



SCREENING, PREVALENCE AND MANAGEMENT OF TYPE 2 DIABETES IN SUB-SAHARAN AFRICA: THE CASE OF ETHIOPIA AND NIGERIA

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**Dissertation for the Doctor of Philosophy Degree in Social and
Administrative Pharmacy**

JUNE 16, 2025

ADDIS ABABA UNIVERSITY

Addis Ababa, Ethiopia

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DIABETES IN SUB-SAHARAN AFRICA**

**A PhD Dissertation submitted to the Department of Social and
Administrative Pharmacy, School of Pharmacy, Addis Ababa University
Presented in partial fulfillment for the Degree of Doctor of Philosophy in Social
and Administrative Pharmacy**

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June 16, 2025

ACKNOWLEDGEMENT

Above all, I would like to express my heartfelt gratitude to loving God for the courage, wisdom and determination; making me curious to explore and analyze.

I am also immensely grateful to my supervisors, Professor Teferi Gedif (BPharm, MPH, Ph.D.) and Dr. Adem Y Dawed (BPharm, MSc, MPH, PhD), for their meticulous and insightful guidance and mentorship throughout my PhD development and during this specific project. Without their strong guidance this dissertation could not have come to success.

I am profoundly thankful to the Addis Ababa University, School of Pharmacy, Department of Social and Administrative Pharmacy for granting me with this remarkable study opportunity and the financial assistance to carry out my dissertation research. My gratitude also extends to the staff members of the School of Pharmacy, friends, and colleagues who have supported me, both directly and indirectly, in my efforts to realize my dreams. The moral support from my colleagues in the Department of Pharmacology and Clinical Pharmacy, especially Mr. Melak Gedamu, Dr Teshome Nedi, Mr Oumer Sada, and others had been tremendous. Their inputs had been helpful throughout the process of this PhD journey including their encouragement to finalize this dissertation.

Furthermore, I extend my thanks to the Diabetes Epidemiologists' Network in Sub-Saharan Africa (DENSSA) project, collaborative research initiative involving the University of Dundee in United Kingdom, Addis Ababa University in Ethiopia and University of Nigeria in Nigeria, for the financial support of the data collection. This support has been pivotal to my success and has been an important enabler for my academic progress. I would also like to thank Madras Diabetes Research Foundation for hosting me in a research conference at Chennai, India. I also extend my acknowledgement to our Nigerian collaborators Dr. Ulasi and Dr Young.

I would like to acknowledge the study participants in this study who provided me with their information. I would also like to acknowledge the data collectors and supervisors and respective field guides to facilitate the data collection. The supervision, facilitation and

support given by Ato Mulugeta and Abiot at Butajira Rural Health Program (BRHP) at the time of data collection is highly acknowledged.

I would humbly acknowledge the love and critical support given to me by my families. I heartfully acknowledge the love, care and support given to me by my wife and life partner Shewaye Gedefaye. Last but importantly, my greatest debt is due to my kids Maranatha, Makiba and Marsena for their love, harmony, motivation and comfort they give me throughout this PhD process.

LIST OF Publications PAPERS

- 1) Baye AM, Fenta TG, Siddiqui MK, Dawed AY: **The Genetics of Adverse Drug Outcomes in Type 2 Diabetes: A Systematic Review.** *Frontiers in Genetics* 2021, **Volume 12 - 2021.** <https://doi.org/10.3389/fgene.2021.675053>
- 2) Baye AM, Fenta TG, Karuranga S, Nnakenyi ID, Young EE, Palmer C, Pearson ER, Ulası II, Dawed AY: **Comparative Analysis of Type 2 Diabetes Prevalence and Clinical Profiles in Ethiopia and Nigeria.** *Journal of Diabetes* 2025, **17(4):e70078.** <https://doi.org/10.1111/1753-0407.70078>
- 3) Baye AM, Fenta TG, Karuranga S, Nnakenyi ID, Young EE, Palmer C, Pearson ER, Ulası II, Dawed AY: **Performance of fasting plasma glucose for community-based screening of undiagnosed diabetes and pre-diabetes in sub-Saharan Africa.** *Frontiers in Endocrinology* 2025, **Volume 16 - 2025.** <https://doi.org/10.3389/fendo.2025.1501383>
- 4) Baye AM, Dawed AY, Fenta TG; **Accuracy of fasting capillary blood glucose test in type 2 diabetes screening in Butajira, Central Ethiopia: a community-based study.** *Int J Diabetes Dev Ctries* [submitted]
- 5) Baye AM, Dawed AY, Taye M, Fenta TG; **Delayed Treatment Intensification as a Barrier to Glycemic Control among Adults with Type 2 Diabetes: Retrospective Cohort Study at a Tertiary Hospital in Ethiopia.** *BMC Endocr. Disord.* [Submitted]

ABSTRACT

Introduction: Diabetes prevalence is rising in Sub-Saharan Africa (SSA), yet many cases remain undiagnosed, delaying treatment. This study assessed diabetes and prediabetes prevalence, evaluated fasting plasma glucose (FPG) and fasting capillary blood glucose (FCG) against the 2-hour plasma glucose (2-h PG) test, and examined glycemic control and treatment intensification delays in type 2 diabetes.

Methods: A community-based cross-sectional study was conducted in Butajira, Ethiopia, and Enugu, Nigeria (2020–2021), involving 1,727 participants. The WHO STEPs tool was used, with FPG, FCG, and 2-h PG tests applied per ADA criteria. Receiver operating characteristic (ROC) curves assessed FPG and FCG performance. A retrospective cohort study at Tikur Anbessa Hospital (2018–2024) evaluated type 2 diabetes management. Statistical tests included ANOVA, chi-square, and logistic regression.

Results: Among participants (50.5% male, mean age 44.6 years), diabetes prevalence was 7.0%, and prediabetes 15.8%; 74.6% were undiagnosed. Impaired fasting glycemia (11.8%) and glucose tolerance (11.5%) were observed. Newly diagnosed diabetes rates were 3.4% (FPG) and 4.0% (2-h PG). Agreement between FPG and 2-h PG was moderate (kappa: 0.56 for diabetes, 0.45 for prediabetes). FCG and 2-h PG showed good agreement (Bland-Altman bias: 0.03). FPG missed 34.1% of prediabetes and 44.4% of diabetes cases; FCG missed 48.0% of diabetes and 14.1% of prediabetes cases. Optimal cut-offs for detecting diabetes were 105 mg/dL (FPG) and 119 mg/dL (FCG). In the type 2 diabetes management study (n = 407, 52.6% female), 48.9% had poor glycemic control. Delay in treatment intensification was longer in uncontrolled cases.

Conclusion: Diabetes and prediabetes prevalence is high in SSA, with significant undiagnosed cases. FPG and FCG effectively ruled out diabetes (99.3% and 99.0% specificity) but missed many cases. Lowering FPG/FCG cut-offs improves detection. Timely treatment intensification is essential for glycemic control.

Keywords: type 2 diabetes, screening, prevalence, Ethiopia, Nigeria, glycemic control.

GLOSSARY OF TERMS AND CONCEPTS USED IN THE STUDY

Screening

Screening is the process of identifying those individuals who are at sufficiently high risk of diabetes to warrant further investigation or direct action (WHO Principles of Screening).

Diagnosis

The term diagnosis refers to confirmation of diabetes in people who have symptoms, or who have had a positive screening test.

Newly diagnosed diabetes

Ascribed to a FPG level of ≥ 126 mg/dL, 2-h PG of ≥ 200 mg/dL or both, excluding previously diagnosed patients.

Impaired fasting glucose (IFG)

Corresponds to fasting plasma glucose levels between 100 mg/dL and 125 mg/dL,

Impaired glucose tolerance (IGT)

defined as a 2-h PG ranging from 140 mg/dL and 199 mg/dL

Isolated IFG (i-IFG)

FPG of 100–125 mg/dl with the 2-h PG value < 140 mg/dl;

Isolated IGT (i-IGT)

2-h PG value of 140–199 mg/dL with the fasting level < 100 mg/dL

Receiver operating characteristics (ROC)

A ROC curve is a graphical representation that classifies a patient's disease state as either positive or negative based on test results and to find the optimal cut-off value with the best diagnostic performance. It plots the true positive rate (TPR) against the false positive rate (FPR). The closer the ROC curve is to the upper left corner of the graph, the better the model's ability to discriminate between positives and negatives. The Area Under the Curve (AUC) value is a widely used metric in clinical studies, succinctly summarizing

index test diagnostic performance. The interpretation and values of AUC for ROC curve is $0.9 \leq \text{AUC}$ as Excellent, $0.8 \leq \text{AUC} < 0.9$ as considerable, $0.7 \leq \text{AUC} < 0.8$ as fair, $0.6 \leq \text{AUC} < 0.7$ as poor and $0.5 \leq \text{AUC} < 0.6$ fail

Sensitivity and Specificity

Sensitivity is defined as the proportion of people who actually have a target disease that are tested positive, and specificity is the proportion of people who do not have a target disease that are tested negative.

Good glycemic control

According to ADA good glycemic control is defined as A1C less than 7.0% (53 mmol/mol) and fasting blood glucose of 80-130 mg/dL. These goals are usually individualized based on duration of diabetes, age and life expectancy, comorbid conditions, known cardiovascular disease or advanced microvascular complications, impaired awareness of hypoglycemia, and individual considerations.

Clinical inertia

Failure to initiate or intensify diabetes treatment in a timely manner despite clinical indications.

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ABBREVIATIONS AND ACRONYMS

2-h PG	2-hour Plasma Glucose
95% CI	95% Confidence Interval
ADA	American Diabetes Association
CI	Clinical Inertia
DENSSA	Diabetes Epidemiologists' Network in Sub-Saharan Africa
FCG	Fasting Capillary Blood Glucose
FPG	Fasting Plasma Glucose
IDF	International Diabetes Federation
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
MET	Metabolic Equivalent of Task
OADs	Oral Antidiabetic Drugs
OGTT	Oral Glucose Tolerance Test
ROC	Receiver Operating Characteristic
SSA	Sub-Sahara Africa
TASH	Tikur Anbessa Specialized Hospital
TI	Treatment Intensification

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CHAPTER 1: INTRODUCTION

1.1. Background of the Study

Diabetes is a chronic disorder characterized by elevated blood glucose levels, caused by either inadequate insulin production in the pancreas or resistance to insulin (World Health Organization, 2018). It poses a significant worldwide health challenge, accounting for more than half a billion cases (11.1% of the world's adult population) and 3.4 million deaths among adults in 2024 (IDF, 2025) projected to rise to 852.5 million by 2050.

The number of individuals with diabetes in Sub-Saharan Africa (SSA) was about 25 million by 2024 with the highest proportion of undiagnosed diabetes cases (72.6%) as compared to high-income countries (29.1%) (IDF, 2025). According to this report, Nigeria and Ethiopia hold the first and fifth positions, respectively, in terms of the highest number of adults with diabetes in SSA.

Societal guidelines stressed the pivotal role of early detection of type 2 diabetes to ensure effective glycemic control and delay the onset of complications (American Diabetes Association Professional Practice Committee, 2022; Aschner, 2017; Davidson et al., 2021). Community-based screening for type 2 diabetes is important for early detection of the disease as it is asymptomatic and high rates of undiagnosed cases (Khunti & Davies, 2012).

Based on the World Health Organization (WHO) diagnostic and screening strategies, clinical questionnaires, urine glucose, fasting plasma glucose (FPG), fasting capillary blood glucose (FCG), 2-h plasma glucose (2-h PG) after 75 gm oral glucose, glycated hemoglobin (HbA1C) and combinations of these tests can be used for screening diabetes (World Health Organization, 2003). The most common testing strategy for community-based screening is the FPG test. But there are several limitations with FPG test as compared to FCG, such as professional venipuncture is required, the test should be conducted in health facilities, and it has high rate of false negative. Instead, FCG test is a preferred method to address the community as it avoids venipuncture, can be tested at every health facility, and can deliver immediate results for timely diagnosis of type 2 diabetes. Studies indicated that the level of glucose in capillary and venous are almost

similar in the fasting state (Haeckel et al., 2002). As a consequence, FCG test may be a suitable alternative screening strategy for detecting undiagnosed type 2 diabetes in resource limited settings and in community-based screening programs. FCG tests are easy-to-use and feasible that makes them ideal for point-of-care testing (POCT) in different setting. This is mainly advantageous in setting with limited-resources where availability of laboratory facilities is inadequate(Zhao et al., 2013).

The American Diabetes Association (ADA) and IDF recommend FPG and the 2-h PG tests for the diagnosis of prediabetes and diabetes(American Diabetes Association Professional Practice Committee, 2022; International Diabetes Federation, 2019a). Each method has distinct advantages and disadvantages in clinical application. Diagnosis of diabetes by FPG is preferred owing to its cost-effectiveness and convenience, particularly in identifying high risk individuals with diabetes. However, the 2-h PG test shows superior sensitivity for identifying individuals with prediabetes and diabetes, although being less feasible in large-scale mass screening (Aschner et al., 2021). As a result, 2-h PG is considered to be the gold standard in the diagnosis of diabetes(American Diabetes Association Professional Practice Committee, 2022).

The increasing burden of diabetes in SSA presents a critical public health challenge, exacerbated by widespread clinical inertia that perpetuates poor glycemic control. Despite growing evidence on complications of diabetes, many healthcare systems in SSA remain ill-equipped to deliver timely, intensive management. Structural barriers, including limited access to insulin, inadequate provider training, and fragmented follow-up care, contribute to delays in treatment escalation even when patients present with persistently elevated HbA1c levels(International Diabetes Federation, 2019a).

Screening for type 2 diabetes faces challenges such as limited access to diagnostic tests, low public awareness, and the asymptomatic nature of early-stage disease, leading to underdiagnosis. Additionally, logistical barriers, cost, and the need for fasting or multiple blood draws hinder widespread screening, particularly in low-resource settings. Pharmacists can play a crucial role in overcoming these challenges by conducting point-of-care glucose testing, providing risk assessments, and educating patients on diabetes prevention. Their accessibility in community settings allows for early detection, timely

referrals, and ongoing monitoring, improving diabetes management and reducing complications. By integrating pharmacists into screening programs, healthcare systems can enhance early diagnosis and bridge gaps in diabetes care(Collins et al., 2011).

1.2. Statement of the Problems

The lack of timely screening for type 2 diabetes can result in a high burden of undiagnosed individuals, with substantial impact on the healthcare systems. Evidences from systematic reviews, meta-analyses and original studies showed that a prominent proportion—often more than half—of individuals living with diabetes in SSA remain unaware of their diabetes, due to the lack of ongoing, community-based screening schemes (Cikomola et al., 2019; Hilawe et al., 2013; Walker et al., 2023)

As a result of late diagnosis of type 2 diabetes, most individuals present to healthcare facilities only after developing symptoms and sever complications of diabetes. In SSA individuals usually visit healthcare providers for type 2 diabetes care and support for the management of retinopathy, neuropathy, nephropathy, diabetic foot ulcer and cardiovascular complications, rather than the diabetes itself (Cikomola et al., 2019; Osei et al., 2003). Delayed diagnosis of diabetes results in an increase in diabetes-related morbidity. As noted by Osei et al.(Osei et al., 2003) , individuals with delayed diagnosis of diabetes usually have severe insulin deficiency and/or resistance, leading to the development of end-organ damage and increased risk of death from preventable complication such as stroke, myocardial infarction, infections associated with immunosuppression, diabetes ketoacidosis and end-stage renal disease(Osei et al., 2003). The progression from undiagnosed hyperglycemia to advanced complications is compounded by poor health literacy, socioeconomic barriers, and limited access to healthcare, fueling a vicious cycle of disability(Osei et al., 2003; Renzaho, 2015).

Moreover, the lack of timely screening of diabetes increases the potential risk and effect of comorbid conditions such as hypertension, dyslipidemia, and obesity, resulting in a snowball effect on the risk for major CV events and further compounding diabetes care(Cikomola et al., 2019; Osei et al., 2003). Systematic reviews have reported a high burden of undiagnosed cases of hypertension and dyslipidemia among individuals with

diabetes, leading to combined impact on complications that would be prevented if screened timely(Padzys et al., 2015).

The challenge of early diabetes screening is highly amplified by “the triple burden” of communicable diseases, noncommunicable diseases (NCDs) and poverty, particularly in low- and middle-income countries. Healthcare facilities in SSA are often congested with multiple responsibilities – managing individuals with chronic infectious diseases such as TB and HIV and injuries combined with the increasing burden of NCDs – leading to system-level failure to develop early diabetes screening and preventive mechanisms(Murphy et al., 2020; Remais et al., 2013). This challenge is further magnified by poverty, which limits access to healthcare, as individuals may not be able to afford screening tests(Behera & Pradhan, 2021; Murphy et al., 2020; Mwangi et al., 2021).

While lack of timely screening for type 2 diabetes remains a significant public health challenge particularly in resource-limited settings, the appropriateness of these screening tests are still a challenge in Africa, resulting in inconsistent diagnostic performance (Cikomola et al., 2019). Even when the screening tests are available, discrepancies and lack of agreement between different screening tests—such as FPG, FCG, 2-h PG and HbA1c—often result in underdiagnosis or misclassification where diabetes status of individuals could be classified differently by different screening tests. Such lack of agreement may stem from measurement inconsistencies, variation with time, or screening tests measure their respective physiological processes(American Diabetes Association, 2013). ADA, IDF and the European Association for the Study of Diabetes (EASD) also indicated that these blood-based methodologies have limitations in interpretation variabilities and missing cases related to concomitant conditions such as haemoglobinopathies and anemias(American Diabetes Association Professional Practice Committee, 2022; Aschner, 2017; Cosentino et al., 2020). This is particularly critical in SSA, where the high prevalence of such comorbidities may contribute to missed cases or variability in interpretations of test results.

In addition to lack of early screening of type 2 diabetes and performance of screening tests, challenges related to diabetes care are further compounded by delayed treatment initiation. As a result, significant number of individuals progress to more complicated

forms of diabetes before effective treatment is initiated. One of the key contributors for poor treatment outcomes among type 2 diabetes is clinical inertia—the failure to initiate or intensify therapy in a timely manner despite clinical indications. Inertia causes various difficulties leading to poor management of diabetes, higher levels of HbA1c and therefore increased complications along with a reduction in life expectancy. Long-term elevation of HbA1c is associated with microvascular complications such as retinopathy, neuropathy, including gastroparesis and bladder dysfunction, and nephropathy, including proteinuria and microalbuminuria, and eventually macrovascular complications (Stratton et al., 2000).

1.3. Rationale for the Study

According to a recent systematic review and meta-analysis, the prevalence of type 2 diabetes in SSA varied from 1.4% to 22.5% (Motala et al., 2022). There are concerns about the accuracy of these findings due to the study methods used, such as sampling strategies and study settings. Previous studies relied on less reliable self-report, random or fasting capillary blood samples, often conducted in health facilities, which may affect the overall reliability of the results (Ekoru et al., 2016). Moreover, most of the studies were focusing on urban population, where rural and semi-urban populations were not considered, which could be in a different risk level and clinical profile (Motala et al., 2003; Padzys et al., 2015). This could bias the prevalence estimates of type 2 diabetes significantly and may not show the complete epidemiological picture of type 2 diabetes in SSA populations (Padzys et al., 2015).

According to ADA, the criteria for the diagnosis of diabetes are FPG ≥ 126 mg/dL and/or 2-h PG ≥ 200 mg/dL (using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water) and/or A1C $\geq 6.5\%$ and/or a random plasma glucose ≥ 200 mg/dL in a person with classic symptoms of hyperglycemia or hyperglycemic complications (American Diabetes Association Professional Practice Committee, 2022). There is an ever-growing discourse underway regarding the current thresholds suggested for the diagnosis and screening of diabetes and prediabetes (Kaur et al., 2020; Saudek et al., 2005). The establishment of these threshold values primarily relied on the outcomes of several studies conducted in Western populations, aiming to identify the most effective

FPG, FCG and other screening tests' cut-off values for predicting diabetes(Droumaguet et al., 2006). Several cohort studies among Asian populations examined FPG and recommended lower cut-off values to predict diabetes(Inoue et al., 2009; Kato et al., 2009; Noda et al., 2010; Ryu et al., 2006). However, epidemiological studies which investigated comparative performance and cut-off values of FPG for predicting type 2 diabetes in SSA population are scarce and it remains uncertain whether the FPG and FCG value of 126 mg/dL is adequate in screening type 2 diabetes in this region.

In order to develop effective and context-specific diabetes interventions, it is crucial to understand the unique sociodemographic and clinical profiles of affected populations. Contrary to the western population, diabetes has also been reported to be common among young and non-overweight individuals especially among Asian and SSA countries (Gujral et al., 2018). Exploring the variability in sociodemographic and clinical characteristics of people with diabetes within SSA provides a foundation for effective interventions. But evidences on anthropometric, socio-demographic and clinical profile of diabetes are limited to formulate tailored recommendations for prevention, screening, diagnosis and treatment of diabetes in SSA.

Few epidemiological investigations in SSA, especially across Ethiopia and Nigeria, have directly assessed the utility of FPG and FCG in identifying undiagnosed type 2 diabetes and prediabetes individuals. Therefore, this research aims to elucidate the screening capacity (sensitivity and specificity) and determine optimal cut-offs for FPG based on 2-h PG-detected prediabetes and diabetes. The outcomes will offer significant insights for healthcare providers, managers and policymakers involved in diabetes and prediabetes care in SSA.

While understanding the burden of diabetes and evaluating the diagnostic capacity of FPG and FCG is valuable for early identification of individuals with diabetes or prediabetes in SSA, optimal management of identified individuals with diabetes is also equally important to prevent long-term complications. However, important limitations exist in current understanding of the care provided for confirmed diabetes cases, particularly in clinical settings where delayed treatment intensification may compromise optimal glycemic control. Given the critical need for better diabetes care, we also explored to

evaluate the level of clinical inertia and glycemic control among individuals with type 2 diabetes at TASH in Addis Ababa.

Thus, there is a need for high-quality population-based studies in SSA to obtain more accurate and comprehensive data on the prevalence of type 2 diabetes, performance of diagnostic and screening tests and glycemic control of type 2 diabetes patients. This research aimed also to produce population-based evidence on the prevalence of diabetes and prediabetes among participants from the two most populous countries in SSA, Ethiopia and Nigeria. Moreover, this paper investigates the heterogeneity of the clinical phenotypes of type 2 diabetes in SSA, using as examples of two populations in the continent.

1.4. Scope of the Study

The scope of this study covers a comprehensive investigation on the prevalence, predictors, performance of screening tests, and glycemic control and treatment intensification of type 2 diabetes in Sub-Saharan Africa, with a focus on Ethiopia and Nigeria. The study determined the prevalence of type 2 diabetes and prediabetes among urban, semi-urban and rural residents from Butajira, Ethiopia, and three Local Government Areas (LGAs) in Enugu State, Nigeria—Enugu North, Enugu West, and Nkanu West. Data for this analysis were collected between November 01, 2020, and October 21, 2021, providing a contemporary assessment of diabetes burden in these regions. Additionally, the study identified key predictors associated with the prevalence of type 2 diabetes.

A significant aspect of this research also involved evaluating the screening performance of FCG and FPG tests in detecting prediabetes and diabetes, using the 2-h PG after 75-gm oral glucose load as the reference standard. The study has determined optimal cut-off values for FCG and FPG to screen diabetes and prediabetes in these populations.

Furthermore, this research explored glycemic control and treatment intensification practice among type 2 diabetes patients attending TASH in Ethiopia, a tertiary hospital where most patients are referred from primary health care facilities. This part of the study covered patients from January 01, 2018, to June 31, 2024 registered in electronic medical

record database. The research assessed the time to treatment intensification and its impact on glycemic outcomes, providing critical evidence on barriers to effective diabetes management in a specialized care setting. By addressing these objectives, the study aims to contribute to improved diabetes screening, diagnosis, and therapeutic strategies in the study settings.

1.5. Significance of the Study

The importance of assessing the screening performance of FCG and FPG tests based 2-h PG-identified diabetes is on enhancing timely and precise diagnosis. By evaluating the performance of FCG and FPG compared to the gold-standard 2-h PG test after 75 gm oral glucose load, our research can inform whether these simpler, more accessible tests can efficiently detect for abnormal glycemic level, especially in low-and-middle-income countries where OGTTs are less practical and feasible.

Reconsidering and setting the optimal thresholds for FCG and FPG by comparing to the standard 2-h PG test-detected prediabetes and diabetes after 75 gm oral glucose load is critical to refine the existing diagnostic criteria and enhancing test accuracy. The existing cut-offs may not be generally acceptable and applicable across the diversified population of the world, resulting in miss-diagnosis or over-diagnosis. Determining population-specific cut-offs can improve the capacity of tests to identify individuals with or without diabetes (sensitivity and specificity), confirming more acceptable test results. This modification could result in also improved diabetes risk level, individualized patient management, and more efficient use of diagnostic logistics.

The results of this study can also inform healthcare providers about existing gaps in diabetes management practices, encouraging the adoption of more proactive and evidence-based approaches to patient care. By highlighting the extent of glycemic control, healthcare professionals can be better equipped to make timely adjustments to treatment regimens, ultimately improving patient health outcomes. This information is vital for guiding clinical practice and ensuring that patients receive optimal care for their condition.

Additionally, the findings of this study will be valuable for hospital administrators and policymakers in Ethiopia and similar settings. This study could also support efforts to

allocate resources more effectively and design educational programs that address the specific needs of healthcare providers and patients, thereby enhancing overall healthcare delivery.

While several studies have reported level of glycemic control in Ethiopia, evidences for root causes of poor glycemic control including inadequate treatment intensification and clinical inertia in the diabetes management in real-world primary care setting is lacking. Therefore, the study will contribute to the body of knowledge on diabetes management, particularly in the context of Ethiopia, where data on glycemic control and inadequate treatment intensifications are limited. The study's findings will provide a foundation for future research on diabetes management in Ethiopia and other similar settings. By identifying key factors associated with poor glycemic control, this research can guide subsequent studies that explore interventions and strategies to overcome these challenges, thereby advancing the field of diabetes care.

1.6. Structure of the Dissertation

The rising burden of type 2 diabetes in SSA demands urgent attention, given the region's dual challenges of limited healthcare resources and escalating NCDs. This dissertation investigates the understudied disparities in type 2 diabetes prevalence, screening efficacy, and clinical management in Ethiopia and Nigeria, two of SSA's most populous nations. First, it conducts a comparative analysis of type 2 diabetes prevalence and clinical profiles, based on the WHO STEPwise surveys framework. Second, we evaluated the performance of FPG and FCG for community-based screening, challenging assumptions about their suitability in resource-limited settings. Third, through a retrospective cohort study at the Ethiopian tertiary hospital, the study examined treatment intensification, a critical barrier to glycemic control, aligning with global studies on therapeutic inertia. By integrating these themes, this dissertation advances evidence for context-specific type 2 diabetes interventions, bridging epidemiology, diagnostics, and clinical practice gaps in SSA.

To address the above themes, the dissertation begins with a title page, which includes the dissertation title, names of investigators, institutional affiliation, and the date of submission. Following this, the abstract provides a brief summary of the research

questions, methodology, key findings, and conclusions. Chapter one, the introduction, sets the stage by providing background information on type 2 diabetes, stating the problem, outlining the rationale of the study, defining the scope, explaining the significance, and stating the structure of the dissertation. The chapter also adds on the literature review, which surveys existing literature on type 2 diabetes. Chapter two, dealt on the study objectives and research questions. Chapter three, the methodology, detailed on the philosophical considerations, research design, study area, population and sampling methods, data collection methods, data analysis techniques, and ethical considerations. Chapter four presents the results using various data representations and analyzes these findings in detail. In addition, this chapter includes the discussion, strength and limitation section, covers the implications, and acknowledges the study's limitations. Chapter five concludes with a summary of findings, conclusions based on these findings, recommendations for future actions, and suggests areas for future research. The References section lists all sources cited, and appendices include supplementary materials that support the research. This structure ensures a comprehensive and logical presentation of the study from inception through conclusion.

1.7. Review of Literature

1.7.1. Overview of diabetes

Diabetes is a major worldwide public health problem. As reported by IDF, about 589 million adults (11.1%) had the disease in 2024, of whom almost half were undiagnosed (Ceriello & Colagiuri, 2025). Moreover, projections suggest 1.1 billion additional adults globally had impaired glucose tolerance or impaired fasting glycaemia, which significantly elevates their risk of progressing to type 2 diabetes. Death as a result of diabetes or its complication exceeded 3.4 million people in 2024 (IDF, 2025).

According to the IDF 2024 report 24.6 million adults (5.0%) had diabetes with three-fourth (72.6%) were undiagnosed. The prevalence of diabetes in the region ranges from 1.28% in Zimbabwe to 10.7% in Sao Tome and Principe. In SSA region, approximately 0.22 million adults are estimated to have died because of diabetes or its complications in 2024 (IDF, 2025).

About 2.3 million Ethiopian adults (3.6%) were reported to have diabetes in 2024 while nearly 3.0 million adults (2.8%) have diabetes in Nigeria in 2024 (IDF, 2025). In a systematic review and meta-analysis, a pooled prevalence of 3.9% for undiagnosed diabetes mellitus among adults was reported with 4.4% in Eastern Africa and 4.7% in Western Africa (Dessie et al., 2020).

1.7.2. Prevalence of Type 2 Diabetes in Sub-Saharan Africa

Existing literature on the prevalence of type 2 diabetes in SSA shows highly variable prevalence estimates due to methodological inconsistencies, including reliance on less reliable self-reported data, random blood glucose tests and/or capillary blood sample tests. In addition, many previously conducted type 2 diabetes prevalence studies are health facility-based, potentially skewing the evidences by increasing the weight of symptomatic cases, while community-based studies were mainly focusing on urban residents, with few studies involving semi-urban and rural communities. Despite this, a fast surge in the prevalence of type 2 diabetes is experienced by SSA as a result of rapid urbanization, changes in lifestyles and increase in life expectancy of the population.

According to the WHO STEPs country/region reports, the prevalence of type 2 diabetes in SSA ranges from 1.4% to 22.5% (World Health Organization, 2020b). Moreover, several studies reported the prevalence of type 2 diabetes ranging from 3.5% to 19.1% in SSA. These include 3.5% in Zambia (Bailey et al., 2016), 5.3% in Kenya (Ayah et al., 2013), 5.8% in Cameroon (Bigna et al., 2018), 7.2% in South Africa (Bailey et al., 2016), 7.8% in Tanzania (Malindisa et al., 2022), 18.7% (Eltom et al., 2018) and (19.1%) (Elmadhoun et al., 2016) in Sudan. The observed variation in the magnitude of DM across these studies might be due to discrepancies in which the diagnosis is based on FPG using either venous or, mostly, finger-prick capillary glucose and/or self-reported history of diabetes. Furthermore, the wide variability in sampling methods, biomarkers and tests (FPG, OGTT and HbA1c) used for the detection of type 2 diabetes limits the comparability of these findings.

In Ethiopia, the National NCDs STEPS Survey in 2015 reported 3.2% prevalence of diabetes (Gebreyes et al., 2018), lower than the age-adjusted estimated national prevalence of diabetes (5.0%) reported by IDF in 2021 (Sun et al., 2022). Furthermore

prevalence rates ranging from 1.9% in Sidama Zone (Zekewos et al., 2018) to 14.9% in DireDawa (Ayele et al., 2020) were also reported in Ethiopia. These reports include 3.1% in Jimma (Tesfaye Yunka et al., 2020), 6.3% in Northwest Ethiopia (Wolde et al., 2020), 9.3% in Mekelle (Gebreegziabiher et al., 2020), 10.2% in Bahir Dar (Bantie et al., 2019), 12.4% in Hawassa Zuria (Seifu et al., 2020), and 14.7% in Menja in South Ethiopia (Assefa & Shifera, 2022). Many of these studies were conducted in urban and/or health facility settings (Ayele et al., 2020; Bantie et al., 2019; Gebreegziabiher et al., 2020; Kassa & Woldesemayat, 2019) exposed to dietary changes, adoption of a sedentary lifestyle, overweight, and obesity all of which fuels the diabetes prevalence (Smyth & Heron, 2006; Whiting et al., 2011)

In Nigeria, a systematic reviews and meta-analyses reported pooled prevalence of type 2 diabetes to be about 5.7% (Adeloye et al., 2017; Uloko et al., 2018). Most of the studies included in these systematic reviews and meta-analyses were based on RBS and/or FBS diagnostic methods. Range of figures were reported in earlier studies in Nigeria. Arugu et al reported the prevalence of diabetes to be 8.0% in the district of Rivers state (Arugu & Maduka, 2017). Similar findings were also reported in Maiduguri of Borno state (7.0%) (Gezawa et al., 2015), in Ekiti State (6.8%) (Oluyombo et al., 2015) and in Calabar city (6.5%) (Enang et al., 2014). Lower than the above prevalence of type 2 diabetes were also reported from various states of Nigeria, 4.8% in Ekiti state (Ogunmola et al., 2013), 4.6% in Lagos state (Idris et al., 2020) and Edo state (Isara & Okundia, 2015), 4.3% in Gagi and Kasarawa districts of Sokoto State (Sabir et al., 2017), 3.0% (Ejike et al., 2015) and 3.6% (Okpechi et al., 2013) in Abia State, 3.3% in a national survey (Kyari et al., 2014) and Katsina state (Rabiu et al., 2020). Majority of these studies utilized RBS as diagnostic criteria which might not be reliable to identify diabetic patients as compared to the ideal blood glucose measurement OGTT.

