based trends in the incidence of type 1 and type 2 diabetes are limited. Existing studies on diabetes are either community-based surveys(38,57) or children and adults mixed reports(37), with health professionals relying on external evidence to manage diabetes and related problems.

Obesity, unhealthy diets, and sedentary lifestyles exacerbate the T2D burden, especially in Ethiopia, due to rapid epidemiologic, economic, societal, and nutritional transitions(27,35). Addressing T2D risk factors is crucial for preventing the disease, reducing healthcare costs, and developing effective interventions to enhance health outcomes and quality of life. Studying T2D risk factors in middle-aged adults(45-64 years) allows investigation of risk factors, hormonal shifts, and metabolic changes, that are crucial for effective intervention, early detection, disease management, prevention, and public health policy influence in the population with the highest

number of incident cases of T2D. However, data on local risk factors for the illness in this age group is scarce. Previous studies in Ethiopia used a community-based cross-sectional study design(38,57) or a health institution-based cross-sectional design (58), with mixed reports for children and adults. At the same time, this study aimed to identify risk factors of T2D among middle-aged adults using a matched case-control study design.

Studying hyperglycemic crises in patients with and without prior diabetes history is crucial for improving diagnosis, treatment, prevention strategies, patient outcomes, reducing healthcare burden, optimizing healthcare resources, and promoting targeted interventions. In the existing studies in SSA, including Ethiopia, most of the studies either focus on DKA (52,55) or only focus on treatment outcomes (50,54). Both did not attempt to differentiate the characteristics of patients with and without prior diabetes history. Understanding differences in clinical characteristics allows researchers and healthcare providers to develop tailored approaches to prevention, diagnosis, and treatment.

Investigating this area of study will guide policymakers in revising their policies, developing suitable screening and treatment guidelines, and designing appropriate prevention and control mechanisms for NCDs, including diabetes mellitus. Likewise, it will be necessary for health institutions to improve the quality of NCD services, including diabetes patients.

Moreover, healthcare professionals in Ethiopia will learn about type 1 and type 2 diabetes trends incidence, risk factors T2D among middle-aged adults, and hyperglycemic crisis and outcomes of care, improving health education, early treatment, and prevention, and designing appropriate treatment, prevention, and promotional approaches. The findings will inspire researchers to conduct additional studies, urge scientists to investigate unrecognized areas of interest, and lay the groundwork for future research.

1.4. Review of Literature

1.4.1. The Biology of Diabetes Mellitus

1.4.1.1. Definition and description of Diabetes Mellitus

Diabetes mellitus (DM) is a chronic progressive group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin-producing beta cells in the pancreas, insulin action, or both, manifested by carbohydrates, fat, protein metabolism, fluid, and electrolyte abnormalities(1). Chronic hyperglycemia, defined as FPG >126 mg/dl, A1C ≥ 6.5%, or 2-hPG ≥ 200 mg/dl, can cause organ damage and dysfunction, leading to symptoms like excessive thirst, frequent urination, blurred vision, and weight loss(2,3). Diabetes classification is crucial for therapy determination, but misdiagnosis is common due to its complex pathogenesis and varied presentation. Diabetes can be divided into four main types: T1D, T2D, GDM, and diabetes caused by specific conditions. WHO classifications 2019 identify two major types(2–4).

Type 1 diabetes, accounting for 5–10% of cases, causes irreversible destruction of pancreatic beta cells, resulting in absolute insulin deficiency. It primarily affects children and young adults, with symptoms like excessive thirst, hunger, frequent urination, weight loss, vision changes, and fatigue(2–4). Type 2 diabetes, accounting for 90–95% of cases, causes insulin resistance and relative insulin deficiency. It mainly affects adults but also occurs in children and adolescents. While often managed with diet, lifestyle changes, and medication, some may require insulin. Prediabetes is typically asymptomatic(1–4).

1.4.2. Aetiology and Pathogenesis of Diabetes

Despite extensive research, diabetes's aetiology remains unknown, influenced by physiological conditions during assessment and diagnosis. Therapeutic approaches for maintaining or improving glucose tolerance could be influenced by β-cell dysfunction and decreased β-cell mass. Diabetes is a complex disease caused by defects in insulin sensitivity and secretion. Genetic and environmental factors can cause β-cell decline. Researchers suggest that various mechanisms can cause β-cell decline or destruction, leading to hyperglycemia in type 1 and 2 diabetes. Genetic and environmental factors can cause this loss, putting patients at risk for chronic complications. Rates of progression may vary(1,2,4,5,59).

1.4.3. Clinical Course of Diabetes Mellitus

An insulin deficiency can lead to significant organ damage, resulting in severe health complications such as cardiovascular diseases, nerve damage, kidney damage, and eye disease if not properly managed(2,5). The primary mechanism underlying both Hyperosmolar Hyperglycemic State (HHS) and Diabetic Ketoacidosis (DKA) is the combination of insulin deficiency and elevated counter-regulatory hormones. This imbalance causes hyperglycemia through increased gluconeogenesis, accelerated glycogenolysis, and reduced glucose utilization by peripheral tissues. Consequently, this leads to osmotic diuresis, hypovolemia, a decreased glomerular filtration rate, and further exacerbation of hyperglycemia(17,60,61). DKA occurs when decreased insulin and increased hormones activate hormone-sensitive lipase in adipose tissue, breaking triglyceride into glycerol and free fatty acids (FFAs). This leads to ketone bodies, decreased serum bicarbonate, and metabolic acidosis(17,62).

In HHS, some insulin reserve prevents lipolysis, leading to minimal or absent ketogenesis. With decreased fluid intake by the patients who are usually elderly, dehydration is severe in HHS. Hence, they are predisposed to prerenal acute kidney injury and hyperosmolarity (62). Literature indicates that high blood glucose levels increase serum concentration(2), leading to glycosuria, polyuria, nocturia, dehydration, polydipsia, fatigue, blurred vision, abdominal pain, and headaches. Manifestations include hyperglycemia, excessive thirst, urination, hunger, weight loss, fatigue, and abdominal pain(2,4,5).

1.4.4. Diagnosis of Diabetes Mellitus

As the literature demonstrates, a diabetes diagnosis can have significant implications for individuals, potentially leading to stigma that affects employment, insurance, driving status, and social opportunities, and can have cultural, ethical, and human rights consequences. Conducting appropriate tests is crucial to prevent disease progression (4).

Blood tests are essential for early diabetes detection, treatment, and risk reduction. The ADA 2020 standards list three diagnostic methods: FPG, OGTT, and A1c. However, research shows less concordance between these tests. 2-hour PG diagnoses more individuals with diabetes or prediabetes than FPG or A1C tests. Haemoglobin A1c tests diagnose only 30% of diabetes cases.

Diabetes is defined as Fasting Plasma Glucose (FPG) value ≥126mg/dl or A1c ≥ 6.5% or 2-hr post-load plasma glucose ≥ (200 mg/dl), or random blood glucose (RBG) ≥ (200 mg/ dl) in the presence of signs and symptoms of diabetes(2–4). The postprandial plasma glucose test uses 75g of anhydrous glucose in water, and random glucose tests can be used in patients with classic hyperglycemia or hyperglycemic crisis symptoms(2,4,5). Diagnosing hyperglycemia requires two abnormal test results from the same or two separate samples, preferably with the same test, to confirm the diagnosis. In symptomatic individuals, one abnormal result is diagnostic(3,63).

The literature demonstrates that diagnosing a hyperglycemic crisis relies on patient history, classic symptoms, and laboratory tests. Diagnosing DKA involves identifying plasma glucose levels greater than 250 mg/dL, positive urine ketones, arterial pH below 7.3, and bicarbonate levels under 15 mEq/L. HHS can be presumed in diabetic patients exhibiting altered mental states, with plasma glucose levels exceeding 600 mg/dL, serum osmolality over 320 mOsm/kg, minimal or no ketonuria or ketonemia, an anion gap below 12, and no significant acidosis (HCO_3 levels above 15 mEq/L or pH above 7.3)(64,65).

1.4.5. Management of Diabetes Mellitus

The goals of diabetes treatment and quality of life depend on maintaining positive health habits and psychological well-being, which includes medical nutrition therapy, weight control, physical activity, alcohol reduction, smoking cessation counseling, and psychosocial care. A study shows that multidisciplinary lifestyle changes can improve glycemic control and reduce complications by 50-75%(66). Non-pharmacological diabetes intervention approaches to enhance overall health and manage diabetes effectively. Personalized treatment goals and strategies are crucial for success(67,68). The ADA and the European Association for the Study of Diabetes have emphasized that personalized treatment goals and therapeutic approaches are essential for the success of T2D(69).

Diabetes self-management education and support (DSMES) is crucial for improving glycemic targets and reducing drug costs. Patient-centered programs using new technology can delay complications and enhance self-efficacy. DSME program was reported to reduce drug costs by 62%(63, 68,70).

Weight reduction and management strategies are crucial for individuals with T2D or prediabetes, as they delay progression and promote sustained diabetes remission(68). A ≤ 800 kcal/day diet replacement can induce weight loss(63,66,71). Medical nutritional therapy is essential for preventing and treating Type 2 Diabetes (T2D). A healthy diet low in saturated fat and sodium high in fruits, vegetables, whole grains, cereals, and legumes is recommended. Individualized meal planning and referral to a registered dietitian nutritionist can help(72,73).

Physical activity, particularly cardiorespiratory fitness, significantly reduces diabetes incidence and impact, improving glycemic control, weight maintenance, and medication use. Combining physical activity with dietary intervention leads to more significant reductions(63). The WHO and ACSM recommend that adults with diabetes engage in 150-300 minutes of moderate-intensity or 75–150 minutes of vigorous-intensity physical activity weekly, including muscle-strengthening activities twice weekly (74,75).

T2D requires medical nutrition and exercise for glucose control, but long-term maintenance often requires medications(76). A paradigm shift is recommended for combination therapy, targeting eight pathophysiological mechanisms underlying T2D, including reduced insulin secretion, elevated glucagon secretion, liver glucose production, neurotransmitter dysfunction, insulin resistance, and impaired peripheral tissue glucose uptake(77). Insulin therapy is crucial for glucose control. Patients with Type 1 Diabetes (T1D) need insulin to sustain life, manage blood glucose, and reduce the risk of complications. For Type 2 Diabetes (T2D) patients unresponsive to or contraindicated for oral hypoglycemic agents, insulin is also necessary to control blood glucose and minimize complications(76).

Multiple studies have demonstrated that the treatment goals for hyperglycemic crises in adults encompass several key objectives. These include identifying and managing the underlying cause, replenishing fluid volume, resolving ketonemia, correcting acidosis, restoring normal blood glucose levels, enhancing mental status, optimizing kidney function, replenishing electrolytes and minerals, and diagnosing and treating coexisting illnesses. Electrolyte levels and venous pH should be monitored every two hours until bicarbonate levels and the anion gap return to regular and electrolyte imbalances are corrected(65,78).

1.4.6. The Epidemiology of Diabetes Mellitus

1.4.6.1. Magnitude and Trends of Diabetes

Prevalence of diabetes mellitus, a global health challenge, is estimated to have increased significantly among adults aged 20-79, from 4.6% in 2000 to 10.5% in 2021. Diabetes prevalence in urban and rural areas is estimated to be 12.1%, 8.3%, 11.1%, 10.8%, and 5.5%, respectively, in high-income, middle-income, and low-income countries, according to the IDF report(3,8). The global age-standardized prevalence of diabetes is estimated to have risen from approximately 4.3% in 1980 to 9.0% in 2014 among men and from 5.0% to 7.9% among women(79). By 2021, the impact and trajectory of estimated diabetes-related health challenges significantly varied across regions and countries, influenced by age, gender, and urban or rural residence(3,5).

In high-income countries, DM prevalence is estimated at 3.5-12.2%(12,14, 15,96–98). In a study in the US, the DM prevalence was estimated at 12.2% of all US adults in 2015(12). A study in Switzerland revealed that the extrapolated overall diabetes prevalence was 4.9%, higher in men than in women [5.7% versus 4.2%]. The prevalence increased from 3.9% in 2006 to 4.9% in 2011 and increased with age, while the incidence of diabetes decreased from 0.63% in 2006 to 0.58% in 2011(9). A study in Sweden from 2007 to 2013 showed a steady increase in diabetes prevalence from 5.8 to 6.8%, but the incidence remained constant at 4.4 per 1000(10). A study in Ireland showed a significant increase in doctor-diagnosed diabetes prevalence from 2.2% in 1998 to 5.2% in 2015, representing a 0.17% annual increase(83).

IDF reported that in some high-income countries, there is evidence of a falling or stable incidence of diabetes, regardless of the inevitable rise in prevalence(3). In particular, diabetes incidence showed a decreasing pattern, which has been seen in the USA[2008-2014], Denmark[2004-2007], Portugal[2008-2014], Israel[2008-2012], Sweden[2008-2012], Germany [2008-2010], Canada[2008-2011], and the UK[2008-2014]. Still, it is not yet clear what is driving the observed falls in incidence(3,84).

According to Sun et al. (2019), the incidence rate of Type 2 Diabetes (T2D) in BRICS countries was 280.2 per 100,000. Between 1990 and 2019, the incidence of T2D in BRICS increased from 152.9 per 100,000 to 280.2 per 100,000. China had the lowest growth rate at 63.6%, while India

had the highest at 110.9%. Overall, the incidence rate of T2D among the BRICS population increased by 83.3% during this period(29).

Investigators from LMICs reported that the trends of diabetes prevalence increased in the previous four decades, possibly due to rapid economic development accompanied by environmental, social, and behavioral changes occurring in many LMICs over the past few decades(79,85). A Kazakhstan study revealed a 1.7-fold increase in Type 1 and Type 2 diabetes prevalence from 2014 to 2019, with the incidence decreasing 1.5 times in T1D, while T2D remained similar over the years(86). A Beijing longitudinal study revealed a significant increase in the incidence of type 1 diabetes from 2.72 in 2007 to 3.60 in 2017 per 100,000 persons(87). The incidence rate of T2D in South Africa has significantly increased from 148 in 1990 to 306 in 2019 per 100,000 adult populations(29). Similarly, Amadi et al.'s study in Nigeria showed a rise in T2D incidence from 4.88% in 2014 to 6.04% in 2018, primarily among men and women, but with a decrease in rural areas(31). Likewise, a study conducted in a northwest Ethiopia hospital indicated that the average increase in the proportion of Type 1 and Type 2 diabetes mellitus cases between 2000 and 2009 was 125%(37).

Different studies pointed out that the prevalence and incidence of diabetes have different reports with various explorative variables such as sex, age, residence, and social class(10,88–91). Other studies in populations of Western origin and globally have consistently reported higher diabetes prevalence in men than in women, and being male is strongly associated with the annualized rates of diabetes per 1,000 individuals. Studies in the US, UK, Sweden, and Thailand reported that males had higher annualized rates of diabetes per 1,000 individuals compared to women (10,88–91). Likewise, a study conducted by Madede et al. in Mozambique revealed that diabetes prevalence increased from 2.9% in 2005 to 7.4% in 2015, with a higher increase among men from 3.5 to 9.5% compared to women 2.4 to 6.0% over the study period(92).

Whereas, studies in Brazil [2006-2014] and Africa[1980-2014] showed a higher increase was observed among women compared to their counterpart men from 6.3 to 8.7 % in women and 6.0 to 7.3 % in men(93), and 4.1 to 8.9% for women and 3.4 to 8.5% for men), respectively(94). Similar studies in Panama and China demonstrated a higher prevalence of diabetes in women

(6.0% of women Vs 4.3% of men; P < 0.0001) in 2015(95) and 5.8% of men Vs 6.1% of women in 2014(96), respectively.

Studies in the US between 1980 and 2012 showed that the prevalence of diabetes is much higher in the age group 65-79 years (9.8% in 1980 and 20.7% in 2012) compared to the age group 20-44 years with a prevalence of 1.1% in 1980 and 2.5% in 2012(97). A study in Sweden reported that the prevalence of diabetes primarily increased with age; 12.8% of women and 18.8% of men ≥ 65 years had diabetes(10). A study in Bulgaria revealed that the prevalence of diabetes primarily increased in the aged group of 50–59 years: 9.4% in 2006 vs 15.7% in 2012 had diabetes (98).

In Panama, a study reported that 13.8% of individuals aged 60 years and older had diabetes in 2015(95). Similarly, in Brazil, research indicated an overall increasing trend in diabetes prevalence from 5.5% in 2006 to 8.0% in 2014, with a notable annual increase of 0.57% among adults aged 65 years and older(93). Furthermore, a study conducted by Madede et al. in Mozambique revealed that diabetes prevalence rose from 4.2% to 10.1% among individuals aged 45 to 64 years, compared to an increase from 2.3% to 5.7% among those aged 25 to 44 years over the study period(92).

Diabetes has emerged as an increasingly prevalent and severe public health challenge affecting both urban and rural areas(48,95,99,100). Studies indicate that the incidence and prevalence of diabetes vary significantly based on individuals' residence and the country's income level. In high-income countries, diabetes rates tend to be higher among rural residents compared to urban residents. For instance, studies in the US have shown that living in higher-density urban communities was associated with lower odds of new-onset Type 2 Diabetes (OR [95% CI]: 0.80 [0.66, 0.97]) compared to rural areas(101). Similarly, in Alberta, Canada, age- and sex-adjusted diabetes prevalence increased by 35% among rural Status Aboriginal populations (from 10.9 per 100 in 1995 to 14.7 per 100 in 2006), compared to a 22% increase in urban areas (from 9.4 per 100 in 1995 to 11.5 per 100 in 2006)(102).

Conversely, in low- and middle-income countries (LMICs), diabetes tends to be more prevalent among urban residents than rural residents (48,95,99,100,103). For example, studies in North Africa have reported higher diabetes prevalence in urban areas, ranging from 2.6% in rural Sudan to 20% in urban Egypt(103). Similar patterns were observed in Kazakhstan (16.3% in

urban vs. 8.6% in rural) (99), China (12.0% in urban vs. 8.9% in rural) (96), and Ethiopia (5.1% in urban vs. 2.1% in rural) (100).

Adult-onset type 1 diabetes incidence varies significantly, from less than one per 100,000 in China to over 30 per 100,000 in Northern Europe and Eastern Africa, reflecting geographical variation in childhood-onset diabetes, whereby countries with high rates in children and adolescents also tend to have higher rates in adulthood(104). A meta-analysis of adult-onset T1D incidence in countries showed mixed trends, with a decrease in Sweden, Korea, Taiwan, and the U.S. from 1983 to 2017, and an increase in Mali from 2007 to 2016, while no change from Spain, the U.K., and Hong Kong(105). Similarly, a study conducted by Vojislav et al. in Serbia indicated that a significant decrease in the incidence of type 1 diabetes was determined in adults aged 25–29, with an annual percentage change of 7.3% between 2006 and 2017(106).

A 2017 study conducted in Finland by Hakkarainen et al. found that the average annual age-standardized incidence rate of Type 1 diabetes among men aged 18–39 was 29 per 100,000/year, marking a 33% increase from 1992 to 2007. Women's incidence rate remained stable at 16 per 100,000/year. For working-age individuals (18–64), the age-standardized prevalence of Type 1 diabetes increased by 39% among women and 33% among men(107). Similarly, findings from Korea indicated that the annual incidence rate of Type 1 diabetes from 2007 to 2013 ranged from 2.73 to 5.02 per 100,000 people, with incidence rates remaining consistent among adults aged over 30 years. In contrast, the incidence rate of atypical Type 1 diabetes in 2013 was higher in individuals aged 40 years and older compared to younger age groups(108).

Similarly, a study in Iran indicated that the incidence of type 1 diabetes increased between 1990 and 2019(109). Likewise, a survey conducted by Sandy et al. in Mali revealed that T1D incidence for 20 to 24 years per 100,000 population/year increased from 0.00 (0.00–0.30) in 2007 to 1.10 (0.64–1.76) in 2016(110). Moreover, Eritrea has the highest documented incidence of adult type 1 diabetes globally, with 46.2/100,000 people affected(3,16).

A study by S. Alemu and colleagues in Gondar and Jimma found an annual incidence of insulin-requiring diabetes of 2.1 per 100,000, twice as high in men as women, peaking at 25 and 29 years of age. Insulin-requiring diabetes incidence in urban Gondar and Jimma is five times higher than in rural areas, primarily among subsistence farmers or unemployed individuals with

low BMI(111). While a case-series study conducted by Balcha et al. in Gondar diabetes clinics over 20 years (1996–2016) reported that there was a striking male predominance of cases with a rural sex ratio, 2.3M:1F was significantly more significant than the urban sex ratio, 1.3M:1F ($P<0.001$). When clinical onset was between 20 and 35 years, this was more marked in the poor rural dwellers than the urban population. While most patients with Type 1 diabetes presented with low BMIs and reduced height, stunting preferentially affected rural men, with an overall annual incidence of 2.75 per 100,000 populations(40).

1.4.6.2. Risk Factors of T2D

The aetiology of diabetes is poorly understood; changes in diet and lifestyle due to rapid economic development are foremost among the principal drives of diabetes. Barring the environmental impact, the genetic component plays a vital role in the development of diabetes. It is a progressive, multi-factorial chronic metabolic disorder with a strong link to demographic, behavioral, and lifestyle factors (dietary habit, sedentary lifestyle, alcohol intake, and cigarette smoking), the most critical factors(42–47).

1.4.6.3. Socio-demographic characteristics

Research indicates that socio-demographic factors like location of residence, age, gender, ethnicity, marital status, education, and income increase the risk of developing T2D, but there is inconsistency in published reports(86,87,112).

The socio-demographic and geographic burdens of T2D are uneven worldwide and closely linked to the neighborhood level. In high-income countries, including the US, Canada, and Australia, people living in deprived neighborhoods are at increased risk of T2D(101,102,113), whereas, in developing countries, the risk is higher in urbanized areas(7,114,115). Previous studies in developing countries in Maynamar[12.1% urban Vs 7.1% rural](114), West Africa[6.2% urban Vs 2.5% rural](115), Algeria[14.5% urban Vs 12.3% rural](7), and North West Ethiopia[5.1% urban Vs 2.1%](100), reported that the risk of developing T2D in urban dwellers higher compared to their rural counterparts. Urbanization in developing countries leads

to changes in eating habits, physical activity, smoking, and alcohol consumption, contributing to obesity and NCDs, including diabetes(114).

Age significantly increases diabetes risk in both men and women, but studies show no uniformity in diabetes prevalence across age ranges. A study in China revealed that the odds of developing diabetes for age ≥65 years was 1.7 in rural and 4.0 in urban residents, higher compared to ages 20-29 years(116). Similarly, a case-control study in Saudi Arabia revealed that cases were more likely to be older than 40 years compared to the group whose age was ≤ 40(the odds ratio of the age > 60 years was 15.6 (117)). A study conducted in Mozambique revealed that higher diabetes prevalence among the age group 45 to 64 years between 2005 and 2015 was 5.9%(1.6-10.2, p= 0.007)(92). Similarly, a study conducted by Issaka et al. showed that the risk of developing T2D was 2.26, 2.93, and 4.35 times higher in age groups 35-44, 45-54, and 55-64 years compared to 25-34 years of age, respectively(115). Moreover, studies in West Africa and North West Ethiopia indicated that **d**iabetes prevalence increased with age up to the oldest age(100,118).

Research shows inconsistencies in findings on the risky gender group for T2D, with health disparities influenced by lifestyle factors and structural determinants, contrasting men's health behaviors. Reports show gender differences in health-protective behaviors, with men's health significantly influenced by their health behaviors and women's health significantly influenced by structural determinants(7,10,96,100,119–123). Findings from South Africa reported that men had an increased risk for the development of T2D compared to women(123). At the same time, other studies in Africa, Brazil, Panama, China, Iran, Senegal, Nigeria, and Northwest Ethiopia demonstrated a higher prevalence of T2D among women than their counterpart men(7,10,96,100,119–122). A study conducted by Issaka et al. in West Africa indicated that being women decreases the risk of developing T2D by 59.0% compared to their men's counterparts, p=0.001(115).

Marriage has been a fundamental social institution since ancient times, playing a significant role in the lives of most people (124). Previous studies produced conflicting findings regarding the association between marital status and T2D(124,125). Research indicates that marriage improves health outcomes, lowers diabetes incidence, and enhances diabetes treatment adherence in partnered patients due to the influence of health behaviors and socioeconomic status(125).

Ramezankhani et al. indicated that being widowed was associated with a lower risk of T2D in Iran(124). Similarly, findings of both urban and rural areas from West Africa revealed that being divorced/widowed lowers the risk of developing T2D, compared to single individuals(115), whereas in Saudi Arabia, being widowed increases the risk of T2D(124). Other studies conducted in Iran indicated that 23.0% of widowed had T2D compared to 13.2% of married women ($p< 0.001$)(7).

Significant studies show that job category is an essential predictor of T2D, which might be related to physical inactivity. According to a Swedish study, compared to university professors and physiotherapists, professional drivers, manufacturing workers, and cleaners had a threefold higher risk of type 2 diabetes(84). In Malaysia, unemployed, senior officials, managers, and homemakers had the highest prevalence of diabetes at 16.1%, 15.9%, and 14.2%, respectively(126). Similarly, a study in Saudi Arabia revealed an increased risk of T2D among jobless/homemakers and employed study participants(112). A study in South East Nigeria indicated that jobless/homemakers, retired, and bankers were found to have a higher prevalence of diabetes than people with non-sedentary jobs(127).

Even though several researchers reported that the prevalence of T2D is rising in all socioeconomic groups, most of the studies revealed that the epidemic is increasing at a greater rate among individuals from a lower socioeconomic position regarding education, occupation, or income to measure. Studies in the USA, Germany, Kazakhstan, and Panama reported that the odds of developing diabetes were higher in less-educated individuals than in educated people(43,95,97,99). A study in West Africa found that individuals with primary and secondary education have higher odds of developing T2D than non-educated individuals(115).

In high-income countries, individuals with sustained low-income status or income decrease have an increased risk of T2D, while those with sustained high-income status or income increase have a lower risk. This is usually related to low-income people who neglect their health behavior and may receive fewer health screenings and healthcare access than those with high income(112,128). A study in Korea reported that individuals who repeatedly experienced low and meager income for five years showed 22% and 57% higher T2D risk compared to those who never experienced low and meager income, respectively(128). At the same time, a case-control

study in Ghana showed that the likelihood of developing T2D was more than fivefold higher in individuals within the middle socio-economic level compared to those with low socio-economic level(129). A study conducted by Dawson et al. in Namibia showed that wealthier individuals had 1.57 increased odds of having diabetes compared to those who were poorer(130).

1.4.6.4. Behavioral risk factors

1.4.6.4.1. Dietary characteristics

Dietary intake, particularly sugar-sweetened beverages and refined carbohydrates, can significantly increase the risk of T2D by affecting glucose metabolism and insulin sensitivity (131,132). High consumption of processed meats, refined grains, sugar-sweetened beverages, and saturated fatty foods increases the risk of T2D(117,133). A US prospective cohort study found that sugar-sweetened beverages are significant risk factors for weight gain and T2D(134). A study on Iranian adults found that tea consumption increases the prevalence of T2D(131), while coffee consumption has a preventive effect (135). High coffee consumption has been associated with better glucose tolerance and a substantially lower risk of T2D(136). A US study found that daily coffee consumption can significantly reduce the risk of T2D by 13% for one cup per day, 42% for 2 to 3 cups per day, and 47% for four or more cups per day compared to nondrinkers (P for trend 0.0001) (135).

A case-control study in Saudi Arabia indicated that routine consumption of Kabsa (OR= 5.5), bakery items (OR =2.4), and French fries (OR= 2.2) increased the risk of T2D(117)**.** A **s**tudy in Lebanon revealed that the traditional Lebanese dietary pattern reduced the risk of T2D by 54%. In contrast, refined grains and fast food patterns significantly increased the risks of T2D in Lebanese adults, with odds of 3.85 and 2.8, respectively(132). Likewise, a study in 21 countries found that consuming more white rice (over 450g/day) increases the risk of T2D(137).

Research indicates that certain dietary items, including whole-grain-rich foods, cereal fibers, legumes, green leafy vegetables, fruits, minerals, and vitamins, can protect against chronic conditions like T2D(117,131,138). Studies in Iran, Saudi Arabia, and Syrian residents reported that routine consumption of vegetables has a protective effect of 14, 60, and 30% reduction in the risk of T2D, respectively(131). A study conducted by Issaka et al. and Gudjinu and Sarfo in West Africa and Ghana demonstrated that eating large quantities/servings of fruits per eating protects against the development of T2D, but null association between vegetable consumption and risk of T2D(115,129). Likewise, a study in Northwest Ethiopia found a higher diabetes prevalence (6.8%) among those eating fruit and vegetables 4-7 times in an atypical week but

found no association(100). A study conducted in Mekelle indicated that the participants' median fruit and vegetable intake was one and two times a week, respectively(57). On the contrary, a study by Manyara et al. in Kenya found that cases consumed more fruits and vegetables and less sugar than controls(139).

1.4.6.4.2. Cigarette smoking and alcohol consumption

Cigarette smoking is an independent modifiable risk factor for T2D. Acute and chronic tobacco exposure significantly impair glucose tolerance, increase insulin resistance, and consequently cause T2D(140). So, tobacco use has a strong association with T2D, either as an independent risk factor or in a cluster with other risk factors, such as centripetal obesity(141). Cigarette smoke, combined with elevated blood glucose, is linked to vascular damage, endothelial dysfunction, and blood-clotting cascade activation, causing further damage in individuals with DM(142,143).

Studies show conflicting results on smoking's association with diabetes mellitus, with most epidemiological studies indicating significant links between smoking and T2D development(142–146). A US study found that smokers have a dose-dependent increased risk of developing Type 2 Diabetes, with relative risks of 1.7 for current smokers of >20 cigarettes per day, 1.5 for current smokers of <20 cigarettes per day, and total pack-years of cigarette smoking was also associated with the risk of T2D (p for trend, both $P<0.01$)(147). A study in Saudi Arabia indicated that smokers had more than 13 times increased possibility of developing T2D compared to non-smokers(148). Similarly, studies in West Africa showed that the probability of developing T2D was higher among smokers to 2.5-fold higher after adjusting for clustered variables(115,118). A systematic review and meta-analysis conducted by Zeru and colleagues in Ethiopia indicated that the odds of developing T2D were 1.72 times higher among smokers compared to non-smokers (149). Other investigators in Ethiopia found no association between smoking and diabetes(57,100,150). On the contrary, studies in China and South Africa indicated that smokers have a lower likelihood of newly diagnosed diabetes than non-smokers(123,151).

Alcohol use is a major contributor to premature death and disability(27). There is a growing agreement that alcohol intake is an influencing factor. Moderate alcohol consumption can improve insulin sensitivity, alter alcohol metabolites, increase HDL-cholesterol concentrations,

and have anti-inflammatory effects, though the exact dose-response relationship remains unclear(152,153).

Epidemiological studies regarding the association between alcohol consumption and T2D risk remain inconsistent. Several studies(58,154–157) revealed that heavy alcohol consumption is the risk factor for the occurrence of T2D, whereas moderate alcohol consumption is protective for T2D in both men and women(58,115). Some studies have shown that light and moderate alcohol consumption is associated with a reduced risk of T2D(152,153,156–158). A prospective survey of 35,625 adults of the Dutch European Prospective Investigation into Cancer and Nutrition (EPIC-NL) cohort found moderate alcohol consumption at 40% lower risk than abstention(155). A study in West Africa demonstrated that alcohol consumption every day reduces the odds of T2D by 45%c compared to non-alcohol drinkers(115). Likewise, a study in North West Ethiopia showed that alcohol consumption was preventive from diabetes for the rural residents(100). On the contrary, a study in Addis Ababa indicated that those who did not drink alcohol were 49% protected from developing T2D(58).

1.4.6.4.3. Physical inactivity and obesity

Obesity and T2D are strongly associated with an unhealthy diet and physical inactivity. Physical and social environments influence diet, physical activity behavior, and economic, psychological, and cultural factors. Lifestyle and habits play a vital role in becoming obese, and almost four out of five people who are newly diagnosed with diabetes are obese(159,160).

Researchers have found that lifestyle modification combining weight loss and physical activity significantly reduces the short-term and long-term incidence of T2D in high-risk groups(74,75). Studies have shown that physical activity can protect T2D(161–163). Studies also show that inverse associations were observed for increasing activity over time, resistance exercise, occupational activity, and cardiorespiratory fitness and risk of T2D(157,161). A study conducted in West Africa revealed that the risk of developing T2D was 1.39 and 1.66 times higher in people with medium and low physical activity compared to those with high physical activity(115). The 2015 NCD STEPS survey reanalysis in Ethiopia revealed that physical activity significantly reduces the 75% risk of diabetes development(150). A similar study in

North West Ethiopia indicated that at least moderate PA lowers the risk of diabetes by 52% among urban residents but not for rural residents(100).

A study in Ghana showed that 73% of cases were physically inactive compared to 33.3% of control groups, and physically inactive participants had a 4.8 times possibility of developing T2D compared to physically active individuals(129). Similarly, a study conducted in urban and rural areas of West Africa revealed that people with low and moderate physical activity had 2.17 and 2.15 times the risk of developing T2D compared to individuals with high physical activity(115). Likewise, a study in Ethiopia found that physically inactive individuals are nearly six times more likely to develop T2D(149).

Excess weight and physical inactivity are significant modifiable risk factors for T2D, as 85-90% of individuals with T2D are overweight or obese(164). Adipose tissue's excessive free fatty acid leads to insulin sensitivity decline, increased glucose levels, insulin resistance, and T2D(165), with higher BMI associated with increased resistance in older individuals in older people with T2D(166–169).

Studies demonstrated that higher waist circumference(WC), waist-to-height ratio(WHtR), and waist-to-hip ratio(WHR) are strong predictors of T2D(115,118,169,170). A study conducted in West Africa reported that the possibility of developing T2D was 2.59 and 2.58 times higher in people with elevated waist circumference and obesity, respectively(115). A study by Danquah et al. in Ghana found that individuals with a higher waist-to-hip ratio risk a 2.6-fold higher risk of T2D(171). A study in West Africa found that individuals with elevated WC, WHtR, and WHR had a 1.54, 1.55, and 1.23 times higher likelihood of developing T2D, respectively(118). A Kenyan study found that a higher waist-to-hip ratio was linked to higher odds of T2D(139). Likewise, a study conducted in Ethiopia showed that in both sexes, a 1-unit higher BMI and WC were positively associated with prediabetes/diabetes(150). Systematic review and meta-analysis indicated that the burden of diabetes mellitus was 5.79 times higher among those adults who had central obesity (169).

Epidemiological evidence from Saudi Arabia suggested that sedentary behavior (e.g., television watching) increases the risk of T2D(117). Many studies have shown the health burden of a sedentary lifestyle, and the WHO rates inadequate physical activities as one of the major threats

to modern health. There is a visible relationship between inactivity and obesity with a subsequent and firm linkage with T2D(127). Findings revealed that individuals, both obese and with low physical activity, had a 7.4-fold increased risk of T2D compared to normal weight, highly physically active participants (172). Similarly, studies in Saudi Arabia and North West Ethiopia came up with supporting findings in that physical inactivity was significantly associated with diabetes mellitus with odds of 2.5 and 1.92, respectively (100,117). Moreover, a study in Ethiopia indicated that physical inactivity increased the risk of developing T2D(149).

1.4.6.5. Medical history and Comorbidities

A family history of diabetes (FHD) is a significant risk factor for developing T2D)(45). A study in China found that diabetes prevalence rates were 32.7% in FH2, 20.1% in FH1, and 8.4% in FH0, with age and gender-adjusted differences(173). Similarly, a study in Korea reported that those with an FHD involving first-degree relatives had a significantly higher prevalence of impaired fasting glucose(14.3 vs. 11.7%) and T2D (6.7 vs. 1.8%) compared to those without a FHD($P < 0.001$)(45). Likewise, a systematic review and meta-analysis conducted by Zeru and colleagues reported that the possibility of developing T2D was more than 6 times higher among those who had FHD compared to those without such experience(149). Moreover, a study in North West Ethiopia indicated that the proportion of diabetes was higher among those who had FHD (18% Vs. 3.1%) compared to those who had not FHD(100).

Diabetes comorbidities increase health risks, complicate diabetes management, and negatively impact emotional health, medication adherence, self-management, and quality of life. Co-morbidity in diabetes patients leads to poorer self-management and higher health service use(174–176). The most common comorbidities in T2D include hypertension, dyslipidemia, obesity, cardiovascular conditions, arthritis, anxiety, and depression across various regions(136,177,178). A similar study in the US reported that the most prevalent T2D-related comorbidities were hypertension (82.5% and 87.2%) and cardiovascular disease (26.9% and 22.3%) in 2008 and 2013, respectively(136).

T2D prevalence is increasing, but longevity may lead to more diverse morbidity. Discover-NOW dataset identified 224,000 T2D cases in North-West London from 2000-2020. A study found that 30% of T2D patients had three or more comorbidities at diagnosis, increasing to 60% ten years

later. Hypertension (73%) was the most common, followed by back pain, depression, asthma, and osteoarthritis. Patients who were obese upon diagnosis exhibited notably distinct comorbidity profiles in contrast to those who were not obese(179). A case-control study in SSA that includes Nigeria, Ghana, and Kenya indicated that 71%, 34%, and 27% of T2D participants had hypertension, hyperlipidemia, and obesity, respectively(180). A prospective study in Rwanda showed that the co-morbidity of diabetes with hypertension, overweight, and dyslipidemia was 31%, 33%, and 28%, respectively(181).

Diabetes and hypertension are linked due to shared risk factors like age, obesity, high cholesterol, sedentary lifestyle, smoking, and stress, with hypertensive individuals more likely to develop diabetes than normal individuals as hypertensive people develop insulin resistance(182). Epidemiological evidence suggests that hypertension is statistically related to T2D(170). Studies from West Africa, Kenya, and Ethiopia indicated that the odds of developing T2D were 2.6, 2.54, and 3 times higher among individuals with hypertension compared to those who do not have hypertension(115,139,149). Besides, a study conducted by Gebreegziabiher et al. in Mekelle City reported that the possibility of developing diabetes was about 6 times higher in people with Systolic hypertension compared to those who had normal systolic blood pressure(57).

Dyslipidemia, a risk factor for T2D, is more common in diabetes patients due to impacted enzymes and lipid metabolism pathways, with low HDL-C, elevated cholesterol, and triglyceride levels significantly associated with new diagnosis. Lipid profile and diabetes are key predictors of metabolic disturbances like dyslipidemia, hypertension, and CVD. Lipids are crucial in diabetes pathogenesis, a common manifestation of uncontrolled diabetes, because insulin has significant regulatory effects on lipid metabolism, and dyslipidemia is increasing globally due to unhealthy diets, reduced physical activity, urbanization, and obesity(57,183–186).

Gudjinu and Sarfo's study in Ghana found that individuals with poorer HDL-cholesterol and total cholesterol higher than 6.3mmol/L had higher odds of developing T2D than those with the best HDL-cholesterol and less cholesterol(129). Similarly, A study in Addis Ababa found that individuals with high triglycerides had a higher risk of developing diabetes. At the same time, those with HDL-C $\geq$ 40 mg/dL lower the risk of diabetes by 44% compared to people with HDL-

C lower than 40 mg/dL(58). Likewise, a study in Mekelle also reported that people with total cholesterol ≥200 mg/dL had a higher risk of developing diabetes compared to those who had < 200 mg/dL(57).

1.4.3. Hyperglycemic Crisis

1.4.3.1. Classification and Magnitude of Hyperglycemic Crisis

Uncontrolled diabetes often leads to hyperglycemic crises (DKA and HHS), which are serious and life-threatening metabolic complications. DKA involves unchecked hyperglycemia, metabolic acidosis, and increased ketone concentration, while HHS is severe hyperglycemia, hyperosmolality, and dehydration without ketoacidosis. Both conditions can occur in different types of diabetes(21,187,188). Uncontrolled type 1 and 2 diabetes mellitus can lead to extreme metabolic derangements in DKA and HHS, resulting in poor patient outcomes, increased mortality rates, and a high risk of infectious complications(21).

Even though the hyperglycemic crisis has either declined or remained stable over time in high-income countries, it remains a significant challenge for low/middle-income countries with unacceptably increasing incidence, intra-hospital morbidity, and mortality from this acute diabetic complication nowadays (189,190). A US study found that 38% of patients with confirmed hyperglycemic crises had DKA, 35% had HHS, and 27% had combined DKA-HHS features(191). Similarly, a study in Japan found that 60.4% of patients with hyperglycemic crises had DKA, 13.2% had HHS, and Mix(192). Likewise, a Nigerian study found that 24.7, 39.2, and 36.1% of diabetes patients with hyperglycemic crises were admitted due to DKA, HHS, and normal-osmolar hyperglycemic state, respectively(193). Moreover, a Jimma University Specialized Hospital study revealed that 93% of participants developed DKA, while 7% developed HHS (50). At Hiwot Fana Specialized University Hospital, 52.3% of patients admitted with hyperglycemic crisis had an HHS diagnosis, while the rest had DKA(54).

DKA and HHS are common in patients with T1D and T2D, with DKA more common in young patients and HHS more common in older patients, with different levels of insulin deficiency, dehydration, ketosis, and metabolic acidosis, often co-existing(17,19–22). A study in Japan found type 1 diabetes was only detected in patients with DKA and mixed, while T2D was observed in all groups, particularly in HHS patients, with a lower rate in DKA patients. It was

still present in 39.1% of patients(192). Similarly, a Danish cohort study revealed that 18.3%, 48.4%, and 33.3% of participants had known type 1 diabetes, known T2D, and had a new diabetes diagnosis, respectively(194). A study conducted among T2D in China revealed that 41.1%, 46.8%, and 12.0% of patients had DKA, HHS, and DKA-HHS, respectively(195). A study conducted in Colombia showed that half of the events of DKA and 57% of the events occurred in people with T2D(196).

In Nigeria, a study found that 64.9% of patients had diabetes, while 35.1% were newly diagnosed upon hospital admission(193). A study in Cameroon among adults 18 and above revealed that 85% of patients with hyperglycemic crises had T2D, and 85% had HHS(197). Diabetes in Ethiopia leads to hospital admissions, complications, and economic losses, affecting individuals, families, healthcare structures, and national economies(50,51). A study at Tikur Anbesa Hospital in Ethiopia revealed a 6.5% diabetes-related hospitalization rate, with diabetic foot ulcers and cardiovascular disease being primary diagnoses for T2D admission. At the same time, DKA was the leading diagnosis for T1D patients(51). Likewise, Hiwot Fana Specialized University Hospital in Ethiopia reported that 44.5% and 55.5% of patients had T1D and T2D, respectively, with 36.4% having no prior DM history at admission(54). A study in JUSH found that 63.8% of participants had type 1 diabetes, while all type 1 and 79.7 % of T2D patients developed DKA, and HHS was noted in T2D ($P < 0.001$)(50).

Diabetes in Ethiopia leads to hospital admissions, complications, and economic losses, affecting individuals, families, healthcare structures, and national economies(50,51). A study at Tikur Anbesa Hospital in Ethiopia revealed a 6.5% diabetes-related hospitalization rate, with diabetic foot ulcers and cardiovascular disease being primary diagnoses for T2D admission. At the same time, DKA was the leading diagnosis for T1D patients, leading to a 21.0% in-hospital mortality rate(51). Studies in Ethiopia found that 34.6-45.4%, 13.2-59%, and 32.3-40.4% of hyperglycemic patients had no prior diabetes history, infection, and non-compliance on admission, respectively, with mortality rate ranges of 9.8-21%(50–55).

1.4.3.2. Precipitating Factors of Hyperglycemic Crisis

Hyperglycemic crises arise from a combination of underlying causes related to insulin deficiency and resistance, compounded by various precipitating factors that exacerbate these conditions.

Infection, insulin omission, new-onset of diabetes, acute medical conditions, certain medications, poor dietary management, pregnancy, comorbid conditions, emotional stress, dehydration, trauma, lack of access to medical care, and non-adherence to diabetes management, cultural and religious beliefs, poor laboratory support, and less emphasis on electrolyte monitoring are the most common precipitating factors for hyperglycemic crisis(21,22,198,199).

Infection is the leading precipitating factor for hyperglycemic crisis admissions and the risk of diabetes death. A US study found that infection was the primary reason for 10% of emergency department visits for adults with diabetes, with urinary tract infections being the most common, accounting for over 30% of these visits. Diabetes patients are more than twice as likely to be hospitalized for infection management, with 8-12% of these patients being hospitalized for this purpose(97). A UK hospital survey found infection as the most common precipitating factor for diabetic ketoacidosis (45%), followed by insulin omission (20%), with other causes including newly diagnosed diabetes and alcohol or drug-related issues(200). A Colombian study revealed that 32% of events were caused by infection, while 27% were due to inadequate therapy(196). A study in China found that infection (70.3%), newly diagnosed diabetes (17.7%), and non-compliance with medications (5.7%) are the most common precipitants of hyperglycemic crises(195).

Similarly, a study in Cameroon revealed that infections (41.7%), newly diagnosed diabetes (33.3%), and non-adherence to medications were the most common causes of hyperglycemic emergency admission(197). Likewise, a study at JUSH found that infections, non-compliance with medications, and newly diagnosed diabetes were the most common precipitants of HCs in 59%, 32.3%, and 45.4% of patients, respectively(50). Moreover, a Hiwot Fana Specialized University Hospital study revealed that infection, noncompliance, and new-onset diabetes were prevalent in 48.0%, 38.6%, and 19.6% of patients admitted due to hyperglycemic crises(54).

The most important signs and symptoms and laboratory markers for diagnosing hyperglycemic emergencies are polydipsia, polyuria, body weight loss, higher blood sugar, level of electrolytes, and body fluid status. A study in Nigeria mentioned that hypokalemia was reported in 37% of the study participants. Elevated urea levels and hyponatremia were noted more in patients with DKA than in patients with HHS (57.5%, 19% versus 53%, 18%)(189). Findings from Taiwan

demonstrated that the classic symptoms and signs of diabetes, like thirst, polydipsia, polyuria, and body weight loss, were predominant in patients without a history of diabetes(56).

1.4.3.3. Case-Fatality/ mortality rate

Diabetes, primarily in developing countries, increases morbidity and mortality due to acute complications like DKA, HHS, and hypoglycemia, with higher mortality rates in patients with HHS(17,201). In a study by Olamoyegun et al. in Nigeria, the hyperglycemic crisis and DFUs were the leading causes of diabetes-related in-hospital admission, with hyperglycemic emergencies accounting for approximately 60% of total admissions(201). Ogbera et al.'s study in Nigeria found a 20% mortality rate for hyperglycemic crises, with 18% and 35% case fatality rates for DKA and HHS, respectively(49). Similarly, a Hiwot Fana Specialized University Hospital study found that hyperglycemic crisis-related mortality was 16.5%, with 21.4% for HHS and 11.1% for DKA(54).

A study in India showed a 20.9% mortality rate related to hyperglycemic crises, with 7.3% in newly diagnosed DM patients and 13.5% among known DM(202). Similarly, findings of JUSH revealed a 9.8% mortality rate related to hyperglycemic crises, with higher rates among known DM patients (14.6%) than newly diagnosed DM patients(4.1%)(50). Likewise, in Taiwan revealed that patients with a history of diabetes had a higher mortality rate(50,203), older, lower Glasgow coma scale, lower classic symptoms of diabetes, higher rate of medical history, higher infection, and a higher proportion of HHS compared to without history of diabetes(203).

In summary, investigators found mixed trends in adult-onset T1D and T2D incidence, with high-income countries experiencing decreased or stable diabetes incidence(3) while increasing in developing countries(29,31,37,85–87,110). Type 1 diabetes incidence: Eritrea has the highest global incidence at 46.2/100,000 people affected(86,105). Balcha et al. found inconsistent results in Ethiopian studies, with urban regions of Gondar and Jimma showing higher T1D risk than rural areas in 2009(111), while in 2024, they reported a notable male predominance in rural Gondar(40). New findings are reported in this review as risk factors of T2D. Higher intake of white rice(137) and tea consumption increases(135) increased the risk of T2D, while high coffee consumption has been associated with better glucose tolerance and a substantially lower risk of

T2D(135,136). Studies in China and South Africa indicated that smokers have a lower likelihood of newly diagnosed diabetes than non-smokers(123,151).

The literature review reveals that hyperglycemic crises are the primary cause of diabetes-related admissions, often precipitated by infection, new-onset diabetes, and non-adherence to diabetes management. In Ethiopia, 19.6-45.4% of hyperglycemic patients have new-onset diabetes at admission(50,52–54), while 47% of Taiwanese patients without diabetes history have HHS. The mortality rate is higher in HHS patients. Hyperglycemic crises in patients without a diabetes history exhibit distinct clinical characteristics from those with known diabetes(203), which has not yet been studied in SSA, including Ethiopia.

1.4.3. Conceptual Framework

The conceptual framework explains how lifestyle, behavioral, and personal factors influence T2D development and hyperglycemic crisis treatment outcomes. The review of research studies, books, and guidelines aimed to identify lifestyle, behavioral, and personal factors that may influence diabetes mellitus and treatment outcomes in patients with hyperglycemia. This study examines lifestyle, behavioral, and personal factors influencing diabetes mellitus and treatment outcomes in hyperglycemic patients, focusing on the association between determinants and diabetes outcomes (see Figure 1).

The framework broadly explains determinants of diabetes and treatment outcome of diabetes care for patients with hyperglycemic crisis, linking them into six groups, namely socio-demographic factors(age, gender, marital status, religion, ethnicity, education, monthly income, residence), behavioral factors (physical inactivity, unhealthy diet, tobacco use, harmful use of alcohol, and khat chewing), co-morbidity and medical history factors (overweight/obesity, raised blood pressure, abnormal blood lipids, infection, non-adherence to treatment, delayed diagnosis, history of GDM, family history diabetes), diabetes-related complications(hyperglycemic crisis(DKA, HHS), long term complications (macro-vascular and micro-vascular complications), hypoglycemia), and treatment outcome of HCs (Discharge, death, transfer/referral).

