ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCEINCES

SCHOOL OF PUBLIC HEALTH

INCIDENCE AND PREDICTORS OF CHRONIC KIDNEY DISEASE AMONG DIABETES MELLITUS PATIENTS IN TWO HOSPITALS IN WOLAITA SODO TOWN, SOUTHERN ETHIOPIA: A RETROSPECTIVE FOLLOW-UP STUDY

BY

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I undersigned agree to accept all responsibilities for the scientific and ethical conduct of this research project and declare that this thesis is my original work in partial fulfillment of the requirement for the Master of Public Health in Epidemiology and Biostatistics

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Approval of the primary advisor

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APRROVAL BY EXAMINATION BOARD

This thesis by Amanuel Arota is accepted in its present form by the board of examiners as satisfying thesis requirements for the review of degree of masters of public health in Epidemiology and Biostatistics

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Abbreviations and Acronyms

AKI	Acute kidney injury
AHR	Adjusted hazard ration
AOR	Adjusted odds ratio
ASIR	Age-specific incidence rate
BMI	Body mass index
CI	Confidence interval
CVD	Cardiovascular disease
CKD	Chronic kidney disease
Dalys	Disability-adjusted life years
DKA	Diabetic ketoacidosis
DKD	Diabetic kidney disease
DN	Diabetic nephropathy
DM	Diabetes mellitus
DR	Diabetic retinopathy
ESRD	End-stage renal disease
eGFR	Estimated glomerular filtration rate
HR	Hazard ratio
HDL	High-density lipoprotein
HDL-C	High-density lipoprotein-cholesterol
ICU	Intensive care unit
IRB	Institution review board

IDR	Incidence density rate
LDL	Low-density lipoprotein
LICs	Low income countries
NCD	Non-communicable disease
ODK	Open data kit
OR	Odds ratio
OPD	Outpatient department
PUD	Peptic ulcer disease
RRT	Renal replacement therapy
SDG	Sustainable development goal
SDI	Socio-demographic index
SBP	Systolic blood pressure
SCGH	Sodo Christian General Hospital
T1DM	Type one diabetes mellitus
T2DM	Type two diabetes mellitus
US	United state
UTI	Urinary tract infection
UK	United Kingdom
WSUCSH	Wolaita Sodo University Comprehensive Specialized Hospital

TABLE OF CONTENTS

List of tables

List of figures

Abstract

Introduction: Chronic kidney disease is type of progressive kidney disease that mainly attributed to diabetes. Ethiopia is one of the developing countries with high incidence of chronic kidney disease among diabetes mellitus patients. However, little is known related to the incidence and predictors of chronic kidney disease among diabetes mellitus patients in Ethiopia.

Objective: The main objective of this study was to determine incidence and predictors of chronic kidney diseases among diabetes mellitus patients in Wolaita Sodo Town, Southern Ethiopia.

Methods: A health facility based retrospective follow-up study was conducted among 495 diabetes mellitus patients in Wolaita Sodo Town during March to May 2023. Simple random sampling technique was used to select individuals. A pre-tested structured data extraction tool was used to collect data from patient's chart using open data kit (ODK). Data were exported to STATA V17 software and cleaned for analysis. The mean and median were used to describe continuous variable. The Kaplan Meir curve along with log rank test was used to estimate and compare survival time. The cox hazard proportional hazard model with p value <0.05 was used to declare significance of association. Assumption was checked using Schoenfeld residual test.

Result: The cumulative incidence of chronic kidney among diabetes mellitus patients and the incidence density is 14.9% (95CI%12-18.03) and 2 cases per 100 person years respectively. The median survival time wa 130 months (IQR128, 133). History of cardiovascular disease [adjusted hazard ratio (AHR) =2.12, 95%CI 1.16, 3.87], diabetic retinopathy [AHR= 1.86 95%CI 1.03–3.36], and acute kidney injury [AHR= 2.49, 95%CI 1.37, 4.54] was associated with higher risk of chronic kidney diseases. However, high density lipoprotein cholesterol ≥ 40 mg/dl was associated with lower risk of chronic kidney disease [AHR= 0.537, 95%CI 0.303, 0.0.95].

Conclusion: Incidence of chronic kidney disease among diabetes has become significant public health problem. Diabetes patients having baseline low level high density lipoprotein, developed diabetic retinopathy, had history cardiovascular disease**,** patients developed acute kidney injury were at high risk to the incidence of chronic kidney disease compared to their counter parts. Thus appropriate health interventions should be implemented to prevent and control the disease.

Key words: Chronic kidney disease, cox proportional hazard model, retrospective study, Ethiopia

1. Introduction

1.1 Background

Chronic kidney disease (CKD) is a progressive condition in which the kidneys are damaged and cannot filter blood as well as they should, which is mainly attributed to diabetes mellitus (DM)(1). DM is a serious, long-term disorder manifested by elevated blood sugar caused when body unable to produce or use insulin(2). The burden of DM is high and increasing(2–4). DM presently affects more than one out of every 10 persons worldwide, with an estimated current prevalence of 537 million adults aged 20 to 79 years in 2021. If sufficient action is not taken and the trend continues, this amount is anticipated to be 643 million and, 783 million adults for the same age group in 2030 and 2045, respectively(2,5). Moreover if not managed appropriately it affects major organs like kidney and results in the most dangerous chronic complication called diabetic kidney disease(DKD)(3).

Diabetic kidney disease (DKD) is a chronic kidney disease(CKD) that may occur in people who have diabetes and one of the most frequent and severe micro vascular complications of DM which is associated with high morbidity and mortality in DM patients (6,7). People with CKD may not feel ill or notice any symptoms and majority of them are unaware of they have it. It is manifested by albuminuria and glomerular filtration rate (GFR) <60Ml/min/1.73m^2 for at least 3 months regardless of clinical manifestation(1).

Globally an estimated 20–50% of patients with DM will ultimately get CKD and it has become the leading cause for end-stage renal disease(ESRD), share about for 50% of problems and the main contributing factor for requiring renal replacement therapy (RRT)(8). The global median duration to acquire CKD among DM ranges from 3.8 to 12 years (9–13). Meanwhile globally the age standardized prevalence of DKD in men and women was 15.48 and 16.5 per 1000 respectively. The prevalence of CKD among DM patients in Africa varied from 11% to 83.7% (14). In Ethiopia the pooled prevalence of CKD among DM patients was found to be 35.2%(15) and the incidence of CKD among DM patients ranges from 10.8% to 15.6% (16–19).

Worldwide the most determining factors for the development of CKD among DM were age, sex, hypertension, body mass index(BMI), duration of diabetes, hemoglobin A1c, albuminuria, vascular complications, positive family history, dyslipidemia and smoking status(15,18,20,21).

1.2 Statement of the problem

CKD is a growing clinical and public health problem related with adverse health outcomes such as ESRD, heart failure, and higher treatment costs (22–24). Worldwide all-age mortality rate duet to CKD increased by 41.5% in the last three decades(24). DM is on rise and CKD is ten times more common among diabetes individual than in the overall population. Consequently increasing toll of DM is linked to premature death and disability(3). In low-income countries (LICs), almost 50% of DM attributed deaths are premature – before the age of 70 years, in contrast to high-income countries where about one-fifth (25%) of deaths are premature. Additionally people with DM and CKD loses 50% higher health care costs compared to those with DM but without CKD(5). Moreover worldwide there are at least 2.284 million people might have died prematurely because of lack of access to RRT attenuated with high treatment gaps like later detection and poorer management in LICs, particularly Asia and Africa(3,22).

According to the studies, population aging, high diabetes prevalence, genetic variation, overweight, and ESRD survival will share about 11-18% increase in the crude incidence rate of CKD among DM between 2015 and 2030. Between 2010 and 2030, the number of persons undergoing RRT is expected to be greater than double globally. Furthermore, in developing countries, the shift from infectious-cause to metabolic disease-related CKD, as well as a huge number of patients with mild CKD, suggests an potential of subjects who may progress to advanced CKD stages(5,8,25). Given the fastest increase of Diabetes-related CKD, it will place an economic crisis on the both health organization and state economy, primarily in low-income countries (2,3,26). In Sub-Saharan Africa, the issue is far worse due to additional factors such as poverty, infections, low health literacy, and the high cost of clinical fees(12-13).

Ethiopia is a low-income country with a high burden of CKD among DM patients (15,27) with median predicted time to detect of CKD ranged from 5 to 8.3 years among DM patients (16–19). Furthermore, 40% of annual deaths in the country are owing to non-communicable disease (NCD), of which diabetes-associated kidney failure makes up 10 to 40 percent of all deaths(28). The WHO Global Action Plan outlines policy options for lowering modifiable risk factors, such as levies on unhealthy foods and drinks, package labeling, and limiting the marketing of such products(3). Ethiopia has also signed the sustainable development program to reduce the premature death due to NCD by third in 2030 through strategies drafted in our setup(29).

However, there is justifiable evidence gap about incidence and predictors of CKD among DM patients in Ethiopia .Therefore this study aimed to determine incidence and predictors of chronic kidney disease among DM patients in Wolaita Sodo Town, southern Ethiopia.

1.3 Rationale and Significance of study

Rationale of the study

Understanding the level public health burden and causes of DM related CKD in our setting, as well as adopting early detection and proper care, are critical steps toward CKD prevention and control. However, there is no well-documented evidence in Ethiopia, and no research has been conducted on this topic in the study area.

Most of the previous studies done in Ethiopia were included only type II diabetes and recommended to include both type of diabetes, so that this study included both type of diabetes.

Significance of study

This study could help with the implementation existing strategies and programs of global and national aimed at cutting the incidence of CKD by providing information that is useful in planning, funding, staffing, and training with the goal of improving patient outcomes.

This study could also be the potential information source for future researchers in the area

It could also be important input to design appropriate policies, strategies, and interventions by health policymakers.

Results from this study could also provide input to decision-makers, program evaluators and clinicians to advance better diabetic care.

It could also enhance public understandings about cause of CKD and improves early care-seeking behavior.

The study results may help health professionals in identifying factors to develop chronic kidney disease and to take intervention accordingly.

This study will also increase knowledge in the public health research advancement.

2. Literature review

2.1 Introduction

After intensive reviewing of different sources related to the problem under study literature review was classified comprehensively into three parts (themes) include the magnitude of chronic kidney disease, predictors of chronic kidney disease, and conceptual framework. In order to identify all relevant publications presented in different sections, databases including PubMed, Google Scholar, Web of Science, Journals, and papers published until 2023 were searched carefully using the title, key word and abstract. The citations are imported to documents using Zotero citation manager.

2.2 Magnitude of chronic kidney disease

Chronic kidney disease (CKD) continues to be a serious public health issue, affecting over 750 million people globally, which is higher than the burden of osteoarthritis, diabetes, or depression combined(1,30–32).

Many studies throughout the word have focused and tried to establish the magnitude of CKD among DM patients. The global burden of kidney disease varies greatly due to differing diagnostic and management procedures in different settings, poor quality, or inadequate data collection, particularly in low-income nations(31,33–35). China carried the highest burden of chronic kidney disease among diabetes followed by the United States and India(8). In china country level cross-sectional assessment of prevalence of CKD found 10.8%, implying that roughly 120 million adults in China have renal disease(36). From 2010 to 2014, patients aged 35 and up receiving treatment for diabetic kidney disease in the United States of America increased dramatically, with an increase in yearly office visits from 772 860 in 2010 to 1,868, 618 in 2014(37). The twelve year retrospective study done in the Australia showed yearly cases of ESRD among DM patients become more than doubled from 528 in 2002 to 1,084 in 2013, with a 4.5% increase in the incidence of ESRD in type 2 diabetes every year(38). Another five year prospective study in Australia showed that 22.6 % of DM patients experienced incident eGFR <60mL/min/1.73 m2 over a median follow-up time of 5.7 years and overall incidence rate was 6.0 cases per 100 person-years(13). Furthermore, retrospective study done in the UK show that 147 and 9284 new cases of CKD ,and the overall incidence rate of 0.5 and 1.5 cases per 100 person-years among cohort of T1DM, and T2DM respectively(10). Cross sectional study done in

the Iran show that the prevalence of CKD among DM was 10% (39). Study done in the Korea found 8.6% prevalent CKD with a mean GFR of 48.1 mL/min/1.73 m2 among DM and higher stage of CKD were revealed among diabetes compared to their counterparts(40).

The trend in the past 30 years shows that Asia carried the heaviest burden of CKD among DM which might be attributed to its high population number. In 1990 the High- in come North American region carried the highest burden of CKD among T1DM with age specific incidence(ASIR) rate and age specific prevalence rate(ASPRP) 2.34 and 104.38 respectively, but thirty year later in 2019 it changed to Eastern Europe with ASIR and ASPR 3.24 and 156 respectively. Similarly, the highest burden of CKD among T2DM changed from High-in come North America in 1990 with ASIR 38.80 to North Africa and Middle East in 2019 with 61.33 ASIR(8). CKD among T2 DM by far put the higher of disease burden compare to CKD-T1DM. World wide CKD-T1DM was 12,900 incident cases, 5.02 million prevalent cases, 8.20 thousand deaths, and 3.22 million Disability adjusted life year (DALYs) in 2019, which increased by 75%, 88%, 89%, and 72% and CKD-T2DM was associated with 2. 5 million incident cases, 12 9.56 million patients, 40 5.99 thousand deaths, and 9.8 7million DALYs, which increased by 156.49%, 94.78%, 172.39%, and 141.73%, over the last 30 years respectively(8).