1.7.3. Prevalence of undiagnosed diabetes

According to the report from IDF, about 43% (251.7 million) of adults living with diabetes were undiagnosed in 2024 (IDF 11th ed). The highest proportion of undiagnosed diabetes is found in Africa (72.6%), accounting 17.9 million individuals (IDF, 2025). According to previous studies in Ethiopia, about three-fourth of individuals were not aware of their

diabetic status as evidenced by the proportion of undiagnosed type 2 diabetes of 72.5% in Dessie town(Endris et al., 2019), 70.0% in Mekelle(Gebreegziabiher et al., 2020), 75% in Hawassa (Seifu et al., 2020), 68.1% in Addis Ababa(Tesfaye et al., 2016). Likewise, the IDF report shows 78.7% of individuals with diabetes are undiagnosed in the Nigerian population(IDF, 2025).

High burden of undiagnosed type 2 diabetes is usually due to the lack of adequate access to healthcare services, insufficient availability of diabetes screening in the healthcare systems to identify individuals with diabetes and lack of awareness on screening of diabetes among the community members (Manne-Goehler et al., 2019). Early screening, diagnosis and the timely management are critical for diabetes cases to avoid or delay complications, prevent premature death, and enhance quality of life(Chan et al., 2021). Moreover, the early diagnosis and treatment of type 2 diabetes can benefit to decrease significant costs associated to diabetes complications(Dall et al., 2014).

1.7.4. Prevalence of prediabetes

Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) represent intermediate states of abnormal glucose homeostasis that occurs between normal glucose regulation and clinical diabetes. IFG is an elevated FPG concentration (≥ 100 and < 126 mg/dL) whereas IGT is an elevated 2-h PG (≥ 140 and < 200 mg/dL) after a 75-g glucose load on the OGTT in the presence of an FPG concentration < 126 mg/dL(Nathan et al., 2007).

According to IDF, 634.8 million adults (12.0%) were reported to have IGT globally in 2024 while an estimated 487.7 million adults (9.2%) of the global adult population were reported to have IFG in the same year(IDF, 2025). Studies in SSA population also reported high prevalences of prediabetes with 15.9% in Ethiopia in Mizan-Aman town (Aynalem & Zeleke, 2018) and 19.5% in Nigeria in Calabar city (Enang et al., 2014). This suggests that the rapid increase in the prevalence of diabetes in the SSA will be further fueled by the progression of prediabetes conditions to diabetes(Ogurtsova et al., 2022). People with IGT or IFG are at high risk for developing diabetes, with up to 50% progressing to diabetes within 5 years(Richter et al., 2018).

According to a report by Faeh, nearly one-fourth of individuals had IFG in Seychelles(Faeh et al., 2007), whereas, a study in Calabar, Cross River state in Nigeria, the prevalence of IFG was 8.8% (Enang et al., 2014). A systematic review and meta-analysis by from South Africa reported a higher pooled prediabetes prevalence of 15.6% among South African populations(Sosibo et al., 2022).

As there is overlap between IFG and IGT, classifications of mutually exclusive isolated IFG (i-IFG) and isolated IGT (i-IGT) have been established to understand their separate characteristics (isolated IFG = FPG of 100–125 mg/dl with the 2-h value <140 mg/dl; isolated IGT = 2-h value of 140–199 mg/dL with the fasting level <100 mg/dL)(Nathan et al., 2007).

A study in Calabar, Nigeria reported an i-IFG and i-IGT prevalence of 19.0% and 8.5%, respectively, where study participants were urban dwellers(Enang et al., 2014). A higher i-IGT prevalence of 22.9% was reported from a study in China by Tian et al (Tian et al., 2021). In individuals with i-IFG, the predominant abnormality is hepatic insulin resistance while the muscle insulin sensitivity is normal. On the other hand, persons with i-IGT have normal to slightly reduced hepatic insulin sensitivity and moderate-to-severe muscle insulin resistance (Nathan et al., 2007).

1.7.5. Consequences of lack of early screening of diabetes

The lack of timely screening for type 2 diabetes can result in a high burden of undiagnosed individuals, with substantial impact on the healthcare systems. Evidences from systematic reviews, meta-analyses and original studies showed that a prominent proportion—often more than half—of individuals living with diabetes in SSA remain unaware of their diabetes, due to the lack of ongoing, community-based screening systems(Cikomola et al., 2019; Hilawe et al., 2013; Walker et al., 2023).

The extensive burden of detected type 2 diabetes directly accounts to delayed diagnosis, with high number of individuals presenting to healthcare only after being symptomatic with severe complications. Research findings in SSA reported that individuals usually demand treatment support for type 2 diabetes when they develop acute or chronic complications, such as retinopathy, neuropathy, nephropathy, foot ulcers, or

cardiovascular events, rather than the diabetes itself (Cikomola et al., 2019; Osei et al., 2003) resulting in a significant rate of diabetes-related morbidity. As stated by Osei et al (Osei et al., 2003), late diagnosis for type 2 diabetes means individuals often had severe insulin deficiency or/and resistance, and the development of severe complications and organ failure by the time of diagnosis is a common pattern in SSA, compared with the western with better screening and timely diagnostic capacity. The progression from undetected hyperglycemia to complicated diabetes is intensified by limited health literacy, social and economic barriers, and inadequate access to healthcare services, perpetuating a vicious cycle of diabetes related disabilities (Osei et al., 2003; Padzys et al., 2015).

Consequently, delayed diagnosis of type 2 diabetes results in an increase in premature mortality that patients die avoidable complications such as stroke, MI, infections, DKA, or end-stage kidney failure (Cikomola et al., 2019; Osei et al., 2003). This pattern of delayed diagnosis coupled with poor glycemic control accounts the high burden of diabetes-associated death reported from literatures in SSA, where individuals acquire the disease at younger ages than is observed in high-income countries (Motala et al., 2003; Osei et al., 2003). Given the connection of diabetes with infections such as TB and HIV, which are highly prevalent in SSA, limited timely diagnosis of diabetes further worsens outcomes and increases the risk of diabetes-related morbidity and mortality (Motala et al., 2003; Renzaho, 2015).

The economic consequences of delayed screening and diagnosis of diabetes are detrimental for both individual patients and the health system at large. Treatment and support for complicated type 2 diabetes such as dialysis for nephropathy, amputations, and CV interventions are more costly than the management and preventive strategies of early-stage and newly-diagnosed diabetes (Cikomola et al., 2019; Renzaho, 2015). Findings from studies have showed that the total costs of diabetes management increase significantly in advanced and complicated cases, with healthcare expenses for these patients far exceeding those with early-identified or well-managed disease (Mbanya & Mbanya, 2003). This increase in expenditure fuels the burden on resource deficient health systems, often shifting funds from other critical health priorities in SSA (Cikomola et al., 2019). For individuals and families of diabetic patients, significantly high health expenses

lead to economic depletion and lost productivity, particularly in communities with high rate of unemployment and security instability(Padzys et al., 2015).

In addition, delayed screening of diabetes worsens the risk and effect of comorbid conditions. Diabetes usually co-exists with other non-communicable chronic diseases, such as hypertension, dyslipidemia, and obesity, causing a multiplier effect on the risk of major CV events and further complicating disease management(Cikomola et al., 2019; Osei et al., 2003). The synergy between type 2 diabetes and communicable diseases including TB and HIV also complicates the management of diabetes as comorbid patients exhibit higher risks of severe complications and poorer health outcomes(Motala et al., 2003; Renzaho, 2015). Literatures have indicated that hypertension and dyslipidemia are usually underdiagnosed in individuals with diabetes, leading to complicated situations that would have been possible to prevent if diagnosed early(Padzys et al., 2015).

1.7.6. Performance of diagnostic test in screening undiagnosed diabetes

According to ADA, diabetes can be diagnosed based on A1C or plasma glucose criteria, either the FPG, 2-h PG using a 75-g OGTT, or random glucose value along with classic hyperglycemic symptoms (e.g., polyuria, polydipsia, and unexplained weight loss) or hyperglycemic crises.(American Diabetes Association Professional Practice Committee, 2023). WHO also recommends different screening strategies for diabetes such as clinical questionnaires, urine glucose, blood glucose (FPG, 2-h PG using 75-g OGTT and FCG tests), glycated hemoglobin (HbA1C) and combinations of the these tests can be used for screening diabetes (World Health Organization, 2003).

Both FPG and 2-h PG after a 75-g OGTT have been widely utilized as the preferred tests to diagnose individuals with pre-diabetes and diabetes. Since the 2-h PG incurs extra cost of OGTT and demands on individuals' time, FPG is the most commonly used test for identifying diabetes and pre-diabetes cases in epidemiological researches and routine screening. However, there are evidences that FPG alone could lead to lower estimate of diabetes prevalence and missed diagnosis of clinical cases. Studies including those in SSA, have been consistently showing that FPG alone detects fewer cases of diabetes and abnormal glucose tolerance than when combined with 2-h PG. Findings from a study

conducted in Cape Town, South Africa, showed that about 44% of those with OGTT-detected diabetes missed by FPG test(Kengne et al., 2017). According to a study in China, about 50% of individuals with undiagnosed diabetes had isolated elevated 2-h PG (Gu et al., 2003; Yang et al., 2010). A systematic review on the prevalence of type 2 diabetes among African older people reported that individuals diagnosed with FPG had lower prevalence of type 2 diabetes (10·9%) compared to those diagnosed with OGTT (23·9%)(Werfalli et al., 2016).

Detection rates of different screening tests vary in both populations and individuals as these tests reflect different characteristics of glucose metabolism, and screening cut-off points for the different tests will identify different groups of people(American Diabetes Association Professional Practice Committee, 2023). Compared with FPG and A1C values, the 2-h PG value identifies more individuals with prediabetes and diabetes (Meijnikman et al., 2017). More importantly, the effectiveness of different interventions for type 2 diabetes primary prevention has mainly been verified among individuals who have IGT with or without abnormal FPG, not for people with isolated IFG or for those with prediabetes diagnosed by A1C values (Knowler et al., 2002; Tuomilehto et al., 2001).

FCG is a point-of-care test and involves only single finger prick using a glucose meter (glucometer). Because it is user friendly and cheap, it is usually utilized as a first-step test for mass screening of individuals in either the fasting or random state(Spijkerman et al., 2002; Toscano et al., 2008). However, evidences from the literature showed that there are significant variations in the performance and accuracy of commonly used glucose meters. This can be affected by many factors including the effects of environmental conditions such as heat, moisture and humidity; and other physiologic substances and drugs in the blood including high triglyceride level, uric acid, acetaminophen, and ascorbic acid which can all affect the measurement of glucose in the blood. The size of blood drop and site of the prick can also influence the level of the glucose as can hemoglobin level, dehydration, reduced peripheral blood flow, improper hand washing and contaminates on the skin surface(Brazg et al., 2013; Ginsberg, 2009; Klonoff et al., 2018). Commonly utilized glucose meters are inaccurate at very high or very low level of glucose in the blood(Ginsberg, 2009).

The screening and diagnostic criteria of diabetes have been evolving over time. Diabetes was previously diagnosed with the cut-off of FPG $\geq 140\text{mg/dL}$ or a 2-h PG level $\geq 200\text{mg/dL}$, using the criteria determined by the National Diabetes Data Group in 1979 (National Diabetes Data Group, 1979). In 1997, the FPG threshold was reduced to 126mg/dL (Gavin III et al., 1997), which was intended to reflect the discrepancy between 2-h PG and FPG where many individuals have a 2-h PG $\geq 200\text{mg/dL}$ and a FPG $< 140\text{mg/dL}$ and to simplify the diagnostic process by using FPG. In 2009, an international expert committee recommended HbA1c as one of the diagnostic criteria for diabetes (Gillett, 2009).

Remarkably, still, there are ongoing concerns on adjusting the cut-off values of FPG and FCG for identifying individuals with diabetes and pre-diabetes as it will increase sensitivity of FPG and FCG for early detection (Katulanda et al., 2019; Mukai et al., 2012). According to a study in Srilanka, a cut off value of 100mg/dL for FPG had an optimal specificity for diagnosis of abnormal hyperglycemia (IFG and/or diabetes) but had a relatively poor sensitivity; suggesting an FPG level of 95.3mg/dL as the optimal cut off value for the study population for the diagnosis of pre-diabetes and/or diabetes (Katulanda et al., 2019).

1.7.7. Glycemic control and treatment intensification among type 2 diabetes patients

The importance of glycemic control in patients with type 2 diabetes is well established (Holman et al., 2008). Although clinical practice guidelines recommend frequent monitoring of HbA1c (usually every three months) with stepwise treatment intensification (TI) until glycemic target is achieved, glycemic control was often found to be inadequate (Davies et al., 2022; Walelgne et al., 2016). A high level of poor glycemic control was reported in Sub-Saharan Africa where 74% had an HbA1c $>7.0\%$ of whom 41% had an HbA1c $>10.0\%$ (Camara et al., 2015). In Ethiopia, a low-income country, a systematic review of 23 studies revealed that only 38.9% achieved the glycemic target (Tegegne et al., 2024).

Better glycemic control leads to microvascular and macrovascular benefits, and studies have shown that early tight control leads to longer-term maintenance of glycemic control. The Efficacy and Durability of Initial Combination Therapy of Type 2 Diabetes (EDICT)

study showed that early intensive therapy in newly diagnosed T2DM was more effective than conventional therapy (Abdul-Ghani et al., 2015). The study demonstrated that triple therapy with metformin, pioglitazone and exenatide was superior to conventional stepped therapy with metformin followed by addition of sulphonylurea and insulin glargine. There was a significant reduction in HbA1c in those receiving triple therapy (5.95%) compared with conventional therapy (6.5%, $p < 0.001$). Additionally, even with the greater reduction in HbA1c in the triple-therapy group, the rate of hypoglycemia was 7.5-fold lower than the conventional group, showing the benefits of early combination therapy (Davies, 2018).

Inadequate treatment intensification and clinical inertia has been associated with a reduced quality of life for the patient, along with increased risks of morbidity and mortality. Osataphan and colleagues demonstrated significantly reduced time to progression of diabetic retinopathy in a population who did not have inertia compared with those who did (Osataphan et al., 2017). There was also a higher incidence of retinopathy progression associated with therapeutic inertia.

Delayed treatment intensification can eventually lead to macrovascular complications. It is a significant factor contributing towards failure to implement national and international guidelines and may be responsible for approximately 80% of CV events (Safford et al., 2007). In addition, a major consequence of inertia is the additional cost on healthcare systems and public health due to the deterioration of patients who suffer from additional complications (Reach et al., 2017).

Diabetes management is significantly influenced by patient-provider dynamics, health literacy, treatment adherence, and clinical inertia. Patients often face challenges such as misconceptions about diabetes, financial barriers, and complex treatment regimens, which hinder adherence (American Diabetes Association Professional Practice Committee, 2022). Low health literacy further exacerbates these issues, leading to poor self-management and glycemic control ((Al Sayah et al., 2013)). On the provider side, delays in treatment intensification despite poor glycemic control is a major barrier, often due to overestimation of patient adherence, competing clinical priorities, or lack of structured follow-up protocols ((Mohan et al., 2020)). Studies in Ethiopia and Nigeria highlight that provider-patient communication gaps and limited access to diabetes

education contribute to suboptimal care. Strategies to address these challenges include culturally tailored patient education, shared decision-making, and regular provider training on guideline updates

1.8. Exiting Policies and Guidelines

Ethiopia has recognized the growing burden of non-communicable diseases (NCDs), including diabetes, and has integrated NCD prevention and control into its national health policy. The *Ethiopian National Strategic Action Plan for the Prevention and Control of Non-Communicable Diseases (2014-2020)* emphasizes early detection through healthcare settings(Shiferaw et al., 2018). The WHO STEPwise Approach to NCD Risk Factor Surveillance (STEPS) has been adopted to monitor diabetes prevalence and risk factors. However, implementation challenges persist, including limited diagnostic tools, inadequate healthcare worker training, and low public awareness. Recent efforts under the *Health Sector Transformation Plan II (HSTP II, 2020-2025)* aim to strengthen NCD services, including expanded screening at health posts and hospitals, though gaps in rural access remain (Ethiopian Ministry of Health, 2021).

Nigeria has developed several policies and guidelines to address the rising burden of diabetes and other non-communicable diseases (NCDs). The *National Policy and Strategic Plan of Action on NCDs (2019-2025)* emphasizes the integration of NCD screening, including diabetes and hypertension, into primary healthcare services (Omokhabi Dr, 2024). Additionally, Nigeria has adopted the WHO STEPwise Approach (STEPS) for NCD surveillance to monitor risk factors and disease prevalence. Despite these policies, challenges such as inadequate healthcare infrastructure, limited funding, and low public awareness hinder effective implementation. Recent initiatives under the *National Multisectoral Action Plan for NCDs (2021-2025) aim to strengthen early detection through community-based screening programs and capacity building for healthcare workers ((Akselrod et al., 2024)). However, disparities in access to screening services persist, particularly in rural and underserved areas.

1.9. Conceptual framework

The conceptual framework of the study outlines the multiple factors affecting the prevalence and management of type 2 diabetes, classified as socioeconomic, biological, and screening test related factors. One of these important issues is delayed screening and diagnosis of type 2 diabetes, which critically worsen the burden of complicated diabetes. As long as type 2 diabetes remains undiagnosed or diagnosed is delayed, people miss the opportunity for early treatments, resulting in chronic hyperglycemia and irreversible end-organ damage(Harris et al., 1992). This delay in screening is the major contributor to the increasing burden of undiagnosed diabetes, as most of these individuals only seek treatment and support once the disease becomes advanced, by which time the diabetes already complicated(Cikomola et al., 2019). Socioeconomic factors including poor health literacy and limited healthcare access, contribute to delayed diabetes screening and associated increased burden of undiagnosed type 2 diabetes, worsening its prevalence(Schillinger et al., 2002). Low health literacy compromises patients' understanding on the importance of time screening leading to missed opportunities for early intervention.

The prevalence of diabetes is also affected by the performance of diagnostic tests, which in turn is also affected by technical barriers, such as variations in assay techniques and types of blood sample (venous vs. capillary blood), which can impact on accuracy and reliability of diagnostic tests (Sacks et al., 2023). Discrepancies in the duration individuals' fasting further complicate diagnostic precision, potentially resulting in misdiagnosis or delayed interventions.

The effects of late screening and diagnosis leads to complicated diabetes, defined by suboptimal glycemic control, microvascular and macrovascular complications (Zoungas et al., 2010). The management of diabetes at advanced-stage becomes more challenging due to the requirement for intensive treatment, multiple and costly medications, and high potential for hospitalization. Moreover, non-adherence to complex treatment regimens usually because of socioeconomic factors including low healthcare and medication literacy and inadequate access to healthcare further complicates these outcomes (Booth et al., 2006).

Fundamentally, delayed screening of diabetes and complications at the time of diagnosis lead to high rate of diabetes-related death. Evidences reported that patients with delayed diagnosis of type 2 diabetes have a significantly increased risk of premature death, majorly from CV events and kidney failure(Gregg et al., 2014). This high extent of progression from undiagnosed type 2 diabetes to advanced complications and mortality calls for the importance of early screening initiatives, particularly in high-risk individuals.

therapeutic inertia, another clinical factor, reflects suboptimal intensification of treatment despite poor glycemic control, further complicating disease management (Khunti et al., 2013).

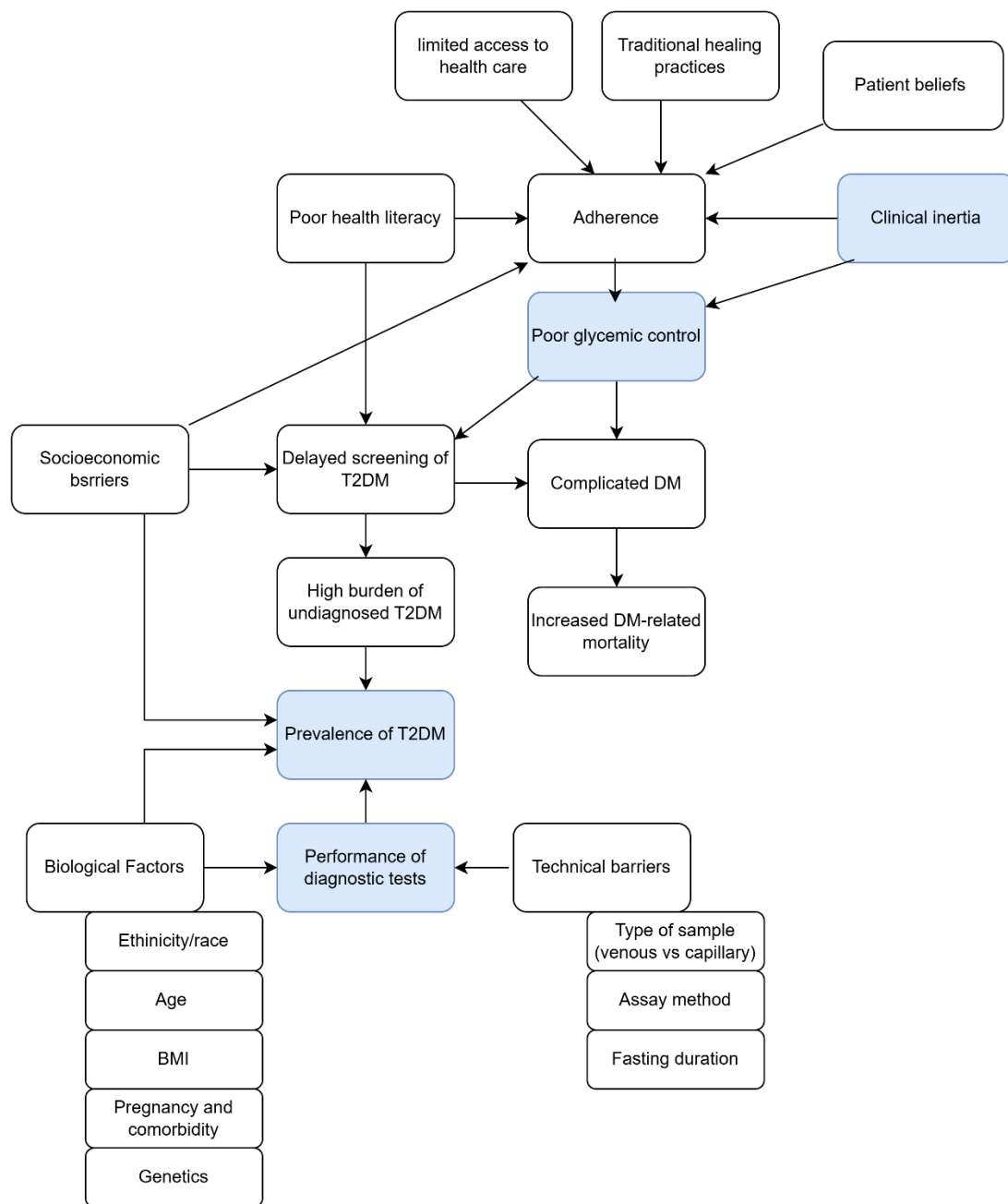


Figure 1. Conceptual model of the study

CHAPTER 2: OBJECTIVES AND RESEARCH QUESTIONS

2.1. Objectives

2.1.1. General objective

To investigate the prevalence and performance of diagnostic tests in Ethiopia and Nigeria, and treatment of type 2 diabetes in Ethiopian.

2.1.2. Specific objectives

- To determine the prevalence and factors associated with type 2 diabetes and prediabetes among participants in Ethiopia and Nigeria
- To evaluate the screening capacity of FCG and FPG tests based on 2-h PG-detected prediabetes and diabetes.
- To determine optimal cut-offs for FCG and FPG tests based on 2-h PG-detected prediabetes and diabetes.
- To assess the extent of glycemic control among type 2 patients attending TASH.
- To evaluate the time to treatment intensification and its association with glycemic control in this population.

2.2. Research questions

1. What are the prevalence and factors associated with type 2 diabetes among study participants in Ethiopia and Nigeria?
2. How is the level of agreement between the FCG and FPG compared to 2-h PG test in screening diabetes and prediabetes
3. What are the sensitivity, specificity and AUC of FCG and FPG tests compared to the 2-h PG gold standard test
4. What are the optimal diagnostic thresholds for FCG and FPG in detecting prediabetes and diabetes when using 2-h PG as a reference?
5. How prevalent is uncontrolled blood glucose among type 2 diabetes patients at TASH?
6. Is delayed treatment intensification associated with poorer glycemic control among type 2 diabetes patients at TASH?

CHAPTER 3: RESEARCH METHODOLOGY

3.1. Philosophical Foundation: Ontological, Epistemological and Axiological Considerations

Ontology is a branch of philosophy that studies the state of being (Maedche, 2002). Conversely, *epistemology* explores the methods of acquiring knowledge, examining how we know, what we know and identifying who qualifies as a knower. It is a philosophical branch concerned with understanding the foundations and scope of knowledge, justification, explanation, and wisdom, questioning the nature of these concepts and the capacity of a knower to grasp them (Gunstone, 2015). *Axiology*, another crucial philosophical component, deals with the study of values and ethics, particularly concerning their role and influence within the research process, including how values shape the relationships among paradigms, methodologies, and methods (Zaidi & Larsen, 2018). The following paragraphs will provide a brief overview of the philosophical stance considered in this study.

This study is grounded in distinct philosophical perspectives—ontological, epistemological, and axiological—that shape the research design, methodology, and ethical considerations.

The study adopts a realist ontology, recognizing type 2 diabetes and prediabetes as objective, measurable conditions influenced by biological, behavioral, and sociodemographic factors. This perspective aligns with biomedical research that assumes disease prevalence and risk factors exist independently of subjective interpretation (Bhaskar, 2013). By employing standardized diagnostic criteria (FCG, FPG, and 2-h PG, A1c), the study reinforces the notion that diabetes can be accurately quantified, supporting evidence-based screening and intervention strategies (American Diabetes Association, 2022; World Health Organization, 2020a).

The research follows a positivist epistemology, relying on quantitative methods to generate generalizable knowledge (Creswell & Creswell, 2017). By analyzing population-based survey data and hospital records, the study identifies statistical associations, determines optimal diagnostic thresholds, and evaluates treatment intensification and

glycemic control through measurable outcomes (e.g., HbA1c levels, time to treatment intensification).

The study incorporates axiological considerations, recognizing the ethical dimensions of diabetes screening, diagnosis, and management in low-resource settings. Given disparities in healthcare access, the research acknowledges potential biases (e.g., self-reporting errors, unequal diagnostic availability) and emphasizes culturally appropriate strategies (Braveman & Gruskin, 2003). The investigation on delayed treatment intensification engages with value-laden questions about healthcare provider decision-making and systemic barriers to optimal care (Khunti et al., 2013).

Together, these philosophical foundations guide the study's methodological rigor, ethical accountability, and interpretation of findings on diabetes screening and treatment in Ethiopia and Nigeria.

3.2. Methods

3.2.1. Study designs

To determine the prevalence of type 2 diabetes and measure the performance of diagnostic tests for type 2 diabetes, a community-based cross-sectional study was carried out from November 01, 2020 to October 21, 2021 initiated by the Diabetes Epidemiologists' Network in Sub-Saharan Africa (DENSSA) that representing collaborative research initiative involving the University of Dundee in United Kingdom, Addis Ababa University in Ethiopia and University of Nigeria in Nigeria. A six-and-half year retrospective open cohort study including data from January 2018 to June 2024 to investigate the extent of glycemic control and time to treatment intensification among type 2 patients attending Tikur Anbessa Specialized Hospital (TASH).

3.2.2. Study settings and population

The epidemiological study objectives of this research were conducted using a population from the Butajira Rural Health Program (BRHP) in central Ethiopia (Figure 2) and Enugu State district in Nigeria (Figure 3). Established in 1986 through a collaborative effort between Addis Ababa University, Ethiopia, and Umeå University, Sweden, BRHP

consisted of one semi-urban and nine rural kebeles, which represent the smallest administrative units in Ethiopia(Emmelin, 2009).

The Butajira Rural Health Program (BRHP) operates in a semi-urban and rural catchment area in the Meskan and Mareko districts of Ethiopia's Gurage Zone, Central Ethiopia. The specific Kebele's are Butajira town, Dobena, Shershera Bido, Bati, Wurib and Dirama. Located 130 km south of Addis Ababa at an altitude of 2,100 meters above sea level, the area has a temperate climate. The surveillance area covers 10 kebeles (smallest administrative units), including the town of Butajira and surrounding rural villages, encompassing a diverse agro-ecological zone with mixed subsistence farming (enset, teff, maize) and small-scale trade. Demographically, the BRHP monitors a dynamic cohort of ~60,000 people across ~12,000 households. The population is predominantly Gurage (85%), with minorities including Oromo (8%), Amhara (5%), and others (2%), reflecting Ethiopia's ethnic diversity.

The study in Nigeria comprises three distinct Local Government Areas (LGAs) in Enugu Stata. Enugu North is the urban hub, housing the state capital and commercial activities. Enugu West blends urban and rural areas, featuring light industries and agriculture. Nkanu West is predominantly rural with farming and natural attractions like Awhum Waterfall. While all share Nkanu ethnic roots, they face different challenges - urban congestion in Enugu North versus erosion in Nkanu West.

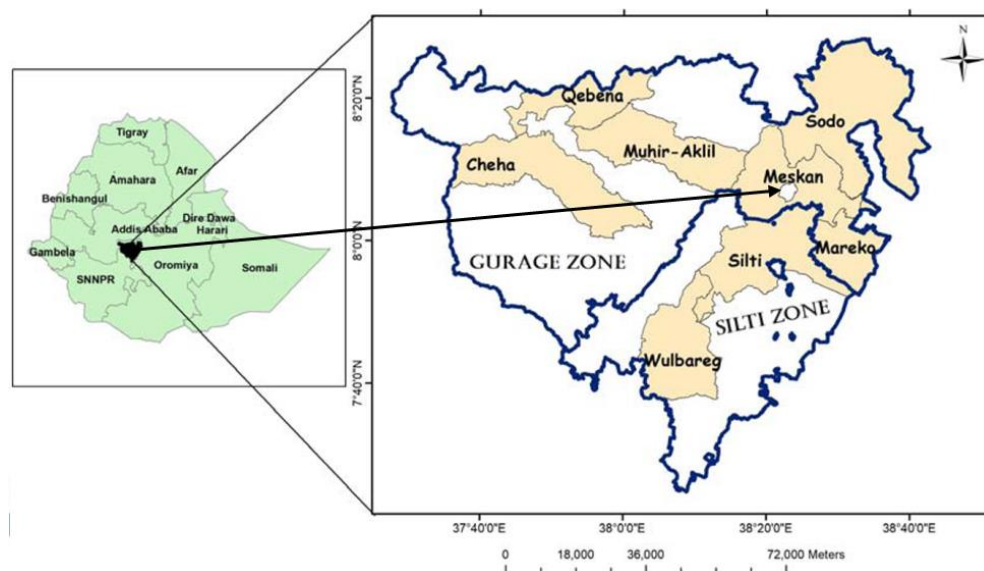


Figure 2: Study Sites in Ethiopia: Butajira Rural Health Program (BRHP) study area

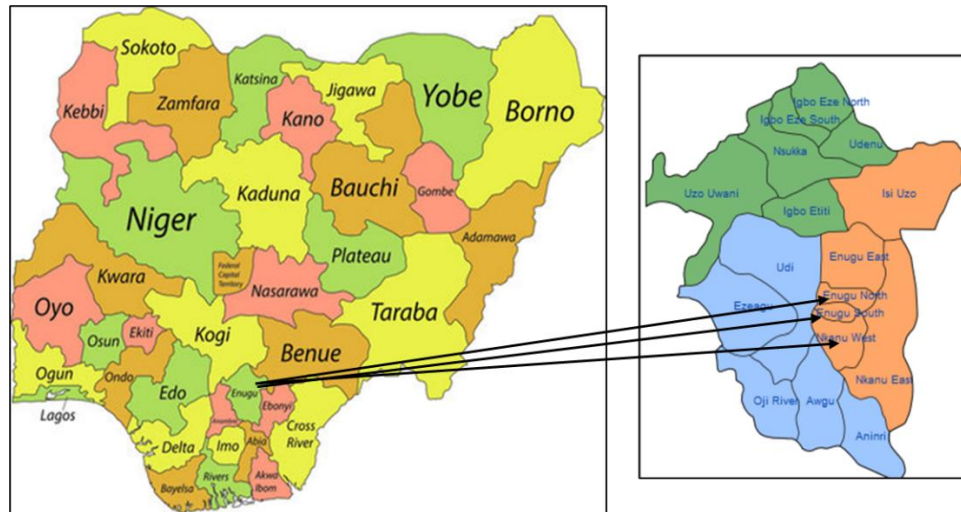


Figure 3: Study Sites in Nigera: Enugu North, Enugu West and Nkanu West in Enugu State,

Investigation of the management practice type 2 diabetes was conducted at Tikur Anbessa Specialized Hospital (TASH), a tertiary hospital in Addis Ababa. TASH has over 700 beds, and serves as a training center for undergraduate and postgraduate medical students, dentists, nurses, midwives, pharmacists, medical laboratory technologists, radiology technologists, and others who shoulder the health problems of the community and the country at large. The cohort consisted of individuals with type 2 diabetes who were on oral antidiabetic drugs (OADs) treatment in the period between January 01, 2018 and December 31, 2023, with end of follow-up on June 31, 2024.