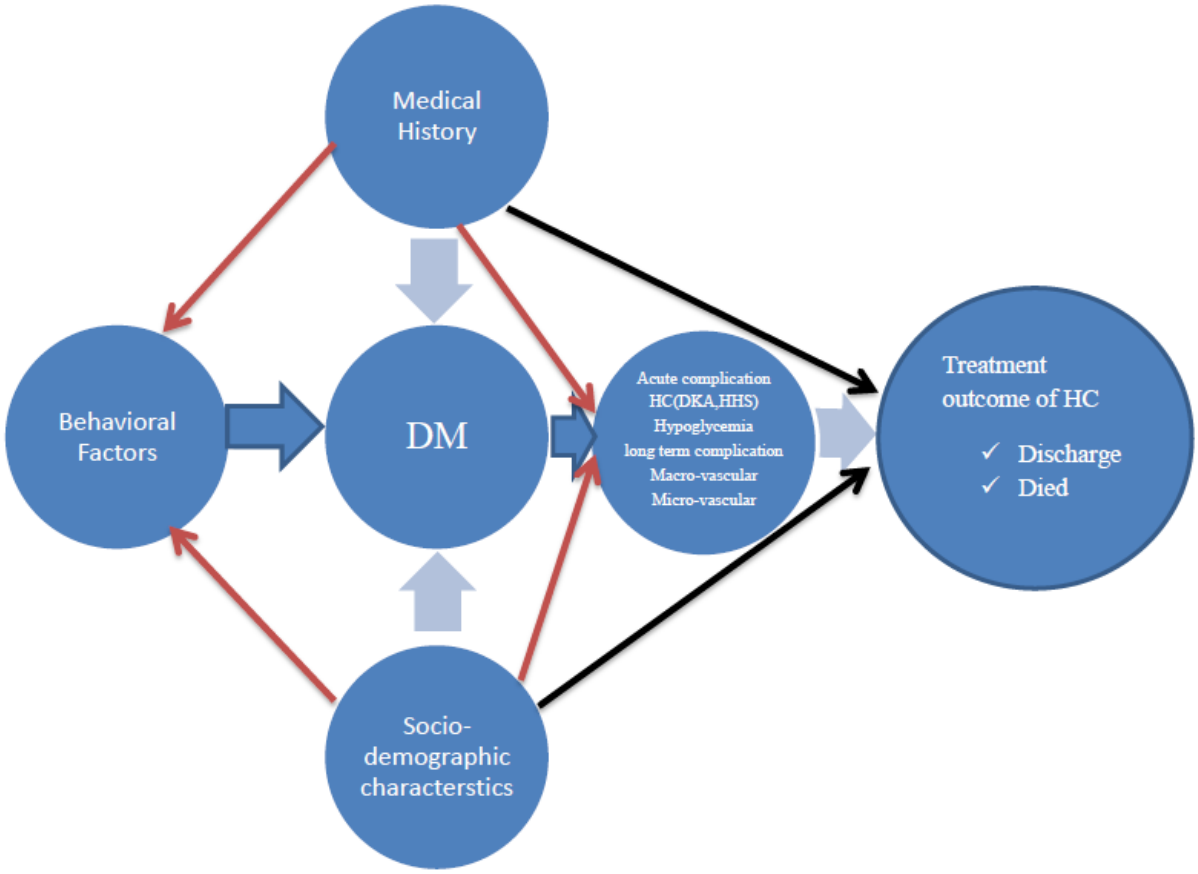

Figure 1: Conceptual Framework of DM: Trend, Risk Factors of T2D and Treatment Outcome of Hyperglycemic Crises (HCs) among adults in selected public hospitals of Tigrai, Ethiopia (Developed)

2. Research Questions

1. What was type 1 and type 2 diabetes magnitude over the last five years (from September 1, 2013, to August 31, 2018) in public hospitals of Tigrai?
2. What was the time trend of type 1 and type 2 diabetes by sex and residence over the study period (from September 1, 2013, to August 31, 2018) in public hospitals of Tigrai, Ethiopia?
3. What were the facilitators or preventive lifestyle behavior factors among hospital-treated middle-aged adults with T2D and those not in public hospitals in Tigrai, Ethiopia?

4. What was the difference in clinical characteristics of hyperglycemic crises (DKA vs. HHS)?
5. What were the differences in the clinical presentation of hyperglycemic crises in patients with a prior diabetes history compared to those without a previous one?
6. What was the treatment outcome of care for hyperglycemic crisis among adult patients with and with no prior diabetes history in public hospitals of Tigrai, Ethiopia?
7. What are the predictors of mortality in patients admitted due to hyperglycemic crises related to admissions in public hospitals in Tigrai, Ethiopia?

Research hypotheses

- ❖ In Tigrai, there is a difference in the time of trend type 1 and type 2 diabetes between urban and rural adults from September 1, 2013, to August 31, 2018, in public hospitals.
- ❖ Middle-aged adults with poor dietary habits and behaviors have a higher risk of developing T2D.
- ❖ In Tigrai hospitals, there is a higher likelihood of higher mortality in patients admitted for HCs with a history of diabetes compared to those without a history of diabetes.

2.1. Objectives:

2.1.1. General objective:

To assess the Trend, Risk Factors of Diabetes, and Treatment Outcome of Hyperglycemic Crises among adults in selected public hospitals in Tigrai, Ethiopia.

2.1.2. Specific objectives:

1. To determine the trend in the time of type 1 and type 2 diabetes among adults who received medical care from September 1, 2013, to August 31, 2018, in selected public hospitals of Tigrai.
2. To assess the risk factors of T2D among middle-aged adults in Ayder Comprehensive Specialized Hospital in Tigrai.
3. To compare the hyperglycemic crisis characteristics of patients with and without a prior diabetes history and care outcomes among adult patients from selected public hospitals in Tigrai.

3. Methods and Materials

3.1. Study Area and Period

The study was conducted in the Tigrai Region, located in northern Ethiopia. Mekelle is the capital of Tigrai. The total projected population of the Tigrai Region was 4,314,456, with 2,124,853 men and 2,189,603 women, with a 2.5% annual growth rate, which gives a projection of 5,738,996 in 2022, of which 2,812,108 men and 2,926,888 women. The Tigrai Region, covering 50,078.64 square kilometers, has 985,654 households, with an estimated density of 86.15 people per square kilometer and an average of 4.4 people per household, with urban households having an average of 3.4 people. In contrast, rural households had an average of 4.6 people. The Tigrai Region is predominantly inhabited by Tigrian people, who make up 96.55% of the population, with other ethnic groups including Amhara, Irob, Afar, Agaw Kamyr, Oromo, and Kunama, and 95.6% of the population follows Orthodox Christianity, and 4% are Muslim(204).

The region comprises 712 health posts, 211 health centers, 22 primary hospitals, 18 general hospitals, and two referral hospitals owned and operated by the government(205). The Ethiopian Service Provision Assessment Survey in 2017 reported among all health facilities, excluding health posts that offer services for NCDs, Tigrai had 56% coverage service for chronic respiratory disease, 36% service coverage for cardiovascular diseases, 29% service coverage for diabetes, and 5% service coverage for cervical cancer among health facilities(206). A Health Resources and Services Availability Monitoring System (HeRAMS) report shows only 3% of NCD clinics have available services, with 19% having asthma and COPD, 23% and 17% having hypertension and diabetes partially available services in Tigrai in June 2023(207). There were 6726 people with type 1 and 17,627 with T2D patients who were receiving regular follow-ups at General and Primary hospitals before November 2020(208). This study was conducted in seven public hospitals of the Tigrai region, namely, Ayder Comprehensive Specialized Hospital (ACSH) and general hospitals Mekelle, Lemlem Karl, Adigrat, St.Marry, Suhul, and Abyi Adi. The data abstraction and collection period was from September 1, 2018 to June 30, 2019.

3.2.Study design

For the time trend of T1D and T2D: a retrospective hospital-based repeated cross-sectional study for each year was employed to describe the trend of T1D and T2D for successive five years from September 1, 2013, to August 31, 2018, in selected public hospitals of Tigrai.

For the risk factors of T2D, a hospital-based matched case-control study design was used for the risk factors associated with T2D among middle-aged adults at ACSH.

For hyperglycemic crisis: A hospital-based retrospective cross-sectional study design was utilized to evaluate the treatment outcomes of adult patients experiencing hyperglycemic crises in selected public hospitals in Tigrai.

3.3.Source and study population

3.3.1. Source population

The time trend of T1D, T2D, and hyperglycemic crises was conducted in six general public hospitals and one Comprehensive Specialized Hospital. In contrast, the risk factors of T2D were conducted at ACSH in selected public hospitals of Tigrai.

For the time trend of T1D and T2D: The registry logbooks documenting medical care provided to adult patients aged 18 years and older in adult medical and emergency outpatient departments (OPD) were reviewed over a consecutive five-year period (September 1, 2013, to August 31, 2018) in selected public hospitals of Tigrai.

For the risk factors of T2D: All middle-aged (45 to 64 years) adults who received medical treatment from ACSH in Tigrai. Cases, controls, and matching are described as follows:

Cases: were known T2D patients for both men and women who have been attending their follow-up at the ACSH diabetes clinic. T2D patients were ascertained from the diabetes clinic by the senior physicians, and the case history of diabetes and diabetes-related complications was verified from the records of diabetes patients by physicians and nurses working in the diabetes clinic.

Controls: patients/healthy individuals who visited the general MOPD for any other reasons but without diabetes confirmed with typical blood glucose values (FPG<100mg/dl) were considered as controls. Controls were ascertained by senior physicians or General practitioners who were providing care in the general MOPD using blood glucose tests and other investigations.

Matching: Cases and controls were matched based on age(100,115,118) and sex(7,10,96,100,119–122), as these factors were identified as associated with T2D in most reviewed studies. Each case was paired with two controls of the same gender and within ±2 years of age. Controls were selected voluntarily from the non-diabetes, meeting the standard blood glucose values criteria, to participate in the study.

For hyperglycemic crisis: All adult patients aged 18 years and above who were admitted and treated from September 1, 2017, to August 31, 2018, in selected public hospitals of Tigrai were the source population.

3.3.2. Study Population

For the time trend of T1D and T2D: The study examined the complete five-year medical records of diabetes patients and registry logbooks documenting medical treatment provided to all adult patients aged 18 years and above in adult medical and emergency outpatient departments (OPD) from September 1, 2013, to August 31, 2018, in selected public hospitals of Tigrai.

For the risk factors of T2D: The study population for cases was sampled T2D patients for both men and women among middle-aged adults who were newly diagnosed with T2D from January 1 to December 31, 2018, and who have been attending their follow-up at ACSH diabetes clinic from March 1 to June 30, 2019. The control study population was sampled men and women among middle-aged adults confirmed without diabetes who visited the medical OPD of ACSH during the data collection period.

For hyperglycemic crises: The review included all selected adult diabetes patients aged 18 years and above admitted and treated for hyperglycemic crises in the medical wards of selected public hospitals in Tigrai from September 1, 2017, to August 31, 2018. Patients were identified and screened using the registry logbooks.

3.4.*Eligibility Criteria*

3.4.1. *Inclusion Criteria*

For the Time Trend of T1D and T2D: All five years' medical records of diabetes patients and registry logbooks of adult patients aged 18 years and above who received medical treatment from adult medical and emergency OPD units during the period of September 1, 2013, to August 31, 2018, aged 18 years and above in the selected public hospitals of Tigrai were included in the study.

For the risk factors of T2D: Cases were newly diagnosed with T2D from January 1 to December 31, 2018, in the middle-aged for both men and women who had been on fellow up willing to participate in the study during the data collection period at ACSH. Controls were middle-aged adult patients or healthy individuals for both men and women who were willing to participate in the research and had the following: never diagnosed with diabetes, patients/participants having FBG of <100mg/dl, and not taking any anti-diabetic medication.

For hyperglycemic crises: All selected medical charts of adult diabetes patients aged 18 years and above who were admitted and treated for hyperglycemic crises(DKA and HHS) in the medical ward of the selected public hospitals of Tigrai during the period September 1, 2017, to August 31, 2018, were included in the study.

3.4.2. Exclusion Criteria

To accurately capture the trends in the time of T1D and T2D, this study excluded medical charts of diabetes patients with missing data, gestational diabetes, and those with referral papers from the studied hospitals. This exclusion was done to reduce the overestimation of cases.

For the risk factors of T2D: Participants/patients having severe co-morbidities like stroke, chronic renal diseases, chronic lung diseases, heart failure, chronic liver disease, end-stage cancer, patients with ascites and edema, adults with spinal problems (kyphosis, lordosis, scoliosis, and kyphoscoliosis), walking using a wheelchair and also pregnant women and women who gave birth in the last six months were excluded from the study to reduce selection, confounding and measurement biases.

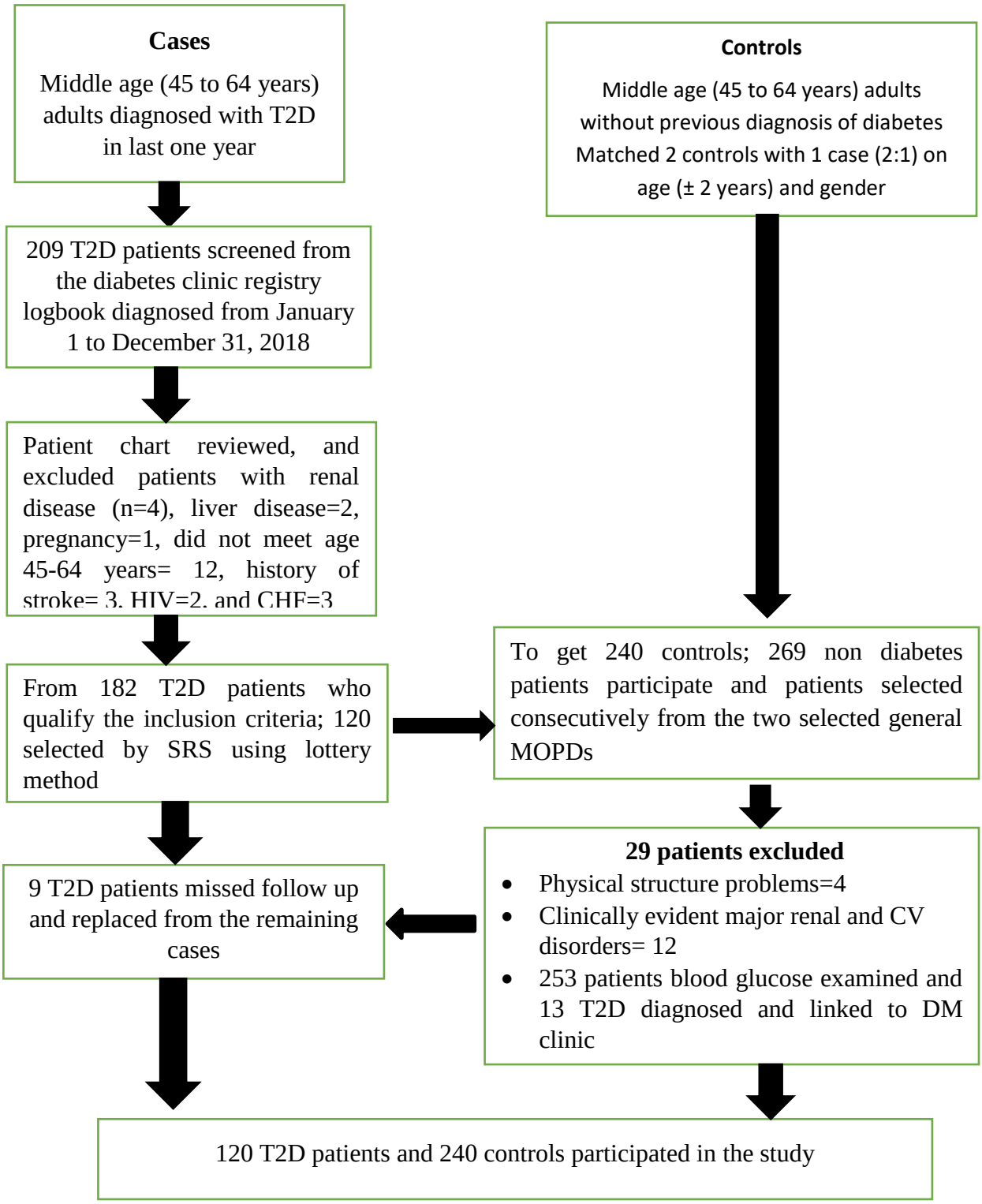

Figure 2: Figure 2: Flow diagram of selection of participants for risk factors associated with T2D included in this study

For hyperglycemic crises, medical charts of adult patients with hyperglycemic crises for not meeting the criteria for DKA or HHS, insufficient data, patients against medical advice, and patients referred to other health institutions were excluded from the study.

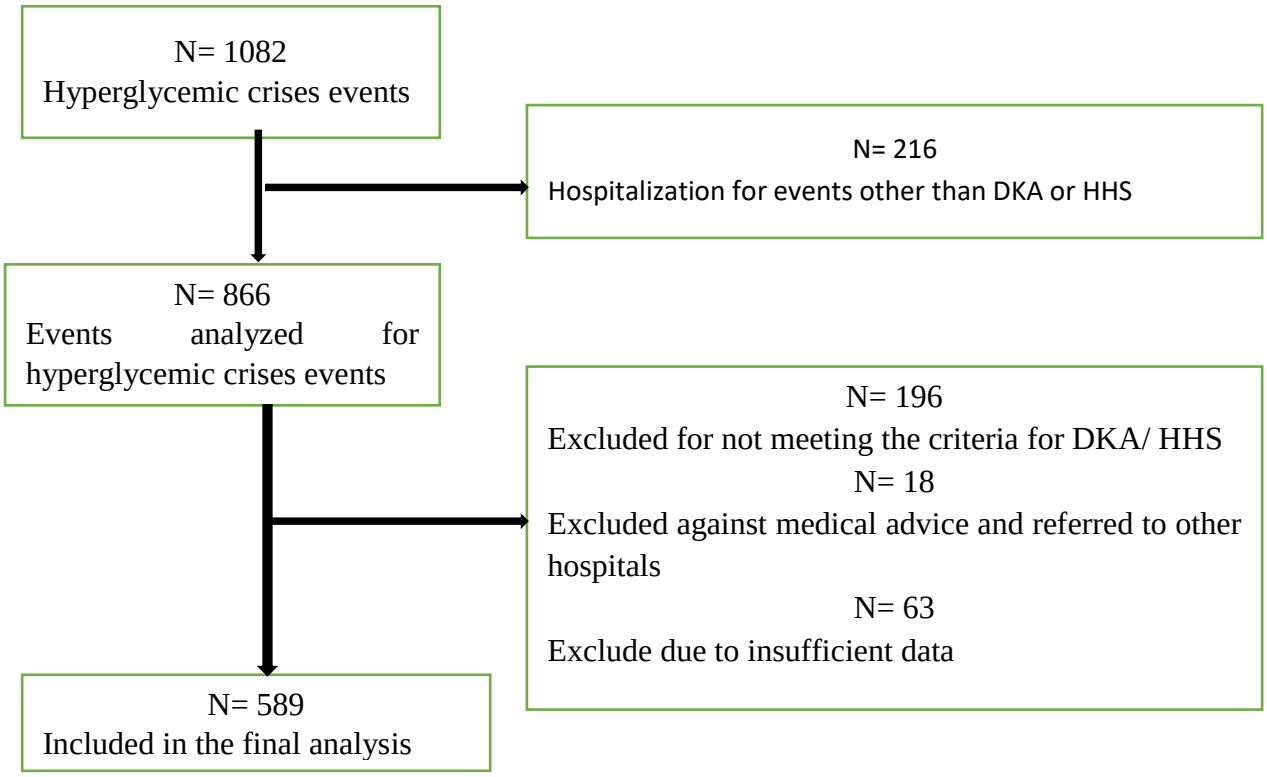

Figure 3: Flow diagram of sampling and clinical characteristics of patients with and without a prior history of diabetes

3.5.Sample Size Determination and Sampling Methods

3.5.1. Sample size determination

For the trend of T1D and T2D: All in the five consecutive years (September 1, 2013, to August 31, 2018), medical records of adult patients aged 18 years and above who received medical treatment were included in the review and screened from the registry logbook. All adult diabetes patients' medical charts were retrieved and reviewed.

For the risk factors of T2D: We used the power command suite procedure of Stata version 14.1 to calculate the sample size according to the following specifications: significance level (α= 0.05); 80% of power, an odds ratio of exposure in cases relative to controls (OR=2.0);

correlations of exposure between cases and controls (r= 0.2), number of matched controls to cases is two and excess body weight assumed rate of exposure among controls is 50% because have not been conducted before in the middle age bracket. The required number of cases was 120, and that of controls was 240.

For hyperglycemic crises: The sample size was determined using a double population proportion formula, assuming in-hospital mortalities of 4.1% and 14.6% in patients without and with a history of diabetes, respectively(50). With a power of 90% and a confidence level of 95%, and assuming a ratio of patients with a history of diabetes to those without of 2, the required sample size was calculated to be 137 patients without a history of diabetes and 274 patients with history of diabetes. The study included all medical records of 589 patients who experienced hyperglycemic crises and were admitted and treated between September 1, 2017, and August 31, 2018, in the six general hospitals and ACSH.

3.5.2. Sampling Methods

For the Time trend of T1D and T2D, the number of adult patients/clients who received medical treatment in five consecutive years was found in the registry logbooks/HMIS records. Information on all adult diabetes patients treated in the five years was retrieved from logbooks and client cards.

For the risk factors of T2D, cases were selected from T2D patients who visited the ACSH diabetes clinic for their follow-up appointments and sampled from the diabetes follow-up registry logbook by simple random sampling using the lottery method. Every time, the selection of controls was governed by the selection of cases in line with the matching. Controls were selected from non-diabetes individuals who came to ACSH medical OPD consecutively, aged between 45 and 64 years and consented to participate in the interview, blood test, and anthropometric examinations. Consecutive patients visiting the ACSH in the two medical OPDs from March 1 to June 30, 2019, who met the eligibility criteria, were requested to participate in the study. In case of refusal, the next patient was approached with the same request. The two medical OPDs participating were required to interview 120 controls during the study period.

For hyperglycemic crisis: all medical charts of hyperglycemic crises treated during the study period of September 1, 2017, to August 31, 2018, were needed. First, the eligible charts were identified and reviewed by each study hospital.

3.6. *Data Collection Techniques and Tools*

3.6.1. Design data collection tools

For the Time Trend of T1D and T2D: Data abstraction checklist format was developed by reviewing different literature (31,41,86,209) to abstract relevant data. Socio-demographic characteristics (age, gender, residence) of patients, type of diabetes, and year of diagnosis were abstracted from the medical records of the studied hospitals.

For the risk factors of T2D: Data on both cases and controls were collected using a unified questionnaire that combined various tools into a single instrument. The primary component of this questionnaire is the WHO STEPwise approach to surveillance(STEPS), a standardized tool specifically designed for surveillance of risk factors for NCDs in member countries(129,141,210). The questionnaire encompassed structured information on various aspects, including socio-demographic characteristics, family history of diabetes, behavioral measurements (such as alcohol consumption, cigarette smoking, and dietary habits including fruit and vegetable intake), physical activity (including occupational, commuting, and recreational activities, as well as sedentary behaviors), physical measurements (such as blood pressure, height, weight, waist circumference, and hip circumference), and biomedical measurements (including blood glucose and blood lipids). It was initially prepared in English and then translated into Tigrigna, with subsequent back-translation to ensure consistency and accuracy.

For hyperglycemic crises, a data abstraction checklist format was developed by reviewing the literature (19,22,50) to abstract relevant data. Socio-demographic characteristics of patients, type of diabetes, type of hyperglycemic crisis, medical history, history of diabetes, and clinical characteristics were abstracted from the medical records of the studied hospitals.

3.6.2. Data collection procedures

Data collectors and supervisors comprised healthcare professionals, including nurses, health officers, and physicians, totaling 14 data collectors and seven supervisors. A two-day training session was conducted for both groups. On the first day, training focused on effective communication with hospital administrations, documentation workers, medical doctors, laboratory experts, and respondents, obtaining informed consent, and administering questionnaires. The second day covered correct measurement techniques for the WHO STEPwise approach to surveillance (STEPS), abstracting data from registry logbooks and patient charts, and adherence to WHO guidelines, with instrument standardization conducted before and during training. A pretest of the STEPs questionnaire was conducted with the data collectors and supervisors, and any questions were clarified during this session.

For the Time Trend of T1D and T2D: Initially, the registry logbook containing records of all patients treated in the adult medical and emergency outpatient departments (OPD) of the hospital, regardless of gender, aged 18 years and above, was obtained. Subsequently, data collectors screened and abstracted data for each patient who qualifies the eligibility criteria within the specified time frame, utilizing a standardized data abstraction format to extract relevant information from the registry logbook. Additionally, medical records of diabetes patients, including both paper files and electronic files/smart records, were accessed to gather further information as needed.

For the risk factors of T2D: First, the required questionnaires were distributed to the study units in ACSH according to the calculated sample size: 120 questionnaires to the diabetes clinic and 240 to the general medical OPD. The controls' patient selection and data collection were governed by the patient flow of the cases in line with matching by age and sex. The data were collected by six trained nurses from the two general medical OPDs and one diabetes clinic, with complete guidance and supervision from the principal investigator and technical assistance from the medical doctors working in the selected medical OPDs. The data collection for the controls was carried out after confirmation of blood glucose level, using a glucometer as they were not diabetes patients.

After completing STEPs, the medical doctor in the medical OPD to provide care was responsible for ordering the biomarkers investigation, and the patient and the data collector went together to

the laboratory unit within the hospital. The laboratory technician collected A venous blood sample in the glucose tube with fluoride. The FPG level and lipid profiles of controls and cases were examined using the enzymatic reference method with hexokinase and COBAS reagents from Roche Diagnostics, Indianapolis, USA. Biochemical analysis was performed within 3 hours after blood samples were taken.

For the Hyperglycemic Crisis: Initially, all adult patients presenting with hyperglycemic crises and subsequently admitted and treated in the medical ward(s) of the hospital were identified by screening the registry logbook. Subsequently, all patient records meeting the eligibility criteria within the specified period were reviewed and abstracted. This process involved utilizing a standardized data abstraction format to collect pertinent information from the medical records, including paper copy files and electronic files/smart records, for further analysis and evaluation.

3.7.Variables and definitions

1) **For the Time trend of T1D and T2D:** the dependent variable was the presence or absence of T1D or T2D in the patient, while the independent variables were age, gender, residence, and year of diagnosis.

New diabetes case: A physician diagnosed with diabetes for the first time, exhibiting Fasting Plasma Glucose (FPG) ≥126 mg/dL or repeated Random Plasma Glucose (RPG) ≥200 mg/dL, fatigue, polyuria, polydipsia, and other symptoms.

Type 1 diabetes: The physician diagnosed a type 1 diabetes patient who presented with FPG ≥ 126 mg/dl or RPG ≥ 200 mg/dl plus classic symptoms of excessive urination, thirst, unexplained weight loss, and increased hunger, were considered as type 1 diabetes patient.

Type 2 diabetes: Physician diagnosed as a T2D patient who presented with FPG ≥126 mg/dl or RPG ≥ 200 mg/dl plus other symptoms such as excess body weight, physical inactivity, unhealthy diet, and family history of diabetes, were considered as T2D patient.

Urban residency: Participants who reside in district/Woreda towns, Zonal towns, or capital cities of the region were considered urban residents.

Rural residency: Participants who reside in rural villages or semi-urban areas were considered rural residents due to most of the society's engagement in agricultural activities.

2) **For the risk factors of T2D,** Exposure variables included:

a. Behavioral measurements:

- **Cigarette smoking status:** The study classified participants into three categories based on their smoking status: current smokers, ex-smokers, and never-smokers, determined by their daily smoking habits. Current smokers were individuals who reported consuming 1-10 cigarettes daily for at least six months, while ex-smokers were those who had stopped smoking for over six months. Among current smokers, further categorization was made based on self-reported daily tobacco consumption: 1-10 cigarettes, 11-20 cigarettes, and more than 20 cigarettes per day(211).
- **Alcohol intake status:** Participants were categorized into three groups based on their alcohol consumption habits: current drinkers, former drinkers, and never-drank individuals(139). Current alcohol drinkers were defined as those who had consumed alcohol at least once within the last 30 days(118). The total amount of alcohol consumed by each individual was calculated using data on the frequency (number of days per week) and amount of common alcoholic beverages, including Ethiopian traditional drinks such as Tella/Suwa, Tej/Meas, beer, wine, and liquor. The amount of alcohol intake per occasion was categorized as follows(157):

1. Non-drinkers: individuals who never drank or were ex-drinkers,
2. Occasional/light drinkers: consuming less than one drink per day,
3. Moderate drinkers: consuming 1-3 drinks per day for men and 1-2 drinks per day for women,
4. Heavy drinkers: consuming more than three drinks per day for men and more than two drinks per day for women.

The frequency of alcohol intake was categorized as never, sometimes, but less than 1 time per week, 1–4 times per week, 5–6 times per week, and every day (115). Ethiopian traditional alcoholic drinks such as Tella, Tej, and Areki were found to have alcohol contents ranging from 3.98% to 6.48%, 8.94% to 13.16%, and 33.95% to 39.90%, respectively, with average values of

5.17%, 11.47%, and 37.22% v/v, respectively (212). One unit of alcohol (1 drink) was defined as a four-ounce glass of wine/Tej, a twelve-ounce can of beer/Tela, or one ounce of liquor. Total alcohol consumption was calculated by summing the intake units for all alcoholic beverages consumed on one drinking occasion(212).

- **Physical Activity Assessment:** The International Physical Activity Questionnaire (IPAQ) was employed to evaluate physical activity (PA), assessing Metabolic Equivalent Task levels (MET) min per week across various life domains, including transportation, work, and leisure. Work-related activity (vigorous, moderate) for at least 30 minutes continuously (yes/no, number of days per week, and duration in hours/minutes), travel to and from places (walking or bicycling) for at least 10 minutes continuously (yes/no, number of days per week, and duration in minutes), and recreational or leisure physical activity (vigorous, moderate) for at least 30 minutes continuously (yes/no, number of days per week, and duration in hours/minutes) were evaluated. The METs min/week for a specific activity (vigorous, moderate, and low-intensity PA) were calculated by multiplying the MET value (3.3 for walking, 4.0 for moderate PA, and 8.0 for vigorous PA) by the duration spent in that activity. Activities lasting at least 10 minutes were considered, with the formula (e.g., walking METs min/week = 3.3 × walking minutes × walking days) (213). The IPAQ scoring protocol categorizes PA levels into low, moderate, and high(213,214). PA levels were categorized as low if less than 600 MET. Min/week, moderate if 600-2999 MET. Min/week, and high if ≥ 3000 MET. min/week(115).

- **Dietary characteristics:** Owing to the low level of fruit and vegetable consumption in this sub-population, individuals who consumed two or more servings of fruits and vegetables daily, or at least 14 servings per week, were considered to have an adequate intake of fruits and vegetables instead of the WHO-recommended five servings(118).
- Additionally, the most frequently consumed or favorite food was categorized, including options such as injera made from teff, barley, wheat or sorghum, bread/bakery, white rice, pasta, and other items (such as ultra-processed foods, saturated fatty acids, butter, etc.).

b. Physical measurements:

Body mass index (BMI) was calculated by dividing body weight in kilograms by height squared in meters. BMI was categorized as follows: normal weight (< 25 kg/m2), overweight (25 kg/m2 to 29.9 kg/m2), and obesity (≥ 30 kg/m2) (57,58,157,215).

Waist circumference (WC) was measured halfway between the lower ribs and the iliac crest, with the subject at minimal respiration. In contrast, hip circumference was measured at the largest circumference around the buttocks. WC values ≥ 94 cm for men and ≥ 80 cm for women were considered elevated WC(57).

Waist-hip ratio (WHR) values of ≥ 0.88 for men and ≥ 0.82 for women were considered elevated WHR. Waist Height Ratio (WHtR) values of ≥ 0.49 for men and ≥ 0.50 for women were considered indicative of central obesity(57).

Blood pressure (BP) was measured using a standard digital sphygmomanometer (OMRON, model HEM-741CINT) on the left arm after 5 minutes of rest in the sitting position. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated as the mean values of three readings. Based on blood pressure, individuals were classified as normotensive (< 130/85 mmHg); hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg, diastolic blood pressure (DBP) ≥ 90 mmHg, or a previous diagnosis by a healthcare worker(115).

c. **Biomarkers:** Dyslipidemia is characterized by a lipid profile containing various abnormalities, individually or in combination. These abnormalities include physician-diagnosed elevation of total cholesterol (≥5.17 mmol/L or ≥200 mg/dL), LDL cholesterol (LDL-C) (≥3.36 mmol/L or ≥130 mg/dL), and triglycerides (≥1.7 mmol/L or ≥150 mg/dL), as well as lower levels of HDL cholesterol (HDL-C) (<1.03 mmol/L or <40 mg/dL for men, <1.3 mmol/L or <50 mg/dL for women)(38,57).
d. **Sociodemographic variables:** The variables assessed included gender, age, education, marital status, and location (urban or rural). Marital status was categorized as (1) Married/cohabitating, (2) divorced, and (3) widowed. Religion was categorized as (1) Orthodox Christian, (2) Muslim, and (3) Catholic/Protestant. Educational attainment was classified into four levels: (1) no formal education, (2) primary education, (3) secondary education, and (4) higher education. Employment status was categorized as (1) farmer, (2)

employed, (3) unemployed, and (4) housewife. Monthly income in Ethiopian birr was divided into quartiles: (Q1) < 2000, (Q2) 2000-3099, (Q3) 3100-5999, and (Q4) ≥ 60000. Location of residence was dichotomized into (1) urban and (2) rural. Medical history included family history of diabetes and history of gestational diabetes mellitus (GDM). Gender was coded as Men = 0 and Women = 1.

3) **For the Hyperglycemic Crisis**:

Dependent variable: In-hospital death after treatment(absence or presence of in-hospital death)

Independent variables:

- Patients with prior history of diabetes: Known diabetes patients: Individuals previously diagnosed with diabetes mellitus by a healthcare professional. While patients with no prior diabetes history who were diagnosed for the first time during admission with fasting plasma glucose (FPG) ≥ 126 mg/dL or repeated random plasma glucose (RPG) ≥ 200 mg/dL in conjunction with symptoms such as fatigue, polyuria, polydipsia, and other relevant symptoms(203).

- Physician-diagnosed hyperglycemic crises (DKA and HHS): Diabetic Ketoacidosis (DKA) is clinically defined by a random blood sugar level ≥ 250 mg/dL, urine glucose (typically > 3+), urine ketones (typically > 2+), and signs and symptoms consistent with DKA. Hyperosmolar Hyperglycemic State (HHS) is characterized by blood glucose levels exceeding 600 mg/dL, accompanied by mental changes, and mild or absent ketonuria(50).

- Level of consciousness: Physician-assessed using the Glasgow Coma Scale (GCS), categorized as mild (GCS ≥ 13), moderate (GCS 9 to 12), and severe levels (GCS ≤ 8).

3.8.Data Processing, Management and Analysis

The data collection process underwent daily scrutiny to detect inconsistencies and errors, with close supervision from the principal investigator. Collected data were securely stored in a locked cabinet. A codebook was prepared to ensure systematic data entry. Data were entered into Epi

Data Manager 4.3 for Windows 10 software daily and analyzed using SPSS Version 25.0 software. Missing values and outliers were thoroughly examined using SPSS version 25 software. Data cleaning procedures were implemented to rectify errors. The mean/median/mode imputation method minimizes missing data. Outliers were either removed or transformed based on their characteristics. These steps ensured the integrity and reliability of the dataset for subsequent analysis.

Data analysis for the Trend of T1D and T2D: The primary covariate of interest was time (in years), enabling the assessment of changes in the prevalence of T1D and T2D over time. Descriptive statistics were calculated, including median (Interquartile Range, IQR) for continuous variables and proportions for categorical variables. To examine trends in diabetes prevalence from September 1, 2013, to August 31, 2018, the extended Mantel-Haenszel chi-square test for linear trends was employed. This analysis was conducted using Epi Info 7.1.5 Statcalc. Trends in both T1D and T2D prevalence were assessed by residence and gender. A p-value of < 0.05 was considered statistically significant for the linear trend analysis. Additionally, the incidence rate (expressed per 1,000 person-years) was calculated by dividing the number of new T1D and T2D cases among adults aged 18 years and above, stratified by urban and rural residence and gender, by the total number of patients receiving medical services from medical and emergency Outpatient Departments (OPDs), separately for each residence and gender category. Similar calculations were performed to determine the five-year prevalence rates.

Data analysis for the risk factors of T2D: The data were analyzed using SPSS version 25 software. Descriptive statistics were computed for each study variable, with percentages and frequencies used for categorical variables. At the same time, numerical data were evaluated for normality using various tests, including normality plots, Q-Q plots, histograms, and statistical tests such as Kolmogorov-Smirnov and Shapiro-Wilk. For normally distributed data, scores, means, and standard deviations were calculated, whereas skewed data were summarized using the median and interquartile range (IQR). Results were summarized using text, tables, and graphs, with population parameters calculated using 95% confidence intervals. Cross-tabulation assessed the crude association between each categorical predictor variable and the outcome variable.

A conditional binary logistic regression model was utilized to demonstrate the relationship between different independent variables and the dependent variable, generating matched odds ratios with their 95% confidence intervals. Variables with a p-value less than 0.25 in bivariate analyses were included in the multivariable analysis. Multicollinearity diagnostics and interaction of variables were tested using the variance inflation factor (VIF) and tolerance, with VIF < 10 considered acceptable. The goodness-of-fit of the logistic regression model was assessed using Hosmer and Lemeshow's test, with a p-value greater than 0.05 indicating model fitness. Multivariable logistic regression was conducted to control for possible confounding effects and identify independent predictors. Adjusted odds ratios and their 95% confidence intervals were reported, with a p-value less than 0.05 (95% CI) considered statistically significant for independent predictors in the final model.

For the Hyperglycemic, Descriptive statistics were computed for each study variable. For categorical variables, percentages and frequencies were utilized. Numerical data underwent assessment for normality through various normality-checking tests, including normality plots, Q-Q plots, histograms, Kolmogorov-Smirnov, and Shapiro-Wilk tests. Data were entered and analyzed using SPSS version 25.0 for Windows. For missing variables, the median was used for continuous variables, and the mode was used for categorical variables to facilitate complete case analysis. Continuous data were presented as medians with interquartile ranges (IQR) and means ± Standard Deviation (SD). Comparisons between the two groups were conducted using independent-sample t-tests (assuming normal distribution) or Mann–Whitney tests (assuming non-normality) for continuous variables. Nominal variables were represented as absolute frequencies and proportions. The $\chi 2$-test was applied for categorical variables. Multivariable logistic regression was conducted to control for possible confounding effects and identify independent predictors. Adjusted odds ratios and their 95% confidence intervals were reported, with a p-value less than 0.05 (95% CI) considered statistically significant for independent predictors in the final model.

3.9.Data quality assurance

Several measures were implemented to enhance the research's quality, from instrument development through data analysis, interpretation, and findings elucidation stages.

For record review (about the Trends of T1D and T2D and hyperglycemic crises), a data abstraction format was devised in English, and abstraction was conducted in English. For case-control studies, the data collection instrument was initially formulated in English and then translated into Tigrigna (local language), followed by a back-translation into English to ensure linguistic consistency, overseen by language experts.

Data collectors possessing prior research experience, particularly in Non-Communicable Diseases (NCDs), were recruited and underwent comprehensive two-day training on the study's objectives, procedures, and the significance of the study tools. Standardized protocols were used to provide precise measurements of height, weight, hip circumference, waist circumference, blood pressure, blood glucose levels, and lipid profile tests among study participants to ensure consistent and accurate measurements. The study implemented rigorous training for data collectors and supervisors, focusing on precise measurement techniques, regular quality control checks, and equipment calibration to ensure uniformity and accuracy. Moreover, the study tools were pre-tested on 5% of the anticipated sample size in institutions not included in the study two weeks before the data collection. Any necessary adjustments in terminologies, question sequencing, and meaning were made accordingly.

Data collectors were instructed to verify the completeness of the instrument immediately after its completion. Each night, the Principal Investigator (PI) and supervisors scrutinized five percent of the data abstraction and questionnaires for completeness. Any errors, ambiguities, incompleteness, or other issues encountered were addressed promptly the following day before commencing the next day's activities.

Furthermore, the collected data underwent coding, cleaning, and exploration before analysis to ensure its quality and reliability.

3.10. Ethical Consideration

Before data collection, ethical clearance was obtained from the Research Ethics Committee of the School of Public Health (REC/SPH) and the Institutional Review Board (IRB) of Addis

Ababa University, College of Health Sciences. Additionally, support letters were secured from Addis Ababa University to the Tigrai Regional Health Bureau and from the Tigrai Regional Health Bureau to the respective hospitals. Permission was also obtained from the administrators of the respective health facilities to access and extract data from patients' records.

Study participants were informed about the study's objectives and procedures, and their willingness to participate was confirmed. They were assured that their decision to withdraw or decline participation would not affect their access to healthcare services. Participants were not exposed to any risks beyond the time spent during the interviews. The study guaranteed anonymity without disclosing participants' identities; their names were not recorded, and all provided information was kept confidential.

Participants were informed that there were no direct benefits to them for participating in the research. Still, the study's outcomes would potentially benefit diabetes patients, healthcare facilities, researchers, policymakers, and the community. Informed consent was obtained from all study participants, and they were informed about their rights and expectations. Those with newly diagnosed diabetes, hypertension, and dyslipidemia were connected to appropriate healthcare units by physicians.

The study adhered to the principles outlined in the Declaration of Helsinki, ensuring the ethical conduct of research involving human participants.

3.11. Dissemination

The findings of this study will be presented to Addis Ababa University School of Graduate Studies College of Health Sciences and Adigrat University and different stakeholders, including the Hospitals, Tigrai Regional Health Bureau, Ethiopian Ministry of Health, in the annual conference of the Ethiopian Public Health Association (EPHA), Ethiopian Diabetes Association and other agencies who are working in NCDs, particularly on diabetes. Finally, the results are also papers I and III published in Dove Medical Press, Diabetes Metab Syndr Obes, and paper II is submitted to BMC Public Health for review in peer-reviewed reputable journals.

3.12. Tabular Summary of the Methods Applied in the Dissertation

Table 1: Summary of methods based on the objectives of the study

S. N	Research objectives	Study design	Study subjects	Sample size utilized	Data collection tools	Data analysis
1	To determine urban-rural differences in the trend of type 1 and type 2 diabetes among adults who received medical care from selected public hospitals of Tigrai, Ethiopia.	Cross sectional study design	Registery logbooks and medical records of newly diabetes patients aged ≥18 years who received medical care from adult medical and emergency OPD units between (2013 and 2018) in 6 general and one referral hospitals	All patients received medical care from 2013-2018 (299,806, of which 3056 were diabetes)	A data abstraction format developed from the literature	Descriptive analysis and Chi-square for trend
2	To identify factors associated with T2D among middle-aged adults who received medical care from ACSH in Tigrai, Ethiopia.	Matched Case-control study design	Adults of middle age (45 to 64 years) with/without T2D who received medical treatment from ACSH.	360(120 cases/T2D, and 240 controls/ Non-diabetes), matched for age and gender	Customized WHO STEPS protocol for NCDs	Descriptive and conditional logistic regression analysis for matched data (Bivariate and multi-variable) Estimated using odds ratio (OR)
3	To compare hyperglycemic crisis characteristics and care outcomes among adult patients without and with a history of diabetes from selected public hospitals of Tigrai.	Cross sectional retrospective record review	Patients aged ≥18 years who were admitted and treated for HC in the medical ward between Sep. 1, 2017, and Aug 31, 2018) in 6 general and one referral hospitals	589(393 with history of diabetes and 196 without history of diabetes)	A data abstraction format developed from the reviewed literature	Descriptive analysis, $\chi 2$-test, t-test, Mann–Whitney/Wilcoxon tests, and logistic regression analysis

4. Results

4.1. Trend of T1D and T2D

4.1.1. Characteristics of study participants

Out of the 299,806 adult patients who received medical care services in the studied hospitals, 128,915 (43.0%) were women, and 126,559 (42.2%) were rural residents. Among these patients, 3,056 (10.2 per 1,000 individuals) were confirmed as having diabetes. The diabetes incidence was higher in urban areas, with 2,011 cases (11.6 per 1,000 urban residents), compared to 1,045 cases (8.6 per 1,000 rural residents) (Table 2).

Nearly quarters (24.2%) of the patients were aged 30 to 39, followed by those aged 18 to 29 (22.9%). The median age at diagnosis for diabetes patients was 46 years (IQR 35–57). For Type 1 diabetes (T1D) patients, the median age was 25 years (IQR 20–30), while for T2D patients, it was 49 years (IQR 40-60) (Table 2).

Among the 3,056 newly diagnosed diabetes patients, 1,705 (55.8%) were men, and 2,011 (66%) were urban residents. Of these patients, 487 (15.9%) had T1D, with almost half (50.1%) being rural residents. Conversely, of the 2,569 T2D patients, 1,768 (68.8%) were urban residents. Nearly half (49.1%) of all diabetes patients were treated with insulin, and almost one-third received treatment at ACSH (Table 2).

Table 2: Characteristics of study participants in selected public hospitals of Tigrai, Ethiopia (September 1, 2013, to August 31, 2018).

Patient characteristics	Frequency	Percent
Gender		
Men	170,819	57.1
Women	128,987	42.9
Residence		
Urban	173,247	57.8
Rural	126,559	42.2
The age category of participants		
< 30	68,723	22.9
30 to 39	72.561	24.2
40 to 49	65.219	21.8
50 to 59	50,631	16.9
60 Years and above	42,672	14.2
Gender of diabetes patients		
Men	1,705	55.8
Women	1,351	44.2
Location of residence of diabetes patients		
Urban	2011	65.8
Rural	1045	34.2
Type of diabetes		
Type 1 diabetes	487	15.9
Type 2 diabetes	2569	84.1
Type 1 diabetes		
Urban resident	243	49.1
Rural residents	244	50.1
Type 2 diabetes		
Urban residents	1,768	68.8
Rural residents	801	31.2
Treatment given at the time of diagnosis		
Advice on lifestyle behavior	185	6.1
OHA	1368	44.8
Insulin	1503	49.1
Co-morbidity		
Yes	761	24.9
No	2295	75.1
Hospital diabetes treated		
Ayder Comprehensive Specialized Hospital	944	30.9
Mekelle hospital	465	15.2
Ma'ychew Lemlem Karl hospital	408	13.4
Adigrat hospital	332	10.9
St Merry hospital	376	12.3
Suhul shire hospital	326	10.7
Abyi Adi hospital	205	6.7

4.1.2. The overall trend in the proportion diabetes by residence and age

The overall time trend in the proportion of diabetes among adult patients increased significantly, rising from 6.8 (95% CI: 6.1-7.5) to 14.3 (95% CI: 13.3-15.1) per 1,000 adult patients, with a statistically significant linear trend ($\chi 2 = 182.6$, $P < 0.001$); with about 110.3% increase in the over study period. This increase was observed in both urban and rural populations. In urban areas, the proportion of diabetes increased from 7.9 (95% CI: 6.9-8.9) to 15.9 (95% CI: 14.6-17.2) per 1,000 adult urban residents, showing a statistically significant rise ($\chi 2 = 78.1$, $P < 0.001$). Similarly, in rural areas, the proportion went up from 5.2 (95% CI: 4.4-6.2) to 12.1 (95% CI: 10.9-13.5) per 1,000 adult residents, also with a statistically significant increase ($\chi 2 = 91.9$, $P < 0.001$) during the observation period, **(**Figure 4).

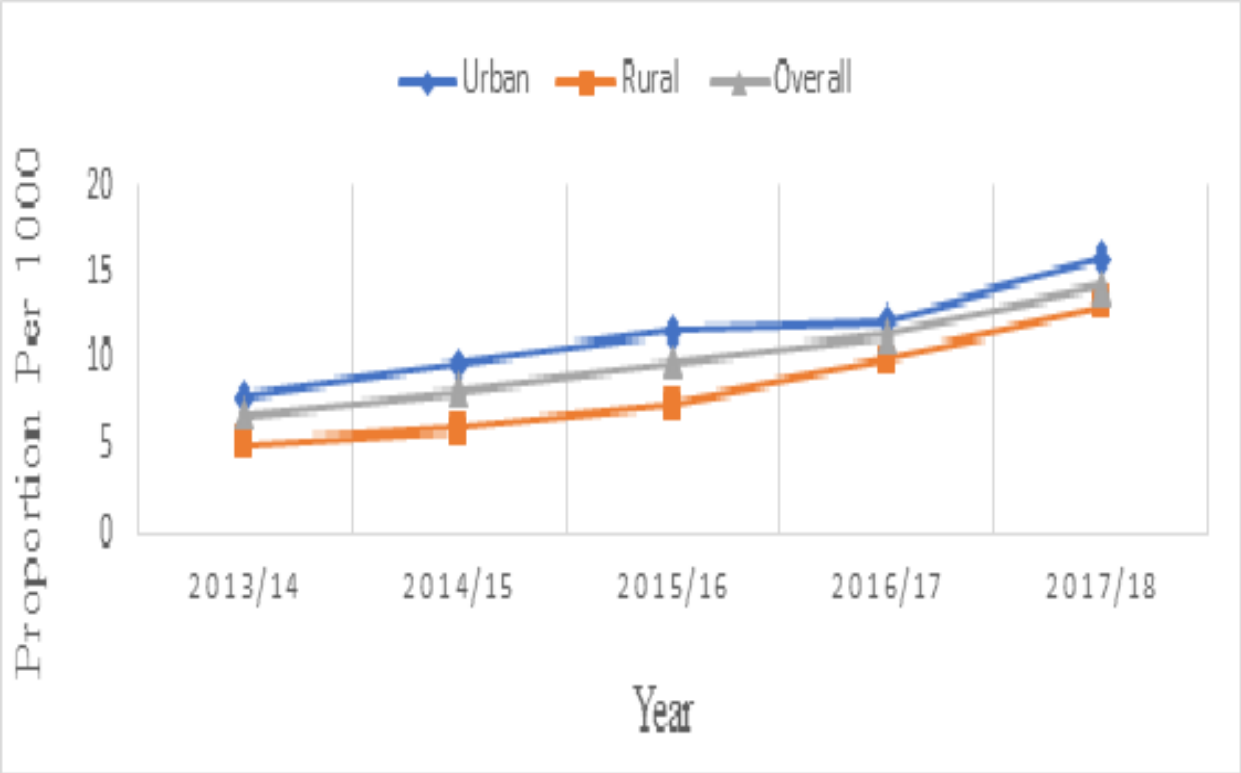

Figure 4: The overall time trends in the proportion of diabetes by residence in selected public hospitals of Tigrai, Ethiopia (September 1, 2013, to August 31, 2018).

The time trend of diabetes showed a steady increase across all age groups during the study period. The proportion per 1,000 patients were 6.8 (95% CI: 6.2-7.4) for ages 18-29, 7.7 (95% CI: 7.1-8.4) for ages 30-39, 11.5(95% CI: 10.7-12.4) for ages 40-49, 12.2 (95% CI: 11.3-13.2) for ages 50-59, and 15.5 (95% CI: 14.4-16.7) for ages 60 and above. This represents a statistically significant linear increase ($\chi 2 = 34.5$, $P < 0.001$) throughout the observation period. **(Figure 5).**

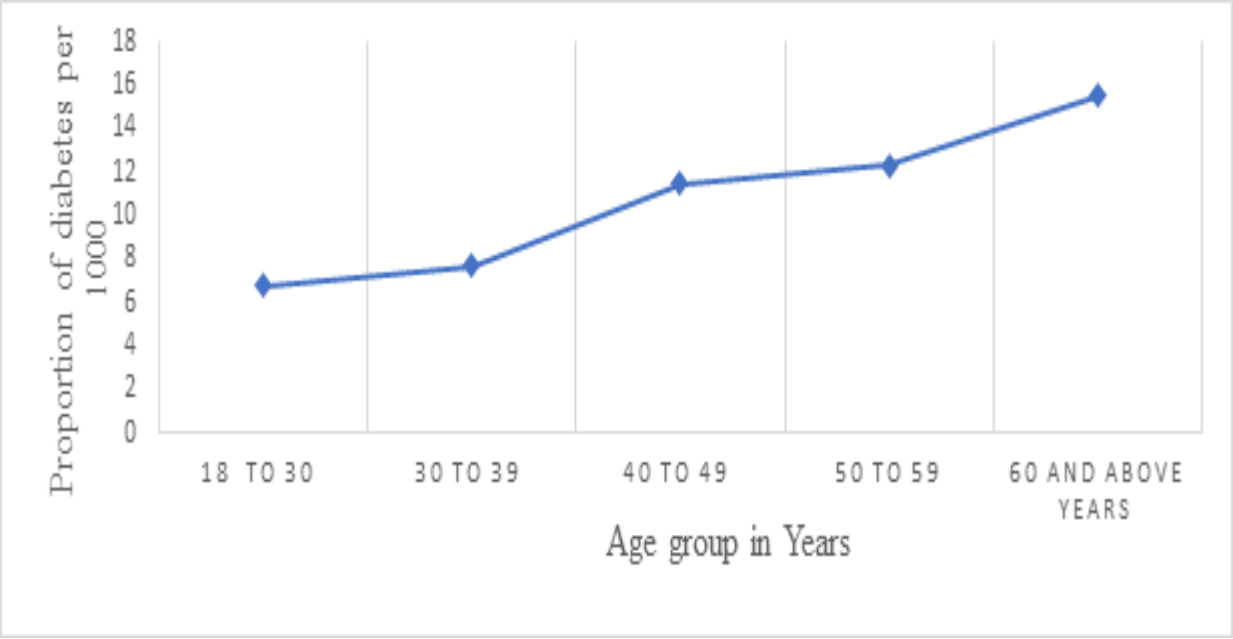

Figure 5: Time Trends in the proportion of diabetes by age category per 1000 adult patients in the selected public hospitals of Tigrai, Ethiopia (September 1, 2013, to August 31, 2018).