Furthermore, African Americans, Asians, and Native Americans continue to have greater rates of diabetic kidney disease (DKD) than Caucasians. A study conducted in Tanzania discovered that the prevalence of chronic kidney disease is 83.7% of diabetics, which is greater than the prevalence reported elsewhere. This result might be confounded by other factors like traditional medicine commonly used in Tanzania (41). Another study done in the south Africa demonstrated that about one quarter of the DM patients have prevalent kidney disease(42). In Uganda the same result were found with overall prevalence of micro-albuminuria in diabetic population was 22.9%(43).

In northern parts of Ethiopia, the retrospective study done among diabetes patients demonstrated that the overall incidence of CKD among DM was 13.6% in Gondar(18) and 10.8% in Amhara regional hospitals(19). Additionally the study done in the central part of country showed that the 14.25% of DM patients developed CKD(16). The only study done in the southwestern parts of country which included both types of DM showed nearly 16% diabetic patients developed

CKD(44). Further more survey done in Ethiopia revealed that high prevalence (26.3%) but low awareness (10%) of CKD was found in DM outpatients attending clinic had Stage 1-5 CKD(45). A Systematic Review and Meta-Analysis done in country also showed that the CKD among DM patients was found to be 35.52%(15). Another cross sectional study done in the central part of the country also reported there is 32% prevalent case(46).

2.3 Predictors of chronic kidney disease among diabetes

Both the prevalence and incidence CKD among diabetes mellitus is determined by a variety of factors, including social, cultural, and political factors, which has resulted in gaps in the current state of CKD prevention and management capabilities in nations around the world.(47).

2.3.1 Socio-demographic factors

Most of the triggering factors of CKD among DM population are related to socio demographic issues. The increased progression of impaired glycemic status to diabetes, the highly alarming prevalence of diabetes as well as the projected increment of current figure is mainly attributed to increasing age of the population. A retrospective medical record review revealed that increasing age were strongly related with increased risks of DKD in patients with both types of DM(10,48,49). Different cross-sectional study again reported that advanced age is significant risk factor for development of DKD(50–52). Systemic review done in Ethiopia also show that older age especially greater than 60 year is significant risk factor for CKD in DM patients with (OR = 2.99; 95% CI: 1.56, 5.73)(15).

The effects of sex in DKD were reported in different manner. Being females had a decreased risk for DKD(38,49,53) and other studies show that being female again have increased risk for DKD than male(15,50). However, other studies assessing eGFR reduction in patients with diabetes mellitus found the effect of sex category to be inconsequential (54). So that it points true effect of sex in the diabetic kidney disease is yet to be proven.

The observational study done in Ethiopia reported that family history of CKD has increased risk for CKD among DM with (adjusted OR = 3.16, CI 1.29-7.77)(50). The review done in Ethiopia show those patients with a family history of CKD were approximately twice as likely as those without a family history of CKD to develop CKD(OR 1.61; 95% CI: 1.09, 3.23)(15). Moreover family history of diabetes in first degree relatives is significantly associated with a rapid decline of eGFR. It has been shown that the mean decline of eGFR was faster in individuals with family

history of diabetes (67.7 vs. 30.4% P<0.002)(55). Again study done in Australia demonstrated that residence is significant predictors of CKD development among DM patients. Living in an inner regional city was associated with a higher incidence than living in an outer regional city (outer regional and remote versus major city: AHR 1.36; 1.17–1.58)(13). Being over weight can increase the risk of CKD significantly high. Overweight has about 44% higher risk to develop CKD than their counter parts (obese class III versus normal: 1.44;1.16–1.80)(13). Similarly study done in Ethiopia showed that increased weight is risk for development of chronic kidney disease(AHR= 1.17, 95%CI 1.1, 1.25)(21)

2.3.2 Medical and clinical factors.

Poor glycemic management is a major risk factor for the onset and progression of diabetic kidney disease. High HbA1c levels are related with an increased risk of developing nephropathy in both T1DM and T2DM patients(56). Population based cohort study in Canada show that regardless of baseline eGFR, a higher HbA1c level was highly correlated with ESRD which was additionally attenuated at a lower baseline eGFR (P <.001)(12). The meta analysis done globally also support the above evidence that HbA1c greater than 7% were significant risk for CKD development and progression of diabetes (HR for both T1DM and T2DM 1.43, 95% CI 1.24-1.64; HR for T1DM 1.70, 95%CI 1.41-2.05; HR for T2DM 1.20, 95%CI 1.12-1.28)(57). The systemic review done in Ethiopia show that tight glycemic control prevents CKD development(15). The other observational study done in southern part of country again says poor glycemic control had increased risk with (adjusted OR = 4.65, CI 1.69-12.76)(50).

Studies showed that medications given for diabetes, lipid lowering agent and renin acceptor inhibitors showed the promising association with development of DKD (10,23,58). The retrospective study done in Ethiopia showed that DM patients taking mixed oral and insulin medication are at less risk compared to those taking oral medication(AHR: 0.07, 95% CI: 0.01, 0.59)(58).

Moreover the attributes of lipid profile in the development of DKD is either insignificant, not represented or having complex relationship. Study reported that patients with DM with high serum triglycerides are associated with eGFR decline(59). The review done in Saudi Arabia showed that hyperlipidemia has increased risk with (OR 95%CI) 1.57 (1.49–1.66) to develop CKD(49). The observational study done in south Africa showed that triglyceride to HDL ratio

has increased risk for diabetic kidney disease(42). On the other hand, the recent studies done in Ethiopia showed that patients with high-density lipoprotein (HDL) greater than 40 mg/dl were less likely to develop CKD than patients with HDL less than 40 mg/dl(15,21,27,44). Another studies done in Ethiopia showed that total cholesterol above 200 mg/dl have increased risk compared to their counter parts (13,19).

Proteinuria measured in different manner in different study and most of the time it was found to be significant predictors of CKD in general as well as in DM patient. Study done in china among type 2 diabetes showed that there is significantly high decline of eGFR among those with proteinuria (4.4(2.4, 6.8) vs. 1.7(0.7, 3.5), P<0.001)(55). Study done in south western parts of Ethiopia showed that presence of proteinuria is significant risk for development of CKD (AHR=2.85,95% CI=1.48–5.55)(44)

The review of diabetes in Africa also show that duration of diabetes increase the risk of developing DKD(14). The cross-sectional study done in Ethiopia show that long duration of diabetes has increased risk of CKD among DM(50). The systematic review in Ethiopia showed that the long duration of DM >10 years was associated with CKD (OR 2.76; 95% CI: 1.38, 5.51)(15). The retrospective study done in the central party of Ethiopia also showed that long duration is the risk for development of chronic kidney disease among diabetes patients(AHR: 1.03, 95%CI: 1.01, 1.06)(58). But the study done in northern parts of Ethiopia showed that long duration above ten years is protective against CKD development(18). Again having type II diabetes is again about two time higher to have CKD than type I(15).

2.3.3 Comorbidity related factors

Comorbidities associated with an increased risk of DKD were also predictors CKD in those without DM. Hypertension, CVD, and cancer were the most predicting comorbidities of CKD(10,13,59). Prospective cohort study done in Australia showed that systolic blood pressure(SBP) above 150 mg/dl were at increased risk to develop CKD than their counter parts among DM(13). Again a review done in Ethiopia reported that those patients who had SBP >140 mmHg were about 3 times more likely to develop CKD than SBP <140 mmHg (OR 3.26; 95% CI: 2.24, 4.74) among DM patients (27). Another studies done in Ethiopia also showed those patients having hypertension have about two time increased hazard to develop CKD than their counter parts among DM patients (AHR 2.31 CI 1.03-5.56)(44). Additionally, retrospective

studies in Ethiopia were repeatedly reporting patients who had diabetic retinopathy were at increased hazard of developing CKD than in patients who did not have diabetic retinopathy(18,21,44). Heart, Stroke and Vascular disease also known as cardiovascular disease or CVD are broad term that describe many different diseases and conditions that affect the heart and blood vessels which most commonly include coronary heart disease, peripheral arterial disease ,stroke and heart failure. Moreover, study has showed patients with cardiovascular disease (CVD) were more likely to develop CKD than their counter parts among DM patients(13,18,19). Again studies shows having one or more episode of AKI has significant effect on the development of CKD among DM patients (60,61). Those patients developed severe form of acute complication can have acute kidney injury, which again lefts scare in the kidney and ends with chronic kidney disease. Diabetic foot ulcer, neuropathy and acute complication of DM were associated with CKD development as well as the decrement of estimated glomerular filtration rate. The decline of estimated glomerular estimation is more rapid in patients with diabetic neuropathy than not having diabetic neuropathy and the coexistence of peripheral neuropathy increases with stages of glomerular filtration rate(62).

Conclusion: Even though the prevalence of CKD is alarmingly high, it does not always imply that the risk of developing CKD is rising. If people with CKD receive better medical support they live longer and, meanwhile prevalence can simply increase. Therefore, it is important to look at incidence the rate at which new cases of CKD are diagnosed and respective contributors

General, many nations, including, Ethiopia, still lack data or data of adequate quality to fully understand the global figure. To fill the evidence gaps, chronic disease organizations across the world continue to enforce the development of high-quality data in all nations. More research is needed to access solid evidence to enhance fully understanding of the impact of CKD and inform national and global health targets. Consequently the findings used for careful and considered use in the support existing actions and to qualify the lives of people with CKD and those at risk of developing the condition and monitor the impact of interventions. Furthermore there has been heterogeneous reporting's even within the same country about the incidence, prevalence and factors associated to CKD. This is attributed to various diagnostic procedures used, differ criteria to diagnose, the source population used, response rates achieved, and geographical scope of each study which informs us there is gap in using common diagnosis and reporting system.

2.4 Conceptual framework.

Conceptual framework below represents of the associations of variables under study. The conceptual framework for the study was prepared from reviewing different literatures(10,16,18,19,44). The straight solid line show hypothesized pathway and the broken line show pathways not originally hypothesized and shows there might be relations among independent variables but nor for all variables inside box. There are four group of variables (socio-demographic, comorbidities, clinical factor, and medication) associated to one outcome variable (Figure1).

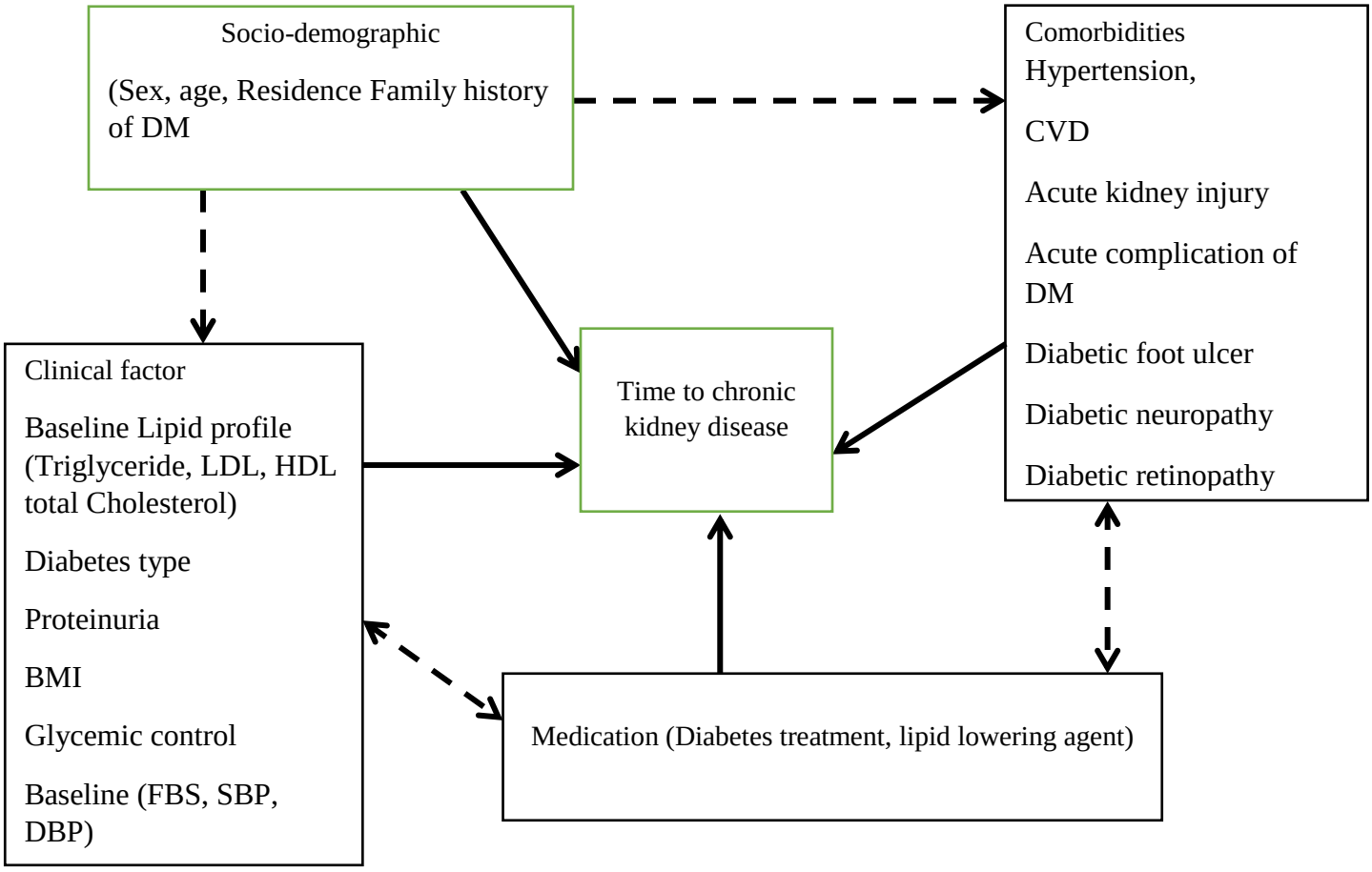


Figure 1: Conceptual frame work for the incidence and predictors of chronic kidney disease among diabetes mellitus patients.