3.2.3. Sample size, sampling and recruitment

For the study objectives to determine the prevalence of type 2 diabetes and compare the performance of diagnostic tests, we planned to involve 1000 study participants from both Butajira, Ethiopia and Enugu state in Nigeria. According to the IDF 2019 report, the estimated prevalence of diabetes is 3.9% for SSA (International Diabetes Federation, 2019b). Sample size was determined using single population proportion formula (Lwanga et al., 1991). Given the prevalence (p) of diabetes in SSA is less than 10%, it's better to take a better precision ($d < 0.05$). Assuming $d = 1.25\%$ and $p = 3.9\%$ and anticipating 10% non-response or missing data, $n = 1014$. Considering a design effect of 2 for complex

multistage design, about 1000 individuals aged ≥ 18 years from each of the two study sites were planned to be included.

We employed a multistage sampling method to choose the participants for the prevalence and test comparison studies. For the Ethiopian study, six kebeles (smallest administrative unit) were nominated randomly out of 10 kebeles that are part of the BRHP whereas three Local Government Areas (LGAs) – Enugu North, Enugu West and Nkanu West in Enugu State, were selected in Nigeria. A proportional sampling method was used to select households from each administrative unit. A randomly selected adult was invited to participate in the study from each household. In households with multiple eligible individuals, a single person was randomly chosen.

Given that the relationship between glycemic control and delayed treatment intensification was undetermined in the study site, we determined a sample of 422 type 2 diabetes individuals attending TASH using the single population proportion formula with a proportion (p) of 50% (or 0.5) and after a 10% contingency for incomplete data. Systematic random sampling technic was employed to select samples for the glycemic control study.

3.2.4. Inclusion and exclusion criteria

For the epidemiological study, we included adults who were 18 years or older and provided their consent to participate. Individuals who did not fast for at least 8 hours, pregnant women and those who were taking certain medications such as corticosteroids, atypical antipsychotics, and protease inhibitors were excluded from the study. Individuals with a history of diabetes were also not included for the OGTT. Eligibility criteria for study participants are indicated in Appendix I.

For the evaluation of management practice at TASH, patients diagnosed with type 2 diabetes and prescribed OADs as the first treatment of diabetes, and aged ≥ 18 years were included. In this study, the index date is defined as the first date of HbA1c $\geq 7.0\%$ (53 mmol/mol) and/or FBS ≥ 130 mg/dL after three months of the first OAD prescription. Patients who received insulin before the index date, on hemodialysis or erythropoietin-

stimulating agents after the first OAD prescription, hospitalization for treatment of type 2 diabetes before the index date were excluded.

3.2.5. Data collection instrument and procedures

3.2.5.1. Survey instrument

For the epidemiological survey, we used the WHO's STEPwise approach to NCD risk factor surveillance (STEPS) instrument version 3.1 to assess the prevalence of type diabetes and related risk factors. This tool has three steps: STEP I for demographic and behavioral data, STEP II for physical measurements, and STEP III for biochemical measurements. The tool was adapted to include detailed diabetes-related questions and locally relevant questions, like Khat chewing. Modifications followed STEPS manual guidelines (World Health Organization. Noncommunicable & Mental Health, 2005). The WHO STEPS instrument is attached in Appendix III.

3.2.5.2. Ewket-care database

Data were extracted from electronic medical record (EMR) of the hospital (formerly I-Care and currently Ewket-care at TASH) by trained clinical pharmacists using data abstraction instrument (Appendix IX). The information extracted from the records included sociodemographic and clinical characteristics such as age, sex, age at diagnosis, duration of follow-up, clinical events during follow-up, including cardiovascular diseases, diabetic neuropathy, and renal complications, along with dates of the events. Detailed information on OADs, insulin and other medications were obtained from the database along with dates. Laboratory test results with respective dates were recorded from the EMR.

3.2.5.3. Training and pre-test

The principal investigator recruited and trained data collectors (nurses, lab technicians and clinical pharmacists) and field supervisors (public health experts, nurses). Training of data collector covered study objectives, survey tools, data extraction from Ewket-care database, physical measurements, and blood sampling collection and testing. The STEPS tools and data abstraction format were pre-tested on 25 participants from each

site to refine the questionnaire's structure, flow, and interview and data abstraction time before data collection.

3.2.5.4. Data collection procedure

The epidemiological survey was conducted from November 01, 2020 to October 21, 2021. Local guides (health workers, volunteers) aided in reaching households. On the first day for STEP 1 data collection, households were visited, and the aim of the survey was explained. Physical measurements and blood samples were taken on the next day after physical measurement (STEP 2 and STEP 3). Blood samples were collected from participants who had fasted for at least eight hours at nearby health facilities.

STEP 1: Questionnaire survey

Questionnaire was used to collect data on respondent's demographic and socioeconomic status; tobacco, alcohol and Khat use; diet, including fruit, vegetable, dietary salt intake; physical activity; history of raised blood pressure, diabetes, raised cholesterol and/or CVDs, and lifestyle advice received.

STEP 2: Physical measurements

A day after the house-to-house survey, participants' blood pressure (BP), heart rate, weight, height, waist, and hip circumference were measured. BP and heart rate were taken twice on the right arm while seated, using a Folee DX-B1 monitor. If BP readings differed by >5 mmHg, a third was taken. In such cases, the mean of two or three readings was used. Raised BP was defined as systolic blood pressure (SBP) $\geq$ 140 mmHg and/or diastolic blood pressure (DBP) $\geq$ 90 mmHg, or taking medication.

STEP 3: Laboratory analysis

Laboratory procedure for diabetes screening is indicated in Appendix II. For all consented study participants, capillary blood glucose level was determined using Fia Biomed Precisa blood glucose monitoring system (Fia Biomed GmbH, Emsdetten, Germany). Participants with a capillary fasting glucose level $\geq$ 126 mg/dL were referred to the nearby health centre. For those with capillary blood glucose level <180mg/dL, two blood samples, 4 mL before and 2 mL after the 75gm oral glucose drink, were collected. The fasting blood and

the 2-hr post glucose load samples were collected into two 2 mL fluoride oxalate tubes (grey top). Full details of study participants were recorded on the collection tubes including the test time. The blood samples for glucose estimation were collected into sterilized disposable vacutainer tubes containing sodium fluoride tubes, which were quickly centrifuged within an hour at the data collection center to separate the plasma. Blood samples were stored in cold boxes maintained at 4–8 °C until transported to a laboratory on the same day as sample collection. OGTT was performed using a standard WHO oral glucose tolerance test solution, Polycal Liquid 200ml (Nutricia Ltd, Wiltshire, UK). Biochemical tests were conducted by the International Clinical Laboratories (ICL) for the Ethiopian samples and at the Chemical Pathology laboratory of the University of Nigeria Teaching Hospital for the Nigerian samples to determine blood glucose concentration.

Individuals with self-reported DM or those already taking any antidiabetic drugs were differed from the OGTT.

3.2.6. Diagnostic criteria and outcome measures

The ADA's diagnostic definitions were utilized to identify diabetes and pre-diabetes cases (American Diabetes Association Professional Practice Committee, 2022). Plasma glucose test results were categorized as follows: impaired fasting glucose (IFG) corresponding to plasma glucose levels between 100 mg/dL and 125 mg/dL, and impaired glucose tolerance (IGT) defined as a 2-h PG ranging from 140 mg/dL and 199 mg/dL. Newly diagnosed diabetes was ascribed to a FPG level of ≥ 126 mg/dL, 2-h PG of ≥ 200 mg/dL or both.

Body mass index (BMI) was delineated according to the WHO criteria into: underweight ($< 18.5 \text{ kg/m}^2$), normal weight ($18.5\text{--}24.9 \text{ kg/m}^2$), overweight ($25.0\text{--}29.9 \text{ kg/m}^2$) and obesity ($\geq 30 \text{ kg/m}^2$)(WHO Consultation, 2000). Waist circumference was classified as normal ($\leq 94 \text{ cm}$ for men and $\leq 80 \text{ cm}$ for women), presenting an increased risk of cardiometabolic complications with measurements of $95\text{--}102 \text{ cm}$ for men and $81\text{--}88 \text{ cm}$ for women, and substantially increased risk of cardiometabolic complications if the waist circumference exceeded $> 102 \text{ cm}$ for men and $> 88 \text{ cm}$ women)(WHO, 2008).

Participants' physical activity was evaluated based on adherence to WHO recommendations, categorizing individuals as either optimal (≥ 600 Metabolic Equivalent of Task (MET) minutes per week) or suboptimal (< 600 MET minutes per week)(World Health Organization, 2012).

For the study investigating type 2 diabetes management practice, our primary outcome of interest was glycemic control. According to ADA good glycemic control is defined as A1c less than 7.0% (53 mmol/mol) and fasting plasma glucose (FPG) of 80-130 mg/dL (American Diabetes Association Professional Practice Committee, 2022). Secondary outcomes of interest were time to treatment intensification and clinical inertia (CI). Clinical inertia is defined as failure of healthcare providers to initiate or intensify therapy when indicated(Almigbal et al., 2023; Milman et al., 2018; Phillips et al., 2001) such as increasing the dose of the current OAD, adding other OADs and switching to other OADs within 90 days of index date. Individuals whose HbA1c is maintained $<7.0\%$ (53 mmol/mol) after the index date were not considered to have clinical inertia, even without TI. TI is defined as: (1) increasing the dose of the current OAD; (2) adding a second OAD or (3) adding insulin to the first OAD (OAD + INS) or switching to a different OAD. Time to TI was calculated by subtracting the index date from the first date of TI. The subjects who do not have increased dose of the current OAD, adding a second OAD or adding insulin to the first OAD were defined as “never intensified” category.

3.2.7. Quality assurance of the research

In order to produce a rigorous and valid research findings, quality assurance was a central step that passed through established protocols, formats, and analysis processes. The following measures were taken into account in order to assure the quality of the data collected in this project.

This study was conducted in accordance with the procedures and principles detailed in the methods section. We developed data collection instruments by reviewing existing literature and including important variables to the study. The questionnaires were primarily produced in English, translated into Amharic for the Ethiopia study participants and into Igbo for the Nigeria participants, and subsequently back-translated into English to

maintain the consistency of linguistics. The Amharic version of the WHO STEPS instrument is Annexed (Appendix VI)

Experienced field data collectors were employed for the house-to-house survey at Butagira and Enugu state. Experienced healthcare providers (nurses, lab technologists and clinical pharmacists) were engaged in the data collection process. Training on the principles of research ethics, patient privacy, confidentiality of the data collected, sample handling and storage was delivered to the data collectors.

To ensure the integrity of the data collected, appropriate preventative measures were implemented at all stages, with a particular focus on the data collection phase. Continuous supervision was maintained throughout all fieldwork processes to minimize potential errors.

To minimize bias in physical measurements such as weight, height, BP, and waist circumference, we implemented standardized protocols and rigorous quality control measures. We followed WHO guidelines in the measurement of these parameters. Proper training was provided for the nurses on these measures to reduce technique-related variations, and periodic observation was conducted maintain accuracy over time.

3.2.8. Data analysis

We utilized Stata V.17 software program (StataCorp. Stata Statistical Software: Release 17. College Station, TX: Stata Corp LP) and R version 4.3.2, (R Core Team, 2023) for data analysis.

In the epidemiological survey, variables with continuous outcomes were reported as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR). Differences in means were assessed using an independent Student's *t*-test. Categorical differences were expressed in proportions and assessed using a Chi-square test. The medians of FPG and 2-h PG were compared across categorical variables utilizing the Wilcoxon rank-sum test or Kruskal-Wallis rank-test. Regression analysis was utilized to evaluate the relationship between FPG and 2-h PG.

The agreement between FPG and 2-h PG was determined using kappa statistics, accompanied by the 95% confidence interval (95% CI). Mean difference (bias) obtained

from FCG and 2-h PG tests were compared by the Bland and Altman's method (Bland & Altman, 2010). Receiver operating characteristic (ROC) curves were computed and plotted and area under the curve (AUC) determined with the FPG and FCG compared to the reference standard 2-h PG to ascertain its diagnostic capacity as a diabetes screening tools. Evaluation metrics such as sensitivity, specificity, and Youden's Index were employed to assess the performance of FPG and FCG tests (Nahm, 2022). Youden's Index, a metric used to express the discriminatory capability of diagnostic tests, is derived from the formula: (sensitivity + specificity) – 1. The index ranges from –1 to 1, with a value closer to 1, indicating superior test performance. Furthermore, the proportion of missed prediabetes by FPG and FCG were calculated against the total number of prediabetes and diabetes cases, respectively.

In the investigation of type 2 diabetes management practice, baseline characteristics were described for the total population by clinical inertia status. These were presented as number (%) for the categorical variables and mean (standard deviation, SD) or median (interquartile range, IQR) for the continuous variables. We used Pearson's chi-square tests to compare the proportions of patients with and without clinical inertia. Independent t-test and ANOVA were used to compare the means while the Mann-Whitney test and Kruskal-Wallis test were used to compare the medians between patients with and without clinical inertia. The proportion of the study population with TI was presented as number (%) with a 95% confidence interval. Associations between patient characteristics and the glycemic control were quantified in terms of adjusted odds ratios (AOR) and 95% confidence intervals (CIs); p values a priori α value of 0.05 were considered significant to determine statistical significance. Model assumption tests, including homoscedasticity, multicollinearity diagnosis were performed. Global model goodness of fit was assessed using the Hosmer and Lemeshow test.

3.2.9. Ethical considerations

We obtained ethical approval from School of Pharmacy Research Ethics Committee (Ref. No. ERB/SoP/54/03/2019), the Institutional Review Board of the College of Health Sciences, Addis Ababa University (Ref.:027/19/SoP) and University of Nigeria Teaching Hospital, Enugu, Health Research Ethics Committee (Ref: UNTH/CSA/329/OL.5).

For the epidemiological survey and evaluation of screening tests, participants were informed that 4 mL of blood sample to be collected by qualified field technicians in the fasting state and 2 mL of blood 2-hours after 75 gm oral glucose challenge. Clients with FCG test results ≥ 126 mg/dL were referred to a local health center (clinic). The client referral form provided in Appendix VIII. In addition, for clients with FCG test result ≥ 180 mg/dL, the subsequent oral glucose tolerance test was omitted, rather they were referred to a local health center (clinic). The diabetes and prediabetes status of clients was notified for each participant once results are available, and a campaign on diabetes prevention and management was conducted for these study participants at Butajira, Ethiopia.

All study participants were notified that participation in this study is voluntary. All information gathered in this study was kept confidential. Clinical information from this study was identified with a code number instead of patient names. Information sheet and consent forms are provided in Appendix IV, V, VI, VII.

For the DM management study, permission to collect the data was obtained from the hospital. To protect the privacy and confidentiality of patient data in this study, strict data security measures were implemented. Access to the electronic medical records was granted through authorized data collectors only via password protected ID. All data was de-identified, and patient identifiers were removed to ensure anonymity. Regular audits and compliance checks were also conducted to safeguard against unauthorized access or data breaches.

CHAPTER 4. RESULTS AND DISCUSSION

4.1. Introduction

This study explores multiple dimensions of type 2 diabetes in Ethiopia and Nigeria, the two most populous countries in SSA, including the epidemiological profile of the disease, screening performance of test for diabetes, and management practices. This chapter deals on the key findings of the study with a number of sections and subsections revealed. Section 4.2 presents detailed sociodemographic, social drug use, dietary patterns, physical activity, physical and anthropometric measurements, and the prevalence and associated factors of diabetes and prediabetes, providing details on the epidemiology of type 2 diabetes in the study areas. Section 4.3 delves into the performance of FPG and FCG in screening type 2 diabetes in the study population. Finally, section 4.4 assesses the level of glycemic control and how it is affected by delayed treatment intensification of type 2 diabetes treatment.

4.2. Diabetes Epidemiologic Survey

4.2.1. Sociodemographic information

Among the 2000 planned samples, 1727 individuals were contacted and given consent for the survey making overall response rate of 86.4%. The rest had insufficient specimen or refused to provide blood samples. The characteristics of individuals refused to provide blood samples were not significantly different from those who provide blood samples.

Out of the entire survey population, 872 individuals (50.5%) were men. The mean age of the participants was 44.6 years, with Ethiopians having a mean age of 41.0 years and Nigerians having a mean age of 47.2 years. More than half of the respondents (54.3%) were under the age of 45 as presented in Table 1.

Table 1. Summary of sociodemographic information, Ethiopia and Nigeria, 2021.

Characteristics	Country		Total, n(%)
	Ethiopia, n(%)	Nigeria, n(%)	
Sex			
Men	272 (37.3)	600 (60.2)	872 (50.5)
Women	458 (62.7)	397 (39.8)	855 (49.5)
Age, years			
Mean (SD)	41.0(±13.62)	47.2(±17.58)	44.6(±16.31)
18-29	149 (20.4)	189 (19.0)	338 (19.6)
30-44	311 (42.6)	289 (29.0)	600 (34.7)
45-59	167 (22.9)	223 (22.4)	390 (22.6)
60-69	71 (9.7)	153 (15.3)	224 (13.0)
≥70	32 (4.4)	143 (14.3)	175 (10.1)
Current Residence			
Urban ^a	455 (62.3)	534 (53.6)	989 (57.3)
Rural	275 (37.7)	463 (46.4)	738 (42.7)
Religion			
Christian	205 (28.1)	985 (98.8)	1190 (68.9)
Muslim	525 (71.9)	3 (0.3)	528 (30.6)
Traditional beliefs	-	9 (0.9)	9 (0.5)
Current marital status			
Never married	63 (8.6)	225 (22.6)	288 (16.7)
Currently married	570 (78.1)	635 (63.7)	1205 (69.8)
Widowed	60 (8.2)	131 (13.1)	191 (11.1)
Divorced/separated	37 (5.1)	6 (0.6)	43 (2.5)
Highest grade of education completed			
No formal education	293 (40.1)	168 (16.9)	461 (26.7)
Some primary education	212 (29.0)	53 (5.3)	265 (15.3)
Completed primary education	77 (10.5)	150 (15.0)	227 (13.1)
Junior secondary education	56 (7.7)	38 (3.8)	94 (5.4)
Senior secondary education	57 (7.8)	226 (22.7)	283 (16.4)
More than secondary education	35 (4.8)	362 (36.3)	397 (23.0)
Occupation			
Government employee	43 (5.9)	204 (20.5)	247 (14.3)
Non-government employee	22 (3.0)	19 (1.9)	41 (2.4)
Self employed	9 (1.2)	261 (26.2)	270 (15.6)
Unpaid	656 (89.9)	513 (51.5)	1169 (67.7)

SD: Standard deviation

^a Semi-urban for the Ethiopian study participants

4.2.2. Social drug use, dietary patterns and physical activity

Among the participants, 6.7% were current smokers while 27.4% of the study participants drank alcohol at least once within 30 days of the survey as presented in Table 2.

Table 2. Pattern of substance use among all respondents by country of residence, Ethiopia and Nigeria, 2021.

Participant characteristics	Ethiopia	Nigeria	Total
Cigarette Smoking			
Current smokers, n (%)	35 (4.8)	81 (8.1)	116 (6.7)
Daily smokers, n (%)	27 (3.7)	42 (4.2)	69 (4.0)
Former smokers, n (%)	23 (3.2)	46 (4.6)	69 (4.0)
Ever smoked, n (%)	58 (7.9)	127 (12.7)	185 (10.7)
Mean (SD) age of smoking started, yrs	28.9±6.7	26.5±7.7	27.2±7.5
Mean (SD) duration of smoking, yrs	19.3±13.1	14.1±11.1	15.5±11.8
Alcohol consumption, n (%)			
Current drinker	107 (14.7)	367 (36.8)	474 (27.4)
Drink in past 12 months, not current	129 (17.7)	473 (47.4)	602 (34.9)
Past 12-month abstainer	494 (67.6)	157 (15.7)	651 (37.7)
Life time abstainer	567 (77.7)	544 (54.6)	707 (59.1)
Khat users, n (%)			
Current chewer	430 (58.9)	NA	430 (58.9)
Past chewer	37 (5.1)	NA	37 (5.1)
Never chewer	264 (36.2)	NA	264 (36.2)

Abbreviation: NA, not applicable; SD, standard deviation

On average, participants consumed fruits 2.7 days and vegetables 4.6 days per week. In terms of servings per day, they had 1.3 servings of fruits and 1.9 servings of vegetables daily. Nearly one-fourth (22%) were not meeting WHO's physical activity recommendations as shown in Table 3.

Table 3. Dietary pattern and physical activity of participants by country of residence, Ethiopia and Nigeria, 2021.

Fruit and Vegetables	Ethiopia	Nigeria	Total
Fruits			
Mean (SD) number of days fruits consumed in a weak	1.9 ± 1.0	3.4±1.7	2.7 ± 1.6
Mean (SD) number of servings of fruits per day	1.5 ± 0.8	1.1 ± 0.5	1.3 ± 0.7
Vegetables			
Mean (SD) number of days vegetables consumed in a weak	4.3 ±2.1	4.9 ± 1.7	4.6 ± 1.9
Mean (SD) number of servings of vegetables per day	2.4 ± 0.8	1.5 ± 0.7	1.9 ± 0.9
Salt^a			
Add salt to food when cooking or preparing food, n (%)	508 (69.6)	113 (11.3)	621 (36.0)
Eat processed foods high in salt, n (%)	110 (15.1)	300 (30.1)	410 (23.7)
Quantity of salt consumption, n (%)			
Far too much or too much	108 (14.8)	19 (1.9)	127 (7.4)
Just the right amount	433 (59.3)	932 (93.5)	1365 (79.0)
Too little or far too little	189 (25.9)	46 (4.6)	235 (13.6)
Physical activity			
Not meeting WHO's recommendations, n (%)	173 (23.7)	205 (20.7)	378 (21.9)
Levels of physical activity ^b , n (%)			
High level	374 (51.2)	621 (62.3)	995 (57.6)
Moderate level	162 (22.2)	243 (24.4)	405 (23.5)
Low level	194 (26.6)	133 (13.3)	327 (18.9)
Contribution of types of activities (%)			
Work-related activity	63.6	55.7	59.0
Transport-related activity	34.6	34.0	34.2
Recreational-related activity	1.8	10.3	8.8

Abbreviations: SD, standard deviation; WHO, World Health Organization

^a Self-reported

^b According to WHO high-level physical activity is vigorous-intensity activity for at least three days per week, achieving at least 1500 MET-minutes per week; or seven or more days of any combination of walking, moderate- or vigorous-intensity activities achieving a at least 3000 MET-minutes per week. Moderate level physical activity is meeting any of the following criteria: three or more days of vigorous-intensity activity of at least 20 minutes per day; or five or more days of moderate-intensity activity or walking for at least 30 minutes per day; or five or more days of any combination of walking, moderate- or vigorous-intensity activities achieving at least 600 MET-minutes per week. Low level physical activity is a person not meeting the criteria for moderate- or high-level categories.

4.2.3. Physical and anthropometric measurements

The prevalence of high BP (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg) was 27.8%. Nigerian participants had an average weight of 72.2 kg, while Ethiopians had 60.4 kg. The overall mean body mass index (BMI) was 26.5 kg/m², with Nigerians having higher BMI (28.6 kg/m²) than Ethiopians (23.6 kg/m²). Nearly two-thirds of the surveyed participants (63.5%) had normal metabolic risk based on waist circumference as shown in Table 4.

Table 4. Distribution of raised BP, weight, height, BMI, waist circumference and WHR by country of residence, Ethiopia and Nigeria, 2021.

Variables	Ethiopia	Nigeria	Total
Blood pressure			
Raised BP, % (95% CI)	17.7 (15.1-20.6)	35.6 (32.5-38.5)	27.8 (25.8-30.0)
Raised SBP, % (95% CI)	11.1 (9.0-13.6)	31.1 (28.3-34.1)	22.6 (20.6-24.6)
Raised DBP, % (95% CI)	14.1 (11.8-16.8)	25.0 (22.4-27.8)	20.3 (18.5-22.3)
Weight and height			
Mean weight, kg (95% CI)	60.4 (59.6-61.3)	72.2 (71.2-73.3)	67.1 (66.4-67.9)
Mean height, cm (95% CI)	159.9 (159.3-160.6)	161.5 (160.6-162.3)	160.8 (160.2-161.4)
BMI, % (95% CI)			
Mean BMI	23.6 (23.3-24.0)	28.6 (27.6-29.6)	26.5 (25.9-27.1)
Underweight	7.0 (5.4-9.1)	2.4 (1.6-3.5)	4.4 (3.5-5.4)
Normal	63.3 (59.7-66.7)	37.8 (34.8-40.9)	48.8 (46.4-51.1)
Overweight	21.2 (18.4-24.4)	29.7 (26.9-32.6)	26.0 (23.0-28.2)
Obese	8.5 (6.7-10.7)	30.2 (27.4-33.1)	20.9 (19.0-22.8)
Waist circumference, % (95% CI)			
Normal	80.6 (77.5-83.3)	50.8 (47.6-53.9)	63.5 (61.2-65.8)
Increased risk	11.1 (9.0-13.6)	20.7 (18.3-23.3)	16.6 (14.9-18.4)
Substantially increased risk	8.4 (6.6-10.6)	28.6 (25.8-31.5)	19.9 (18.1-21.9)
Waist to hip ratio (WHR), % (95% CI)			
Mean WHR	0.85 (0.84-0.86)	NA	0.85 (0.84-0.86)
Normal	65.0 (61.5-68.4)	NA	65.0 (61.5-68.4)
Obese	35.0 (31.6-38.5)	NA	35.0 (31.6-38.5)

Abbreviations: BP, blood pressure; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure; WHR, waist-to-hip ratio

4.2.4. History of cardiovascular disorders

Nearly half (49.2%) of the participants had never had their BP measured. Of those who had measurements, 22.2% were diagnosed with high BP, accounting for 11.3% of the study participants (Table 5).

Table 5. History cardiovascular diseases by country of residence, Ethiopia and Nigeria, 2021.

History	Ethiopia, % (95% CI)	Nigeria, % (95% CI)	Total, % (95% CI)
History of hypertension			
Never measured	73.4 (70.1-76.5)	31.5 (28.7-34.4)	49.2 (46.9-51.6)
Hypertensive	9.7 (7.8-12.1)	12.4 (10.5-14.6)	11.3 (9.9-12.9)
Non-hypertensive	16.8 (14.3-19.7)	56.1 (53.0-59.1)	39.5 (37.2-42.8)
History of raised cholesterol			
Never tested	97.1 (95.6-98.1)	91.1 (89.1-92.7)	93.6 (92.4-94.7)
High cholesterol	1.8 (1.0-3.0)	1.5 (0.9-2.5)	1.6 (1.1-2.3)
Normal cholesterol	1.1 (0.5-2.1)	7.4 (5.9-9.2)	4.7 (3.8-5.9)
History of heart attack or chest pain	6.6 (5.0-8.6)	8.1 (6.6-10.0)	7.5 (6.3-8.8)

Abbreviations: CI, confidence interval

4.2.5. Prevalence of diabetes and prediabetes

In the survey, 15.8% (265 individuals) met prediabetes criteria. Impaired fasting glycaemia (IFG) was present in 11.8% while 11.5% exhibited impaired glucose tolerance (IGT). Among 1550 individuals tested by both fasting and OGTT, isolated IFG and IGT were observed in 5.5% and 5.8% of participants, respectively (Table 6).

Table 6. Percentage of prediabetes and diabetes by sex and country of residence, Ethiopia and Nigeria, 2021.

Test results	Number of tests	Sex		Country		Total, n(%)
		Men, n(%)	Women, n(%)	Ethiopia, n(%)	Nigeria, n(%)	
Prediabetes						
IFG	1614	101 (12.4)	89 (11.2)	31 (4.8)	159 (16.4)	190 (11.8)
IGT	1588	105 (13.3)	79 (9.9)	27 (4.1)	156 (16.8)	184 (11.5)
i-IFG	1550	45 (5.8)	38 (4.9)	13 (2.1)	70 (7.5)	83 (5.4)
i-IGT	1550	53 (6.8)	39 (5.1)	15 (2.4)	77 (8.3)	92 (5.9)
All prediabetes	1682	146 (17.2)	119 (14.3)	41 (5.8)	224 (22.9)	265 (15.8)
Diabetes						
Known people with diabetes	1725	20 (2.3)	10 (1.2)	19 (2.6)	11 (1.1)	30 (1.7)
New diabetes by fasting	1614	42 (5.1)	12 (1.5)	4 (0.6)	50 (5.2)	54 (3.3)
New diabetes by 2-h PG	1588	35 (4.4)	28 (3.5)	20 (3.0)	43 (4.6)	63 (4.0)
All newly diagnosed diabetes	1574	58 (7.3)	30 (3.9)	20 (3.2)	68 (7.2)	88 (5.6)
Overall prevalence of diabetes	1682	78 (9.2)	40 (4.8)	39 (5.5)	79 (8.1)	118 (7.0)

Abbreviation: 2-h PG, 2-hour Plasma Glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; i-IFG, Isolated IFG; i-IGT, Isolated IGT

Among the survey participants, 118 individuals (7.0%) met at least one of the criteria for diabetes, 5.5% in Ethiopia and 8.1% in Nigeria. Three-fourth (74.6%) of the people diagnosed with diabetes were not aware of their diabetes status prior to the survey, yielding 5.6% prevalence of undiagnosed diabetes in the region. In addition to the 30 (1.7%) participants with history of diabetes, we identified 54 (3.4%) new individuals with diabetes by FPG measurement and 63 (4.0%) by OGTT (Figure 4).

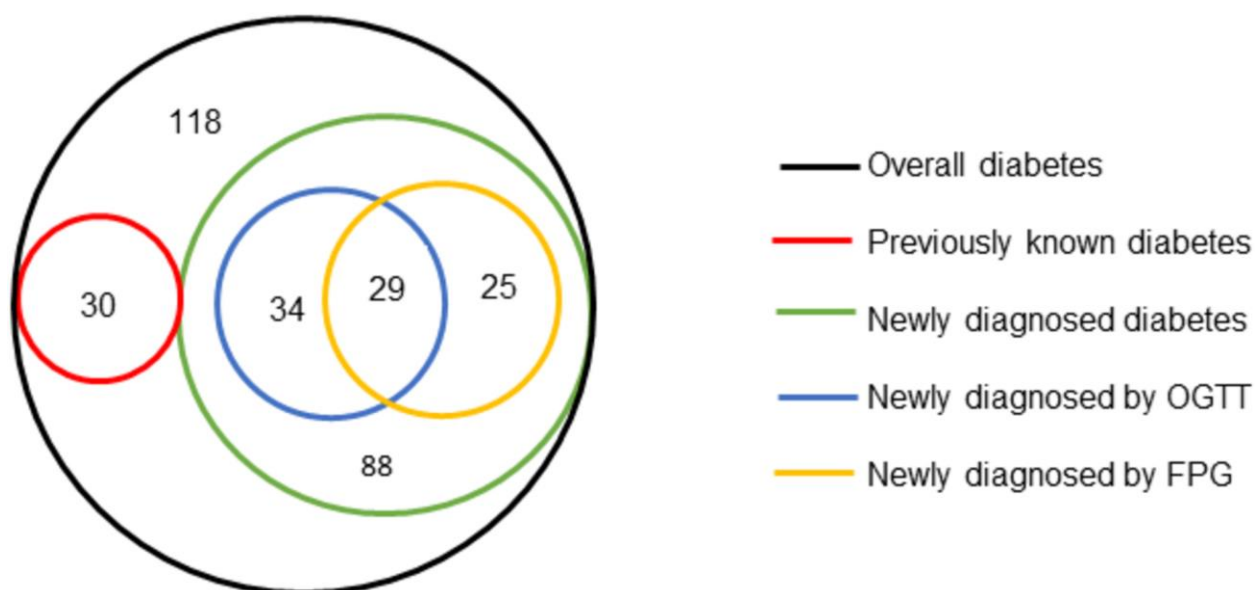


Figure 4. Number of previously diagnosed and newly diagnosed diabetes cases identified by FPG and 2 h PG, Ethiopia and Nigeria, 2021.

FPG, fasting plasma glucose; 2-h PG, 2-hour Plasma Glucose.

As presented in Table 7 and 8, the mean (SD) age of Ethiopians with diabetes was 47.4 years (SD 14.2), nearly 7 years older compared to the non-diabetic cases. Furthermore, the mean weight among Ethiopians with diabetes is 68.6 kg (SD 17.0 kg), significantly higher than their non-diabetic counterparts ($p < 0.001$). Similarly, Ethiopians with diabetes had significantly higher mean BMI ($26.8 \pm 5.8 \text{ kg/m}^2$) and waist circumference ($85.1 \pm 13.7 \text{ cm}$) compared to non-diabetic participants, ($p < 0.01$).