4.1.3. The Time trend of T1D and T2D by residence and gender

The overall five-year prevalence rate of T1D was 1.6 (95% CI: 1.5-1.8) per 1,000 patients, showing a statistically significant linear increase ($\chi 2 = 34.5$, Ptrend < 0.001). Among urban residents, the proportion was 1.4 (95% CI: 1.2-1.6) per 1,000 patients, significantly increasing ($\chi 2 = 9.1$, $P = 0.002$). For rural residents, the proportion was higher at 1.9 (95% CI: 1.7-2.2) per 1,000 patients, with a significant linear trend ($\chi 2 = 17.8$, $P < 0.001$). Women had a proportion of 1.7 (95% CI: 1.2-1.6) per 1,000 patients, showing a significant increase ($\chi 2 = 20.2$, $P < 0.001$), while the time trend for men was not statistically significant ($\chi 2 = 3.1$, $P = 0.08$), (Table 3).

The overall trend in the proportion of type 1 diabetes increased from 1.1 (95% CI: 0.8-1.4) to 2.4 (95% CI: 2.1-2.8) per 1,000 adult patients. For urban residents, the incidence rose from 1.0 (95% CI: 0.7-1.4) to 2.2 (95% CI: 1.8-2.8) per 1,000 adult urban residents. In rural areas, the proportion increased from 1.2 (95% CI: 0.8-1.7) to 2.6 (95% CI: 2.1-3.3) per 1,000 adult rural residents over the observation period (Figure 6).

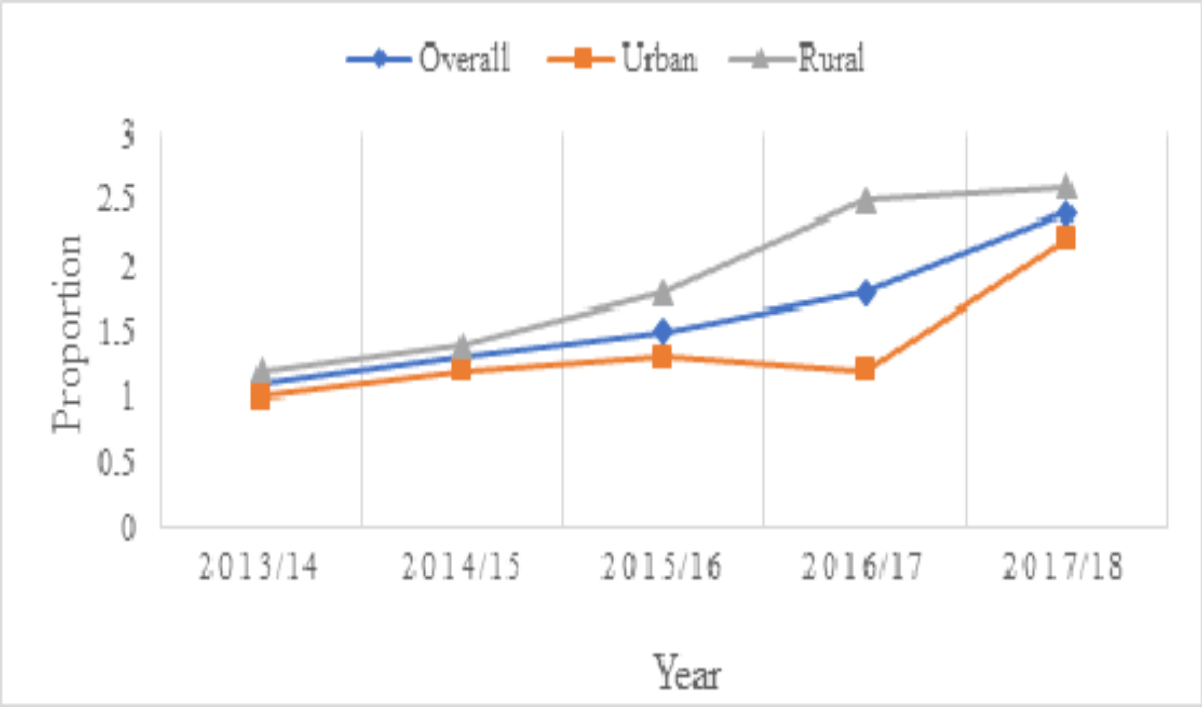

Figure 6: Time Trends in the proportion of type 1 diabetes by residence per 1000 adult patients in the selected public hospitals of Tigrai, Ethiopia (September 1, 2013 to August 31, 2018).

Table 3: The trends of T1D by residence and gender (Extended Mantel-Haenszel chi-square and proportion) in the selected hospitals of Tigrai, Ethiopia (September 1, 2013 to August 31, 2018).

Variable	Year	DM patients	OPD+EOPD patients	Proportion per 1000	95% CI per 1000	MH-OR
The overall Proportion of of T1D	2013/14	59	55734	1.1	[0.8-1.4]	1.000
	2014/15	76	58806	1.3	[1.0-1.6]	1.221
	2015/16	91	60221	1.5	[1.2-1.9]	1.428
	2016/17	109	61805	1.8	[1.4-2.1]	1.667
	2017/18	152	63240	2.4	[2/1-2.8]	2.274
	Total	487	299,806	1.6	[1.5-1.8]	$\chi2$= 34.5, P<0.001
Proportion of of T1D in urban	2013/14	31	31,914	1.0	[0.7-1.4]	1.000
	2014/15	42	34,370	1.2	[0.9-1.6]	1.254
	2015/16	45	34,645	1.3	[1.0-1.7]	1.334
	2016/17	44	36,244	1.2	[0.9-1.6]	1.250
	2017/18	81	36,074	2.2	[1.8-2.8]	2.315
	Total	243	173,247	1.4	[1.2-1.6]	$\chi2$= 9.1, P=0.002
Proportion of T1D in rural	2013/14	28	23,820	1.2	[0.8-1.7]	1.000
	2014/15	34	24,436	1.4	[1.0-1.9]	1.188
	2015/16	46	25,576	1.8	[1.3-2.4]	1.536
	2016/17	65	25,561	2.5	[2.0-3.2]	2.173
	2017/18	71	27,166	2.6	[2.1-3.3]	2.233
	Total	244	126,559	1.9	[1.7-2.2]	$\chi2$=17.8, P<0.001
Proportion of T1D for men	2013/14	39	31,312	1.2	[0.9-1.7]	1.00
	2014/15	39	34,273	1.1	[0.8-1.6]	0.914
	2015/16	45	34,267	1.3	[1.0-1.8]	1.054
	2016/17	63	36,579	1.7	[1.3-2.2]	1.383
	2017/18	77	34,460	2.2	[1.8-2.8]	1.796
	Total	263	170,891	1.5	[1.4-1.7]	$\chi2$= 3.1, P= 0.08
Proportion of T1D for women	2013/14	20	24,422	0.8	[0.5-1.3]	1.000
	2014/15	37	24,533	1.5	[1.1-2.1]	1.828
	2015/16	46	25,952	1.8	[1.3-2.3]	2.235
	2016/17	46	25,226	1.8	[1.4-2.4]	2.211
	2017/18	75	28,780	2.6	[2.1-3.3]	3.162
	Total	224	128,915	1.7	[1.5-2.0]	$\chi2$=20.2, P<0.001

DM: Diabetes, MH-OR: Mantel-Haenszel-Odd Ratio, OPD: Out Patient Department, EOPD: Emergency Out Patient Department

The overall proportion of T2D was 8.6(95% CI: 8.2-8.9) per 1000 adult patients, showing a statistically significant increase (χ^2 =151.0, p_{trend}<0.001). The five-year trend in the proportion of T2D increased from 5.7(95%CI: 5.1-6.3) to 12.0(95%CI: 11.0-13.0) per 1000 adult patients, (P_{trend}<0.001), with urban from 6.9 to 14.0 per 1000 adult urban residents, (P_{trend}=0.001) and rural from 4.0 to 9.5 per 1000 adult rural residents, (P_{trend}=0.001). The proportion of for men and

women were 8.4(95% CI: 7.9-8.8) per 1000 men and 8.8(95% CI: 8.3-9.4) per 1000 women, respectively, both showing statistically significant increases ($\chi^2 = 32.0$, $P < 0.001$ for men and $\chi^2 = 70.3$, $P < 0.001$ for women), (Table 4).

Table 4: The Time Trends of T2D by residence and gender (Extended Mantel-Haenszel chi-square and proportion) in hospitals of Tigrai, Ethiopia (September 1, 2013 to August 31, 2018).

Variable	Year	DM patients	OPD+EOPD patients	Proportion per 1000	95% CI per 1000	MH-OR
Overall Proportion of T2D	2013/14	317	55734	5.7	[5.1-6.3]	1.000
	2014/15	407	58806	6.9	[6.3-7.6]	1.216
	2015/16	502	60221	8.3	[7.6-9.1]	1.470
	2016/17	593	61805	9.6	[8.9-10.0]	1.694
	2017/18	750	63240	12.0	[11.0-13.0]	2.098
	Total	2569	299,806	8.6	[8.2-8.9]	$\chi2$=151, P<0.001
Proportion of T2D in urban residents	2013/14	221	31,914	6.9	[6.0-7.9]	1.000
	2014/15	294	34,370	8.6	[7.7-9.6]	1.237
	2015/16	359	34,645	10.0	[9.3-11.0]	1.497
	2016/17	402	36,244	11.0	[10.0-12.0]	1.608
	2017/18	492	36,074	14.0	[12.0-15.0]	1.983
	Total	1768	173,247	10.0	[9.7-11.0]	$\chi2$=68.4, P<0.001
Proportion of T2D in rural residents	2013/14	96	23,820	4.0	[3.3-4.9]	1.000
	2014/15	113	24,436	4.6	[3.8-5.6]	1.148
	2015/16	143	25,576	5.6	[4.7-6.6]	1.389
	2016/17	191	25,561	7.5	[6.5-8.6]	1.860
	2017/18	258	27,166	9.5	[8.4-11.0]	2.369
	Total	801	126,559	6.3	[5.9-6.8]	$\chi2$=74.2, P<0.001
Proportion of T2D for men	2013/14	184	31,312	5.9	[5.1-6.8]	1.000
	2014/15	225	34,273	6.6	[5.8-7.5]	1.118
	2015/16	281	34,267	8.2	[7.3-9.2]	1.399
	2016/17	351	36,579	9.6	[8.6-11.0]	1.639
	2017/18	389	34,460	11.3	[10.2-12.5]	1.932
	Total	1,430	170,891	8.4	[7.9-8.8]	$\chi2$=32.0, P<0.001
Proportion of T2D for women	2013/14	133	24,422	5.4	[4.6-6.4]	1.000
	2014/15	182	24,533	7.4	[6.4-8.6]	1.365
	2015/16	221	25,952	8.5	[7.5-9.7]	1.569
	2016/17	242	25,226	9.6	[8.5-11.0]	1.769
	2017/18	361	28,780	11.3	[11.0-13.9]	2.320
	Total	1,139	128,915	8.8	[8.3-9.4]	$\chi2$=70.3, P<0.001

DM: Diabetes, MH-OR: Mantel-Haenszel-Odd Ratio, OPD: Out Patient Department, EOPD: Emergency Out Patient Department

The time trend in the proportion of T2D increased from 5.7 (95% CI: 5.1-6.3) to 12.0 (95% CI: 11.0-13.0) per 1000 adult patients. For urban residents, the proportion rose from 6.9 (95% CI: 6.0-7.9) to 14.0 (95% CI: 12.0-15.0) per 1000 adult urban residents. Among rural residents, the proportion increased from 4.0 (95% CI: 3.3-4.9) to 9.5 (95% CI: 8.4-11.0) per 1000 adult rural residents during the observation period (Figure 7).

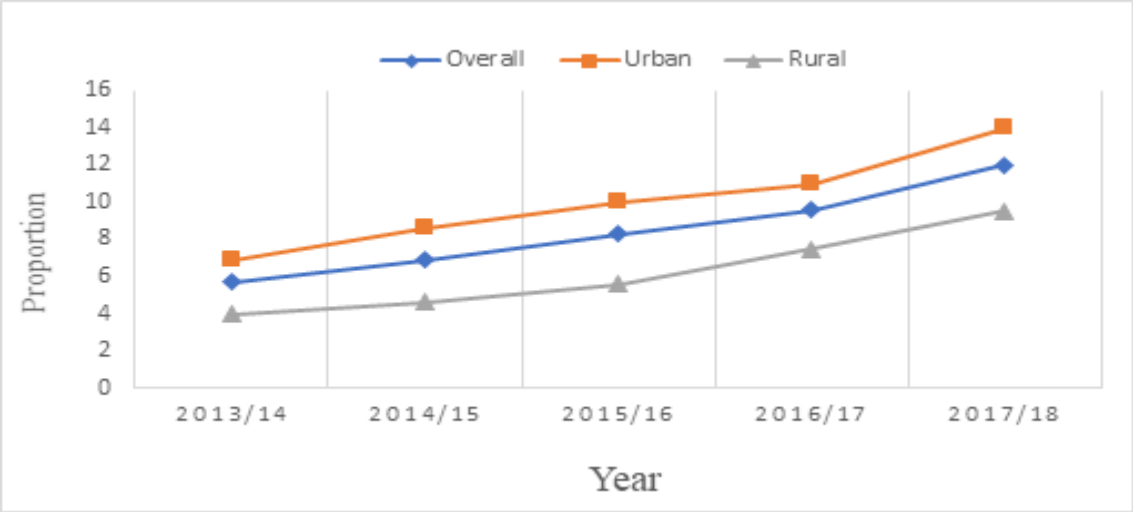

Figure 7: Time Trends in the proportion of T2D by residence per 1000 adult patients in the selected public hospitals of Tigrai, Ethiopia (September 1, 2013 to August 31, 2018).

4.2. Associated Factors of T2D

4.2.1. Socio-demographic of cases and controls

During the study period from March 1 to June 30, 2019, 360 patients were interviewed and measured for their socio-demographic and medical history, behavioral characteristics, physical measurements, and biomarker indices. Among these participants, 120 T2D cases were matched by age and gender, with 240 controls to identify risk factors for T2D. The focus was primarily on examining socio-demographic characteristics, family history of diabetes, lifestyle behaviors, dietary characteristics, physical measurements, and biomarker indices.

The mean (SD) ages of the cases and controls were 55.9 (±5.0) and 55.7 (±4.8) years, respectively. Among the cases, 113 (94.2%) were urban residents compared to 169 (70.4%) of the controls. Regarding religious affiliation, 111 (92.5%) of the cases and 216 (90.0%) of the controls followed Orthodox Christianity. Marital status revealed that 87 (73.3%) of the cases and 201(83.8%) of the controls were married, while 19 (15.8%) of the cases and 18 (7.5%) of the controls were widowed. In terms of education, 44 (36.7%) of the cases and 99 (41.3%) of the controls had completed primary education, and 24 (20.0%) of the cases and 38 (15.9%) of the controls had attained higher education. Employment status showed that 74 (61.7%) of the cases and 126 (52.5%) of the controls were employed, while 24 (20.0%) of the cases and 38 (15.8%) of the controls were homemakers. Additionally, 31(25.8%) of the cases and 63 (26.3%) of the controls had a monthly family income of ≥ 6000 Ethiopian Birr(Table 5).

In the cases, nearly half (48.3%) had been previously diagnosed with raised blood pressure, whereas among controls, this was reported in only one-fifth (17.1%). Among those with raised blood pressure, 45 (71.4%) of the cases and 21 (46.7%) of the controls had received treatment prescribed by a healthcare provider within the past two weeks. Similarly, 61 (50.8%) cases had been diagnosed with raised cholesterol at some point, compared to 56(23.3%) controls. Among those with raised cholesterol, 37(60.7%) of the cases and 27(46.4%) of the controls had received treatment within the past two weeks as prescribed by a healthcare provider. Additionally, 28 (23.3%) of the cases reported a family history of diabetes (FHD), while 19 (7.9%) of the controls had the same family history (Table 5).

Table 5: Socio-demographic characteristics of cases and controls at ACSH, Tigrai, 2019(n=360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	COR[95%CI], t(df),	p-value
Age in years(Mean ± SD)	55.9±5.0	55.7±4.8	t(358)=-0.24	p= 0.8
Residence, n (%)				
Rural	7(5.8)	71(29.6)	1	
Urban	113(94.2)	169(70.4)	6.8[3.0, 15.3]	P< 0.001
Religion, n (%)				
Orthodox	112(93.3)	216(90.0)	0.78[0.13, 4.7]	P= 0.5
Muslim	6(5.0)	21(8.8)	0.43[0.06, 3.2]	
Catholic/protestant	2(1.7)	3(1.3)	1	
Marital status, n(%)				
Married	87(72.5)	201(83.8)	1	
Divorced/separated	14(11.7)	21(8.8)	1.6[0.6, 4.0]	
Widowed	19(15.8)	18(7.5)	2.4[1.2, 4.9]	P=0.029
Educational level (%)				
No formal education	22(18.3)	55(22.9)	1	
Primary education	44(36.7)	99(41.3)	1.0[0.51, 2.0]	
Secondary education	30(25.0)	48(20.0)	1.4[0.76, 2.7]	
Higher education	24(20.0)	38(15.9)	1.6[0.76, 3.2]	P=0.4
Employment status, n (%)				
Employed	74(61.7)	126(52.5)	3.6[1.5, 9.0]	
Unemployed	16(13.3)	39(16.3)	0.93[0.52, 1.7]	
House-wife	24(20.0)	38(15.8)	1.4[0.75, 2.7]	P=0.031
Farmer	6(5.0)	37(15.4)	1	
Quartiles of family income in EB				
Q1(< 2000)	9(7.5)	25(10.4)	1	
Q2(2000-3099)	40(33.3)	106 (44.2)	1.1[0.45, 2.4]	
Q3(3100-5999)	40(33.3)	46(19.2)	2.4[1.01,5.8]	P=0.023
Q4(≥ 6000)	31(25.8)	63(26.3)	1.4[0.57, 3.3]	
Ever told as having raised BP, n (%)				
No	62(51.7)	199(82.9)	1	p< 0.001
Yes	58(48.3)	41(17.1)	4.5[2.8, 7.4]	
Ever told of having raised cholesterol				
No	59(49.2)	184(76.7)	1	
Yes	61(50.8)	56(23.3)	3.4[2.1, 5.4]	p< 0.001
Family History of Diabetes				
No	92(76.7)	221(92.1)	1	
Yes	28(23.3)	19(7.9)	3.5[1.6, 3.7]	P< 0.001

4.2.2. Behavioral Factors of Cases and Controls

4.2.2.1.Cigarette Smoking and alcohol consumption

Almost 5.3% of the participants were current smokers of tobacco products, such as cigarettes, with a slightly higher proportion among cases (8.3%) compared to controls (3.8%), although this difference was not statistically significant (p=0.19). Notably, all current smokers were men. Among the current smokers, 60.0% of the cases and 44.4% of the controls smoked more than 20 cigarettes per day. The mean age at which cigarette smoking started was 28.4 ± 5.5 years for cases and 32.4 ± 5.3 years for controls. The duration of cigarette smoking was 26.6 ± 5.5 years for cases and 23.9 ± 5.4 years for controls (Table 6).

In both the cases and controls, a high proportion of participants reported current alcohol consumption: 82.5% among cases and 78.8% among controls. Among those who consumed alcohol, the traditional local alcoholic drink ‘Suwa/Tela’ was the most commonly consumed, with 51.5% of cases and 61.4% of controls preferring it. Beer was the second most popular alcoholic beverage, consumed by 35.4% of cases and 31.2% of controls. Liquor consumption was reported in 18.2% of cases and 7.9% of controls, with a statistically significant difference observed (p=0.01) (Table 6).

Among the cases, 44 (36.7%) were heavy alcohol drinkers compared to 55 (22.9%) of the controls. Among men, heavy alcohol consumption was reported by 37 (61.7%) cases and 46 (38.3%) controls, whereas among women, it was 7 (11.7%) cases and 9 (7.5%) controls. In terms of residence, 4 (57.1%) rural cases and 40 (35.4%) urban cases reported heavy alcohol consumption, while among controls, 17 (23.9%) rural residents and 38 (22.5%) urban residents were heavy alcohol drinkers, (Table 6).

On average, cases reported consuming 2.06 (±1.6) standard alcoholic drinks per occasion in the past 30 days, which was higher than controls who reported 1.7 (±1.3) drinks (p=0.01). A higher proportion of cases (7.5%) reported drinking alcohol daily compared to controls (2.9%). The median (IQR) number of standard alcoholic drinks per week was 11 (1–12) for cases and 6.25 (0.5–6.75) for controls in a typical week (Table 6).

Table 6: Cigarette smoking and Alcohol drinking behavior of study participants at ACSH, Tigrai, Ethiopia, 2019(n= 360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	COR[95%CI], t(df)	P-value
Cigarette smoking status				
Never smoker	105(87.5)	222(92.5)	1	
Ex-smoker	5(4.2)	9(3.8)	1.2[0.38, 3.6]	
Current smoker	10(8.3)	9(3.8)	2.4[0.93, 6.0]	P= 0.19
Number of cigarettes smoked/day				
≤ 10 cigarettes	2(20.0)	2(22.2)	1	
11 to 20 cigarettes	2(20.0)	3(33.3)	0.67[0.1, 9.5]	
> 20 cigarettes	6(60.0)	4(44.4)	1.5[0.2, 15.5]	P= 0.76
Drinking status				
Life-time abstainer	5(4.2)	25(10.4)	1	
Ex – drinker	16(13.3)	26(10.8)	3.1[0.98, 9.7]	
Current drinker	99(82.5)	189(78.8)	2.6[0.97, 7.1]	P=0.13
During the past 30 days, on average, standard alcoholic drinks on one occasion (%)				
Non-drinker	21(17.5)	51(21.3)	1	
Light drinker	13(10.8)	21(8.8)	1.5[0.67, 3.6]	
Moderate drinker	42(35.0)	113(47.1)	0.9[0.45, 1.7]	
Heavy drinker	44(36.7)	55(22.9)	1.9[1.02, 3.47	P= 0.029
During the past 30 days, how frequently have you had at least one alcoholic drink?				
Non-drinker	21(17.5)	51(21.3)	1	
Less than once per week	3(2.5)	17(7.1)	0.43[0.1,1.6]	
1-4 days per week	65(54.2)	147(61.3)	1.1[0.6, 1.9]	P=0.004
5 -6 days per week	22(18.3)	18(7.5)	3.0[1.3, 6.6]	
Every day	9(7.5)	7(2.9)	3.1[1.03, 9.5]	
Common types of alcoholic drinks drunk				
‘Suwa/Tela’ (yes, %)	51(51.5)	116(61.4)	0.7[0.4, 1.1]	P=0.1
‘Meas/Tej’ (yes, %)	9(9.1)	8(4.2)	2.3[0.9, 6.1]	P=0.1
Beer (yes, %)	35(35.4)	59(31.2)	1.2[0.7, 2.0]	P=0.4
Wine (yes, %)	10(10.1)	18(9.5)	1.1[0.5, 2.4]	P=0.8
Liquor (yes, %)	18(18.2)	15(7.9)	2.6[1.2, 5.4]	P=0.01

4.2.2.2.Dietary Characteristics of Cases and Controls

According to the study participants, injera made from teff/barley/sorghum/wheat was reported as the favorite diet by 72 (60%) of the cases and 174 (72.5%) of the controls. The second most commonly consumed diet was bread/bakery made from wheat, with 24 (20.0%) of cases and 33 (13.8%) of controls preferring it **(**Table 7**).**

Forty-nine (40.8%) of the cases and 88 (36.7%) of the controls reported not using fruit in their dishes in a typical week. Only 1.7% of cases and 3.3% of controls consumed 14 or more servings of fruits in their dishes in a typical week. The median (IQR) number of days fruit was used in a dish for the cases and controls was 2(0.0–2.0) and 3(0.0–3.0), respectively. Similarly, the median (IQR) number of dishes of fruit used per day in a typical week for the cases and controls was 1.0 (0.0–1.0) (Table 7).

Fourteen (11.7%) of the cases and 34 (14.2%) of the controls reported not using vegetables in their dish in a typical week. Only 5.8% of the cases and 8.8% of the controls consumed 14 or more vegetables in their dish in a typical week. The median (IQR) number of days vegetables were used in a dish in a typical week for the cases and controls was 1 (2.0–3.0) and 2 (1.0–3.0), respectively. The mean (SD) number of dishes of vegetables used per day in a typical week was 1.4 (±0.72) for the cases and 1.4(±0.76) for the controls. The median (IQR) number of dishes of vegetables used in a typical week for the cases and controls was 4 (2.0–6.0) and 5 (1.0–6.0), respectively (Table 7).

Over 73% of the cases and 67.1% of the controls consumed one to three cups of coffee daily. Forty-one (34.5%) of the cases and 72 (30.0%) of the controls consumed two or more cups of tea daily. In a typical week, 28 (23.3%) of the cases and 30 (12.5%) of the controls consumed one to two bottles of sugar-containing soft drink beverages (p=0.033) (Table 7).

Table 7: Dietary characteristics of cases and controls at ACSH, Tigrai, Ethiopia, 2019(n= 360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	COR[95%CI], t(df)	P-value
Your most favorite and regularly used food				
Injera made from Teff/barely/sorghum	72(60.0)	174(72.5)	1	
Bread/injera made from wheat	24(20.0)	33(13,8)	0.57[0.31, 1.03]	
White rice	12(10.0)	11(4.6)	0.38[0.16, 0.90]	
Pasta	9(7.5)	13(5.4)	0.6[0.25, 1.5]	
Others	3(2.5)	9(3.8)	1.2[0.33, 4.7]	P=0.085
Fruit-eating in a typical week				
0-13 servings	118(98.3)	232(96.7)	1	
14 and above	2(1.7)	8(3.3)	0.49[0.1, 2.4]	p=0.37
Vegetables eating in a typical week				
0-13 servings	113(94.2)	219(91.2)	1	
14 and above	7(5.8)	21(8.8)	0.67[0.27, 1.6]	p=0.33
Coffee consumption per day				
None	26(21.7)	58(24.2)	1	
1-3 cups	88(73.3)	161(67.1)	0.52[0.2, 1. 3]	
> 3 cups	6(5.0)	21(8.8)	0.64[0.23, 1.8]	P=0.35
Tea consumption per day				
None	35(29.4)	67(27.9)	1	
1 cup	43(36.1)	101(42.1)	1.1[0.62, 1. 1]	
≥ 2 cups	41(34.5)	72(30.0)	1.3[0.79, 2.3]	P=0.5
Soft drink beverages consumption per week				
None	83(69.2.3)	187(77.9)	0.48[0.27, 0.85]	
1-2 bottles	28(23.3)	30(12.5)	0.71[0.25, 2.0]	
≥ 3 bottles	9(7.5)	23(9.6)	1	P=0.033

Others: Processed, fast foods, and fatty acid foods,

4.2.2.3.Occupational and Leisure Physical Activities(LPA) of Cases and Controls

A comparison of self-reported occupational activity engagement between cases and controls revealed that only 15(12.5%) of the cases and 79 (32.9%) of the controls engaged in vigorous-intensity occupational activity. Among those involved in vigorous-intensity occupational activity, the mean hours of engagement were 16.7 ± 8.2 hours per week for cases and 18.1 ± 7.3 hours per week for controls. Rural residents showed better engagement in vigorous-intensity occupational activity, with 6 (85.7%) cases and 48 (67.6%) controls compared to urban residents, where only 9(8.0%) cases and 31(18.3%) controls engaged in vigorous-intensity occupational activity (Figure 8). A higher proportion of men reported vigorous-intensity occupational activity, with 8 (13.3%) cases and 46 (38.3%) controls, compared to women, where 7 (11.7%) cases and 33 (27.5%) controls engaged in such activity, Table 8).

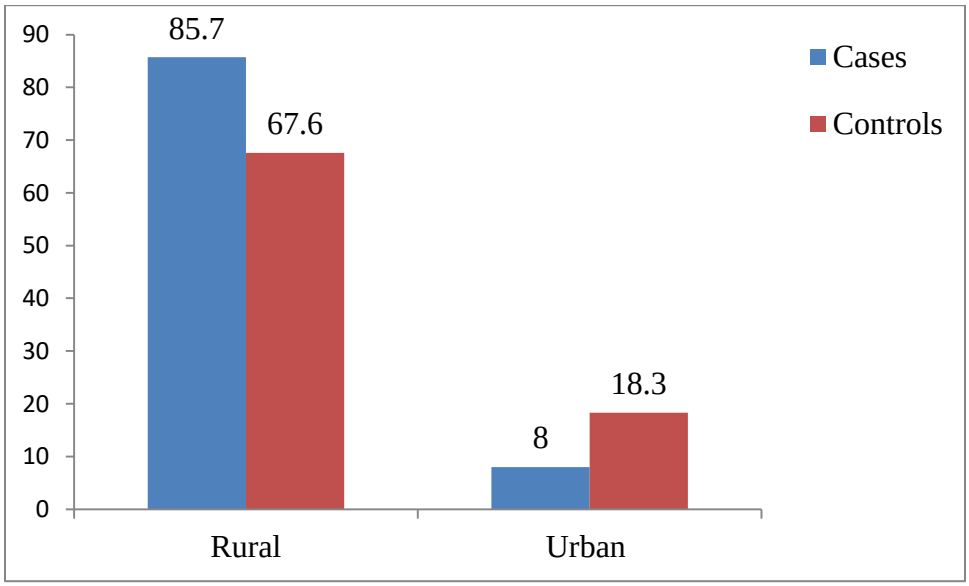

Figure 8: Percent of urban and rural residents' engagement in the vigorous-intensity occupational activity of cases and controls, Tigrai, Ethiopia, 2019(n= 360).

Forty-eight (40.0%) cases and 151 (62.9%) controls were involved in moderate-intensity occupational activity. The mean hours of engagement in moderate-intensity occupational activity were 22.5 ± 8.6 hours per week for cases and 24.5 ± 10.2 hours per week for controls. Rural residents showed better engagement in moderate-intensity occupational activity, with 5 (71.4%) cases and 61 (85.9%) controls compared to urban residents, where 43 (38.1%) of the cases and 90 (53.3%) of the controls were involved in moderate-intensity occupational activity. Similarly, a higher proportion of men reported moderate-intensity occupational activity, with 8 (13.3%) cases and 46 (38.3%) controls, compared to women, where 7 (11.7%) cases and 33 (27.5%) controls engaged in such activity, (Table 8).

Seventeen (14.2%) of the cases and 43 (17.9%) of the controls did not walk or use a bicycle (pedal cycle) for at least 10 minutes continuously to get to and from places. Five (4.9%) of the cases and 23 (11.7%) of the controls continuously walked or used a bicycle for at least 10 minutes to get to and from places seven days a week. Nineteen (16.0%) of the cases and 53 (22.1%) of the controls reported walking or using a bicycle for at least 150 minutes per week. Only 1 (0.8%) of the cases and 4 (1.7%) of the controls were engaged in walking or using a bicycle for 300 minutes or more in a typical week (Table 8).

Only 6(5.0%) of the cases and 18(7.5%) of the controls were involved in vigorous-intensity sports, fitness, or recreational (leisure) activities. Among the cases and controls who were engaged in vigorous-intensity sports, fitness, or leisure activities, 4(66.7%) of the cases and 15(83.3%) of the controls were involved for 75 minutes or more in vigorous-intensity sports, fitness, or leisure activities in a typical week. Of those cases and controls that involved vigorous-intensity sports, fitness, or leisure activities, only 2(33.3%) of the cases and 3(16.7%) of the controls engaged for 150 minutes per week. Only 8(6.7%) of the cases and 25(10.4%) controls were involved in moderate-intensity sports, fitness or leisure activities. Three (37.5%) of the cases and 4(16.7%) of the controls were engaged for 150 minutes or more in moderate-intensity sports, fitness, or leisure activities in a typical week (Table 8).

Sixty-one (50.8%) of the cases and 64(26.7%) of the controls had low physical activity, and 48(40.0%) of the cases and 152(63.3) of the controls had high physical activity. Six(85.7%) of the cases and 61(85.9%) of the controls of rural residents were highly active, while only 42(37.2%) and 91(53.8%) of the controls of urban residents were highly active. Thirty-three (55.0%) of the cases and 27(22.5%) of the controls among men, and 28(46.7%) of the cases and 37(30.8%) of the controls among women had low PA. Only 9(7.5%) cases and 33(13.7%) controls were engaged in moderate-vigorous leisure physical activity. Regarding the sedentary behavior of the cases and controls, 63(52.5%) of the cases and 88(37.1%) of the controls spent 6 hours or more in sedentary activities (Table 8).

Table 8: Occupational and LPA of cases and Controls at ACSH, Tigrai, Ethiopia, 2019(n= 360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	COR[95%CI], t(df)	P-value
Vigorous-intensity of occupational PA				
Yes	15(12.5)	79(32.9)	0.3[0.2, 0.5]	
No	107(87.5)	161(67.1)	1	P< 0.001
Moderate-intensity of occupational PA				
Yes	48(40.0)	151(62.9)	0.4[0.3, 0.6]	
No	72(60.0)	89(37.1)	1	P< 0.001
Walk or use a bicycle (pedal cycle) for at least 10 minutes continuously				
Yes	103(85.8)	197(82.1)	1.3[0.7, 2.4]	
No	17(14.2)	43(17.1)	1	P<=0.35
Vigorous-intensity sports, fitness/LPA				
Yes	6(5.0)	18(7.5)	0.7[0.3, 1.7]	
No	114(95.0)	222(92.5)	1	P=0.37
Moderate-intensity sports, fitness/LPA				
Yes	8(6.7)	25(10.4)	0.6[0.3, 1.4]	
No	112(93.3)	215(89.6)	1	P=0.25
Physical activity (%)				
Low	61(50.8)	64(26.7)	3.0[1.9, 4.9]	
Medium	11(9.2)	24(10.0)	1.5[0.7, 3.2]	
High	48(40.0)	152(63.3)	1	P<0.001
Leisure MVPA				
None	111(92.5)	207(86.3)	2.0[0.9, 4.3]	
Yes	9(7.5)	33(13.7)	1	P=0.086
Sedentary behavior				
< 4 hours/day	10(8.3)	55(23.2)	1	
4 to 6 hours/day	47(39.2)	94(39.7)	1.4[0.9, 2.3]	
> 6 hours	63(52.5)	88(37.1)	3.9[1.9, 8.3]	P=0.001

4.2.3. Physical and Biomarkers Characteristics of Cases and Controls

Fifty-seven (47.5%) of the cases and 76(31.5%) of the controls were overweight, and 36(30.0%) of the cases and 32(13.3%) of the controls were obese. For cases and controls, 94(78.3%) of the cases and 98(40.8%) controls had high waist circumference. Ninety-one (75.8%) of the cases and 136(56.7%) of the controls had high WHR, and also 107(89.2%) of the cases and 131(54.6%) of the controls had high WHtR (Table 9).

Fifty-four (45.0%) cases and 60(25.0%) controls had a raised total cholesterol. Thirty-four (28.3%) of the cases and 42(17.5%) of the controls had Men/women < 40/50 mg/dL HDL-C. Fority one (34.2%) of the cases and 44(18.3%) of the controls had raised raised LDL-C. Moreover, elevated triglyceride was also detected in 73(60.8%) cases and 117(48.8%) controls. Fifty-two (43.3%) of the cases and 52(21.7%) of the controls had raised SBP, and 41(34.2%) of cases and 43(17.9%) controls had elevated DBP. Sixty-eight (56.7%) of the cases and 70(29.2%) of the controls had hypertension. Fifty-eight (48.3%) of the cases and 60(25.0%) of the controls had dyslipidemia (Table 9).

Table 9: Physical and biomarker characteristics of Cases and Controls at ACSH, Tigrai, 2019(n= 360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	COR[95%CI], t(df)	P-value
FPG(IQR): Un categorized	55(98-153)	12(84-96)		
BMI				
Normal	27(22.5)	132(55.0)	1	
Overweight	57(47.5)	76(31.7)	3.7[2.1, 6.3]	p< 0.001
Obese	36(30.0)	32(13.3)	5.5[2.9, 10.3]	
Waist Circumference				
Men/women < 94/80	26(21.7)	142(59.2)	1	
Men/women ≥ 94/80	94(78.3)	98(40.8)	5.2[3.2, 8.7]	p< 0.001
WHR				
Men/women < 0.88/0.82	29(24.2)	104(43.3)	1	
Men/women ≥ 0.88/0.82	91(75.8)	136(56.7)	2.4[1.5, 3.9]	p< 0.001
WHtR				
Men/women < 0.49/0.50	13(10.8)	109(45.4)	1	
Men/women ≥ 0.49/0.50	107(89.2)	131(54.6)	6.8[3.7, 12.9]	p< 0.001
Total cholestrol				
< 200 mg/dl	66(55.0)	180(75.0)	1	P<0.001
≥ 200 mg/dl	54(45.0)	60(25.0)	2.5[1.5, 3.9]	
HDL-C				
Men/women ≥ 40/50 mg/dl	86(71.7)	198(82.5)	1	P=0.019
Men/women < 40/50 mg/dl	34(28.3)	42(17.5)	1.9[1.1, 3.1]	
LDL-C				
< 130 mg/dl	79(65.8)	196(81.7)	1	
≥ 130 mg/dl	41(34.2)	44(18.3)	2.3[1.4, 3.8]	p= 0.001
Triglycerides				
< 150 mg/dl	47(39.2)	123(51.2)	1	
≥ 150 mg/dl	73(60.8)	117(48.8)	1.6[1.1, 2.6]	P=0.031
SBP				
< 130 mmHg	43(35.8)	145(60.4)	1	
130 to 139 mmHg	25(20.8)	43(17.9)	1.7[0.92, 3.2]	
≥ 140 mmHg	52(43.3)	52(21.7)	3.4[2.0, 5.6]	p< 0.001
DBP				
< 85 mmHg	54(45.0)	165(68.8)	1	
85 to 89 mmHg	25(20.8)	32(13.3)	1.2[0.62, 2.4]	
≥ 90 mmHg	41(34.2)	43(17.9)	2.9[1.7, 4.9]	p< 0.001
Hypertension				
No	52(43.3)	170(70.8)	1	
Yes	68(56.7)	70(29.2)	3.2[2.0, 5.0]	p< 0.001
Dyslipidemia				
No	62(51.7)	180(75.0)	1	
Yes	58(48.3)	60(25.0)	2.8[1.8, 4.8]	p< 0.001

4.2.4. Potential risks of T2D Binary logistic regression adjusted odds ratio

According to the results of multivariable logistic regression (Table 10), several factors were significantly associated with increased odds of T2D. These include urban residence, widowhood or divorce status, FHD, hypertension, dyslipidemia, consumption of white rice, alcohol consumption, elevated waist circumference (WC), and high WHtR. Conversely, engagement in MVPA during leisure was found to be protective against T2D.

The odds of developing T2D were more than fivefold higher among urban residents than rural dwellers [AOR=5.1, 95%CI (2.0, 13.2)]. Likewise, those being divorced and widowhood were nearly three times and more than three times more likely to have T2D compared to their married counterparts [AOR=2.8, 95%CI (1.1, 7.3)] and [AOR=3.3, 95%CI (1.3, 8.6)], respectively (Table 10).

The odds of having T2D among participants who had hypertension were 3.0 times higher than those who did not have hypertension [AOR=**3.0,** 95%CI **(**1.7, 5.5)**]**. Besides, the chances of developing T2D among those with dyslipidemia were almost three times higher than those without dyslipidemia [AOR=2.8, 95%CI (1.5, 5.4)]. Similarly, those who had a family history of diabetes experienced more than fivefold higher odds of developing T2D than those who did not have the same history [AOR=5.4, 95%CI (2.4, 12.5)] (Table 10).

The risk of developing T2D was threefold higher among those who consumed 5 to 6 days in a typical week and 3.5 times higher in those who drank alcohol every day compared to non-drinkers [AOR=3.0, 95%CI (1.1, 3.6)] and [AOR=3.5, 95%CI (1.2, 10.2)], respectively. The odds of developing T2D were 3.8 times higher in those who used white rice as their favorite diet than those who ate injera made of teff/barely/sorghum[AOR=3.8,95%CI (1.2, 11.6)].

The risk of T2D among those with elevated waist circumferences was almost twice as high as those with a normal waist circumference [AOR= 2.4, 95%CI (1.1, 5.0)]. Likewise, the odds of developing T2D among those with an elevated WHtR was 4.4 times higher than those with a normal WHtR [AOR=4.4, 95%CI (1.7, 11.2)]. Leisure MVPA was associated with lower odds of T2D compared to those who did not in leisure MVPA[AOR= 0.27,95%CI(0.1, 0.72)] (Table-10).

Table 10: Potential risk factors of T2D at ACSH, Tigrai, Ethiopia, 2019(n= 360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	AOR[95% CI],	p-value
Residence, n (%)				
Rural	7(5.8)	71(29.6)	1	
Urban	113(94.2)	169(70.4)	5.1[2.0, 13.2]	p= 0.001
Marital status, n(%)				
Married	87(72.5)	201(83.8)	1	
Divorced/separated	14(11.7)	21(8.8)	2.8[1.1, 7.3]	
Widowed	19(15.8)	18(7.5)	3.3[1.3, 8.6]	P=0.008
Hypertension				
No	52(43.3)	170(70.8)	1	
Yes	68(56.7)	70(29.2)	3.0[1.7, 5.5]	p< 0.001
Dyslipidemia				
No	62(51.7)	180(75.0)	1	
Yes	58(48.3)	60(25.0)	2.8[1.5, 5.4]	p=0.002
Family History of Diabetes				
No	92(76.7)	221(92.1)	1	
Yes	28(23.3)	19(7.9)	5.4[2.4, 12.5]	P< 0.001
Cigarette smoking status				
Never smoker	105(87.5)	222(92.5)	1	
Ex—-smoker	5(4.2)	9(3.8)	1.5[0.3, 6.3]	
Current smoker	10(8.3)	9(3.8)	3.4[0.82, 13.9]	P= 0.22
Frequency of alcohol intake per week				
Non-drinker	21(17.5)	51(21.3)	1	
Less than once per week	3(2.5)	17(7.1)	0.2[0.1,1.1]	
1-4 days per week	65(54.2)	147(61.3)	1.1[0.5, 2.1]	
5 -6 days per week	22(18.3)	18(7.5)	3.0[1.1, 3.6]	P=0.012
Every day	9(7.5)	7(2.9)	3.5[1.2, 10.2]	
Most favorite and regularly used food				
Injera of teff/barely/sorghum	72(60.0)	174(72.5)	1	
Bread/injera made from wheat	24(20.0)	33(13,8)	1.7[0.8, 4.0]	
White rice	12(10.0)	11(4.6)	3.8[1.2, 11.6]	
Pasta	9(7.5)	13(5.4)	1.3[0.4, 4.7]	
Others	3(2.5)	9(3.8)	0.3[0.1, 1.6]	P=0.059
Waist Circumference				
Men/women < 94/80	26(21.7)	142(59.2)	1	
Men/women ≥ 94/80	94(78.3)	98(40.8)	2.4[1.1, 5.0]	P= 0.027
WHtR				
Men/women < 0.49/0.50	13(10.8)	109(45.4)	1	
Men/women ≥ 0.49/0.50	107(89.2)	131(55.6)	4.4[1.7, 11.2]	p=0.002
Engagement in leisure MVPA				
None	111(92.5)	207(86.3)	1	
Yes	9(7.5)	33(13.7)	0.27[0.1, 0.72]	P=0.009

4.3. Hyperglycemic Crisis

Among the 1082 admissions related to hyperglycemic crises, only 589 (54.4%) met the inclusion criteria for DKA or HHS. Among these patients, 196 (33.3%) had no prior history of diabetes, while 393 (66.7%) had a known history of diabetes and were included in the study (Figure 3).

4.3.1. Characteristics of Hyperglycemic crisis(DKA and HHS)

The mean age of patients experiencing hyperglycemic crises was 47.3±14.9 years, with those diagnosed with DKA having a mean age of 42.9±13.6 years and those with HHS averaging 59.3±11.2 years. Middle-aged patients (45 to 64 years) comprised 193 (44.6%) of DKA cases and 103(66.0%) of HHS cases, while 6% of DKA patients and 27.6% of HHS patients were aged 65 years or older. Nearly 60% of both DKA and HHS patients were men. Among them, 181 (41.8%) DKA patients and 42 (26.9%) HHS patients resided in rural areas (Table 11).

Fatigue was reported in 414 (95.6%) DKA patients and 139 (89.1%) HHS patients. Among those with a medical history, 60 (80.0%) DKA patients and 90 (90.9%) HHS patients had a history of cardiovascular disease (CVD). Infection precipitated hyperglycemic crises in 105 (24.2%) DKA patients and 65 (41.7%) HHS patients, 163 (37.6%) DKA patients, and 33 (21.2%) HHS patients who were newly diagnosed with diabetes (Table 11).

Among the hyperglycemic crisis cases, 301 (69.5%) of DKA patients had type 1 diabetes, while 154 (98.7%) of HHS patients had T2D. The median (IQR) Glasgow Coma Scale scores were 12 (9, 15) for DKA and 9 (7, 11) for HHS. Additionally, DKA patients had a mean baseline urine ketone level of 2.84±0.7, compared to 0.79±0.65 for HHS patients (Table 11).

The median (IQR) hospital stay for DKA and HHS patients was 7 (6, 13) days and 7 (7, 14) days, respectively. The in-hospital death was 8.1% (35 patients) for DKA and 27.6% (43 patients) for HHS (Table 11).

.

Table 11: Characteristics of DKA and HHS among adults, Tigrai, Ethiopia, 2019(n= 589).

Patient characteristics	DKA (n, %)	HHS(n, %)	Total (%)
Age in years (Mean ±SD)	42.9(±13.6)	59.3(±11.2)	47.3(±14.9)
Age in years(%)			
18 to 44 years	214(49.4)	10(6.4)	224(38.0)
45 to 64	193(44.6)	103(66.0)	296(50.3)
≥ 65 years	26(6.0)	43(27.6)	69(11.7)
Sex			
Male	261(60.3)	95(60.9)	356(60.4)
Female	172(39.7)	61(39.1)	233(39.6)
Residence			
Urban	252(58.2)	114(73.1)	366(62.1)
Rural	181(41.8)	42(26.9)	223(37.9)
Symptoms on diagnosis (yes,%)			
Vomiting	271(62.6)	8(5.1)	279(47.4)
Abdominal pain	99(22.9)	2(1.3)	101(17.1)
Excessive urination	326(75.3)	54(34.6)	380(64.5)
Excessive thirsty	351(81.1)	107(68.6)	458(77.8)
Fruit odor	377(87.1)	32(20.5)	409(69.4)
Weight loss	360(83.1)	48(30.8)	408(69.3)
Fatigue	414(95.6)	139(89.1)	553(93.9)
Medical history (yes, %)			
CKD	10(13.3)	35(35.4)	45(25.9)
DFS	6(8.0)	19(19.2)	25(14.4)
CVD	60(80.0)	90(90.9)	150(86.2)
Stroke	12(16.0)	48 (48.5)	60(34.5)
Pancreatitis	12(13.3)	10(12.1)	22(12,6)
Precipitating factors of HC			
Infection	105(24.2)	65(41.7)	170(28.9)
Noncompliance to treatment	135(31.2)	15(9.6)	150(25.5)
New onset of diabetes	163(37.6)	33(21.2)	196(33.3)
Recurrent illness	30(6.9)	43(27.6)	73(12.4)
Types of patient			
With prior diabetes history	270(62.4)	123(78.8)	393(66.7)
Without prior diabetes history	163(37.6)	33(21.2)	196(33.3)
Diabetes type			
Type 1 diabetes	301(69.5)	2(1.3)	303(51.4)
Type 2 diabetes	132(30.5)	154(98.7)	286(48.6)
Glasgow Coma Scale in Median (IQR)	3(12, 15)	2(9, 11)	4(11,15)
Urine Ketones: Uncategorized (Mean ±SD)	2.84±0.7	0.79±0.65	2.3±1.13
Hospital Stay in Days in Median (IQR)	7(6,13)	7(7, 14)	7(6, 13)
Treatment outcome			
Discharge home	398(91.9)	113(72.4)	511(86.8)
In-hospital death	35(8.1)	43(27.6)	78(13.2)

4.3.2. Characteristics of patients with and without a prior diabetes diagnosis

The distribution of sociodemographic and clinical characteristics varied significantly between patients with and without a prior history of diabetes. Patients without prior diabetes were younger on average compared to those with diabetes history (mean age 43.9±12.6 vs. 48.4±14.8 years; $p<0.001$) and were less likely to be elderly (3.6% vs. 15.8%; $p<0.001$). They also resided more frequently in rural areas (53.1% vs. 30.3%; $p<0.001$) compared to those with a diabetes history (Table 12).

Regarding clinical features during hyperglycemic crises, patients without prior diabetes exhibited a higher proportion of classic symptoms such as vomiting (69.4% vs. 36.4%; $p<0.001$), polyuria (75.5% vs. 59.0%; $p<0.001$), polydipsia (83.7% vs. 74.8%; $p=0.015$), fruity breath odor (84.2% vs. 72.3%; $p=0.001$), and weight loss (79.6% vs. 64.1%; $p<0.001$). Conversely, patients with a prior diabetes history had a higher prevalence of comorbidities, including Chronic Kidney Disease (10.7% vs. 1.5%; $p<0.001$), Cardiovascular diseases (31.3% vs. 13.8%; $p<0.001$), and stroke (12.5% vs. 5.6%; $p=0.014$), (Table 12).

Patients with a prior diabetes history also showed higher rates of type 2 diabetes (53.7% vs. 38.3%; $p<0.001$), hyperosmolar hyperglycemic state (31.8% vs. 15.8%; $p<0.001$), and in-hospital death (15.5% vs. 8.7%; $p=0.02$) compared to those without prior diabetes. Additionally, patients with prior diabetes had a higher median baseline blood pressure and a lower mean baseline urine ketone level (2.1±1.1 vs. 2.7±1.1 mg/dl; $p<0.001$) compared to patients without diabetes history (Table 12).

Table 12: Comparison of clinical characteristics of adult patients with a hyperglycemic crisis without and with a history of diabetes in a resource-poor community:

Clinical characteristics	Diabetes history		p-value
	No (n= 196)	Yes (n= 393)	
Age in years (Mean ± SD)	43.9±12.6	48.4±14.9	p<0.001*
Elderly, aged ≥65 years (%)	7(3.6)	62(15.8)	p<0.001*
Gender, Men (%)	118(60.2)	238(60.6)	1.00
Residence (%)			
Urban	92(46.9)	274(69.7)	
Rural	104(53.1)	119(30.3)	p<0.001*
Clinical feature; yes (%)			
Vomiting	136(69.4)	143(36.4)	p<0.001*
Abdominal pain	47(24.0)	54(13.7)	0.002*
Polyuria	148(75.5)	232(59.0)	p<0.001*
Polydipsia	159(81.1)	294(74.8)	0.015*
Fruit breath odor	165(84.2)	284(72.3)	0.001*
Fatigue	181(92.3)	372(94.7)	0.3
Weight loss	156(79.6)	252(64.1)	P<0.001*
Medical history, yes(%)			
CKD	3(1.5)	42(10.7)	p<0.001*
DFS	1(0.5)	24(6.1)	0.003*
CVD	27(13.8)	123(31.3)	p<0.001*
Stroke	11(5.6)	49 (12.5)	0.014*
Pancreatitis	12(6.1)	10(2.5)	0.054
Type of DM (%)			
Type 1 DM	121(61.7)	182(46.3)	
Type 2 DM	75(38.3)	211(53.7)	0.001*

CVD: Cardiovascular Diseases, CKD: Chronic Kidney Disease, DFS: Diabetes Foot Syndrome, DBP: Diastolic Blood Pressure, GCS: Glasgow Coma Scale**,** IQR: Inter Quartile Range, RBS: Random Blood Sugar, SBP: Systolic Blood Pressure, SD: Standard Deviation; *: Statistically significant.