Foote note *;* ***HDL*** *high density lipoprotein* ***LDL:*** *low density lipoprotein* ***SBP:*** *systolic blood pressure* ***DBP*** *:diastolic blood pressure* ***DM :****diabetes mellitus* ***CVD :*** *cardiovascular disease* ***FBS:*** *fasting blood sugar* ***BMI*** *:body mass index*

3 Objectives

3.1 General objectives

To determine incidence and predictors of chronic kidney disease among diabetes mellitus patients in Wolaita Sodo University Comprehensive Specialized Hospital and Sodo Christian General Hospital, Southern Ethiopia

3.2 Specific objectives

- To determine the incidence of chronic kidney disease among diabetes mellitus patients at Wolaita Sodo University Comprehensive Specialized Hospital and Sodo Christian General Hospital, Southern Ethiopia 2012 to 2023
- To determine the median time to detection of chronic kidney disease in diabetes mellitus patients at Wolaita Sodo University Comprehensive Specialized Hospital and Sodo Christian General Hospital ,Southern Ethiopia 2012 to 2023
- To investigate predictors of chronic kidney disease among diabetes mellitus patients at Wolaita Sodo University Comprehensive Specialized Hospital and Sodo Christian General Hospital, Southern Ethiopia 2012 to 2023

4. Methods and materials

4.1 Study area

The study was conducted at Wolaita Sodo University Comprehensive Specialized Hospital and Sodo Christian General Hospital which are found in Wolaita Sodo Town. Wolaita Sodo is the capital of Wolaita zone capital located 390 km south of Addis Ababa and 167 km south west of Hawassa. The city is located 6049" N latitude and 37045'' E longitude. Population size of the city according to the data from city finance Economic Development office, recently the total number of the city's residents exceed 120,000. To this end, the annual growth rate of the city's population is 5.4%.

Wolaita Sodo University Comprehensive Specialized Hospital (WSUCSH) was found in 1928. For the last five decades it has been serving as primary hospital and then become general hospital. In 2012, Wolaita Sodo University (WSU) takeover the hospital as a teaching and referral hospital with academic, research and community service responsibilities. The college has clinical, academic and administration wings. In clinical part, it delivers different medical services for outpatients (adult outpatient department (OPD), Pediatric OPD, Gynecology and obstetric OPD), emergency (adult, pediatric, intensive care unit (ICU), Obstetric) and inpatients (adult, Pediatric, maternal) for nearly 500-750 patients per day for 24 hours. The total service coverage of the hospital is about 3.5 million people of catchment areas. Currently; about 620 clients with DM visit these hospitals to receive regular follow-up care.

The second study setup is Sodo Christian General Hospital (SCGH) which is one of the three private hospitals in the town. The hospital was found in 2004. The same to Ottona, Christian hospital also has clinical, academic and administration wings. The hospital gives a full range of medical, surgical, maternity, and pediatric care. The hospital has an emergency clinic and outpatient rooms and an optometry and dental clinic. Currently 235 DM patients visit this hospital to receive routine care.

The study period: The study was conducted between March 28, 2023 and May 2, 2023.

4.2 Study design

A Health facility-based retrospective follow-up study was conducted by reviewing medical records of newly diagnosed DM patients enrolled to treatment between 2012 January to 2018 December.

4.3 Populations

4.3.1 Source populations

Medical charts of individual newly diagnosed with diabetes mellitus and started follow up in Wolaita Sodo Ottona Comprehensive Specialized and Sodo Christian General Hospitals.

4.3.2 Study population

Medical charts of individuals diagnosed with DM and started follow-up between 2012 and 2023.

4.4 Eligibility criteria

4.4.1 Inclusion criteria

Medical charts of all individuals diagnosed with DM Between, 2012-2018 and age of 15 years and above

4.4.2 Exclusion criteria

Medical charts of patients who had CKD during diagnosis of DM, those charts not found, patients who had less than three visits, the diagnosis time of DM and CKD not known

4.5 Sample size determination and sampling procedure

4.5.1 Sample size determination

To calculate the sample size the parameters used from two previous studies done in Ethiopia. The studies were chosen because they are most recent, large sample compared to others and socio-demographically related to our study area(19,44).

For specific objective one (1)

The sample was calculated using single population formula

$$\mathbf{(N)} = \frac{\left(\frac{z\alpha}{2}\right)2pq}{(d)2}$$

- Where 'N' is the required sample size;
- "Z a/2 is the critical value of standard normal distribution variable at 95%
- d" is the margin of error(0.05)

- P=the proportion of individuals developed event:
- q=the proportion of individuals not developed event or 1-P

Previous study(19) (N) $= \frac{(1.96)2(0.11)(0.89)}{(0.05)2}$ =150, adding 10% LTF =**166**

Previous study(44) (N) = $\frac{(1.96)2(0.1556)(0.8444)}{(0.05)2}$ =201, adding 10% LTF =**221**

For specific objective two (2)

The sample size determined in time to event formula by the power analysis for cox proportional hazard model in STATAV17 taking significantly related covariates with chronic kidney disease from previous studies(19,44).

By inserting the following parameters from previous study in STATA

- "Z a/2 is the critical value of standard normal distribution variable at 95%
- Zβ" is the critical value of the standard normal distributed variable at 20% β;
- The hazard ratio for selected covariates.
- The probability of CKD from previous study; and 10% lost to follow-up

Table 1: The minimum calculated sample size using STATA for CKD patients in (WSOCSH) and (SCGH), Southern Ethiopia 2023

Assumption	Previous study	Significant Variables	Hazard ration	Probability of event	Sample size ,n
Type I error =0.05 Power =80 Lost to follow-up=0.1	(19)	Cardiovascular disease	3.82	0.11	239
		Total cholesterol	3.31	0.11	177
	(44)	Hypertension	2.31	0.1556	320
		Sex(female)	0.51	0.1556	495
		HDL	3.19	0.1556	167
		Proteinuria	2.85	0.1556	205

For specific objective three (3)

The sample size determined by the Epi@Info taking significantly related covariates with chronic kidney disease from previous studies using double population formula

By inserting the following parameters from previous study in Epi Info

- "Z a/2 is the critical value of standard normal distribution variable at 95%
- "Zβ" is the critical value of the standard normal distributed variable at 20% β;
- "P1" the proportion of outcome among exposed
- "p2" the proportion of outcome among unexposed and 10% lost to follow-up

Table2: The minimum calculated sample size using Epi-Info for CKD patients in (WSUCSH) and (SCGH), Southern Ethiopia 2023

Assumption	Previous study	Significant Variables	P1%, p2% ,r%	Sample size ,n
Type I error =0.05 Power =80 Lost to follow-up=0.1	(19)	Cardiovascular disease	32.5%,5.4%,1	85
		Total cholesterol	19.8%, 4.4%,1	187
	(21)	Diabetic retinopathy	11.6%,48%,1	63
		HDL	22.5%,8.6%,1	240

As we can see from summaries of above equations of all three objective the **495** maximum samples from calculated were taken as final sample.

4.5.2 Sampling technique and procedures

There is one governmental and three private hospitals in the city. Two hospitals were selected purposely (WSUCSH and SCGH) because the rest two were found in the last three years, thus they not include our study population. Before proportionally allocation of calculated sample to each hospitals number of newly diagnosed DM patients were identified for both hospitals by enrollment year (2012-18) from log books and databases (Table 3).

Table 3: The number of newly diagnosed DM patients of age 15 years and above in WSUCSH and SCGH from 2012-2018.

Year Institution	2012	2013	2014	2015	2016	2017	2018	Total
WSOCSH	77	106	76	127	107	139	132	764
SCGH	68	71	59	57	56	69	66	446
Total	145	177	135	184	163	208	198	1210

The calculated sample 495 was proportionally allocated to both hospitals based on the DM patient flow (figure 2).

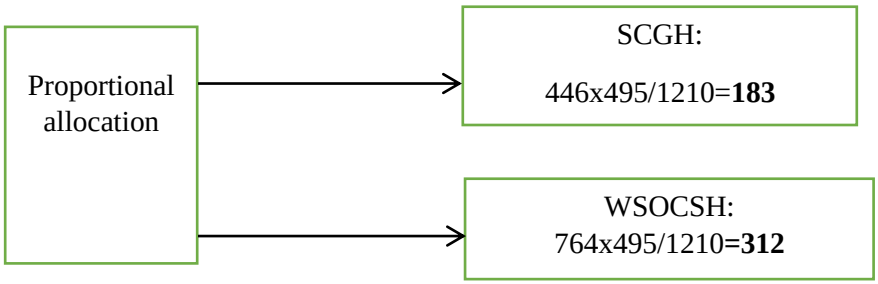
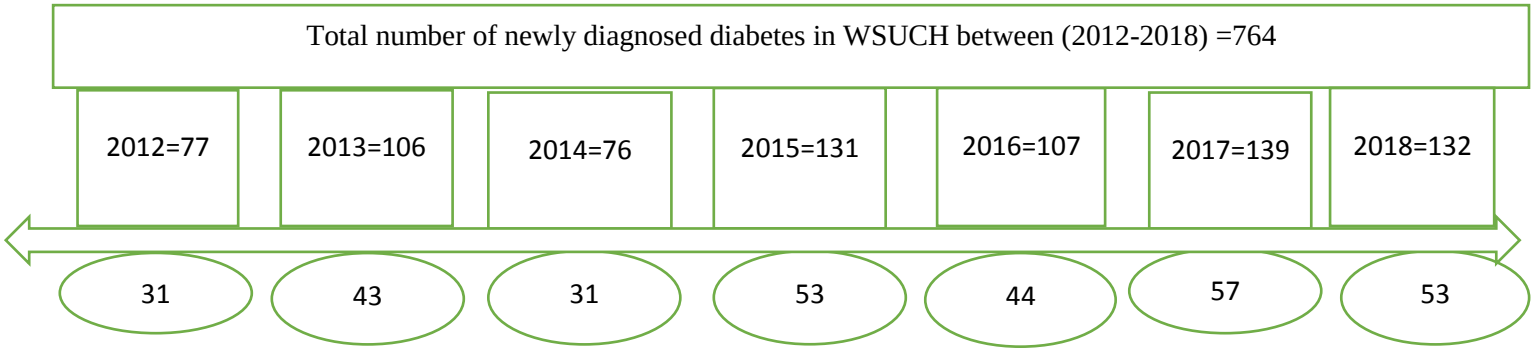


Figure 2: Proportional allocation of sample to WSUCSH and SCGH based on DM patient flow.

After proportionally allocation of calculated sample to each hospital, the samples were distributed to each enrollment year based on patient flow to those years for hospitals. After proportionally allocation of total sample to each year based on the patient flow during that year, then simple random sampling technique was done using computer to generate the medical registration number to access the patient charts. Those who had not diagnosis time registered for DM and CKD, chart that were not found, individual with less than three visits were replaced by other charts(figure 3)

Enrollment year (2012-2018) based allocation to the Wolaita Sodo University comprehensive specialized hospital.



Enrollment year (2012-2018) based allocation to the Sodo Christian General Hospital

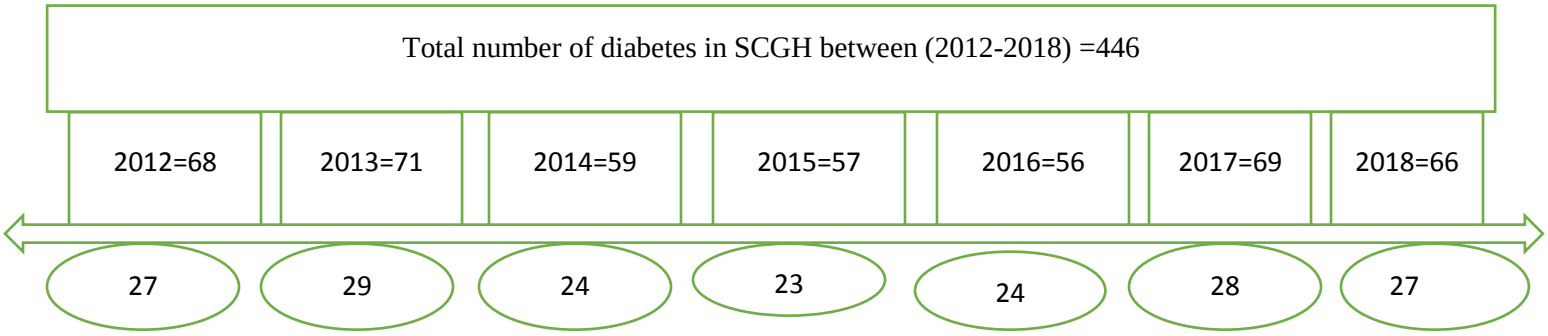


Figure 3: Study year based allocation of samples to both hospitals based on the patient flow of the enrollment year.

4.6 Study variables

Dependent variable

Time to CKD; which means the time from diagnosis of the DM to detection of chronic kidney disease calculated in months.