The mean (SD) age among Nigerians with diabetes was 53.5 years (SD 14.2), which was over 8 years higher than the mean age of non-diabetic cases, recorded at 45.2 years (SD 18.2). Moreover, Nigerians with diabetes had higher mean weight 83.9 kg (SD 25.5 kg) compared to their non-diabetic counterparts ($p < 0.001$). In addition, Nigerian diabetes cases had significantly higher mean BMI, waist circumference, DBP and SBP as compared to non-diabetic participants ($p < 0.001$).

With the multivariable logistic regression analysis, sex is identified as a common predictor of the prevalence of type 2 diabetes in both Nigeria and Ethiopia. Ethiopian males were nearly four times more likely to have DM than their female counterparts (AOR = 3.80,

95% CI = 1.22–11.82, $p = 0.021$), while Nigerian males were nearly three times more likely to have DM than females (AOR 2.89, 95% CI 1.35–6.18, $p = 0.007$). In addition, older age and urban residence are significant predictors in Nigeria, with urban dwellers over twice as likely to develop type 2 diabetes (AOR = 2.45, 95% CI = 1.33–4.49, $p = 0.004$). Central obesity is also a strong predictor in Ethiopia, with higher risks linked to greater odds of DM, whereas, weight is a significant factor instead in Nigeria. Hypertension is also a key predictor in Ethiopia, increasing DM odds by 4% (AOR 3.68, 95% CI 1.07–12.61, $p = 0.038$).

Table 7. Clinical profile of diabetes individuals in Ethiopia and Nigeria, 2021

Variables	Total (N = 1682)	Ethiopia (n=704)				Nigeria (n=978)			
		Normal (n=624)	Prediabetes (n=41)	Diabetes (n=39)	P-value	Normal (n=675)	Prediabetes (n=224)	Diabetes (n=79)	P-value
Men	848 (50.4)	226 (36.2)	14 (34.1)	18 (46.2)	0.432	398 (59.0)	132 (58.9)	60 (75.9)	0.013
Age (yrs)	1682	40.5±13.5	42.5±13.1	47.4±14.2	0.007	45.2±18.2	50.7±15.9	53.5±14.2	<0.001
Urban	883 (52.5)	248 (39.7)	15 (36.6)	9 (23.1)	0.112	346 (51.3)	122 (54.5)	59 (74.7)	<0.001
Current smoker	114 (6.8)	33 (5.3)	-	1 (2.6)	0.246	56 (8.3)	20 (8.9)	4 (5.1)	0.549
Current alcohol use	468 (27.8)	94 (15.1)	8 (19.5)	3 (7.7)	0.317	241 (35.7)	90 (40.2)	32 (40.5)	0.393
Current Khat chewer	414 (58.8)	372 (59.6)	20 (48.8)	22 (56.4)	0.375	NA	NA	NA	NA
No. of days fruits consumed in a week	1682	1.7±1.12	1.9±1.10	1.5±1.04	0.299	2.9±1.90	3.2±2.10	2.6±1.98	0.073
Consumed fruits in the past week	1460 (86.8)	564 (90.4)	39 (95.1)	34 (87.2)	0.705	571 (84.6)	192 (85.7)	60 (75.9)	0.075
No. of days vegetables consumed in a week	1682	4.2±2.19	3.9±2.16	3.9±1.76	0.518	4.2±2.30	4.5±2.17	3.5±2.41	0.005
Consumed vegetables in the past week	1521 (90.4)	603 (96.6)	39 (95.1)	39 (100.0)	0.652	578 (85.6)	202 (90.2)	60 (75.9)	0.031
Optimal physical activity ^a	1317 (78.3)	478 (76.6)	32 (78.0)	29 (74.4)	0.925	535 (79.3)	183 (81.7)	60 (75.9)	0.522
Weight (kg)	1674	59.5 ±10.8	65.0±14.3	68.6±17.0	<0.001	70.2 ±14.6	74.3±17.0	83.9±25.5	<0.001
BMI	1674	23.3±4.1	25.9±5.4	26.8±5.8	<0.001	27.7±17.9	29.0±11.9	35.5±12.6	<0.001
Obese	351 (21.0)	39 (6.3)	8 (15.8)	12 (30.8)	<0.001	159 (23.7)	83 (37.6)	50 (64.9)	<0.001
WC, overall	1682	76.3±10.7	81.4±11.5	85.1±13.7	<0.001	87.4±13.4	91.1±14.8	95.4±15.1	<0.001
WC, men	848	78.4±8.9	85.4±9.5	87.1±14.9	<0.001	88.2±13.9	91.8±16.7	96.6±15.9	<0.001
WC, women	834	75.1±11.4	79.2±12.0	83.4±12.8	0.002	86.2±12.6	90.0±11.6	91.8±11.9	0.012
Substantially increased risk of central obesity	337 (20.0)	39 (6.3)	8 (19.5)	11 (28.2)	<0.001	166 (24.6)	80 (35.7)	33 (42.3)	<0.001
WHR	703	0.85 ±0.12	0.87±0.10	0.88±0.11	0.242	NA	NA	NA	NA
Abnormal WHR	251 (35.7)	210 (33.7)	17 (41.5)	24 (63.2)	<0.001	NA	NA	NA	NA

DBP (mm Hg)	1680	78.4 ±10.7	83.7 ±14.2	82.1±12.2	0.002	80.5 ±12.5	85.4 ±13.9	83.7 ±12.3	<0.001
SBP (mm Hg)	1680	118.3 ±16.3	129.2 ±19.4	124.3 ±18.4	<0.001	130.1 ±20.7	136.7 ±23.0	140.0 ±23.3	<0.001
Raised BP	470 (28.0)	100 (16.0)	10 (24.4)	14 (35.9)	0.003	206 (30.6)	98 (43.8)	42 (53.8)	<0.001
Reported history of hypertension	193 (11.5)	51 (8.2)	4 (9.8)	14 (35.9)	<0.001	60 (8.9)	44 (19.6)	20 (25.3)	<0.001
Reported history of high cholesterol	28 (1.7)	7 (1.1)	1 (2.4)	5 (12.8)	0.005	8 (1.2)	6 (2.7)	1 (1.3)	0.255

Table 8: Nigerian vs Ethiopian diabetes cases with phenotypic differences

Variables	Ethiopian	Nigerian
Mean age (SD)	47.4±14.2	53.5±14.2
Mean weight	68.6±17.0	83.9±25.5
Mean BMI	26.8±5.8	35.5±12.6
Mean WC, Mean	87.1±14.9	96.6±15.9
Mean WC, women	83.4±12.8	91.8±11.9

4.3. Performance of Diabetes Screening Tests

4.3.1. Patterns of FPG and 2-h PG results

Among the total of 1727 participants, 1550 individuals were included in the analysis following the exclusion of 30 previously diagnosed with type 2 diabetes and 147 who were not tested by either FPG or 2-h PG.

Of the 1550 participants, 72 individuals (4.6%) were identified as having diabetes through either FPG or 2-h PG, whereas 261 individuals (16.8%) demonstrated prediabetes, and 1217 individuals (78.5%) exhibited normal glucose tolerance. Among all tested individuals, 11 (15.3%) displayed abnormalities in FPG alone (false positive results), 32 (44.4%) in 2-h PG alone (false negative results for FPG), and 29 (40.3%) in both. Of those

with prediabetes, 83 (31.8%) presented with IFG, 89 (34.1%) had IGT and 89 (34.1%) with a combination of both.

Median FPG among all participants was 83 mg/dL (IQR: 76 – 92), while the median 2-h PG level was 94 mg/dL (IQR: 77-116). Notably, men demonstrated a significantly higher median 2-h PG compared to women (97 mg/dL, IQR: 78-123 vs 91 mg/dL, IQR: 76-112; $P < 0.0006$) (Figure 5A). Moreover, the age group of 45-59 years exhibited the highest median FPG levels (84.5 mg/dL, IQR 79 – 95, $p < 0.0001$), while the ≥ 70 age group had the highest median 2-h PG levels (102 mg/dL, IQR 81 - 139, $p < 0.0001$) (Figure 5B).

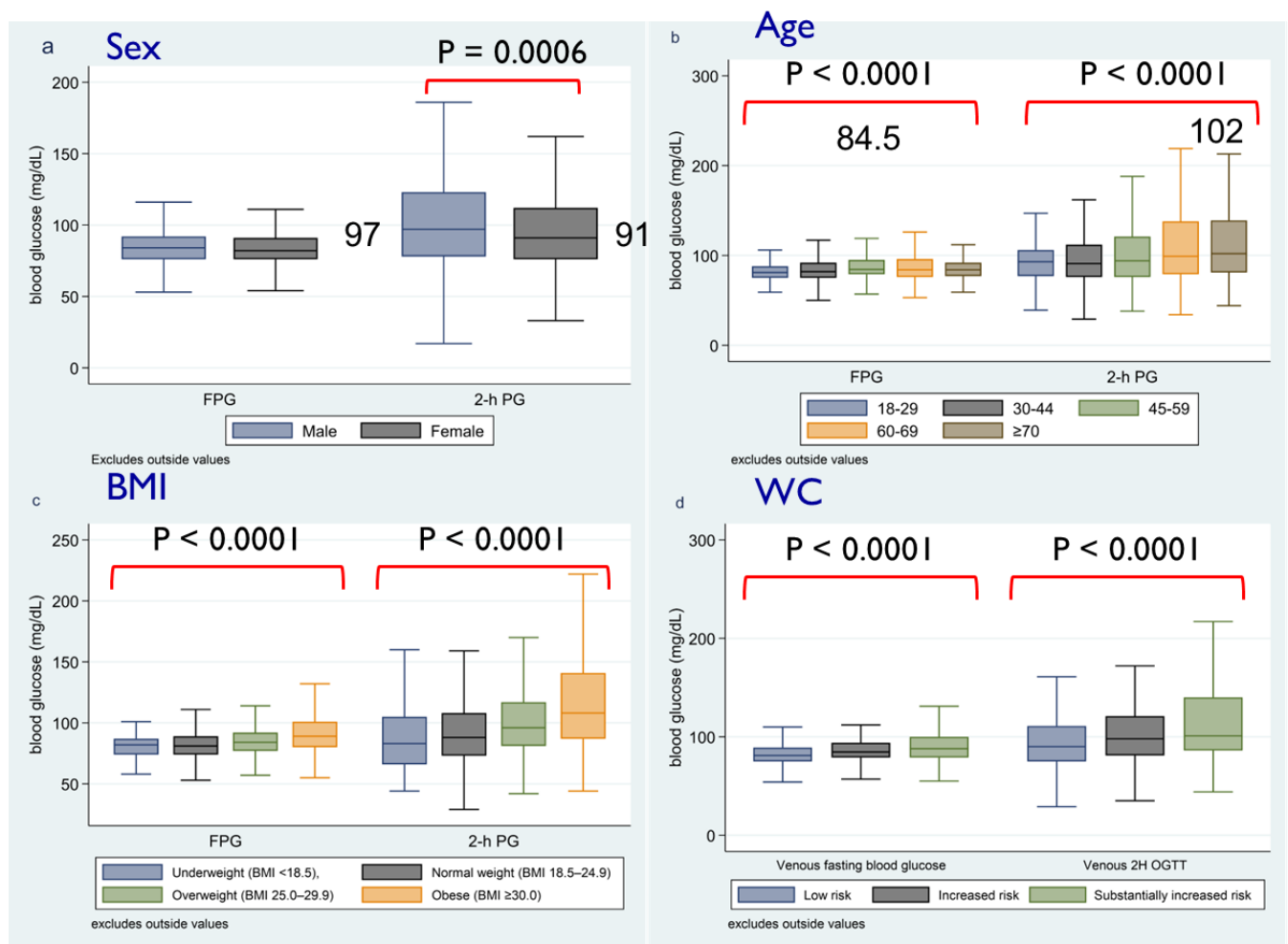


Figure 5: Box plots for median FPG and 2-h PG by sex (A), age category (B), body mass index (BMI) (C) and waist circumference (D).

FPG, fasting plasma glucose; 2-h PG, 2-hour plasma glucose.

In addition, FPG values increased from underweight individuals to those classified as obesity (underweight 82 mg/dL, IQR 74-87; normal weight 81 mg/dL, IQR 74-89; overweight 84 mg/dL, IQR 77-92; obese 89 mg/dL, IQR 80-101; $P < 0.0001$; as determined by WHO BMI criteria). Likewise, 2-h PG values progressively increased from individual with underweight to obese participants (underweight 83 mg/dL, IQR 66-105; normal weight 88 mg/dL, IQR 73-108; overweight 96 mg/dL, IQR 81-117; obese 108 mg/dL, IQR 87-141; $P < 0.0001$; by WHO BMI criteria) (Figure 5C). Similarly, both FPG and 2hPG showed progressive elevation across low-risk to substantially increased risk groups, based on waist circumference (Figure 5D).

4.3.2. Agreement between of FPG/FCG and 2-h PG tests

The regression analysis revealed a statistically significant, moderately robust positive correlation ($r = 0.57$, $P < 0.0001$) between FPG and 2-h PG. Employing regression analysis, an equivalent FPG value was derived in relation to 2-h PG (Figure 6). In the study population, both FPG and 2-h PG demonstrated a strong correlation within a linear relationship represented by $\text{FPG (mg/dL)} = 57.05 + 0.28 \times \text{2-h PG (mg/dL)}$. Utilizing this equation, an FPG level of 113 mg/dL (6.3 mmol/L) corresponds to a 2-h PG level of 200mg/dL (11.1mmol/L).

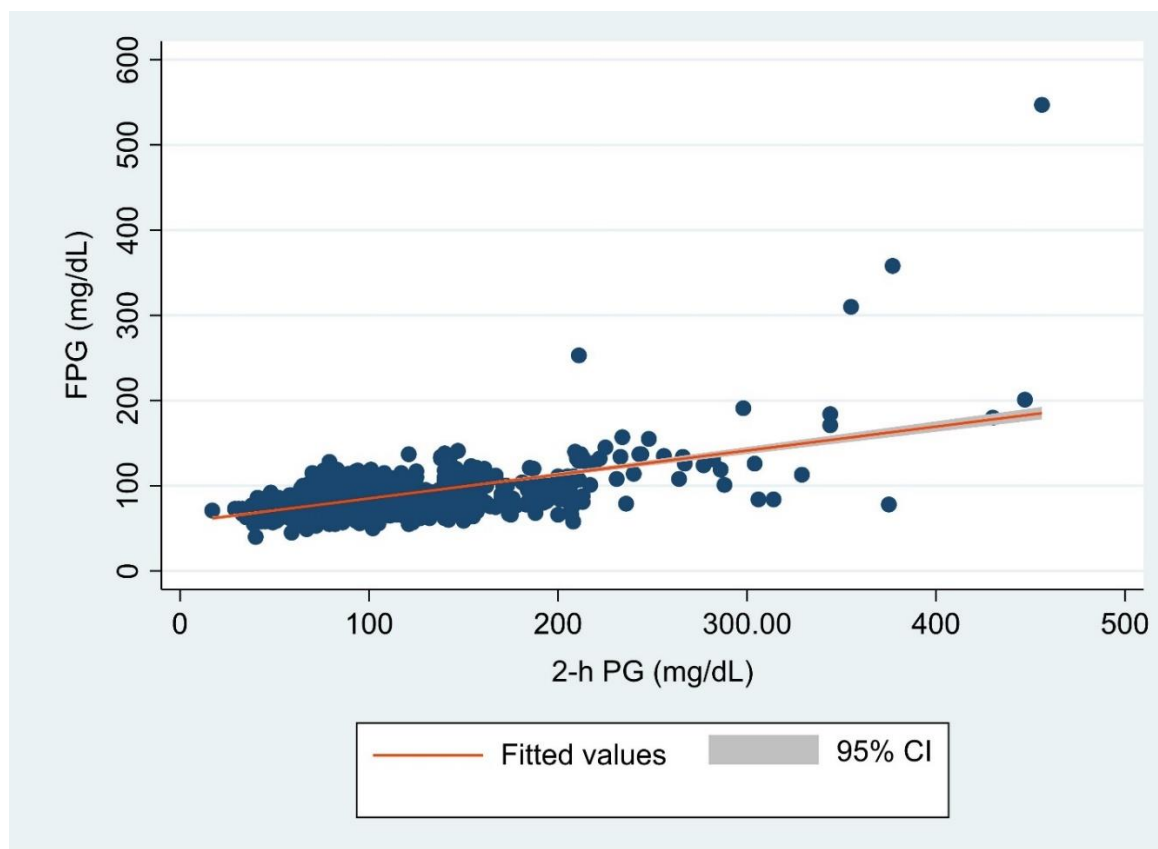


Figure 6. Scatter plot of hour plasma glucose (2-h PG, in mg/dL) and fasting plasma glucose (FPG in mg/dL) with a fitted regression line and 95% confidence interval (CI).

The overall concordance between FPG and 2-h PG in identifying diabetes and prediabetes was moderate, with kappa statistic of 0.56 (95% CI, 0.51 – 0.61; $p < 0.0001$) for diabetes and 0.45 (95% CI, 0.40 – 0.50; $p < 0.0001$) for prediabetes. More specifically, the concordance between these two methods for detection of negative cases is very high with a negative predictive value (NPV) of 97.9%.

The performance of FCG was tested against the standard 2-h PG test on 619 Ethiopian study participants. The Bland–Altman plot (Figure 7) was developed to explore the limits of agreement between the FCG and 2-h PG tests. The mean bias predicted for these tests was 0.03 and the 1.96 SD ranged from -67.2 to +67.3. Overall, there is good agreement between the two tests.

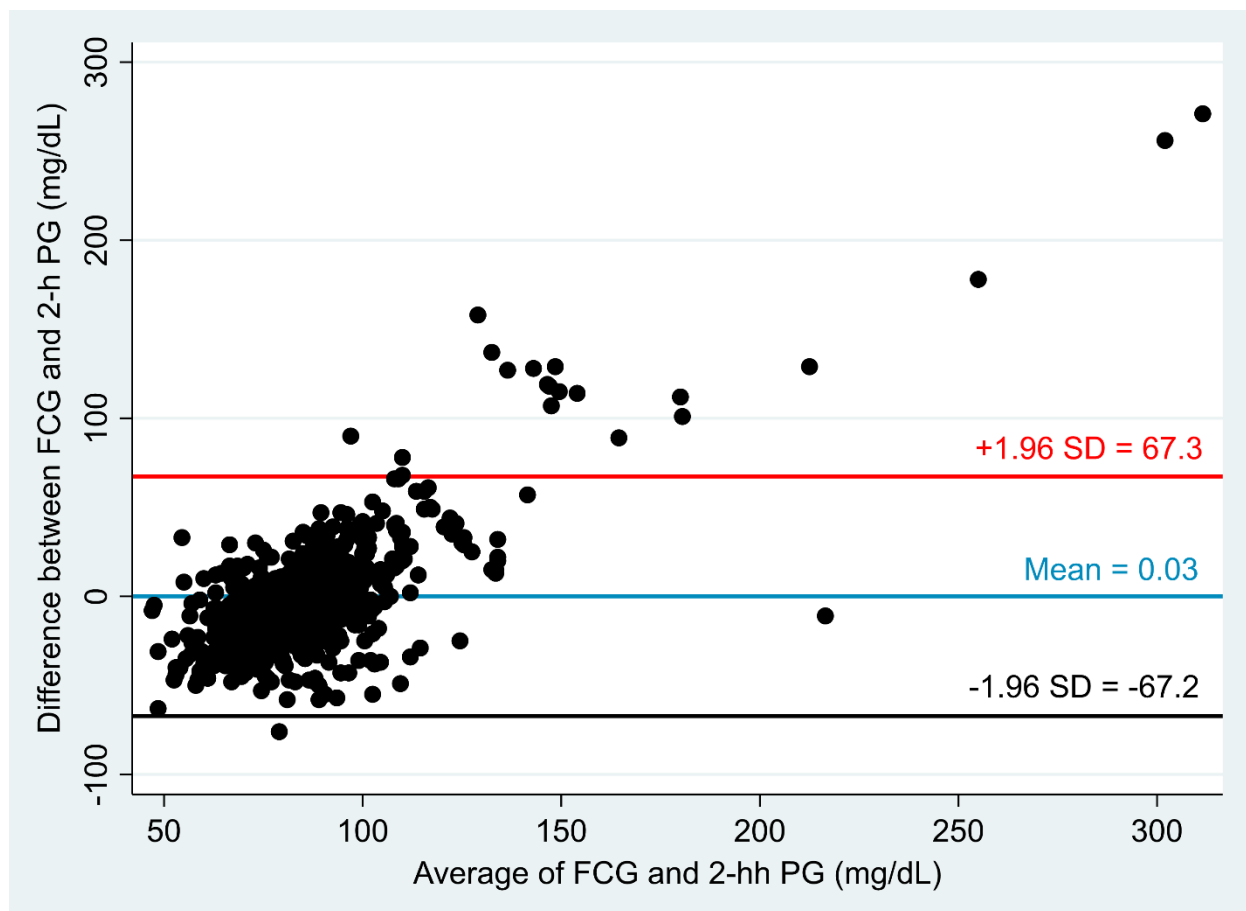


Figure 7. Bland–Altman plot of fasting capillary blood glucose concentration and 2-hour plasma glucose concentration after 75 gm oral glucose load.

4.3.3. Performance of FPG and FCG tests

The receiver operating characteristic (ROC) for FPG and FCG tests to identify cases with diabetes and prediabetes is outlined in Figure 8 and 9 and Table 7. The FPG test exhibited good and acceptable discriminatory power in identifying individuals with diabetes, an overall AUC of 0.83 (95% CI: 0.76–0.90) (Figure 8A and Table 7). The AUC for men, 0.88 (95% CI: 0.80–0.95), was higher than that for women, 0.77 (95% CI: 0.65–0.89), but this difference was not statistically significant ($P=0.142$) (Table 7). Moreover, the AUC for Nigerian participants, 0.89 (95% CI: 0.83–0.95) was significantly higher than that of Ethiopian counterparts, 0.70 (95% CI: 0.53–0.86) ($P\text{-value} = 0.034$) (Figure 8B and Table 7).

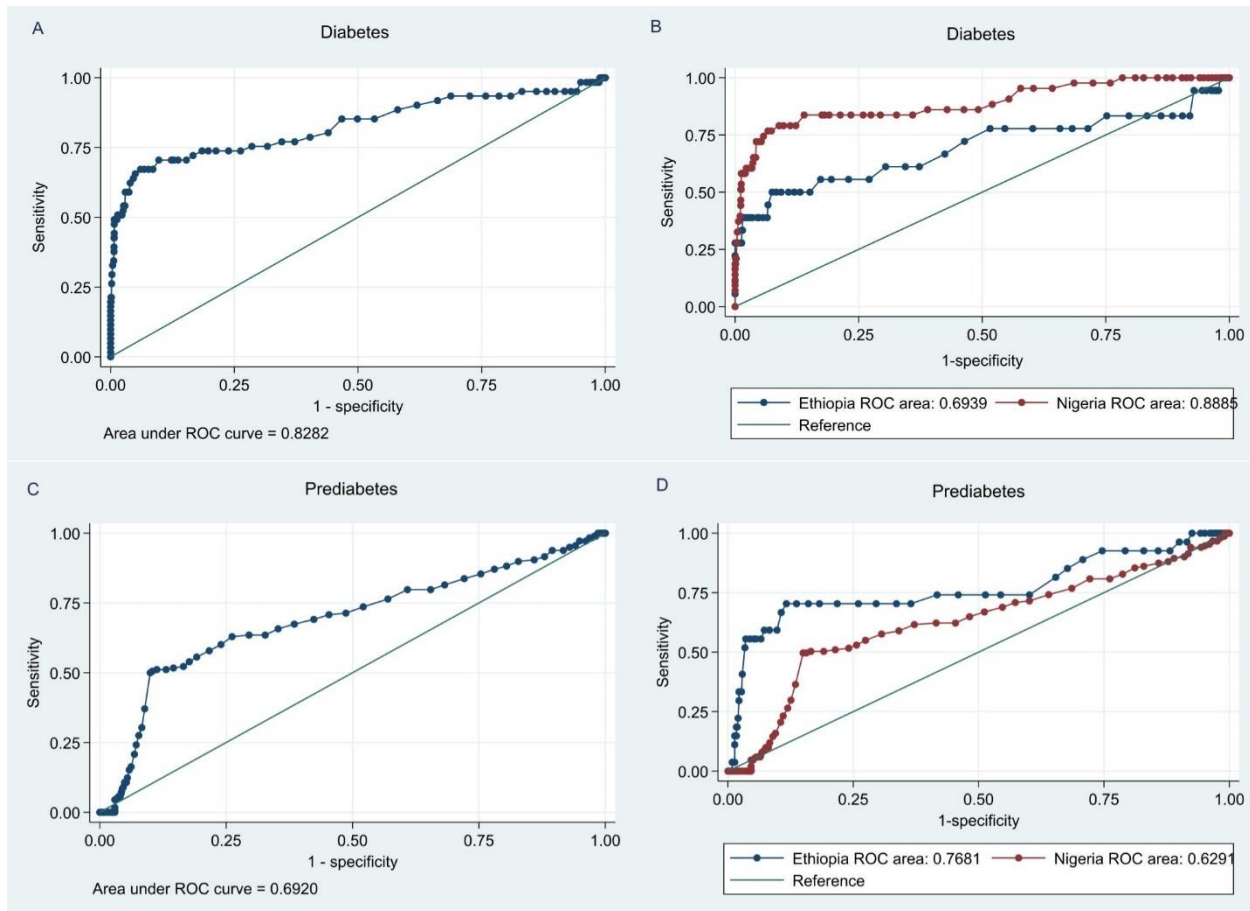


Figure 8. Receiver operating characteristic (ROC) curve for fasting plasma glucose (FPG) to assess the presence of undiagnosed diabetes and prediabetes.

These figures show the overall AUC for diabetes (A), the AUC for diabetes in each country (B), overall AUC for prediabetes (C) and the AUC for prediabetes in each country (D).

Similarly, the FPG test had nearly fair performance in identifying individuals with prediabetes, with an overall AUC of 0.69 (95% CI: 0.67-0.72) (Figure 8C and Table 7). The performance of the FPG test to identify people with prediabetes revealed a significantly higher AUC among the Ethiopians, 0.77 (95% CI: 0.65-0.89), compared to the Nigerians, 0.63 (95% CI: 0.58-0.68) (Figure 8D and Table 7). Nonetheless, the performance of the FPG test to identify individuals with prediabetes was comparable between male and female participants (Table 7). These ROC curves for FPG were calculated based on the detection of diabetes by 2-h PG ≥ 200 mg/dL and prediabetes by 2-h PG ≥ 140 mg/dL.

Table 9. Area under the curve (AUC) for fasting plasma glucose (FPG) and fasting capillary blood glucose (FCG) to screen undiagnosed diabetes and prediabetes

Performance of FPG				
Variables	Prediabetes		Diabetes	
	AUC (95% CI)	P-value	AUC (95% CI)	P-value
Overall	0.69 (0.67-0.72)	-	0.83 (0.76-0.90)	-
Country				
Nigeria	0.63 (0.58-0.68)	0.039	0.89 (0.83-0.95)	0.034
Ethiopia	0.77 (0.65-0.89)		0.70 (0.53-0.86)	
Sex				
Men	0.68 (0.61-0.74)	0.505	0.88 (0.80-0.95)	0.149
Women	0.71 (0.64-0.78)		0.77 (0.64-0.89)	
Performance of FCG				
Overall	0.77 (0.68-.0.86)	-	0.69 (0.52-.0.86)	-
Residence				
Urban	0.82 (0.72-0.91)	0.225	0.71 (0.50-0.92)	0.623
Rural	0.69 (0.51-0.87)		0.62 (0.36-0.89)	
Sex				
Men	0.69 (0.51- 0.87)	0.223	0.79 (0.51-1.0)	0.353
Women	0.82 (0.72-0.92)		0.63 (0.43-0.82)	

Diagnostic accuracy of FPG test in distinguishing between prediabetes and diabetes in different groups based on country and sex by using the area under the curve (AUC) from a Receiver Operating Characteristic (ROC) curve. A higher AUC (closer to 1) indicates better diagnostic performance

The FCG test also exhibited nearly fair accuracy in identifying individuals with diabetes, with an overall AUC of 0.69 (95% CI: 0.52-.0.85) (Figure 9A and Table 7). The AUC for men, 0.79 (95% CI: 0.51-1.0), was higher than that for women, 0.63 (95% CI: 0.43-0.82), but this difference was statistically insignificant (P=0.353). In addition, the FCG test also exhibited a fair accuracy in identifying individuals with prediabetes, with an overall AUC of 0.77 (95% CI: 0.68-.0.86).

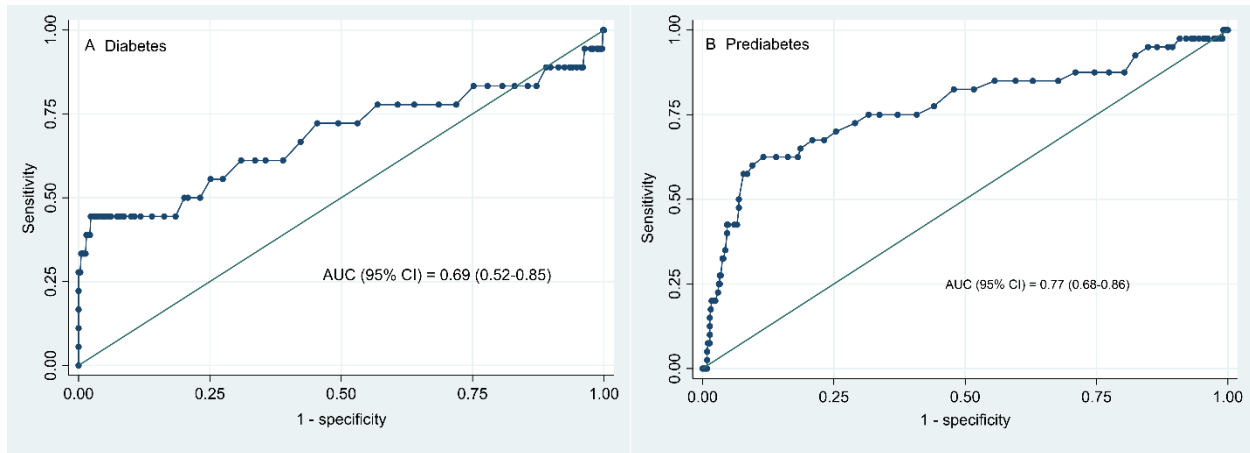


Figure 9. Receiver operating characteristic (ROC) curve for fasting capillary blood glucose (FCG) test to assess the presence of undiagnosed diabetes and prediabetes.

Similarly, the FCG test had good and acceptable performance in identifying individuals with prediabetes, with an overall AUC of 0.77 (95% CI: (0.68.-0.86)) (Figure 9B and Table 7). The performance of the FCG test to identify people with prediabetes revealed higher AUC among the females, 0.82 (95% CI: 0.72-0.92), compared to the men, 0.69 (95% CI: 0.51-0.87), although this is also statistically insignificant.

4.3.4. FPG and FCG cut-off points for diabetes and pre-diabetes screening

Based on the ROC curve, the optimal cut point of FPG for detecting newly diagnosed diabetes by 2-h PG was determined to be 105 mg/dL, associated with a sensitivity of 67.2% and specificity of 94.0% (AUC 0.83, 95% CI: 0.76 – 0.90; NND 1.6) (Table 7). Applying this cut-off point, an additional 59 undiagnosed cases of diabetes (3.8%) among the 1550 participants could be identified.

Likewise, the optimal cut-off points of FPG in detecting prediabetes diagnosed by 2-h PG was determined to be 99 mg/dL, with a sensitivity of 52.2% and specificity of 90.0% (AUC 0.69, 95% CI:0.67-0.72).