Table 13 (Continued).

Clinical characteristics	Prior diabetes history		p-value
	No (n= 196)	Yes (n= 393)	
Type of hyperglycemic crisis (%)			
DKA	165(84.2)	268(68.2)	
HHS	31(15.8)	125(31.8)	P<0.001*
In-hospital mortality (%)	17(8.7)	61(15.5)	0.03*
SBP in mmHg in Median (IQR)	90(70; 100)	90(80; 150)	0.02*
DBP in mmHg in Median (IQR)	60(50; 70)	60(50; 100)	0.01*
Body Temperature (℃) (Mean ± SD)	36.8± 0.8	37.3± 1.04	P<0.001*
Respiratory rate(Mean ± SD)	23.4 ± 2.0	22.07 ± 2.4	p<0.001*
Pulse rate (Mean ± SD)	100.2 ± 7.3	98.1± 7.0	0.001*
GCS in Median (IQR)	14(11, 14)	12(11;14)	0.002*
RBS in mg/dl (Median (IQR))	538.5(499, 591)	517(472; 600)	0.032*
Urine ketones (Mean ± SD)	2.7± 1.1	2.1± 1.1	P<0.001*
Length of hospital stay (days) Median (IQR)	9(7; 13)	9(6; 13)	0.4

CVD: Cardiovascular Diseases, CKD: Chronic Kidney Disease, DFS: Diabetes Foot Syndrome, DBP: Diastolic Blood Pressure, GCS: Glasgow Coma Scale**,** IQR: Inter Quartile Range, RBS: Random Blood Sugar, SBP: Systolic Blood Pressure, SD: Standard Deviation; *: Statistically significant.

A higher proportion of in-hospital mortality was observed in rural residents compared to urban residents for both patients with (21.8% vs. 12.8%; p=0.03) and without (13.5% vs. 3.3%; p=0.023) prior history of diabetes (Table 13).

In patients with prior diabetes history, higher in-hospital mortality was observed in patients who did not present with polyuria (21.1% vs. 11.6%; p=0.016), polydipsia (23.2% vs. 12.9%; p=0.022), fruity breath odor (26.6% vs. 11.3%; p<0.001), and weight loss (22.0% vs. 11.9%; p=0.012) compared to those who had these symptoms on admission. Patients with No Prior Diabetes History: Higher in-hospital mortality was observed in patients who did not have a fruity breath odor on admission (25.8% vs. 5.5%; p=0.001) compared to those who did. In both groups (with and without prior diabetes history), higher in-hospital mortality was observed in patients with a medical history of Chronic Kidney Disease, Cardiovascular diseases, and stroke compared to those without such history (Table 13).

Type 2 vs. Type 1 Diabetes: In patients without a history of diabetes, in-hospital mortality was higher in Type 2 diabetes patients compared to Type 1 (16.0% vs. 4.1%; p=0.009). Similarly, in patients with a history of diabetes, in-hospital mortality was higher in Type 2 diabetes patients compared to Type 1 (22.3% vs. 7.7%; p<0.001) (Table 13).

Patients with HHS had a higher proportion of in-hospital mortality compared to patients with DKA in both groups without a history of diabetes (29.0% vs. 4.8%; p<0.001) and with a history of diabetes (27.2% vs. 10.1%; p<0.001). Lower mean baseline urine ketones were associated with higher in-hospital mortality in both groups: without diabetes history (1.9±1.3 vs. 2.8±1.1; p=0.008) and with diabetes history (1.64±1.2 vs. 2.2±1.04; p=0.002). Among patients with a prior diabetes history, higher median baseline blood pressure (p<0.01) and random blood sugar (RBS) readings in mg/dl (p=0.003) were significantly associated with higher in-hospital mortality (Table 13).

Table 13: Comparison of participant characteristics and clinical outcomes of adult patients with a hyperglycemic crisis without and with a history of diabetes in Tigrai, Ethiopia:

Clinical characteristics	With no diabetes history (%)		P-value	With a diabetes history (%)		p-value
	In-hospital Death (n= 17)	Discharge home (n= 179)		In-hospital Death (n= 61)	Discharge home (n= 332)	
Age in years(Mean ± SD)	46.9±14.8	43.6±12.3	0.4	51.8±14.6	47.7±14.7	0.047*
Gender, Men(%)	10(8.5)	108(91.5)	0.9	38(16.0)	200(84.0)	0.9
Residence						
Urban	3(3.3)	89(96.7)		35(12.8)	239(87.2)	
Rural	14(13.5)	90(86.5)	0.023*	26(21.8)	93(78.2)	0.03*
Clinical presentations						
Vomiting	11(8.1)	125(91.9)	0.9	16(11.2)	127(88.8)	0.07
Abdominal pain	2(4.3)	45(95.8)	0.4	4(7.4)	50(92.6)	0.1
Polyuria	11(7.4)	137(92.6)	0.4	27(11.6)	205(88.4)	0.016*
Polydipsia	8(5.0)	151(95.5)	0.001*	38(12.9)	256(87.1)	0.02*
Fruit breath odor	9(5.5)	156(94.5)	0.001*	32(11.3)	252(88.7)	p<0.001*
Fatigue	16(8.8)	165(91.2)	1.00	58(15.6)	314(84.4)	1.00
Weight loss	14(9.0)	142(91.0)	1.00	30(11.9)	222(88.1)	0.012 *
Medical history						
CKD	2(66.7)	1(33.3)	0.02*	13(31.0)	29(69.0)	0.007*
DFS	0(0.0)	1(100.0)	1.00	6(25.0)	18(75.0)	0.2
CVD	6(22.2)	21(77.8)	0.017*	31(25.2)	92(74.8)	0.001*
Stroke	4(36.4)	7(63.6)	0.009*	17(37.4)	32(65.3)	p<0.001*
Pancreatitis	2(16.7)	10(83.3)	0.3	3(30.0	7(70.0)	0.4
Type of diabetes (%)						
Type 1 DM	5(4.1)	116(95.9)	0.009*	14(7.7)	168(92.3)	
Type 2 DM	12(16.0)	63(84.0)		47(22.3)	164(77.7)	<0.001*
Hyperglycemic crisis (%)						
DKA	8(4.8)	157(95.2)	p<0.001	27(10.1)	241(89.9)	
HHS	9(29.0)	22(71.0)		34(27.2)	91(72.8)	p<0.001*
Length of hospital stay (days) in Median (IQR)	13(8; 16)	9(7;12)	0.07	8.5(6;12)	9(6;13)	0.5

CVD: Cardiovascular Diseases, CKD: Chronic Kidney Disease, DFS: Diabetes Foot Syndrome, DBP: Diastolic Blood Pressure, GCS: Glasgow Coma Scale**,** IQR: Inter Quartile Range, RBS: Random Blood Sugar, SBP: Systolic Blood Pressure, SD: Standard Deviation; *: Statistically significant

Table 14 (Continued).

Clinical characteristics	With no diabetes history (%)		P-value	With a diabetes history (%)		P-value
	In-hospital death (n= 17)	Discharge home (n= 179)		In-hospital death (n= 17)	Discharge home (n= 179)	
SBP (Median (IQR))	90(70; 90)	90(70; 100)	0.4	110(82.5;160)	90(74;120)	0.001*
DBP (Median (IQR))	60(50; 60)	60(50, 70)	0.6	80(60;100)	60(50;80)	0.006*
BT (°C) (Mean ± SD)	36.9± 0.9	36.8± 0.9	0.8	37.3± 1.0	37.3± 1.0	0.6
RR(Mean ± SD)	23.4± 2.5	23.4±2.0	0.9	21.2± 2.7	22.3± 2.3	0.004*
PR (Mean ± SD)	101.7± 8.9	100.1±7.2	0.5	96.7± 6.7	98.4±7.0	0.09
GCS in Median (IQR)	12(9; 15)	14(11;15)	0.2	12(10;14)	13(11;14)	0.2
RBS (Median (IQR))	578(498;600)	538(498,585)	0.3	600(471.5;600)	512(470;600)	0.003*
Urine ketones (Mean ± SD)	1.9± 1.3	2.8± 1.1	0.008*	1.6± 1.2	2.2± 1.0	0.002*

CVD: Cardiovascular Diseases, CKD: Chronic Kidney Disease, DFS: Diabetes Foot Syndrome, DBP: Diastolic Blood Pressure, GCS: Glasgow Coma Scale**,** IQR: Inter Quartile Range, RBS: Random Blood Sugar, SBP: Systolic Blood Pressure, SD: Standard Deviation; *: Statistically significant

On the multivariable logistic regression model (Table 15), independent predictors of in-hospital mortality were rural residents [AOR=3.1, 95% CI 1.8, 5.4], patients with a medical history of stroke [AOR=2.7, 95% CI 1.3, 5.6], type 2 diabetes [AOR=2.3, 95% CI (1.1, 4.7)], hyperosmolar hyperglycemic state [AOR=2.4, 95% CI (1.1, 5.4)], and patients with a prior diabetes history[AOR=2.0, 95% (CI 1.04, 3.8)]; while presentation with polydipsia on admission was preventive [AOR= 0.47, 95% CI 0.27, 0.81]; (Table 14).

Table 14: Potential risks of hyperglycemic crisis-related mortality among patients without and with a history of diabetes in a resource-poor community in Tigrai, Ethiopia:

Clinical characteristics	Outcomes of care (%)		COR(95 % CI)	AOR(95 % CI)
	In-hospital mortality (n= 17)	Discharge home (n= 179)		
Residence				
Urban	38(10.4)	328(89.6)	1	1
Rural	40(17.9)	183(82.1)	1.9[1.2, 3.1]	3.1[1.8, 5.4]*
Stroke				
Yes	21(35.0)	39(65.0)	4.6[2.5, 8.1]	2.7[1.3, 5.6]*
No	57(10.8)	472(89.2)	1	1
Vomiting				
Yes	27(9.7)	252(90.3)	0.5(0.33, 0.90)	1.5(0.74, 3.13)
No	51(16.5)	259(83.5)	1	1
Excessive thirst				
Yes	46(10.2)	407(89.8)	0.37(0.22, 0.61)	0.47(0.27, 0.81)*
No	32(23.5)	104(76.5)	1	1
Type of DM				
T1D	19(6.3)	284(93.7)	1	1
T2D	59(20.6)	227(79.4)	3.9(2.25, 6.7)	2.3(1.1, 4.7)*
Type of hyperglycemic crisis				
DKA	35(8.1)	398(91.9)	1	1
HHS	43(27.6)	113(72.4)	4.3(2.6, 7.1)	2.4(1.1, 5.4)*
Type of patient				
With a prior known DM	61(15.5)	332(91.9)	1.94(1.1, 3.4)	2.0(1.04, 3.8)*
With no prior DM diagnosis	17(8.7)	179(91.3)	1	1

T1D: Type 1 diabetes, T2D: Type 2 diabetes, *: Statistically significant,

4.4. Summary of the main findings of the dissertation

In this section, the main findings from the three manuscripts are outlined & reviewed.

Table 15: Summary of main findings from the three manuscripts

S.N	Objectives	Major findings
1	To determine the trend in the proportion of type 1 and type 2 diabetes among adults who received medical care from selected public hospitals in Tigrai, Ethiopia.	• Two hundred ninety-nine thousand eight hundred six adult patients received medical care from adult medical OPD and emergency units in the five years (September 1, 2013 to August 31, 2018). • Out of these patients, 10.2(95%CI: 9.8-10.6) per 1000 adult patients were confirmed as diabetes patients from September 1, 2013 to August 31, 2018. • The overall proportion of diabetes increased significantly from 6.8(95%CI: 6.1-7.5) to 14.3(95%CI: 13.3-15.1) per 1000 adult patients over the study period. • The time trend in the proportion of diabetes increased for both urban from 7.9(95%CI: 6.9-8.9) to 15.9(14.6-17.2) per 1000 adult urban residents, (p_{trend}<0.001) and rural from 5.2(95%CI: 4.4-6.2) to 12.1(95%CI: 10.9-13.5) per 1000 adult rural residents, (p_{trend}<0.001) in the observation. • The five-year proportion of T1D was 1.6(95% CI: 1.5-1.8) per 1000 patients, with a statistically significant increase ((p_{trend}<0.001)) for a linear trend. The trend of type 1 diabetes increased for both urban areas from 1.0 to 2.2 per 1000 adult urban residents (Ptrend=0.002) and rural areas from 1.2 to 2.6 per 1000 adult rural residents (P_{trend}=0.001). • The five-year trend of T2D increased from 5.7(95%CI: 5.1-6.3) to 12.0(95%CI: 11.0-13.0) per 1000 adult patients (P_{trend}<0.001), with urban urban from 6.9 to 14.0 per 1000 adult urban residents, (P_{trend}=0.001) and rural from 4.0 to 9.5 per 1000 adult rural residents, (P_{trend}=0.001). • Notably, a higher increase for T1D and T2D was observed among women patients.

2	To assess the risk factors associated with T2D among middle-aged adults who received medical care	The mean (SD) ages of cases and controls were 55.9(±5.0) and 55.7(±4.8) years old, respectively. **The odds of T2D was significantly higher among**: • urban residents (AOR=5.1, 95%CI ([2.0, 13.2]), • widowhood(AOR=3.3, 95%CI ([1.3, 8.6]) and divorced(AOR=2.8, 95%CI([1.1,7.3]), • hypertension (AOR=3.0, 95%CI ([1.7,5.5]), • dyslipidemia(AOR=2.8, 95%CI ([1.5, 5.4]), • positive family history of diabetes(AOR=5.4, 95%CI ([2.4, 12.5]), • consuming alcohol 5 to 6 days in a week(AOR=3.0, 95%CI ([1.1, 3.6]), • consumed alcohol every day(AOR=3.5, 95%CI ([1.2,10.2]), • consuming white rice as favorite food(AOR=3.8,95%CI([1.2,11.6]), • elevated waist circumference(AOR= 2.4, 95%CI ([1.1, 5.0]), • elevated WHtR(AOR=4.4, 95%CI([1.7, 11.2]), **The odds of T2D reduced among people:** • Engaged in leisure MVPA(AOR= 0.27, 95%CI ([0.1, 0.72]) were preventive
3	To compare hyperglycemic crisis characteristics and care outcomes among adult patients with and without a history of diabetes from selected public hospitals in Tigrai.	• The mean age of patients with DKA and HHS was 42.9(±13.6) and 59.3(±11.2) years, respectively. • About 42% of patients with DKA and 27% with HHS were rural residents. • Infection was found in 24.2% of DKA and 42% of HHS patients, and 163(37.6%) DKA and 33(21.2%) of HHS patients were newly diagnosed diabetes patients. • The overall mortality was 78(13.2%), of which 43(7.3%) deaths were in patients with HHS. In comparison, the remaining (5.9%) was due to DKA, and mortality was higher in the rural residents (17.9%) compared to their urban counterparts (10.4%).

		• Compared to patients with a prior diabetes history; patients no prior diabetes history were more younger with ≥ 65 years(3.6% Vs. 15.8%; p< 0.001) ✓ Patients with no prior diabetes history were more rural residents (53.1% Vs. 30.3%, P< 0.001), ✓ had more significant signs and symptoms of diabetes, ▪ better consciousness, higher median RBS (538.5 Vs. 517, p= 0.032), higher urine ketones (3 Vs. 2, p<0.001), the lower mortality rate (8.7% Vs. 15.5%, p= 0.015) ✓ had a higher mortality rate in rural residents(7.1% Vs. 1.6%, p= 0.01), T2D (6.6% Vs. 2.1%, P<0.001), and HHS(4.6% Vs. 4.1%) with lower urine ketones(2 Vs. 3; p=0.002) compared to urban residents, type 1 diabetes and diabetic ketoacidosis, respectively. **The odds of in-hospital mortality was significantly higher among**: ✓ rural residents [AOR=3.1, 95% CI 1.8, 5.4], ✓ patients with a medical history of stroke [AOR=2.7, 95% CI 1.3, 5.6], ✓ type 2 diabetes [AOR=2.3, 95% CI (1.1, 4.7)], ✓ hyperosmolar hyperglycemic state [AOR=2.4, 95% CI (1.1, 5.4)], and ✓ patients with a prior diabetes history[AOR=2.0, 95% (CI 1.04, 3.8)]; ✓ while presentation with excessive thirst on admission was preventive [AOR= 0.47, 95% CI 0.27, 0.81];

5. Discussion

The current study attempts to determine the trends of type 1 and 2 diabetes, factors associated with T2D, and treatment outcomes of hyperglycemic patients among hospital-treated adult patients (aged ≥ 18 years) in selected public hospitals in Tigrai. For more details, see the discussion section, which is organized into sections and papers below as follows:

5.1. Trend of Type 1 and Type 2 diabetes

The findings of this study revealed that diabetes affected 10.2 per 1000 adult patients, with 11.6 per 1000 urban residents and 8.6 per 1000 rural residents. Over time, there was a consistent rise in adult diabetes proportion in both urban and rural areas, encompassing both type 1 and type 2 diabetes and affecting both men and women patients. Particularly noteworthy was the increasing trend among women during the observation period.

The study's findings indicate a significant increase, more than doubling, in the proportion of adult diabetes over the past five years, aligning with findings from prior research(31,41,86,216). This alarming trend suggests potential influences from rapid epidemiological, economic, and societal shifts, childhood nutritional stunting(40), chronic undernutrition, and enhancements in diabetes detection and recording mechanisms(114,217). However, the findings of this study are inconsistent with findings from high-income countries, and diabetes is declining(3,9). This inconsistency might be due to better health literacy, healthy diet, regular physical exercise, and decreasing coexisting illnesses (218,219). The proportion of this doctor-diagnosed diabetes is lower than findings from previous studies in Ireland(83), Kazakhstan(86), China(220), Iran(221), Brazil(85), and Nigeria(31). The observed variation could stem from disparities in urbanization levels, varying health literacy, differences in diagnostic criteria, the tendency to underestimate diabetes among patients with co-existing conditions, and deficiencies in documentation practices(37,219).

The study highlighted a notable increase in the five-year prevalence of adult diabetes across all age brackets, with the most significant rise observed among individuals aged 60 years and older. This trend is consistent with findings from previous studies with similar objectives, indicating a concerning escalation in diabetes prevalence, particularly among older age groups

(10,86,92,95,98,220). Aging can lead to impaired insulin secretion due to impaired β-cell function and adaptation to insulin resistance, possibly due to lifestyle changes, like obesity and diminished physical activity, poor diet, and increased comorbidity(222).

In the twenty-first century, diabetes affects both urban and rural populations and is a profound, challenging, and widespread public health concern, especially in emerging nations' urbanized areas(3,13,114,223). The current study reveals that despite an increasing trend of adult diabetes among urban and rural residents, the urban population exhibits the highest proportion , consistent with previous studies in Nigeria(31). Urbanization alters eating habits, physical activity, smoking, and alcohol consumption, which is linked to obesity and NCDs. Urbans have better healthcare access, including reliable diabetes screening, anti-diabetic medications, education, and social services, while rural populations lack it, potentially leading to premature death before diagnosis(115,224). Rural areas face disproportionate health resource allocation, contributing to poverty, food insecurity, illiteracy, poor sanitation, and communicable diseases. The degradation of diabetes infrastructure leads to inadequate screening, non-adherence to guidelines, lack of counseling, and long-distance travel to health services. Addressing this inequality is crucial for improving diabetes intervention(225). In high-income countries, diabetes incidence and prevalence are higher in rural residents compared to urban. This might be due to rural residents having lower incomes, limited access to healthcare, and reduced opportunities for physical activity, which may lead to poor dietary habits, higher obesity rates, and increased diabetes prevalence(101,102).

The study indicates a consistent increase in type 1 diabetes prevalence over the study period, consistent with previous research in Finland, Korea, Iran, Mali, and Eritrea(107–110). In contrast, other similar studies in Serbia reported that a significant decrease in the incidence of type 1 diabetes was determined in adults aged 25–29 with an annual percentage change -of 7.3% between 2006 and 2017(106). The variation in the newly diagnosed type 1 diabetes between countries is multifactorial, involving complex interactions between genetic, environmental, healthcare-related, and socioeconomic factors(40,105). Evidence supports that geographical variation in adult-onset type 1 diabetes is similar to childhood-onset type 1, with countries with high rates in children and adolescents often having higher rates in adulthood(104). In this study, the proportion of adult type 1 diabetes is 1.6 per 1000 adult patients, which is higher than in

previous studies by Gondar and Jimma(111) and Gondar(40) 2.1 and 2.75 per 100000 population, respectively. The variation might be due to differences in study settings, denominator of the study, and genetic, environmental, healthcare-related, and socioeconomic factors. Moreover, Eritrea has the highest documented type 1 diabetes proportion globally, with 46.2/100,000 people affected, which has a similar culture, feeding habits, and geographical locations to our study participants(3,16). Even though the type 1 diabetes proportion observed in this study is higher than in previous studies, this is likely due to the study being conducted in general and referral hospitals. The actual proportion of type 1 diabetes may be even more significant because many individuals may die before receiving a diagnosis and accessing treatment. Additionally, some patients presenting with DKA might be incorrectly classified as having T2D(226,227).

The findings of this study align with previously published research, indicating a notable proportion of type 1 diabetes among rural residents(40,217). The annual proportion of type 1 diabetes is higher in rural areas, at 1.9 per 1000 people, compared to 1.4 per 1000 in urban areas. The increase in type 1 diabetes proportion among rural residents may be attributed to poverty and childhood malnutrition. Tigrai has faced numerous severe famines, predominantly affecting rural areas, prompting residents to seek medical care due to the acute nature of the disease. S. Fekadu et al. reported a strong association between insulin-requiring diabetes, poor education, and indicators of poverty indicators (217). The findings of this research indicated that the trend of type 1 diabetes significantly increased among women compared to their men counterparts. However, this contradicts the findings of a study by Hakkarainen et al. in Finland, which showed that the proportion of type 1 diabetes among men aged 18–39 was 29 per 100,000 per year, with a 33% increase from 1992 to 2007; in contrast, the proportion among women remained stable during the same period(107). The disparity might be due to differences in structural determinants, nutritional status, hormonal differences, and behavioral factors. It might be more marked detection bias in Ethiopia than Finland because women are more likely to be tested for diabetes because they are more likely to access health services (eg during pregnancy or for other reasons) than men.

The proportion of all diabetes that is T2D is higher in low-income countries than in higher-income countries. It affects the productive age groups(3), particularly in SSA countries like Ethiopia, due to rapid epidemiologic transition and low health literacy(32). T2D prevalence is

higher in developing countries' urban populations and higher in high-income countries' rural populations (13,101,114,223). The study revealed a higher prevalence of T2D in urban residents than in rural residents, a trend observed in other developing countries(13,114). Aung WP et al. reported that being a rural resident is 38% protective compared to being an urban resident (114). Urbanization leads to changes in eating habits, physical activity, smoking, and alcohol consumption, contributing to obesity and comorbidity, with sedentary lifestyles and unhealthy diets persisting due to epidemiologic and demographic transitions, with a notable increment trend (2,3,29,31,114). This finding is consistent with a study in Nigeria, the trend of T2D decreasing in rural residents(31), but inconsistent with studies in high-income countries, where diabetes prevalence vary by income level, with rural areas experiencing higher diabetes incidence in high-income countries and the urban regions having lower odds of new-onset diabetes. T2D proportion incidence is higher in rural and urban residents (101,223). The increasing trend of T2D in urban and developing countries and rural areas in high-income countries may be due to epidemiologic and demographic transitions(101,228). The study reveals a significant rise in T2D proportion among women, possibly due to biological, lifestyle, socioeconomic, and cultural factors. Factors include processed food, stress due to multiple roles, frequent healthcare visits, obesity, and cultural norms and practices influencing diet, physical activity, and healthcare access for women(94,229).

The rising T2D proportion in low-income countries is posing significant public health challenges, including delayed diagnosis, increased complications, and affecting healthcare systems and economic stability. To combat T2D, a multifaceted approach involving healthcare access, prevention programs, socioeconomic disparities, and supportive policies is needed at local, national, and international levels(2,3).

5.2. Risk Factors Associated with T2D

This study endeavored to determine factors associated with T2D in the hospital setting of Tigrai. The study found that urban residency, widowhood/divorce, family history of diabetes, hypertension, dyslipidemia, consumption of white rice, alcohol consumption, elevated waist circumference, and WHtR levels were significantly associated with increased odds of T2D, while leisure MVPA is found preventive.

The socio-demographic and geographic burdens of T2D are uneven throughout the world, with neighborhoods in high-income countries like the US, Canada, and Australia showing increased risk for those living in deprived areas. Deprived neighborhoods have limited access to healthy foods, physical activity, healthcare, education, social support, and environmental pollutants, increasing their risk of developing T2D(101,113,223,230), whereas, in developing countries, the risk is higher in urbanized areas(114,115,129). The study found that urban residents have more than five times higher odds of developing T2D compared to rural residents, which is consistent with previous studies in Myanmar(114), West Africa(115), Ghana(129), Algeria(7), and North West Ethiopia(100). Urbanization in developing countries leads to dietary changes, increased smoking, alcohol consumption, and sedentary lifestyles, contributing to obesity and NCDs like diabetes(115,228).

Marriage, a vital social institution since ancient times, has been linked to various health issues. Still, previous studies have found conflicting findings regarding the association between marital status and T2D(7,115,124,125). Previous studies in Brazil and West Africa indicated being divorced/widowed lowers the risk of developing T2D compared to married and single, respectively(115,125). The study reveals that divorced and widowhood individuals are 2.8 and 3.3 times more likely to develop T2D compared to married individuals, consistent with research from Iran and Saudi Arabia(7,124). Inconsistencies may be attributed to geographical location, culture, and socio-economic status disparities. Studies suggest that marriage improves health outcomes, lowers diabetes incidence, and improves adherence to treatment in partnered patients influenced by health behaviors and socioeconomic status(125). The death of a spouse can lead to significant stress and anxiety, lack of social support, change in lifestyles, financial strain, and feelings of loneliness and isolation, which could lead to a lack of motivation to engage in healthy behaviors and poorer health outcomes, including an increased risk of developing T2D.

Studies have demonstrated that an FHD is linked to various metabolic abnormalities and is a significant risk factor for developing T2D. In the current study, patients with an FHD have over five times the risk of developing T2D compared to those without a family history, consistent with previous research findings(42,100,173,231–234). FHD can include environmental factors besides the genetic risk that provides for obesity and some lifestyle factors, such as alcohol consumption, smoking, and diet. Individuals with an FHD may share similar lifestyle habits and

environmental exposures with their relatives, such as unhealthy dietary patterns, sedentary behavior, and obesity, which were reported to be associated with an FHD(42,235).

Cigarette smoking significantly impairs glucose tolerance and increases insulin resistance, leading to T2D, either independently or in clusters with other risk factors like centripetal obesity(140,141,147). Experience with cigarette smoke, combined with elevated blood glucose, is linked to vascular damage, endothelial dysfunction, and blood-clotting cascade activation, causing further vascular damage in individuals with diabetes(142,143). Studies show conflicting results on the link between smoking and T2D. While most epidemiological studies show a higher likelihood of developing T2D in smokers in Saudi Arabia, West Africa, and North Ethiopia(115,148,149), China and South Africa reported smokers have a lower probability of newly diagnosed diabetes than non-smokers(123,151). At the same time, the findings of this study indicated a null association between smoking and T2D. Possibly only one in twenty participants (5.3%) are current smokers of any tobacco products, such as cigarettes, with a higher proportion of cases (8.3%) compared to controls (3.8%) with an insignificant difference (p=0.19), which might be a negligible number to give important facts, and all smokers are men. Similarly, other investigators in Ethiopia found no association between smoking and T2D(57,100,150).

Previous studies(154–157) indicate that heavy alcohol consumption is a risk factor for Type 2 Diabetes, while moderate alcohol consumption is protective in both men and women. Even though the biological mechanisms remain poorly understood, moderate alcohol consumption has been linked to improved insulin sensitivity, changes in alcohol metabolites, increased HDL cholesterol concentrations, and anti-inflammatory effects. However, the exact dose-response relationship remains unclear(152,153). A study in West Africa demonstrated that alcohol consumption every day reduces the odds of T2D by 45%(115). Likewise, a study in North West Ethiopia showed that alcohol consumption was preventive for diabetes for rural residents(100). In the present study, alcohol consumption everyday increases 3.5 times the risk of T2D compared to non-drinkers. The variance may be attributed to lifestyle differences, patient characteristics, type, and alcohol consumption.

Dietary intake is a significant environmental risk factor for developing and preventing T2D, with nutritional patterns potentially having more substantial health effects than individual foods,

nutrients, or food groups(168). Consuming sugar-sweetened beverages, refined carbohydrates, processed meats, refined grains, and fatty foods can increase the risk of T2D by disrupting glucose metabolism and insulin sensitivity(117,133). The current study found that white rice consumption increases the risk of T2D by 3.8 times compared to those who ate injera made of teff/barely/sorghum. This is consistent with a large-scale study that found that consuming more white rice (over 450 g/day) increases the risk of diabetes (137). This may be due to white rice's high glycemic index(GI) and low fiber content, which can lead to weight gain, insulin resistance, and T2D risk, while replacing healthier carbohydrates like whole grains, legumes, and vegetables, which have lower GI, higher fiber content, and more nutrients, increasing metabolic diseases, including T2D(236,237).

Epidemiological studies demonstrated that elevated waist circumference, WHR, and WHtR are imperative indicators of central obesity, which is strongly linked with insulin resistance, inflammation, hormonal imbalances, and genetic factors that contribute to the development of T2D in both men and women (159,170,238); which is consistent with the finding of the present study, the risk of developing T2D is 2.4 and 3.2 times higher among individuals with elevated waist circumference and WHtR compared to those who have normal waist circumference and WHtR, respectively. Excessive abdominal fat accumulation, especially visceral fat, indicated by increased waist circumference, WHR, and WHtR, releases fatty acids and inflammatory substances, potentially causing insulin insensitivity and elevated glucose levels, potentially leading to T2D(57,165). Managing central obesity through lifestyle modifications, including healthy eating, regular PA, and weight loss, can significantly reduce the risk of developing T2D(3).

Previous studies have established that hypertension is an independent predictor of T2D (239). The current study found that individuals with hypertension are 3.0 times more likely to develop T2D compared to those with normal blood pressure. This finding is consistent with studies conducted in West Africa(115), Ethiopia(149), and Tigrai(57), where the risk of developing T2D in hypertensive patients was found to be 2.6, 3, and 6 times higher, respectively, compared to individuals with normal blood pressure. This might be due to both hypertension and T2D frequently coexist and contribute to each other's complications through shared pathophysiological mechanisms that justify their co-existence.

Dyslipidemia has recently been recognized as a risk factor for T2D. Literature shows that low levels of HDL-C, elevated levels of triglycerides, LDL-C, and total cholesterol are significantly associated with newly diagnosed T2D(57,166,183–185,240–243). In the current study, the possibility of developing T2D is nearly three times higher among individuals with dyslipidemia compared to those who do not. This finding is parallel with findings in Ghana(129), Addis Ababa(58), and Tigrai (57). This coexistence might be due to elevated levels of free fatty acids derived from triglycerides contribute to insulin resistance by interfering with insulin signaling pathways in peripheral tissues, with the inclination of increasing concentration of blood glucose and cholesterol nearly in the same manner as physical inactivity, body weight in general and central obesity in particular(165,244).

Previous studies on the impact of fruit and vegetable intake on type 2 diabetes (T2D) risk have yielded inconsistent results(245–248). Some studies have found an inverse association between higher intakes of total fruit (247,249) and total vegetables (246,247,250) with the risk of T2D. Conversely, other studies found no significant associations between total fruit (246,248,251) and vegetables(248,251). Similarly, the current study found no significant association between fruit and vegetable consumption and T2D. Perhaps only 2 (1.7%) of the cases and 8 (3.3%) of the controls reported consuming 14 or more servings of fruits in a typical week, with an insignificant difference (p=0.37). Similarly, only 7 (5.8%) of the cases and 21 (8.8%) of the controls consumed 14 or more servings of vegetables in a typical week, also with an insignificant difference (p=0.33). These numbers may not provide substantial insights due to their negligible proportion. The variations among these studies could be attributed to differences in the types of fruits or vegetables consumed and variances in participant characteristics, study designs, and assessment methods. Nonetheless, fruits and vegetables are abundant sources of dietary fiber, antioxidants, and phytochemicals, which can regulate blood sugar levels, enhance insulin sensitivity, and potentially mitigate the risk of type 2 diabetes(115,129).

Studies consistently show that regular physical activity, including resistance exercise, occupational activities, and cardiorespiratory fitness, can protect against T2D, emphasizing the importance of incorporating these activities into daily routines(157,161). In the present study, involvement in MVPA, moderate-intensity, and vigorous-intensity occupational activities, as well as engaging in moderate and vigorous-intensity sports, fitness, or leisure activities, and

regular walking or bicycling for at least 10 minutes continuously, did not show a significant association with a reduction in the risk of developing T2D, including total physical activity (PA) and occupational moderate-to-vigorous physical activity (MVPA). However, individuals engaged in leisure MVPA experienced a 27.0% protective effect against T2D. This discrepancy might be due to differences in the activity type, duration, participants' characteristics, study design, and assessment methods. However, the findings of this study are consistent with findings from Japan reported that occupational physical activity and walking to and from work are not associated with diabetes.

In contrast, leisure MVPA reduces the risk of diabetes(46). The WHO and ACSM recommend that adults with diabetes engage in 150-300 minutes of moderate-intensity or 75–150 min of vigorous-intensity physical activity per week, including muscle-strengthening activities twice a week. Regular physical activity is essential in reducing the risk of developing T2D and improving outcomes for those already diagnosed. Regular MVPA is crucial for diabetes prevention and management, improving insulin sensitivity, glycemic control, cardiovascular health, and mental well-being. Healthcare providers should encourage personalized physical activity(74,75).

5.3. Hyperglycemic Crisis

The study reveals DKA is the most common diagnosis among diabetic patients with hyperglycemic crises; the hospital stay and in-hospital mortality of HCs are higher in HHS. Similarly, in this study, patients with no prior diabetes history had a higher proportion of classic signs and symptoms of diabetes. Patients with a diabetes history have higher T2D, HHS, and chronic diseases and a higher mortality rate, particularly in rural residents. Besides, patients with certain conditions, such as T2D, HHS, lower urine ketones, chronic kidney disease, cardiovascular disease, stroke, diabetes, and rural residences, have higher in-hospital mortality. At the same time, excessive thirst on admission is protective.

The study reveals that 73.5% of hyperglycemic crisis admissions are linked to DKA, higher than Hiwot Fana Specialized University Hospital's(HFSUH) 52.3%(54) but lower than Jimma University's (JUSH) 93%(50) admitted due to DKA, respectively. This discrepancy might be due to differences in type of diabetes, rate of onset, symptoms and severity, population differences,

precipitating factors, diagnosis, and recognition. The reason for the higher proportion of DKA could be the combined effect. DKA, a common symptom of type 1 diabetes, is more frequent due to its rapid onset, often precipitated by factors that are more immediately recognized and managed like missed insulin doses or acute illnesses, severe symptoms like nausea, vomiting, abdominal pain, and deep rapid breathing, and younger individuals with insulin variability, leading to more frequent hospital admissions(50,64). In the present study, DKA patients in our study had 70% type 1 diabetes, severe symptoms (see Table 12), 31.2% non-compliance to medication, 37.6% newly diagnosed diabetes, and higher ketone bodies in the urine. Effective management of diabetes, prompt recognition of symptoms, and patient education are essential in reducing the incidence of DKA and HHS.

The most common precipitants of hyperglycemic crises in our study are the new onset of diabetes 33.3 %, infections 28.9 %, non-compliance to antidiabetic medications 25.5 %, and recurrent illness 12.4%. There is a higher proportion of newly diagnosed diabetes than in Jimma(50) and Haramaya(54) studies. These discrepancies might be related to differences in study settings where our study was predominantly conducted in general hospitals, with two-fifths of admitted patients with hyperglycemic crises being rural residents, which could be related to limited access to healthcare services and screening practices. Furthermore, there is a higher infection rate on admission in patients with HHS compared to DKA (41.7% Vs 24.2%). The reasons could be related to the combination of impaired immune function, mucosal barrier dysfunction, impaired wound healing, and history of hospitalization, which increases the risk of infection in patients with HHS compared to those with DKA.

This research's findings are consistent with those in Jimma(50) and Taiwan(203), where DKA patients are younger than patients with HHS. Young adults with type 1 diabetes are more likely to develop DKA due to disrupted diabetes management behaviors like irregular eating, substance abuse, and skipping insulin doses, leading to a higher incidence of DKA(17). Elderly individuals are more likely to develop T2D, characterized by insulin resistance and deficiency, and may also have comorbidities like CVDs, CKD, or infections exacerbated by hyperglycemia and lead to HHS. Besides, elderly individuals may experience impaired thirst sensation and reduced kidney function, increasing their susceptibility to dehydration and electrolyte imbalances, common characteristics of HHS.

Understanding hyperglycemic crises in patients with and without a prior diabetes history is crucial for improving clinical outcomes, treatment protocols, patient education, self-management, and public health planning and resource allocation to better address diabetes challenges(56). The study found that patients with no prior diabetes history had better consciousness compared to those with a previous diabetes history. They had more pronounced signs and symptoms of hyperglycemic crisis (vomiting, abdominal pain, polyuria, polydipsia, fruity breath odor, and body weight loss) compared to patients with a prior diabetes history, which is in line with findings in Taiwan(203). We believe that it could be due to two-thirds of patients without diabetes history presenting with classic diabetes symptoms due to high blood glucose levels causing urination, nocturia, thirst, fatigue, blurred vision, weight loss, and abdominal pain(2,4,5).

The study reveals that rural residents face a higher hyperglycemic crisis in patients without a diabetes history than those with diabetes. Rural residents face health challenges like low health literacy, treatment gaps, limited healthcare access, long-distance travel to health services, lower income, and lack of health insurance, healthcare provider shortages, cultural and behavioral factors, leading to diabetes diagnosis delays(252). To combat diabetes, a comprehensive approach involving improved healthcare access, increased diabetes education, preventive care services, and socioeconomic barriers, particularly in rural areas, is crucial. We suggest expanding diabetes care services to primary healthcare units, integrating diabetes screening into health extension packaging programs, and offering diabetes self-care management education.

Additionally, diabetic ketoacidosis (DKA) was more prevalent among patients with no prior history of diabetes (84.7%). In contrast, hyperosmolar hyperglycemic state (HHS) was more prominent in patients with a pre-existing diabetes history. Consequently, a higher in-hospital mortality was observed in patients with known diabetes. This finding contrasts with a study conducted in Jimma(50) but aligns with findings from studies conducted in Taiwan and South Africa(203,253). The higher proportion of DKA in patients with no prior diabetes history may be related to a relatively younger age, and more than half of the patients are rural residents, which could be associated with poverty(217,254).

The hyperglycemic crisis-related in-hospital mortality is 13.2%, which is higher than studies in Colombia, China, Taiwan, and Jimma that reported in-hospital mortality ranging from 2.27 to 10.6%(50,96,203,255) but lower than in Nigeria(20%)(256), Haramaya(16.5%) (54) and Tikur Anbesa Hospital Addis Ababa(21%)(51). The disparity might be due to differences in study settings, patient characteristics, access to diabetes commodities, severity, treatment delay, comorbidities, elderly age, infections, neurological impairment, electrolyte imbalances, inpatient management protocol of hyperglycemic crisis, inadequate laboratory investigations at presentation, and insufficient laboratory monitoring during treatment to monitor patient response(50,187,257). The study reveals that most patients are treated in general hospitals, less equipped with diabetes commodities and trained diabetes care providers, and 40% of patients are rural residents, with 53.1% having no diabetes history. Rural residents may face challenges in accessing healthcare services, leading to delayed diagnosis and increased risk of severe diabetic complications.

The study found a higher in-hospital mortality in patients with HHS compared to DKA. This higher in-hospital mortality in HHS patients may be due to delayed diagnosis, dehydration, hyperosmolality, underlying comorbidities, increased complications, management challenges, and age-related complications compared to DKA patients(54). The study found a lower in-hospital mortality among patients with no prior diabetes history compared to those with a pre-existing diabetes history. However, it's important to note that many diabetes patients might pass away undiagnosed or before receiving access to diabetes treatment, especially in rural areas. Despite this, the in-hospital mortality observed in this study was still higher compared to studies conducted in China, Taiwan, and Jimma(50,96,203). The disparity may be due to delayed diagnosis of T2D, where patients seek medical attention only after experiencing the disease's complications. The study revealed a more than threefold increase in-hospital mortality among rural patients compared to urban patients, a trend consistent with findings from a survey conducted in China (96). Rural patients face higher in-hospital mortality due to limited access to diabetes screening preventive services, lower income, lack of health insurance, long-distance travel, and lack of awareness, leading to complications and worsening conditions.

Patients with a medical history of chronic kidney disease, cardiovascular disease, and stroke are linked to higher in-hospital mortality compared to those without such conditions. Specifically,

with a medical history of stroke, patients have a 2.7 times greater likelihood of death upon admission, consistent with findings from a study in Taiwan (96,203). Additionally, the study revealed that patients with T2D and HHS experienced more than a twofold higher in-hospital mortality compared to patients with type 1 diabetes and DKA, respectively. Moreover, higher in-hospital mortalities were observed in patients with lower mean urine ketone levels, which is common in T2D and HHS patients. The increased in-hospital mortality in diabetes patients is attributed to inadequate inpatient management, inadequate laboratory monitoring, delayed recognition, and ignorance of complications, leading to severe dehydration and neurological deficits, ultimately resulting in death.

Moreover, there was a twofold higher in-hospital mortality in patients with a prior diabetes history compared to those with no prior diabetes, consistent with a study conducted in Taiwan (203). Prolonged hyperglycemia resulting from poorly managed diabetes and lack of awareness about diabetes complications could potentially contribute to increased in-hospital mortality (50). Lack of the presence of a routine annual checkup policy for NCDs- in Ethiopia, including diabetes, has led to delayed recognition and treatment after developing diabetes-related complications. Early identification, swift treatment initiation, and aggressive management are crucial for improving outcomes and reducing mortality in patients with hyperglycemic crises.

The study findings indicate that patients presenting with classic signs and symptoms of diabetes (such as vomiting, polydipsia, polyuria, fruity breath odor, and weight loss) upon admission had lower proportions of in-hospital mortality compared to those who did not exhibit these symptoms. This reduction in mortality for patients presenting with polydipsia on admission highlights the importance of early symptom recognition of hyperglycemia, which can prompt earlier medical intervention, potentially reducing complications and improving outcomes. However, failure to promptly recognize hyperglycemic symptoms in type 2 diabetes and lack of awareness about diabetes complications could result in mortality(96,203).

6. Validity and Generalizability

Internal validity refers to the extent of inferring that the independent variable is indeed causing or influencing the dependent variable(258). The research utilized various procedures to ensure

internal validity and minimize bias, chance, and confounding effects, evaluating these factors as alternate explanations for the findings.

The dissertation evaluated chance's impact using large, representative samples and confidence intervals. However, small sample sizes in some independent variables necessitated re-categorization by merging or excluding these categories during multivariate analysis.

In our efforts to minimize bias, a series of comprehensive actions spanned from the initial design of data collection tools to the eventual analysis of gathered data. We meticulously tailored questionnaires and checklists, drawing from established protocols and relevant literature. Additionally, we sought to enhance its validity by seeking feedback from senior endocrinologists or diabetes experts, leading to several adjustments. Experienced nurses, public health professionals, collectors, and supervisors proficient in NCD research were recruited. During this time, our supervisors and data collectors received thorough training sessions to ensure proficiency in their roles, where they gained valuable skills to handle the project's objectives smoothly. They learned how to interact with study participants gently, avoiding any unintentional hints that could affect their responses that could indicate agreements, disagreements, or a kind of surprise in the answers provided by study participants, with diligent supervision maintained throughout the data collection process. Standardized protocols were used to ensure accurate measurements of height, weight, hip circumference, waist circumference, blood pressure, blood glucose levels, and lipid profile tests among study participants. The study implemented rigorous training for data collectors and supervisors, focusing on precise measurement techniques, regular quality control checks, and equipment calibration to ensure uniformity and accuracy, and these concerted efforts aimed to mitigate potential interviewer and measurement biases, thereby enhancing the integrity of our study. The data collectors and participants were blind about the study's hypothesis to minimize bias.

Content validity concerns the degree to which an instrument has an appropriate sample of items for the measured construct (258). Thus, a comprehensive literature review was conducted to abstract the variables measured to ensure content validity. To improve the instrument's validity, we adopted the WHO STEPS protocol and similar kinds of literature and customized it to our

context. In addition, the instrument was pre-tested in 5% of the sample size in Wukro General Hospital, and the tool was modified accordingly.

To enable statistical conclusion validity, adequate statistical power was achieved by taking a sufficient sample size, and variables were clearly defined. We included all patients from the registry logbook and patient charts over the study period for paper I and III to minimize the potential for selection biases, and we also used simple random sampling for paper II. In addition, Matching was done in the design stage for the case-control study, and multivariable binary logistic regression analysis was done for papers II and III to control the effect of potential confounders. The study used robust statistical methods to analyze complex data, setting a significance threshold of $p < 0.05$ and employing a 95% confidence interval. We ensured rigorous interpretation while mitigating the influence of random chance. The study used a comprehensive approach to analyze data, including hypothesis testing, diagnostic tools, and statistical tests. The study used diagnostic tools like histograms, Q-Q plots, and rigorous statistical tests such as Kolmogorov-Smirnov and Shapiro-Wilk to improve evidence quality in Paper III. We used non-parametric tests and multivariable statistical analyses to ensure internal validity and minimize confounding factors, ensuring the reliability and robustness of our findings during the design and analysis stages. We used the mean/median/mode imputation technique for papers I and III to minimize missing data.

External validity refers to generalizing the research findings to other settings or populations. It allows findings to be generalized beyond the specific context (258,259). In healthcare systems, where factors like patient demographics, resource availability, and healthcare professionals are similar, findings can be extrapolated to other settings. This homogeneity in operational dynamics allows for the adoption of interventions across different settings. Since the health care system organizations in the country operate in similar settings regarding patient mix, resources, and professional mix, the findings can reasonably apply to other similar health facilities. Therefore, external validity is essential in research to advance healthcare practices on a broader scale.

7. Strengths and Limitations

This study exhibits several strengths. Firstly, in Paper I, the study utilized a large sample size that included all 18 years and above adult patients who sought medical care from all adult medical OPDs and EOPDs with all medical records of diabetes patients who had been diagnosed over the review years, which gave us the actual image of the target population. In Paper III, the study meticulously examined all patient charts treated for hyperglycemic crises in the study year.

Another strength of the study is its utilization of the standardized WHO STEPS method, which ensures comparable results across countries. In the case-control study, unlike many previous studies in Ethiopia that used a cross-sectional study design, this study used a matched case-control study design. Previous studies included their target population as all age groups or adults aged 18 and older. In contrast, our target groups were the most risky age brackets (middle-aged 45 to 64 years old) only. Most of the previous Ethiopian studies assessed all types of diabetes, while this study targeted the most commonly extensively explored risk factors of T2D. Unlike the existing studies in the country, which often relied on Random Plasma Glucose tests from the capillary blood samples, our study employed both fasting and venous blood samples, producing more accurate glucose concentration estimates. Moreover, we used a better, fully automated clinical chemistry analyzer machine to analyze biomarkers. Further enhancing the precision and reliability of our findings.

Besides, T2D patients were ascertained from the diabetes clinic by the senior physicians. The controls were ascertained by senior physicians or General practitioners providing care in the general medical OPD, using blood glucose tests and other investigations. At Ayder Comprehensive Specialized Hospital, better-experienced healthcare providers, equipment, and material supplies were available.

It is necessary to acknowledge the study's limitations. A key limitation of this study is the lack of a comprehensive critical appraisal of the studies included in the literature review. The potential roles of chance, bias, and confounding in these studies were not systematically assessed, which may affect the robustness of the conclusions drawn from the literature. Future reviews should rigorously evaluate study quality to improve the interpretation of evidence.

The nature of record-reviewed data had limitations as there were incomplete data to address objectives I and III. Regarding the incompleteness of the data, the review charts had some missing data for some variables, which could have led to differences in an unmeasured independent variable for which no correction could be made. Data were not validated, which could have led to misclassification of diabetes type and types of hyperglycemic crises. The data were retrospective chart reviews, and the total number of adults with diabetes was underestimated because some patient charts were lost. Not all adult patients who received medical services from the study units were tested for diabetes for those who came for other medical illnesses. As a result, the findings of this study may not show the true magnitude of diabetes. The study is limited to medical and emergency units, which do not include obstetrics and surgical units, which may further underestimate the proportion of diabetes. The study was limited in including critical diagnostic criteria for classifying hyperglycemic crises because studies in general hospitals lack advanced laboratory setups. Approximately 8% of the data from the charts and logbooks were missing, primarily affecting key variables like age, gender, and place of residence for objective I, while was about 12.1% missing data for objective III, which majorly affects medication dosage and frequency, frequency of admission, clinical presentations, diabetes-related complications, laboratory results, and follow-up results. The data appeared to be missing at random for most variables, but non-random patterns were observed in the documentation of follow-up visits. To minimize the limitations, diabetes patients' data in the logbooks with a diagnosis of diabetes were cross-checked with the data in the patient chart and electronic medical record. For the third objective, the possible limitation was minimized by cross-checking the charts with electronic medical records during the data collection. We used the mean/median/mode imputation technique during the data analysis to minimize missing data.

The researcher utilized a comparative cross-sectional study design, opting for a snapshot approach instead of follow-up due to data limitations, such as incomplete records, inconsistencies in accuracy, and disparities in availability between exposed and unexposed groups. These challenges could introduce bias by affecting unmeasured independent variables. Recognizing this limitation, the study objective was tailored accordingly. A prospective cohort study is recommended for a more accurate assessment of in-hospital mortality rate differences between patients with and without a prior history of diabetes.

In this study, despite matching cases and controls by age and gender, residual confounding factors—such as family history, stress, healthcare access, comorbidities (hypertension, hyperlipidemia), social support, and neighborhood environment may still affect the relationship between the exposures and T2D. Similarly, for both cases and controls, we measured dietary assessment, alcohol consumption, cigarette smoking, and PA at one point in time, and this may not represent habitual behavior levels across the lifetime. Measurement error in self-reporting is unavoidable and frequently skew results toward the hypothesis due to biased self-reported behaviors—social desirability and approval further influence these reports. Likewise, as this study is hospital-based, its findings may not apply to the broader community in the region or country.

Likewise, we could not compare our findings with the existing data from Ethiopia or other sub-Saharan African countries. No studies have investigated the trend of type 1 and type 2 diabetes among urban and rural residents aged 18 years and above, risk factors of T2D in middle-aged adults (45 to 64 years), and treatment outcomes hyperglycemic crises in patients with and with no prior diabetes history. Therefore, some comparisons made with high- and middle-income countries are of limited value due to participant characteristics, study methods, health literacy, health service utilization, and healthcare system differences.

The researcher used a physician's diagnosis for type 1 diabetes, T2D, hyperglycemic crises (DKA and HHS), hypertension, and dyslipidemia without input in diagnosis. The diagnosis of type 1 diabetes was based on clinical assessment, considering age, presentation, clinical features, and immediate requirement for insulin, without indications of T2D or another diabetes type. The researcher didn’t attempt to examine autoantibodies and C-peptide test results to confirm the diagnosis due to a lack of resources and testing capacity within the Hospitals and the Region.

8. Conclusions and Recommendations

8.1. Conclusion

Over the five-year study, the proportion of diabetes in this study was 10.2 per 1000 adult patients, with 11.6 per 1000 urban residents and 8.6 per 1000 rural residents. The trend of adult diabetes mellitus steadily increased over time for both type 1 and type 2 diabetes among urban

and rural residents for both men and women in the observation period. Notably, the proportion of type 1 diabetes increased more in rural residents, especially among women.