Independent variable

Socio-demographic factors; Sex, age, residence, family history of diabetes

Clinical factors; LDL, HDL, Triglyceride, Total cholesterol, baseline SBP, baseline DBP, baseline FBS, proteinuria, type of diabetes, glycemic control

Comorbidities; Hypertension, CVD, diabetic retinopathy, diabetic neuropathy, diabetic foot ulcer, acute kidney injury, acute complications of DM

Medications; Diabetes regimen, lipid lowering agents

4.7 Data collection tool and procedures

The study used secondary data. Data abstraction tool was developed from extensive reviewing of different literature(16–19,46). The tool includes socio-demographic, clinical, comorbid condition, medication history, follow-up time and patient's status (outcome)**.** After accessing charts by their respective medical registration number medical charts intake form, follow-up format and databases were used as data sources. Starting from first confirmed diagnosis of time DM to the detection of chronic kidney disease, death, lost follow-up or until study is ended, the

patient's history were retrospectively reviewed**.** The ODK data collection app was used to collect the patient data from cards. Three experienced data collectors (one MPH graduating class students from Wolaita Sodo University and two BSc nurses from Sodo town health center) were assigned to extract data. One MPH students were assigned as supervisor with Principal investigator (PI). Health information technologist (HIT) focal personal of Christian general hospital were facilitating data extraction from data base.

4.8 Operational definitions and measurements

Patient status; outcome of the participants; either event developed or censored

Censored; Individuals who did not develop the desired outcome during the follow-up time. This includes those who were lost to follow-up, died, or did not acquire CKD until the end of the follow-up time.

Event; chronic kidney disease

Follow-up time: the time from diagnosis with DM until either event or censorship occurs (2012 January -2023 April).

Death: if the individuals died from other case and if recorded in the charts.

Glycemic control: **Poor**: The average of fasting blood sugar from their last three consecutive visits >= 130 or<=70 mg/dl

Good: The average of fasting blood sugar from their last three consecutive visits< 130 mg/dl or >70 mg/dl(63).

Residence; Urban; address recorded as Sodo Town in the chart.

Rural; address other than Sodo Town in the chart, and the residence of those individuals who follows our study area from out of wolaita zone defend on the remoteness from major city.

Hypertension: The patient is on the antihypertensive medication or diagnosed as hypertensive on charts.

Proteinuria: Baseline dipstick proteinuria +1 and above.

Cardiovascular disease: confirmed history of cardiovascular disease/s on the medical charts

Chronic kidney disease: abnormalities of the kidney structure or function that is marked by a glomerular filtration rate (GFR) <60 mL/min/1.73 m2) present for >3 months and albuminuria >30 mg/24 hours and history of kidney transplantation or based on the clinical decision of physicians (1)

Acute kidney injury (AKI): This is a rapid decrease in kidney function characterized by an increase in Serum Creatinine by ≥0.3mg/dl (≥26.5μmol/L) versus baseline or increase in Serum Creatinine≥1.5 time's baseline value or based on the clinical decision of the physician(61).

To categorized lipid profiles Mayo clinic and guidelines from the National Cholesterol Education Program were used (64,65).

Elevated (low density lipoprotein (LDL)) ≥100 mg/dl

Low level of (high density lipoprotein (HDL) <40 mg/dl and<50mg/dl for Male and Female, respectively

High triglyceride (TGL) ≥150 mg/dl

Elevated total cholesterol level ≥200 mg/dl

4.9 Data management

Data was entered using ODK software directly during data collection and daily collected data was sent to the central server (to the PI SMART PHONE). The data collection template was prepared in Microsoft excels and changed to XLS form by uploading to kobo toolbox. The uploaded form was deployed to data collector's SMART phone. They used their SMART phone to access the extraction tool through getting blank form from ODK app.

4.10 Data analysis

The data was exported and cleaned for analysis using STATA statistical software version 17.

Specific objective1: Incidence density rate (IDR) was estimated for the entire study period and consequently, the incidence within the study period was divided by the total person months on follow-up and reported per person months. The patient status after end of follow-up were declared to event or censored.

Specific objective 2: Log-rank with Kaplan Meier was used to estimate and compare median survival time across groups and calculate cumulative probability of survival.

Specific objective 3: Categorical independent variables were calculated using frequency distribution. Patient's cohort characteristic of continuous independent variables was described by mean and median with respective measure of dispersion. The covariates such as baseline SBP, baseline DBP, baseline FBS was treated as continuous and the rest were categorical. The Cox proportional hazard regression model was used to determine the relationship between independent and outcome variables (incident CKD over follow-up time). Bivariate analysis was done and, variables with a p-value $\leq$ 0.25, fulfills the proportionality assumptions were transferred to multivariable analysis. The proportional hazard assumptions were checked using Schoenfeld residual test (global test) and graphically. In multivariable analysis, $p< 0.05$ was considered statistically significant. Hazard ratios (HR) with its corresponding p value were computed to determine statistical significance and strength of association. The over all model fitness to the data was checked by cox Snell residuals. Then, relationship among outcome and predictors were reported using an adjusted hazard ratio. Lastly, texts, tables, and graphs were used to describe the results.

Handling of missing value

All 495 charts were reviewed by replacing those charts with exclusion criteria. The missing value of variable of interest ranges from 0.15% to 7.2%. The pattern of missing data was checked statistically using littles MCAR test .The pattern of missing was missing completely at random(MCAR (p value 0.0625>0.05). The variable BMI has missing value greater than 40% and dropped from inferential analysis. The complete case analysis approach was used, so that there is variation of samples (n) from variable to variable in descriptive and bivariate analysis. Because statistical articles suggest that bias could be happen when analyzing variable with more than 10% of missing observations and, if more than 40% of missing observations were for important variable ,then the result should be used only for hypothesis(66).

4.11 Data quality control

Before one week of data collection extraction tool was pre-tested among 5% of the patient charts in the study setup (WSUCSH) for consistency of understanding and measurement's of variables, adequacy of instrument, and completeness of data for charts to improve the data quality. The tool

was modified and necessary corrections were done after pretest. The variables like socio-demographic factors (education status, marital status); behavioral factors (history of smoking, drinking alcohol) were not recorded in the medical charts and removed from extraction checklist. One day training was given for data collectors and supervisor two days before actual data collection on the aim of the study, about the ODK app, the data extraction tool (checklist), and any ethical issue might be during data collection. The same data collectors were used for both institutions. The supervisor with principal investigator was supervising the data collectors.

4.12 Ethical considerations

Ethical clearance was obtained from research and ethical review board of the School of Public Health at the College of Health Sciences in Addis Ababa University. A formal letter of cooperation from the University was submitted to the hospitals administrative body to get permission for data collection. The proposal was reviewed again by Sodo Christian General Hospitals ethical review committee to permit for data collection in their SCGH. The hospitals respective management body allowed data collection. The health information technologists and data clerks of the hospitals were adequately explained about the purpose, and feature benefits of the study. Any personal identifiers were removed from the data collection format to assure the confidentiality. As long as this is secondary data informed consent is not needed or not applicable but waiver consent was considered throughout data collection.

4.13 Dissemination of the results

The result will be submitted to Addis Ababa University, College of Health Sciences, and School of public health. Also, the result will be submitted to Wolaita Sodo University Comprehensive Specialized Hospital and Sodo Christian General Hospital. Further effort will be made to present it at a workshop and conference and publish it on a highly reputable journal.

5. Results

5.1 Description of study participants

From randomly selected patients charts those charts with exclusion criteria were excluded and replaced with other charts of the same year. Charts were reviewed until all 495 samples were reached. Even though there is variation of sample (n) from variable to variable during descriptive and bivariate analysis, our multivariable analysis was restricted to 424 full cases for our variable of interest in final analysis (Figure 4).

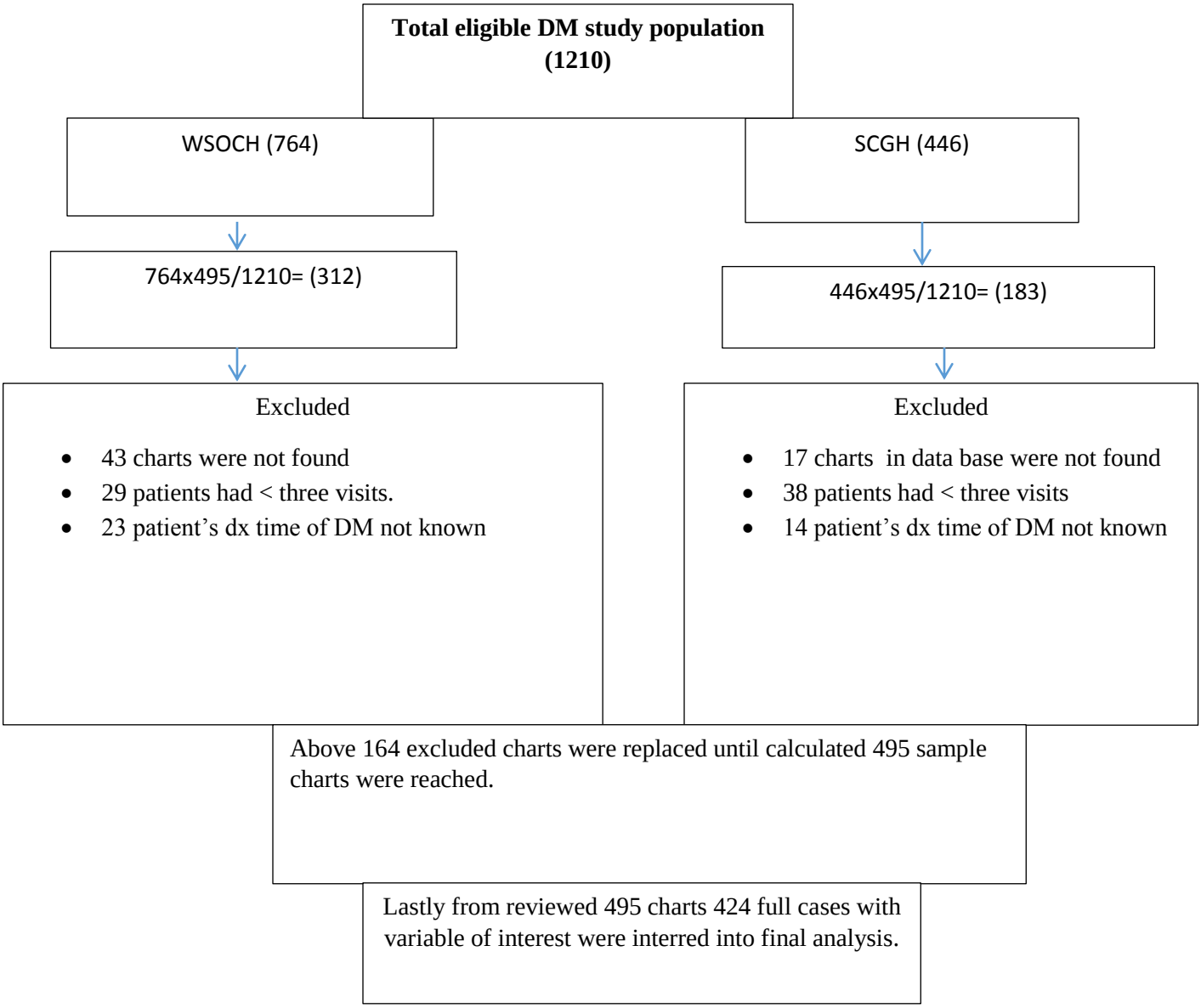


Figure 4: General description of sampling and study participants

5.2 Socio -demographic characteristics.

Out of 495 patients 318 (64.24%) were male and 74.3% CKD is among this population. Majority of the patients were urban dwellers 353(71.31%) and the rest 28.6% were from rural. The highest number of patients developed CKD (71.6%) were urban. The mean age of study participants was 45 (95% CI 43.7, 46.2) and majority (26.6%) of them are between age group 40-50. Large number of patients developed chronic kidney after the age of 40. Out 474 DM patients 210 (44.3%) had positive family history of DM (Table 4).

Table 4: Socio-demographic characteristics of DM patients in WSUCSH and SCGH, Southern Ethiopia 2023

Variable	Category	Patient status		Hospitals		Total n(%)
		Event n,(%)	Censored, n(%)	WSOCSH n, (%)	SCGH n, (%)	
Sex	Male	55(74.3)	263(63.3)	206(41.6)	112(22.6)	318(64.2)
	Female	19(25.7)	153(36.7)	106(21.4)	77(15.5)	177(35.7)
Age	15-19	4(5.4)	15(3.6)	18(3.6)	2(0.4)	30(3.8)
	20-29	5(6.7)	50(12.0)	37(7.4)	18(3.6)	55(11.1)
	30-39	17(22.9)	115(27.6)	54(10.9)	31(6.2)	85(17.2)
	40-49	11(14.8)	74(17.7)	88(17.7)	44(8.8)	132(26.6)
	50-59	31(41.8)	96(23.1)	75(15.2)	52(10.5)	127(25.6)
	≥60	6(8.1)	71(17.1)	40(8.0)	37(7.4)	77(15.5)
Residence	Urban	53(71.6)	300(71.2)	219(44.2)	134(27)	353(71.3)
	Rural	21(28.4)	121(28.7)	93(18.7)	49(9.8)	142(28.6)
Family(n=474)	Yes	31(43.6)	179(44.4)	108(21.8)	102(20.6)	210(44.3)
	No	40(56.4)	224(55.5)	183(36.9)	81(16.6)	264(55.7)

5.3 Clinical, treatment and laboratory related characteristics

Three hundred sixty-seven (74.14%) of the study participants had type II diabetes, while the remaining had type I diabetes. During their most recent visit to the hospital, about one-third (31.92%) were taking oral medication, followed by insulin (31.72%). Over a quarter of the patients (27.27%) were taking combined both insulin and oral drugs.