Table 10. Sensitivity and specificity for FPG in diagnosing diabetes and prediabetes

FPG cut-offs	Diabetes					Prediabetes				
	Se (%)	Sp (%)	Youden J	LR+	LR-	Se (%)	Sp (%)	Youden J	LR+	LR-
80 mg/dL	90.2	38.1	0.282	1.46	0.26	80.4	39.3	0.198	1.326	0.497
85 mg/dL	80.3	56.0	0.363	1.83	0.35	70.1	57.9	0.281	1.667	0.516
90 mg/dL	75.4	71.5	0.469	2.64	0.34	64.1	74.2	0.383	2.487	0.483
95 mg/dL	73.8	81.5	0.553	3.99	0.32	53.8	83.9	0.377	3.338	0.551
100 mg/dL	70.5	87.7	0.582	5.74	0.34	51.6	90.5	0.421	5.421	0.535
105 mg/dL	67.2	94.0	0.612	11.12	0.35	23.4	93.6	0.170	3.667	0.818
110 mg/dL	59.0	96.6	0.557	17.58	0.42	13.6	95.6	0.092	3.091	0.904
115 mg/dL	50.8	97.7	0.485	22.26	0.50	8.7	96.5	0.052	2.473	0.946
120 mg/dL	49.2	98.7	0.479	38.54	0.51	7.6	97.5	0.051	3.055	0.948
125 mg/dL	47.5	99.3	0.468	64.35	0.53	3.3	97.6	0.008	1.349	0.991
130 mg/dL	39.3	99.3	0.387	58.58	0.61	3.3	98.0	0.013	1.649	0.987
135 mg/dL	29.5	99.7	0.292	109.84	0.71	1.6	98.7	0.003	1.236	0.997
140 mg/dL	21.3	99.9	0.212	317.33	0.79	0.5	99.1	-0.003	0.618	1.003
145 mg/dL	19.7	100.0	0.197	Inf	0.80	0.0	99.2	-0.008	0.000	1.008
150 mg/dL	18.0	100.0	0.180	Inf	0.82	0.0	99.3	-0.007	0.000	1.007

Comparison of diagnostic performance metrics for fasting plasma glucose (FPG) cut-off values ranging from 80 mg/dL – 150 mg/dL in diagnosing diabetes and prediabetes to identify which FPG levels offer the best sensitivity, specificity, and diagnostic balance for the two conditions. Youden J is summary statistic combining Se and Sp to show the overall diagnostic effectiveness, it is computed as Youden's index = Sensitivity + Specificity - 1. A higher value of Youden's index indicates better overall diagnostic accuracy. FPG, Fasting Plasma Glucose; LR-, negative likelihood ratio; LR+, Positive likelihood ratio; Se, Sensitivity; Sp, Specificity

When utilizing the guideline recommended cut-off 126 mg/dL, the sensitivity of FPG in identifying diabetes is 44.3%, with a specificity of 99.3%. A lower FPG cut-off value 105 mg/dL revealed markedly increased sensitivity (67.2%) and high specificity (94.0%) for identifying individuals with diabetes. Furthermore, for diagnosing individuals with prediabetes, guideline recommended cut-off value for FPG, 100 mg/dL, demonstrated a sensitivity of 51.6% and specificity of 90.5%. Lowering the FPG cut-off to 90 mg/dL

resulted in increased sensitivity (64.1%) and reasonable specificity (74.2%) to identify individuals with pre-diabetes (Table 8).

Similarly, based on the ROC curve analysis, the optimal cut point of FCG for detecting newly diagnosed diabetes by 2-h PG was determined to be 119 mg/dL, associated with a sensitivity of 44.4% and specificity of 97.7% (AUC 0.69, 95% CI: 0.52-0.85) (Table 9). Applying this cut-off point, an additional 9 undiagnosed cases of diabetes could be identified, making the prevalence of diabetes 3.6% in the study population.

Table 11. Sensitivity and specificity for FCG in diagnosing diabetes and prediabetes, Butajira, Ethiopia, 2021

FCG cut-off	Diabetes			Prediabetes		
	Se (%)	Sp (%)	Youden J	Se (%)	Sp (%)	Youden J
70.5 mg/dL	88.9	8.7	-0.025	97.5	9.2	0.067
75.5 mg/dL	83.3	17.0	0.003	92.5	17.6	0.101
76.5 mg/dL	83.3	19.3	0.026	87.5	19.7	0.072
80.5 mg/dL	77.8	31.4	0.092	85.0	32.3	0.173
85.5 mg/dL	72.2	50.6	0.228	82.5	52.2	0.347
90.5 mg/dL	61.1	66.4	0.275	75.0	68.4	0.434
95.5 mg/dL	50.0	79.2	0.292	65.0	81.3	0.463
99.5 mg/dL	44.4	86.0	0.305	62.5	88.4	0.509
100.5 mg/dL	44.4	88.2	0.326	60.0	90.5	0.505
105.5 mg/dL	44.4	92.2	0.366	42.5	93.4	0.359
110.5 mg/dL	44.4	94.8	0.393	35.0	95.7	0.307
115.5 mg/dL	44.4	96.5	0.410	25.0	96.7	0.217
119.0 mg/dL	44.4	97.7	0.421	20.0	97.6	0.176
125.5 mg/dL	33.3	98.8	0.322	12.5	98.6	0.111
126.5 mg/dL	33.3	99.0	0.323	10.0	98.6	0.086
135.5 mg/dL	27.8	99.8	0.276	2.5	99.1	0.016
170.0 mg/dL	16.7	100.0	0.167	0.00	99.5	-0.005

Likewise, the optimal cut-off-point of FCG in detecting prediabetes diagnosed by 2-h PG was determined to be 99.5 mg/dL with a sensitivity of 62.5% and specificity of 88.4% (AUC 0.77, 95% CI:0.68-0.86). This cut-off was equivalent to the ADA recommended cut-off for prediabetes.

When utilizing the guideline recommended cut-off 126 mg/d, the sensitivity of FPG in identifying diabetes is extremely low, 33.3%, with a specificity of 99.0%. A lower FCG cut-off value 119 mg/dL revealed an increased sensitivity (44.4%) and high specificity (97.7%) for identifying individuals with diabetes.

4.3.5. Prediabetes and diabetes missed by FPG and FCG tests

Table 10 highlights the percentages of prediabetes and diabetes cases missed by either FPG or 2-h PG alone. Among the total 1550 participants tested by both FPG and 2-h PG, FPG would miss 34.1% of all prediabetes and 44.4% of all diabetes cases, whereas the corresponding percentages missed by 2-h PG were 31.8% and 15.3%, respectively.

The rates of missed prediabetes cases using FPG and 2-h PG were similar for men and women study participants. In contrast, FPG demonstrated a higher rate of missed cases of diabetes in women compared to men ($p = 0.047$), whereas 2-h PG presented a higher rate of missed diabetes cases in men compared to women, despite this was not statistically significant.

Moreover, the rate of missed cases of prediabetes by FPG was higher among individuals aged 70 years and above as compared to middle-aged and young study participants ($p = 0.006$). The percentage of missed diabetes cases by FPG was significantly higher among non-obese participants compared to obese individuals with diabetes ($p = 0.013$), while the opposite trend was observed in 2-h PG. However, there was no significant difference in the rate of missed prediabetes cases by FPG and 2-h PG among obese and non-obese individuals.

Table 12. Percentages of diabetes and prediabetes missed by FPG and 2-h PG.

Diabetes							
	All diabetes	Diabetes missed by FPG			Diabetes missed by 2-h PG		
		Missed (%)	Not missed (%)	p-value	Missed (%)	Not missed (%)	p-value
All (N=1550)	72	32 (44.4)	40 (56.6)	-	11 (15.3)	61 (84.7)	-
Sex							
Men	43	15 (34.9)	28 (60.1)	0.047	9 (20.9)	34 (79.1)	0.105
Women	29	17 (58.6)	12 (41.4)		2 (6.9)	27 (93.1)	
Age							
< 65 years	62	29 (46.8)	33 (53.2)	0.322	9 (14.5)	53 (85.5)	0.655
≥ 65 years	10	3 (30.0)	7 (70.0)		2 (20.0)	8 (80.0)	
Residence							
Urban	26	12 (46.2)	14 (53.8)	0.826	1 (3.8)	25 (96.2)	0.043
Rural	46	20 (43.5)	26 (56.5)		10 (21.7)	36 (78.3)	
WHO global recommendations on physical activity ^a							
Optimal	56	24 (42.9)	32 (57.1)	0.612	10 (17.9)	46 (82.1)	0.255
Suboptimal	16	8 (50.0)	8 (50.0)		1 (6.3)	15 (93.7)	
BMI ^b							
Non-obese	35	21 (60.0)	14 (40.0)	0.013	1 (2.9)	34 (97.1)	0.004
Obese	36	11 (30.6)	25 (69.4)		10 (27.8)	26 (72.2)	
Waist circumference ^c							
Low risk	31	15 (48.4)	16 (51.6)	0.484	7 (22.6)	24 (77.4)	0.302
Increased risk	16	5 (31.3)	11 (68.8)		2 (12.5)	14 (87.5)	
Substantially increased risk	25	12 (48.0)	13 (52.0)		2 (8.0)	23 (92.0)	
Raised BP							
Yes	33	14 (42.4)	19 (57.6)	0.751	5 (15.2)	28 (84.8)	0.978
No	39	18 (46.2)	21 (53.9)		6 (15.4)	33 (84.6)	
Prediabetes							
	All prediabetes	Prediabetes missed by FPG			Prediabetes missed by 2hPG		
		Missed (%)	Not missed (%)	p-value	Missed (%)	Not missed (%)	p-value
All (N=1550)	261	89 (34.1)	172 (65.9)	--	83 (31.8)	178 (68.2)	--
Sex							
Men	145	52 (35.9)	93 (64.1)	0.502	45 (31.0)	100 (69.0)	0.766
Women	116	37 (31.9)	79 (68.1)		38 (32.8)	78 (67.2)	
Age							
< 65 years	202	60 (29.7)	142 (70.3)	0.006	72 (35.6)	130 (64.4)	0.014
≥ 65 years	59	29 (49.2)	30 (50.8)		11 (18.6)	48 (81.4)	
Country							
Ethiopia	40	13 (32.5)	27 (67.5)	0.817	13 (32.5)	27 (67.5)	0.918
Nigeria	221	76 (34.4)	145 (65.6)		70 (31.7)	151 (68.3)	
Residence							
Urban	125	34 (27.2)	91 (72.8)	0.024	44 (35.2)	81 (64.8)	0.258
Rural	136	55 (40.4)	81 (59.6)		39 (28.7)	97 (71.3)	

WHO global recommendations on physical activity ^a							
Optimal	212	75 (35.4)	137 (64.6)	0.365	68 (32.1)	144 (67.9)	0.843
Suboptimal	49	14 (28.6)	35 (71.4)		15 (30.6)	34 (69.4)	
BMI ^b							
Non-obese	168	64 (38.1)	104 (61.9)	0.065	55 (32.7)	113 967.3)	0.525
Obese	90	24 (26.7)	66 (73.3)		26 (8.9)	64 (71.1)	
Waist circumference ^c							
Normal risk	126	49 (38.9)	77 (61.1)	0.265	42 (33.3)	84 (66.7)	0.594
Increased risk	47	15 (31.9)	32 (68.1)		12 (25.5)	35 (74.5)	
Substantially	88	25 (28.4)	63 (71.6)		29 (33.0)	59 (67.0)	
increased risk							
Raised BP							
Yes	107	41 (38.3)	66 (61.7)	0.231	33 (30.8)	74 (69.2)	0.781
No	154	48 (31.2)	106 (68.8)		50 (32.5)	104 (67.5)	

^a According to WHO global recommendations on physical activity for health optimal physical activity is 150 minutes of moderate-intensity physical activity; or 75 minutes of vigorous-intensity physical activity; or an equivalent combination of moderate- and vigorous-intensity physical activity achieving at least 600 MET-minutes.

^b obese is based on WHO BMI classification (BMI $\geq$ 30 kg/m²)

^c Waist circumference classification is based on WHO recommendation where normal risk is $\leq$ 94 cm for men and $\leq$ 80 cm for women; increased risk is >94 – 102 cm for men and >80 – 88 cm for women; and substantial increased risk is >102 cm for men and >88 cm for women.

BP, blood pressure; FPG, fasting plasma glucose; 2-h PG, 2-hour plasma glucose; BMI, body mass index

Table 11. highlight the percentages of prediabetes and diabetes cases missed by FCG. Among the total 619 participants tested by both FCG and 2-h PG, FCG would miss 13 cases (14.1%) of all prediabetes and 13 cases (48.0%) of all diabetes cases.

The rates of diabetes misdiagnosis were higher among women (2.3%) than men (1.3%) using FCG test, while the rate of misdiagnosis for prediabetes was higher among men (2.2%) compared to women (2.0%), despite these differences were not statistically significant. Moreover, the rate of missed cases of diabetes by FCG was higher among older individuals (2.2%) as compared to middle-aged and young study participants (1.8%). This difference is also statistically insignificant.

Table 13. Percentages of diabetes and prediabetes missed by FCG, Butajira, Ethiopia, 2021

Characteristics	Diabetes			Prediabetes		
	All diabetes (%)	Diabetes missed by FCG		All prediabetes (%)	Prediabetes missed by FCG	
		Missed (%)	Not missed (%)		Missed (%)	Not missed (%)
All (N=619)	25 (4.0)	12 (1.9)	13 (98.1)	92 (14.9)	13 (2.1)	606 (97.9.0)
Sex						
Men	11 (4.9)	3 (1.3)	222 (98.7)	33 (14.7)	5 (2.2)	220 (97.8)
Women	14 (3.6)	9 (2.3)	385 (97.7)	59 (15.0)	8 (2.0)	386 (98.0)
Age						
< 45 years	14 (3.6)	7 (1.8)	386 (98.2)	51 (13.0)	11 (2.8)	382 (97.2)
≥ 45 years	11 (4.9)	5 (2.2)	221 (97.8)	41 (18.1)	2 (0.9)	224 (98.1)
Residence						
Urban	15 (4.2)	7 (2.0)	347 (98.0)	50 (14.1)	6 (1.7)	348 (98.3)
Rural	10 (3.8)	5 (1.9)	260 (98.1)	42 (15.8)	7 (2.6)	258 (97.4)
WHO global recommendations on physical activity ^a						
Optimal	19 (3.9)	10 (2.0)	478 (98.0)	78 (16.0)	2 (1.5)	129 (98.5)
Suboptimal	6 (4.6)	2 (1.5)	129 (98.5)	14 (10.7)	11 (2.3)	477 (97.7)
BMI ^b						
Non-obese	21 (3.7)	10 (1.7)	565 (98.3)	80 (13.9)	13 (2.3)	562 (97.7)
Obese	4 (9.1)	2 (4.5)	42 (95.5)	12 (27.3)	0	44 (100.0)
Waist circumference ^c						
Low risk	17 (3.4)	8 (1.6)	497 (98.4)	70 (13.9)	12 (2.4)	493 (97.8)
Increased risk	4 (5.9)	3 (4.4)	65 (95.6)	12 (17.6)	0	68 (100.0)
Substantially increased risk	4 (8.7)	1 (2.2)	45 (97.8)	10 (21.7)	1 (2.2)	45 (97.8)
Raised BP						
Yes	8 (7.5)	4 (3.7)	103 (96.3)	17 (15.9)	3 (2.8)	104 (97.2)
No	17 (3.3)	8 (1.6)	504 (98.4)	75 (14.6)	10 (2.0)	502 (98.0)

4.4. Diabetes Management at TASH

4.4.1 Demographic and clinical characteristics

Table 12 shows the characteristics of all type 2 diabetes patients and by clinical inertia. A total of 407 patients were identified as eligible for the study. Overall, more than half (57.0%) of the patients had clinical inertia. Among the total cohort, 214 (52.6%) were younger adults (<60 years), and 214 (52.6%) females. The majority of patients (57.0%) had follow-ups every three months, with this pattern being similar among those with clinical inertia (59.1%) and those without it (54.3%). Community-based health insurance

(CBHI) was the most common payment modality, accounting for 54.3% of the cohort, followed by out-of-pocket payments (43.0%) and free services (2.7%).

Table 14. Characteristics of individuals with type 2 diabetes at baseline and follow-up, Tikur Anbessa Specialized Hospital, Ethiopia

Characteristics	Total (n = 407)	Clinical inertia		P-value
		Yes, 232 (57.0%)	No, 175 (43.0%)	
Age, mean (SD)	58.5 (10.8)	57.8 (10.5)	59.3 (11.2)	0.169
Younger adults (<60 years)	214 (52.6)	125 (58.4)	89 (41.6)	0.546
Older adults (≥60 years)	193 (47.4%)	107 (55.4)	86 (44.6)	
Age at diagnosis of DM, mean (SD)	48.7 (11.2)	47.4 (11.1)	50.4 (11.1)	0.006
Sex				
Male	193 (47.4)	107 (46.1)	86 (49.1)	0.546
Female	214 (52.6)	125 (53.9)	89 (50.9)	
Follow-up duration (yrs), mean (SD)	4.6 (1.9)	5.1 (1.5)	3.9 (2.1)	<0.001
<5 year	144 (35.4)	56 (24.1)	88 (50.3)	<0.001
≥5 year	263 (64.6)	176 (75.9)	87 (49.7)	
Follow-up schedule				
Every month	33 (8.1)	17 (7.3)	16 (9.1)	0.523
Every three month	232 (57.0)	137 (59.1)	95 (54.3)	
Every four month	13 (3.2)	9 (3.8)	4 (2.3)	
Every six month	129 (31.7)	69 (29.7)	60 (34.3)	
Payment modality				
CBHI	221 (54.3%)	131 (56.5)	90 (51.4)	0.279
Out-of-pocket	175 (43.0%)	97 (41.8)	78 (44.6)	
Free	11 (2.7%)	4 (1.7)	7 (4.0)	
Duration of diabetes, Median (IQR)	8.0 (5.3-13)	9.5 (6.0-14.0)	7.0 (4.0-13)	0.002
<5 years	85 (20.9)	34 (14.7)	51 (29.1)	0.002
5 – 10 years	171 (42.0)	104 (44.8)	67 (38.3)	
> 10 years	151 (37.1)	94 (40.6)	57 (32.6)	
Recent HbA1c (%), median (IQR)	7.3 (6.4-8.7)	8.0 (7.0-9.3)	6.7 (6.1-7.4)	<0.001
Recent FBS (mg/dL), median (IQR)	135.0 (116.0-169.0)	145 (122.5-182.0)	124 (111.0-146.0)	<0.001
Lipid profile				
TC (mg/dL), median (IQR)	148.0 (119.2-171.5)	140.6 (121.5-176.0)	135.5 (118.0-168.0)	0.281
LDL (mg/dL), median (IQR)	79.0 (60.0-106.0)	81.0 (60.5-107.1)	77.2 (59.7-100.8)	0.289

HDL (mg/dL), median (IQR)	41.0 (35.0-48.0)	41.0 (36.0-47.3)	40.0 (34.0-48.0)	0.452
TG (mg/dL), median (IQR)	122.0 (93.0-173.0)	127.0 (99.8-176.3)	113.0 (89.0-162.9)	0.032
Blood pressure				
SBP (mmHg), mean (SD)	131.9 (18.1)	133.3 (18.0)	129.9 (18.1)	0.075
DBP (mmHg), mean (SD)	77.2 (11.8)	77.9 (12.0)	76.2 (11.4)	0.180
Comorbidities				
	364 (89.4)	202 (87.1)	162 (92.6)	0.074
Hypertension	264 (64.9)	149 (64.2)	115 (65.7)	0.556
Dyslipidaemia	83 (20.4)	45 (19.4)	38 (21.7)	0.790
IHD	38 (9.3%)	19 (8.2)	19 (16.6)	0.471
CKD	30 (7.4%)	18 (7.8)	12 (6.9)	0.604
Stroke	16 (3.9%)	8 (3.4)	8 (4.6)	0.651
DM complications				
	131 (32.2%)	70 (30.2)	61 (34.9)	0.317
Types of complications				
Neuropathy	54 (13.3)	31 (13.4)	23 (13.1)	0.949
Nephropathy	36 (8.8)	23 (9.9)	13 (7.4)	0.382
Retinopathy	17 (4.2)	10 (4.3)	7 (4.0)	0.877
Diabetic foot ulcer	7 (1.7)	2 (0.9)	5 (2.9)	0.125
Unspecified	7 (1.7)	2 (0.9)	5 (2.9)	0.125
Other*	10 (2.5)	2 (0.9)	8 (4.6)	0.015
Number of indices OAD agents				
Monotherapy	194 (47.7)	96 (41.4)	98 (56.0)	0.003
Dual therapy	213 (52.3)	136 (58.8)	77 (44.0)	
Index OAD agents				
Metformin	389 (95.6)	222 (95.7)	167 (95.4)	0.899
Sulfonylureas	220 (54.1)	141 (60.8)	79 (45.1)	0.002
SGLT2 inhibitors	8 (2.0)	2 (0.9)	6 (3.4)	0.065
DPP4 inhibitors	4 (1.0)	2 (0.9)	2 (1.1)	0.776
Number of current antidiabetes				
Monotherapy	118 (29.2)	57 (24.6)	61 (34.9)	0.074
Dual therapy	205 (50.4)	123 (53.0)	82 (46.9)	
Triple therapy	84 (20.6)	52 (22.4)	32 (18.3)	
Current antidiabetes drugs				
OAD agents	297 (73.0)	156 (67.2)	141 (80.6)	0.010
Insulin	17 (4.2)	11 (4.7)	6 (3.4)	
Both insulin and OADs	93 (22.9)	65 (28.0)	28 (16.0)	

Statin therapy	389 (95.6)	224 (96.6)	165 (94.3)	0.271
Antiplatelet therapy	133 (32.7)	68 (29.3)	65 (37.1)	0.095

4.4.2 Time to Treatment intensification

Table 13 shows characteristics related to TI. The diabetes management of majority of individuals (58.8%) was intensified by increasing the dose of OADs. The main type of antidiabetic agents for treatment intensification were OADs (79.7%). In about five of six cases, treatment of type 2 diabetes was intensified with monotherapy. About half (52.3%) of patients experienced treatment de-escalation. Among the types of treatment de-escalation, the removal of antidiabetics was the most common (66.2%), with only 39.0% achieving glycemic control.

Table 15. Treatment intensification and de-escalation among individuals with type 2 diabetes attending Tikur Anbessa Specialized Hospital, Ethiopia

	Characteristics	Frequency (%)
Treatment intensified (n=352)	Yes	320 (90.9)
	No	32 (9.1)
Methods of TI (n = 320) *	Increase dose of OADs	188 (58.8)
	Addition of new OAD	77 (24.1)
	Addition of Insulin	45 (14.1)
	Other [#]	10 (3.1)
Type of antidiabetic drugs for TI	OADs	255 (79.7)
	Insulin	36 (11.3)
	Both insulin and OADs	29 (9.1)
Number of medications for TI	One	271 (84.7)
	Two	47 (14.7)
	Three	2 (0.5)
Treatment de-escalation	Yes	213 (52.3)
	No	194 (47.7)
Type of treatment de-escalation	Dose reduction	41 (19.2)
	Removal of antidiabetics	141 (66.2)
	Both dose reduction and removal of antidiabetics	31 (14.6)

Both new OAD and increase dose of OADs, addition of both insulin and new OADs

* TI-related characteristics is documented for 320 individuals with treatment intensification, be it timely or delayed

As shown in Table 14, among all patients who require TI (n=352) with index HbA1c $\geq 7.0\%$ (53 mmol/mol) and clinical judgement, slightly more than half (58.5%) were intensified in less than 6 months, and 18.5% were intensified within 6 - 12 months, while nearly a quarter of cases (23.0%) were not intensified within 12 months. TI was not deemed necessary for the remaining 55 cases as their HbA1c was $< 7.0\%$ (53 mmol/mol) throughout the follow-up period.

Over all, the median time to TI was 6 months (95% CI: 4.3 – 7.7). Men experienced shorter median times to TI (4.0 months, 95% CI: 2.3–5.7) compared to women, whose median time to TI was more than double (9.0 months, 95% CI: 3.8–14.2). Inline to this, a higher proportion of men (61.5%) had TI within 6 months compared to women (55.7%).

Table 16. Time to treatment intensification among individuals with type 2 diabetes attending Tikur Anbessa Specialized Hospital, Ethiopia

Variables		Median time to TI (months) (95% CI)	Intensified in <6 months, n (%)	Intensified within 6-12 months, n (%)	Not intensified in 12 months, n (%)	P-value
All cases		6.0 (4.3-7.7)	206 (58.5%)	65 (18.5%)	81 (23.0%)	
Sex	Men	4.0 (2.3-5.7)	104 (61.5)	33 (19.5)	32 (18.9)	0.218
	Women	9.0 (3.8-14.2)	102 (55.7)	32 (17.5)	49 (31.7)	
Age	<60 years	6.0 (3.9-8.2)	108 (57.4)	39 (20.9)	41 (21.8)	0.480
	≥ 60 years	5.0 (1.7-8.2)	98 (59.8)	26 (15.9)	49 (26.8)	
Age at diagnosis	<45 years	8.0 (4.0-12.0)	71 (54.2)	28 (21.4)	32 (24.4)	0.406
	≥ 45 years	4.3 (2.1-6.6)	135 (61.1)	37 (16.7)	49 (22.2)	
Duration of DM since diagnosis	< 5 years	6.0 (0.8-11.2)	40 (67.8)	6 (10.2)	13 (22.0)	0.185
	5 – 10 years	4.3 (1.3-7.4)	82 (59.4)	26 (16.8)	37 (23.9)	
	>10 years	6.0 (2.8-9.2)	74 (53.6)	33 (23.9)	31 (22.5)	
Index HbA1c	<8.5%	4.0 (3.2-4.8)	52 (67.5)	9 (11.7)	16 (20.8)	0.547
	$\geq 8.5\%$	6.0 (3.3-8.7)	65 (59.6)	16 (14.7)	28 (25.7)	

Complications	Yes	8.0 (2.6-13.4)	57 (50.9)	27 (24.1)	28 (25.0)	0.093
	No	4.0 (2.4-5.6)	149 (62.1)	38 (15.8)	53 (22.1)	
Index treatment	MTF alone	4.0 (1.8-6.2)	88 (64.2)	18 (13.1)	31 (22.6)	0.062
	MTF+SU	8.0 (0.9-15.1)	101 (52.9)	45 (23.6)	45 (23.6)	
	Other*	3.0 (2.3-3.7)	17 (70.8)	2 (8.3)	5 (20.8)	
Taking aspirin	Yes	6.0 (2.8-9.2)	65 (58.0)	23 (20.5)	24 (21.4)	0.753
	No	5.3 (3.1-7.6)	141 (58.5)	42 (17.5)	57 (23.8)	
Number of index treatment	Monotherapy	4.0 (1.9-6.1)	100 (64.9)	19 (14.3)	35 (22.7)	0.024
	Dual therapy	7.8 (1.8-13.8)	106 (53.5)	46 (23.2)	46 (23.2)	

* Canagliflozin, Dapagliflozin, Metformin + Dapagliflozin, Metformin + Vildagliptin

4.4.3 Glycemic control

Figure 10 shows the relationship between glycemic control and time of TI. Among the total 407 participants, nearly half, 199 (48.9%), had poor glycemic control as determined by their latest HbA1c or FBS and clinical judgement. Early TI was significantly associated with glycaemic control as half (51.9%) of individuals intensified with less than 6 months achieved glycaemic control while only a third of individuals intensified after six months achieved glycaemic control ($p=0.003$). Similarly, less than 40.0% of individuals who never intensified in 12 months achieved glycemic control.

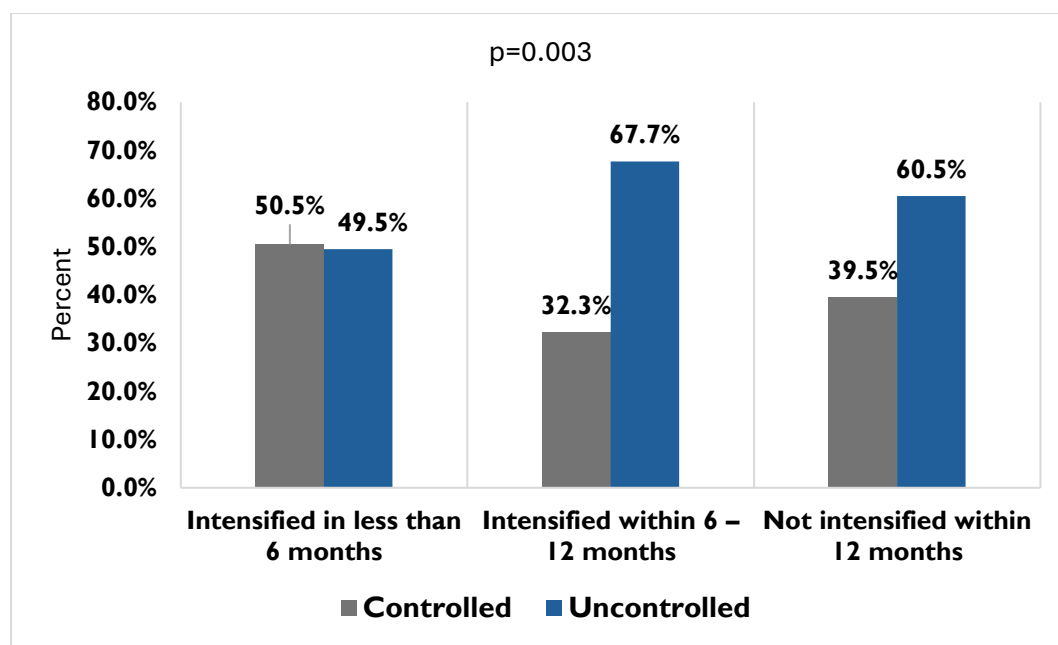


Figure 10. Status glycemic control by time of treatment intensification

4.4.4 Factors associated with glycemic control

In the univariate analysis variables significantly associated with poor glycemic control include age (COR = 0.97, 95% CI: 0.95-0.99, $p = 0.001$), diagnosis of DM before the age of 45 years (COR = 1.98, 95% CI: 1.31-3.00, $p = 0.001$), dual (COR = 2.64, 95% CI: 1.64-4.25, $p < 0.001$) and triple (COR = 3.22, 95% CI: 1.80-5.78, $p < 0.001$) antidiabetic therapy, lack of aspirin therapy (COR = 1.89, 95% CI: 1.24–2.88, $p = 0.003$), dual index therapy (COR = 2.30, 95% CI: 1.55–3.43, $p < 0.001$), and delayed treatment intensification (COR = 2.08, 95% CI: 1.34–3.22, $p = 0.001$). In the multivariable analysis, poor glycemic control was significantly associated with the number of current antidiabetic drugs, dual index treatment, and delayed treatment intensification. Patients with delayed treatment intensification had about twice higher odds of experiencing poor glycemic control compared to those with timely treatment intensification (AOR = 2.08, 95% CI: 1.34–3.22, $p = 0.001$). Similarly, patients who had been on dual index treatment had more than twice higher odds of experiencing poor glycemic control than patients on single index treatment (AOR = 2.30, 95% CI: 1.55-3.43, $p = 0.043$). Moreover, patients on dual and triple current antidiabetic treatments had more than twice (AOR = 2.64, 95% CI: 1.64 – 4.25, $p < 0.001$) and three time (AOR = 3.22, 95% CI: 1.80 – 5.78, $p < 0.001$) higher odds

of having poor glycemic control than patients taking single current antidiabetic treatment (Table 15).

Table 17. Factors associated with poor glycemic control among type 2 diabetes individuals attending Tikur Anbessa Specialized Hospital, Ethiopia

Variables	Glycemic control		COR (95% CI)	P-value	AOR (95% CI)	P-value
	Controlled, 208 (51.1%)	Uncontrolled, 199 (48.9%)				
Age, mean (SD)	60.1 (10.72)	56.7 (10.73)	0.97 (0.95-0.99)	0.001	0.99 (0.96-1.02)	0.324
Age at diagnosis						
<45 year	57 (40.1)	85 (58.9)	1.98 (1.31-3.00)	0.001	1.24 (0.66-2.34)	0.507
>/=45 year	151 (57.0)	114 (43.0)	1		1	
Gender						
Men	106 ((54.9)	87 (45.1)	0.75 (0.51-1.11)	0.144	0.91 (0.59-1.45)	0.676
Women	102 (47.7)	112 (52.3)	1			
Number current antidiabetics						
Monotherapy	81 (68.6)	37 (31.4)	1		1	
Dual therapy	93 (45.4))	112 (54.6)	2.64 (1.64-4.25)	<0.001	1.78 (1.03-3.20)	0.045
Triple therapy	34 (40.5)	50 (59.5)	3.22 (1.80-5.78)	<0.001	2.03 (1.03-4.11)	0.048
On aspirin therapy						
Yes	82 (61.7)	51 (38.3)	1		1	
No	126 (46.0)	148 (54.0)	1.89 (1.24-2.88)	0.003	1.55 (0.94-2.55)	0.082
On statin						
Yes	202 (51.9)	187 (48.1)	0.46 (0.17-1.26)	0.131	0.43 (0.11-1.85)	2.18
No	6 (33.3)	12 (66.7)	1		1	
Number of index treatment						
One	120 (61.9)	74 (38.1)	1			
Two	88 (41.3)	125 (58.7)	2.30 (1.55-3.43)	<0.001	1.80 (1.04-2.58)	0.043
Delayed TI						
Not delayed	107 (51.9)	99 (48.1)	1			
Delayed	50 (34.2)	96 (65.8)	2.08 (1.34-3.22)	0.001	2.15 (1.35-3.42)	0.001

4.5. Discussion

The aim of this study is to explore the prevalence of type 2 diabetes among Ethiopian and Nigerian participants, the two most populous countries in Africa. We also evaluated the performance of FCG and FPG against the standard 2-h PG test after 75-gm oral glucose load. These findings are based on data from Butajira in Ethiopia and Enugu State in Nigeria and should not be generalized to all of SSA without further research. We found an overall prevalence of diabetes to be 7.0%; higher among Nigerians (8.1%) than the Ethiopian (5.5%). The management of type 2 diabetes is also explored at the highest Ethiopian tertiary care hospital, Tikur Anbessa Specialized Hospital (TASH).