We found that being an urban resident, widowhood/divorced, FHD, hypertension, dyslipidemia, consumption of rice, alcohol consumption, high waist circumference, and WHtR were confirmed possible risk factors of T2D, while leisure MVPA is protective.

The proportion of in-hospital mortality for hyperglycemic crises was 13.2%. Patients with a prior diabetes history had a higher proportion of in-hospital mortality (15.5%) compared to those with no prior diabetes history (8.7%). Furthermore, mortality was also higher among rural residents and among patients with type 2 diabetes and hyperglycemic hyperosmolar state in both patients. Independent predictors for in-hospital mortality included living in rural areas, having T2D, experiencing HHS, a history of stroke, and a history of diabetes, while excessive thirst was a preventive factor.

8.2. Recommendations

To Tigrai Regional Health Bureau:

- Develop and evaluate in a piolet diabetes screening protocol for all adults with coexisting diseases, 45+ years old, and NCD risk factors in healthcare settings.
- Enhancing health education programs to raise awareness about the health risks associated with alcohol, tobacco, intake of processed foods, and sedentary behaviors
- Encouraging people to consume a healthful diet and discouraging sugar-containing processed unhealthy foods.
- Promote the enhancement of dependable diabetes care services at primary healthcare units and integrate diabetes screening into health extension programs.
- Develop an efficient bidirectional referral system between hospitals, health centers, and health posts to decentralize diabetes services to the grassroots level of the primary health care unit, including health posts closer to where patients reside, which will help in the early detection of complications.

- Create tailored informational materials about diabetes and related risk factors, including obesity, physical inactivity, tobacco use, alcohol abuse, and poor nutrition, emphasizing primary prevention strategies.
- With concerned bodies, mainly the Bureau of Agriculture means must be developed to increase affordable access and availability of vegetables and fruits in local markets.
- Promote diabetes awareness and healthy lifestyles at work by allocating time, room, and supplies with essential physical exercise equipment and access to a healthful diet.
- Formulate policies guaranteeing access to quality, available, and affordable insulin and other diabetes commodities at the community level.

- Develop guidelines and protocols to improve the inpatient management of hyperglycemic crises and equip advanced laboratory investigations in general hospitals.

To Woreda Health offices/ Health care managers

- Healthcare managers and administrators across all levels of the healthcare system should prioritize diabetes prevention and control due to its escalating prevalence and the higher rates of complications and mortality.
- Ensure timely essential diagnostic and treatment supplies are available, supported by robust supervision and mentorship initiatives.
- Healthcare institutions should implement robust screening strategies for diabetes and its risk factors and other NCDs, such as obesity, high blood pressure, and elevated cholesterol levels.
- Implement screening (blood glucose testing) programs to identify and diagnose pre-diabetes and diabetes earlier among high-risk groups. These groups include individuals with a family history of diabetes, obesity, hypertension, elevated cholesterol levels, and those with a history of significant laboratory findings or gestational diabetes.
- Ensure that physicians are trained to seize the opportunity for medical screening of patients aged 45 and above and pregnant women to detect conditions like gestational diabetes during routine visits for other purposes.
- Implement screening programs for patients already diagnosed with diabetes to detect complications like retinopathy, nephropathy, coronary heart disease, and foot problems early, aiming to minimize associated morbidities and mortalities.

- Establish appropriate consultation and screening for DM and HTN in health centers;
- Conduct mass screening campaigns for diabetes and hypertension

Health care professionals

- Healthcare professionals need to prioritize timely identification and effective management of patients with diabetes to alleviate the burden of the condition.
- Health professionals should raise awareness in rural communities about the risk factors, symptoms, and potential complications of diabetes. Moreover, they should ensure diligent monitoring of diagnosed diabetes patients due to the heightened risk of complications.

Research Institutions/ Researchers

- Investigate characteristics of type 1 diabetes in Tigrai
- Conduct prospective cohort studies on the management of hyperglycemic crises in both government and private healthcare institutions at different levels.
- Investigate diabetes-related morbidities and mortalities at different levels of healthcare institutions and in the community.
- Assess psycho-social trauma and quality of life in patients with diabetes
- Determine the cost of inpatient diabetes management
- Assess the bidirectional referral linkage between health centers and hospitals and its effectiveness on the treatment outcome of diabetes patients

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Annex I: English Version Checklist and Questionnaire

Part I: Data extraction sheet from the logbooks

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General instruction for data collectors/supervisors

This is a checklist for abstracting data from patient registry logbooks who received medical care from September 1, 2013 to August 31, 2018 to be filled by the respective data collectors you as part of research team are responsible to adhere to the ethical issues in maintaining confidentiality and hand over the logbooks and charts to the records office immediately after taking the necessary information needed, and say thank you to the record office staffs.

Name of data extracter: _____

Name of hospital: _____

Name of hospital: _____

Data extraction sheet report form from the registry logbooks and record a count in each box

Year of diagnosis	Patients visited												Age group	Count
	Urban						Rural							
	Men			Women			Men			Women				
	Count			Count			Count			Count				
2013/4													18-29	
2014/5													30-39	
2015/6													40-49	
2016/7													50-59	
2017/8													≥ 60	
Total														

Name of the data abstracter: _____ Signature: _____

Name of the data abstracter: _____ Signature: _____

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General instruction for data collectors/supervisors

This is a checklist for collecting data from patient chart of patients with diabetes mellitus who were newly diagnosed from September 1, 2013 to August 31, 2018 to be filled by the respective data collectors, you as part of research team are responsible to adhere to the ethical issues in maintaining confidentiality and hand over the logbooks and charts to the records office immediately after taking the necessary information needed, and say thank you to the record office staffs.

Name of the nurse/health officer: _____

Name of hospital: _____

QN	**Identification information:**		
101	Patient card no _____	105	Date of OPD visit_____
102	Age in years_____	106	Year of diagnosed:_____
103	Sex: 1. Male 2. Female	107	Referral (if any)_____
104	Residence: 1. Urban 2. Rural		
Characteristics of newly diagnosed adult diabetes patients at OPD during diagnosis			
QN	**Variable**	QN	**Variable**
108	Reason the patient has sought medical care (you can circle more than one) 1. Polyuria 2. Polydepsia 3. Polyphagia 4. Fever 5. Fatigue 6. Others (specify)_____ 7. Not stated……66	109	What were the vital sign at the time of diagnosis 1. BP: SBP_____DBP_____ 2. Pulse rate:_____ 3. Temperature: _____ 4. Respiratory Rate:_____ 5. Weight :_____Kg 6. Height : _____m
110	Family history of diabetes 1. Yes 2. No 3. Not stated……66	111	If QN 107 is yes, which family members 1. Father 2. Mother 3. Siblings 4. Grand father 5. Grand mother 6. Others (specify)_____ 7. Not stated……66
112	Type of Diabetes Mellitus 1. Type I DM 2. Type II DM	113	What were the laboratory test findings at time of diagnosis 1. FBS /RBS/ A1C (circle one)

	3. Gestational DM 4. Others (specify)_____ 5. Not stated…….66		2. Lipid profile a. LDL_____ b. HDL_____ c. Total triglycerides _____ d. Total cholesterol level_____ e. Other lab tests (specify)_____ 3. Not stated…….66
114	Did the patient had additional disease 1. Yes 2. No 3. Not stated…….66	115	If Q 111 is yes; what was the co-morbidity with diabetes 1. Hypertension 2. Heart disease 3. Kidney disease 4. Diabetic foot ulcer 5. Others (specify)_____ 6. Not stated……66
116	What was the treatment for the patient 1. Advice 2. OHAs 3. Insulin 4. Others (specify)_____ 5. Not stated…….66	117	N.B. Any special information available from the chart should be documented in this check list

Suggestions after completing the checklist by the data collector (report any missing data, vague sentences, spoiled or unreadable statements, etc below)

_____
_____
_____
_____
_____
_____
_____

Data collector's Signature_____

Supervisor's Signature_____

Part II: A Semi-Structured Questionnaire

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Consent Form

This questionnaire is prepared to assess risk factors of T2D among adult diabetes patients treated in selected public hospitals, Tigrai, Ethiopia.

Subject Information Sheet

Dear respondent

Good morning/Good afternoon. Thank you for your interest in talking with me today. My name is _____. I am working with Mr. Getachew Gebremedhin who is a member of a team conducting a study **to assess the risk of T2D among hospital treated adult patients** in your locality. The research is to be conducted as partial fulfillment for the requirement of Doctor of Philosophy under college of health sciences, Addis Ababa University; you are randomly selected to take part in this research interview.

The purpose of my visit today is to take information from you on the aforementioned issue. If you are willing to participate in the study, I will ask you few questions lasting for 30 minutes. I will measure your body weight and height in order to assess your nutritional status, and my working mate will take also 10ml venous blood from your arm for analysis of your glycaemic level and lipid profile. And then at end; I will tell you your result; and if you are found to have diabetes or any other disease, you will be referred for treatment and advice. In addition; the questionnaire will not be used for any other analysis apart from this study and won't be stored in anyway. However, no financial payment will be made for your participation.

Your name will not be written on this form and will never be used in connection with any of your information. You do not have to answer any question that you do not feel comfortable with, and you may end this task any time you want to. However, your honest answers to these questions and your continuous interest to participate in the study will help us in better understanding of common risk factors for T2D in your locality, and will eventually help in designing and implementing appropriate prevention and intervention programs to alleviate the problem. Hence, we would greatly appreciate your help in involving in the study. Your

participation in the study is fully based on your interest and choice. Your participation or non-participation will not be related with the health service that you will get from this health institution.

If you have any un-clarity on my visit you can ask me now so that I can elaborate it. If you come across with any concern during my stay with you, you can stop me and raise it anytime you want. It is also possible to communicate the principal investigators Getachew Gebremedhin through the telephone address **+251914 155081.**

Informed Consent Form

With due understanding of the aforementioned information, are you willing to participate in the study?

Yes ☐ (Proceed with the interview)
Signature of the interviewee Name _____ Signature _____ date _____

No ☐ (Terminate the interview)

Signature of the interviewer Name _____ Signature _____ date _____

Supervisors/Researcher remark and signature _____ Name _____ Signature _____ date _____

Part I: Socio-Demographic characteristics				
No.	**Question**	**Response**		**Code**
301	Sex	Male	1	C1
		Female	2	
302	What is your date of birth in Ethiopian Calendar? *Don't Know 99*	_____/ ____/ _____ *If known, Go to C4* dd mm year		C2
303	How old are you?	Years	_____	C3
304	What is your religion?	Orthodox Muslim Protestant Catholic Others (specify)_____ Refused	1 2 3 4 5 88	C4
305	What is your ethnicity?	Tigreway/ti Amharay/ti Afar Others(Specify)_____ Refused	1 2 3 4 88	C5
306	What is your marital status?	Single Married Divorced Widowed Refused	1 2 3 4 88	C6
307	What is the highest level of education you have completed?	Illiterate Grade 1-4 Grade 5-8 Grade 9-10 Grade 11-12 College/University complete Post graduate degree Refused	1 2 3 4 5 6 7 88	C7
308	Which of the following best describes your main work status over the past 12 months?	Civil servant Self employed Farmer Student Homemaker Unemployed Retired Housewife	1 2 3 4 5 6 7 8	C8

		Refused	88	
309	Taking the past year, can you tell me what the average earnings of the household have been?	Per month_____ Or Per year_____ Refused	Go to C10 88	C9
310	Where is your residence?	Rural Urban Refused	1 2 88	C10
History of chronic diseases				
311	Do you ever told by a doctor as have raised blood pressure?	1. Yes 2. No	If yes, Go to C12 88	**C11**
312	If C11 is yes; did the doctor or other health care providers prescribed medication?	1. Yes 2. No		
313	Do you ever told by a doctor as have raised cholestrol?	3. Yes 4. No	If yes, Go to C13 88	**C12**
314	If C11 is yes; did the doctor or other health care providers prescribed medication?	3. Yes 4. No		
313	Do you have family history of diabetes	1. Yes 2. No 3. Don't know	**If yes, Go to C14** **88**	**C13**
314	If C12 is yes, which family members	1. Father 2. Mother 3. Siblings 4. Grand father 5. Grand mother 6. Others (specify)_____ 7. Refused	**88**	**C14**

Part II: Behavioral Measurements			
No.	**Question**	**Response**	**Code**
314	What is your status in cigarrete smoking?	1. Never smoke 2. Ex-smoker	T1

		3. Current smoker	
315	Do you currently smoke tobacco products **daily**?	Yes 1 No 2, If No Go to A1	T2
316	If yes Q≠315, on average, how many cigarettes do you smoke per day?	1. 1-9 cigarettes/day 2. 10-20 cigarettes/day 3. > 20 cigarettes/day	T3
317	How old were you when you **first started** smoking daily?	Age in years_____ Don't know ……..99	T4
318	If yes Q≠115, do you remember how long ago it was?	In years_____ In months____ In weeks_____	T5a T5b T5c
Alcohol consumption			
No.	**Question**	**Response**	**Code**
319	What is your status in alcohol consumption? such as beer, wine, wisky, ArekiTella, Teji, or *others*?	1. Never drink 2. Ex-drinker 3. Current drinker; If never or ex-drinker Go to D1	**A1**
320	Have you consumed an alcoholic drink within the **past 30 days**?	**Yes = 1** **No = 2**	**A3**
321	If yes for Q≠320; how frequently did you drink alcoholic?	1. Daily 2. Three times a week 3. Once a week 4. _____/week 5. Don't know ……99 6. Refused…… 88	**A3**
322	During the past 30 days, **on average**, how many **bottle/glass of alcoholic drinks** did you have during one drinking occasion?	1. Number bottle____ 2. Don't know…. 99 3. Refused…….. 88	**A4**

323	During the past 30 days, what was the **largest number** of alcoholic drinks you had (glass, bottle and the like) on a single occasion, counting all types of alcoholic drinks together?	Largest number_____ Don't know 99 Refused 88	**A5**
CORE: Diet			
The next questions ask about the foods, fruits and vegetables that you usually eat. I have a nutrition card here that shows you some examples of local fruits and vegetables. Each picture represents the size of a serving. As you answer these questions, please think of a typical week in the last year.			
No.	Question	Response	Code
324	Which one of the food items do you consumed regularly/your favorite/staple food?	1. Injera made of Teff/Sorgum/barely 2. Injera/bread/bakery/kita made of wheat 3. Rice 4. Pasta 5. Red meat 6. Faty acid rich foods (butter,) 7. Processed foods 8. Others_____	**D1**
326	In a typical week, on how many days do you **eat fruit**?	No. of days____ *If Zero days, go to D5* Don't Know 99	**D3**
327	How many **servings** of fruit do you eat on **one** of those days?	No. of servings_____ Don't Know 99	**D4**
328	In a typical week, on how many days do you **eat vegetables**?	No. of days____ *If Zero days, go to D7* Don't Know 99	**D5**
329	How many **servings** of vegetables do you eat on one of those days?	No. of servings_____ Don't Know 99	**D6**
330	What sugar contained beverages/caffeine commonly do you drink?	1. Coffee with sugar/or without sugar 2. Tea 3. Soft drinks 4. Others _____	**D7**
331	In a typical week, on how many days do you drink these beverages	1. Coffee _____ 2. Tea _____	**D8**

		3. Soft drinks _____ 4. Others _____	
332	How many **servings** of these beverages do you drink on **one** of those days? (cups)	1) Coffee with/or without sugar _____ 2) Tea _____ 3) Soft drinks _____ 4) Others _____	**D9**

Physical Activity

Next I am going to ask you about the time you spend doing different types of physical activity in a typical week. Please answer these questions even if you do not consider yourself to be a physically active Person. There are various domains of activity which need to be included; work activities in and around the home and garden, to get from place-to-place (transport-related) and recreation (discretionary or leisure-time) exercise or sports activities. This opening statement **should not** be omitted.

No.	**Questions**	**Response**	**Code**
	Activity at work		
333	Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like [carrying or lifting heavy loads, digging or Construction work] for at least 30 minutes continuously?	**Yes 1** **No 2** **If no go to P4**	**P1**
334	In a typical week, on how many days do you do vigorous intensity activities as part of your work?	No. of days_____	**P2**
335	How much time do you spend doing vigorous-intensity activities at work on a typical day?	Hours : minutes___:___	**P3**
336	Does your work involve moderate-intensity activity that causes small increases in breathing or heart rate such as brisk walking *[or carrying light loads*] for at least 30 minutes continuously?	Yes 1 No 2; If No go to P7	**P4**
337	In a typical week, on how many days do you do moderate intensity activities as part of your work?	Number of days _____	**P5**
338	How much time do you spend doing moderate-intensity activities at work on a typical day?	Hours : minutes___:___	**P6**
Travel to and from places:			
The next questions exclude the physical activities at work that you have already mentioned. Now I would like to ask you about the usual way you travel to and from places. For example to work, for shopping, to market, to place of worship. [insert other examples if needed]			
No.	**Questions**	**Response**	**Code**

339	Do you walk or use a bicycle (*pedal cycle*) for at least 10minutes continuously to get to and from places?	**Yes 1** **No 2; If no go to P10**	**P7**
340	In a typical week, on how many days do you walk or bicycle for at least 30 minutes continuously to get to and from places?	No. of days _____	**P8**
341	How much time do you spend walking or bicycling for travel on a typical day?	Hours : minutes___:___	**P9**
Recreational activities:			
The next questions exclude the work and transport activities that you have already mentioned. Now I would like to ask you about sports, fitness and recreational activities (leisure),[insert relevant terms].			
342	Do you do any vigorous-intensity sports, fitness or recreational (leisure) activities that cause large increases in breathing or heart rate like [running or football] for at least 30 minutes continuously?	Yes 1 No 2; If no go to P13	**P10**
343	In a typical week, on how many days do you do vigorous intensity sports, fitness or recreational (*leisure*) activities?	No. of days _____	**P11**
344	How much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?	Hours : minutes___:___	**P12**
Sedentary behavior:			
The following question is about sitting or reclining at work, at home, getting to and from places, or with friends including time spent [sitting at a desk, sitting with friends, travelling in car, bus, train, reading, playing cards or watching television], but do not include time spent sleeping.			
345	How much time do you usually spend sitting or reclining on a typical day?	Hours : minutes___:___	**P13**
Part III: Physical Measurements			
CORE: Blood Pressure			
No.	**Question**	**Response**	**Code**
346	Interviewer ID	**_____**	**M1**
347	Blood pressure reading	Systolic_____mmHg	M2a
		Diastolic_____mmHg	M2b
348	During the past two weeks, have you been treated for raised BP with drugs prescribed by a doctor or other health worker?	1. Yes 2. No	M3
CORE: Height and Weight			
349	**For women:** Are you pregnant?	1. Yes; if yes go to part IV 2. No	M4
350	Record participant's **height** in cm with one decimal point.	_____cm	M5
351	Record participant's **weight in kg** with one decimal point.	_____kg	M6
352	Record participant's **waist circumference** in centimetres with	_____cm	M7

	one decimal point.		
353	**Hip circumference** in centimetres with one decimal point.	_____cm	M8
Part IV: Biochemical Measurements			
CORE: Blood Glucose			
354	During the past 12 hours have you had anything to eat or drink, other than water? It is essential that the participant has fasted.	1. Yes 2. No	B1
355	Time of day blood specimen taken (24 hour clock), Enter time measurement started.	Hours : _____:_____ Minutes hrs minutes	B2
356	Fasting blood glucose [choose accordingly: mmol/l or mg/dl] Double check that the participant has fasted.	mmol/l_____ *mg/dl*_____	B3
357	A1C	_____%	B4
358	Today, have you taken insulin or other drugs (medication) that have been prescribed by a doctor or other health worker for raised blood glucose? Select appropriate response.	1. Yes 2. No	B5
CORE: Blood Lipids			
359	Total cholesterol [choose accordingly: mmol/l or mg/dl]Record value for total cholesterol.	mmol/l_____ mg/dl_____	B6
360	During the past two weeks, have you been treated for raised cholesterol with drugs (medication) prescribed by a doctor or other health worker? Select appropriate response.	1. Yes 2. No	B7
361	Triglycerides [choose accordingly: mmol/l or mg/dl] Record Value For Triglycerides.	mmol/l_____ mg/dl_____	B8
362	HDL Cholesterol [Choose Accordingly: Mmol/L Or Mg/Dl] Record Value For HDL Cholesterol.	mmol/l_____ mg/dl_____	B9
363	LDL Cholesterol [Choose Accordingly: Mmol/L Or Mg/Dl] Record Value For LDL Cholesterol.	mmol/l_____ mg/dl_____	

Thank you for giving us your time!!

Part III: Checklist for hyperglycemic crisis data extraction

ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF PUBLIC HEALTH

General instruction for data collectors/supervisors

This is a checklist for collecting data from patient chart of patients with hyperglycemic emergencies to be filled by the respective nurses/health officers/public health experts, you as part of research team are responsible to adhere to the ethical issues in maintaining confidentiality and hand over the charts to the records office immediately after taking the necessary information needed, and say thank you to the record office staffs.

Name of the data collector: _____
Name of hospital: _____

QN	**Identification information:**		
201	Patient card no _____	205	Year of first diagnosed:_____
202	Age in years_____	206	Duration with diabetes _____ years
203	Sex: 1. Male 2. Female	207	Date and year of admission_____
204	Residence: 1. Urban 2. Rural	208	Date of discharge_____
209	Referral (if any)_____	210	Number of admission_____

Characteristics of adult diabetes patients with hyperglycemic emergencies

QN	**Variable**	QN	**Variable**
211	Type of Diabetes Mellitus 1. Type I DM 2. Type II DM 3. Gestational DM 4. Others (specify)_____ 5. Not stated……66	212	Patients medication for the diabetes before admission 1. Insulin; a. Type of Insulin_____ 2. Oral hypoglycemic agents a. Type of OHAs_____ 3. Insulin and OHAs, if both a. Type of Insulin_____ b. Type of OHAs_____ 4. Not stated……66

213 Type of Hyperglycemic Emergencies
1. Diabetic Ketoacidosis
2. Hyperosmolar Hyperglycemic state
3. Mixed
4. Others (specify)_____
5. Not stated……..66

214 What were the precipitating factors for HEs
1. Infection
2. Noncompliance to treatment
3. New diagnosis of diabetes
4. Trauma/Injury
5. Cultural and religious beliefs
6. Others (specify)_____
7. Not stated…….66

215 If QN 214 is infection; what type of infection/s
1. UTI
2. Pneumonia
3. Sepsis
4. Pulmonary TB
5. Insulin site infection
6. Diabetic foot ulcer
7. Oral infection
8. Osteomyelitis
9. Others (Specify)_____
10. Not stated……66

216 If Q 214 is noncompliance to treatment; what is the reason
1. Medication discontinuation
   - Reason of discontinuation _____
2. Missed dose of medication
   - Reason for missed doses _____
3. Others(specify)_____

217 What clinical manifestations was the patient had
1. Vomiting
2. Abdominal pain
3. Polyuria
4. Polydipsia
5. Shortness of breath
6. Impaired LOC
7. Fever
8. Others (specify)_____
9. Not stated …….66

218 What was the vital sign of the patient
1. Weight of patient in Kg_____
2. Height of patient in meter _____
3. BP: SBP_____DBP_____
4. Temperature_____
5. Respiratory rate_____
6. Pulse rate_____
7. Others(specify)_____
8. Not stated……..66

219 What were the laboratory test findings at admission
1. FBS / RBS / A1C (circle one)
2. Lipid profile
   a. LDL_____
   b. HDL_____
   c. Total triglycerides _____
3. Total cholesterol level_____

220 What was the medication that the patient has taken for HEs
1. Insulin;
   a. Regular insulin
   b. Lente insulin
   c. Mixed insulin
   d. Others (specify)_____
2. Oral hypoglycemic agents
   Type of OHAs_____

4. Not stated……66

3. Insulin and OHAs, if both
   Type of Insulin_____
   Type of OHAs_____

221 What type of IV fluids the patient had taken with in the first 24 hours of admission per hour

1. Normal saline_____litres
2. Ringer lactate_____litres
3. D5W_____litres
4. DNS_____Liters

222 Does the patient had additional disease

1. Yes
2. No
3. Not stated…….66

223 If Q222 is yes; what was the co-morbidity with diabetes

1. Hypertension
2. Heart disease
3. Diabetic foot ulcer
4. Tuberculosis
5. HIV/AIDS
6. Others (specify)_____
7. Not stated…….66

224 What was the treatment outcome of the patient

1. Discharge with improvement
2. Died
3. Others(specify)_____

225 N.B. Any special information available from the chart should be documented in this check list

Suggestions after completing the checklist by the data collector (report any missing data, vague sentences, spoiled or unreadable statements, etc below)

_____
_____
_____
_____
_____
_____
_____

Data collector's Signature_____

Supervisor's Signature_____

Annex II: Tigrigna version of Questionnaires

ተወሳኺ ፅሑፍ 2: ትግርኛ ስሪት ዝርዝር መፈተሺን መሕተትን
ክፍሊ ሓደ ሀ)፡- መረዳእታ ካብ ናይ ተሓካሚ መዝገብ ምእካብ

አዲስ አበባ ዩኒቨርስቲ

ኮሌጅ ሳይንስ ጥዕና

ክፍሊ ትምህርቲ ሕብረተሰብ ጥዕና

አጠቃላሊ መምርሒ ንአከብትን ተቆፃፀርትን መረዳእታ

ቀሚሉ ዘሎ ቐጥዒ ካብ መስከረም 1/2005 ክሳብ ነሓሰ, 2010 አብቲ ተመድብኹሙሉ ዘሎ ሆስፒታል ኣብ ናይ ዓበይቲ ተመላለስቲ ዉሽጣዊ ሕክምና ግልጋሎት ዝረኸቡ ተሓከምቲ በብዓመቱ ኣብቲ ቀፅሉ ዘሎ ቅጥዒ ምልኡ፡፡ ካብቶም ናይቶም ኣብዚ ጊዜ ተመርሚሮም ሓዱሽ ሕማም ሽኮርያ አለኩም ዝተብሃሉ ሰባት ናይ ሕክምና ካርዶም ብምርኣይ ሙሉእ መረዳእታ ዝምላእ ኮይኑ ንሶም ከም አባል ናይዚ መፅናዕቲ ዘለዎም ግዴታ ናይ ሓበሬታ ኣተኣኻክባ ስነ ምግባር ከምኡውን ምስጢር ምሕላው ሙሉእ ብሙሉእ አብ ተግባር ምውዓሎም ምክትታል ከምኡ እውን ዝተመልአ መረዳእታ ናብ ቢሮ / ካርዲ ክፍሊ ምብፃሕ ጥራይ እዩ። አድላዩ ሓበሬታ ምስተአከበ ምስጋና ብምሃብ ናብ ካርዲ ክፍሊ ይምለሱ።

Annex II: Tigrigna version of Questionnaires

ተወሳኺ ፅሑፍ 2: ትግርኛ ስሪት ዝርዝር መፈተሺን መሕተትን
ክፍሊ ሓደ ሀ)፡- መረዳእታ ካብ ናይ ተመላላሲተሓካሚ ባሕሪ መዝገብ ምእካብ

አዲስ አበባ ዩኒቨርስቲ

ኮሌጅ ሳይንስ ጥዕና

ክፍሊ ትምህርቲ ሕብረተሰብ ጥዕና

አጠቃላሊ መምርሒ ንአከብትን ተቆፃፀርትን መረዳእታ

እዚ ካብ መስከረም11, 2005 ክሳብ 25 ነሓሰ 2010 ዓ/ም ሕክምናዊ ክንክን ካብ ናይ ዝረኸበ ተመላላሲ ተሓካሚ ባሕሪ መዝገብ ሕሙማት መረዳእታ ንምእካብ ዝሕግዝ ዝርዝር መፈተሺ ኮይኑ በቶም ዝምልከቶም ኣከብቲ መረዳእታ ንስኻ/ንስኺ ከም ኣካል ናይዚ መጽናዕቲ ጉጅለ ክትሕዞም ሓላፍነት ዘለካ ስነ-ምግባራዊ ጉዳያት ኣብ ምሕላው ምስጢራዊነትን ዘድሊ ሓበሬታ ምስ ወሰዱ ብቕልጡፍ ናብ ካርዲ ክፍሊ ኣረኪቡ፡ ንሰራሕተኛታት ቤት ጽሕፈት መዝገብ የቕንየልና ምባል።

ስም መረዳኢታ ኣካቢ: _____

ስም ሆስፒታል: _____

Name of hospital: _____

Data extraction sheet report form from the registry logbooks and each box is for 1000 count

Year of diagnosis	Patients visited												Age group	Count
	Urban						Rural							
	Men			Women			Men			Women				
	Count			Count			Count			Count				
2013/4													**18-29**	
2014/5													**30-39**	
2015/6													**40-49**	
2016/7													**50-59**	
2017/8													**≥ 60**	
Total														

Name of the data abstracter: _____ **Signature:** _____

Name of the data abstracter: _____ **Signature:** _____

ተወሳኺ ፅሑፍ 2: ትግርኛ ስሪት ዝርዝር መፈተሺን መሕተትን
ክፍሊ ሓደ ለ)፡- መረዳኢታ ካብ ናይ ተሓካሚ መዝገብ ምእካብ

አዲስ አበባ ዩኒቨርስቲ

ኮሌጅ ሳይንስ ጥዕና

ክፍሊ ትምህርቲ ሕብረተሰብ ጥዕና

አጠቃላሊ መምርሒ ንአከብትን ተቆፃፀርትን መረዳኢታ

ቀፂሉ ዘሎ ቐጥጢ ካብ መስከረም 1/2005 ክሳብ ነሓሰ, 2010 አብቲ ተመድብኹሙሉ ዘሎ ሆስፒታል ኣብ ናይ ዓበይቲ ተመላለስቲ ዉሽጣዊ ሕክምና ግልጋሎት ዝረኽቡ ተሓካምቲ በብዓመቱ ኣብቲ ቀፅሉ ዘሎ ቅጥጢ ምልኡ፡፡ ካብቶም ናይቶም ኣብዚ ጊዜ ተመርሚሮም ሓዱሽ ሕማም ሽኮርያ አለኩም ዝተብሃሉ ሰባት ናይ ሕክምና ካርዶም ብምርኣይ ሙሉእ መረዳኢታ ዝምላእ ኮይኑ ንሶም ከም አባል ናይዚ መፅናዕቲ ዘለዎም ግዴታ ናይ ሓበሬታ ኣተኣኻክባ ስነ ምግባር ከምኡውን ምስጢር ምሕላው ሙሉእ ብሙሉእ አብ ተግባር ምውዓሎም ምክትታል ከምኡ እውን ዝተመልአ መረዳኢታ ናብ ቢሮ / ካርዲ ክፍሊ ምብፃሕ ጥራይ እዩ። አድላዩ ሓበሬታ ምስተአከበ ምስጋና ብምሃብ ናብ ካርዲ ክፍሊ ይምለሱ።

ስም መረዳኢታ ኣካቢ _____

ስም ሆስፒታል _____

N	መፍለይ ሓበሬታ		
101	ካርዲ ቁፅሪ _____	105	Date of OPD visit_____
102	ዕድመ ተሓካማይ_____	106	ሕ/ሽኮርያ ዝተረጋገፀሉ ዓ/ምህረት_____
103	ፆታ ተሓካማይ: 1. ተባዕታይ 2. አንስታይ	107	ሪፈራል ተሃልዩ_____
104	መንበሪ ቦታ 1. ከተማ 2. ገጠር		
ኩነታት ሓደሽቲ ተሓከምቲ ሕማም ሽኮርያ ካብ ጥሪ 1/2005 ክሳብ ታሕሳስ 30/2010 ዓ/ም			
ሕቁ	ሕቶ	ሕቁ	ሕቶ
108	ተሓካማይ ሕክምና ዝደለየሉ ምክንያት 1. ብዙሕ ሽንቲ ምሸናው 2. ብዙሕ ማይ ምፅማእ 3. ብዙሕ ምግቢ ምብላዕ 4. ረስኒ 5. ናይ ርእሲ ምሕማም 6. ምድካም 7. ካሊእ(ይገለፅ)_____ 8. አይተገለፀን……66	109	አብ እዋን ሕማም ዝተፈለጠሉ ስዓት ኩነታት ቀንዲ ወሰንቲ ምልክታት እንታይ ይመስል ነይሩ 1. ድፍኢት ደም፡- systolic ____ Dyastolic_____ 2. ውቅዒት ልቢ 3. ናይ ረስኒ መጠን 4. ስርዓት አተነፋፍሳ መጠን 5. ክብደት ብኪ.ግ 6. ቁመት ብኪ.ግ_____ 7. አይተገለፀን……66
110	ካብ ቤተሰብኩም ሕማም ሽኮርያ ዘለዎ ሰብ ነይሩዶ ? 1. እወ 2. አይኮነን 3. አይተገለፀን……66	111	ሕቶ ቐፅሪ 110 መልሶም እወ እንተኮይኑ አየናይ 1. ኣቦ 2. ኣዶ 3. ሓው/ሓፍቲ 4. ኣቦ ሓጎ 5. እነምበይተ 6. ካሊእ ግለፅ_____ 7. አይተገለፀን……66
112	ዓይነት ሕማም ሽኮርያ 1. ሕማም ሽኮርያ ዓይነት ሓደ 2. ሕማም ሽኮርያ ዓይነት ክልተ 3. ምስ ጥንሲ ዝተተሓሓዘ ሕማም ሽኮርያ 4. ካሊእ ግለፅ_____	113	አብ እዋን ሕማም ዝተፈለጠሉ ላበራቶሪ ዝተረኽበ ውፅኢት እንታይ ነይሩ? 1. አብ እዋን ፆም ዝርከብ ናይ ደም ስኳር/አብ ዝኾነ እዋን ዝርከብ ናይ ደም ስኳር መጠን 2. ናይ ስብሒ መጠን

	5. አይተገለፀን…….66		ሀ. LDL_____ ለ. HDL_____ ሐ. Total trigly cerides_____ መ. Total cholestrol level_____ ረ. ካልኦት መዐቀንታት(ግለፅ)____ አይተገለፀን…….66
114	ተሓካማይ ተወሳኪ ሕማም አለዎ ዶ ? 1. እወ 2. አይኮነን 3. አይተገለፀን…….66	115	ንጥያቄ 207 መልሶም እወ እንተኾይኑ እንታይ ዓይነት ተደራቢ ሕማም እዩ ዘለዎም ? 1. ደም ድፍኢት 2. ሕማም ልቢ 3. ናይ ሽኮርያ ቁስሊ አብ እግረ 4. ሕማም ቲቢ 5. ኤች ኣይቪ ኤድስ 6. ካሊእ (ግለፅ) 7. አይተገለፀን…….66
116	ናይ ተሓካማይ ሕክምና እንታይ ነይሩ 1. ምኽሪ 2. ብኣፍ ዝውሰዱ ናይ ሽኮርያ መድሓኒት 3. ኢንሱሊን 4. ካሊእ 5. አይተገለፀን…….66	117	መዘኻኸሪ ፡-ካሊእ ፍልይ ዝበለ ሓበሬታ ካብቲ ካርዲ እንተሃልዩ ኣብዚ ቼክሊስት እዙይ ከፅሓፍ ግድን እዩ?

ርኢቶ ፡- ቼክሊስት ምስተመልአ ብኣካባይ ሓበሬታ ዝውሃብ ሪኢቶ(ዘይተመልአ፣ ግልፂ ዘይኮነ ሙሉእ ሓሳብ ወይ ከዓ ዘይንበብን ዘይምዕሩይ ሓሳብ እንተልዩ አብ ታሕቲ ሪፖርት ይግበሩ)

_____
_____
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<u>ኣካባይ ሓበሬታ</u> <u>ተቆፃሪ</u>

ፊርማ_____ ፊርማ _____

ክፍሊ ሰለስተ 3: ቃለ መሕትት 1

አብ ዞባታት ትግራይ ዝርከባ መንግስታዊ ናይ ዞባ ሆስፒታላት ክትትሎም ዝገብሩ ዓበይቲ ተሓከምቲ ሕማም ሽኮርያ ዝካየድ ቃለ መሕትት ኮይኑ ንሕማም ሽኮርያ ዘቃልው ኩነታት ንምፍላይ ዝግበር መፅናዕቲ እዩ:: ትግራይ; ኢትዮድያ

ዩንቨርሲቲ አዲስ አበባ ኮሌጅ ሳይንስ ጥዕና

ክፍሊ ትምህርቲ ሕብረተሰብ ጥዕና

ናይ ስምምዕነት ቅጥዒ

እዙይ ቃለ መሕተት ዝተሰናድአሉ ዋና ዕላማ አብ ናይ ዞባ ሆስፒታላት ዝሕከሙ ተሓከምቲ ሕማም ሽኮርያ ንሕማም ሽኮርያ ዘቃለዕዎም ኣቃለዕቲ ነገራት ንምፍላይ ዘድሃበ እዩ:: ትግራይ; ኢትዮድያ::

መብራህርሂ ሓሳባት

ዝሽበርካ ተሓታታይ

ከመይ ሓዲርካ/ውዒልካ

ሎማዕንቲ ምሳይ ዘተ ንምግባር ፍቃደኛ ስለዝኾንካ አቀዲመ ከመስግን ይፎቱ:: ስመይ _____ይብሃል :: ምስ አይተ ጌታቸው ገብረመድህን አባል ናይዚ መፅናዕቲ ዝሰርሕ ኮይነ እዙይ መፅናዕቲ አብ ዙርያ ተሓከምቲ ሕማም ሽኮርያ ዓይነት ክልተ ዘድሃበ አብ ከባቢኩም ዝካየድ ዘሎ መፅናዕቲ እዩ:: እዙይ መፅናዕቲ እዙይ ከም መመረቂ ፅሑፍ ናይ ፍልስፍና ዶክትሬት ዲግሪ አብ አዲስ አበባ ዩንቨርሲቲ ኮሌጅ ሳይንስ ጥዕና ዘገልግል እዩ:: አብዙይ መፅናዕቲ እዙይ ቃለ መሕትት ንክትገብሩ/ራ ብፅጫ ዝተመረፅኩም ምኻንክን ክገልፅ ይፎቱ:: ናይ ሎማዕንቲ መፅናዕቲ ዋና ዕላማ ቅድም ኢለን አብ ዝተጠቀሳ ጉዳያት ሓበሬታ ንምእካብ እዩ:: አብዚ መፅናዕቲ እዙይ ንምስታፍ ፍቃደኛ እንተኮይንክንኩም ውሕዳት ሕቶታት ን ሰላሳ ደቂቃ ዝአክል ከምኡውን ናይ አመጋግባ ኩነታትኩም/ክን ንምፍላጥ ዘለክን ቁመትን ክብደትን ክዕቅን እየ:: ብተወሳኺ ከዓ መሳርሕተይ 10 ሚሊ ሊትር ቬነሰ ደም ብምውሳድ ዘለኩም/ክን ናይ ስኳር መጠንን ናይ ስብሒ መጠንን ዓቂንና ውፅኢትኩም ክንነግረኩም ኢና:: እንድሕር ድኣ ሕማም ሽኮርን ካልኦት ተዛመድቲ ሕማማትን ተረኪብኩም ንምክርን ንሕክምናን ናብ ዝምልከቶም ላዕለዎት አካላት ክንልእኽኩም ኢና:: ብተወሳኺ እዙይ ቃለ መሕትት እዙይ ንካሊእ ዕላማ ዘይውዕልን ንዙይ መፅናዕቲ እዙይ ጥራሕ ዘገልግል ከምኡውን ዝህቡና መረዳእታ ንነዊሕ እዋን ተዓቂቡ ዘይፀንሕ ምኻኑ ክንገልፅ ንፎቱ:: ኮይኑ ግና አብዙይ መፅናዕቲ እዙይ ብምስታፎም ዝረክብዎ ምንም ዐይነት ክፍሊት ከምዘየለ ክንገልፅ ንፎቱ:: ስሞም አብዙይ ቃለመሕትት እዙይ ብምንም መልክዑ ዘይፅሓፍን ከምኡውን ምስዝህቡና መረዳእታ ከምዘይነተሓሕዞ ክነረጋግፅ ንደሊ:: አብዙይ ቃለ መሕትት እዙይ ምቾት ዘይሃበኩም ጥያቄ ናይዘይ ምምላስ ከምኡውን አብዝኮነ እዋን ናይ ምቁራፅ መሰለን/መሰሎም ዝተሓለወ እዩ:: ኮይኑ ግና ናቶም/ናተን ቅንዕና ዝተመልአ መልሲ ንሕቶትና ከምኡውን አብዙይ መፅናዕቲ ንምስታፍ ዘለኩም/ዘለክን ልዑል ድልየት እዙይን ብሕማም ሽኮር ዐይነት ክልተ ዝተጠቅዑ አብ ዙርያ ብውልቀን ብጉጅለ ዝውሃቡ ናይ ደም ስኳር መጠን ንምቁፅፃር ዝሕግዙ ትምህርታዊ ድጋፋት ንምንፅፃር አብ ከባቢኩም ዘሎ ሀዋህው ንምርዳእ ስለዝሕግዘናን እቲ ዘሎ ፀገም ንምፍታሕን ንምክልካልን ዘክእሉ መንገድታትን ስትራተጅታትን ንምሕንፃፅ ስለዘገልግል ተሳትፎኩም ከምዘይፍለየና ንኣምን:: አብዙይ መፅናዕቲ እዙይ ናይ ምስታፍ ናትኩም/ክን ድልየት ጥራሕ መሰረት ዝገበረ እዩ:: አብዙይ መፅናዕቲ እዙይ ብምስታፍኩም/ክን ወይ ብዘይምስታፍኩም/ክን ካብ መንግስታውን ዘይ መንግስታውን ትካላት ጥዕና ምስ ክረኽብኦ ተዳሊወን/ተዳሊዎም ዘለዎ ሕክምናዊ ግልጋሎት ፈፂሙ ኣይተሓሓዝን::

ሕጂ ክሓቶም ተዳሊወ አብ ዘለኩዎ ጉዳይ ዘይበርህልኩም/ክን ጉዳይ ተሃልዩ ንክብራህርህልክን ክትሓታኒ ትኽእላ ኢኽን:: አብ ከይዲ ዘይበርህልክን ጉዳይ እንተልዩ አብ ዝኮነ እዋን ጠጠው አቢልክን ክሓቱ/ታ ትኽእላ ኢኽን:: ዝበለፀ መብራህርሂ እንተደልዮን ዋና መተሓባበርቲ እዙይ መፅናዕቲ አይተ ጌታቸው ገብረመድህን ብስልኪ ቀፅሪ +251914 155081 ከምኡውን ፕሮፌሰር ፍቅሬ እንቁስላሴ +251912 45 97 07 ደዊሎም/ደዊለን ክሓቱ/ታ ይኽእላ እየን::

ውዕሊ ስምምዕነት ቅጥዒ

አብ ላዕሊ ካብ ዝተሓበረ መብራህርሂ ብምብጋስ አብዙይ መፅናዕቲ ንምስታፍ ፍቃደኛ ድዮም/ድየን?

እወ ☐ ቃለ መሕትት ይቀፅል

ቃለ መሕትት ዝተገበረላ ፊርማ

ስም _____ ፊርማ_____ ዕለት_____

አይኮነን ☐ ቃለ መሕትት ይቋረፅ

ቃለ መሕትት ዝተቋረፀላ ፊርማ

ስም _____ ፊርማ_____ ዕለት_____

ዋና ተቆፃፃሪ/አፅናዓይ ፊርማን ምልክትን

ስም _____ ፊርማ _____ ዕለት _____

ክፍሊ ሓደ: ማሕበራዊን ኢኮኖሚያውን ዝምልከቱ ሕቶታት

ወሰንቲ ናይ ስነ ህዝቢ ሕቶታት				
ቁ	**ሕቶ**	**መልሲ**		**ኮድ**
301	*ፆታ*	ተባዕታይ	1	C1
		አንስታይ	2	
302	ብኢትዮድያ አቆፃፅራ ዝተወለድሉ/ዳሉ ዓመተ ምህረት መእዝ እዩ? *ኣይፈልጥን 99*	_____/_____/_____ *ዝፈልጥዎ እንተኾይኖም ናብ C4 ዕለት ወርሒ ዓመት*		C2
303	ዕድሚአም/ኣን ክንደይ እዩ ?	*ዕድመ*	_____	C3
304	ሀይማኖትኩም/ክን እንታይ እዩ?	ኦርቶዶክስ ሙስሊም ፕሮቴስታንት ካቶሊክ ካሊእ (ይገለፅ)_____ ፍቃደኛ አይኮነን	1 2 3 4 5 88	C4
305	ብሄርኩም/ክን እንታይ እዩ ?	ትግራዋይ/ቲ አምሓራይ/ይቲ ኢሮብ አፋር ካሊእ ይገለፅ_____ ፍቃደኛ አይኮነን	1 2 3 4 5 88	C5
306	ኩነታት ሓዳርኩም/ክን እንታይ ይመስል?	*ዘይተመርዐወ/ት* አብ ሓዳር *ዘለ/ላ* ዝተፋትሐ/ት በዓል ገዝኡላ ዝሞተ/ታ ፍቃደኛ አይኮነን	1 2 3 4 88	C6
307	ዝልዓለ ናይ ትምህርቲ ደረጅኦም/ኣን ክንደይ እዩ/ያ?	*ዘይተምሃረ/ት* ካብ $1^{ይ}$ ክሳብ $4^{ይ}$ ካብ $5^{ይ}$-$8^{ይ}$ ካብ $9^{ይ}$-$10^{ይ}$ ካብ 11-12 ኮሌጅ ዩንቨርሲቲ ካልኣይ ዲግሪን ልዕሊኡን ፍቃደኛ አይኮንኩን	1 2 3 4 5 6 7 88	C7
308	ካብዞም ቀሊሎም ዝተጠቀሱ መማረፂታት አብ ዝሓለፉ 12 አዋርሕ ዝሰራሕኩምዎ ቀንዲ ስራሕ ዝገልፅ አየናይ እዩ?	*መንግስቲ ሰራሕተኛ* *ዘይመንግስታዊ ሰራሕተኛ* ናይ ግሊ ሰራሕተኛ ሓረስታይ ተምሃራይ ናይ ገዛ ስራሕ	1 2 3 4 5	C8

		ስራሕ አልቦ ጡረተኛ ሙሉእ እዋን አብ ገዛ ፍቃደኛ አይኮንኩን	6 7 8 9 88	
309	ዝሓለፈ ዓመት ከም መበገሲ ብምውሳድ ናይዚ ገዛ ማእኸላይ እቶት ክንደይ ነይሩ?	ብሰሙን_____ወይም ብ ወርሒ_____ወይም ብዓመት _____ ፍቃደኛ አይኮንኩን	Go to C10 88	C9
310	መንበሪ ቦታኹም አበይ እዩ?	ገጠር ከተማ ፍቃደኛ አይኮንኩን	1 2 88	C10
ታሪኽ ሕዱር ሕማማት				
311	ናይ ደም ጸቕጥኻ ከም ዝለዓለ ተነግርካዶ ይፈልጥ ብዶክተርዶ?	1. እወ 2. አይኮነን 3. አይፈልጥን	**እወ እንተኾይኑ ናብ C11**	**C11**
312	ኣብ C11 እወ እንተኾይኑ መድሓኒት ትኣዝሁልኻ ዶ?	4. እወ 5. አይኮነን 6. አይፈልጥን	**እወ**	
313	ናይ ስብሒ መጠንካ ከም ዝለዓለ ተነግርካዶ ይፈልጥ ብዶክተርዶ?	1. እወ 2. አይኮነን 3. አይፈልጥን	**እወ እንተኾይኑ ናብ C13**	**C12**
314	ኣብ C13 እወ እንተኾይኑ መድሓኒት ትኣዝሁልኻ ዶ?	4. እወ 5. አይኮነን 6. አይፈልጥን	**እወ እንተኾይኑ ናብ C14**	
313	ብ ሕማም ሽኮርያ ዝተትሓዘ ኣብ ቤተሰብኩም ነይሩ ይፈልጥ ዶ ?	7. እወ 8. አይኮነን 9. አይፈልጥን	**እወ እንተኾይኑ ናብ C14**	**C13**
314	መልሲ ሕቶ ቁፅሪ C12 እወ እንተኾይኑ አየናይ ቤተሰብኩም/ ቤተሰብክን እዩ?	8. አቦ 1. አዶ 2. ሓው/ሓፍቲ 3. አቦ ሕጎ 4. እነምበይተ 5. ካሊእ/ይገለፅ_____ 6. ፍቃደኛ አይኮንኩን	**88**	**C14**
ክፍሊ ክልተ: ኩነታት ውልቀ ባህሪ ዝምልከት				
ቁ	**ሕቶ**	**መልሲ**		**ኮድ**
315	ኣብዚ ሐዚ እዋን ቱምባኾ ዝሓዙ ነገራት ተትክኽ ዶ ከምኒ ሲጋራ: ብወረቀት ተጠቕሊሉ ዝስተ ቆፅሊ ቱምባኾ: ቱቦ ብዝመስል መሳርሒ ተሓኒዝካ ዝስተ ቱምባኾ?	1. እወ 2. አይኮነን		T1
316	ቱምባኾ ዝሓዙ ነገራት በብመዓልቱ ትጥቀም ዶ?	1. እወ 2. አይኮነን, አይኮነን እንተኾይኑ ናብ		T2

		A1 ቀፅል	
317	ሕቶ ቁፅሪ 316 መልሲ እወ እንተኾይኑ ብ ማእኸላይ ክንደይ ሲጋራ አብ መዓልቲ ተትክኽ?	1. 1-9 ሲጋራ አብ መዓልቲ	T3a
		2. 10-20 ሲጋራ አብ መዓልቲ	T3b
		3. >20 ሲጋራ አብ መዓልቲ	T3c
318	በብመዓልቱ ሲጋራ ምትካኽ አብ ዝጀመርካሉ እዋን ዕድሜኻ ክንደይ ነይሩ?	ዕድመ ብዓመት_____ ኣይፈልጦን_____	T4
319	ክንደይ እዋን ከምዝገበረ ክተሰታውሶ ዶ ትኽእል?	ብዓመት_____ ብወርሒ____ ብ ሰሙን_____	T5a T5b T5c
መጠን አወሳስዳ አልኮል			
ቁ	**ሕቶ**	**መልሲ**	**ኮድ**
320	አልኮላዊ ትሕዝቶ ዘለዎም መስተታት ከምኒ ቢራ: ወይን : ዊስኪ: አረቂ: ስዋ: ሜስ ወይም ካልኦት ሰቲኻ ትፈልጥ ዶ ?	1. እወ 1 2. ኣይኮነን; መልሲ ኣይኮነን እንተኮይኑ ናብ D1 ቀፅል	**A1**
321	አብ ዝሓለፉ ሰላሳ መዓልቲታት ናይ አልኮል ትሕዝቶ ዘለዎም መስተታት ሰቲኻ ዶ ትፈልጥ ዶ ?	1. እወ 2. ኣይኮነን	**A2**
321	ሕቶ ቁፅሪ 321 መልሲ እወ እንተኾይኑ ብ ማእኸላይ ክንደይ ብርጭቆ: ጠርሙስ ወይም ካሊእ ተመሳሳሊ ናይ አልኮል መስተ ይሰትዮ?	1. Daily 2. Three times a week 3. Once a week 4. _____/week 5. Don't know ……99 6. Refused…… 88	**A3**
322	አብ ዝሓለፉ ሰላሳ መዓልቲታት ብማእኸላይ ክንደይ ዝአክል ናይ መስተ ብርጭቆ አብ ሓደ ናይ መስተ እዋን ይሰትዩ?	ቁፅሪ_____ ኣይፈለጦን……. 99	**A4**
323	አብ ዝሓለፉ ሰላሳ መዓልቲታት አብ ሓደ ናይ መስተ ሰዓት ዝበዝሐ ዝሰተይዎ መጠን አልኮል ብ ብርጭቆ: ጠርሙስ ወይም ካሊእ ተመሳሳሊ ነገር ኩሉም ዐይነታት መስተ ሓዊስካ ክንደይ እዩ?	ዝበዝሐ ቁፅሪ_____ ኣይፈልጦን ……99 ፍቃደኛ ኣይኮንኩን ……88	**A5**
ዋና ሐሳብ: ስነ አመጋግባ			
ቀፃሊ ዘለዉ ሕቶታት መብዛሕቲኡ ግዜ ዝምገብዎም ምግቢታት: ኣሕምልትን ፍራምረን ዝምልከት እዩ:: ናይ አመጋግባ ካርዲ አለኒ እዙይ ካርዲ እዙይ መብዛሕቲኡ ገዜ አብ ከባቢኩም እትምገብዎም ምግብታት ዘርኢ እዩ:: ሕድሕድ ምሰሊ መጠን አመጋግባኩም ዘመልክት እዩ:: ንሕድ ሕድ ሕቶ መልሲ አብ ዝህብሉ እዋን ካብ ዝሓለፈ ዓመት ወካላይ ክኾን ዝኽእል ሰሙን ከም አብነት ይውሰዱ::			
ቁ	**ሕቶ**	**መልሲ**	**ኮድ**
324	አየናይ ምግቢ ብተኪታታሊ ኩልግዜ ይምገብዎ?	1. እንጀራ ጣፍ/መሸላ/ስገም' 2. 'እንጀራ/ሕምባሻ/ባኒ/ቂጫ ስርናይ 3. ፃዕዳ ሩዝ	