Above one-quarter had a high-density lipoprotein of less than 40 mg/dl and below half (42%) had a LDL of more than 100 mg/dl. Their mean value of baseline systolic hypertension and baseline fasting blood sugar was 143 mg/dl and 183 mg/dl respectively. One hundred patients

had dipstick proteinuria at baseline. Taking the average fasting blood sugar of their last three consecutive visits, more than half of the patients (54.95%) showed poor glycemic control. One hundred and nine (38.2%) of the study participants were taking a lipid-lowering medication (statin). Again there is highest proportion of CKD were presented among type two diabetes mellitus (Table5).

Table 5 : Clinical, treatment and laboratory related characteristics of DM patients in WSUCSH and SCGH, Southern Ethiopia 2023

Variables	Category	Patient status		Total (%)
		Event	Censored	
Type of DM	Type 2 Type 1	63(85.1) 11(14.9)	304(72.2) 117(27.8)	367(74.14) 128(25.86)
DM of therapy	1 oral therapy >1 oral medication Insulin Both	7(9.4) 21(28.8) 20(27.0) 26(35.1)	38(9.0) 137(32.5) 137(32.5) 109(25.9)	45(9.1) 158(31.9) 157(31.7) 135 (27.3)
HDL(459)	<40 ≥40	40(55.6) 32(44.4)	97(25.06) 290(74.3)	137(29.8) 322(70.1)
LDL(472)	<100 ≥100	45(65.3) 24(34.7)	156(38.7) 247(61.2)	271(57.4) 201(42.5)
Triglyceride(475)	<150 ≥150	48(67.6) 23(32.4)	162(40.1) 242(59.9)	265(55.7) 210(44.2)
Total Cholesterol (461)	<200 ≥200	35(48.3) 37(51.3)	74(18.3) 315(77.9)	352(76.3) 109(23.6)
Proteinuria	No Yes	31(41.9)) 43(58.1	364(90.1) 57(14.1)	395(79.8)) 100(20.2
SBP	Mean 139.27 ± 22.00	73	422	495
DBP	Mean83.33 ±14.19472	73	422	495
FBS	Mean 182.45 ± 59.7	74	421	495
Lipid lowering agent	Yes No	41(55.4) 33(44.6)	265(62.9) 156(37.05)	306(61.8) 189(38.1)
Glycemic control	Good Poor	47(63.5) 27(36.6)	225(53.4) 196(46.5)	222(45.0) 272(54.9)
BMI(285)	≥30 25-30 18.5-25 <18.5	8(16.6) 12(25.0) 27(56.2) 1(2.08)	15(6.3) 39(16.5) 181(76.4) 2(0.84)	23(8.07) 51(17.9) 208(72.9) 3(8.07)

5.4 Comorbidity characteristics

During follow-up time, just above half of the DM patients (55.96%) had a history of hypertension. Almost all hypertensive patients (98.2%) began taking antihypertensive medication. During their most recent visit to the hospital, 166 (61.03%) of the patients on the anti-hypertensive medicine were taking enalapril (antihypertensive agent).

About a quarter (21.41%) of the 495 patients had a history of anemia, and sixty-six (13.33%) experienced acute kidney damage (AKI) during the study period. There was a history of cardiovascular illness in 87 (17.58%) of diabetic patients. The majority (61.36%) had congestive heart failure, followed by ischemic heart disease (42%).

Ninety-seven patients (19.59%) had history retinopathy, and 21.01% had a history of peripheral neuropathy. Only 9% had a history of diabetic foot ulcers. Out of 495 patients, approximately 31.31% had a history of acute complication, and from them majority (74%) had at least one episode of DKA. The proportion of CKD is higher among patients with AKI, CVD and hypertension (Table 6).

Table6: Comorbidity characteristics of DM patients in WSUCSH and SCGH, Southern Ethiopia 2023

Variables	Category	**Patient status**		Total (%)
		Event	**Censored**	
Retinopathy	Yes	36(48.6)	61(14.5)	97(19.59)
	No	38(51.4)	360(85.5)	398(80.40)
Neuropathy	Yes	20(27.0)	84(19.9)	104(21.01)
	No	54(72.9)	337(80.0)	391(78.9)
Diabetic ulcer	Yes	13(17.5)	32(7.6)	45(9.09)
	No	61(82.4)	389(92.4)	340(90.9)
Acute complication	Yes	29(39.2)	130(30.8)	159(31.3)
	No	45(60.8)	291(69.1)	336(68.69)
Type of acute complication	DKA	21(72.4)	98(75.4)	159(74.2)
	HHS	5(17.2)	25(19.2)	30(18.87)
	Both	2(6.9)	3(2.31)	5(4.52)
	Hypoglycemia	3(10.3)	10(7.6)	13(8.8)
Hypertension	Yes	64(86.5)	213(50.6)	277(55.9)
	No	10(13.5)	208(49.4)	218(44.0)
Started-antihypertensive medication	Yes	64(86.5)	208(49.4)	272(45.0)
	No	10(13.5)	213(50.6)	223(54.9)

Type of antihypertensive therapy	Enalapril Nifedifine Combined	35(54.7) 2(3.13) 24(37.5)	131(62.9) 18(8.65) 38(18.3)	166(61.0) 20(7.3) 86(31.6)
CVD	Yes No	46(62.2) 28(37.8)	41(9.7) 380(90.2)	87(17.5) 408(82.4)
Type of CVD	CHF IHD PAD Stroke	34(73.9) 15(32.6) 5(10.8) 3(6.5)	20(48.8) 21(51.2) 2(4.8) 2(4.88)	54(61.3) 36(42.0) 7(14.1) 5(5.6)
AKI	Yes No	39(52.7) 35(47.3)	27(6.4) 394(93.6)	66(13.3) 86.6
Other comorbidities	RVI UTI Pneumonia TB Asthma Goiter Cancer PUD Anemia	2(2.7) 16(29) 29(39.2) 6(8.1) 2(2.7) 2(2.7) 3(4.0) 20(27.0) 48(64.8)	5(1.2) 39(29.1) 119(28.3) 25(5.9) 7(1.6) 10(2.3) 10(2.3) 42(9.9) 58(13.7)	7(1.4) 55(11.1) 148(29.9) 31(6.2) 9(1.8) 12(2.4) 13(2.6) 62(12.5) 106(21.4)

5.5 Incidence density of chronic kidney disease

Of the total 495 diabetic patients at risk 74(14.95% 95CI% 12-18.03) patients developed CKD over the median follow-up time 7.1 (IQR 6.0-9.0) years. The over all duration of follow-up is 44064 months .The patients were followed for minimum of 32 and maximum 133 months. The overall incidence rate of chronic kidney was 16.7 (95% CI 13.3–21.0) cases per 10,000 person-months or 2 cases per 100 person-years. The cumulative incidence of CKD for patients in WSUCSH and SCGH were 20.5 % and 5.46% respectively. The median time to develop CKD was 130 (interquartile range (IQR) 128-132) months. The incidence density below shows the number of event in each group with person time and how fast the event was happening in the follow-up period in the study population. There is highest incidence rate among age above 50 years 20.6(95% CI 14.9-28.46) compared to below 50 year with 14.1(10.0-19.54*)* incidence rate. The incidence rate is again high in HDL <40 32.7 (95%CI 23.6-43.8) compared with 11.3(95%7.9-15.9*)* in their counter parts. The DM patients who has of retinopathy has incidence

rate 39.9 cases per 100,000 person months compared to those who had not experienced the problem (Table 7)

Table 7: Incidence density of CKD patients among DM in WSUCSH & SCGH, by groups of significant covariates on log-rank test

Variable	Category	Person time	Events	Incidence rate(95%CI) per 10,000PMs
Age	≥50	26126	37	20.6(14.9-28.46)
	<50	17938	37	14.1(10.0-19.54)
HDL	≥40	28296	32	11.3(7.9-15.9)
	<40	12429	40	32.18(23.6-43.8)
LDL	≥100	18213	45	24.7(18.4-33.09)
	<100	23608	24	10.16(6.8-15.16)
Triglyceride	≥150	23230	23	9.9(0.6-1.48)
	<150	18937	48	25.3(19.1-33.6)
Cholesterol	≥200	10351	35	33.8(24.2-47.09)
	<200	30500	37	12.1(8.79-16.74)
Retinopathy	Yes	9092	36	39.59(28.56-54.89)
	No	34972	38	10.8(7.9-14.9)
Hypertension	Yes	25198	64	25.39(19.8-32.45)
	No	18866	10	5.3(2.8-9.8)
CVD	Yes	8374	46	54.9(41.1-73.3)
	No	35690	28	7.8(5.4-11.30
Presence of AKI	Yes	6313	39	61.7(66.6-129.1)
	No	37751	35	9.2(6.6-12.9)
Type of DM	Type 2	32477	63	19.3(15.15-24.8)
	Type 1	11587	11	9.49(5.2-17.1)
Type of DM therapy	Oral	25716	47	18.27(13.7-24.3)
	Insulin	14669	20	13.6(8.7-24.3)
	Both	3679	7	19.0(9.07-39.9)

5.6 The over all Kaplan Meir survival curve estimate

The graph of over Kaplan–Meir survival curve represented that in patients with DM the probability of developing CKD increased over time (Figure 5). A highest number of CKD diagnosed were detected after 100 months of follow-up time. The cumulative survival probability of developing chronic kidney disease among DM patients who were free from the disease at the start of treatment was 0.9820 at 72 month, 0.9175 at 96 month, 0.8712 at 108 months, and 0.5692 at 132 month. The fist case was detected after 36 months of follow-up (**Table 8**).

Table8: Life table of DM patients at WSUCSH and SCGH, southern Ethiopia 2023

Time in months	Beg. Total	Events	Censored	Probability of survival	Standard error	95% CI
24-36	495	0	1	1.00	0.00	..
36-48	494	2	12	0.9939	0.0035	0.9811, 0.9980
48-60	479	0	16	0.9939	0.0035	0.9811, 0.9980
60-72	463	5	84	0.9820	0.0063	0.9644, 0.9910
72-84	374	14	74	0.9413	0.0123	0.9118, 0.9611
84-96	286	6	96	0.9175	0.0153	0.8817, 0.9428
96-108	184	8	51	0.8712	0.0216	0.8219, 0.9076
108-120	125	2	13	0.8565	0.0236	0.8029,0.8965
120-132	110	27	59	0.5692	0.0477	0.4704, 0.6564
132-144	24	9	15	0.2587	0.0731	0.1306, 0.4075

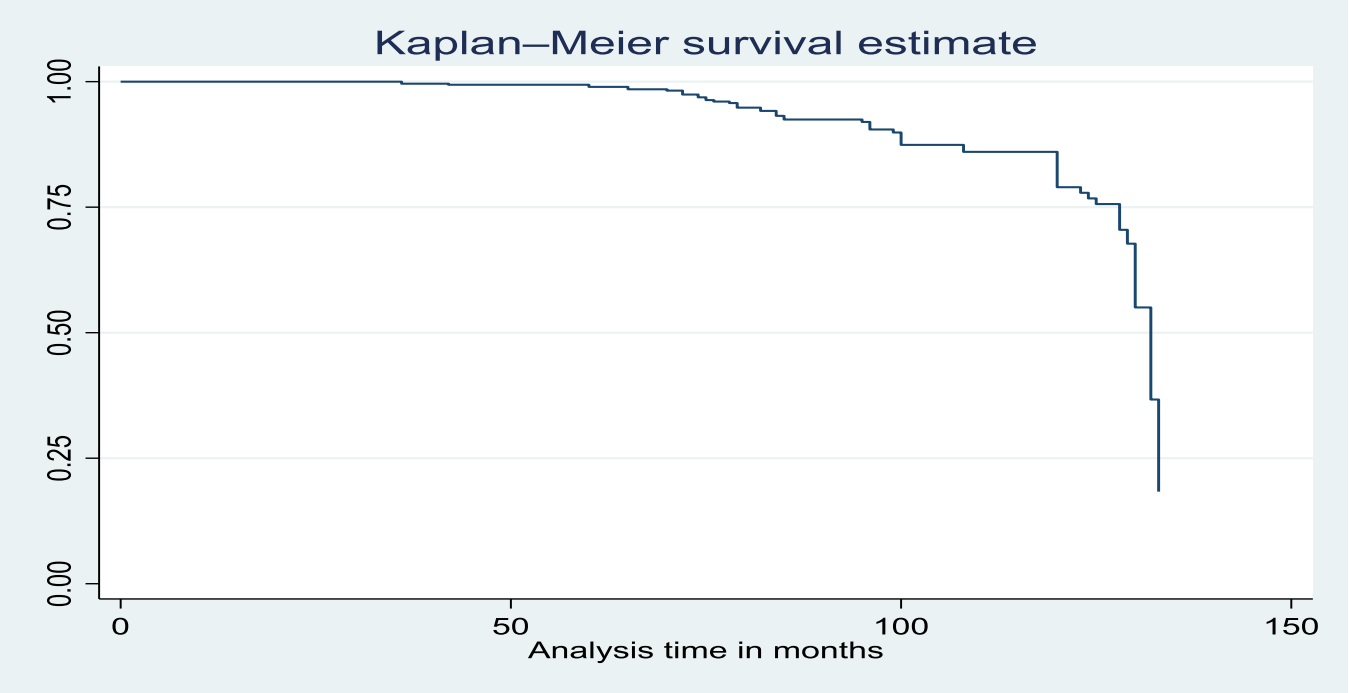


Figure 5: Show the overall Kaplan Meir survival curve estimate of diabetes patients in WSOCSH and SCGH

5. 7 Kaplan- Meier survival graphs for selected predictors

Patients whose HDL level 40mg/dl and above vis-à-vis less than 40 mg/dl, their survival time was equal for the first 5 years. But after that diabetes patients with HDL level above 40mg/dl have better survival with median survival time of 132 months compared to below 40 mg/dl whose median survival time were 128 months (**Figure 6**).