According to WHO STEPS reports(Motala et al., 2022), the prevalence of type 2 diabetes in SSA ranged from 1.4% to 22.5%. The prevalence of type 2 diabetes in the current study (7.0%) is higher than findings reported from Zambia (3.5%) (Bailey et al., 2016) and Kenya (4.4%) (Oti et al., 2013) but lower than a study in South Africa (15.3%) (Pheiffer et al., 2021). The prevalence of diabetes in Butajira, Ethiopia 5.5% corresponds to the national prevalence estimate of 5.0% by IDF in 2021 (Sun et al., 2022), but exceeds the 2015 National NCDs STEPS Survey (3.2%) (Gebreyes et al., 2018). The 8.1% prevalence among Nigerian participants contrasts with previous systematic review and meta-analysis showing a pooled prevalence of diabetes at 5.7% (Adeloye et al., 2017). The discrepancies in these findings may stem from differences in diagnostic criteria and tests, and sampling methods; limiting direct comparison. Unlike earlier studies relying mainly on random or FPG, this research employed both OGTT and FPG to identify diabetes cases.

Alarmingly, three-quarters (74.6%) of the individuals with diabetes were not aware of their diabetes status prior to the survey comparable with the previous findings in Nairobi (75.0%) (Oti et al., 2013). Failure to diagnose diabetes promptly and left untreated, it can lead to severe complications, enduring disabilities, and premature mortality.

This study identified a prediabetes prevalence of 15.8%, comparable to rates in previous Ethiopian(Gebreegziabiher et al., 2020) and Nigerian(Enang et al., 2014) studies, suggesting increased risk of progression of prediabetes to diabetes. Among prediabetes cases, 11.8% had IFG whereas 11.5% had IGT.

The study found that adults diagnosed with diabetes in Ethiopia are younger indicating early disease onset, comparable to a study in Indian (Chaudhary et al., 2019). Prediabetes was the highest in 45-59 age group in Ethiopian, where as it was invariably higher after age 30 in Nigeria. Ethiopian participants with diabetes had lower body weight, waist circumference and WHR comparable to previous studies in Ethiopia(Alemu et al., 2009) and Asian(Bhowmik et al., 2014; Borah & Goswami, 2017). In contrast, diabetes in Westerns appears to develop later in life (> 50 years) and is common among overweight and obese individuals (Tonstad et al., 2009). In line to this, multivariable analysis showed that age was significantly associated with type 2 diabetes in Nigerian individuals. Unlike the Ethiopian participants, Nigerians showed phenotypes more comparable to Western individuals.

Central obesity is found to be a strong predictor of DM in Ethiopia, where individuals with increased risk of central obesity are more likely to have type 2 diabetes compared to low risk for central obesity as measured by waist circumference. These findings highlight the critical role of abdominal fat in driving type 2 diabetes prevalence in Ethiopia. In contrast, central obesity is not found to be a predictor of type 2 diabetes in the Nigerian, but higher weight is significantly associated with type 2 diabetes. This suggests that cut-offs for waist circumference for predicting type 2 diabetes in African populations vary significantly from international standards, highlighting the need for tailored thresholds(Goedecke et al., 2022; Manyara, 2021).

In overweight or obese individuals, type 2 diabetes is most likely to result from adiposity-induced insulin resistance, followed by compensatory insulin secretion and subsequent β -cell dysfunction, and ultimately manifest with overt hyperglycemia(Kasuga, 2006). Conversely, in individuals who are not overweight, the underlying pathophysiology is not well comprehended and is often ascribed to the deposition of ectopic fat (Chan et al., 2009) and impairments in insulin secretion(Kibirige et al., 2019). Primary pancreatic beta cell secretory dysfunction might explain why diabetes in Ethiopia is occurring at lower age, BMI, waist circumference and waist-to-hip ratio while insulin resistance could be important among Nigerian participants as majority (64.9%) of them were obese. Inline to this, a previous Nigerian study reported a high dual burden of insulin resistance and

pancreatic beta cell secretory dysfunction among individuals with type 2 diabetes (Oli et al., 2009).

Hypertension often coexists with type 2 diabetes (Petrie et al., 2018). In the present study, it was also observed that a significant proportion of individuals with diabetes had associated hypertension (53.8% among the Nigerians and 35.9% for Ethiopians) compared to non-diabetic cases (30.6% among Nigerians and 16.0% among Ethiopians). Inline to this, Ethiopian individuals reporting a history of hypertension were more likely to have type 2 diabetes than individuals without history of hypertension. This dual adversity raises cardiovascular risk, demanding strict control of blood pressure and blood sugar levels. Hypertension also worsens micro- and macrovascular complications in diabetes, stressing the need for effective management strategies.

In SSA, the clinical management of adults with diabetes predominantly guided by clinical guidelines formulated by international diabetes associations such as ADA(American Diabetes Association Professional Practice Committee, 2022). It is noteworthy, however, that these international guidelines are developed from evidence generated through phenotyping studies conducted on Caucasian or mixed ancestry populations. Hence, it might not be applicable directly to the SSA population.

The performance of FPG and FCG to identify undiagnosed prediabetes and diabetes cases has been investigated based on 2-h PG after 75-gm oral glucose load in this study. According to ADA and IDF, both FPG and 2-h PG during 75-g oral glucose load are equally appropriate for screening of diabetes (American Diabetes Association Professional Practice Committee, 2022; Aschner, 2017), but the agreement between them was moderate for identifying diabetes and prediabetes, indicating that these tests did not consistently categorize the same individuals with abnormal blood glucose. Existing evidence from western populations and this study suggests limited agreement between FPG and 2-h PG. In the National Health and Nutrition Examination Survey (NHANES) in the US, concordance between FPG and 2-h PG was limited with a kappa statistic of 0.310(Huang et al., 2015). Nevertheless, the concordance of FPG with 2-h PG to identify non-diabetes individuals is very high with a negative predictive value (NPV) of 97.9%. In previous studies, the agreement between FPG and 2-h PG was shown to be inconsistent,

implicating the call for comprehensive studies across diverse populations to improve guidelines for the diagnosis of diabetes.

The Bland–Altman plot (Bland & Altman, 2010) showed a small mean bias (0.03) between FCG and 2-h PG tests, with 95% limits of agreement ranging from -67.2 to +67.3, with overall good agreement. This finding is similar to previous studies comparing FCG and 2-h PG. For example, a study found reasonable agreement between FCG and 2-h PG in screening for diabetes (García-Claver et al., 2020), though with notable discrepancies in some individuals, particularly at higher glucose levels.

Most importantly, with the current study, FPG was able to correctly identify 99.3% of individuals with no diabetes as measured by the 2-h PG. Several community-based studies also reported FBP is highly specific to rule-out diabetes. In an Iranian study from diabetes screening program, the specificity of FBG was comparable to the current study reported at 95.7%, indicating its reliability in screening in the community (Kianpour et al., 2021). The DECODE study compared the diagnostic performance of FPG and 2-h PG in large European populations. The study found that FPG had high specificity for identifying individuals without diabetes, with a low rate of misclassification when compared to the 2-h PG (DECODE Study Group, 1999). The ADA guidelines indicated that FPG is a reliable screening method for identifying individuals without diabetes (American Diabetes Association Professional Practice Committee, 2022). Hence, results of the current and previous studies indicate that the usefulness of FPG for screening of diabetes and prediabetes in this and other populations.

Although FPG is reported to have higher specificity and lower intra-individual coefficients of variation compared to 2-h PG (Barr et al., 2002), it was found to identify a smaller number of individuals with diabetes (Aekplakorn et al., 2015; Sinnott et al., 2015). This study showed that a significant number of individuals with diabetes would have been missed if the screening relied only on FPG. Moreover, while about three-fourth (72.5%) of individuals screened to be diabetes through FPG were also detected by 2-h PG, the latter disclosed an additional 2.1% prevalence of diabetes. These findings were consistent with results from earlier studies (Alberti et al., 2007; Cosson et al., 2010; Cowie et al., 2009). In addition, studies in Africa have consistently reported that the use of FPG

alone identified fewer diabetes cases and IGT compared to 2-h PG (Kengne et al., 2017; Werfalli et al., 2016).

In this study, the FCG test also effectively identified 99.0% of individuals with no diabetes (high specificity), but its sensitivity is low in identifying individuals with diabetes compared to the 2-h PG test, leading to a high rate of missed cases if used alone. This limitation calls the importance of incorporating the 2-h PG or other more sensitive tests in diagnostic guidelines to enhance the accuracy of diabetes detection, as FCG alone may not adequately identify individuals with IGT or postprandial hyperglycemia (Dungan et al., 2007; International Diabetes Federation, 2019a).

Screening in an apparently healthy population with lower FPG cut-off point may enhance the early detection of individuals with IGT. The current study has determined the optimal FPG cut-off values for identifying individuals with prediabetes and diabetes. This emphasizes the need to reassess screening thresholds for identifying diabetes and prediabetes in the African populations, given their significant importance for public health. The FPG cut-off value of 126 mg/dL had a very high specificity (99.3%) for identifying diabetes cases but had a relatively lower sensitivity (44.3%). Variations in sensitivity ranging from 40% to 94% and specificity from 83% to 100% for FPG 126 mg/dL was reported in a systematic review and meta-analysis (Kaur et al., 2020). Once the cut-off value was lowered furthermore it improved the sensitivity at the expense of a minor lowering of specificity. We identified an FPG level of 99 mg/dL and 105 mg/dL as the optimal cut-off values for our population in screening pre-diabetes and diabetes cases, respectively. Our finding of the optimal cut-off for FPG is consistent with the 104 mg/dL cut-off reported in a systematic review and meta-analysis for detecting diabetes (Kaur et al., 2020). But our finding of optimal threshold for FPG differs from that estimated by Hoyer, et al., 2018 (Hoyer et al., 2018).

Based on the standard 2-h PG after 75 gm oral glucose test, we also proposed an optimal FCG cut-off of 119 mg/dL to screen type 2 diabetes with improved sensitivity (44.4%) while maintaining high specificity (97.7%) compared to the conventional WHO, IDF and ADA-recommended threshold of 126 mg/dL yielding a 33.3% sensitivity in the study population (American Diabetes Association Professional Practice Committee, 2023; IDF,

2025; World Health Organization, 2003). This underscores that in screening type 2 diabetes, particularly in high-risk populations, a slightly lower threshold may help to identify more undiagnosed type 2 diabetes cases without substantially increasing false positives. Similarly, the FCG cut-off for prediabetes (99.5 mg/dL) closely matched the ADA guideline (100 mg/dL), reinforcing its validity in screening programs.

Studies from Asian countries have also suggested reduced threshold values for FPG in the range of 95.0–113.4 mg/dL for screening diabetes (Katulanda et al., 2019; Mukai et al., 2012). Similar to our results for screening pre-diabetes, other studies recommended a threshold value of 100 mg/dL as a good cut-off with acceptable sensitivity and specificity (Katulanda et al., 2019).

The study's findings emphasize the need for complementary tests, such as 2-h PG, to mitigate the limitations of a single screening method. By using multiple tests, healthcare providers can reduce the likelihood of missing true cases (false negatives) and improve the overall reliability of diabetes diagnosis. As recommended by the 2019 European Society of Cardiology (ESC) guidelines on diabetes, pre-diabetes, and CVDs developed in collaboration with the European Association for the Study of Diabetes (EASD), it may be wise to implement a sequential screening framework (Cosentino et al., 2020). In this strategy, the FPG or FCG serve as the initial blood glucose tests. An FPG $\geq 105\%$ is diagnostic for diabetes, whereas an additional 2-h PG test is recommended in individuals who did not fulfil FPG criteria but can be considered at high risk of developing diabetes. When this sequential approach would have been used in this population, about two-third of the diabetes cases would have been identified by FPG alone. Screening in this manner is less laborious with a reasonable cost and thus might be a better patient care practice by prioritizing those individuals with a genuine need for 2-h PG, thereby mitigating the risk of overdiagnosis.

In addition to high burden of diabetes and limited performance of current screening tests for early identification of individuals with diabetes or prediabetes in SSA, suboptimal management of diagnosed individuals with diabetes is also an important challenge, particularly in clinical settings where clinical inertia may compromise optimal glycemic control.

In the current study at TASH, nearly half (48.9%) of the study participants had poor glycaemic control as determined by their latest HbA1c or FBS or clinical judgement. A higher pooled prevalence of poor glycemic control (61.1%) was reported by a recent systematic review and meta-analysis in Ethiopia by Tegegne et. al. (Tegegne et al., 2024). Delay in treatment intensification (TI) is an important reason for poor glycemic control contributing to a higher risk of DM-related complications, potentially due to prolonged periods of hyperglycaemic level (García-Pérez et al., 2013; Reach et al., 2017). In the current study, patients with delayed treatment intensification had more than twice higher odds of experiencing poor glycemic control compared to those with timely treatment intensification. Other studies also indicated that patients who experienced delays in intensifying their treatment are at a higher risk of poor glycemic control and diabetes-related complications. Patients with delayed TI (≥ 5 years) had higher HbA1c levels compared to those with early intensification, indicating poorer glycemic control (Shabnam et al., 2024; Tong et al., 2018). The findings support the recommendation of early intervention through TI to optimizing glycemic outcomes. Early TI was linked to a significant decrease in both microvascular and macrovascular complications, with studies showing a 56% higher risk of complications for those with delayed TIs (Gavin et al., 2023; Shabnam et al., 2024). Initiating insulin or other therapies early can reduce HbA1c levels by approximately 1.4%, leading to better overall glycemic control (Gavin et al., 2023). Concern of hypoglycemia and limited therapeutic options are often cited as reasons for longer delays in TI among individuals with DM complications (Gavin et al., 2023).

Conversely, several studies have shown that timely intensification of antidiabetic therapy can significantly improve glycemic control in type 2 diabetes. Furthermore, it has demonstrated a significant reduction in diabetes related complications (Fu & Sheehan, 2016; Paul et al., 2015). In the current study, the median time for TI among individuals with type 2 diabetes on OAD treatment is 6 months. In comparison to the median time to TI observed in our study, previous studies have reported longer duration. A Malaysian study reported a median time to TI of 1.29 years (15.5 months) (Wan et al., 2020) while a Japanese cohort study found median times of 6.7 months for insulin intensification, 8.1 months for OAD and 9.1 months for GLP-1 receptor agonists (Maegawa et al., 2021).

Individuals on index dual therapy at the index date had longer median time to TI compared to those on monotherapy. Likewise, patients on dual index treatment had more than twice higher odds of experiencing poor glycemic control than patients on index monotherapy. Patients on initial monotherapy, such as metformin or sulfonylureas, often show a clear need for intensification when glycemic targets are not met, prompting quicker adjustments in treatment (Desai et al., 2018), whereas those on dual therapy may have more complex treatment regimens, leading to a slower recognition of inadequate control and a subsequent delay in intensification (Tan et al., 2023).

The result of this study shows that more than half of the cohort had clinical inertia. A systematic review revealed that over 50% of individuals with T2D globally experienced clinical inertia, with notably higher rates (68%) reported in developing countries such as Brazil and Thailand (Almigbal et al., 2023). This inertia can lead to prolonged periods of inadequate glycemic management, thereby increasing the risk of complications (Gavin et al., 2023).

During the course of their follow-up, over half of patients experienced treatment de-escalation. The combination of delayed TI and frequent de-escalation represents a critical clinical challenge where patients not only miss timely interventions but are also subjected to regressive treatment practices. Physicians may reduce treatment intensity to mitigate risks associated with hypoglycaemia, which can lead to adverse outcomes (Gavin et al., 2023; Tanaka et al., 2016). Frequent de-escalation can result in inadequate glycemic control, further complicating diabetes management and increasing long-term health risks (Reach et al., 2017).

In summary, using recent electronic medical record data from January 2018 to June 2024 in a real-world type 2 diabetes population, we observed that nearly half of the study participants had poor glycemic control and more than half had clinical inertia. Delayed TI by six or more months was associated with higher odds of poor glycemic control. In addition, poor glycemic control was significantly associated with the number of current and index antidiabetic drugs. We recommend healthcare providers to intensify DM treatment to enhance better glycemic control and reduce complications.

4.6. Implication of the Study

4.6.1. Practice implication

The findings of this study highlight several critical areas for improving diabetes care and prevention in rural and peri-urban populations in SSA. Given the high prevalence of undiagnosed diabetes (75%) and prediabetes (16.5%), healthcare providers should prioritize community-based screening programs. Since FPG alone misses nearly half of diabetes cases, combining FPG with other diagnostic measures, such as 2-h PG after 75-gm oral glucose tolerance tests, may enhance detection. Additionally, adopting a lower FPG cut-off could improve early identification of at-risk individuals, allowing for timely lifestyle interventions and treatments. In Ethiopia, where diabetes presents atypically—with younger, leaner individuals—clinicians should maintain a high index of suspicion even in non-obese patients to avoid missed diagnoses. Furthermore, the high rates of uncontrolled blood glucose levels and clinical inertia emphasize the need for structured diabetes management protocols, including regular follow-ups and prompt treatment intensification to prevent complications.

4.6.2. Policy implication

Policymakers in SSA should integrate these findings into national diabetes strategies by expanding screening initiatives, particularly in underserved rural and peri-urban areas. Given the limitations of FPG, health systems should invest to enhance the affordability and accessibility of diagnostic tools, such as 2-h PG after 75-gm OGTT, to improve detection rates. Policies in SSA shall promote public health campaigns to raise awareness about diabetes risk factors, especially in Ethiopia, where atypical presentations may lead to underdiagnosis. Policies should also mandate regular provider training to reduce clinical inertia and ensure timely treatment adjustments, particularly at referral hospitals like TASH. Finally, MoH should collaborate with international organizations to align FPG cut-offs with global standards including ADA, WHO and IDF recommendations to facilitate early intervention and reduce the long-term burden of diabetes in the region.

4.7. Strength and Limitation of the Study

4.7.1. Strength of the study

This study employed a community-based multi-center design on 1727 study participants from SSA, facilitating the extrapolation of outcomes to the broader population of the research settings within the region. In contrast to numerous prior investigations in the region that relied on random or fasting blood glucose measurements, we have used both fasting and 2-hr OGTT, thereby enhancing the accuracy of diabetes detection.

The diagnostic capacity of FPG was evaluated against the reference 2-h PG test, to our knowledge, one of the first such studies in the SSA population. Furthermore, setting the FPG and FCG cut-off levels corresponding to a 2-h PG of 200 mg/dL and 140 mg/dL, the gold standard for diabetes diagnosis, substantially adds to the novelty of this study in the SSA setting.

4.7.2. Limitation of the study

It is crucial to acknowledge that the cross-sectional nature of the design for the epidemiologic predictors precludes the confirmation of the course of causal pathways. In addition, a single FCG, FPG or 2-h PG measurement was utilized to identify individuals with pre-diabetes or diabetes while the criteria for the diagnosis of diabetes requires repeated measurement in asymptomatic individuals. However, given the large study population, the consequences of this limitation are expected to be negligible.

The findings are specifically tailored to the study settings at the two most populous countries in SSA and may not be fully applicable to other regions in SSA with different healthcare systems, cultural contexts, or economic conditions. This limitation restricts the broader application of the study's conclusions beyond the immediate geographical areas of study sites.

The reliability of the six-and-half year-long dataset used in the diabetes management study at TASH is dependent on the accuracy of optimal recording of clinical information from the Iwket-care registry. Potential inconsistencies and missing data could affect the study's analysis and the conclusions on timely treatment intensification and glycemic control.

Chapter 5. CONCLUSION AND RECOMMENDATION

5.1. Conclusion

In the present study, there is a notable occurrence of diabetes at a relatively high rate of 7.0% among rural, peri-urban and urban populations in SSA, higher among Nigerians (8.1%) than the Ethiopian (5.5%). The prevalence of prediabetes was 16.5% in the present study. Three-quarters of diabetes cases were undiagnosed in the region.

We observed that individuals with diabetes in Ethiopia are characterized by younger age of onset, leanness, lower BMI and waist circumference compared to those in Nigeria. The diabetes phenotype encountered in Ethiopia is very different from the classical type 2 diabetes seen in the West while Nigerian diabetes cases had comparable phenotypes to Westerns.

FPG and FCG were able to correctly identify 99.3% and 99.0% of individuals without diabetes, respectively, indicating its usefulness for screening of diabetes. But, a significant percentage, 44.4% and 48.0%, of diabetes cases would have remained undetected if FPG or FCG, respectively, had been used alone. The use of a lower cut-off values, at 105 mg/dL for FPG and 119 mg/dL for FCG, enhanced the detection of individuals with diabetes. Likewise, an FPG and FCG cut-off at 99 mg/dL, comparable to that of ADA and IDF, can improve early detection of individuals at risk of type 2 diabetes.

We observed that more than half of individuals with type 2 diabetes had uncontrolled blood glucose levels and clinical inertia at TASH. Delayed TI by six or more months was associated with an increase in uncontrolled blood glucose levels.

5.2. Recommendation

As three-quarters of diabetes cases were undiagnosed in SSA, intensified early screening of type 2 diabetes is strongly recommended in the region.

As the clinical profiles of individuals with type 2 diabetes in SSA, particularly in Ethiopia, is unique, careful considerations when formulating therapeutic strategies for diabetes specifically tailored to the distinct physiological and clinical characteristics of populations in SSA. This underscores the imperative need for further research. The use of 2-h PG

test is recommended to identify older individuals, females and non-obese persons with diabetes who would be missed by measuring only FPG. In all cases implementing a sequential screening model has the potential to enhance patient care, minimize unnecessary over-diagnosis, and optimize efficient resource use.

Overall, re-evaluation of screening thresholds for FPG and FCG for the early identification of individuals with diabetes and prediabetes has pivotal public health implications. Our study emphasizes the need for a thorough and careful revision of diabetes screening guidelines tailored to demographic, clinical, and lifestyle factors influencing the screening and diagnosis of diabetes.

We also recommend healthcare providers for early and timely intensification of type 2 diabetes treatment to enhance better glycemic control and reduce complications.

5.3. Direction for Further Research

The findings of this study highlight several critical gaps in diabetes research within SSA that warrant further investigation. Future studies should explore the underlying reasons for the differing diabetes phenotypes between Ethiopia and Nigeria. Genetic, environmental, and lifestyle factors contributing to these variations should be examined to tailor prevention and treatment strategies. In addition, given the high proportion of undiagnosed diabetes and the limitations of FPG and FCG in detection of diabetes, research should evaluate cost-effective, alternative screening methods in low-resource settings.

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ORIGINAL PAPERS

Publication – 1

ORIGINAL ARTICLE OPEN ACCESS

Comparative Analysis of Type 2 Diabetes Prevalence and Clinical Profiles in Ethiopia and Nigeria

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Received: 4 October 2024 | **Revised:** 6 February 2025 | **Accepted:** 10 March 2025

Funding: This work was supported by National Institute for Health Research, 34558a_CRT.

Keywords: clinical characteristics | diabetes | oral glucose tolerance test | sub-Saharan Africa

ABSTRACT

Aims: We aimed to determine the prevalence of diabetes and the clinical profiles of Type 2 diabetes in Ethiopia and Nigeria.

Methods: A community-based cross-sectional study was carried out from November 01, 2020 to October 21, 2021 among 1727 participants using a multistage sampling method. The WHO's STEPs tool was employed. Both fasting and oral glucose tolerance tests were used for screening and American Diabetes Association's (ADA's) diagnostic criteria was used. Stata version 17 was used for analysis. Analysis of Variance (ANOVA) and the Chi-square test were used to compare variables. Significance was declared at a *p*-value less than 0.05.

Result: Of the surveyed participants, 872 (50.5%) were men and the mean age was 44.6 years. The overall prevalence of prediabetes and diabetes was 15.8% and 7.0%, respectively. Impaired fasting glycaemia and glucose tolerance were 11.8% and 11.5%, respectively. The prevalence of newly diagnosed diabetes was 3.4% by fasting and 4.0% by oral glucose tolerance test. Participants with normal blood glucose were younger and had a lower weight, body mass index (BMI), waist circumference, diastolic, and systolic blood pressure, and history of hypertension than those with prediabetes and diabetes.

Conclusion: In the present study, there is a notably high diabetes and prediabetes prevalence in the study settings. Individuals with diabetes in Ethiopia compared to Nigeria and the West have different anthropometric and clinical profiles characterized by a young age of onset, leanness, lower BMI, and waist circumference. Hence, the management of diabetes shall be tailored to the unique physiologic and clinical profiles of the population.

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1 | Introduction

Diabetes is a chronic disorder characterized by elevated blood glucose levels, caused by either inadequate insulin production in the pancreas or resistance to insulin [1]. It poses a significant worldwide health challenge, accounting for more than half a billion cases (10.5% of the world's adult population) and 6.7 million deaths among adults in 2021 [2] projected to rise to 643 million by 2030.

The number of individuals with diabetes in Sub-Sahara Africa (SSA) was about 24 million by 2021, with the highest proportion of undiagnosed diabetes cases (53.6%) as compared to high-income countries (28.8%) [2]. According to the report from the International Diabetes Federation (IDF) [2], Nigeria and Ethiopia hold the second and fourth positions, respectively, in terms of the highest number of people with diabetes in SSA.

Guidelines recommend the early detection of diabetes to achieve adequate plasma glucose control and delay the onset of complications [3, 4]. Both the American Diabetes Association (ADA) and IDF recommend fasting plasma glucose (FPG) and the 2-h postprandial oral glucose tolerance test (OGTT) to identify prediabetes and diabetes [4, 5]. These methods come with distinct advantages and disadvantages in practical use. In healthcare settings, FPG is preferred for identifying diabetes in high-risk groups due to its convenience and cost-effectiveness compared to OGTT. However, it should be noted that OGTT surpasses FPG in sensitivity, diagnosing a greater number of individuals with prediabetes and diabetes [6], despite being less feasible for mass screening [5].

According to a recent systematic review and meta-analysis, the prevalence of Type 2 diabetes in SSA varied from 1.4% to 22.5% [7]. There are concerns about the accuracy of these findings due to the study methods used, such as sampling strategies and study settings. Moreover, studies relied on less reliable self-report, random, or fasting capillary blood samples, often conducted in health facilities, which may affect the overall reliability of the results [8].

In order to develop effective and context-specific diabetes interventions, it is crucial to understand the unique sociodemographic and clinical profiles of affected populations. Contrary to the western population, diabetes has also been reported to be common among young and non-overweight individuals, especially among Asian and SSA countries [9]. Exploring the variability in sociodemographic and clinical characteristics of people with diabetes within SSA provides a foundation for effective interventions. But evidence on the anthropometric, socio-demographic, and clinical profile of diabetes is limited to formulate tailored recommendations for prevention, screening, diagnosis, and treatment of diabetes in SSA.

Thus, there is a need for high-quality population-based studies in SSA to obtain more accurate and comprehensive data on the prevalence of Type 2 diabetes. This research aimed also to produce population-based evidence on the prevalence of diabetes and prediabetes among participants from the two most populous countries in SSA, Ethiopia and Nigeria. Moreover, this paper investigates the heterogeneity of the clinical phenotypes of type 2 diabetes in SSA, using examples from two populations on the continent.

2 | Methods

2.1 | Study Design

The Diabetes Epidemiologists' Network in Sub-Saharan Africa (DENSSA) represents a collaborative research initiative involving the University of Dundee in the United Kingdom, Addis Ababa University in Ethiopia, and the University of Nigeria in Nigeria. A community-based cross-sectional study was carried out from November 01, 2020 to October 21, 2021.

2.2 | Survey Population

The study was conducted using a population from the Butajira Rural Health Program (BRHP) in central Ethiopia and Enugu State district in Nigeria. BRHP consisted of one semi-urban and nine rural kebeles, which represent the smallest administrative units in Ethiopia.

2.3 | Sample Size Determination and Sampling Procedure

Sample size was determined using the single population proportion formula, using a 3.9% prevalence of diabetes for SSA [10], $d = 1.25\%$ for better precision, and considering a design effect of two for complex multistage design. Anticipating a 10% non-response, about 1000 individuals aged ≥ 18 years from each of the two study sites were included.

We employed a multistage sampling method to choose the participants for the study. For the Ethiopian study, six kebeles (smallest administrative unit) were selected randomly out of 10 kebeles that are part of the BRHP, whereas three Local Government Areas (LGAs)—Enugu North, Enugu West, and Nkanu West in Enugu State—were selected in Nigeria. A proportional sampling method was used to select households from each administrative unit. A randomly selected adult was invited to participate in the study. In households with multiple eligible individuals, a single person was randomly chosen.

2.4 | Inclusion and Exclusion Criteria

This study included adults who were 18 years or older and provided their consent to participate. Individuals who did not fast for at least 8 h, pregnant women, and those who were taking medications such as corticosteroids, atypical antipsychotics, and protease inhibitors were excluded from the study. Individuals with a history of diabetes were also not included for the OGTT.

2.5 | Survey Instrument

The study used the WHO's STEPwise approach to NCD risk factor surveillance (STEPS) instrument version 3.1 to assess diabetes risk factors [11].

Summary

- We found that Ethiopian individuals with diabetes had a different anthropometric and clinical profile characterized by a young age of onset, leanness, lower BMI, and waist circumference compared to Nigerians and the west.
- This study highlights the imperative need for further research and careful considerations when formulating therapeutic strategies for diabetes specifically tailored to the distinct physiological and clinical characteristics of populations in Ethiopia, Nigeria, and Sub-Saharan Africa at large.

2.6 | Data Collection Procedure

Data collectors were trained on study objectives, survey tools, physical measurements, and blood sampling collection and testing. Tools were pre-tested on 25 participants from each site to refine the questionnaire's structure, flow, and interview time before data collection. Local guides (health workers, volunteers) aided in reaching households. On the first day for STEP I data collection, households were visited, and the aim of the survey was explained. Then respondent's demographic and socioeconomic status; tobacco, alcohol, and Khat use; diet, including fruit, vegetable, dietary salt intake; physical activity; history of raised blood pressure, diabetes, raised cholesterol and/or CVDs, and lifestyle advice received were collected. Physical measurements (STEP 2) including blood pressure (BP), heart rate, weight, height, waist, and hip circumference, and laboratory tests (STEP 3) were taken on the next day after the questionnaire survey. Blood pressure and heart rate were taken twice on the right arm while seated, using a Folee DX-B1 monitor (Jiangsu Folee Medical Equipment, China). If BP readings differed by > 5 mmHg, a third was taken and the mean of two (or three) readings was used. Blood samples were collected from participants who had fasted for at least 8 h at nearby health facilities.

Capillary blood glucose level was determined using Fia Biomed Precisa blood glucose monitoring system (Fia Biomed GmbH, Emsdetten, Germany). Participants with a capillary fasting glucose level ≥ 126 mg/dL were referred to the nearby health center. For those with capillary blood glucose level < 180 mg/dL, two blood samples, 4 mL before and 2 mL after the 75 g oral glucose drink, were collected. The fasting blood and the 2-h post glucose load samples were collected into two 2 mL fluoride oxalate tubes (gray top). OGTT was performed using a standard solution, Polycal Liquid 200 mL (Nutricia Ltd., Wiltshire, UK).

2.7 | Diagnostic Criterion

The definition of the ADA is used to identify diabetes and pre-diabetes cases [4]. The results of plasma glucose testing are classified as follows: isolated impaired fasting glucose (IFG) is defined as plasma glucose levels between 100 mg/dL and 125 mg/dL, with a 2-h PG of < 140 mg/dL. Isolated impaired glucose tolerance (IGT) is defined as a glucose level < 100 mg/dL of fasting and a 2-h PG between 140 mg/dL and 199 mg/dL. Newly

diagnosed diabetes is defined as a FPG level of ≥ 126 mg/dL or 2-h OGTT of ≥ 200 mg/dL or both. When people receive a medical diagnosis of diabetes from healthcare providers previously, it is regarded as a known diabetes case.

2.8 | Data Quality Assurance

The items of the tool were translated into local languages, then translated back to English to assure consistency and accuracy. Based on the results of the pre-test and back translation, the questionnaires were further reviewed and completed. Field data supervisors carried out intensive monitoring and follow-up during each phase of data collection.

2.9 | Statistical Analysis

Data analysis was conducted on Stata V.17 software program (StataCorp. Stata Statistical Software: Release 17. College Station, TX: Stata Corp LP). Estimates of continuous variables were summarized as mean (SD) and frequencies and proportions (95% CI) for categorical variables. Comparison of means of quantitative variables across different diabetes categories was done by analysis of variance. Association between categorical variables was checked using chi-square testing. Statistical significances were tested at $p < 0.05$.

3 | Results

3.1 | Demographic Information Results

Among the 2000 planned samples, 1727 individuals were contacted and given consent for the survey, making the overall response rate 86.4%. The rest refused to provide blood samples. The characteristics of individuals who refused to provide blood samples were not significantly different from those who provided blood samples, as shown in [Supporting Information \(Data S1\)](#).

Out of the entire survey population, 872 individuals (50.5%) were men. The mean age of the participants was 44.6 years, with Ethiopians having a mean age of 41.0 years and Nigerians having a mean age of 47.2 years. More than half of the respondents (54.3%) were under the age of 45, as presented in [Table 1](#).

3.2 | Social Drug Use

Among the surveyed participants, 6.7% were current smokers, while 27.4% of the study participants drank alcohol at least once within 30 days of the survey, as presented in [Table 2](#).

3.3 | Dietary Patterns and Physical Activity

On average, participants consumed fruits 2.7 days and vegetables 4.6 days per week. In terms of servings per day, they had

TABLE 1 | Summary of sociodemographic information by country of residence, Ethiopia and Nigeria, 2021.