		4. ፓስታ 5. ቀይሕ ስጋ 6. ስብሒ ዝበዝሖ ምግቢ(ጠስሚ) 7. ዝተዓሸጉ ምግብታት 8. ካሊእ (ይገለፅ) _____	*D1*
326	አብ ሰሙን ንክንደይ መዓልቲታት ፍራምረ ይምገቡ?	በዝሒ መዓልቲ_____ ; *ዜሮ እንተኾይኑ ናብ D5* ኣይፈልጥን 99	*D3*
327	አብ ሰሙን ካብ ዘለዉ መዓልቲታት ውሽጢ እቲ ሓደ አብ ክንደይ ናይ ምግቢ እዋናት ፍራምረ ተመጊቦም?	በዝሒ_____ ኣይፈልጦን 99	D4
328	አብ ሰሙን ክንደይ ጊዜ ንክንደይ መዓልቲታት አሕምልቲ ተመጊቦም?	በዝሒ መዓልቲ_____ ; *ዜሮ እንተኾይኑ ናብ D7* ኣይፈልጥን 99	D5
329	አብ ሰሙን ካብ ዘለዉ መዓልቲታት ውሽጢ እቲ ሓደ አብ ክንደይ ናይ ምግቢ እዋናት አሕምልቲ ተመጊቦም?	በዝሒ_____ ኣይፈልጦን 99	D6
330	አየናይ ልሱሉስ መስተ ወይም መነቃቐሒ ብበዝሒ ይጥቀሙ?	1. ቡና 2. ሻይ 3. ኮካ ኮላ 4. ሚሪንዳ 5. ካሊእ_____	D7
331	አብ ሓደ ሰሙን ንክንደይ መዓልቲታት እዞም መስተታት ይሰትዩ?	1. ቡና _____ 2. ሻይ_____ 3. ኮካ ኮላ_____ 4. ሚሪንዳ _____	D8
332	እዞም ዝተጠቀሱ መስተታት አብ ሓደ መዓልቲ ክንደይ ኩባያ ይሰትዩ?	1. ቡና _____ 2. ሻይ_____ 3. ኮካ ኮላ_____ 4. ሚሪንዳ _____	D9
አካላዊ ምንቅስቓስ			
ቀሚለ አብ ሓደ ዝተወሰነ ሰሙን ዝተፈላለዩ አካላዊ ምንቅስቓሳት ንምግባር እተሕልፎ ግዜ ዝምልከት ክሓተካ እየ:: በይዝአም ዋላኳ ንጡፍ ዝኾነ ስፖርታዊ ምንቅስቓስ አይግበሩ ቀሚሎም ዘለው ሕቶታት ብምምላስ ይተሓባበሩና:: ዝተፈላለዩ ዐይነታት ምንቅስቓሳት ክካተቱ ክኽእሉ አለዎም:: ዝተፈላለዩ ንጥፈታት አብ ገዛ ውሽጥን መረባን፣ካብ ቦታ ናብ ቦታ ንምንቅስቃስ /መጓዓዝያ መንገድታት/ ፣መዘናግዒ መንገዲታት አብ እዋን መዘናግዒ እዋን ከምኡውን ስፖርታዊ እንቅስቃሴታት:: እዙይ መእተዊ ሓሳብ ብምንም መልክዑ ክይተነበበ ክሓልፍ የብሉን::			
ቁ	**ሕቶ**	**መልሲ**	**ኮድ**
	ምንቅስቓስ አብ እዋን ስራሕ		
333	ዝሰርሕዎ ዐይነት ስራሕ ከቢድ ጉልበትን እንቅስቃሴን ዝሓትት ኮይኑ ስርዓተ ምትንፋስን ውቅዒት ልብን ይውስኽ ዶ? (ን አብነት ከም ምሽካምን ምልዓልን፣ ምኹዓት፣ ዐበይቲ አቕሑ ወይም ናይ ኮንስትራክሽን ስራሕቲ) ብውሕዱ ን ሰላሳ ደቂቃ ዝአክል ብተኸታታሊ?	**እወ 1** **ኣይኮነን 2** **ኣይኮነን እንተኾይኑ ናብ P4**	**P1**
334	አብ ሓደ ሰሙን ውሽጢ ንክንደይ መዓልቲታት እዩ ፅዕቅ ዝበለ ምንቅስቓስ ዘለዎ መዓልታዊ ስራሕ ዝሰርሑ?	በዝሒ መዓልቲ_____	**P2**

335	አብ ሓደ መዓልቲ ንክንደይ ጊዜ ዝአክል እዩ ፅዕቅ ዝበለ አካላዊ ምንቅስቓስ ዘለዎ ስራሕ ዝሰርሕሉ?	ሰዓት : ደቂቃ___:___	**P3**
336	ስርሑም ማእከላይ ምንቅስቓስ ብምፍጣር ንኡሽተይ ወሰኽ አብ ምትንፋስ ወይከዓ ውቅዒት ልቢ የስዕብ ዶ ከም እኒ ፈጣን ናይ እግሪ ጉዕዞ ወይም ቀለልቲ ነገራት ምሸካም ብውሕዱ ን ሰላሳ ደቂቃ	1. እወ **2.** አይኮነን;አይኮነን እንተኮይኑ ናብ P7	**P4**
337	አብ ሰሙን ንክንደይ መዓልቲታት ማእከላይ እንቅስቃሴ ዝሓቱ ስራሕቲ ብመልክዕ መደበኛ ስራሕ ይሰርሑ?	በዝሒ መዓልቲ _____	**P5**
338	አብ ሓደ መዓልቲ ንክንደይ ዝአክል ግዜ ማእከላይ ጉልበት ዝሓቱ ስራሕቲ ብምስራሕ አብ ስራሕ የሕልፉ?	ሰዓት : ደቂቃ _____: _____	**P6**
ካብ ቦታ ናብ ቦታ ምግዑዛዝ			
ቀሊሎም ዘለው ሕቶታት ቅድም ኩበል ዝተጠቀሱ አብ እዋን ስራሕ እትገብርዎም ምንቅስቃሳት አየጠቃልልን:: ሕጂ ቀጺለ ካብ ቦታ ናብ ቦታ ንምንቅስቃስ እትጥቀምሎም መንገድታት ክሓቶም እየ:: ንአብነት ሽቀጥ ንምሽቃጥ ናብ ዕዳጋ፣ ናብ ቤተ እምነት ዝግዓዝሎም መንገድታት ክሓቶም እየ:: (ካልኦት አብነታት ከም ኣድላይነቱ ምጥቃስ ይከኣል እዩ)			
ቁ	**ሕቶ**	**መልሲ**	**ኮድ**
339	ካብ ቦታ ናብ ቦታ ንምንቅስቃስ ብ እግሪ ምጉዓዝ ወይ ከዓ ሳይክል እንተንኣሰ ን 10 ደቂቃ ይጥቀሙዶ?	1. እወ 2. አይኮነን; አይኮነን እንተኮይኑ ናብ P10	**P7**
340	አብ ሓደ ሰሙን ን ክንደይ መዓልቲታት ብእግሮም ወይ ከዓ ሳይክል ብምግናሕ እንተንኣሰ ን ሰላሳ ደቂቃ ብተከታታሊ ካብ ቦታ ናብ ቦታ ይግዓዙ?	በዝሒ መዓልቲ _____	**P8**
341	አብ ሓደ መዓልቲ ንክንደይ ግዜ እዮም ብእግሪ ብምካድ ወይ ከዓ ሳይክል ብምግናሕ ካብ ቦታ ናብ ቦታ ንምግዓዝ ግዜኦም ዘሕልፉ?	ሰዓት: ደቂቃ ___: ___.	**P9**
መዘናግዒ ምንቅስቓሳት			
ቀሊሎም ዘለው ሕቶታት ብመልክዕ ስራሕን መጓዓዝያን ዝተሓተትኩምዎ ሕቶታት አየጠቃልልን:: ቀሊለ ብዛዕባ ስፖርት ን ንመዘናግዒነት እንጥቀመሎም ዐይነታት ስፖርትን ጥዕናን ዘጠቃለለ እዩ::			
342	እንተንኣሰ ን 30 ደቂቃ ዝአክል ዐብይ ጉልበት ዝሓቱ እስፖርታዊን ጥዕናዊን እንቅስቃሴታት ወይም መዘናግዒ ስፖርትታት ብምሰራሕ አብ አተነፋፍሳ ወይከዓ አብ ውቅዒት ልቢ ከም ምጉያይ ወይ ከዓ እግሪ ኩዕሾ ይሰርሕዶ?	1. እወ 2. አይኮነን; አይኮነን እንተኮይኑ ናብ P13	**P10**
343	አብ ሓደ ሰሙን ንክንደይ መዓልቲታት ዐብይቲ ጉልበት ዝሓቱ ናይ ስፖርትን (መዘናግዕን) ንጥዕና ዝግበሩ እንቅስቃሴታት ይሰርሑ?	በዝሒ መዓልቲ_____	**P11**
344	አብ ሓደ መዓልቲ ንክንደይ ግዜ እዮም ዐበይቲ ጉልበት ከውፅኡ ዝክእሉ ናይ ስፖርትን መዘናግዕን ንጥዕና ዝግበሩ እንቅስቃሴታት ዝሰርሑ?	ሰዓት: ደቂቃ ___: __	**P12**
ትሑት ምንቅስቃስ ሰውነት ዘለዎም ስራሕቲ			
ቀሊሎም ዘለው ስራሕቲ ብዛዕባ ምቅማጥ ወይ ከዓ ጋደም ኢልካ ምቅማጥ አብ ስራሕ ፣አብ ገዛ፣ ካብ ቦታ ናብ ቦታ አብ ዝግዓዝሉ እዋን ወይም ምስ የዕሩኽ ዝሓልፍ ግዜ (አብ ወንበር፣ ምስ የዕሩኽ ከፍ ምባል፣ አብ መኪና ምጉዓዝ፣ አብ ባቡር፣ ምንባብ፣ ካርታ ምፅዋት፣ ቴሌቪዥን ምክትታል ነገር ግን ደቂሶም ዘሕልፍዎ ሰዓት አይምልከትን::			
345	ንክንደይ ሰዓት ዝአክል አብ ሓደ መዓልቲ ኮፍ አሎም ወይ ከዓ ጋደም ኢሎም ግዜኦም የሕልፉ?	ሰዓት: ደቂቃ ___: ___	**P13**
ክፍሊ ሰለስተ: አካላዊ ኩነታት መዐቀኒ ረቋሒታት			
CORE: Blood Pressure			

ቁ	ሕቶ	መልሲ	ኮድ
346	ናይ ሓታታይ ኮድ	_____	**M1**
347	አንበብ	Systolic_____mmHg	M2a
		Diastolic_____mmHg	M2b
348	አብ ዝሓለፉ ክልተ ሰሙናት ናይ ፀቅጢ ደሞም ብምውሳኹ ብ ሓኪም ወይም ብናይ ጥዕና በዓል ሙያ ትእዛዝ መድሓኒት ወሲዶም ዶ ይፈልጡ?	1. እወ 2. ኣይኮነን	M3
COዋና : ቁምትን ክብደትን			
349	ናይ ተሳታፈይ ቁመት ብ ሴሜ ይፅሓፉ? ካብ ሓደ ደሲማል ብዘይዘልል	_____ሴሜ	M4
350	ናይ ተሳታፋይ ክብደት ብኪሎ ግራም ፀሓፍ? ካብ ሓደ ደሲማል ብዘይዘልል መልክዑ .	_____ኪግ	M5
351	ናይ ተሳታፈይ ናይ ሽምጢ ዙርያ መጠን ብሴ.ሜ ክንደይ እዩ ካብ ሓደ ደሲማል ብዘይዘልል መልክ	_____ሴሜ	M6
352	ናይ ተሳታፋይ ናይ ጎድኒ (ዳሌ) ዙርያ መጠን ብ ሴ.ሜ ክንደይ እዩ?ካብ ሓደ ደሲማል ብዘይዘልል መልክዑ?	_____ሴሜ	M7
ክፍሊ IV: ባዮ ኬሚካል መዐቀኒታት			
ዋና: ናይ ደም ውሽጢ ስኳር መጠን			
353	አብ ዝሓለፈ 12 ሰዓት ውሽጢ ካብ ማይ ወፃኢ ካሊእ ዝብላዕ ወይም ዝስተ ነገር ወሲድካ ዶ ነይርካ? ተሳታፋይ ክፀውም ክኽእል ግዴታ እዩ	1. እወ 2. ኣይኮነን	B1
354	ናይ ደም ምርመራ ዝተወሰደሉ ሰዓት መአዝ እዩ (አብ 24 ሰዓት ውሽጢ) ዓቀን ዝተጀመረሉ ሰዓት ይፅሓፉ	ሰዓት: _____:_____ ደቂቃ ሰዓት ደቂቃ	B2
355	ምግቢ ከይበላዕካ ዝውሰድ ናይ ደም መጠን ብ መልክዕ mmol/l or mg/dl] ይፅሓፉ: እቲ ተሳታፋይ ምንም ምግቢ ከምዘይወሰደ ደጊሞም የረጋግጹ.	mmol/l_____ *mg/dl*_____	B3
356	A1C	_____%	B4
357	ናይ ደሞም ስኳር መጠን ስለዝወሰከ ሎማዕንቲ ብ ሓኪም ወይ ካዓ ብ በዓል ሙያ ጥዕና ዝተአዘዘሎም ኢንሱሊን ወይ ከዓ መድሓኒት ወሲዶም ዶ?	1. እወ 2. ኣይኮነን	B5
ናይ ስብሒ መጠን አብ ደም			
358	በዝሒ ጠቅላላ ኮሌስትሮል [ብ: mmol/l or mg/dl] ይፅሓፉ	mmol/l_____ mg/dl_____	B6
359	አብ ዝሓለፉ ክልተ ሰሙናት ናይ ኮሌስትሮል መጠኖም ስለ ዝልዓለ ብሓኪም ወይ ከዓ ናይ ጥዕና በዓል ሙያ ዝተአዘዘ መድሓኒት ወሲዶም ዶ ነይሮም? ትክክለኛ መልሲ ይምረፁ	1. እወ 2. ኣይኮነን	B7
360	መጠን Triglycerides [ብ mmol/l or mg/dl] ይፅሓፍ?	mmol/l_____ mg/dl_____	B8
361	መጠን HDL Cholesterol [ብ : Mmol/L Or Mg/Dl] ይፅሓፍ?.	mmol/l_____ mg/dl_____	B9
362	መጠን LDL Cholesterol [ብ : Mmol/L Or Mg/Dl] ይፅሓፍ?.	mmol/l_____	

		mg/dl_____	

ንዝሃቡና ግዜ ነመስግን!

ክፍሊ ሰለስተ፡- **ካብ ናይ ተሓካሚ ካርዲ መረዳታ መእከቢ ቅጥዒ**
ዩኒቨርስቲ አዲስ አበባ
ኮሌጅ ሳይንስ ጥዕና
ክፍሊ ትምህርቲ ሕብረተሰብ ጥዕና
ሓፈሻዊ መምርሒ ንኣከብቲ ሓበሬታን ተቆፃፀርትን
እዙይ ቼክሊስት እዙይ ንህፁፅ ሕክምና ግልጋሎት ብሰንኪ ምውሳኽ ናይደም ስካር መጠን ናብ ጥዕና ትካል ዝኣተዉ ግለሰባት ካርዶም ብምርኣይ ብ ነርስ ወይ ከዓ ብ ጥዕና መኮነን ዝምላእ እዩ:: ንሶም/ንሰን ከም ኣባል እዙይ ምፅናዕቲ እዙይ ሕግታት ስነ ምግባር መፅናዕቲን ምስጢር ምሕላውን ሙሉእ ብ ሙሉእ ኣብ ታግባር እናዉዓሉ ምካኖም ምክትታል ከምኡዉን ዝተመልኡ ካርድታት ናብ ካርዲ ክፍሊ ወድያውን ንክበፅሕ ምግባርን ንሰራሕተኛታት ካርዲ ክፍሊ ምምስጋንን እዩ;:

ስም ነርስ ወይ ከዓ ጥዕና መኮነን _____

ስም ሆስፒታል _____

N	መፍለይ ሓበሬታ		
201	ካርዲ ቁፅሪ _____	205	ምስ ሕ/ሽኮርያ ዝፀንሓሉ ዓመት_____
202	ዕድመ ተሓካማይ_____	206	ናብ ሆስፒታል ዝኣተወሉ ዕለት_____
203	ፆታ ተሓካማይ: 1. ተባዕታይ 2. አንስታይ	207	ካብ ሆስፒታል ዝወፅሉ ዕለት _____
204	መንበሪ ቦታ 1) ከተማ 2) ገጠር	208	ሪፈራል ተሃልዩ_____
ኩነታት ድንገተኛ ምዉሳኽ ናይ ስኳር መጠን ንዓበይቲ ተሓከምቲ ካብ 23/4/2008 ክሳብ 22/4//2010 ዓ/ም			
ሕቁ	ሕቶ	ሕቁ	ሕቶ
209	ዓይነት ሕማም ሽኮርያ 1. ሕማም ሽኮርያ ዓይነት ሓደ 2. ሕማም ሽኮርያ ዓይነት ክልተ 3. ምስ ጥንሲ ዝተትሓሓዘ ሕማም ሽኮርያ 4. ካሊእ(ምግላፅ)_____ 5. ኣይተገለፀን…….66	210	ናይ ተሓካማይ መድሓኒት 1. ኢንሱሊን ዓይነት ኢንሱሊን_____ 2. ብ ኣፍ ዝውሰድ መድሓኒት ዓይነት ብ ኣፍ ዝውሰድ መድሓኒት ____ 3. ኣይተገለፀን…….66
210	ዓይነት ድንገተኛ ምዉሳኽ ናይ ስኳር መጠን 1. Diabetic keto acidosis 2. Hyperosmolar hyperglycemic state 3. ካሊእ(ምግላፅ)_____ 4. ኣይተገለፀን…….66	211	ንክንደይ ዝኣክል ተሓካማይ ኣብ ሆስፒታል ደቂሶም 1. ንመጀመርታ ግዘ 2. ንካልኣይ ግዘ 3. ንሳለሳይግዘ 4. ንራብዓይን ልዕሊኡን 5. ኣይተገለፀን…….66
212	ን ድንገተኛ ምዉሳክ ሕማም ሽኮርያ ምክንያት ዝኮነ እንታይ እዩ? 1. ረክሲ 2. መድሓኒት በኣናባቡ ዘይምክትታል 3. ሓድሽ ሕማም ሽኮርያ ስለዝፈለጠ 4. መድሓኒት ዘይ ምህላው 5. መውቃዕቲ 6. ሃይማኖታዉን ባህላውን እምነት 7. ካሊእ(ምግላፅ)_____ 8. ኣይተገለፀን…….66	213	ንጥያቄ ቁፅሪ 212 መልሱ ረክሲ እንተኮይኑ እንታይ ዓይነት ረክሲ? 1. ናይ ላዕለዋይ መተንፈሲ ኣካላት ረኽሲ 2. ናይ ሳንባ ምቹ 3. መላእ ሰውነት ዝተሰራጨወ እንፈኽሽን 4. ናይ ሕማም ቲቢ 5. ኢንሱሉን ኣብ ዝውግኣሉ ቦታ ኢንፈክሽን 6. ናይ ሽኮሪያ ኣብ እግሪ ዝወፅእ ቁስሊ 7. ናይ ኣፍ ኢንፈክሽን 8. ናይ ዓፂሚ ኢንፈክሽን 9. ካሊእ(ምግላፅ)_____ 10. /ኣይተገለፀን…….66
214	ጥያቄ ቁፅሪ 212 መልሲ መድሓኒት ብኣግባቡ ዘይምክትታልእንተኮይኑ ምክንያቱ እንታይ እዩ፡ 1. መዳሓኒት ምቁራፅ	215	እንታይ ዓይነት ምልክታት እዮም እቲ ተሓካማይ ዝነበሮ 1. ንዓቕብ ምባል 2. ሕማም ካብዲ

	ምክንያት መድሓኒት ምቁራፅ--------- 1. መድሓኒት ሙሉእ ብሙሉእ ዘይምውሳድ መድሓኒት ከይተወሰደ ዝተረፈሉ ምክንያት---------- ------		3. ብዙሑ ምሻን 4. ማይ ምፅማእ 5. ምትንፋስ ምሕፃር 6. ውነ ምሳሓት 7. ረስኒ ምውሳኽ 8. ካሊእ /ይጋለፅ/---------- 9. አይተገለፀን……66
216	ናይቲ ተሓካማይ ቀንዲ ምልክታት ጥዕና እንታይ ይመስል? 1. ክብደት ተሓካማይ ብኪ.ግ 2. ቁመት ተሓካማይ ብ.ሜ 3. ፀቕጢ ደም ተሓካማይ . SBP__DBP__ 4. ረስኒ ምውሳኽ 5. መጠን አተነፋፍሳ 6. ውቅዒት ልቢ 7. ካሊእ /ይጋለፅ/---------- 8. አይተገለፀን……66	217	ናይ ሆስፕታል ኣብ ዝኣተወሉ ስዓት እንታይ ዓይነት ላብራቶሪ ኣስሪሑ ነይሩ 3. FBS /RBS /A1C / ሓደ ምረፅ_____ 4. መጠን ስብሒ_____ e.LDL_____ f. HDL_____ g.total triglyceride_____ h. total cholesterol level_____ 5. ኤሌክትሮላይት ኣብ ሰውነተ_____ a. b. serum ceratinize_____ b. serum potassium_____ c. serum urea_____ d. serum chloride_____ e. serum sodium_____ f. g. others/ ግፅ/_____
218	ንድንገታዊ ወሰኽ ሽኮር እቲ ተሓካማይ ዝወሰዶ መድሓኒት እንታይ ነይሩ? 1.ኢንሱሉን ሀ. ሬጉላር ኢንሱሉን ለ. ሌንት ኢንሱሉን ሐ. ሚክሲያ ኢንሱሉን መ. ካሊእ /ግልፅ/ 2. ብኣፍ ዝውሰድ መድሓኒት ዓይነት ብኣፍ ዝውሰድ መድሓኒት ------- 3. ኢንሱሊንን ካልኦት ብኣፍ ዝውሰዱ መድሓኒታት ብሓባር ዓይነት ኢንሱሊን ---------- ዓይነት ብኣፍ ዝውሰዱ መድሓኒት ------	219	ኣየናይ ዓይነት ብደም ሱር ዝወሰድ ፈሳሲ ወሲዱ መጠኑን ብሳዓት ወይ ካዓ ብደቒቓ 1. ኖርማል ሳላይን --ብሊትር-- ggt/min 2. ሪንገር ላክቴት --ብሊትር--ggt/min 3. D5W --ብሊትር---ggt/min 4. DNS ---ብሊትር--ggt/min
220	እቲ ተሓካመይ ተወሳኺ ሕማም ኣለዎዶ 1. እወ 2. ኣይኮነ	221	ጥያቄ ቁፅሪ 315 መልሲ እወ እንተኾይኑ እንታይ ዓይነት ተደራቢ ሕማም እዩ፡፡ 1. ምስ ሽኮርያ ዘለዎ 2. ድፊኢት ደም 3. ሕማም ልቢ 4. ኣብ እግሪ ዝወፅእቁስሊ 5. ሕማም ቲቢ 6. ኤች ኣይቪ 7. 13. ካሊእ /ግለፅ/----------
222	ናይቲ ተሓካማይ ውፅኢት እንታይ ነይሩ 1. ድሒኑን ለውጢ ኣምጺኡ ወፂኡ 2. ብሞት ተፈልዩ	223	መዘኻኸሪ ፡-ካሊእ ፍልይ ዝበለ ሓበሬታ ካብቲ ካርዲ እንተሃልዩ ኣብዚ ቼክሊስት እዙይ ክፅሓፍ ግድን እዩ?

ርኢቶ ፡- ቼክሊስት ምስተመልአ ብኣካባይ ሓበሬታ ዝውሃብ ሪኢቶ(ዘይተመልአ፣ ግልፂ ዘይኮነ ሙሉእ ሓሳብ ወይ ከዓ ዘይንበብን ዘይምዕሩይ ሓሳብ እንተልዩ አብ ታሕቲ ሪፖርት ይግበሩ)

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<u>ኣካባይ ሓበሬታ</u>
ፊርማ_____

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ፊርማ _____

Annex III: Original papers and manuscripts

Orginal Paper -One

Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy Dovepress
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Open Access Full Text Article ORIGINAL RESEARCH

Urban-Rural Differences in the Trends of Type 1 and Type 2 Diabetes Among Adults Who Received Medical Treatment from Public Hospitals in Resource-Poor Community Tigray, Ethiopia

This article was published in the following Dove Press journal:
Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

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†Fikre Enqueselassie passed away on October 28, 2019

Objective: This study carried out to describe urban-rural differences in the trend of type 1 and type 2 diabetes among adults who have received medical treatment from public hospitals over the last five years.

Methods: The trends of adult diabetes assessed from September 1, 2013, to August 31, 2018, using hospital-based retrospective medical records of 299,806 adult patients in the adult medical outpatient and emergency units. Data were collected using a uniform data abstraction format. An extended Mantel-Haenszel chi-square test of the linear trend used to examine the trend over time.

Results: Of the total 299,806 adult patients, 3056 (1.02% (95% CI: 0.98–1.06)) patients were confirmed diabetes patients. The overall trend in the proportion of diabetes had increased from 6.8 to 14.3 per 1000 adult patients. The trend of type 1 diabetes increased for both urban from 1.0 to 2.2 per 1000 adult urban residents and rural from 1.2 to 2.6 per 1000 adult rural residents, with statistically a significant increase (χ^2= 9.1, P=0.002) and (χ^2=17.8, P<0.001) for linear trend, respectively. The trend of type 2 diabetes increased for both urban from 6.9 to 14.0 per 1000 adult urban residents and rural from 4.0 to 9.5 per 1000 adult rural residents, with a statistically significant increase (χ^2=68.4, P<0.001) and (χ^2=74.2, P<0.001) for linear trend, respectively. The higher increase in the proportion of both type 1 and type 2 diabetes observed among women patients.

Conclusion: The trend in the proportion of type 1 and type 2 diabetes increasing for both urban and rural residents, with a higher increase observed among women. These findings highlight health-care professionals and policymakers to design effective public health policies to treat each type of disease.

Keywords: urban, rural, trend, type 1 diabetes, type 2 diabetes

Introduction

Diabetes is one of the most epidemic diseases of this century. The global size of diabetes has grown from 108 million in 1980 to 425 million in 2017, and this could be reached 693 million by 2045 and varies by age, gender and residence.[1,2] In the modern era, diabetes has no border that imposes unacceptably high human, social, and economic costs on countries at all income levels worldwide. In 2015, roughly 5 million people aged 20 to 79 years died from diabetes-related deaths, which is equivalent to one death every six seconds, and about 14.5% of the global all-cause mortality among adults.[1–3]

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Acute and long-term diabetes complications bring about substantial economic loss by increased use of health services, loss of productivity, disability, and premature death. As a result, diabetes imposes the economic burden on individuals, families, national health systems and the economy of a country.[1,2,4]

Even though incidence rates of diabetes are decreasing in the developed countries in the previous two decades such as in the United States (US) and Switzerland;[4,5] still, it is alarmingly increasing in low and middle-income countries (LMICs) such as China, India, and Brazil.[6–8] In 2017, about 80% of people with diabetes live in LMICs, since these countries were on rapid economic and societal transitions.[1,9–11]

Ethiopia is the leading country in Sub-Saharan Africa (SSA), with over 2.6 million adult diabetes patients; with an estimated diabetes prevalence of 5.2% in 2017,[1,3] probably catalyzed by economic and societal transitions, and childhood malnutrition, with about 70% of adults with undiagnosed diabetes.[1,10,12] Recent studies in Ethiopia[13–15] indicated that more than one-third of patients admitted with hyperglycemic emergencies were undiagnosed diabetes, which suggests people die undiagnosed and the prevalence of diabetes could be beyond this magnitude.

Studies indicated that type 1 diabetes (T1D) and type 2 diabetes (T2D) are the two major public health concerns types of diabetes elsewhere in the world, including Ethiopia.[16,17] Even though both type 1 and type 2 diabetes results in hyperglycemia, pathophysiology, and etiology of the diseases are distinct and require us to consider each type of diabetes independently.[18] Study in the US suggested that type 1 and type 2 diabetes accounted for about 6% and 91% of all cases of diagnosed diabetes, respectively.[19] Recent studies in Italy and Ethiopia indicated, type 1 diabetes is strongly associated with poverty and markers of undernutrition, most marked in the rural cases and excess among men compared to women.[17,20] The trend on the prevalence of T2D is alarmingly increased over time in developing countries, including SSA countries due to marked economic and epidemiologic transitions, which result in altering lifestyle practices, and marked increases in overweight and obesity.[6,21]

Studies indicate that both type 1 and type 2 diabetes have become an increasingly prevalent, problematic and severe public health issue for both urban and rural residents, with the highest prevalence in urban areas.[6,22,23] Studies in Ethiopia, Myanmar, India, and Peru showed the prevalence of diabetes is higher for urban dwellers compared to rural residents.[6,24–26] Location of residence is also important in terms of access to care and health outcomes; people living in rural areas have increased treatment gaps and acute complications with their diabetes.[1,2,27]

Sex-related differences in lifestyle may lead to differences in the risk of developing diabetes mellitus and, in consequence, to differences in the prevalence of this condition in women and men.[27,28] Studies in the US, Italy, and Ethiopia indicate that male participants had a higher risk than female study participants in all age-groups for both type 1 and type 2 diabetes.[17,19,20] But other studies in SSA countries suggested that the prevalence of diabetes is higher among women compared to men; this is due to higher rates of obesity among women,[29,30] or history of gestational diabetes mellitus, which is associated with an increased risk of subsequent T2D in mothers and their offspring.[11,28]

Although diabetes brings real economic loss by increased use of health services, loss of productivity, disability and premature death in the developing nations including Ethiopia, robust data on adult diabetes are scarce in Ethiopia as well in Tigray; where most clinical data are not timely assessed and made accessible for policy and decision-makers. This study demonstrated the trend in the proportion of adult T1D and T2D for both urban and rural residents, which will have a crucial input in shifting healthcare priorities for policymakers and planners for planning health services for the needy and preventing premature adult deaths.

Methods and Materials

Study Period and Population

The study was conducted in seven public hospitals of Tigray in northern Ethiopia among adult patients aged 18 years and above, who received medical treatment from adult medical outpatient and emergency units from September 1, 2013, to August 31, 2018.

Study Design and Data Collection

This study was a hospital-based retrospective record review of patients registered in the study period and units. All five years' medical records of adult patients aged 18 years and above who received medical treatment were included in the review and screened from the registry log book. But adult patients with gestational diabetes and diabetes patients with referral papers were excluded from the study to decrease over enumeration of cases.

Data abstracted using a uniform data abstraction format prepared to gather relevant data from the medical records both paper copy file and e file/smart care/after the data abstraction format pretested from 295,806 adult patients. Nursing and public health experts recruited for data abstraction. Data collectors and supervisors were trained for one day on how to retrieve, abstract relevant data from the medical records, and keep records back in the original location. The data abstraction format pretested in 300 adult medical records two weeks before the actual data abstraction period for fitness and consistency.

Operational Definitions

New diabetes case: Physician diagnosed as a diabetes patient for the first time with fasting blood sugar (FBS) ≥126 mg/dL, or repeated random blood sugar (RBS) ≥200 mg/dL plus fatigue, polyuria, polydipsia, and other symptoms, we considered a new diabetes patient.[1,2]

Type 1 diabetes: When the patient presented with FBS ≥ 126 mg/dL or RBS ≥ 200 mg/dL plus classic symptoms excessive urination, excessive thirst, unexplained weight loss, and increased hunger, we considered as type 1 diabetes patient.[2]

Type 2 diabetes: When the patient presented with FBS ≥ 126 mg/dL or RBS ≥ 200 mg/dL plus other symptoms such as excess body weight, physical inactivity, unhealthy diet, and family history of diabetes, we considered as T2D patient.[2]

Data Analysis

Data entered in Epi data manager 4.3 for Windows 10 software and analyzed using SPSS Version 25.0 software, and we used a list-wise deletion for missing variables to have a complete case analysis across time. The key covariate of interest was the time (in years), which allowed the estimation of change in the prevalence of type 1 and type 2 diabetes over time. We calculated Mean and Standard Deviation (SD), and proportions for continuous variables and categorical variables, respectively. Extended Mantel-Haenzel chi-square test for linear trends used to examine trends in diabetes proportion for the period September 1, 2013, to August 31, 2018, using Epi info 7.1.5 STAT CALC, and the trends of both type 1 and type 2 diabetes observed by residence and gender. A p-value of <0.05, considered statistically significant for the linear trend, and findings presented in text, table, and figures.

Ethical Statement

The ethical statement protocol approved by the Institution Review Board (IRB) of Addis Ababa University-College of Health Sciences (AAU-CHS), and waiver letter obtained. In addition, a written permit obtained from the Tigray Regional State Health Bureau and respective hospitals' administrative bodies after submitting the protocol and explaining the purpose of the study. For the sake of privacy and confidentiality, no personal identifiers, such as names, were collected.

Results

Out of the total 299,806 adult patients who received medical care services in the studied hospitals, 128,915 (43.0%) of the patients were women, and 126,559 (42.2%) of them were rural residents. From those patients who received medical treatment, 3056 (10.2 per 1000 adult patients) were confirmed, diabetes patients. The proportion of diabetes was 11.6 per 1000 urban residents, and 8.6 per 1000 rural residents. The mean (±SD) age of adult diabetes patients at diagnosis was 46.04 (±14.96) years, with 26.41 (±9.45), and 49.65 (±12.98) years, for Type 1 diabetes (T1D) and Type 2 diabetes (T2D), respectively. Of the total of 3056 newly diagnosed adult diabetes patients, 1705 (55.8%) were men and 2011 (66%) of the diabetes patients were urban residents. Four hundred eighty-seven (15.9%) of adult diabetes patients, were type 1 diabetes patients and half of these were rural residents. Of the total 2569 T2D patients, 1768 (68.8%) were urban residents. Almost one-third of the diabetes patients treated at Ayder comprehensive specialized hospital (ACSH) (Table 1). Supporting information available (PPTX) in Tables S1 and S2.

The overall trend of diabetes had increased from 6.8 to 14.3 per 1000 adult patients, with increased for both urban (7.9 to 15.9 per 1000 adult urban residents) and rural (from 5.2 to 13.2 per 1000 adult rural residents) in the observation period (Figure 1). Supporting information available in Tables S1 and S2.

The trend of diabetes had a higher increase in those ages group 60 and above years, with 15.5 per 1000 adult patients compared to those in the age group of 18 to 29 years with 6.8 per 1000 adult patients in the observation period (Figure 2). Supporting information available in Table S3.

The overall proportion of Type 1 diabetes was 0.16% (95% CI: 0.15–0.18), with a statistically significant

Table 1 Characteristics of Newly Diagnosed Adult Diabetes Patients in Selected Public Hospitals of Tigray, Ethiopia (September 1, 2013 to 2018, August 31, 2018)

Patient Characteristics	Frequency	Percent
Gender		
Men	1705	55.8
Women	1351	44.2
Residence		
Urban	2011	65.8
Rural	1045	34.2
Age		
<29	466	15.3
30 to 39	561	18.4
40 to 49	750	24.5
50 to 59	617	20.2
60 Years and above	662	21.7
Type of diabetes		
Type 1 diabetes	487	15.9
Type 2 diabetes	2569	84.1
Type 1 Diabetes		
Urban resident	243	49.1
Rural residents	244	50.1
Type 2 Diabetes		
Urban residents	1768	68.8
Rural residents	801	31.2
Hospital Diabetes Treated		
Ayder comprehensive specialized hospital	944	30.9
Mekelle hospital	465	15.2
Ma'ychew Lemlem karl hospital	408	13.4
Adigrat hospital	332	10.9
St Merry hospital	376	12.3
Suhul shire hospital	326	10.7
Abyi Adi hospital	205	6.7

increase (χ^2= 34.5, P<0.001) for linear trend. The proportion of T1D for both urban and rural residents was 0.14% (95% CI: 0.12–0.16) and 0.19% (95% CI: 0.17–0.22), with a statistically significant increase (χ^2= 9.1, P=0.002) and (χ^2=17.8, P<0.001) for linear trend, respectively. The proportion of T1D for women was 0.17% (95% CI: 0.12–0.16), with statistically significant increase (χ^2=20.2, P<0.001) for linear trend, but not for men (χ^2= 3.1, P= 0.08) (Table 2).

The overall trend of type 1 diabetes had increased from 1.1 to 2.4 per 1000 adult patients, with the trend of type 1 diabetes increased for both urban (1.0 to 2.2 per 1000 adult urban residents) and rural (from 1.2 to 2.6 per 1000 adult rural residents) in the observation period (Figure 3).

The overall proportion of T2D was 0.86% (95% CI: 0.82–0.89), with statistically significant increase (χ^2=151.0, P<0.001) for linear trend. The proportion of T2D for both urban and rural residents was 1.0% (95% CI: 0.97–1.10) and 0.63% (95% CI: 0.59–0.68), with statistically significant increase (χ^2=68.4, P<0.001) and (χ^2=74.2, P<0.001) for linear trend, respectively. The proportion of T2D for both men and women was 0.84% (95% CI: 0.79–0.88) and 0.88% (95% CI: 0.83–0.94), with statistically significant increase (χ^2=32.0, P<0.001) and (χ^2=70.3, P<0.001) for linear trend, respectively (Table 3).

The overall trend of T2D has increased from 5.7 to 12.0 per 1000 adult patients, with increased for both urban (6.9 to 14.0 per 1000 adult urban residents) and rural (from 4.0 to 9.5 per 1000 adult rural residents) in the observation period (Figure 4).

Discussion

The present study used a retrospective record administrative health care data from hospital logbook and patient charts to investigate urban-rural differences in the trend of type 1 and type 2 diabetes among adult patients in resource-poor community Tigray between September 1, 2013, and August 31, 2018. The proportion of diabetes in this study was 10.2 per 1000 adult patients, with 11.6 per 1000 urban residents and 8.6 per 1000 rural residents with age. The trend in the proportion of adult diabetes steadily increased with time in

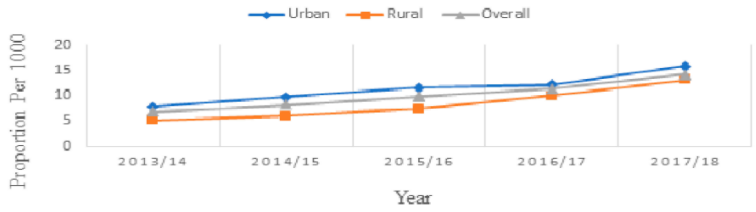

Figure 1 The overall trends in the proportion of diabetes by residence in the selected public hospitals of Tigray, Ethiopia (September 1, 2013 to August 31, 2018).

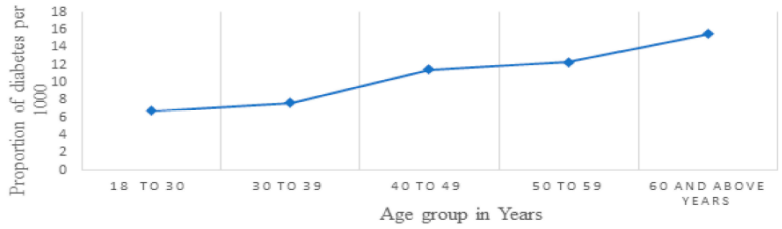

Figure 2 Trends in the proportion of diabetes by age category per 1000 adult patients in the selected public hospitals of Tigray, Ethiopia (September 1, 2013 to August 31, 2018).

both urban and rural residents for both T1D and T2D, and for both men and women patients in the observation period.

The finding of this study suggests, the trend in the proportion of adult diabetes has definitely risen more than double over the last five-years observation period,

Table 2 The Trends of T1D by Residence and Gender (Extended Mantel-Haenszel Chi-Square and Proportion) in the Selected Hospitals of Tigray, Ethiopia (September, 2013 to August, 2018)

Variable	Year	DM Patients	OPD Patients	Proportion of DM (%)	95% CI	MH-OR
Overall Proportion of T1D	2013/14	59	55,734	0.11	[0.08–0.14]	1.000
	2014/15	76	58,806	0.13	[0.10–0.16]	1.221
	2015/16	91	60,221	0.15	[0.12–0.19]	1.428
	2016/17	109	61,805	0.18	[0.14–0.21]	1.667
	2017/18	152	63,240	0.24	[0.21–0.28]	2.274
	Total	487	299,806	0.16	[0.15–0.18]	χ^2= 34.5, P<0.001
Proportion of T1D Among Urban Residents	2013/14	31	31,914	0.10	[0.07–0.14]	1.000
	2014/15	42	34,370	0.12	[0.09–0.16]	1.254
	2015/16	45	34,645	0.13	[0.10–0.17]	1.334
	2016/17	44	36,244	0.12	[0.09–0.16]	1.250
	2017/18	81	36,074	0.22	[0.18–0.28]	2.315
	Total	243	173,247	0.14	[0.12–0.16]	χ^2= 9.1, P=0.002
Proportion of T1D Among Rural Residents	2013/14	28	23,820	0.12	[0.08–0.17]	1.000
	2014/15	34	24,436	0.14	[0.10–0.19]	1.188
	2015/16	46	25,576	0.18	[0.13–0.24]	1.536
	2016/17	65	25,561	0.25	[0.20–0.32]	2.173
	2017/18	71	27,166	0.26	[0.21–0.33]	2.233
	Total	244	126,559	0.19	[0.17–0.22]	χ^2=17.8, P<0.001
Proportion of T1D Among Men	2013/14	39	31,312	0.12	[0.09–0.17]	1.00
	2014/15	39	34,273	0.11	[0.08–0.16]	0.914
	2015/16	45	34,267	0.13	[0.10–0.18]	1.054
	2016/17	63	36,579	0.17	[0.13–0.22]	1.383
	2017/18	77	34,460	0.22	[0.18–0.28]	1.796
	Total	263	170,891	0.15	[0.14–0.17]	χ^2= 3.1, P= 0.08
Proportion of T1D Among Women	2013/14	20	24,422	0.08	[0.05–0.13]	1.000
	2014/15	37	24,533	0.15	[0.11–0.21]	1.828
	2015/16	46	25,952	0.18	[0.13–0.23]	2.235
	2016/17	46	25,226	0.18	[0.14–0.24]	2.211
	2017/18	75	28,780	0.26	[0.21–0.33]	3.162
	Total	224	128,915	0.17	[0.15–0.20]	χ^2=20.2, P<0.001

Abbreviations: DM, diabetes; MH-OR, mantel-haenszel-odd ratio; OPD, out patient department.

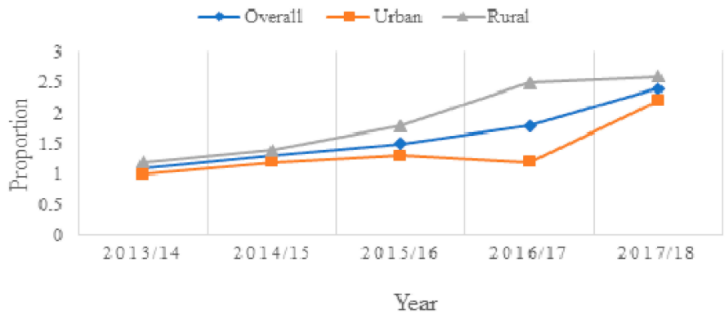

Figure 3 Trends in the proportion of type 1 diabetes by residence per 1000 adult patients in the selected public hospitals of Tigray, Ethiopia (September 1, 2013 to August 31, 2018).

and this is consistent with studies in Ethiopia, Brazil, China, and India.[6,24,28,31] Therefore, rapid economic and societal transitions, childhood nutritional stunting, chronic undernutrition, improving recording, and diabetes detection mechanisms could lie behind these alarmingly increasing trends of diabetes.[17,25]

Even though the findings of this study showed faster increase in the trend of adult diabetes, the prevalence is lower than from the findings of Ethiopia, Tanzania, Iran, and India.[6,22,31,32] The discrepancy might be due to differences in the level of urbanization, health literacy, diagnostics criteria, underestimating diabetes for patients with other illnesses.[1,25,32] The current finding is also much lower compared to the national estimated prevalence of diabetes with 5.2%, which might be due to people die undiagnosed, and about 70% of people with diabetes do not know that they have diabetes.[1]

This study pointed out the trend in the proportion of adult diabetes has increased among all age groups and most pronounced being with people aged 60 and older years. This finding is in line with similar studies in the US, Sweden, Bulgaria, and Panama, with increasing the trend of diabetes with age over time.[4,33–35] Aging could impair β-cell function and impaired β-cell adaptation to insulin resistance leading to impaired insulin secretion, which might be related to obesity and decreased physical activity.[36]

Studies indicated that diabetes becomes an increasingly prevalent, challenging, and severe public health issue in the 21st century, for both the urban and rural residents, with the highest prevalence in urbanized regions.[1,6,25,27] In the current study, even though the trend of adult diabetes is increasing for both urban and rural residents, but the highest proportion observed in urban residents. This study is consistent with studies in Ethiopia, Myanmar, Iran, India, and Kazakhstan.[6,22,24,25,37] Affluent people live in urban areas, reducing the number of people living in traditional rural livelihoods, which might result in obesity associated with rising living standards.[1,6,25,38] Likewise, urban life is a more complicated, stressful, and competitive life compared with the rural ones.[25,38,39] Although the urban population has better access to the healthcare services, including reliable screening methods and diabetes treatment, people die undiagnosed due to lack of health services in rural residents.[39]

A study in the US suggested that type 1 and type 2 diabetes accounted for about 6% and 91% of all cases of diagnosed diabetes, respectively.[19] Recent studies in Italy and Ethiopia indicated, type 1 diabetes is strongly associated with poverty and markers of undernutrition, most marked in the rural cases and excess among men compared to women.[17,20,40] The trend in the prevalence of T2D is alarmingly increasing over time in developing countries, including SSA countries due to marked economic and epidemiologic transitions, which result in altering lifestyle practices and marked increases in overweight and obesity.[21,28,41]

In several epidemiological studies, T1D in adults is a significant and widespread health problem associated with unacceptably high rates of morbidity and mortality in SSA countries, as a result of childhood nutritional stunting, chronic undernutrition, and environmental factors.[17,20,42] Although the proportion of T1D in the current study is 1.6 per 1000 adult patients, the potential proportion might be greater than that indicated finding. It might be due to many people die before they are diagnosed and access to diabetes treatment and some type 1 diabetes misclassified as

Table 3 The Trends of T2D by Residence and Gender (Extended Mantel-Haenszel Chi-Square and Proportion) in Hospitals of Tigray, Ethiopia (September, 2013 to August, 2018)

Group of Proportion	Year	DM Patients	OPD Patients	Proportion of DM (%)	95% CI	MH-OR
Overall Proportion of T2D	2013/14	317	55,734	0.57	[0.51–0.63]	1.000
	2014/15	407	58,806	0.69	[0.63–0.76]	1.216
	2015/16	502	60,221	0.83	[0.76–0.91]	1.470
	2016/17	593	61,805	0.96	[0.89–1.00]	1.694
	2017/18	750	63,240	1.20	[1.10–1.30]	2.098
	Total	2569	299,806	0.86	[0.82–0.89]	χ^2=151, P<0.001
Proportion of T2D Among Urban Residents	2013/14	221	31,914	0.69	[0.60–0.79]	1.000
	2014/15	294	34,370	0.86	[0.77–0.96]	1.237
	2015/16	359	34,645	1.00	[0.93–1.10]	1.497
	2016/17	402	36,244	1.10	[1.00–1.20]	1.608
	2017/18	492	36,074	1.40	[1.20–1.50]	1.983
	Total	1768	173,247	1.00	[0.97–1.10]	χ^2=68.4, P<0.001
Proportion of T2D Among Rural Residents	2013/14	96	23,820	0.40	[0.33–0.49]	1.000
	2014/15	113	24,436	0.46	[0.38–0.56]	1.148
	2015/16	143	25,576	0.56	[0.47–0.66]	1.389
	2016/17	191	25,561	0.75	[0.65–0.86]	1.860
	2017/18	258	27,166	0.95	[0.84–1.10]	2.369
	Total	801	126,559	0.63	[0.59–0.68]	χ^2=74.2, P<0.001
Proportion of T2D Among Men	2013/14	184	31,312	0.59	[0.51–0.68]	1.000
	2014/15	225	34,273	0.66	[0.58–0.75]	1.118
	2015/16	281	34,267	0.82	[0.73–0.92]	1.399
	2016/17	351	36,579	0.96	[0.86–1.10]	1.639
	2017/18	389	34,460	1.10	[1.10–1.20]	1.932
	Total	1430	170,891	0.84	[0.79–0.88]	χ^2=32.0, P<0.001
Proportion of T2D Among Women	2013/14	133	24,422	0.54	[0.46–0.64]	1.000
	2014/15	182	24,533	0.74	[0.64–0.86]	1.365
	2015/16	221	25,952	0.85	[0.75–0.97]	1.569
	2016/17	242	25,226	0.96	[0.85–1.10]	1.769
	2017/18	361	28,780	1.30	[1.10–1.40]	2.320
	Total	1139	128,915	0.88	[0.83–0.94]	χ^2=70.3, P<0.001

Abbreviations: DM, diabetes; MH-OR, mantel-haenszel-odd ratio; OPD, out patient department.