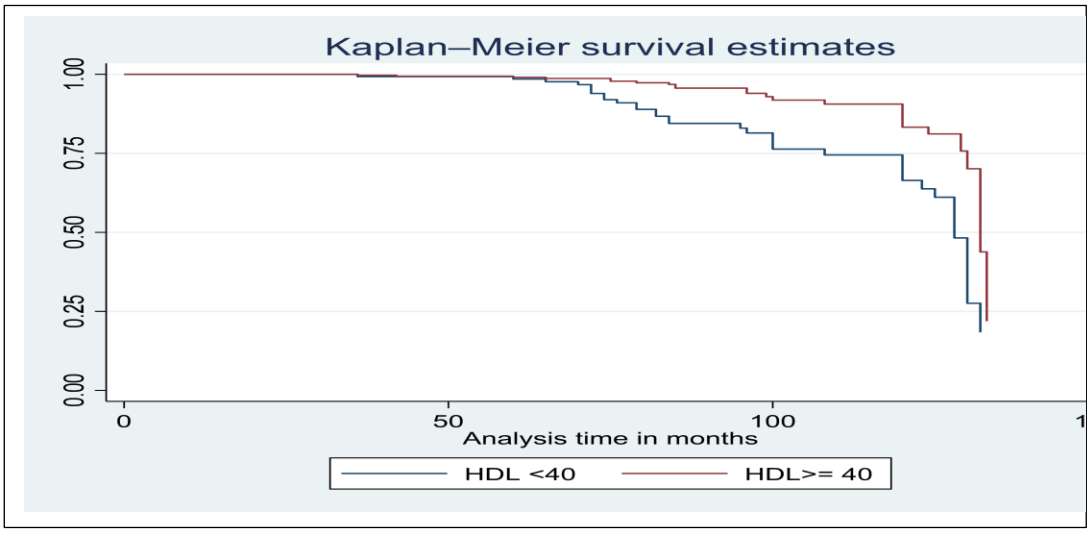


Figure 6: KM curve of DM patients with HDL >= and< 40mg/dl.

Diabetes patients with history of cardiovascular disease have low survival with median survival time of 120 months compared to their counter parts (Figure 7).

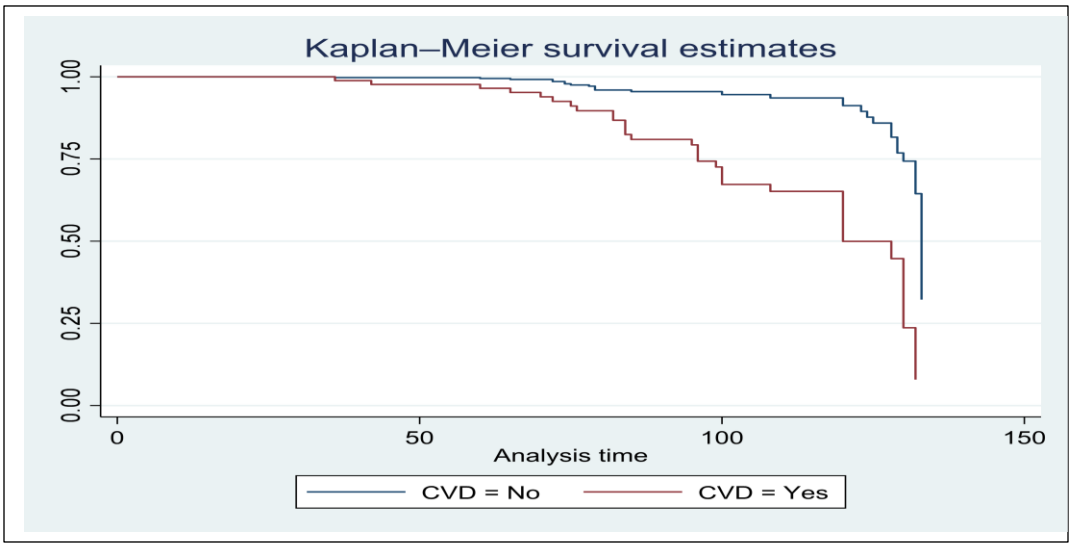


Figure 7: KM curve of DM patients with history of CVD.

Diabetes patients with history of diabetic retinopathy have low survival with median survival time of 125 months compared to their counter **(Figure 8).**

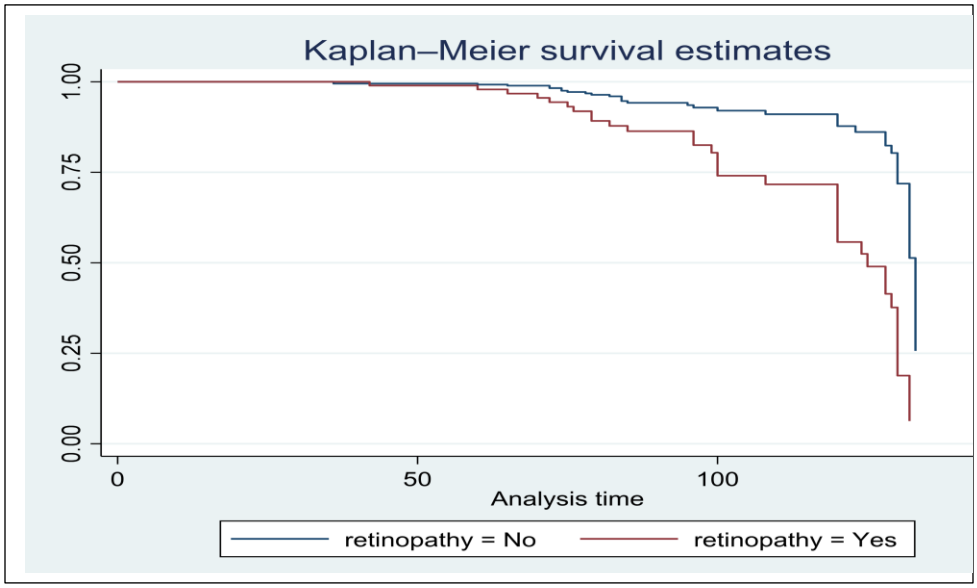


Figure 8: KM curve of DM patients with history of Diabetic retinopathy (DR)

Diabetes patients with history of acute kidney injury have low survival with median survival time of 120 months **(Figure 9).**

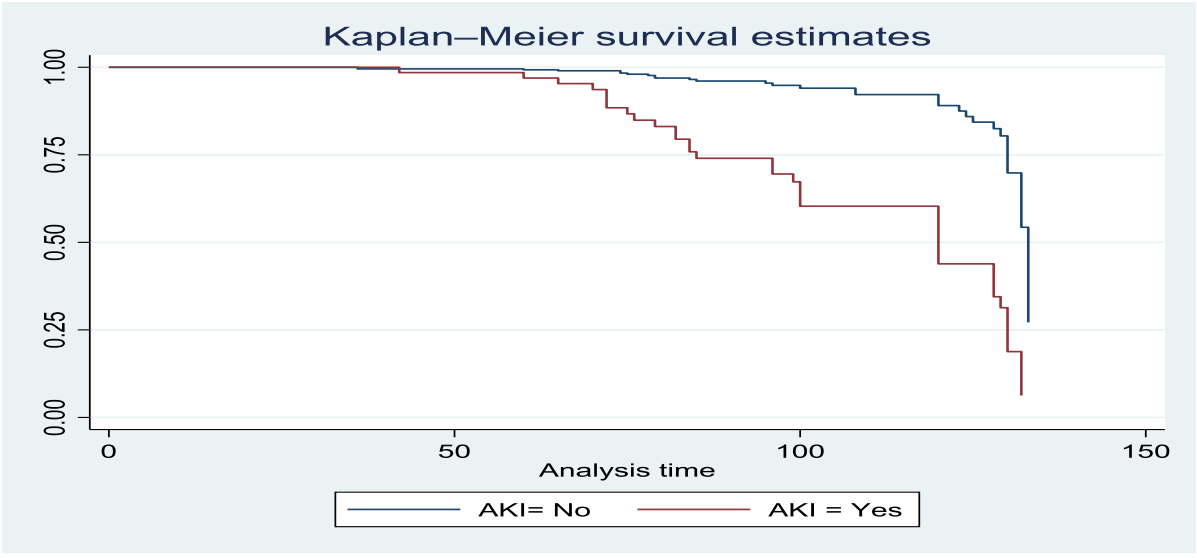


Figure 9: KM curve of DM patients with AKI

The Kaplan-Meier estimate of survival functions using a statistical log-rank test was used to test for differences in significance between the factors categories. The log rank test below showed that difference between groups of covariates in selected covariates. Those variables include; age (**pr>x2**0.0082), HDL (**pr>x2** 0.00), LDL (0.0043) and type of DM (0.0018) have significant difference from their groups. Additionally variable like family history of DM, sex and type of DM regimen have not significant difference in log rank test. Other variables were showed in the table below (Table 9).

Table 9: Log-rank test for equality of survival function of CKD patients among DM in WSOCSH &SCGH using selected covariates

Variable		**Observed effects**	**Expected effects**	**X^2 test**	**Log-rank test (pr>x2)**
Age	<50	37	47.46	7.00	0.0082
	>=50	37	26.54		
Sex	Male	55	49.77	1.81	0.1780
	Female	19	24.77		
Family history of DM	Yes	31	25.23	2.26	0.1329
	No	40	45.77		
HDL	<40	40	23.09	19.92	0.0000
	>=40	32	48.91		
LDL	>=100	45	33.65	8.16	0.0043
	<100	24	35.35		
Triglyceride	>=150	48	34.75	10.79	0.0010
	<150	23	36.25		
Cholesterol	>=200	35	37.22	8.88	0.0029
	<200	37	23.17		
Type of DM	Type 2	63	51.19	9.70	0.0018
	Type 1	11	22.81		
Type of DM therapy	Oral	47	37.86	7.5	0.0235
	Insulin	20	31.01		
	Both	7	5.12		
Retinopathy	Yes	36	15.69	35.89	0.0000
	No	38	58.31		
Peripheral neuropathy	Yes	20	19.71	0.01	0.9374
	No	54	54.29		
Hypertension	Yes	64	43.71	24.81	0.000
	No	10	30.29		
Proteinuria	Yes	43	22.61	29.97	0.0000
	No	31	51.39		

CVD	Yes	46	19.57	54.41	0.0000
	No	28	54.43		
Presence of AKI	Yes	39	13.69	63.20	0.000
	No	35	60.31		
Glycemic control	Poor	47	42.97	0.97	0.3244
	Good	27	31.03		
Lipid lowering agents	Yes	41	45.89	1.49	0.2218
	No	33	28.77		

5.8 Cox proportional hazard assumption checking

The Schoenfeld residual global test showed overall full model satisfies the proportionality assumption ($X2$= 15.30, P < 0.6414). Again Cox Snell residual plot which is used to assess the overall goodness of fit in survival models. This is done graphically using the usual Cox-Snell plots and it is observed that residuals from a properly fitted model follow an exponential unity distribution along the 45-degree slope (baseline) below showed was the assumption was satisfied (Figure 10).