Characteristics	Country		Total, <i>n</i> (%)
	Ethiopia, <i>n</i> (%)	Nigeria, <i>n</i> (%)	
Sex			
Men	272 (37.3)	600 (60.2)	872 (50.5)
Women	458 (62.7)	397 (39.8)	855 (49.5)
Age, years			
Mean (SD)	41.0 ($\pm$ 13.62)	47.2 ($\pm$ 17.58)	44.6 ($\pm$ 16.31)
18–29	149 (20.4)	189 (19.0)	338 (19.6)
30–44	311 (42.6)	289 (29.0)	600 (34.7)
45–59	167 (22.9)	223 (22.4)	390 (22.6)
60–69	71 (9.7)	153 (15.3)	224 (13.0)
≥ 70	32 (4.4)	143 (14.3)	175 (10.1)
Current residence			
Urban ^a	455 (62.3)	534 (53.6)	989 (57.3)
Rural	275 (37.7)	463 (46.4)	738 (42.7)
Religion			
Christian	205 (28.1)	985 (98.8)	1190 (68.9)
Muslim	525 (71.9)	3 (0.3)	528 (30.6)
Traditional beliefs	—	9 (0.9)	9 (0.5)
Current marital status			
Never married	63 (8.6)	225 (22.6)	288 (16.7)
Currently married	570 (78.1)	635 (63.7)	1205 (69.8)
Widowed	60 (8.2)	131 (13.1)	191 (11.1)
Divorced/separated	37 (5.1)	6 (0.6)	43 (2.5)
Highest grade of education completed			
No formal education	293 (40.1)	168 (16.9)	461 (26.7)
Some primary education	212 (29.0)	53 (5.3)	265 (15.3)
Completed primary education	77 (10.5)	150 (15.0)	227 (13.1)
Junior secondary education	56 (7.7)	38 (3.8)	94 (5.4)
Senior secondary education	57 (7.8)	226 (22.7)	283 (16.4)
More than secondary education	35 (4.8)	362 (36.3)	397 (23.0)
Occupation			
Government employee	43 (5.9)	204 (20.5)	247 (14.3)
Non-government employee	22 (3.0)	19 (1.9)	41 (2.4)
Self employed	9 (1.2)	261 (26.2)	270 (15.6)
Unpaid	656 (89.9)	513 (51.5)	1169 (67.7)

Abbreviation: SD: Standard deviation.

^aSemi-urban for the Ethiopian study participants.

1.3 servings of fruits and 1.9 servings of vegetables daily. Nearly one-fourth (22%) were not meeting WHO's physical activity recommendations, as shown in Table 3.

3.4 | History Cardiovascular Disorders

Nearly half (49.2%) of the participants had never had their BP measured. Of those who had measurements, 22.2% were diagnosed with high BP, accounting for 11.3% of the study participants (Table 4).

3.5 | Physical Measurements

The prevalence of high BP (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg) was 27.8%. Nigerian participants had an average

weight of 72.2 kg, while Ethiopians had 60.4 kg. The overall mean body mass index (BMI) was 26.5 kg/m², with Nigerians having a higher BMI (28.6 kg/m²) than Ethiopians (23.6 kg/m²). Nearly two-thirds of the surveyed participants (63.5%) had normal metabolic risk based on waist circumference as shown in Table 5.

3.6 | Prevalence of Diabetes and Prediabetes

In the survey, 15.8% (265 individuals) met prediabetes criteria. Impaired fasting glycaemia (IFG) was present in 11.8%, while 11.5% exhibited impaired glucose tolerance (IGT). Among 1550 individuals tested by both fasting and OGTT, isolated IFG and IGT were observed in 5.5% and 5.8% of participants, respectively (Table 6).

Among the survey participants, 118 individuals (7.0%) met at least one of the criteria for diabetes. Three-fourths (74.6%) of the people diagnosed with diabetes were not aware of their diabetes status prior to the survey, yielding a 5.6% prevalence of undiagnosed diabetes in the region. In addition to 30 (1.7%) participants with a history of diabetes, we identified 54 (3.4%) new individuals with diabetes by FPG measurement and 63 (4.0%) by OGTT (Figure 1).

As presented in Table 7, the mean (SD) age of Ethiopians with diabetes was 47.4 years (SD 14.2), nearly 7 years older compared to the non-diabetic cases. Furthermore, the mean weight among Ethiopians with diabetes is 68.6 kg (SD 17.0 kg), significantly higher than their non-diabetic counterparts ($p < 0.001$). Similarly, Ethiopians with diabetes had significantly higher mean BMI (26.8 ± 5.8 kg/m²) and waist circumference (85.1 ± 13.7 cm) compared to non-diabetic participants ($p < 0.01$).

The mean (SD) age among Nigerians with diabetes was 53.5 years (SD 14.2), which was over 8 years higher than the mean age of non-diabetic cases, recorded at 45.2 years (SD 18.2). Moreover, Nigerians with diabetes had a higher mean weight of 83.9 kg (SD 25.5 kg) compared to their non-diabetic counterparts ($p < 0.001$). In addition, Nigerian diabetes cases had significantly higher mean BMI, waist circumference, DBP, and SBP as compared to non-diabetic participants ($p < 0.001$).

With the multivariable logistic regression analysis (Data S1), sex is identified as a common predictor of the prevalence of Type 2 diabetes in both Nigeria and Ethiopia. Ethiopian males were nearly four times more likely to have DM than their female counterparts (AOR = 3.80, 95% CI = 1.22–11.82, $p = 0.021$), while Nigerian males were nearly three times more likely to have DM than females (AOR 2.89, 95% CI 1.35–6.18, $p = 0.007$). In addition, older age and urban residence are significant predictors in Nigeria, with urban dwellers over twice as likely to develop type 2 diabetes (AOR = 2.45, 95% CI = 1.33–4.49, $p = 0.004$). Central obesity is also a strong predictor in Ethiopia, with higher risks linked to greater odds of DM; whereas, weight is a significant factor instead in Nigeria. Hypertension is also a key predictor in Ethiopia, increasing DM odds by 4% (AOR 3.68, 95% CI 1.07–12.61, $p = 0.038$).

TABLE 2 | Pattern of substance use among all respondents by country of residence, Ethiopia and Nigeria, 2021.

Participant characteristics	Ethiopia	Nigeria	Total
Cigarette smoking			
Current smokers, <i>n</i> (%)	35 (4.8)	81 (8.1)	116 (6.7)
Daily smokers, <i>n</i> (%)	27 (3.7)	42 (4.2)	69 (4.0)
Former smokers, <i>n</i> (%)	23 (3.2)	46 (4.6)	69 (4.0)
Ever smoked, <i>n</i> (%)	58 (7.9)	127 (12.7)	185 (10.7)
Mean (SD) age of smoking started, years	28.9 $\pm$ 6.7	26.5 $\pm$ 7.7	27.2 $\pm$ 7.5
Mean (SD) duration of smoking, years	19.3 $\pm$ 13.1	14.1 $\pm$ 11.1	15.5 $\pm$ 11.8
Alcohol consumption, <i>n</i> (%)			
Current drinker	107 (14.7)	367 (36.8)	474 (27.4)
Drink in past 12 months, not current	129 (17.7)	473 (47.4)	602 (34.9)
Past 12-month abstainer	494 (67.6)	157 (15.7)	651 (37.7)
Life time abstainer	567 (77.7)	544 (54.6)	707 (59.1)
Khat user, <i>n</i> (%)			
Current chewer	430 (58.9)	NA	430 (58.9)
Past chewer	37 (5.1)	NA	37 (5.1)
Never chewer	264 (36.2)	NA	264 (36.2)

Abbreviations: NA, not applicable; SD, standard deviation.

TABLE 3 | Dietary pattern and physical activity of participants by country of residence, Ethiopia and Nigeria, 2021.

Fruit and vegetables	Ethiopia	Nigeria	Total
Fruits			
Mean (SD) number of days fruits consumed in a week	1.9 ± 1.0	3.4 ± 1.7	2.7 ± 1.6
Mean (SD) number of servings of fruits per day	1.5 ± 0.8	1.1 ± 0.5	1.3 ± 0.7
Vegetables			
Mean (SD) number of days vegetables consumed in a week	4.3 ± 2.1	4.9 ± 1.7	4.6 ± 1.9
Mean (SD) number of servings of vegetables per day	2.4 ± 0.8	1.5 ± 0.7	1.9 ± 0.9
Salt^a			
Add salt to food when cooking or preparing food, <i>n</i> (%)	508 (69.6)	113 (11.3)	621 (36.0)
Eat processed foods high in salt, <i>n</i> (%)	110 (15.1)	300 (30.1)	410 (23.7)
Quantity of salt consumption, <i>n</i> (%)			
Far too much or too much	108 (14.8)	19 (1.9)	127 (7.4)
Just the right amount	433 (59.3)	932 (93.5)	1365 (79.0)
Too little or far too little	189 (25.9)	46 (4.6)	235 (13.6)
Physical activity			
Not meeting WHO's recommendations, <i>n</i> (%)	173 (23.7)	205 (20.7)	378 (21.9)
Levels of physical activity^b, <i>n</i> (%)			
High level	374 (51.2)	621 (62.3)	995 (57.6)
Moderate level	162 (22.2)	243 (24.4)	405 (23.5)
Low level	194 (26.6)	133 (13.3)	327 (18.9)
Contribution of types of activities (%)			
Work-related activity	63.6	55.7	59.0
Transport-related activity	34.6	34.0	34.2
Recreational-related activity	1.8	10.3	8.8

Abbreviations: SD, standard deviation; WHO, World Health Organization.

^aSelf-reported.

^bAccording to WHO, high-level physical activity is vigorous-intensity activity for at least 3 days per week, achieving at least 1500 MET-min per week; or seven or more days of any combination of walking, moderate- or vigorous-intensity activities achieving a at least 3000 MET-min per week. Moderate-level physical activity is meeting any of the following criteria: three or more days of vigorous-intensity activity of at least 20 min per day; or five or more days of moderate-intensity activity or walking for at least 30 min per day; or five or more days of any combination of walking, moderate- or vigorous-intensity activities achieving at least 600 MET-min per week. Low-level physical activity is a person not meeting the criteria for moderate- or high-level categories.

TABLE 4 | History cardiovascular diseases by country of residence, Ethiopia and Nigeria, 2021.

History	Ethiopia, % (95% CI)	Nigeria, % (95% CI)	Total, % (95% CI)
History of hypertension			
Never measured	73.4 (70.1–76.5)	31.5 (28.7–34.4)	49.2 (46.9–51.6)
Hypertensive	9.7 (7.8–12.1)	12.4 (10.5–14.6)	11.3 (9.9–12.9)
Non-hypertensive	16.8 (14.3–19.7)	56.1 (53.0–59.1)	39.5 (37.2–42.8)
History of raised cholesterol			
Never tested	97.1 (95.6–98.1)	91.1 (89.1–92.7)	93.6 (92.4–94.7)
High cholesterol	1.8 (1.0–3.0)	1.5 (0.9–2.5)	1.6 (1.1–2.3)
Normal cholesterol	1.1 (0.5–2.1)	7.4 (5.9–9.2)	4.7 (3.8–5.9)
History of heart attack or chest pain			
	6.6 (5.0–8.6)	8.1 (6.6–10.0)	7.5 (6.3–8.8)

Abbreviation: CI, confidence interval.

TABLE 5 | Distribution of raised BP, weight, height, BMI, waist circumference, and WHR by country of residence, Ethiopia and Nigeria, 2021.

Variables	Ethiopia	Nigeria	Total
Blood pressure			
Raised BP, % (95% CI)	17.7 (15.1–20.6)	35.6 (32.5–38.5)	27.8 (25.8–30.0)
Raised SBP, % (95% CI)	11.1 (9.0–13.6)	31.1 (28.3–34.1)	22.6 (20.6–24.6)
Raised DBP, % (95% CI)	14.1 (11.8–16.8)	25.0 (22.4–27.8)	20.3 (18.5–22.3)
Weight and height ^a			
Mean weight, kg (95% CI)	60.4 (59.6–61.3)	72.2 (71.2–73.3)	67.1 (66.4–67.9)
Mean height, cm (95% CI)	159.9 (159.3–160.6)	161.5 (160.6–162.3)	160.8 (160.2–161.4)
BMI ^{b,c} % (95% CI)			
Mean BMI	23.6 (23.3–24.0)	28.6 (27.6–29.6)	26.5 (25.9–27.1)
Underweight	7.0 (5.4–9.1)	2.4 (1.6–3.5)	4.4 (3.5–5.4)
Normal	63.3 (59.7–66.7)	37.8 (34.8–40.9)	48.8 (46.4–51.1)
Overweight	21.2 (18.4–24.4)	29.7 (26.9–32.6)	26.0 (23.0–28.2)
Obese	8.5 (6.7–10.7)	30.2 (27.4–33.1)	20.9 (19.0–22.8)
Waist circumference ^d , % (95% CI)			
Normal risk	80.6 (77.5–83.3)	50.8 (47.6–53.9)	63.5 (61.2–65.8)
Increased risk	11.1 (9.0–13.6)	20.7 (18.3–23.3)	16.6 (14.9–18.4)
Substantially increased risk	8.4 (6.6–10.6)	28.6 (25.8–31.5)	19.9 (18.1–21.9)
Waist to hip ratio (WHR), % (95% CI)			
Mean WHR	0.85 (0.84–0.86)	NA	0.85 (0.84–0.86)
Normal	65.0 (61.5–68.4)	NA	65.0 (61.5–68.4)
Obese	35.0 (31.6–38.5)	NA	35.0 (31.6–38.5)

Abbreviations: BP, blood pressure; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure; WHR, waist-to-hip ratio.

^aOverall, 27 values were missing.

^bOverall, 29 values were missing.

^cWHO cut off for BMI classification is used.

^dWaist circumference classification is based on WHO recommendation where normal risk is ≤ 94 cm for men and ≤ 80 cm for women; increased risk is > 94 – 102 cm for men and > 80 – 88 cm for women; and substantial increased risk is > 102 cm for men and > 88 cm for women.

4 | Discussion

The aim of this study is to explore the prevalence and phenotypes of Type 2 diabetes among Ethiopian and Nigerian participants, the two most populous countries in Africa. The findings from this study are based on data from Butajira in Ethiopia and Enugu State in Nigeria and should not be generalized to all of SSA without further research. We found an overall prevalence of diabetes to be 7.0%; higher among Nigerians (8.1%) than the Ethiopians (5.5%).

According to WHO STEPS reports [7], the prevalence of Type 2 diabetes in SSA ranged from 1.4% to 22.5%. The prevalence of Type 2 diabetes in the current study (7.0%) is higher than findings reported from Zambia (3.5%) [12] and Kenya (4.4%) [13] but lower than a study in South Africa (15.3%) [14]. The prevalence of diabetes in Butajira, Ethiopia 5.5% corresponds to the national prevalence estimate of 5.0% by IDF in 2021 [2], but exceeds the 2015 National NCDs STEPS Survey (3.2%) [15]. The 8.1% prevalence among Nigerian participants contrasts

with a previous systematic review and meta-analysis showing a pooled prevalence of diabetes at 5.7% [16]. The discrepancies in these findings may stem from differences in diagnostic criteria and tests, and sampling methods; limiting direct comparison. Unlike earlier studies relying mainly on random or FPG, this research employed both OGTT and FPG to identify diabetes cases.

Alarming, three-quarters (74.6%) of the individuals with diabetes were not aware of their diabetes status prior to the survey, comparable with the previous findings in Nairobi (75.0%) [13]. Failure to diagnose diabetes promptly and, if left untreated, it can lead to severe complications, enduring disabilities, and premature mortality.

This study identified a prediabetes prevalence of 15.8%, comparable to rates in previous Ethiopian [17] and Nigerian [18] studies, suggesting an increased risk of progression of prediabetes to diabetes. Among prediabetes cases, 11.8% had IFG, whereas 11.5% had IGT. Among the study participants tested by both OGTT and fasting, isolated-IFG was found in 5.4% of

TABLE 6 | Percentage of prediabetes and diabetes by sex and country of residence, Ethiopia and Nigeria, 2021.

Test results	Number of tests	Sex		Country		Total, <i>n</i> (%)
		Men, <i>n</i> (%)	Women, <i>n</i> (%)	Ethiopia, <i>n</i> (%)	Nigeria, <i>n</i> (%)	
Prediabetes						
Impaired fasting glucose	1614	101 (12.4)	89 (11.2)	31 (4.8)	159 (16.4)	190 (11.8)
Impaired glucose tolerance	1588	105 (13.3)	79 (9.9)	27 (4.1)	156 (16.8)	184 (11.5)
Isolated impaired fasting glucose	1550	45 (5.8)	38 (4.9)	13 (2.1)	70 (7.5)	83 (5.4)
Isolated impaired glucose tolerance	1550	53 (6.8)	39 (5.1)	15 (2.4)	77 (8.3)	92 (5.9)
All prediabetes	1682	146 (17.2)	119 (14.3)	41 (5.8)	224 (22.9)	265 (15.8)
Diabetes						
Known people with diabetes	1725	20 (2.3)	10 (1.2)	19 (2.6)	11 (1.1)	30 (1.7)
New diabetes by fasting	1614	42 (5.1)	12 (1.5)	4 (0.6)	50 (5.2)	54 (3.3)
New diabetes by 2 h OGTT	1588	35 (4.4)	28 (3.5)	20 (3.0)	43 (4.6)	63 (4.0)
All newly diagnosed diabetes	1574	58 (7.3)	30 (3.9)	20 (3.2)	68 (7.2)	88 (5.6)
Overall prevalence of diabetes	1682	78 (9.2)	40 (4.8)	39 (5.5)	79 (8.1)	118 (7.0)

Abbreviation: 2 h OGTT, 2-hour oral glucose tolerance test.

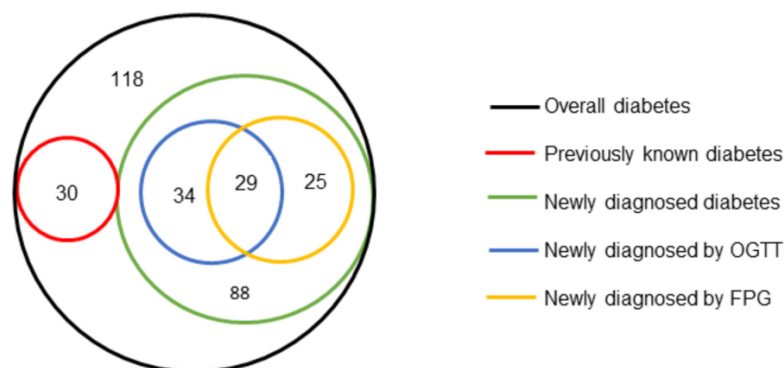


FIGURE 1 | Number of previously diagnosed and newly diagnosed diabetes cases identified by FBG and 2h OGTT, Ethiopia and Nigeria, 2021. FPG, fasting plasma glucose; OGTT, oral glucose tolerance test.

participants, while isolated-IGT was present in 5.9% of participants. The slightly higher I-IGT rates emphasize the importance of OGTTs for early detection of abnormal glucose regulation, better identifying those at risk for diabetes and its complications. In individuals with I-IFG, the major disturbance is hepatic insulin resistance, while I-IGT individuals have normal to slightly reduced hepatic insulin sensitivity and moderate-to-severe muscle

insulin resistance; those with combined IFG and IGT tend to have both muscle and hepatic insulin resistance [19].

The African continent has the most genetic heterogeneity in the world that could implicate the diversified clinical profiles of diabetes [20]. SSA is also unique in that it continues to have a high rate of infectious diseases and other problems including

TABLE 7 | Characteristics of study participants by diabetes status and country, Ethiopia and Nigeria (N=1682).

Variables	Total (N=1682)	Ethiopia (n=704)				Nigeria (n=978)			
		Normal (n=625)	Prediabetes (n=41)	Diabetes (n=39)	p	Normal (n=678)	Prediabetes (n=224)	Diabetes (n=79)	p
Men	848 (50.4)	226 (36.2)	14 (34.1)	18 (46.2)	0.432	398 (59.0)	132 (58.9)	60 (75.9)	0.013
Age (years)	1682	40.5 ± 13.5	42.5 ± 13.1	47.4 ± 14.2	0.007	45.2 ± 18.2	50.7 ± 15.9	53.5 ± 14.2	< 0.001
Urban	883 (52.5)	248 (39.7)	15 (36.6)	9 (23.1)	0.112	346 (51.3)	122 (54.5)	59 (74.7)	< 0.001
Current smoker	114 (6.8)	33 (5.3)	—	1 (2.6)	0.246	56 (8.3)	20 (8.9)	4 (5.1)	0.549
Current alcohol use	468 (27.8)	94 (15.1)	8 (19.5)	3 (7.7)	0.317	241 (35.7)	90 (40.2)	32 (40.5)	0.393
Current Khat chewer	414 (58.8)	372 (59.6)	20 (48.8)	22 (56.4)	0.375	NA	NA	NA	NA
Number of days fruits consumed in a week	1682	1.7 ± 1.12	1.9 ± 1.10	1.5 ± 1.04	0.299	2.9 ± 1.90	3.2 ± 2.10	2.6 ± 1.98	0.073
Consumed fruits in the past week	1460 (86.8)	564 (90.4)	39 (95.1)	34 (87.2)	0.705	571 (84.6)	192 (85.7)	60 (75.9)	0.075
Number of days vegetables consumed in a week	1682	4.2 ± 2.19	3.9 ± 2.16	3.9 ± 1.76	0.518	4.2 ± 2.30	4.5 ± 2.17	3.5 ± 2.41	0.005
Consumed vegetables in the past week	1521 (90.4)	603 (96.6)	39 (95.1)	39 (100.0)	0.652	578 (85.6)	202 (90.2)	60 (75.9)	0.031
Optimal physical activity ^a	1317 (78.3)	478 (76.6)	32 (78.0)	29 (74.4)	0.925	535 (79.3)	183 (81.7)	60 (75.9)	0.522
Weight (kg)	1674	59.5 ± 10.8	65.0 ± 14.3	68.6 ± 17.0	< 0.001	70.2 ± 14.6	74.3 ± 17.0	83.9 ± 25.5	< 0.001
BMI	1674	23.3 ± 4.1	25.9 ± 5.4	26.8 ± 5.8	< 0.001	27.7 ± 17.9	29.0 ± 11.9	35.5 ± 12.6	< 0.001
Obese	351 (21.0)	39 (6.3)	8 (15.8)	12 (30.8)	< 0.001	159 (23.7)	83 (37.6)	50 (64.9)	< 0.001
WC, overall	1682	76.3 ± 10.7	81.4 ± 11.5	85.1 ± 13.7	< 0.001	87.4 ± 13.4	91.1 ± 14.8	95.4 ± 15.1	< 0.001
WC, men	848	78.4 ± 8.9	85.4 ± 9.5	87.1 ± 14.9	< 0.001	88.2 ± 13.9	91.8 ± 16.7	96.6 ± 15.9	< 0.001
WC, women	834	75.1 ± 11.4	79.2 ± 12.0	83.4 ± 12.8	0.002	86.2 ± 12.6	90.0 ± 11.6	91.8 ± 11.9	0.012
Substantially increased risk of central obesity	337 (20.0)	39 (6.3)	8 (19.5)	11 (28.2)	< 0.001	166 (24.6)	80 (35.7)	33 (42.3)	< 0.001
WHR	703	0.85 ± 0.12	0.87 ± 0.10	0.88 ± 0.11	0.242	NA	NA	NA	NA
Abnormal WHR	251 (35.7)	210 (33.7)	17 (41.5)	24 (63.2)	< 0.001	NA	NA	NA	NA
DBP (mm Hg)	1680	78.4 ± 10.7	83.7 ± 14.2	82.1 ± 12.2	0.002	80.5 ± 12.5	85.4 ± 13.9	83.7 ± 12.3	< 0.001
SBP (mm Hg)	1680	118.3 ± 16.3	129.2 ± 19.4	124.3 ± 18.4	< 0.001	130.1 ± 20.7	136.7 ± 23.0	140.0 ± 23.3	< 0.001

(Continues)

TABLE 7 | (Continued)

Variables	Total (N = 1682)	Ethiopia (n = 704)			Nigeria (n = 978)		
		Normal (n = 625)	Prediabetes (n = 41)	Diabetes (n = 39)	Normal (n = 678)	Prediabetes (n = 224)	Diabetes (n = 79)
Raised BP	470 (28.0)	100 (16.0)	10 (24.4)	14 (35.9)	206 (30.6)	98 (43.8)	42 (53.8)
Reported history of hypertension	193 (11.5)	51 (8.2)	4 (9.8)	14 (35.9)	60 (8.9)	44 (19.6)	20 (25.3)
Reported history of high cholesterol	28 (1.7)	7 (1.1)	1 (2.4)	5 (12.8)	8 (1.2)	6 (2.7)	1 (1.3)
							<i>p</i>
							< 0.001
							< 0.001
							0.255

Note: Data are presented as *n* (%), mean $\pm$ SD.

Abbreviations: BMI, body mass index; NA, not applicable; SD, standard deviation; WHO, World Health Organization; WHR, waist-to-hip ratio.

^aWHO global recommendations on physical activity.

famine, civil conflict, and malnutrition, which may modulate the pathogenesis and clinical course of diabetes. Famine and food insecurity related history of Ethiopia may have led to metabolic changes that could result in variations in different phenotypes in insulin resistance and diabetes [21, 22]. In Nigeria, the history of malnutrition, particularly in civil-conflict affected areas, could have led to insufficient dietary consumptions and contributed to diversified diabetes phenotypic characteristics including differences in obesity levels, dyslipidemia, and other chronic diseases [23].

The study found that adults diagnosed with diabetes in Ethiopia are younger, indicating early disease onset, comparable to a study in Indian [24]. Prediabetes was the highest in the 45–59 age group in Ethiopia, whereas it was invariably higher after age 30 in Nigeria. Ethiopian participants with diabetes had lower body weight, waist circumference, and WHR, comparable to previous studies in Ethiopia [25] and Asian [26, 27]. In contrast, diabetes in Western individuals appears to develop later in life (> 50 years) and is common among overweight and obese individuals [28]. In line with this, multivariable analysis showed that age was significantly associated with type 2 diabetes in Nigerian individuals. Unlike the Ethiopian participants, Nigerians showed phenotypes more comparable to Western individuals.

Central obesity is found to be a strong predictor of DM in Ethiopia, where individuals with increased risk of central obesity are more likely to have Type 2 diabetes compared to low risk for central obesity as measured by waist circumference. These findings highlight the critical role of abdominal fat in driving Type 2 diabetes prevalence in Ethiopia. In contrast, central obesity is not found to be a predictor of Type 2 diabetes in Nigeria, but higher weight is significantly associated with Type 2 diabetes. This suggests that waist cut-offs for waist circumference for predicting Type 2 diabetes in African populations vary significantly from international standards, highlighting the need for tailored thresholds [29, 30].

In overweight or obese individuals, Type 2 diabetes is most likely to result from adiposity-induced insulin resistance, followed by compensatory insulin secretion and subsequent β -cell dysfunction, and ultimately manifest with overt hyperglycemia [31]. Conversely, in individuals who are not overweight, the underlying pathophysiology is not well comprehended and is often ascribed to the deposition of ectopic fat [32] and impairments in insulin secretion [33]. Primary pancreatic beta cell secretory dysfunction might explain why diabetes in Ethiopia is occurring at a lower age, BMI, waist circumference, and waist-to-hip ratio, while insulin resistance could be important among Nigerian participants, as the majority (64.9%) of them were obese. In line with this, a previous Nigerian study reported a high dual burden of insulin resistance and pancreatic beta cell secretory dysfunction among individuals with Type 2 diabetes [34].

Hypertension often coexists with Type 2 diabetes [35]. In the present study, it was also observed that a significant proportion of individuals with diabetes had associated hypertension (53.8% among the Nigerians and 35.9% for Ethiopians) compared to non-diabetic cases (30.6% among Nigerians and 16.0% among Ethiopians). In line with this, Ethiopian individuals

reporting a history of hypertension were more likely to have Type 2 diabetes than individuals without a history of hypertension. This dual adversity raises cardiovascular risk, demanding strict control of blood pressure and blood sugar levels. Hypertension also worsens micro- and macrovascular complications in diabetes, stressing the need for effective management strategies.

In SSA, the clinical management of adults with diabetes is predominantly guided by clinical guidelines formulated by international diabetes associations such as ADA [4]. It is noteworthy, however, that these international guidelines are developed from evidence generated through phenotyping studies conducted on Caucasian or mixed ancestry populations. Hence, it might not be applicable directly to the SSA population.

5 | Conclusion

In the present study, there is a notable occurrence of diabetes at a relatively high rate of 7.0% among rural and peri-urban populations in SSA, higher among Nigerians than Ethiopians. The prevalence of prediabetes was 16.5% in the present study. Given that three-quarters of diabetes cases were undiagnosed, there may be a large number of people with diabetes in the study settings who do not know their status. It is recommended that screening and early detection efforts be intensified in SSA.

The findings of this study showed that individuals with diabetes in Ethiopia compared to Nigeria are characterized by a young age of onset, leanness, lower BMI, and waist circumference. The diabetes phenotype encountered in Ethiopia is very different from the classical Type 2 diabetes seen in the West, while Nigerian diabetes cases had comparable phenotypes to Westerners. This underscores the imperative need for further research and careful consideration when formulating therapeutic strategies for diabetes specifically tailored to the distinct physiological and clinical characteristics of populations in SSA.

This research relied on data from specific study areas within Ethiopia (Butajira) and Nigeria (Enugu State). While the findings from these areas provide important insights on the burden and clinical profiles of Type 2 diabetes, it is important to emphasize that the results may not be generalized to all of SSA. Because of genetic and environmental variabilities across SSA, the prevalence of Type 2 diabetes may vary considerably across the region. Nevertheless, the inclusion of individuals from Ethiopia and Nigeria, which together account for a substantial proportion of SSA's population, offers important insight that can inform future studies and public health strategies. Further studies on a wider range of countries from the region are recommended to build a more comprehensive understanding of the epidemiology of diabetes in SSA.

6 | Strength and Limitation

This study employed a community-based multi-center design, facilitating the extrapolation of outcomes to the broader population of the research settings within SSA. In contrast to numerous prior investigations in the region that relied on random

or fasting blood glucose measurements, we have used both fasting and 2-h OGTT, thereby enhancing the accuracy of diabetes cases. However, it is crucial to acknowledge that the cross-sectional nature of the design precludes the confirmation of the course of causal pathways.

Author Contributions

Assefa Mulu Baye, Adem Y. Dawed, Teferi Gedif Fenta, Ewan R. Pearson, and Colin Palmer designed the study. Assefa Mulu Baye, Ifeyinwa Dorothy Nnakenyi, Ekenechukwu Esther Young, and Ifeoma Isabella Ulasi conducted the research. Assefa Mulu Baye, Ifeyinwa Dorothy Nnakenyi, and Teferi Gedif Fenta contributed to the data analysis and interpretation. Assefa Mulu Baye, Adem Y. Dawed, and Ifeoma Isabella Ulasi performed statistical analysis. Assefa Mulu Baye and Adem Y. Dawed wrote the draft manuscript. All the authors contributed to the discussion and revision of the manuscript. Assefa Mulu Baye confirmed that all authors included in the list meet the necessary authorship criteria. As the guarantor of this work, Assefa Mulu Baye had complete access to all data analyzed in the study and bears responsibility for ensuring the data's integrity and accuracy in the analysis.

Acknowledgments

We thank all the participants of the study. We also thank International Clinical Laboratories, Ethiopia, and the Chemical Pathology Laboratory of the University of Nigeria Teaching Hospital, Nigeria, for conducting the glucose assays.

Ethics Statement

This study was conducted with the approval of the Institutional Review Board of the College of Health Sciences, Addis Ababa University (Ref: 027/19/SoP), Ministry of Education, Ethiopia (Ref: 17/152/407/23) and University of Nigeria Teaching Hospital, Enugu, Health Research Ethics Committee (Ref: UNTH/CSA/329/OL.5). Written informed consent was obtained from the participants.

Conflicts of Interest

The authors declare no conflicts of interest.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Publication – II



OPEN ACCESS

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RECEIVED 27 September 2024
ACCEPTED 03 March 2025
PUBLISHED 25 March 2025

CITATION
Baye AM, Fenta TG, Karuranga S, Nnakenyi ID,
Young EE, Palmer C, Pearson ER, Ulasi II and
Dawed AY (2025) Performance of fasting
plasma glucose for community-based
screening of undiagnosed diabetes and
pre-diabetes in sub-Saharan Africa.
Front. Endocrinol. 16:1501383.
doi: 10.3389/fendo.2025.1501383

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Performance of fasting plasma glucose for community-based screening of undiagnosed diabetes and pre-diabetes in sub-Saharan Africa

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Introduction: Early diabetes screening is critical in sub-Saharan Africa (SSA), where the prevalence is increasing, yet a large proportion of cases remain undiagnosed. This study aimed to evaluate the performance of fasting plasma glucose (FPG) in screening diabetes and/or prediabetes compared to the 2-hour plasma glucose (2-h PG)-level in SSA.

Methods: Data from a population-based, cross-sectional diabetes screening survey involving 1550 individuals in Butajira, Ethiopia, and Enugu state, Nigeria were analyzed. Fasting plasma glucose and a 2-hour 75-g oral glucose tolerance test (OGTT) were utilized for diabetes screening. In addition, we determined and plotted the receiver operating characteristic curve for FPG against the reference standard 2-h PG to evaluate the screening tool's sensitivity and specificity.