T2D.[20,42,43] The overall trend of type 1 diabetes is increasing in the current study, which is consistent with other studies in the US, Sweden, and SSA countries.[18, 44,45]

Different studies suggest that there are major differences in the age and gender of presenting cases together with marked urban-rural variations in the incidence of T1D.[17,19,20] We found differences in the proportion of type 1 diabetes between urban and rural areas with almost twofold higher in the rural compared to the urban residents. Type 1 diabetes is strongly associated with poverty and markers of undernutrition most marked in the rural cases,[17,46] and acute nature of the disease made rural residents seek medical care.[47] This is inconsistent with studies in Ethiopia urban centers had higher incidence rates than the surrounding rural areas,[17] which could be due to genetic, environmental, cultural, and socioeconomic variations. Another striking feature of the disease in this study was an excess proportion of T1D in women compared to their men counterparts. It could be due to little attention given to girls in their childhood which lead to undernutrition, genetic susceptibility, and undernutrition at particular times in pregnancy affects many genes that control hepatic and pancreatic function.[17,19,20,36] This finding is inconsistent with findings in Ethiopia and Italy, where the proportion of type 1 diabetes is excess among men.[17,19,20]

Even though T2D prevalence is reaching epidemic proportions elsewhere in the world, it is disproportionately

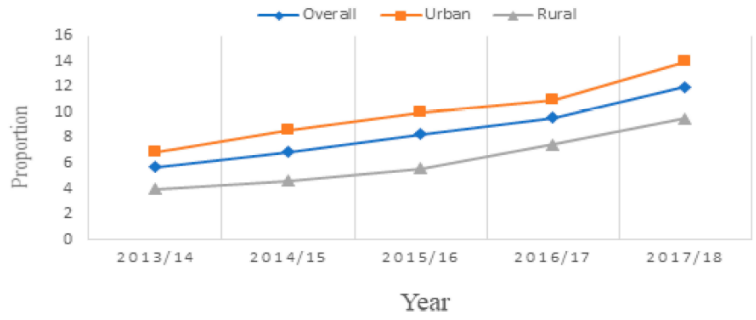

Figure 4 Trends in the proportion of T2D by residence per 1000 adult patients in the selected public hospitals of Tigray, Ethiopia (September 1, 2013 to August 31, 2018).

higher in low-income countries.[1,2] SSA countries, including Ethiopia, take the lion share in the magnitude of diabetes due to a rapidly epidemiologic and demographic transition.[1,6,26] In developing countries, the prevalence of T2DM is higher among urban residents compared to their rural counterparts; however, it is higher for rural residents in developed countries.[6,25,27]

The trend of T2DM is increasing with time for both urban and rural residents. In this study, we found a higher proportion of T2DM in an urban resident compared to a rural resident. These marked urban and rural differences in the prevalence of T2DM have reported in other developing countries in India, Bangladesh, and Peru.[6,23,48] This increase might be due to epidemiologic and demographic transitions, with a sedentary lifestyle and unhealthy diet are still problematic and with a notable increment trend.[1,25] This study is inconsistent with study in Canada where prevalence of T2DM is higher among rural residents compared to urban residents.[27]

Several studies indicated that the prevalence of T2DM is higher among men compared to women.[6,25,49] Unlike other studies, we found in this study, women with a higher proportion of T2DM compared to men. This discrepancy could be due to a higher rate of obesity among women compared to their men counterparts[29,30] and history of gestational diabetes mellitus, which is associated with increased risk of subsequent T2D in mothers.[11,28]

It is imperative to acknowledge, as our results must be viewed in light of several important limitations. The first limitation, the incompleteness of the data in the review charts had some missing data for some variables, which could have led to differences in an unmeasured independent variable for which no correction could be made. The second limitation, data were not validated, which could have led to misclassification of diabetes type. Third, the data were retrospective chart review and underestimate the total number of adults with diabetes, due to some patient charts were lost and not all adult patients who received medical service from the study units were tested for diabetes for those who came for other medical illnesses. The fourth, the study is limited to medical outpatient and emergency units, which do not include obstetrics and surgical units, which might underestimate the proportion of diabetes. Although this finding is not representative of the entire nation, it can generalize for those who are receiving medical services from adult medical outpatient and emergency units of general hospitals of Tigray.

Conclusion

The overall trend of diabetes is increasing with age over time in the study period. We observed significant increases in the trend of both type 1 and type 2 diabetes among adult patients, for both urban and rural residents steadily with time. A higher proportion of type 1 diabetes is increased in rural residents, and with a statistically significant increase in women study participants, but not in men. Type 2 diabetes has a higher proportion of increase among urban residents, and women participants with time in the observation period.

Our study results might hasten the academia and public interest, resulting in renewed efforts to design effective public health policies. Knowledge about regional prevalence and trend of type 1 and type 2 diabetes in both urban and rural residents might facilitate assessment of the burden of disease and long-term cost-effectiveness of public health interventions and policies aimed at improving diabetes management and help to prioritize regional and national plans for future type-specific health services.

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The sudden death of Professor Fikre Enquo Selassie is extremely painful and hurting. He was not only a good professor of epidemiology and biostatistics but also, he had a unique human entity to his family, students and staff. It pains me to notify you that my supervisor, professor Fikre, left for his heavenly abode on October 28, 2019, on account of sudden death. Professor Fikre was heartily involved in all activities of the study from the proposal development to manuscript approval for publication. The authors express their gratitude to the Addis Ababa University for funding this project. Additionally, we would like to express our heartfelt thanks to the selected public hospitals' administrative bodies, staff, data collectors and supervisors and Tigray Regional Health Bureau office for granting access to these data.

Author Contributions

All authors contributed from the development of the proposal to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work. Specifically, GG conceived the idea and developed the study proposal, did the fieldwork, analyzed data, interpreted the findings, and led the manuscript writing. FEQ was involved in proposal development, planning the fieldwork, data analysis and interpretation, manuscript editing and manuscript review. ND and HY were involved in proposal development, planning the fieldwork, data interpretation, manuscript editing, and manuscript review.

Disclosure

The authors report no conflicts of interest in this work.

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Orginal Paper –Two

Risk factors for type 2 diabetes mellitus among middle-aged adults' out-patients in Ayder comprehensive specialized hospital, Tigrai: Matched Case-Control study.

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Risk factors for type 2 diabetes mellitus among middle-aged adults' out-patients at Ayder comprehensive specialized hospital, Tigrai: Matched Case-Control study.

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Abstract

Background: Type 2 diabetes mellitus (T2D) is a growing global health concern, with limited knowledge about risk factors among middle-aged adults in Africa, including Tigrai. The study aimed to identify the possible risk factors of T2D among middle aged adults in Tigrai, Ethiopia.

Methods: A matched case-control study was conducted on 120 cases and 240 controls at Ayder Comprehensive Specialized Hospital in Tigrai. Cases were known T2D patients who were diagnosed from January 1 to December 31, 2018; and who were on follow up while controls were patients without diabetes. Data on socio-demographic, medical, behavioral, and physical measurements were collected and analyzed using SPSS software to determine associations between exposure and outcome variables.

Results: The mean ages of the cases and controls were 55.9±5.0 and 55.7±4.8 years old, respectively. The odds of Type 2 diabetes were significantly higher among urban residents (AOR=5.1, 95%CI ([2.0, 13.2]), widowhood(AOR=3.3, 95%CI ([1.3, 8.6]) and divorced(AOR=2.8, 95%CI([1.1, 7.3]), hypertension (AOR=3.0, 95%CI ([1.7,5.5]), dyslipidemia(AOR=2.8, 95%CI ([1.5, 5.4]), positive family history of diabetes(AOR=5.4, 95%CI ([2.4, 12.5]), consumed alcohol every day(AOR=3.5, 95%CI ([1.2, 10.2]), consuming white rice as staple diet(AOR=3.8,95%CI ([1.2, 11.6]), elevated waist circumference(AOR= 2.4, 95%CI ([1.1, 5.0]), and elevated waist to height ratio(AOR=4.4, 95%CI([1.7, 11.2]), while moderate to vigorous intensity leisure physical activity (AOR= 0.27, 95%CI ([0.1, 0.72]) was preventive.

Conclusion: We found, urban residency, widowhood, diabetes history, daily alcohol consumption, white rice diet, hypertension, dyslipidemia, elevated waist circumference and waist-to-height ratio, hypertension, and dyslipidemia increase risk of type 2 diabetes, engagement in leisure moderate to vigorous intensity physical activity was preventive. Future actions policy makers have to be focused on appropriate timely action plans for the prevention and control of risks of T2D from early years of life.

Keywords: Type 2 diabetes, risk factors, adults, middle age, Tigrai

Introduction

Diabetes mellitus (DM) is one of a global, multifactorial and complex clinical and public health challenge that has reached epidemic proportions, and whose social and economic impact is growing(260). Diabetes is among the top 10 causes of death in adults aged 20–79 years worldwide and was estimated to have caused 6.7 million deaths globally in 2021(3). Diabetes is becoming a major challenge in the healthcare system; which is usually associated with disability, reduced life expectancy, and has a high cost of treatment. It also imposes an economic burden on individuals, families, national health systems, and the economy of a country(5,6).

According to International Diabetes Federation (IDF) report; the number of diabetes cases has progressively increased from 151 million in 2000 to 463 million in 2019 worldwide. In 2019, about 79.4% of the diabetes cases live in low- and middle-income countries (LMIC). China, India, and Pakistan are the diabetes capitals of the world, where nearly half of diabetes cases are found in these countries (5,8,261–263).

Type 2 diabetes mellitus (T2D) is the main driver of the epidemic, accounting for approximately 90% of all diabetes cases. The mortality, morbidity, social and economic burden of T2D has been steadily increasing worldwide at an alarming pace. T2D is a heterogeneous disorder most commonly characterized by insulin resistance, a state of reduced insulin-mediated glucose uptake, in the presence of incapacity of the pancreatic beta cells to produce and provide sufficient insulin to meet the required needs(2,5,79,264).

The etiology of T2D is complex and multifactorial; behavioral factors (physical inactivity, unhealthy diet, alcohol consumption, smoking, and obesity) are the most pivotal factor for the occurrence of T2D for both men and women(5,216).

Different studies have reported significant links between smoking and the development of T2D (142,146). However, contrary findings are reported, smokers have a lower likelihood of newly diagnosed diabetes than non-smokers in Chinese men with normal weight (151).

Certain prospective studies confirmed that moderate alcohol consumption was inversely associated with the occurrence of T2D(155,156), whereas heavy alcohol consumption as being

the risk factor for the for the development of T2D in the Western populations(144,154), and also other studies have reported a null association(156,157).

Findings regarding the intake of fruit and vegetables on T2D have been inconsistent(245–250). Some of the studies have shown an inverse association with risk of T2D with higher intakes of total fruit(247,249), and total vegetables(246,247,250), whereas other studies did not find associations for total fruit (246,248,251) or total vegetables(248,251).

Some epidemiological studies reported a contradict findings regarding physical activity over the occurrence of T2D. The incidence of T2D was significantly inversely associated with moderate-intensity activity alone(162), vigorous-intensity activity alone(46,162), typical walking pace(157,162), and vigorous-intensity exercise combined with moderate-intensity exercise(46,157); whereas moderate-intensity exercise alone(46,157), and vigorous-intensity exercise combined with moderate-intensity exercise(162,265) were null association with T2D. Study in Japan, walking for at least 30 min per day was shown to reduce the risk of T2D by approximately 50%(266).

Studies confirmed that increased time spent in sedentary behaviors was conversely positively associated with the occurrence of T2D. Being inactive in physical activity is the main reason for being overweight and obese (162,265). Obesity is well recognized to be one of the major modifiable risk factors for the development of T2D. Many epidemiological studies have suggested a progressive increase in the prevalence of T2D with obesity(170,267,268).

The importance of lifestyle factors in the etiology of T2D has been well documented in Western and Asian populations, with its contradicting findings, and inconclusive. However, evidence is limited in SSA, including Tigrai regarding physical activity, alcohol consumption, smoking, fruit and vegetable consumption over the occurrence of T2D among adults, specifically among middle aged adults. The aim of this study was to identify the possible risk factors of T2D among middle aged adults in Tigrai.

Methods and Materials

Study design and population

The study was conducted in Tigrai among adult patients aged 45-64 years who received medical care at Ayder Comprehensive Specialized Hospital (ACSH) from adult medical outpatient units from March 1 to June 30, 2019.

A hospital-based matched case-control study design was used to compare the association between SES, physical activity, smoking, alcohol consumption, fruit and vegetable consumption, physical measures, biomarkers and T2D risk.

Cases: were known T2D patients for both men and women among middle-aged adults who were newly diagnosed with T2D from January 1 to December 31, 2018, and have been attending their follow up at ACSH diabetes clinic. The case history of diabetes was verified from the record of diabetes patients by physicians and nurses working in the diabetes clinic. **Controls:** were patients/healthy individuals who visited the general medical outpatient department (OPD) for any other reasons but without diabetes confirmed with normal blood glucose values (FBS<100mg/dl) were considered as controls(Figure 1).

Matching: cases and controls were matched by age and sex as they were found to be associated with T2D in majority of the studies reviewed. Two controls were matched to each case based on gender and age (± 2 years). The gender and age (±2 years), matched individuals who were willingly selected to become participants of the study with normal blood glucose values were considered as controls(Figure 1).

Participants/patients having severe co-morbidities like stroke, chronic renal diseases, chronic lung diseases, heart failure, chronic liver disease, end-stage cancer, and also pregnant women and women who gave birth in the last 6 months, adults with spinal problems (kyphosis, lordosis, scoliosis, and kyphoscoliosis), amputation of the leg and patients on wheel chair were excluded from the study(Figure 1).

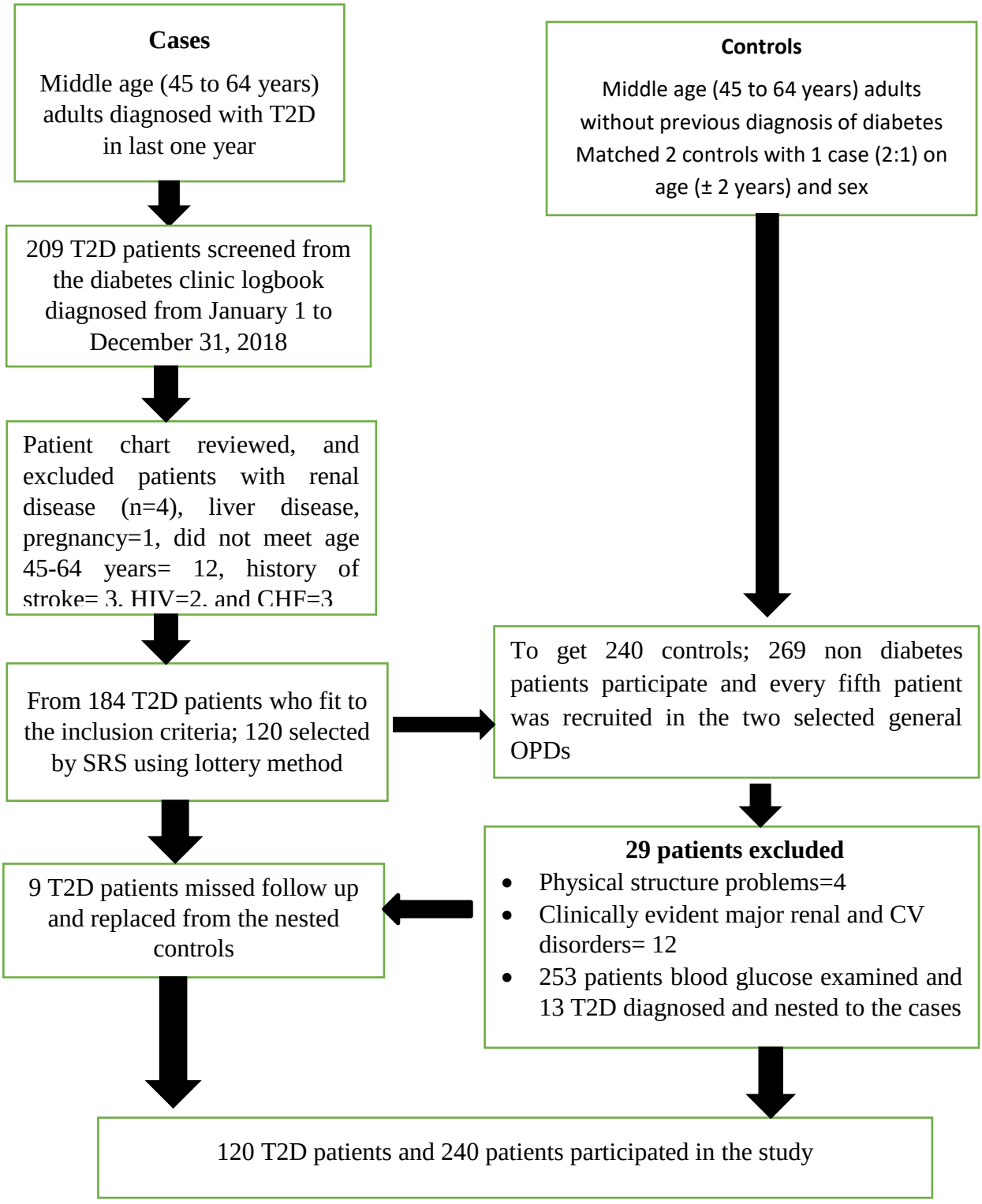

Figure 9:Flow diagram of selection of participants for factors associated with T2D included in this study

We used the StatCalc procedure of Stata version 14.1 to calculate the sample size according to the following specifications: significance level (α= 0.05); 80% of power, an odds ratio of exposure in cases relative to controls (OR=2.0); correlations of exposure between cases and controls (r= 0.2), number of matched controls to cases is 2 and excess body weight assumed rate of exposure among controls is 50% because have not been conducted before in the middle age bracket. The required numbers of cases were 120; and that of controls were 240.

Cases were selected from T2D patients who visited the ACSH diabetes clinic for their follow-up appointments and sampled from the diabetes follow-up registry book by simple random sampling using the lottery method who consented to participate were selected for the interview and anthropometric examinations. Controls were selected from non-diabetes individuals who came to ACSH medical OPD and sampled consecutive method, whose age was between 45 and 64 years, who consented to participate were selected for the interview, and blood test and anthropometric examinations. Consecutive patient visiting the ACSH in the 2 medical OPDs from March 1 to June 31, 2019, who met the eligibility criteria, was requested to participate in the study. In case of refusal, the next patient was approached with the same request. Each of the 2 medical OPDs participating was required to interview 120 controls during the study period.

Data collection tools and techniques

A semi-structured interviewer-administered questionnaire was adopted and adapted from the WHO STEPS protocol and similar kinds of literature (269–272). The questionnaire included structured information on socio-demographic characteristics and medical history of patients, family history of diabetes, behavioral measurements (alcohol consumption, cigarette smoking, diet(fruits and vegetables)), physical activity(activity at work, travel to and from place, recreational activities, and sedentary behaviors)), physical measurements(blood pressure, height and weight, waist circumference, hip circumferences), biomedical measurements(blood glucose, blood lipids). The questionnaire was prepared in English and translated into Tigrigna and back-translated to ensure consistency in the phrasing of questions.

Data collectors and supervisors were health care professionals (nurses and physicians). A total of 6 data collectors and 2 supervisors were recruited. Training was given for the data collectors and supervisor for two days. The first day of training highlighted how to communicate with respondents and how to obtain informed consent and how to conduct questionnaires, medical doctors, and laboratory experts. During the second day, the correct measuring methods for all three STEPs were in focus, in accordance with the standardized methods of WHO guidelines. The standardization of instruments was carried out before and during the training. A pretest was conducted for STEPs with the data collectors and supervisors, and questions were also clarified.

First the required numbers of questionnaire were distributed to the study units in ACSH according to the calculated sample size, 120 questionnaires to the diabetes clinic and 240 to the general medical OPD. The patient selection and data collection of the controls were governed by patient flow of the cases in line with matching by age, sex and day of interview. The data were collected by six trained nurses from the two general medical OPDs and one diabetes clinic with full guidance and supervision of the principle investigator, and also with technical assistance of the medical doctors working in the selected medical OPDs. The data collection, for the controls were carried out after confirmation blood glucose level using glucometer as they were not diabetes patients.

After completing STEPs, the medical doctor who was in the medical OPD to provide care was responsible to order the biomarkers investigation and the patient and the data collector went together to the laboratory unit within the hospital. A venous blood sample was collected by the laboratory technician in the glucose tube with fluoride, and according to the standard of procedure (SOP), the FPG level for the controls, and the lipid profiles for both the controls and cases were investigated on plasma from whole blood with the enzymatic reference method with hexokinase, using reagents of COBAS from Roche Diagnostics, Indianapolis, USA. Biochemical analysis was started within 3 hours after blood samples were taken.

The exposure variables included socio-demographic characteristics (age, sex, marital status, religion, educational level, family monthly income, and employment status), medical history and family history of diabetes, behavioral measurements (Smoking, alcohol consumption, physical activity(occupational PA, walking to and from places, leisure-time PA, and sedentary behaviors),

dietary characteristics(most favorite/staple diet, coffee and tea, sugar contained beverages, vegetable and fruit consumptions), physical measurements (height and weight, waist circumference, hip circumferences, BMI, WHR, and WHtR), biomedical characteristics (biomarkers)

Data collectors and supervisors were recruited based on their research experiences. Data collectors and supervisors were nurse experts. The training was given for data collectors and supervisors for two days on the objective of the study, data collection tools, and procedures to ensure consistency of interviewing, measuring anthropometrics, and high-quality data. Appropriate customization and modifications were made after the instrument was pretested on 10% of the study population for cultural appropriateness and clarity. Anthropometric measurement tools were calibrated before measurement to maintain the accuracy of the data.

Measurements

Body mass index (BMI) was calculated as body weight (kg) divided by height squared (m2). BMI was categorized as normal weight (< 25kg/m2), overweight (25 kg/m2 to 29.9 kg/m2) and obesity (≥ 30 kg/m2) (57,58,215,272).

Waist circumference (WC) was measured halfway between the lower ribs and the iliac crest while the subject was at minimal respiration, while hip circumference is measured at the largest circumference around the buttocks. WC values ≥ 94cm for men and ≥ 80 cm for women is considered as elevated WC(57).

Waist Hip Ratio (WHR) was the WHR Values of ≥0.88 for men and ≥ 0.82 for women were regarded as elevated WHR. Waist Height Ratio (WHtR) values of ≥0.49 for men and ≥0.50 for women were considered central obesity(57).

Blood pressure (BP) was measured using a standard digital sphygmomanometer (OMRON, model HEM-741CINT) on the left arm after 5 minutes of rest in the sitting position. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated from the mean value of three readings. Based on blood pressure, an individual is classified as normotensive (< 130/85 mmHg); Pre-hypertensive (130-139/85-89 mmHg), and hypertensive (≥140/90 mmHg or by the use of antihypertensive medications) for SBP and DBP, respectively(57).

Dyslipidemia treatment was defined by the use of lipid-lowering drugs.

Blood collection was standardized, and laboratory assays were conducted in the same clinical chemistry laboratory. The fasting status was declared by the participants at the time of blood collection and the duration of 8 hours was requested.

One unit of alcohol (1 drink) was defined as four-ounce glass of wine/Me'as, or twelve-ounce can of beer/'Suwa', or One- ounce of liquor. Total alcohol consumption was calculated by adding units of intake for all alcoholic beverages that the patient has taken in one drinking occasion.

Level of alcohol consumption was categorized by 1) Non-drinkers: Never/ex-drinker, 2) Occasional/light: < 1 drinks/day, 3) Moderate drinker: M: 1-3 drinks & W: 1-2 drinks/day, 4) Heavy drinker: M: ≥ 4 drinks and W: ≥ 3 drinks per day.

The Ethiopian traditional alcoholic drinks have the alcohol contents of Tella, Tej and Areki samples ranged from 3.98 to 6.48, 8.94 to 13.16 and 33.95 to 39.90 with average values of 5.17, 11.47 and 37.22 %v/v, respectively(212).

Vigorous-intensity occupational physical activity: These are tasks that require significant physical effort and result in elevated heart rate, breathing rate, and sweating. Such as heavy lifting, carrying heavy loads, digging, chopping wood, plowing fields, harvesting crops, and handling large livestock, operating heavy machinery, laying bricks or concrete, and carrying heavy building materials or other tasks that involve intense muscular effort and energy expenditure.

Moderate-intensity occupational physical activities: These are tasks that require some physical effort but are not as strenuous as vigorous activities. Such as walking or standing for extended periods, light lifting or carrying, sweeping the floor, washing windows, gardening, hanging laundry on a clothesline, moving light furniture, walking and putting household items away, carrying water or firewood, housework that involves intense scrubbing/cleaning.

Urban residency: participants whose residency is in district/Woreda towns or Zonal towns or capital city of the Region were considered urban residency.

Rural residency: participants whose residency is in rural villages or in semi urban areas were considered rural residency.

Once the data were collected; it was handled confidentially, a codebook was prepared, the data were coded, and be double entered into SPSS version 25 daily. Data checking was done to verify the consistency and backups were saved. Data cleaning was conducted for errors and implausible values that might result from an incorrect reading, incorrect reporting, incorrect filling, and incorrect sensing, incorrect coding, and incorrect typing.

After cleaning the data, frequency tables, graphs, and proportions were used to present the results. In addition, the association between the exposure and the outcome variables was determined using bivariate and multivariate logistic regression analysis. Odds ratios with 95% confidence intervals and p-values were calculated to measure the strength of association.

To assure the quality of the data/research the adapted questionnaire and checklist were prepared using a simple and easily understandable Tigrigna language. Standardization on translation was given emphasis during training. A pre-test was conducted on 10% of study subjects to evaluate the completeness and consistency of the tools. Accordingly, appropriate modifications and corrections were made. At the end of every data collection day, each questionnaire was examined, and pertinent feedback was given to the data collectors and supervisors. Data entry was carried out by the experienced data entry clerk with close supervision by the principal investigator. Data cleaning was conducted out exclusively by the principal investigator, and finalized questionnaires/checklists and the data were stored in a well-secured cabinet.

The ethical statement protocol approved by the Institution Review Board (IRB) of Addis Ababa University-College of Health Sciences (AAU-CHS), and letter approval obtained. In addition, a written permit obtained from the Tigrai Regional State Health Bureau and a written permit was obtained from the ACSH medical director and respective administrative bodies after submitting the protocol and explaining the purpose of the study. All participants were informed about the purpose of the study and individual written informed consent was obtained before the interview and before obtaining blood sample at the time of data collection, anthropometric examination, and blood testing, and the data collectors and the principal investigator were blinded about the cases and controls of T2D, only the nurse and physician in the selected diabetes clinic and

medical OPD in charge were aware because they were in charge of providing all necessary care concerning diabetes. Respondents were not identified by name; they were also informed that they had the right to participate, not to participate, and to withdraw any time they like during the study. Respondents were also informed; no information other than for this study was collected.

Result

Socio-demographic characteristics

In the study period from March 1 to June 30, 2019, a total of 360 patients were interviewed and measured for their socio-demographic and medical history, behavioral characteristics, physical measurements, and biomarker indices. Of those, 120 T2D cases were matched on age and sex with 240 controls to identify risk factors of T2D, primarily focusing on socio-demographic characteristics, family history of diabetes, lifestyle behaviors, dietary characteristics, physical measurements, and biomarkers.

The mean (SD) ages of the cases and the controls were 55.9 (±5.0) and 55.7 (±4.8), respectively. One hundred thirteen (94.2%) cases and 169(70.4%) controls were urban residents. One hundred eleven (92.5%) of the cases and 216(90.0%) of the controls were Orthodox Christianity followers. Eighty seven (73.3%) of the cases and 201(83.8%) of the controls were married, and 19(15.8 %) of the cases and 18(7.5%) of the controls were widowed. Forty-four (36.7%) of the cases and 99(41.3) of the controls had primary education, and 24(20.0%) of the cases and 38(15.9%) of the controls attained higher education. Seventy-four (61.7%) of the cases and 126(52.5%) of the controls were employed, and 24(20.0%) of the cases and 38(15.8%) of the controls were housewives. Thirty-one (25.8%) of the cases and 63(26.3%) of the controls had a monthly family income ≥ 6000 Ethiopian Birr (Table 6).

In the cases and controls, almost half (48.3%) of the cases and one-fifth (17.1.0%) of the controls were ever told as having raised blood pressure. Of those who had raised BP, 45(71.4%) of the cases and 21(46.7%) of the controls were treated for raised BP during the past two weeks prescribed by a doctor or other health care providers. Sixty-one (50.8%) of the cases and 56(23.3%) of the controls were ever told as having raised cholesterol. Thirty-seven (60.7%) of the cases and 27(46.4%) of the controls were treated for raised cholesterol during the past two

weeks prescribed by a doctor or other health care providers. Twenty-eight (23.3%) of the cases and 19(7.9%) had FHD, (Table 1).

Table 16: Socio-demographic characteristics of cases and controls at ACSH, Tigrai, 2019(n=360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	COR[95%CI], t(df),	p-value
Age in years(Mean ± SD)	55.9±5.0	55.7±4.8	t(358)=-0.24	p= 0.8
Residence, n (%)				
Rural	7(5.8)	71(29.6)	1	
Urban	113(94.2)	169(70.4)	6.8[3.0, 15.3]	P< 0.001
Religion, n (%)				
Orthodox	112(93.3)	216(90.0)	0.78[0.13, 4.7]	P= 0.5
Muslim	6(5.0)	21(8.8)	0.43[0.06, 3.2]	
Catholic/protestant	2(1.7)	3(1.3)	1	
Marital status, n(%)				
Married	87(72.5)	201(83.8)	1	
Divorced/separated	14(11.7)	21(8.8)	1.6[0.6, 4.0]	
Widowed	19(15.8)	18(7.5)	2.4[1.2, 4.9]	P=0.029
Educational level (%)				
No formal education	22(18.3)	55(22.9)	1	
Primary education	44(36.7)	99(41.3)	1.0[0.51, 2.0]	
Secondary education	30(25.0)	48(20.0)	1.4[0.76, 2.7]	
Higher education	24(20.0)	38(15.9)	1.6[0.76, 3.2]	P=0.4
Employment status, n (%)				
Employed	74(61.7)	126(52.5)	3.6[1.5, 9.0]	
Unemployed	16(13.3)	39(16.3)	0.93[0.52, 1.7]	
House wife	24(20.0)	38(15.8)	1.4[0.75, 2.7]	P=0.031
Farmer	6(5.0)	37(15.4)	1	
Quartiles of family income in EB				
Q1(< 2000)	9(7.5)	25(10.4)	1	
Q2(2000-3099)	40(33.3)	106 (44.2)	1.1[0.45, 2.4]	
Q3(3100-5999)	40(33.3)	46(19.2)	2.4[1.01,5.8]	P=0.023
Q4(≥ 6000)	31(25.8)	63(26.3)	1.4[0.57, 3.3]	
Ever told as having raised BP, n (%)				
Yes	62(51.7)	199(82.9)	1	p< 0.001
No	58(48.3)	41(17.1)	4.5[2.8, 7.4]	
Ever told as having raised cholesterol				
No	59(49.2)	184(76.7)	1	
Yes	61(50.8)	56(23.3)	3.4[2.1, 5.4]	p< 0.001
Family History of Diabetes				
No	92(76.7)	221(92.1)	1	
Yes	28(23.3)	19(7.9)	3.5[1.6, 3.7]	P< 0.001

Cigarette Smoking and alcohol

Almost one in twenty participants (5.3%) are current smokers of any tobacco products, such as cigarettes, with a higher proportion of cases (8.3%) compared to controls (3.8%) with insignificant differences (p=0.19), and all smokers are men. Of the current smokers, only 6(60.0%) of the cases and 4(44.4%) of the controls smoke >20 cigarettes per day. The mean (±SD) ages of cigarette smoking started among cases (28.4±5.5) and controls (Vs. 32.4±5.3) years old, and the duration of cigarette smoking between cases and controls was 26.6±5.5 and 23.9±5.4, respectively, (Table 7).

In the cases and the controls, the proportion of current drinkers of alcohol was 82.5% and 78.8%, respectively. In both the cases and controls from those who consumed alcohol, the traditional local alcoholic drink 'Suwa/Tela' was the most commonly consumed by 51.5% of the cases and 61'4% of the controls. Among those who drank alcoholic drinks, beer was the second most widely consumed alcoholic drink in 35(35.4%) of the cases and 59(31.2%) of the controls. The proportion of liquor consumption among the cases and controls was 18(18.2%) and 15(7.9%). (p=0.01), (Table 7).

Forty four (36.7%) of the cases and 55(22.9%) of the controls were heavy alcohol drinkers. Thirty sven (61.7%) of men and 7(11.7%) of women among the cases, and 46(38.3%) of men and 9(7.5%) of women among the controls were heavy alcohol drinkers. Four (57.1%) of rural and 40(35.4%) of urban residents among the cases, and 17(23.9%) of rural and 38(22.5%) of urban residents among the controls were heavy alcohol drinkers. The overall average number (±SD) of standard alcoholic drinks during the past 30 days in one drinking occasion was higher among the cases 2.06(±1.6) compared to the controls 1.7(±1.3), p=0.01). Higher proportion of cases (7.5%) compared to controls (2.9%) drank alcohol every day. The median (IQR) number of standard alcoholic drinks per week for the cases and the controls was 11(1–12) and 6.25(0.5–6.75) alcoholic beverages, in a typical week, (Table 2).

Table 17: Cigarette smoking and Alcohol drinking behavior of study participants at ACSH, Tigray, Ethiopia, 2019(n= 360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	COR[95%CI], t(df)	P-value
Cigarette smoking status				
Never smoker	105(87.5)	222(92.5)	1	
Ex – smoker	5(4.2)	9(3.8)	1.2[0.38, 3.6]	
Current smoker	10(8.3)	9(3.8)	2.4[0.93, 6.0]	P= 0.19
Number of cigarettes smoked/day				
≤ 10 cigarettes	2(20.0)	2(22.2)	1	
11 to 20 cigarettes	2(20.0)	3(33.3)	0.67[0.1, 9.5]	
> 20 cigarettes	6(60.0)	4(44.4)	1.5[0.2, 15.5]	P= 0.76
Drinking status				
Life time abstainer	5(4.2)	25(10.4)	1	
Ex – drinker	16(13.3)	26(10.8)	3.1[0.98, 9.7]	
Current drinker	99(82.5)	189(78.8)	2.6[0.97, 7.1]	P=0.13
During the past 30 days, on average, standard alcoholic drinks on one occasion (%)				
Non-drinker	21(17.5)	51(21.3)	1	
Light drinker	13(10.8)	21(8.8)	1.5[0.67, 3.6]	
Moderate drinker	42(35.0)	113(47.1)	0.9[0.45, 1.7]	
Heavy drinker	44(36.7)	55(22.9)	1.9[1.02, 3.47	P= 0.029
During the past 30 days, how frequently have you had at least one alcoholic drink?				
Non-drinker	21(17.5)	51(21.3)	1	
Less than once per week	3(2.5)	17(7.1)	0.43[0.1,1.6]	
1-4 days per week	65(54.2)	147(61.3)	1.1[0.6, 1.9]	P=0.004
5 -6 days per week	22(18.3)	18(7.5)	3.0[1.3, 6.6]	
Every day	9(7.5)	7(2.9)	3.1[1.03, 9.5]	
Common types of alcoholic drinks drunk				
'Suwa/Tela' (yes, %)	51(51.5)	116(61.4)	0.7[0.4, 1.1]	P=0.1
'Meas/Tej' (yes, %)	9(9.1)	8(4.2)	2.3[0.9, 6.1]	P=0.1
Beer (yes, %)	35(35.4)	59(31.2)	1.2[0.7, 2.0]	P=0.4
Wine (yes, %)	10(10.1)	18(9.5)	1.1[0.5, 2.4]	P=0.8
Liquar (yes, %)	18(18.2)	15(7.9)	2.6[1.2, 5.4]	P=0.01

Dietary Characteristics of Cases and Controls

As the study participants reported, seventy-two (60%) of the cases and 174(72.5%) of the controls reported injera made from teff/barely/sorghum as their favorite/staple diet they usually ate. Bread/injera made of wheat was the second most commonly consumed diet in 24(20.0%) of cases and 33(13.8%) of the controls **(**Table 3**).**

Forty-nine (40.8%) of the cases and 88(36.7%) of the controls reported that they did not use fruit in their dish in a typical week. Only 1.7% of cases and 3.3% of controls consumed 14 or more servings of fruits in their dishes in a typical week. In a typical week, the median (IQR) number of days fruit use in a dish for the cases and the controls were 2(0.0–2.0) and 3(0.0–3.0), respectively. The median (IQR) number of dishes fruit use for the cases and the controls were the same 1.0(0.0-1.0) number of dishes per day in a typical week. Similarly, the median (IQR) number of dishes of fruit used in a typical week for the cases and controls were 3(0.0–3.0) and 4(0.0–4.0), respectively. Fourteen (11.7%) of the cases and 34(14.2%) of the controls reported that they did not use vegetables in their dish in a typical week. Only 5.8% of the cases and 8.8% of the controls consumed 14 and above servings vegetables in their dish in a typical week. The median (IQR) number of days vegetables use in a dish in a typical week for the cases and controls were 1(2.0–3.0) and 2(1.0–3.0), respectively. In a typical week, the mean (SD) number of dishes of vegetable use per day was 1.4(±0.72) for the cases and 1.4 (±0.76) dishes for the controls. In a typical week, the median (IQR) number of dishes of vegetable use for the cases and controls were 4(2.0–6.0) and 5(1.0–6.0), respectively (Table 3).

More than 73% of the cases and 67.1% of the controls consumed one to three cups of coffee per day. Forty-one (34.5%) of the cases and 72(30.0) of the controls consumed two or more cups of tea every day. In a typical week, 28(23.3%) of the cases and 30(12.5%) of controls consumed one to two bottles of sugar-contained soft drink beverages (p=0.033) (Table 3).

Table 18: Dietary characteristics of cases and controls at ACSH, Tigrai, Ethiopia, 2019(n= 360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	COR[95%CI], t(df)	P-value
Your most favorite and regularly used food				
Injera made from Teff/barely/sorghum	72(60.0)	174(72.5)	1	
Bread/injera made from wheat	24(20.0)	33(13,8)	0.57[0.31, 1.03]	
Rice	12(10.0)	11(4.6)	0.38[0.16, 0.90]	
Pasta	9(7.5)	13(5.4)	0.6[0.25, 1.5]	
Others	3(2.5)	9(3.8)	1.2[0.33, 4.7]	P=0.085
Fruit eating in a typical week				
0-13 servings	118(98.3)	232(96.7)	1	
14 and above	2(1.7)	8(3.3)	0.49[0.1, 2.4]	p=0.37
Vegetables eating in a typical week				
0-13 servings	113(94.2)	219(91.2)	1	
14 and above	7(5.8)	21(8.8)	0.67[0.27, 1.6]	p=0.33
Coffee consumption per day				
None	26(21.7)	58(24.2)	1	
1-3 cups	88(73.3)	161(67.1)	0.52[0.2, 1. 3]	
> 3 cups	6(5.0)	21(8.8)	0.64[0.23, 1.8]	P=0.35
Tea consumption per day				
None	35(29.4)	67(27.9)	1	
1 cup	43(36.1)	101(42.1)	1.1[0.62, 1. 1]	
≥ 2 cups	41(34.5)	72(30.0)	1.3[0.79, 2.3]	P=0.5
Soft drink beverages consumption per week				
None	83(69.2.3)	187(77.9)	0.48[0.27, 0.85]	
1 -2 bottles	28(23.3)	30(12.5)	0.71[0.25, 2.0]	
≥ 3 botltles	9(7.5)	23(9.6)	1	P=0.033

Others: Processed, fast foods, and fatty acid foods,

Occupational and Leisure Physical Activities (LPA) of Cases and Controls

A comparison of self-reported occupational activity engagement between the cases and controls revealed that only 15 (12.5%) of the cases and 79 (32.9%) of the controls engaged in vigorous-intensity occupational activity. Of those who were involved in vigorous-intensity occupational activity, the mean hour engagement was 16.7±8.2 hours per week for cases and 18.1±7.3 hours per week for controls. Rural residents had better engagement in vigorous-intensity occupational activity, with 6(85.7%) cases and 48(67.6%) for controls compared to the urban residents, only 9(8.0%) of the cases and 31(18.3%) of the controls engaged in vigorous-intensity occupational activity (Figure 2). A higher proportion of vigorous-intensity occupational activity was self-

reported in 8(13.3%) of cases and 46(38.3%) for controls among men compared to 7(11.7%) of cases and 33(27.5%) for controls among women (Table 4).

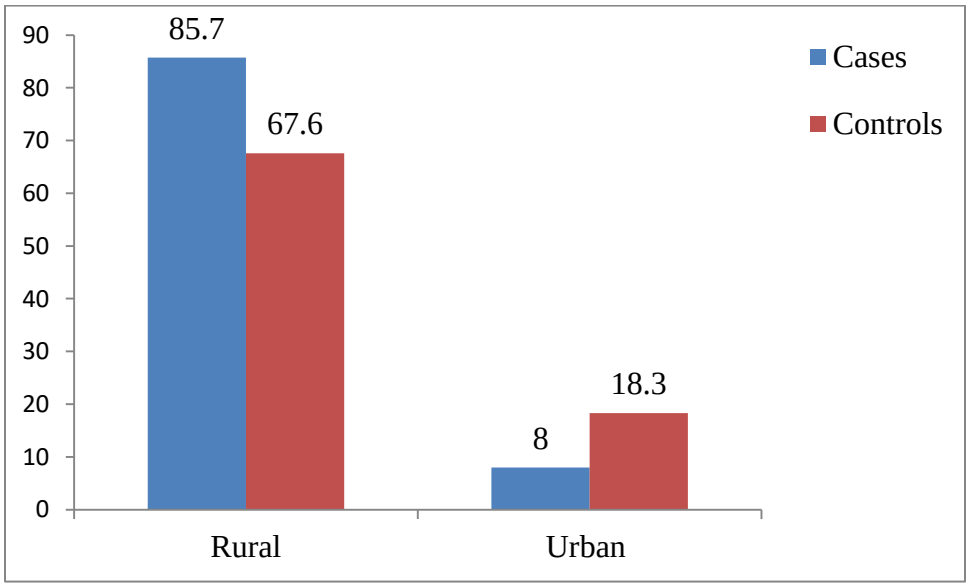

Figure 10: Percent of urban and rural residents' engagement in the vigorous-intensity occupational activity of cases and controls, Tigrai, Ethiopia, 2019(n= 360).

Forty-eight (40.0%) of the cases and 151(62.9%) of the controls were involved in moderate-intensity occupational activity. The mean hour engagement in moderate-intensity occupational activity was 22.5±8.6 hours per week for cases and 24.5±10.2 hours per week for controls. Rural residents had better engagement in moderate-intensity occupational activity, with 5(71.4%) cases and 61(85.9%) for controls compared to the urban residents, 43(38.1%) of the cases and 90(53.3%) of the controls involved in moderate-intensity occupational activity. Similarly, a higher proportion of moderate-intensity occupational activity was self-reported in 8(13.3%) of cases and 46(38.3%) for controls among men compared to 7(11.7%) of cases and 33(27.5%) for controls among women (Table 4).

Seventeen (14.2%) of the cases and 43(17.9%) of the controls did not walk or use a bicycle (pedal cycle) for at least 10 minutes continuously to get to and from places. Five (4.9%) of the cases and 23(11.7%) of the controls spent walking or using a bicycle for at least 10 minutes continuously getting to and from places for seven days a week. Nineteen (16.0%) of the cases and 53(22.1) of the controls spent walking or using a bicycle for 150 minutes per week. Only

1(0.8%) of the cases and 4(1.7%) of the controls spent walking or using a bicycle for 300 minutes and more in a typical week (Table 4).

Only 6(5.0%) of the cases and 18(7.5%) of the controls were involved in vigorous-intensity sports, fitness, or recreational (leisure) activities. Among the cases and controls who were engaged in vigorous-intensity sports, fitness, or leisure activities, 4(66.7%) of the cases and 15(83.3%) of the controls were involved for 75 minutes or more in vigorous-intensity sports, fitness, or leisure activities in a typical week. Of those cases and controls that involved vigorous-intensity sports, fitness, or leisure activities, only 2(33.3%) of the cases and 3(16.7%) of the controls engaged for 150 minutes per week. Only 8(6.7%) of the cases and 25(10.4%) of the controls were involved in moderate-intensity sports, fitness or leisure activities. Three (37.5%) of the cases and 4(16.7%) of the controls were engaged for 150 minutes or more in moderate-intensity sports, fitness, or leisure activities in a typical week (Table 4).

Sixty one (50.8%) of the cases and 64(26.7%) of the controls had low physical activity, and 48(40.0%) of the cases and 152(63.3) of the controls had high physical activity. Six (85.7%) of the cases and 61(85.9%) of the controls of rural residents were highly active, while only 42(37.2%) and 91(53.8%) of the controls of urban residents were highly active. Thirty-three (55.0%) of the cases and 27(22.5%) of the controls among men, and 28(46.7%) of case and 37(30.8%) of the controls among women had low PA. Only 9(7.5%) of the cases and 33(13.7%) of the controls were engaged in moderate-vigorous leisure physical activity. Regarding the sedentary behavior of the cases and controls, 63(52.5%) of the cases and 88(37.1%) of the controls spent 6 hours or more in sedentary activities (Table 4).

Table 19: Occupational and LPA of cases and Controls at ACSH, Tigrai, Ethiopia, 2019(n= 360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	COR[95%CI], t(df)	P-value
Vigorous-intensity of occupational PA				
Yes	15(12.5)	79(32.9)	0.3[0.2, 0.5]	
No	107(87.5)	161(67.1)	1	P< 0.001
Moderate-intensity of occupational PA				
Yes	48(40.0)	151(62.9)	0.4[0.3, 0.6]	
No	72(60.0)	89(37.1)	1	P< 0.001
Walk or use a bicycle (pedal cycle) for at least 10 minutes continuously				
Yes	103(85.8)	197(82.1)	1.3[0.7, 2.4]	
No	17(14.2)	43(17.1)	1	P<=0.35
Vigorous-intensity sports, fitness/LPA				
Yes	6(5.0)	18(7.5)	0.7[0.3, 1.7]	
No	114(95.0)	222(92.5)	1	P=0.37
Moderate-intensity sports, fitness/LPA				
Yes	8(6.7)	25(10.4)	0.6[0.3, 1.4]	
No	112(93.3)	215(89.6)	1	P=0.25
Physical activity (%)				
Low	61(50.8)	64(26.7)	3.0[1.9, 4.9]	
Medium	11(9.2)	24(10.0)	1.5[0.7, 3.2]	
High	48(40.0)	152(63.3)	1	P<0.001
Leisure MVPA				
None	111(92.5)	207(86.3)	2.0[0.9, 4.3]	
Yes	9(7.5)	33(13.7)	1	P=0.086
Sedentary behavior				
< 4 hours/day	10(8.3)	55(23.2)	1	
4 to 6 hours/day	47(39.2)	94(39.7)	1.4[0.9, 2.3]	
> 6 hours	63(52.5)	88(37.1)	3.9[1.9, 8.3]	P=0.001

Physical and biomarkers characteristics of Cases and Controls

Fifty-seven (47.5%) of the cases and 76(31.5%) of the controls had overweight, and 36(30.0%) of the cases and 32(13.3%) of the controls were obese. For cases and controls, 94(78.3%) of the cases and 98(40.8%) controls had high waist circumference. Ninety-one (75.8%) of the cases and 136(56.7%) of the controls had high WHR, and also 107(89.2%) of the cases and 131(54.6%) of the controls had high WHtR (Table 10).

Fifty-four (45.0%) of the cases and 60(25.0%) of the controls had a raised total cholesterol. Thirty-four (28.3%) of the cases and 42(17.5%) of the controls had Men/women < 40/50 mg/dL HDL-C. Fority one (34.2%) of the cases and 44(18.3%) of the controls had raised raised LDL-C. Moreover, elevated triglyceride was also detected in 73(60.8%) of the cases and 117(48.8%) of the controls. Fifty two (43.3%) of the cases and 52(21.7%) had raised SBP, and 41(34.2%) of cases and 43(17.9%) had elevated DBP. Sixty-eight (56.7%) of the cases and 70(29.2%) of the controls had hypertension. Fifty-eight (48.3%) of the cases and 60(25.0%) of the controls had dyslipidemia (Table 5).

Table 20: Physical and biomarker characteristics of Cases and Controls at ACSH, Tigrai, 2019(n= 360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	COR[95%CI], t(df)	P-value
BMI				
Normal	27(22.5)	132(55.0)	1	
Overweight	57(47.5)	76(31.7)	3.7[2.1, 6.3]	p< 0.001
Obese	36(30.0)	32(13.3)	5.5[2.9, 10.3]	
Waist Circumference				
Men/women < 94/80	26(21.7)	142(59.2)	1	
Men/women ≥ 94/80	94(78.3)	98(40.8)	5.2[3.2, 8.7]	p< 0.001
WHR				
Men/women < 0.88/0.82	29(24.2)	104(43.3)	1	
Men/women ≥ 0.88/0.82	91(75.8)	136(56.7)	2.4[1.5, 3.9]	p< 0.001
WHtR				
Men/women < 0.49/0.50	13(10.8)	109(45.4)	1	
Men/women ≥ 0.49/0.50	107(89.2)	131(54.6)	6.8[3.7, 12.9]	p< 0.001
Total cholestrol				
< 200 mg/dl	66(55.0)	180(75.0)	1	P<0.001
≥ 200 mg/dl	54(45.0)	60(25.0)	2.5[1.5, 3.9]	
HDL-C				
Men/women ≥ 40/50 mg/dl	86(71.7)	198(82.5)	1	P=0.019
Men/women < 40/50 mg/dl	34(28.3)	42(17.5)	1.9[1.1, 3.1]	
LDL-C				
< 130 mg/dl	79(65.8)	196(81.7)	1	
≥ 130 mg/dl	41(34.2)	44(18.3)	2.3[1.4, 3.8]	p= 0.001
Triglycerides				
< 150 mg/dl	47(39.2)	123(51.2)	1	
≥ 150 mg/dl	73(60.8)	117(48.8)	1.6[1.1, 2.6]	P=0.031
SBP				
< 130 mmHg	43(35.8)	145(60.4)	1	
130 to 139 mmHg	25(20.8)	43(17.9)	1.7[0.92, 3.2]	
≥ 140 mmHg	52(43.3)	52(21.7)	3.4[2.0, 5.6]	p< 0.001
DBP				
< 85 mmHg	54(45.0)	165(68.8)	1	
85 to 89 mmHg	25(20.8)	32(13.3)	1.2[0.62, 2.4]	
≥ 90 mmHg	41(34.2)	43(17.9)	2.9[1.7, 4.9]	p< 0.001
Hypertension				
No	52(43.3)	170(70.8)	1	
Yes	68(56.7)	70(29.2)	3.2[2.0, 5.0]	p< 0.001
Dyslipidemia				
No	62(51.7)	180(75.0)	1	
Yes	58(48.3)	60(25.0)	2.8[1.8, 4.8]	p< 0.001

Potential risks of T2D Binary logistic regression adjusted odds ratio

On multivariable logistic regression (Table-6), urban residence, widowhood/divorce, FHD, hypertension, dyslipidemia, consumption of rice, alcohol consumption, elevated WC and WHtR were significantly associated with increased odds of T2D, while leisure MVPA is protective.

The odds of developing T2D were more than fivefold higher among the urban residents compared to the rural dwellers [AOR=5.1, 95%CI (2.0, 13.2)]. Likewise, those being divorced and widowed were nearly three times and more than times more likely to have T2D compared to their married counterparts [AOR=2.8, 95%CI (1.1, 7.3)] and [AOR=3.3, 95%CI (1.3, 8.6)], respectively (Table-6).

The odds of having T2D among participants who had hypertension were 3.0 times higher than those who did not have hypertension [AOR=**3.0,** 95%CI **[**1.7,5.5**]**. Besides, the chances of developing T2D among those who had dyslipidemia were almost three times higher compared to those who had not dyslipidemia [AOR=2.8, 95%CI (1.5, 5.4)]. Similarly, those who had a family history of diabetes experienced more than fivefold higher odds of developing T2D than those who did not have the same history [AOR=5.4, 95%CI (2.4, 12.5)] (Table-6).

The risk of developing T2D were threefold higher among those who consumed 5 to 6 days in a typical week and 3.5 times higher in those who consumed alcohol everyday compared to non-drinker [AOR=3.0, 95%CI (1.1, 3.6)] and [AOR=3.5, 95%CI (1.2, 10.2)], respectively. The odds of developng T2D were 3.8 times higher in those who used rice as favourite/regular diet compared to those who ate injera made of teff/barely/sorghum[AOR=3.8,95%CI (1.2, 11.6)]. The risk of developing T2D among those with a elevated waist circumferences was almost more than times higher compared to those with a normal waist circumference [AOR= 2.4, 95%CI (1.1, 5.0)]. Likewise, the odds of developing T2D among those with an elevated WHtR was 4.4 times higher compared to those with a normal WHtR [AOR=4.4, 95%CI (1.7, 11.2)]. Participants who engaged in leisure MVPA reduced their risk of T2D by 27% compared to those who did not engaged in leisure MVPA [AOR= 0.27, 95%CI (0.1, 0.72)] (Table-6).