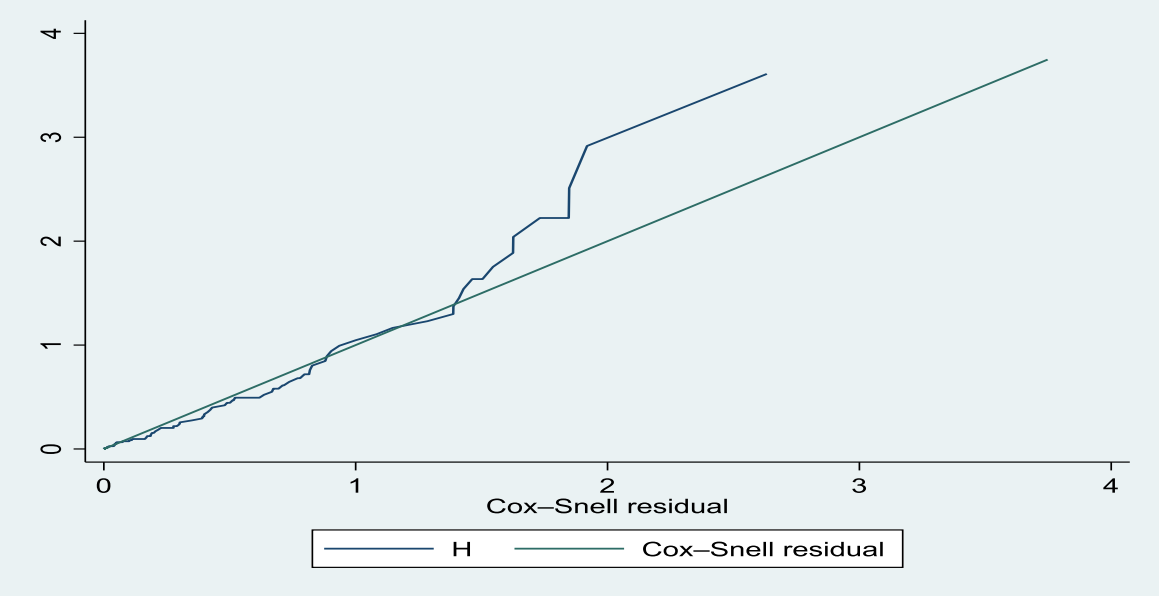


Figure 10: Cox-residual assumption graph for over all model fitness

Graphical assumption checking for those covariates significantly associated with outcome using the–ln(-ln(survival)) against –ln(analysis time) graphs are roughly parallel (not crossed each other) ;which represents the assumption is roughly fulfilled(**Figure 11**). It shows that applying multivariable cox regression analysis is suitable for this data

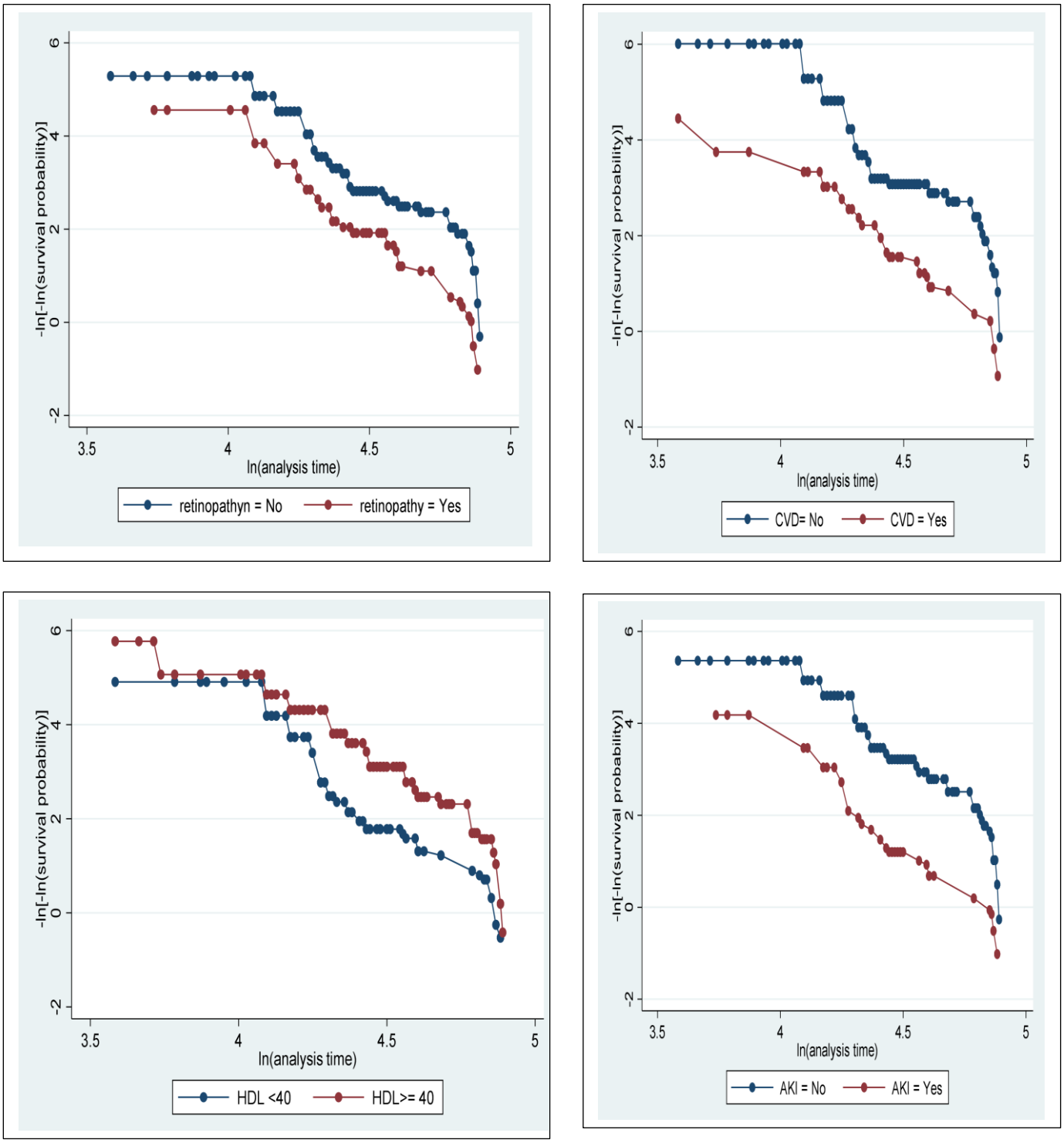


Figure 11: Graphically assumption checking for statistically significant factors

Foot note HDL; high density lipoprotein, **CVD;** cardiovascular disease AKI; acute kidney injury

5.7 Predictors of incidence of chronic kidney disease among diabetes patients

Bivariate analysis

The relationship between the independent variables and the outcome variables was analyzed using the Cox proportional hazards regression model. In bivariate Cox proportional regression analysis sex, age, family history of diabetes ,lipid profiles(HD, LDL, total cholesterol, triglyceride),SBP, DBP, type of DM ,history of hypertension, retinopathy, proteinuria ,having cardiovascular disease, history of AKI , lipid lowering agent and diabetes regimen were associated with chronic kidney disease at p value ≤0.25. Moreover variables such as, lipid profiles (HD, LDL, total cholesterol, triglyceride),SBP, DBP, type of DM ,history of hypertension, retinopathy, proteinuria ,having cardiovascular disease, history of AKI were associated with chronic kidney disease at p value ≤0.05 in bivariate analysis.

Multivariable cox regression analysis

Variables with p ≤0.25 on bivariate analysis and meet assumption of proportionality test were sent for multivariable analysis. Therefore sex, age, family history of diabetes, lipid profiles (HD, LDL, Total cholesterol, triglyceride), retinopathy, acute kidney injury, baseline systolic blood pressure, baseline diastolic blood pressure, CVD, type of DM ,history of hypertension, lipid lowering agent, proteinuria and diabetes regimen were fulfilled the above criteria and interred into multivariate model. From that high density lipoprotein, acute kidney injury, history of confirmed cardiovascular disease, history of diabetic retinopathy, was become significant independent predictors to chronic kidney disease among diabetes adjusted for sex, age, family history of diabetes, LDL, Total cholesterol, triglyceride, SBP, DBP, type of DM ,hypertension, lipid lowering agent, proteinuria and diabetes regimen at p-value 0.05.

Diabetic patients having baseline elevated high density lipoprotein were about 46.3% less risk of having chronic kidney disease than those with lower high density lipoprotein **(AHR 0.537 95% CI 0.303, 0.95).** Patients who developed diabetic retinopathy had 86% increased risk of having CKD than their counter parts **(AHR 1.86 95% 1.03-3.36).** Those who had history of confirmed CVD had about 2 times higher risk of developing CKD **(AHR 2.12 95% CI (1.16-3.87)** compared to those not having disease**.** DM patients who developed one or more episodes of AKI had 2.49 times higher risk than their counter parts **(AHR 95% 2.49(1.37-4.54)** (Table 10)

Table 10: Bivariate and Multivariable survival model analysis for predictors of CKD among DM patients in WSUCSH and SCGH, Southern Ethiopia 2023

		Patient status				
Variable	Category	Censored	Event	CHR(95%CI)	AHR(95% CI)	P-value
Sex	Male	55	263	1.41(0.83-2.3)	0.97(0.53-1.76)	0.923
	Female	19	153	**Ref**	**Ref**	
Age	>=50	48	231	1.81(1.14-2.86)	1.08(0.605-1.92)	0.792
	<50	26	190	**Ref**	**Ref**	
Family history of diabetes	Yes	31	179	1.42(0.88-2.28)	1.16(0.68-2.00)	0.569
	No	40	224	**Ref**	**Ref**	
HDL	>=40	40	97	0.371(0.23-0.59)	0.537(0.303-0.95)	**0.033***
	<40	32	290	**Ref**	**Ref**	
LDL	>=100	45	156	1.98(1.20-3.27)	1.433(0.755-2.72)	0.270
	<100	24	247	**Ref**	**Ref**	
Triglyceride	>=150	48	162	2.18(1.32-3.59)	1.09(0.614-1.95)	0.755
	<150	23	242	**Ref**	**Ref**	
Cholesterol	>=200	35	74	1.94(1.22-3.10)	1.109(0.63-1.93)	0.713
	<200	37	315	**Ref**	**Ref**	
Retinopathy	Yes	36	61	3.60(2.27-5.72)	1.86(1.03-3.36)	**0.039***
	No	38	360	**Ref**	**Ref**	
Hypertension	Yes	64	208	4.45(2.28-8.67)	1.31(0.501-3.43)	0.579
	No	10	208	**Ref**	**Ref**	
Proteinuria	Yes	43	57	3.34(2.02-5.37)	1.15(0.579-2.28)	0.687
	No	31	364	**Ref**	**Ref**	
CVD	Yes	46	41	4.86 (3.00-7.87)	2.12(1.16-3.87)	**0.013***
	No	28	380	**Ref**	**Ref**	
Lipid lowering agents	Yes	41	265	0.75(0.477-1.20)	1.033(0.568-1.87)	0.913
	No	33	156	**Ref**	**Ref**	
SBP		73	422	1.015(1.00-1.02)	1.004(0.99-1.01)	0.713
DBP		73	422	1.02(1.01-1.04)	1.013(0.99-1.03)	0.238
History of AKI	Yes	39	27	5.08(3.18-8.05)	2.49(1.37-4.54)	**0.003***
	No	35	394	**Ref**	**Ref**	
Type of DM	Type 2	63	304	2.58 (1.35-4.91)	0.68(0.258-1.80)	0.44
	Type 1	11	117	**Ref**	**Ref**	
Type of DM therapy	Oral	19	138	0.910(0.41-2.019)	1.08(0.42-2.76)	0.866
	Insulin	45	248	0.466(0.19-1.16)	0.49(0.153-1.609)	0.244
	Both	9	38	**Ref**	**Ref**	

Foote note: **ref**; reference, * significant at p value 0.05

6. Discussion

CKD is the sever form of renal kidney disease that could be irreversible and leads to death which is commonly observed in patients with NCD primarily DM and has become serious public health problem both in developing and developed world. However it is highly increasing in developing country compared to the developed(8). Therefore this study was investigated incidence and predictors of chronic kidney disease among diabetes mellitus patients in Wolaita Sodo town hospitals Southern Ethiopia.

Majority of CKD patients in this study were male 55 (74.4%). Above one-quarter of study participant's had a baseline HDL of less than 40 mg/dl and below half (42%) had a LDL of more than 100 mg/dl. More than half (55.96%) had a history of hypertension. Sixty-six (13.33%) of study participants experienced AKI during the study period. There was a history of cardiovascular illness in 87 (17.58%) of DM patients. Moreover 74(14.9% 95CI%12-18.03) out of 495 DM patients in the follow-up years were developed CKD. The average follow-up time in this study was 7.4 years. Further more AKI, CVD, retinopathy and HDL have strong association with CKD development.

The cumulative incidence of CKD in this study is (14.9% 95CI%12-18.03). This result is inline with study done in central (14.25%)(16), Northern13.6%(18) and south western parts of Ethiopia (15.6%) (44) and ,Italy 13.5% (67). But the result is lower than study done in Australia 22.2% (13),United Kingdom 28%(68), Nigeria 76.2%(69) and Sweden 20%(70). This might be due to longer follow-up duration, the study done UK followed for average of fifteen years ,however this study only followed for average of seven years which is about half of them and the patients in the united kingdom had high risky life style compared our study populations. Again this study is retrospective, while the study done in the UK and Australia was prospective which had high chance for cases to be diagnosed and they had large sample (n=4029) and (n=9331) respectively compared (495) to this study. Meanwhile the study done in Australia included only age group 45 years and above. Additionally, Sweden is developed nation with the better patients' health-seeking behavior, the high capabilities and skills of health professionals, and the presence of sophisticated investigation machines may help patients to motivate and check for their kidney status (71). Furthermore study done in Nigeria used albuminuria to diagnose CKD.

Beside the incidence is higher than the study done Spain 10.23% (72) . This might be due to our study included both types of diabetic (I&II) patients that might be the reason for the higher cumulative incidence compared to other which included only one type of diabetes (type two). Even though Study done in Spain is prospective it only assessed CKD stage 3-5 and the duration of follow-up is only (5 years) related to current study in which the average follow-up time is seven years. Again the study setup this study included was both governmental and private settings in which those risky individuals were following. Again in the private settings there is high chance of detection of case.

The median survival time to develop chronic kidney disease in this study was 10.8(IQR 10.6-11) years .This result go inline with study done in UK 12 years (68). However it is higher than study in Ethiopia 5.9 and 9 years (16,19),and Australia 5.7 years (13). This discrepancy might be due to the subset of DM populations, the previous study used was only type II DM .However this study included both type of DM patients ,so that they have longer duration to develop chronic kidney disease. The individuals in the study setup are remote compared above studies, in that they might be less motivated to check or know their kidney status early. Most of individual in the study setup are farmers and labor workers, which prevents risks related to sedentary life that in turn might shorten the duration of CKD incidence.