Table 21: Potential risk factors of T2D at ACSH, Tigrai, Ethiopia, 2019(n= 360).

Patient characteristics	Cases n=120(%)	Controls n=240(%)	AOR[95% CI],	p-value
Residence, n (%)				
Rural	7(5.8)	71(29.6)	1	
Urban	113(94.2)	169(70.4)	5.1[2.0, 13.2]	p= 0.001
Marital status, n(%)				
Married	87(72.5)	201(83.8)	1	
Divorced/separated	14(11.7)	21(8.8)	2.8[1.1, 7.3]	
Widowed	19(15.8)	18(7.5)	3.3[1.3, 8.6]	P=0.008
Hypertension				
No	52(43.3)	170(70.8)	1	
Yes	68(56.7)	70(29.2)	3.0[1.7, 5.5]	p< 0.001
Dyslipidemia				
No	62(51.7)	180(75.0)	1	
Yes	58(48.3)	60(25.0)	2.8[1.5, 5.4]	p=0.002
Family History of Diabetes				
No	92(76.7)	221(92.1)	1	
Yes	28(23.3)	19(7.9)	5.4[2.4, 12.5]	P< 0.001
Cigarette smoking status				
Never smoker	105(87.5)	222(92.5)	1	
Ex – smoker	5(4.2)	9(3.8)	1.5[0.3, 6.3]	
Current smoker	10(8.3)	9(3.8)	3.4[0.82, 13.9]	P= 0.22
Frequency of alcohol intake per week				
Non-drinker	21(17.5)	51(21.3)	1	
Less than once per week	3(2.5)	17(7.1)	0.2[0.1,1.1]	
1-4 days per week	65(54.2)	147(61.3)	1.1[0.5, 2.1]	
5 -6 days per week	22(18.3)	18(7.5)	3.0[1.1, 3.6]	P=0.012
Every day	9(7.5)	7(2.9)	3.5[1.2, 10.2]	
Most favorite and regularly used food				
Injera of teff/barely/sorghum	72(60.0)	174(72.5)	1	
Bread/injera made from wheat	24(20.0)	33(13,8)	1.7[0.8, 4.0]	
Rice	12(10.0)	11(4.6)	3.8[1.2, 11.6]	
Pasta	9(7.5)	13(5.4)	1.3[0.4, 4.7]	
Others	3(2.5)	9(3.8)	0.3[0.1, 1.6]	P=0.059
Waist Circumference				
Men/women < 94/80	26(21.7)	142(59.2)	1	
Men/women ≥ 94/80	94(78.3)	98(40.8)	2.4[1.1, 5.0]	P= 0.027
WHtR				
Men/women < 0.49/0.50	13(10.8)	109(45.4)	1	
Men/women ≥ 0.49/0.50	107(89.2)	131(55.6)	4.4[1.7, 11.2]	p=0.002
Engagement in leisure MVPA				
None	111(92.5)	207(86.3)	1	
Yes	9(7.5)	33(13.7)	0.27[0.1, 0.72]	P=0.009

Discussion

This study endeavored to determine factors associated with T2D in the hospital setting of Tigrai. The study found that urban residency, widowhood/divorce, family history of diabetes, hypertension, dyslipidemia, regular consumption of rice, alcohol consumption, elevated waist circumference and WHtR levels were significantly associated with increased odds of T2D, while leisure MVPA is found preventive

The socio-demographic and geographic burdens of T2D are uneven throughout the world, with neighborhoods in high-income countries like the US, Canada, and Australia showing increased risk for those living in deprived areas. Deprived neighborhoods have limited access to healthy foods, physical activity, healthcare, education, social support, and environmental pollutants, increasing their risk of developing T2D(101,113,223,230), whereas, in developing countries, the risk is higher in urbanized areas(114,115,129). The study found that urban residents have more than times higher odds of developing T2D compared to rural residents, which is is consistent with previous studies in Myanmar(114), West Africa(115), Ghana(129), Algeria(7), and North West Ethiopia(100). Urbanization in developing countries leads to dietary changes, increased smoking, alcohol consumption, and sedentary lifestyles, contributing to obesity and NCDs like diabetes(115,228).

Marriage, a vital social institution since ancient times, has been linked to various health issues, but conflicting findings have been found in previous studies, regarding the association between marital status and T2D(7,115,124,125). Previous studies in Brazil and West Africa indicated being divorced/widowed lowers the risk of developing T2D compared to married and single, respectively(115,125). The study reveals that divorced and widowed individuals are 2.8 and 3.3 times more likely to develop T2D compared to married individuals, consistent with research from Iran and Saudi Arabia(7,124). Inconsistencies may be attributed to disparities in geographical location, culture, and socio-economic status. Studies suggest marriage improves health outcomes, lowers diabetes incidence, and improves adherence to treatment in partnered patients, influenced by health behaviors and socio-economic status(125). The death of a spouse can lead to significant stress and anxiety, lack of social support, change in lifestyles, financial strain, and feelings of loneliness and isolation, which could lead to a lack of motivation to

engage in healthy behaviors and poorer health outcomes, including an increased risk of developing T2D.

Epidemiological studies have shown that a family history of diabetes (FHD) is associated with a range of metabolic abnormalities and is a strong risk factor for the development of T2D. In the current study, patients with a FHD have a more than fivefold risk of developing T2D compared to those with a negative FHD, which is consistent with previous studies(42,100,173,231–234). FHD can include environmental factors besides the genetic risk that provides for obesity and some lifestyle factors, such as alcohol consumption, smoking, and diet. Individuals with an FHD may share similar lifestyle habits and environmental exposures with their relatives, such as unhealthy dietary patterns, sedentary behavior, and obesity, which were reported to be associated with an FHD(42,235).

Cigarette smoking significantly impairs glucose tolerance and increases insulin resistance, leading to T2D, either independently or in clusters with other risk factors like centripetal obesity(140,141,147). Experience with cigarette smoke, combined with elevated blood glucose, is linked to vascular damage, endothelial dysfunction, and blood-clotting cascade activation, causing further vascular damage in individuals with diabetes(142,143). Studies show conflicting results on the link between smoking and T2D. While most epidemiological studies show a higher likelihood of developing T2D in smokers in Saudi Arabia, West Africa, and North Ethiopia(115,148,149), China and South Africa reported smokers have a lower likelihood of newly-diagnosed diabetes than non-smokers(123,151). At the same time, the findings of this study indicated a null association between smoking and T2D. Possibly only one in twenty participants (5.3%) are current smokers of any tobacco products, such as cigarettes, with a higher proportion of cases (8.3%) compared to controls (3.8%) with an insignificant difference ($p=0.19$), which might be a negligible number to give important facts, and all smokers are men. Similarly, other investigators in Ethiopia found no association between smoking and T2D(57,100,150).

Previous studies(154–157) indicate that heavy alcohol consumption is a risk factor for Type 2 Diabetes, while moderate alcohol consumption is protective in both men and women. Even though the biological mechanisms remain poorly understood, moderate alcohol consumption has

been linked to improved insulin sensitivity, changes in alcohol metabolites, increased HDL cholesterol concentrations, and anti-inflammatory effects, though the exact dose-response relationship remains unclear(152,153). A study in West Africa demonstrated that alcohol consumption every day reduces the odds of T2D by 45%(115). Likewise, a study in North West Ethiopia showed that alcohol consumption was preventive for diabetes for rural residents(100). While in the present study, alcohol consumption everyday increases 3.5 times higher risk of T2D compared to non-drinker. The variance may be attributed to various factors such as difference in lifestyle, patient characteristics, type, amount, and frequency of alcohol consumption.

Dietary intake is a significant environmental risk factor for developing and preventing T2D, with dietary patterns potentially having greater health effects than individual foods, nutrients, or food groups(168). Consuming sugar-sweetened beverages, refined carbohydrates, processed meats, refined grains, and fatty foods can increase the risk of T2D by disrupting glucose metabolism and insulin sensitivity(117,133). The current study found that regular rice consumption increases the risk of T2D by 3.8 times compared to those who ate injera made of teff/barely/sorghum. This is consistent with a large-scale study found that consuming more white rice (over 450 g/day) increases the risk of diabetes (137). This may be due to white rice has high glycemic index(GI) and low fiber content can lead to weight gain, insulin resistance, and T2D risk, while replacing healthier carbohydrates like whole grains, legumes, and vegetables, which have lower GI, higher fiber content, and more nutrients, increasing metabolic diseases, including T2D(236,237).

Epidemiological studies demonstrated that elevated waist circumference, WHR, and WHtR are imperative indicators of central obesity, which is strongly linked with insulin resistance, inflammation, hormonal imbalances, and genetic factors that contribute to the development of T2D in both men and women (159,170,238); which is consistent with the finding of the present study, the risk of developing T2D is 2.4 and 3.2 times higher among individuals with elevated waist circumference and WHtR compared to those who have normal waist circumference and WHtR, respectively. The excessive non-essential fat accumulation around the abdomen, particularly visceral fat with increased waist circumference, WHR, and WHtR, releases fatty acids and inflammatory substances that interfere with insulin action, which may lead to raised glucose levels, low secretion of insulin by the pancreas or insulin insensitivity, both leads to

T2D(57,165). Managing central obesity through lifestyle modifications such as healthy eating, regular physical activity, and weight loss can help reduce the risk of T2D.

Previous studies have shown that hypertension is an independent predictor of T2D(239). The findings of the current study showed that the possibility of developing T2D is 3.0 times higher in patients with hypertension compared to individuals with normal blood pressure. This finding is consistent with studies in West Africa(115), Ethiopia(149), and Mekelle City (57), and the risks of developing T2D are 2.6, 3, and 6-fold higher in patients with hypertension compared to individuals with normal blood pressure, respectively. This might be due to both hypertension and T2D frequently coexist and contribute to each other's complications through shared pathophysiological mechanisms that justify their coexistence.

Dyslipidemia has recently been recognized as a risk factor for T2D. Literature shows that low levels of HDL-C, elevated levels of triglycerides, LDL-C, and total cholesterol are significantly associated with newly diagnosed T2D(57,166,183–185,240–243). In the current study, the possibility of developing T2D is nearly three times higher among individuals with dyslipidemia compared to those who do not. This finding is parallel with findings in Ghana(129), Addis Ababa(58), and Mekelle city (57). This coexistence might be due to elevated levels of free fatty acids derived from triglycerides contribute to insulin resistance by interfering with insulin signaling pathways in peripheral tissues, with the inclination of increasing concentration of blood glucose and cholesterol nearly in the same manner as physical inactivity, body weight in general and central obesity in particular(165,244).

Findings of previous studies regarding the intake of fruit and vegetables on T2D have been inconsistent(245–248). Some of the studies have shown an inverse association with the risk of T2D with higher intakes of total fruit(247,249) and total vegetables(246,247,250). In contrast, other studies did not find associations for total fruit (246,248,251) or total vegetables(248,251). The study found no significant association between fruit and vegetable consumption and T2D. Probably only 2(1.7%) of the cases and 8(3.3%) of the controls consumed 14 and more servings of fruits in a typical week, with an insignificant difference (p=0.37), and only 7(5.8%) of the cases and 21(8.8%) of the controls consumed 14 and more servings of vegetables in a typical week, with an insignificant difference (p=0.33), which might be a negligible number to give important facts. The inconsistency among these studies may be explained by differences in the

types of fruits or vegetables consumed in different study populations as well as a difference in participants' characteristics, study design, and assessment methods. Fruits and vegetables are a rich source of dietary fiber, antioxidants, and phytochemicals, which can help regulate blood sugar levels, improve insulin sensitivity, and potentially reduce T2D risk(115,129).

Findings of various observational studies demonstrated that physical activity has a protective effect on T2D, and inverse associations were observed for increasing activity over time, resistance exercise, occupational activity, and cardiorespiratory fitness and risk of T2D(157,161).

In the current study, engagement in moderate-intensity, vigorous-intensity occupational, moderate and vigorous-intensity sports, fitness or leisure activities, and walking or using a bicycle (pedal cycle) for at least 10 minutes continuously are not significantly associated with reduction of T2D. This discrepancy might be due to differences in the type of activity, duration of the activity, participants' characteristics, study design, and assessment methods. Regular physical activity plays an essential part in reducing the risk of developing T2D and improving outcomes for those who have already been diagnosed with the condition.

Strengths and Limitations

This study has several strengths, including the use of the standardized WHO STEPS method, which ensure comparable results across countries. The strength of the present study was, unlike many previous studies in Ethiopia that they used is cross- sectional study design, meaning that associations cannot be assumed to be causal; this study uses matched case control study design. Similarly, previous studies include their target population was either all age groups or adults aged 18 years old and more, whereas our target groups were the most risky groups (middle age 45 to 64 years old) only. In most of previous Ethiopian studies, they assessed all types of diabetes while this study targeted the most common, T2D. In most of previous studies, unlike various earlier studies in the country that have used a random capillary blood sample, we have used both fasting and venous blood samples, which produces more accurate estimates of glucose concentration. Moreover, we have used a better fully automated clinical chemistry analyzer machine for analysis of biomarkers.

Besides, T2D patients were ascertained from the diabetes clinic by the endocrinologists, and the controls were ascertained by senior physician or General practitioner who were providing care in

the in the general medical OPD using blood glucose test and other investigations, and it was at Ayder Comprehensive Specialized Hospital where better experienced health care providers, equipment and material supply is available. The selections of the controls were governed by the follow up of T2D patients selected from the diabetes clinic. The selected T2D patients were who was diagnosed in the last one year to minimize the recall bias. Moreover, the data collectors were kept blinded for the cases and non-cases during the data collection process of the case control study.

It is imperative to acknowledge, as our results must be viewed in light of some important limitations. For both the cases and controls; we measured dietary assessment, alcohol consumption, cigarette smoking, and physical activity at one point in time, and this may not have represented habitual behavior levels across the lifespan. Measurement error in self-report is inevitable, and the misclassification attributed to self-reported behaviors likely biased the association toward the hypothesis. Besides, social desirability and/or social approval could also affect self-reported behaviors. Likewise, since the current study is hospital based it might not be generalized to the whole community in the region and the country.

Conclusion

We found, being an urban resident, widowhood/divorced, FHD, hypertension, dyslipidemia, consumption of rice, alcohol consumption, elevated waist circumference and waist-to-height ratio were confirmed possible risk factors of T2D, while leisure MVPA is protective. Normal individuals should practice healthy lifestyle behaviors like exercising regularly to prevent weight gain, eating healthily, and controlling blood pressure.

Abbreviations

BMI, body mass index; CVD, cardiovascular disease, DBP, diastolic blood pressure; DM, diabetes mellitus; ETB, Ethiopian Birr; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; IQR: Inter Quartile Range; IDF, International Diabetic Federation; LDL-C, low-density lipoprotein cholesterol; NCDs, non-communicable diseases; SD: Standard Deviation; SBP, systolic blood pressure; WC, waist circumference; WHO, World Health Organization, WHR, Waist Hip Ratio; WHtR, Waist Height Ratio

Ethics approval and informed consent

The ethical clearance was obtained from the Institutional Review Board (IRB) of Addis Ababa University College of Health Sciences. The study followed basic ethical principles of Helsinki declaration for medical research involving human participants which illustrates that the right to make informed decisions, recognition of vulnerable groups and others. All of the study participants were informed about the purpose and procedure of the research and their right to withdrawal from the study at any time. Written informed consent was obtained from each of the study participants. Meanwhile, the study participants were agreed to the extent that the finding of this study will be subjected to publication. Participants were well informed not to disclose their information to a third person. The information was kept secured and put confidentially with the first author.

Data availability

Data will be available up on request

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Authors' contributions

All authors contributed from the conception of idea up to data analysis and write up. They also participated in drafting or revising of the article and have agreed on to which journal the article shall be submitted and have given final approval of the version to be published, and agreed to be accountable for all aspects of the work. Specifically, GG was conceptualized the topic of interest, involved in data collection, coding, cleaning, analysis, interpretation of the result unto preparation of this manuscript. FE was involved in proposal development, planning the fieldwork and result section, and ND and HY were involved in proposal development, data analysis and write up and have participated in critical reviewing of the manuscript.

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Orginal Paper –Three

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ORIGINAL RESEARCH

Hyperglycemic Crisis Characteristics and Outcome of Care in Adult Patients without and with a History of Diabetes in Tigrai, Ethiopia: Comparative Study

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Objective: To compare hyperglycemic crisis characteristics and outcomes of care in adult patients without and with a history of diabetes in Tigrai, Ethiopia.

Methods: A retrospective record review of diabetes patients, 196 without and 393 with a history of diabetes who had been treated in the medical wards from September 1/2017 to August 31/2018, aged 18 years and above was included. An independent-samples *t*-test/Mann–Whitney tests, χ^2-test, and logistic regression analysis were used to analyze the data using SPSS version 25.0.

Results: Patients without history of diabetes were younger [43.9±12.6 vs 48.4±14.9], more rural residents [53.1% vs 30.3%], lower proportion of type 2 diabetes [38.3% vs 53.7%], hyperosmolar hyperglycemic state [15.8% vs 31.8%], with lower mortality rate [8.7% vs 15.5%] compared to with a history of diabetes. A higher mortality reported in rural residents [13.5% vs 3.3%; without vs 21.8% vs 12.8%; with history], and lower urine ketones [1.9± 1.3 vs 2.8± 1.1; without vs 1.6± 1.2 vs 2.2± 1.0; with a history] compared to their counterparts in both patients, respectively. Rural residents [AOR (95% CI); 3.1 (1.8, 5.4)]; medical history of stroke [AOR (95% CI); 2.7 (1.3, 5.6)]; type 2 diabetes [AOR (95% CI); 2.3 (1.1, 4.7)], hyperglycemic hyperosmolar state [AOR (95% CI); 2.4 (1.1, 5.4)]; and with a history of diabetes [AOR (95% CI); 2.0 (1.04, 3.8)] were significantly associated with mortality, but polydipsia [AOR (95% CI); 0.47 (0.27, 0.81)] was preventive.

Conclusion: This finding suggests that rural residents, medical history of stroke, type 2 diabetes, hyperglycemic hyperosmolar state, and with a history of diabetes were independent predictors of mortality while polydipsia was preventive. Therefore, the need for more public health awareness campaigns, screening for people having known risk factors, and expansion of diabetes care services to the primary health care units is a fundamental measure.

Keywords: hyperglycemic crisis, mortality, new-onset, with history, outcome

Plain Language Summary

This study aims to compare hyperglycemic crisis characteristics and outcomes of care in adult patients without and with a history of diabetes in Tigrai, Ethiopia. A retrospective medical chart review of all adult patients aged 18 years and above with a hyperglycemic crisis of 196 without and 393 with a history of diabetes admitted in a medical ward from September 1/2017 to August 31/2018; are included in the study. Patients without a history of diabetes are younger with a mean age of (44 vs 49 years), more rural residents (53.1% vs 30.3%), lower the proportion of type 2 diabetes (38.3% vs 53.7%) and hyperosmolar

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hyperglycemic state (15.8% vs 31.2%) compared to with a history of diabetes. Mortality is higher in patients with a history of diabetes [15.5% vs 8.7%], rural residents [13.5% vs 3.3%; without, and 21.8% vs 12.8%; with], and with lower urine ketones [1.9± 1.3 vs 2.8± 1.1; without and 1.6± 1.2 vs 2.2± 1.0; with] compared to their counterparts. A 30 days cases of mortality is 3.0, 2.7, 2.3, 2.4, and 2.0 times higher in rural residents, who had a stroke, type 2 diabetes, hyperglycemic hyperosmolar state, and with a history of diabetes, respectively; but reduced by 47% in patients with excessive thirst. In general, rural residents, a history of stroke, type 2 diabetes, hyperglycemic hyperosmolar state, and with a history of diabetes are risk factors for mortality while excessive thirst is preventive. Therefore, the need for more public health awareness campaigns, screening for people having known risk factors, and expansion of services to health centers is a fundamental measure.

Introduction

The hyperglycemic crisis is the most common life-threatening acute metabolic-complication, which results in significant morbidity and mortality.[1–3] Diabetic ketoacidosis (DKA), and hyperosmolar hyperglycemic state (HHS), are the two most common hyperglycemic crises, where patients requiring intensive treatment and hospitalization.[3–5] Both DKA and HHS are extreme metabolic derangements associated with uncontrolled types 1 and 2 diabetes mellitus. DKA is more common in young people with type 1 diabetes (T1D) and HHS is more frequently reported in adult and elderly patients with type 2 diabetes (T2D); however, each type of diabetes may be associated with DKA or HHS. Hyperglycemic crises are a continuum of metabolic derangements that differ in the rapidity of onset, clinical features, the severity of dehydration, and the degree of ketosis.[2,3,6–8]

The hyperglycemic crisis is becoming a major challenge in the healthcare system; which is usually associated with disability, reduced life expectancy, and has a high cost of treatment.[2,7] The annual incidence of the hyperglycemic crisis is estimated to be 9.5 per 1000 persons with diabetes, and there were 207,000 hospitalizations for the hyperglycemic crisis reported in the United States of America (USA) in 2014.[9] In the USA, about 43% of the total medical cost for diabetes is spent on hospital inpatient care.[10]

8A study in Taiwan reported that about one-fourth of hyperglycemic crisis admission was patients without a history of diabetes. Patients without a history of diabetes were younger and less elderly, had better consciousness and renal function, more significant diabetic signs and symptoms, higher blood sugar, a higher proportion of DKA and less proportion of HHS, less opportunity of infection, medical history, and a 30 days cases of mortality.[11]

In Africa, the hyperglycemic crisis was the main reason for hospital admission of patients with diabetes ranging from about 26% in South Africa to 40% in Nigeria with mortality rates ranging, from 7.5% in South Africa to 34% in Nigeria.[12–14] Admissions for HHS, in contrast to DKA, were more common in patients with a new diagnosis of diabetes in South Africa and Ethiopia.[2,15] Studies in Ethiopia, 23.6–43% of patients with the hyperglycemic crisis were with new onset of diabetes at admission with a 30 days cases of mortality 4.1%; but 14.6% with a history of diabetes.[2,16,17]

Although the hyperglycemic crisis is a major challenge in the healthcare system in developing nations, including Ethiopia; but robust data on the hyperglycemic crisis characteristics and outcome of care in patients without and with a history of diabetes is lacking, which will have a crucial input in shifting healthcare priorities and management protocol.

Methods

Study Design, Population and Data Collection

The study conducted in randomly selected six general and one referral hospitals of Tigrai in northern Ethiopia among adult patients aged 18 years and above, who admitted and treated for a hyperglycemic crisis in the medical wards from September 1, 2017, to August 31, 2018. Data extracted from January to March 2019. This study was a hospital-based retrospective record review and all one-year medical records of adult patients aged 18 years and above who had been admitted and treated were included in the review if they met the inclusion criteria. But, adult patients who left against medical advice, referred to other health institutions, and pregnant mothers were excluded from the study.

The sample size calculated using a double population proportion formula with the assumption of 4.1% and 14.6% mortality rates in patients without and with a history of diabetes, respectively,[2] a power of 90% and confidence interval of 95% and a ratio of patients with history diabetes to without a history of diabetes is 2. Then, the required sample size was 137 patients without a history of diabetes and 274 patients with a history of diabetes. But, finally, all medical records of patients (196 without

and 393 with a history of diabetes) with hyperglycemic crisis who were admitted and treated between September 1, 2017, to August 31, 2018, in the six general hospitals and Ayder Comprehensive specialized hospital were included.

Data were abstracted using a uniform data abstraction format prepared to gather relevant data from the medical records both from paper copy file and e file/smart care/. The data were abstracted from 196 patients without a history of diabetes and 393 patients with a history of diabetes with DKA and HHS. By Nurse and public health experts recruited for data abstraction. Data collectors and supervisors trained for one day on how to retrieve, and abstract relevant data from the medical records. The data abstraction format was pretested in 60 adult medical records two weeks before the actual data abstraction period.

Operational Definitions

Type 1 diabetes: When the patient presented with FBS ≥ 126 mg/dl or RBS ≥ 200 mg/dl plus classic symptoms excessive urination, excessive thirst, and unexplained weight loss.

Type 2 diabetes: When the patient presented with FBS ≥ 126 mg/dl or RBS ≥ 200 mg/dl plus other symptoms such as excess body weight, physical inactivity, unhealthy diet, and family history of diabetes.[18,19]

Diabetic Ketoacidosis (DKA): DKA was defined as admission blood glucose >250 mg/l and urine dipstick ketone level ≥ +2.[2]

Hyperosmolar Hyperglycemic State (HHS): HHS was defined as blood glucose >600 mg/dL, alteration in mental status, and mild or absent ketonuria.[2]

Level of consciousness: Based on the Glasgow Coma Scale (GSC); the level of consciousness is classified as better consciousness (mild) when GSC ≥ 13; Moderate level of consciousness when GSC is 9 to 12; Severe altered level of consciousness when the GSC ≤ 8.

Without a history of diabetes: Patients who denied and had no medical record of diabetes and diagnosed for the first time with fasting blood sugar (FBS) ≥ 126 mg/dl, or repeated random blood sugar (RBS) ≥ 200 mg/dl plus fatigue, polyuria, polydipsia, and other symptoms.[11]

Definition of End-Point: We used 30-day mortality as the primary end-point. People who survived at least 30 days whether or not they were still hospitalized were considered 'survivors' for this analysis. We used 30-day mortality as the primary end-point because the hospital stay of 98.8% of patients was within 30 days in the present study. Also, 30 days is a universally acceptable endpoint for outcome studies.[11]

Data Analysis

Data entered and analyzed using SPSS version 25.0 for Windows. Continuous data presented as the median and interquartile range (IQR) [25th; 75th percentiles] and means ± Standard Deviation (SD). Comparisons between two groups made using either an independent-samples *t*-test (assuming a normal distribution) or Mann–Whitney/Wilcoxon tests (assuming non-normality) of the continuous variables.

The nominal variables presented as absolute frequencies and proportions, and the χ^2-test or a Fisher's exact test was used for categorical variables. The association between the exposure and outcome variables was determined using a logistic regression model with 95% confidence intervals (CI). Significance was set at $p < 0.05$ (two-tailed) to extract variables effective in a model.

Ethical Statement

The ethical statement protocol was approved by the Institution Review Board (IRB) of Addis Ababa University-College of Health Sciences (AAU-CHS), following the Helsinki Declaration, and a waiver letter was obtained. Besides, written permission was obtained from the health bureau of the Tigrai Regional State after submitting the protocol and explaining the purpose of the study. For the sake of privacy and confidentiality, all charts used in this research were kept private and confidential; where data were password protected and filled checklists were kept locked in a cabinet. No information other than for this study purpose was collected from the patient charts, including personal identifiers.

Results

Of the 1082 hyperglycemic crisis-related admissions, only 589 (54.4%) of them met the inclusion criteria for DKA or HHS. Out of those patients with a hyperglycemic crisis, 196 (33.3%) patients without a history of diabetes, and 393 (66.7%) patients with a history of diabetes were included in the study (Figure 1).

The distribution of socio-demographic and clinical characteristics differs between those patients without and with a history of diabetes. Those patients without a history of diabetes were comparatively younger than those with a history of diabetes with a mean (±SD) age of

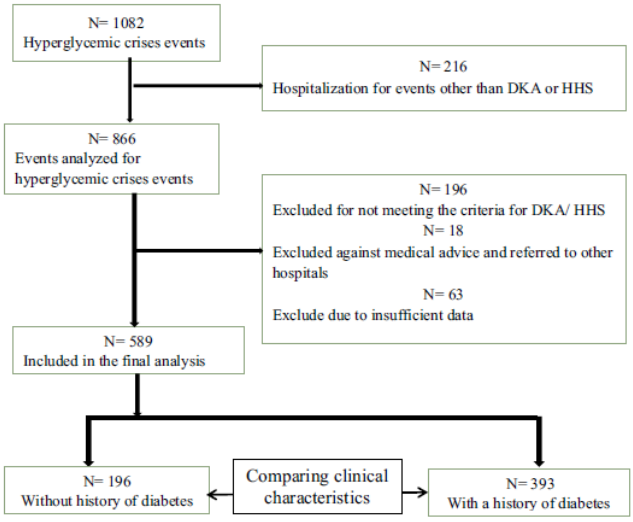

Figure 1 Flow diagram of analyzed events and comparing clinical characteristics of patients without and with a history of diabetes.

[43.9±12.6 vs 48.4±14.8 years; p<0.001], and also they were less elderly [3.6% vs 15.8%; p< 0.001]. Similarly, patients without a history of diabetes were more rural residents [53.1% vs 30.3%; p<0.001] compared to patients with a history of diabetes. Regarding to the clinical characteristics of hyperglycemic crisis, patients without a history of diabetes had relatively higher proportion of classic signs and symptoms of diabetes [vomiting (69.4% vs 36.4%; p<0.001), polyuria (75.5% vs 59.0%; p<0.001), polydipsia (83.7% vs 74.8%; p=0.015), fruit breath odor (84.2% vs 72.3%; p=0.001), and weight loss (79.6% vs 64.1%; p<0.001)]. Whilst, patients with a history of diabetes had a comparatively higher proportion of medical history of Chronic Kidney Disease (10.7% vs 1.5%; p<0.001), Cardiovascular diseases (31.3% vs 13.8%; p<0.001), and stroke (12.5% vs 5.6%; p=0.014); compared to their counterparts. Besides, patients with a history of diabetes had comparatively a higher proportion of Type 2 diabetes, hyperosmolar hyperglycemic state, and a 30 days cases of mortality rate (53.7% vs 38.3%; p<0.001), (31.8% vs 15.8%; p<0.001), and (15.5% vs 8.7%; p=0.02) compared to patients without a history of diabetes, respectively. Likewise, comparatively, patients with a history of diabetes had a higher median of baseline blood pressure readings in mmHg than patients without a history of diabetes. However; patients with a history of diabetes had relatively lower mean baseline body urine ketones (2.1± 1.1 vs 2.7± 1.1; p<0.001) in mg/dl compared to their counterparts, respectively, (Table 1).

As Table 2 showed, comparatively a higher proportion of mortality was observed in rural residents than urban residents in both patients without and with a history of diabetes (13.5% vs 3.3%; p= 0.023), and (21.8% vs 12.8%; p= 0.03); respectively. In patients with a history of diabetes, a higher proportion of mortality was observed in patients who did not presented with polyuria (21.1% vs 11.6%; p=0.016), polydipsia (23.2% vs 12.9%; p=0.022), fruit breath odor (26.6% vs 11.3%; p<0.001), and weight loss (22.0% vs 11.9%; p=0.012) compared to patients who had on admission. Whereas, in patients without a history of diabetes, a higher proportion of mortality was observed in patients who had not fruit breath odor on admission (25.8% vs 5.5%; p= 0.001) compared to those who had the presentation on admission. In both patients without and with a history of diabetes, a higher proportion of mortality was observed in patients who had a medical history of Chronic Kidney Diseases, Cardiovascular diseases, and stroke than without a medical history. Similarly, 30 days of cases mortality was higher in Type 2 diabetes patients than type 1 diabetes (16.0% vs 4.1%; p= 0.009) and (22.3% vs 7.7%; p<0.001) in both patients without and with a history of diabetes, respectively. Besides, patients with HHS had comparatively a higher proportion of

Table 1 Comparison of Clinical Characteristics of Adult Patients with a Hyperglycemic Crisis without and with a History of Diabetes in a Resource-Poor Community

Clinical Characteristics	History of Diabetes		p-value
	Without (n= 196)	With (n= 393)	
Age in years (Mean ± SD)	43.9±12.6	48.4 ±14.9	p<0.001*
Elderly, aged ≥65 years (%)	7 (3.6)	62 (15.8)	p<0.001*
Gender, Men (%)	118 (60.2)	238 (60.6)	1.00
Residence (%)			
Urban	92 (46.9)	274 (69.7)	p<0.001*
Rural	104 (53.1)	119 (30.3)	
Clinical feature; yes (%)			
Vomiting	136 (69.4)	143 (36.4)	p<0.001*
Abdominal pain	47 (24.0)	54 (13.7)	0.002*
Polyuria	148 (75.5)	232 (59.0)	p<0.001*
Polydipsia	159 (81.1)	294 (74.8)	0.015*
Fruit breath odor	165 (84.2)	284 (72.3)	0.001*
Fatigue	181 (92.3)	372 (94.7)	0.3
Weight loss	156 (79.6)	252 (64.1)	P<0.001*
Medical history, yes (%)			
CKD	3 (1.5)	42 (10.7)	p<0.001*
DFS	1 (0.5)	24 (6.1)	0.003*
CVD	27 (13.8)	123 (31.3)	p<0.001*
Stroke	11 (5.6)	49 (12.5)	0.014*
Pancreatitis	12 (6.1)	10 (2.5)	0.054
Type of DM (%)			
Type 1 DM	121 (61.7)	182 (46.3)	0.001*
Type 2 DM	75 (38.3)	211 (53.7)	
Type of hyperglycemic crisis (%)			
DKA	165 (84.2)	268 (68.2)	P<0.001*
HHS	31 (15.8)	125 (31.8)	
The 30 day mortality (%)	17 (8.7)	61 (15.5)	0.03*
SBP in mmHg in Median (IQR)	90 (70; 100)	90 (80; 150)	0.02*
DBP in mmHg in Median (IQR)	60 (50; 70)	60 (50; 100)	0.01*
Body Temperature (°C) (Mean ± SD)	36.8± 0.8	37.3± 1.04	P<0.001*
Respiratory rate (Mean ± SD)	23.4 ± 2.0	22.07 ± 2.4	p<0.001*
Pulse rate (Mean ± SD)	100.2 ± 7.3	98.1± 7.0	0.001*
GCS in Median (IQR)	14 (11, 14)	12 (11;14)	0.002*
RBS in mg/dl (Median (IQR))	538.5 (499, 591)	517 (472; 600)	0.032*
Urine ketones (Mean ± SD)	2.7± 1.1	2.1± 1.1	P<0.001*
Length of hospital stay (days) Median (IQR)	9 (7; 13)	9 (6; 13)	0.4

Note: *Statistically significant.
Abbreviations: CVD, cardiovascular diseases; CKD, chronic kidney disease; DFS, diabetes foot syndrome; DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; IQR, inter quartile range; RBS, random blood sugar; SBP, systolic blood pressure; SD, standard deviation.

mortality than patients with DKA (29.0% vs 4.8%; p< 0.001) and (27.2% vs 10.1%; p<0.001) in both patients without and with a history of diabetes, respectively. Similarly, in both patients without and with a history of diabetes; lower mean baseline urine ketones (1.9± 1.3 vs 2.8± 1.1; p=0.008); and (1.64± 1.2 vs 2.2± 1.04; p=0.002) was statistically significantly associated with a 30 days cases of mortality, respectively. Also, in patients with a history of diabetes a higher median blood pressure in mmHg (p<0.01), and RBS in mg/dl (p= 0.003) readings at baseline was statistically significantly associated with a 30 days cases of mortality.

On the multivariate logistic regression model (Table 3), independent predictors of a 30 days case of mortality were a rural residents [AOR=3.1, 95% CI 1.8, 5.4], patients with a medical history of stroke [AOR=2.7, 95% CI 1.3, 5.6], type 2 diabetes [AOR=2.3, 95% CI (1.1, 4.7)], hyperosmolar hyperglycemic state [AOR=2.4, 95% CI (1.1, 5.4)], and patients with history of diabetes [AOR=2.0, 95% (CI 1.04, 3.8)]; while presentation with polydipsia on admission was preventive [AOR= 0.47, 95% CI 0.27, 0.81]; (Table 3).

Table 2 Comparision of Hospital Management and Clinical Outcomes Adult Patients with a Hyperglycemic Crisis without and with a History of Diabetes in a Resource-Poor Community

Clinical Characteristics	Without History (%)		P-value	With a History (%)		p-value
	Died (n= 17)	Alive (n= 179)		Died (n= 61)	Alive (n= 332)	
Gender, Men (%)	10 (8.5)	108 (91.5)	0.9	38 (16.0)	200 (84.0)	0.9
Residence						
Urban	3 (3.3)	89 (96.7)	0.023*	35 (12.8)	239 (87.2)	0.03*
Rural	14 (13.5)	90 (86.5)		26 (21.8)	93 (78.2)	
Clinical presentations						
Vomiting	11 (8.1)	125 (91.9)	0.9	16 (11.2)	127 (88.8)	0.07
Abdominal pain	2 (4.3)	45 (95.8)	0.4	4 (7.4)	50 (92.6)	0.1
Polyuria	11 (7.4)	137 (92.6)	0.4	27 (11.6)	205 (88.4)	0.016*
Polydipsia	8 (5.0)	151 (95.5)	0.001*	38 (12.9)	256 (87.1)	0.02*
Fruit breath odor	9 (5.5)	156 (94.5)	0.001*	32 (11.3)	252 (88.7)	p<0.001*
Fatigue	16 (8.8)	165 (91.2)	1.00	58 (15.6)	314 (84.4)	1.00
Weight loss	14 (9.0)	142 (91.0)	1.00	30 (11.9)	222 (88.1)	0.012 *
Medical history						
CKD	2 (66.7)	1 (33.3)	0.02*	13 (31.0)	29 (69.0)	0.007*
DFS	0 (0.0)	1 (100.0)	1.00	6 (25.0)	18 (75.0)	0.2
CVD	6 (22.2)	21 (77.8)	0.017*	31 (25.2)	92 (74.8)	0.001*
Stroke	4 (36.4)	7 (63.6)	0.009*	17 (37.4)	32 (65.3)	p<0.001*
Pancreatitis	2 (16.7)	10 (83.3)	0.3	3 (30.0)	7 (70.0)	0.4
Type of diabetes (%)						
Type 1 DM	5 (4.1)	116 (95.9)	0.009*	14 (7.7)	168 (92.3)	<0.001*
Type 2 DM	12 (16.0)	63 (84.0)		47 (22.3)	164 (77.7)	
Hyperglycemic crisis (%)						
DKA	8 (4.8)	157 (95.2)	p<0.001*	27 (10.1)	241 (89.9)	p<0.001*
HHS	9 (29.0)	22 (71.0)		34 (27.2)	91 (72.8)	
Age in years (Mean ± SD)	46.9±14.8	43.6±12.3	0.4	51.8±14.6	47.7±14.7	0.047*
SBP (Median (IQR))	90 (70; 90)	90 (70; 100)	0.4	110 (82.5;160)	90 (74;120)	0.001*
DBP (Median (IQR))	60 (50; 60)	60 (50, 70)	0.6	80 (60;100)	60 (50;80)	0.006*
BT (°C) (Mean ± SD)	36.9± 0.9	36.8± 0.9	0.8	37.3± 1.0	37.3± 1.0	0.6
RR (Mean ± SD)	23.4± 2.5	23.4±2.0	0.9	21.2± 2.7	22.3± 2.3	0.004*
PR (Mean ± SD)	101.7± 8.9	100.1±7.2	0.5	96.7± 6.7	98.4±7.0	0.09
GCS in Median (IQR)	12 (9; 15)	14 (11;15)	0.2	12 (10;14)	13 (11;14)	0.2
RBS (Median (IQR))	578 (498;600)	538 (498;585)	0.3	600 (471.5;600)	512 (470;600)	0.003*
Urine ketones (Mean ± SD)	1.9± 1.3	2.8± 1.1	0.008*	1.6± 1.2	2.2± 1.0	0.002*
Length of hospital stay (days) in Median (IQR)	13 (8; 16)	9 (7; 12)	0.07	8.5 (6;12)	9 (6;13)	0.5

Note: *Statistically significant.
Abbreviations: CVD, cardiovascular diseases; CKD, chronic kidney disease; DFS, diabetes foot syndrome; DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; IQR, inter quartile range; RBS, random blood sugar; SBP, systolic blood pressure; SD, standard deviation.

Discussion

In this study, patients without a history of diabetes had a higher proportion of classic signs and symptoms of diabetes. Whilst, the proportion of Type 2 diabetes, hyperosmolar hyperglycemic state, and medical history of chronic diseases were higher among those patients with

Table 3 Potential Risks of Hyperglycemic Crisis-Related Mortality Among Patients without and with a History of Diabetes in a Resource-Poor Community

Clinical Characteristics	Outcomes of Care (%)		COR (95% CI)	AOR (95% CI)
	Died (n= 17)	Alive (n= 179)		
Residence				
Urban	38 (10.4)	328 (89.6)	1	1
Rural	40 (17.9)	183 (82.1)	1.9 [1.2, 3.1]	3.1 [1.8, 5.4]*
Stroke				
Yes	21 (35.0)	39 (65.0)	4.6 [2.5, 8.1]	2.7 [1.3, 5.6]*
No	57 (10.8)	472 (89.2)	1	1
Vomiting				
Yes	27 (9.7)	252 (90.3)	0.5 (0.33, 0.90)	1.5 (0.74, 3.13)
No	51 (16.5)	259 (83.5)	1	1
Excessive thirst				
Yes	46 (10.2)	407 (89.8)	0.37 (0.22, 0.61)	0.47 (0.27, 0.81)*
No	32 (23.5)	104 (76.5)	1	1
Type of DM				
T1D	19 (6.3)	284 (93.7)	1	1
T2D	59 (20.6)	227 (79.4)	3.9 (2.25, 6.7)	2.3 (1.1, 4.7)*
Type of hyperglycemic crisis				
DKA	35 (8.1)	398 (91.9)	1	1
HHS	43 (27.6)	113 (72.4)	4.3 (2.6, 7.1)	2.4 (1.1, 5.4)*
Type of patient				
With a history of DM	61 (15.5)	332 (91.9)	1.94 (1.1, 3.4)	2.0 (1.04, 3.8)*
Without a history of DM	17 (8.7)	179 (91.3)	1	1

Note: *Statistically significant.
Abbreviations: T1D, type 1 diabetes; T2D, type 2 diabetes.

a history of diabetes. Also, the mortality rate was comparatively higher in those patients with a history of diabetes. A higher proportion of mortality was observed in patients from rural. Similarly, higher a 30 days case of mortality was reported among those patients with T2D, HHS, a lower mean of urine ketones, had a medical history of chronic kidney disease, cardiovascular disease, and stroke. Rural residence patients, type 2 diabetes, hyperglycemic hyperosmolar state, had a medical history of stroke, and history of diabetes were independent predictors of mortality while had polydipsia on admission was preventive.

In the current findings, although patients without a history of diabetes had better consciousness compared to with a history of diabetes, but had more pronounced signs and symptoms for hyperglycemic crisis (vomiting, abdominal pain, polyuria, polydipsia, fruity breath odor, and body weight loss) compared to patients with a history of diabetes; which is in line with findings in Taiwan.[11] We believe that it could be due to two-third of the patients without a history of diabetes had type 1 diabetes that presents with these classic signs and symptoms of diabetes mellitus.[18,19]

In the current study, comparatively a higher proportion of the hyperglycemic crisis among rural residents in patients without a history of diabetes than those with a history of diabetes. This is due to people living in rural areas have increased treatment gaps, less access to health care services, and long-distance travel to health services. On the other hand, somewhat a greater proportion of

hyperglycemic crisis among urban residents in patients with a history of diabetes compared to those patients without a history of diabetes. This might be due to poor compliance, unaffordability of insulin medicine, and inaccessibility of anti-diabetes medicines. We suggest expansion diabetes care services to the primary health care units, integrate diabetes screening in the health extension packaging programs, and providing diabetes self-care management education.

Furthermore, DKA was more common in patients without a history of diabetes (84.7%), while HHS is more pronounced in patients with a history of diabetes. As a result, a higher mortality rate is reported in patients with a history of diabetes. This finding contradicts a study conducted in other parts of Ethiopia[2] but consistent with findings from Taiwan and South Africa.[11,15] The higher incidence of DKA in patients without a history of diabetes may be related to a relatively younger age and more than half of the patients are from rural residents which could be associated with poverty.[20,21]

The overall 30 days case of hyperglycaemic crisis-related mortality is 13.2%; which is higher than studies in Colombia, China, Taiwan, and other parts of Ethiopia that reported mortality rates ranging from 2.27 to 10.6%;[1,2,11,22] but lower than 20% mortality in Nigeria.[23] The disparity might be due to differences in inpatient management protocol of hyperglycemic crisis, inadequate laboratory investigations at presentation, insufficient laboratory monitoring during treatment to monitor patient response, and also the absence of routine annual checkup policy for NCDs- in Ethiopia. Besides a delayed diagnosis of T2D, and then present for medical attention after developing diabetes complications.

In this study, a lower mortality rate in patients without a history of diabetes than patients with a history of diabetes is reported. Many diabetes patients might die undiagnosed and before access to diabetes treatment particularly in rural areas. This finding is still higher than studies in other parts of Ethiopia, China, and Taiwan.[2,11,22] This disparity might be due to a delayed diagnosis of T2D and then present for medical attention after developing diabetes complications. And also; the absence of inpatient management protocol, and insufficient laboratory monitoring during treatment to monitor patient response in the studied hospitals. The researchers suggest the expansion of reliable diabetes care services to the primary health care units and integrating diabetes in the health extension packaging. Furthermore, the inpatient management protocol of the hyperglycemic crisis has to be equipped with adequate laboratory investigations and sufficient laboratory monitoring during treatment to monitor patient response. Also, routine annual checkup policies for NCDs, including diabetes have to be implemented.

In this finding, more than three times higher a 30 days cases of mortality among rural patients than urban; which is consistent with a study in China.[22] This higher mortality in rural patients might be people living in rural areas have less access to diabetes screening and preventive services. Besides, long-distance travel to health care services, and have increased treatment gaps. Likewise, these individuals are unaware of their glycemic state and then present for medical attention after developing diabetes complications and worsening of the conditions. Therefore, the need for more public health awareness campaigns about diabetes, and the expansion of diabetes care services to the primary health care units particularly in the rural areas is a fundamental measure.

The findings of this study revealed that lower mortality is reported in patients who had classic signs and symptoms of diabetes (vomiting, polydipsia, polyuria, fruity breath odor, and body weight loss) than those who had not on admission. Mortality is reduced by 47% in patients who had polydipsia on admission. Nevertheless, delayed recognition of hyperglycemic symptoms in T2D and ignorance of diabetes complications might lead to mortality.[11,22] Public health awareness campaigns have to be made to increase health-seeking behavior to make annual checkups and the classic symptoms of diabetes.

In both patients, a higher proportion of mortality is reported in patients who had a medical history of chronic kidney disease, cardiovascular disease, and stroke compared to patients who had not. Patients who had a medical history of stroke are 2.7 times as great as the likelihood of mortality those who had not a medical history of the stroke on admission. This study is consistent with the study in Taiwan.[11,22] Medical attention after developing diabetes complications, absence of integrated inpatient management protocol of hyperglycemic crisis and co-morbidity, and inadequate laboratory monitoring during treatment to monitor patient response might be the reasons for higher mortality.

In this study, patients with type 2 diabetes, and hyperosmolar hyperglycemic state had more than two folds higher mortality than patients with type 1 diabetes, and DKA respectively. A higher 30 days cases of mortality are

observed in patients with a lower mean of urine ketones which is common T2D and HHS in both patients without and with a history of diabetes. This higher mortality might be due to delayed diagnosis of T2D and ignorance of diabetes complications which results in severe dehydration and neurologic deficit that can lead to death. We recommend more public health awareness campaigns and diabetes screening for people with known risk factors.

Furthermore, two folds higher a 30 days of cases mortality in patients with a previous history of diabetes than without a history of diabetes; which is parallel with a study in Taiwan.[11] Long-standing hyperglycemia due to poorly controlled diabetes and ignorance of diabetes complications might be the reason for the higher mortality.

Nevertheless, the present study had several limitations. The first limitation, the data were obtained retrospectively from patient charts, where clinical presentations or records might not have been completely documented. Some patients may have been excluded due to a lack of data for analysis. The second limitation, data were not validated, which could have led to misclassification of type hyperglycemic crisis, though the overlaps do not affect the present study results. Third, the study is limited to include important diagnostic criteria for the classification of hyperglycemic crises due to the study is conducted in general hospitals with a lack of advanced laboratory setups. Fourth, the study is limited to medical wards, and do not include patients against medical advice, pregnant mothers, and patients referred to other hospitals. Fifth, this was a single- Regional State study, where findings from our database might not be generalizable to the entire national hospitals, but it can generalize for hospitals in Tigrai.

Conclusions

Comparatively a higher 30 days cases of mortality in patients with a history of diabetes compared to patients without a history of diabetes. Moreover, a higher proportion of mortality is rural residents in both patients. Also, mortality was higher among patients with type 2 diabetes and hyperosmolar hyperglycemic state in both patients. Rural residents, Type 2 diabetes, hyperosmolar hyperglycemic state, had a medical history of stroke, and with a history of diabetes were independent predictors of 30 days cases of mortality; while polydipsia was preventive. We suggest regular check-ups and screening for NCDs and more public health awareness campaigns. We also recommend expanding diabetes care services to the primary health care units and integrate diabetes screening in the health extension packaging programs. Furthermore, improving the inpatient management protocol of hyperglycemic crisis and equipped advanced laboratory investigations.

Abbreviations

AAU-CHS, Addis Ababa University-College of Health Sciences; DBP, CKD, chronic kidney disease; Diastolic blood pressure; DFS, diabetic foot syndrome; DKA, diabetic ketoacidosis; DM, diabetes mellitus; GCS, Glasgow Coma Scale; HEs, hyperglycemic emergencies; HHS, hyperosmolar hyperglycemic state; IRB, Institution Review Board; IQR, Interquartile ranges; T1D; type 1 diabetes; T12D; type 2 diabetes SD, standard deviation; SBP, systolic blood pressure; SD, Standard Deviation.

Data Sharing Statement

All data about the findings are presented in this paper. However, the data can be obtained from the corresponding author at any time on reasonable request.

Acknowledgments

The sudden death of Professor Fikre Enquo Selassie is really painful and hurting. He was not only a good professor of epidemiology and biostatistics but also, he had a unique human entity to his family, students, and staff. It pains me to notify you that, professor Fikre, left for his heavenly abode on October 28, 2019, on account of sudden death. Professor Fikre was vigorously involved in all activities of the study from the proposal development to manuscript approval for publication. The authors express their gratitude to the Addis Ababa University for its financial support to conduct this study. Additionally, we would like to express our heartfelt thanks to the selected public hospitals' administrative bodies, staff, data collectors and supervisors, and the Tigrai Regional Health Bureau office for granting access to these data.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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Annex IV: Summary of Curriculum Vitae

My name is Getachew Gebremedhin Tedla I was born in 1984 in Northern Ethiopia, Tigrai. I am married and father of two girls and a boy. I obtained my BSc degree in Nursing in 2006 from Jimma University. I also obtained my MSc in Adult Health Nursing from Jimma University in 2011. Since March 2016, I am a PhD candidate at the SPH of AAU.

I started my career in October 2006 as a Head Nurse of OPD and clinician at Mekelle Hospital in Tigrai and worked until October 2009. I joined Sheba University College from June 2011 to September 2014; and I served the University College as head and lecture in department of Nursing for about 3 and half years.

I have joined at Department of Nursing of College of Medicine and Health Sciences (CMHS) of Adigrat University on October 2014 with the rank of lecturer of nursing and served the university as a lecturer of nursing courses and participated in different committee of the college. Since 2016, I have been working as an assistant professor of Nursing at the CMHS of Adigrat University with different responsibilities of the CMHS of Adigrat University.

I have been involving in various capacities, in more than two research projects conducted by different organizations, including projects from Tigrai Regional Health Bureau and emergency response of Tigrai, including COVID-19, Cholera, and member of mobile health team in Tigrai crisis. I have also attended more than 10 national conferences and also presented scientific papers.

I have attended a number of short-term trainings to mention some of them; I have been taking training on pre service training organized by AIDSTAR-One Ethiopia, instructional design organized by Jhpiego, training on data analysis organized by Mekelle University and KOICA International, trainings on different qualitative and quantitative research methods.

I have about 20 publications in pear reviewed scientific journals, of which 2 are emanated from this PhD dissertation.