In our study we found that the presence of history diabetic retinopathy diagnosed prior to CKD among diabetes patients was become significantly associated with CKD development. This finding is supported by other studies done among adult diabetic populations in central and south westerns of Ethiopia, Japan, UK (21,68,73). This might be due to having of diabetic retinopathy itself may put individuals at risk for CKD among DM patients. According to studies, the vascular networks of the kidney and eye are comparable in structure, development routes, and disease progression, including atherosclerosis, endothelial dysfunction, oxidative stress, and inflammation because of various pleiotropic genes(74). The presence of DR may indicate concurrent renal small vessel injury, elevated cardiac biomarkers, prompt endothelial dysfunction, increased albuminuria, and decreased vascular reactivity, all of which are indicators of systemic factors that may attribute to the development and increased risk of chronic kidney disease(75).

In this study patients with elevated level of baseline high density lipoprotein ≥ 40 mg/dl are at less risk compared to their counter parts. This finding is consistent with study done in Ethiopia and Italy (21,44,76). This association may be caused by biological properties of HDLC-cholesterol, such as its ability to reverse the transfer of lipids from artery walls to the liver and its anti-inflammatory and antioxidant effects. As a result, the artery wall's ability to accumulate fat and develop atherosclerosis is finally reduced. Additionally, it guards against artery damage, which lowers the likelihood of vascular complications from DM, such as CKD. Patients with decreased HDL levels may therefore lack this utility and have an increased risk of getting CKD. The development of micro-albumuria and diabetic kidney disease has been demonstrated to be facilitated by reduced levels of HDL(76,77).

This study again revealed that DM patients with history confirmed cardiovascular diseases are significantly at higher risk to get CKD compared to their counter parts. Our study showed hazards of CKD among DM patients who had CVD are approximately two times higher than patients who didn't have the disease. The finding is supported by studies done in Ethiopia, Spain, Australia and the UK (13,18,21,68,72). The relationship between cardiovascular morbidity and renal disease is based on the fact that when the heart is unable to pump blood effectively due to blood clots, pressure builds up in the blood vessels leads to congestion in the kidneys. The heart continuously pumps oxygen-rich blood to all organs. The kidney removes waste from the blood and controls the water and salt levels. This association was further supported by studies showing that decreased pump volume and effective circulating blood cause baroreceptor stimulation, increased sympathetic nervous activity, renin secretion, which causes an increase in sodium reabsorption, and constriction of the glomerular-mesangial cells, which would affect the filtration rate (78). Therefore, the results of this study highlight the importance of paying close attention to cardiac issues in DM patients and preventing the condition to lower the risk of CKD.

Having history of one or more episode of AKI is also become the significant predictors of the CKD experience among DM patients in this study. This result is supported by study done in the united states (60,61,79). Endothelial dysfunction caused by an increase in the production of the vasoconstrictor endothelial-1 (ET-1), a decrease in the production of nitric oxide, proximal tubular injury, and a maladaptive process that results in insults like scarring and tubule-interstitial fibrosis that leads to CKD progression and ESKD are among the hypothesized

mechanisms to explain why DM patients are more susceptible to AKI(80,81). DM itself is also risk for acute kidney injury. However the association between AKI and CKD was also reported in various ways. The true impact of acute kidney damage in the diabetes population on the development of CKD relies on which comes first. AKI can predict for CKD, and conversely, CKD can also predict AKI. Even though this study highlighted the effect of previously diagnosed AKI before CKD to ascertain temporality, being the chronicity and silent symptoms might made the CKD to be diagnosed later.

Further more the study resulted in some inconsistent findings. In our study patients having history of hypertension have weak relation to CKD development. This result is inconsistent with studies done in Ethiopia(44) and UK(68). The possible reason might be almost all hypertensive population in this study has started taking antihypertensive medication. Again the proportion of hypertension in this this is lower compare to above studies. However, despite of its statistically insignificant p-value, hypertension is clinically significant variable based on the biological plausible study for patients with DM. So, patients with hypertension and DM should get attention equally with individuals with statistically significant variables.

Additionally the effect of sex in this study also becomes statistically insignificant. Some other studies done before in Ethiopia(15,18,44) ,UK(68) and Spain(72) had reported the strong relation of sex in the development of CKD among DM patients. Even if sex had significant effect in the studies before, the effect varies from one study to other (in one study male and in other study female becomes significant predictors). In contrary to them, in our study and study done in Australia (13) sex has no effect in the outcome. This might be due to different design used, proportion of sex in study or different cultural effect ascribed to sex. In generally this warrants us the effect of sex in the CKD prediction among diabetes is yet to be proven.

Many study across world repeatedly demonstrated that old age has established association with getting CKD in diabetes(13,15,68). However the effect of age adjusted for covariates in full model is insignificant in our study. This might be due to most of the studies selected advanced age, while this study only included less risky age compare to them with mean age of 45.

7. Strengths and limitations of the study

7.1 Strengths

Though the study is retrospective ,it has some strengths like including both types of DM populations in which other studies done in Ethiopia were only included type two DM, this study also included patients having their follow-up in the private health setup who are more or less risky compared to others which enables us to external validity (generalization). Again using ODK to collect data is very important to control data quality issue that might be formed during paper based data collection, entering collected data manually. The second of its type in Ethiopia by assessing the incidence among both types of DM, and the first for the study area

7.2 Limitations

Having above shortlisted strengths, however there are undeniable shortcomings of the study. Its retrospective nature and missing of variables such as socio-demographic, behavioral, and laboratory parameters which are very indicative and their presence might have effect on the variable that are included in the study. This might leads to unmeasured or omitted variable bias.

Again the study is prone to selection biases because it only included facility.

With baseline kidney status was not actively done for all DM patients, this study is again in difficulty to say the result is only the incidence.

The data extraction tool was not standard or validated.

8. Conclusion and Recommendations

8. 1 Conclusion

CKD was found to be significant public health problem and it is comparatively high to previous studies done in Ethiopia Approximately fifteen percent of diabetic patient experienced CKD throughout study time with median time to 11 years to get the problem. Further, diabetic retinopathy, HDL, AKI and history of CVD have increased the hazard of developing CKD.

The clinical significance of these findings is to inform healthcare providers about the incidence and risk factors for CKD so that they can take appropriate action to reduce those risks and focus their efforts on preventing it. By finding the factor most substantially associated with CKD, this study has the potential to improve public health by preventing the financial loss related to dialysis and transplantation in ESRD.

8.2 Recommendations

Patients: They should consult care providers especially those above 100 months with disease about their CKD status and follow their caregiver advice and treatment recommendations.

Clinicians: Health professionals are also suggested to give more emphasis and inform patients to prevent risk of cardiovascular disease, diabetic retinopathy, HDL, AKI as well as to encourage them to know their kidney status early.

Policymakers and program planners: Awareness creation on all promising risk factors as well as signs and symptoms for CKD should be focused on all responsible body to the public

Training of first-line health professionals about the problem engaging them to community to promote reduction modifiable risk factors like cholesterol .Promotion of having good diabetes self care and increasing access to treatment of DM shall be emphasized.

R**esearchers** in the field are suggested to conduct a prospective study to identify predictors fully. So that clinicians will uptake the evidence and prioritize patients during treatment.

To WSOCSH and SCGH: Inclusion of detailed patient behavioral and socio-demographic characteristics in patients charts, active follow up of patients, and establishing and making compressive of existing electronically data managing system will be important for quality of care

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ANNEX: I Extraction tool

PART I Socio-demographic characteristics.

S.N	VARIABLES	Value	SKIP
1	Baseline Age		
2	Sex	Male ……..1 Female ……2	
3	Family history of diabetes	Yes …1 No……2	
4	Residence	Urban Rural	

Part II Clinical factors

S.N	VARIABLES	CATEGORY	SKIP
1	Duration of diabetes in months		
2	HDL		
3	LDL		
4	BMI		
5	Baseline FBS		
6	Type of DM therapy	1 Oral medication……1 > 1 Oral medication….2 Insulin…….,3 Both ……..4	
7	Antihypertensive medication	Yes ……1 No …….2	
8	Total cholesterol, mg/d		
9	Triglyceride, mg/dl		
10	Baseline SBP		
11	Baseline DBP		
12	Baseline FBS		
13	Glycemic control		

Part III **Comorbidities**

1	Hypertension	Yes ……1 No ……..2	
	Started antihypertensive medication	Yes No	
	Type of antihypertensive medication	Nifedipine Enalapril Combined	

2	Retinopathy	Yes ……1 No ……..2	
3	Peripheral Neuropathy	Yes ……1 No ……..2	
4	CVD	Yes ……1 No ……..2	
5	Type of CVD	IHD PAD Stroke CHF	
6	Acute complication	Yes No	
7	Type of acute complication	DKA HHS BOTH(DKA,HHS) Hypoglycemia	
8	Acute kidney injury	Yes ……1 No ……..2	
9	Diabetic foot ulcer	Yes ……1 No ……..2	
10	Other comorbidities	RVI TB Pneumonia Asthma Goiter Cancer Pud Uti Anemia	

ANNEX II: Information sheet

(English version)

Research Title: Incidence And Predictors of chronic kidney disease among Diabetes Patients In Wolaita Sodo University Comprehensive Specialized Hospital and Sodo Christian General Hospital Southern Ethiopia, Retrospective follow-up Study

Name of principal investigator: Amanuel Arota

Name of the sponsor: Addis Ababa University

Introduction: This information sheet is prepared for Wolaita Sodo University Comprehensive Specialized Hospital and Sodo Christian General Hospital. The aim of the form is to make the institution clear about the purpose of the research, data collection procedures and finally to get permission to conduct the research.

Purpose of the research project: Primarily, the result of these study will be submitted to Addis Ababa University School of Public Health for the requirements to earn Masters of Public Health in Epidemiology and Biostatics. Additionally there are few studies were done so far in the area of diabetic kidney disease due to the fact in Ethiopia. The international and national non-communicable disease control program had mentioned improving research capacity on chronic kidney disease as one strategy to control the disease. Thus, the finding of this study will contribute its part in filing the information gap regarding diabetic kidney disease and its care by isolating factors those results in its development among diabetes patients so as to guide specific interventions on those factors. Therefore, it will contribute for policies that focus on diabetic kidney disease prevention, care and treatment.

Procedure: All patient cards and data base information's of diabetes patients who are under follow up from 2012 to 2018 in Wolaita Sodo University Comprehensive Specialized Hospitals and Sodo Christian General Hospital will be selected and a review of the required information from the records will be made using extraction tool. Two nurses and two MPH students will be trained and review the charts using ODK.

Risk: There will be no risk at all on patients whom their records are reviewed.

Benefits: There will be no incentive or direct benefit to patient's charts involved in the study. In dead, they will benefit indirectly from the research when the result of the study is used for program Planning to improve diabetes care and treatment. Therefore, this research will have a

paramount direct benefit for health care planners and managers working on diabetes prevention, care and treatment

Confidentiality: All patient rights will be highly respected. Patients name will not be used, instead, number codes will be used for every patient. Patient's information will be kept confidentially so as no other parties can obtain except the principal investigator and it will be locked with password in a computer.

Person to contact: This research project were reviewed and approved by the institutional review board of Public health College of Health Sciences at Addis Ababa University. In case, if you want to know more information about the research and its undertakings, you can contact the committee through the following address.

Addis Ababa University College of Medicine and Health Science Research Review Committee

Amanuel Arota (MPH Candidate): Tel: +251904696568

Permission: Therefore, you are kindly requested to permit and forward your permission to concerned body in your organization so that the researcher can get cooperation from data clerks and other responsible bodies.

With regards!

To be filled by Medical Directors:

I have properly examined the objective of the study, understood patient rights are respected patient confidentiality is assured and there will be no risks on patients related to the study.

Therefore, I gave a formal permission for the study to begin on behalf _____hospital.

Medical Director Name:

Signature:

Date:

ANEXXI III. Training guide for medical chart data extraction

First of all, the potentially challenging areas during data collection are identified and this data guide is developed to overcome the challenge. Therefore, this guide will be used for training of data collectors, supervisor and as a reference when data collectors are abstracting data from the medical records, and interviewing of diabetic patients in WSUCSH and SCGH. This guide will explain; source of data for every variable, the most frequently used abbreviations by physicians in the hospital, Protocols and steps for data collection from records. Therefore, data collectors were easily perform their tasks with this reference.

Objective of the study: To determine incidence and predictors of chronic kidney disease among diabetic patients in WSUCSH and SCGH.

Inclusion criteria: All diabetic patients diagnosed and started follow-up in WSUCSH and SCGH during 2012-2018 and age 15 and above years.

Exclusion criteria: Those patient charts were not found, the diagnosis time of CKD and DM were not known, not had visits at least three times were removed from the study

Sources of data: Medical records, Data base, log book

Criteria for data collectors and Supervisor: data collectors and supervisor are going to be experienced in data collection and have smart phone.

Part I: Data collection from Medical records

Time required: a maximum of 25 minutes for every patient chart

How each variable is extracted?

1. Socio-demographic variables

Sex and age: are usually written in the patient chart

Place of residence: this can be fully or partially available on the cover page of patient chart. Family history, are not usually available on the patient chart However, if there is a nursing process sheet in the chart, you can record from it.

2. Clinical data

Duration of diabetes: will be determined by calculating date of diagnosis of diabetes to CKD **.**HDL, LDL, glyceride, cholesterol, are going to be reviewed from laboratory investigation sheet.

3. **Comorbidities**: this variable is going to be filled from discharge diagnosis of the patients.

Commonly used Abbreviations on patients' chart: dx (diagnosis), Ass (assessment), DM (Diabetes Mellitus), CKD (chronic kidney disease), GFR (glomerular filtration rate)