Results: The mean (SD) age of the study participants was 44.5 ($\pm$ 16.43) years, with men comprising 50.4% of the cohort. Among 1550 individuals analyzed, 4.6% and 16.8% demonstrated diabetes and prediabetes, respectively, as identified by either FPG or 2-h PG. The agreement between FPG and 2-h PG in identifying diabetes and prediabetes was moderate, with kappa statistic of 0.56 (95% CI, 0.51 – 0.61; $p < 0.0001$) for diabetes and 0.45 (95% CI, 0.40 – 0.50; $p < 0.0001$) for prediabetes. FPG failed to detect 34.1% of all prediabetes and 44.4% of all diabetes cases. The sensitivity of FPG in identifying diabetes cases was 44.3% at a cut-off 126 mg/dL with a specificity of 99.3%. We identified the optimal FPG cut-off for detecting newly identified diabetes cases using 2-h PG to be 105 mg/dL associated with a sensitivity and specificity of 67.2% and 94.0%, respectively.

Conclusion: FPG was able to correctly identify 99.3% of individuals with no diabetes but a significant percentage of diabetes cases would have remained undiagnosed if only FPG had been utilized instead of the 2-h PG. The use of 2-h PG test is recommended to diagnose diabetes in older individuals, females and non-obese persons who would be missed if tested by only FPG. Lowering the cut-off value for FPG to 105 mg/dL substantially increases the identification of individuals with diabetes, thus improving the effectiveness of FPG as a screening test for type 2 diabetes.

KEYWORDS

diabetes, fasting plasma glucose, 2-h plasma glucose, sub-Saharan Africa, sensitivity, specificity

1 Introduction

Diabetes is an important worldwide health concern, with 830 cases (14% of the adult population aged 18 years and older) were living with diabetes (1) and 6.7 million deaths among adults in 2021 (2). Projections from the International Diabetes Federation (IDF) forecast a surge to 643 million cases by 2030. In addition, diabetes results in serious complications such as visual impairment and blindness, kidney problems, heart diseases, and cerebrovascular diseases (3).

Societal guidelines stressed the pivotal role of early detection of type 2 diabetes to ensure effective glycemic control and delay the onset of complications (4–6). Community-based screening for type 2 diabetes is important for early detection of the disease as it is asymptomatic and high rates of undiagnosed cases (7).

The American Diabetes Association (ADA) and IDF recommend FPG and the 2-hour postprandial oral glucose tolerance test (OGTT) for the diagnosis of prediabetes and diabetes (4, 8). Each method has distinct advantages and disadvantages in clinical application. Diagnosis of diabetes by FPG is preferred owing to its cost-effectiveness and convenience, particularly in identifying high risk individuals with diabetes. However, the 2-hour postprandial glucose (2-h PG) test shows superior sensitivity for identifying individuals with prediabetes and diabetes, although being less feasible in large-scale mass screening (8). As a result, 2-h PG is considered to be the gold standard in the diagnosis of diabetes (4).

According to ADA, the criteria for the diagnosis of diabetes are FPG ≥ 126 mg/dL and/or 2-h PG ≥ 200 mg/dL (using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water) and/or A1C $\geq 6.5\%$ and/or a random plasma glucose ≥ 200 mg/dL in a person with classic symptoms of hyperglycemia or hyperglycemic complications (4). There is an ever-growing discourse underway regarding the current thresholds suggested for the diagnosis and screening of diabetes and prediabetes (9, 10). The establishment of these threshold values primarily relied on the outcomes of several

studies conducted in Western populations, aiming to identify the most effective FPG and other screening tests' cut-off values for predicting diabetes (11). Several cohort studies among Asian populations examined FPG and recommended lower cut-off values to predict diabetes (12–15). However, epidemiological studies which investigated comparative performance and cut-off values of FPG for predicting type 2 diabetes in Sub-Saharan Africa (SSA) population are scarce and it remains uncertain whether a FPG value of 126 mg/dL is adequate in screening type 2 diabetes in this region. In addition, evidence is limited in investigating those individuals whose diabetes status could be classified differently by different screening tests. Such lack of agreement may stem from measurement inconsistencies, variation with time, or screening tests measure their respective physiological processes (16). ADA, IDF and the European Association for the Study of Diabetes (EASD) also indicated that these blood-based methodologies have limitations in interpretation variabilities and missing cases related to concomitant conditions such as haemoglobinopathies and anemias (4, 8, 17). This is particularly critical in SSA, where the high prevalence of such comorbidities may contribute to missed cases or variability in interpretations of test results.

Few epidemiological investigations in SSA, especially across Ethiopia and Nigeria, have directly assessed the utility of FPG in identifying undiagnosed type 2 diabetes and prediabetes individuals. Therefore, this research aims to elucidate the screening capacity (sensitivity and specificity) and determine optimal cut-offs for FPG based on 2-h PG-detected prediabetes and diabetes. The outcomes will offer significant insights for healthcare providers, managers and policymakers involved in diabetes and prediabetes care in SSA.

2 Materials and methods

2.1 Study design and setting

The Diabetes Epidemiologists' Network in Sub-Saharan Africa (DENSSA): represents collaborative research initiative involving the University of Dundee in United Kingdom, Addis Ababa University in Ethiopia and University of Nigeria in Nigeria. Within this framework, a

Abbreviations: FPG, Fasting plasma glucose; IFG, Impaired fasting glucose; IGT, Impaired glucose tolerance; 2-h PG, 2-hour plasma glucose; OGTT, Oral glucose tolerance test; ROC, Receiver operating characteristic.

community-based, cross-sectional study was conducted as a crucial facet of the project, encompassing the Butajira Rural Health Program (BRHP) in central Ethiopia and at Enugu State in Nigeria. Data was collected between November 2020 to October, 2021.

2.2 Study participants

The study participants comprised individuals from six villages in Butajira, Ethiopia and three Local Government Areas (LGAs) – Enugu North, Enugu West and Nkanu West in Enugu State, Nigeria. Utilizing a multi-stage random cluster sampling technique, a representative sample of 1000 community-based adults ≥ 18 years were planned to be selected from each of the two study settings. The sample of participants in each district was allocated using a probability proportional to the size technique. We utilized computer generated list from Butajira Rural Health Program (BRHP) register in Ethiopia and Enugu State in Nigeria to select households. Pregnant women, acutely ill individuals, and those taking medications including steroids, second generation antipsychotics, and protease inhibitors as well as those refused to participate were excluded from the study.

2.3 Data collection

After study participants were interviewed on the first day, they were requested to visit health centers on the subsequent day, between 7:30 a.m. and 9:00 a.m. following an overnight fast of 10–12 hours. A structured and pre-coded questionnaire administered by a trained interviewer, was used for data collection. Measurement of blood pressure (BP), heart rate, weight, height, waist, and hip circumference were conducted at the nearby health facilities. Blood samples for FPG were collected from participants who had fasted overnight for at least ten hours. Thereafter, all participants drank a standard solution of 75g of anhydrous glucose dissolved in 300ml of water. Two hours after ingesting the drink, a second venous blood sample was collected. The blood samples for glucose estimation were collected into sterilized disposable vacutainer tubes containing sodium fluoride, which were quickly centrifuged within an hour at the data collection center to separate the plasma. Blood samples were stored in cold boxes maintained at 4–8°C until transported to a laboratory on the same day as sample collection. Biochemical tests were conducted on the same day by the International Clinical Laboratories (ICL) for the Ethiopian samples and at the Chemical Pathology laboratory of the University of Nigeria Teaching Hospital for the Nigerian samples to determine blood glucose concentration.

2.4 Diagnostic criteria

The ADA's and IDF's diagnostic definitions were utilized to identify diabetes and pre-diabetes cases (4, 18). Plasma glucose test results were categorized as follows: impaired fasting glucose (IFG) corresponding to plasma glucose levels between 100 mg/dL and 125 mg/dL, and impaired glucose tolerance (IGT) defined as a 2-h PG

ranging from 140 mg/dL and 199 mg/dL. Newly diagnosed diabetes was ascribed to a FPG level of ≥ 126 mg/dL, 2-h PG of ≥ 200 mg/dL or both.

Body mass index (BMI) was delineated according to the WHO criteria into: underweight (< 18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²) and obesity (≥ 30 kg/m²) (19). Waist circumference was classified as normal (≤ 94 cm for men and ≤ 80 cm for women), presenting an increased risk of cardiometabolic complications with measurements of 95–102 cm for men and 81–88 cm for women, and substantially increased risk of cardiometabolic complications if the waist circumference exceeded > 102 cm for men and > 88 cm women) (20).

Participants' physical activity was evaluated based on adherence to WHO recommendations, categorizing individuals as either optimal (≥ 600 Metabolic Equivalent of Task (MET) minutes per week) or suboptimal (< 600 MET minutes per week) (21).

2.5 Data analysis

We utilized Stata V.17 software program (StataCorp. Stata Statistical Software: Release 17. College Station, TX: Stata Corp LP) and R version 4.3.2, (22) for data analysis. Variables with continuous outcome were reported as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR). Differences in means were assessed using an independent Student's *t*-test. Categorical differences were expressed in proportions and assessed using a Chi-square test. The medians of FPG and 2-h PG were compared across categorical variables utilizing the Wilcoxon rank-sum test or Kruskal-Wallis rank-test. Regression analysis was utilized to evaluate the relationship between FPG and 2-h PG.

The agreement between FPG and 2-h PG was determined using kappa statistics, accompanied by the 95% confidence interval (95% CI). We considered $P < 0.05$ to declare statistically significant. Receiver operating characteristic (ROC) curves were computed and plotted, with the FPG compared to the reference standard 2-h PG to ascertain its diagnostic capacity as a diabetes and prediabetes screening tool. Evaluation metrics such as sensitivity, specificity, and Youden's Index were employed to assess the performance of FPG tests (23). Youden's Index, a metric used to express the discriminatory capability of diagnostic tests, is derived from the formula: (sensitivity + specificity) – 1. The index ranges from –1 to 1, with a value closer to 1, indicating superior test performance.

Furthermore, the proportion of missed prediabetes by FPG and 2-h PG, as well as the proportion of missed diabetes cases by FPG, were calculated against the total number of prediabetes and diabetes cases, respectively.

3 Results

3.1 Sociodemographic and clinical information

Among the total of 1727 participants, 1550 individuals were included in the analysis following the exclusion of 30 previously diagnosed with type 2 diabetes and 147 who were not tested by

either FPG or 2-h PG. The mean age of the study population was 44.5 (SD 16.4) years, with women comprising 49.6% of the analyzed cohort (Table 1).

Of the 1550 participants, 72 individuals (4.6%) were identified as having diabetes through either FPG or 2-h PG, whereas 261 individuals (16.8%) demonstrated prediabetes, and 1217 individuals (78.5%) exhibited normal glucose tolerance. Among all tested individuals, 11 (15.3%) displayed abnormalities in FPG alone (false positive results), 32 (44.4%) in 2-h PG alone (false negative results for FPG), and 29 (40.3%) in both. Of those with prediabetes, 83 (31.8%) presented with IFG, 89 (34.1%) had IGT and 89 (34.1%) with a combination of both.

3.2 Patterns of FPG and 2-h PG results

Median FPG among all participants was 83 mg/dL (IQR: 76 – 92), while the median 2-h PG level was 94 mg/dL (IQR: 77–116). Notably, men demonstrated a significantly higher median 2-h PG compared to women (97 mg/dL, IQR: 78–123 vs 91 mg/dL, IQR: 76–112; $P < 0.0006$) (Figure 1A). Moreover, the age group of 45–59 years

exhibited the highest median FPG levels (84.5 mg/dL, IQR 79 – 95, $p < 0.0001$), while the ≥ 70 age group had the highest median 2-h PG levels (102 mg/dL, IQR 81 – 139, $p < 0.0001$) (Figure 1B).

In addition, FPG values increased from underweight individuals to those classified as obesity (underweight 82 mg/dL, IQR 74–87; normal weight 81 mg/dL, IQR 74–89; overweight 84 mg/dL, IQR 77–92; obese 89 mg/dL, IQR 80–101; $P < 0.0001$; as determined by WHO BMI criteria). Likewise, 2-h PG values progressively increased from individual with underweight to obese participants (underweight 83 mg/dL, IQR 66–105; normal weight 88 mg/dL, IQR 73–108; overweight 96 mg/dL, IQR 81–117; obese 108 mg/dL, IQR 87–141; $P < 0.0001$; by WHO BMI criteria) (Figure 1C). Similarly, both FPG and 2hPG showed progressive elevation across low-risk to substantially increased risk groups, based on waist circumference (Figure 1D).

3.3 Concordance between FPG and 2-h PG

The regression analysis revealed a statistically significant, moderately robust positive correlation ($r = 0.57$, $P < 0.0001$) between FPG and 2-h PG. Employing regression analysis, an equivalent FPG value was derived in relation to 2-h PG (Figure 2). Both FPG and 2-h PG demonstrated a strong correlation within a linear relationship represented by $\text{FPG (mg/dL)} = 57.05 + 0.28 \times 2\text{-h PG (mg/dL)}$. Utilizing this equation, an FPG level of 113 mg/dL (6.3 mmol/L) corresponds to a 2-h PG level of 200mg/dL (11.1mmol/L).

The overall concordance between FPG and 2-h PG in identifying diabetes and prediabetes was moderate, with kappa statistic of 0.56 (95% CI, 0.51 – 0.61; $p < 0.0001$) for diabetes and 0.45 (95% CI, 0.40 – 0.50; $p < 0.0001$) for prediabetes. More specifically, the concordance between these two methods for detection of negative cases is very high with a negative predictive value (NPV) of 97.9%.

The ROC for each calculated FPG test and cut-off points to identify cases without diabetes and prediabetes is outlined in Figure 3. Table 2. The FPG test exhibited good and acceptable discriminatory power in identifying individuals with no diabetes, an overall AUC of 0.83 (95% CI: 0.76–0.90) (Figure 3A, Table 2). The AUC for men, 0.88 (95% CI: 0.80–0.95), was higher than that for women, 0.77 (95% CI: 0.65–0.89), but this difference was statistically insignificant ($P = 0.142$) (Table 2). Moreover, the AUC for Nigerian participants, 0.89 (95% CI: 0.83–0.95) was significantly higher than that of Ethiopian counterparts, 0.70 (95% CI: 0.53–0.86) ($P\text{-value} = 0.034$) (Figure 3B, Table 2).

Similarly, the FPG test had good performance in identifying individuals without prediabetes, with an overall AUC of 0.69 (95% CI: 0.67–0.72) (Figure 3C, Table 2). The performance of the FPG test to identify people without prediabetes revealed a significantly higher AUC among the Ethiopians, 0.77 (95% CI: 0.65–0.89), compared to the Nigerians, 0.63 (95% CI: 0.58–0.68) (Figure 3D, Table 2). Nonetheless, the performance of the FPG test to identify individuals without prediabetes was comparable between male and female participants (Table 2). These ROC curves for FPG were calculated based on the detection of diabetes by 2-h PG ≥ 200 mg/dL and prediabetes by 2-h PG ≥ 140 mg/dL.

TABLE 1 Summary of sociodemographic and clinical information by country of residence, Sub-Sahara Africa, 2021.

Characteristics	Country		Total
	Ethiopia	Nigeria	
Sex, women	394 (63.7)	375 (40.3)	769 (49.6)
Age (years)	40.8 $\pm$ 13.5	46.9 $\pm$ 17.7	44.5 $\pm$ 16.4
Urban residence	354 (57.2)	431 (46.3)	785 (50.60)
BMI (kg/m ²) ^a	23.3 $\pm$ 4.1	28.1 $\pm$ 10.3	28.2 $\pm$ 8.7
Waist circumference (cm)	76.8 $\pm$ 11.0	88.7 $\pm$ 14.0	83.9 $\pm$ 14.1
WHR ^b	0.86 $\pm$ 0.1	–	0.86 $\pm$ 0.1
Diastolic BP (mm Hg)	78.9 $\pm$ 11.2	81.8 $\pm$ 13.1	80.6 $\pm$ 12.5
Systolic BP (mm Hg)	119.1 $\pm$ 16.7	132.1 $\pm$ 21.6	126.9 $\pm$ 20.8
FPG (mg/dL)	79 (73–85)	87 (79–96)	83 (76–92)
2-h PG (mg/dL)	81 (67–98)	103 (86–129)	94 (77–116)
IFG	27 (4.4)	145 (15.5)	172 (11.1)
IGT	27 (4.4)	151 (16.2)	178 (11.5)
Prediabetes	40 (6.5)	221 (23.7)	261 (16.8)
New diabetes by FPG	4 (0.6)	36 (3.9)	40 (2.6)
New diabetes by 2-h PG	18 (2.9)	43 (4.6)	61 (3.9)
Overall New diabetes	18 (2.9)	54 (5.8)	72 (4.6)
Normal glucose tolerance	561 (90.6)	656 (70.5)	1217 (78.5)

Data are presented as n (%), mean $\pm$ SD or median (IQR).

^aSeven values were missing.

^bWHR is available for the Ethiopian data only.

BMI, body mass index; FPG, fasting plasma glucose; IQR, interquartile range; 2-h PG, 2-hour plasma glucose; SD, standard deviation; WHR, waist-to-hip ratio; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

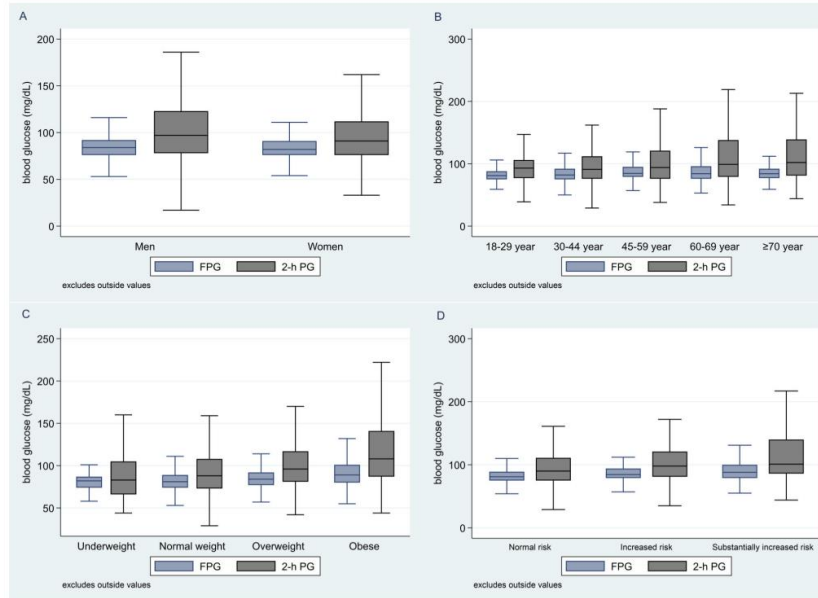


FIGURE 1
Box plots for median FPG and 2-h PG by sex (A), age category (B), body mass index (BMI) (C) and waist circumference (D). FPG, fasting plasma glucose; 2-h PG, 2-hour plasma glucose.

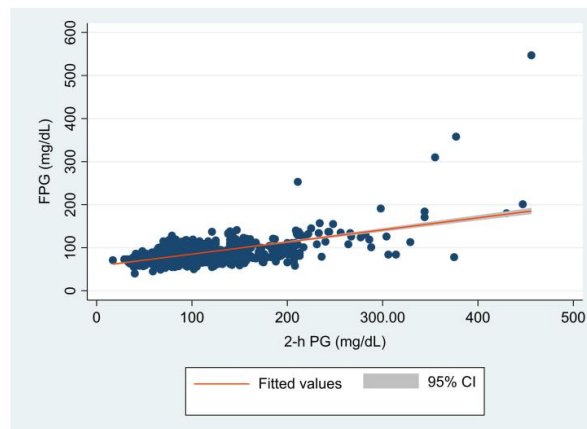


FIGURE 2
Scatter plot of hour plasma glucose (2-h PG, in mg/dL) and fasting plasma glucose (FPG in mg/dL) with a fitted regression line and 95% confidence interval (CI). The figure demonstrates the overall correlation between FPG and 2-hr PG.

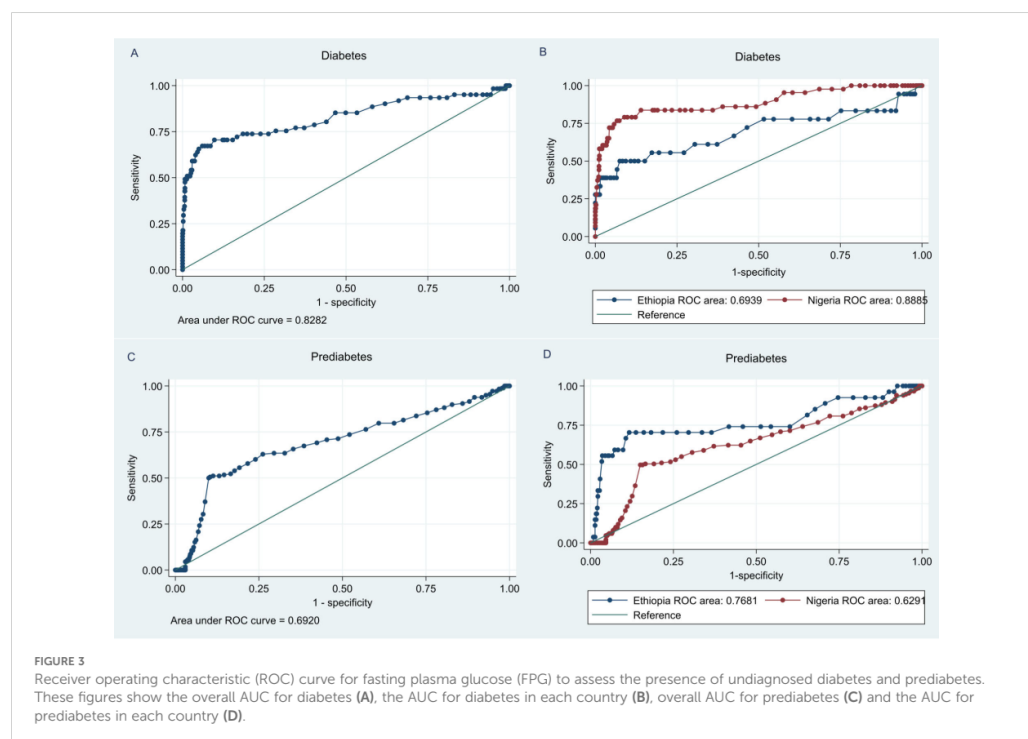


TABLE 2 Area under the curve (AUC) for fasting plasma glucose (FPG) to assess the presence of undiagnosed diabetes and prediabetes by country and sex.

Variables	Prediabetes			Diabetes		
	AUC (95% CI)	χ2	P-value	AUC (95% CI)	χ2	P-value
Overall	0.69 (0.67-0.72)	-	-	0.83 (0.76-0.90)	-	-
Country						
Nigeria	0.63 (0.58-0.68)	4.26	0.039	0.89 (0.83-0.95)	4.50	0.034
Ethiopia	0.77 (0.65-0.89)			0.70 (0.53-0.86)		
Sex						
Men	0.68 (0.61-0.74)	0.45	0.505	0.88 (0.80-0.95)	2.09	0.149
Women	0.71 (0.64-0.78)			0.77 (0.64-0.89)		

Diagnostic accuracy of FPG test in distinguishing between prediabetes and diabetes in different groups based on country and sex by using the area under the curve (AUC) from a Receiver Operating Characteristic (ROC) curve. A higher AUC (closer to 1) indicates better diagnostic performance.

3.4 FPG cut-off points for pre-diabetes and diabetes screening

Based on the ROC curve, the optimal cut point of FPG for detecting newly diagnosed diabetes by 2-h PG was determined to be 105 mg/dL, associated with a sensitivity of 67.2% and specificity of 94.0% (AUC 0.83, 95% CI: 0.76 – 0.90; NND 1.6) (Table 3).

Applying this cut-off point, an additional 59 undiagnosed cases of diabetes (3.8%) among the 1550 participants could be identified.

Likewise, the optimal cut-off point of FPG in detecting prediabetes diagnosed by 2-h PG was determined to be 99 mg/dL, with a sensitivity of 52.2% and specificity of 90.0% (AUC 0.69, 95% CI: 0.67-0.72).

When utilizing the guideline recommended cut-off 126 mg/d, the sensitivity of FPG in identifying diabetes is 44.3%, with a specificity of

TABLE 3 Sensitivity and specificity for FPG in diagnosing diabetes and prediabetes.

FPG cut-offs	Diabetes					Prediabetes				
	Se (%)	Sp (%)	Youden J	LR+	LR-	Se (%)	Sp (%)	Youden J	LR+	LR-
80 mg/dL	90.2	38.1	0.282	1.46	0.26	80.4	39.3	0.198	1.326	0.497
85 mg/dL	80.3	56.0	0.363	1.83	0.35	70.1	57.9	0.281	1.667	0.516
90 mg/dL	75.4	71.5	0.469	2.64	0.34	64.1	74.2	0.383	2.487	0.483
95 mg/dL	73.8	81.5	0.553	3.99	0.32	53.8	83.9	0.377	3.338	0.551
100 mg/dL	70.5	87.7	0.582	5.74	0.34	51.6	90.5	0.421	5.421	0.535
105 mg/dL	67.2	94.0	0.612	11.12	0.35	23.4	93.6	0.170	3.667	0.818
110 mg/dL	59.0	96.6	0.557	17.58	0.42	13.6	95.6	0.092	3.091	0.904
115 mg/dL	50.8	97.7	0.485	22.26	0.50	8.7	96.5	0.052	2.473	0.946
120 mg/dL	49.2	98.7	0.479	38.54	0.51	7.6	97.5	0.051	3.055	0.948
125 mg/dL	47.5	99.3	0.468	64.35	0.53	3.3	97.6	0.008	1.349	0.991
130 mg/dL	39.3	99.3	0.387	58.58	0.61	3.3	98.0	0.013	1.649	0.987
135 mg/dL	29.5	99.7	0.292	109.84	0.71	1.6	98.7	0.003	1.236	0.997
140 mg/dL	21.3	99.9	0.212	317.33	0.79	0.5	99.1	-0.003	0.618	1.003
145 mg/dL	19.7	100.0	0.197	Inf	0.80	0.0	99.2	-0.008	0.000	1.008
150 mg/dL	18.0	100.0	0.180	Inf	0.82	0.0	99.3	-0.007	0.000	1.007

Comparison of diagnostic performance metrics for fasting plasma glucose (FPG) cut-off values ranging from 80 mg/dL to 150 mg/dL in diagnosing diabetes and prediabetes to identify which FPG levels offer the best sensitivity, specificity, and diagnostic balance for the two conditions. Youden J is summary statistic combining Se and Sp to show the overall diagnostic effectiveness, it is computed as Youden's index = Sensitivity + Specificity - 1. A higher value of Youden's index indicates better overall diagnostic accuracy. FPG, Fasting Plasma Glucose; LR-, negative likelihood ratio; LR+, Positive likelihood ratio; Se, Sensitivity; Sp, Specificity.

99.3%. A lower FPG cut-off value 105 mg/dL revealed markedly increased sensitivity (67.2%) and high specificity (94.0%) for identifying individuals with diabetes. Furthermore, for diagnosing individuals with prediabetes, guideline recommended cut-off value for FPG, 100 mg/dL, demonstrated a sensitivity of 51.6% and specificity of 90.5%. Lowering the FPG cut-off to 90 mg/dL resulted in increased sensitivity (64.1%) and reasonable specificity (74.2%) to identify individuals with pre-diabetes (Table 3).

3.5 Prediabetes and diabetes missed by FPG and 2-h PG

Table 4 highlight the percentages of prediabetes and diabetes cases missed by either FPG or 2-h PG alone. Among the total 1550 participants tested by both FPG and 2-h PG, FPG would miss 34.1% of all prediabetes and 44.4% of all diabetes cases, whereas the corresponding percentages missed by 2-h PG were 31.8% and 15.3%, respectively.

The rates of missed prediabetes cases using FPG and 2-h PG were similar for men and women study participants. In contrast, FPG demonstrated a higher rate of missed cases of diabetes in women compared to men ($p = 0.047$), whereas 2-h PG presented a higher rate of missed diabetes cases in men compared to women, despite this was not statistically significant.

Moreover, the rate of missed cases of prediabetes by FPG was higher among individuals with aged 70 years and above as

compared to middle-aged and young study participants ($p = 0.006$). The percentage of missed diabetes cases by FPG was significantly higher among non-obese participants compared to obese individuals with diabetes ($p = 0.013$), while the opposite trend was observed in 2-h PG. However, there was no significant difference in the rate of missed prediabetes cases by FPG and 2-h PG among obese and non-obese individuals.

4 Discussion

The performance of fasting plasma glucose (FPG) to identify undiagnosed prediabetes and diabetes cases has been investigated based on 2-hour plasma glucose (2-h PG) during an oral glucose tolerance test (OGTT) in this study. According to ADA and IDF, both FPG and 2-h PG during 75-g OGTT are equally appropriate for screening of diabetes (4, 8), but the agreement between them was moderate for identifying diabetes and prediabetes, indicating that these tests did not consistently categorize the same individuals with abnormal blood glucose. Existing evidence from western populations and this study suggests limited agreement between FPG and 2-h PG. In the National Health and Nutrition Examination Survey (NHANES) in the US, concordance between FPG and 2-h PG was limited with a kappa statistic of 0.310 (24). Nevertheless, the concordance of FPG with 2-h PG to identify non-diabetes individuals is very high with a negative predictive value (NPV) of 97.9%. In previous studies, the agreement between FPG

TABLE 4 Percentages of diabetes and prediabetes missed by FPG and 2-h PG.

Diabetes							
	All diabetes	Diabetes missed by FPG			Diabetes missed by 2-h PG		
		Missed (%)	Not missed (%)	p-value	Missed (%)	Not missed (%)	p-value
All (N=1550)	72	32 (44.4)	40 (56.6)	–	11 (15.3)	60 (84.7)	–
Sex							
Men	43	15 (34.9)	28 (60.1)	0.047	9 (20.9)	34 (79.1)	0.105
Women	29	17 (58.6)	12 (41.4)		2 (6.9)	27 (93.1)	
Age							
< 65 years	62	29 (46.8)	33 (53.2)	0.322	9 (14.5)	53 (85.5)	0.655
≥ 65 years	10	3 (30.0)	7 (70.0)		2 (20.0)	8 (80.0)	
Residence							
Urban	26	12 (46.2)	14 (53.8)	0.826	1 (3.8)	25 (96.2)	0.043
Rural	46	20 (43.5)	26 (56.5)		10 (21.7)	36 (78.3)	
WHO global recommendations on physical activity ^a							
Optimal	56	24 (42.9)	32 (57.1)	0.612	10 (17.9)	46 (82.1)	0.255
Suboptimal	16	8 (50.0)	8 (50.0)		1 (6.3)	15 (93.7)	
BMI ^b							
Non-obese	35	21 (60.0)	14 (40.0)	0.013	1 (2.9)	34 (97.1)	0.004
Obese	36	11 (30.6)	25 (69.4)		10 (27.8)	26 (72.2)	
Waist circumference ^c							
Low risk	31	15 (48.4)	16 (51.6)	0.484	7 (22.6)	24 (77.4)	0.302
Increased risk	16	5 (31.3)	11 (68.8)		2 (12.5)	14 (87.5)	
Substantially increased risk	25	12 (48.0)	13 (52.0)		2 (8.0)	23 (92.0)	
Raised BP							
Yes	33	14 (42.4)	19 (57.6)	0.751	5 (15.2)	28 (84.8)	0.978
No	39	18 (46.2)	21 (53.9)		6 (15.4)	33 (84.6)	
Prediabetes							
	All prediabetes	Prediabetes missed by FPG			Prediabetes missed by 2hPG		
		Missed (%)	Not missed (%)	p-value	Missed (%)	Not missed (%)	p-value
All (N=1550)	261	89 (34.1)	172 (65.9)	–	83 (31.8)	178 (68.2)	–
Sex							
Men	145	52 (35.9)	93 (64.1)	0.502	45 (31.0)	100 (69.0)	0.766
Women	116	37 (31.9)	79 (68.1)		38 (32.8)	78 (67.2)	
Age							
< 65 years	202	60 (29.7)	142 (70.3)	0.006	72 (35.6)	130 (64.4)	0.014
≥ 65 years	59	29 (49.2)	30 (50.8)		11 (18.6)	48 (81.4)	

(Continued)

TABLE 4 Continued

Prediabetes							
	All prediabetes	Prediabetes missed by FPG			Prediabetes missed by 2hPG		
		Missed (%)	Not missed (%)	p-value	Missed (%)	Not missed (%)	p-value
All (N=1550)	261	89 (34.1)	172 (65.9)	–	83 (31.8)	178 (68.2)	–
Country							
Ethiopia	40	13 (32.5)	27 (67.5)	0.817	13 (32.5)	27 (67.5)	0.918
Nigeria	221	76 (34.4)	145 (65.6)		70 (31.7)	151 (68.3)	
Residence							
Urban	125	34 (27.2)	91 (72.8)	0.024	44 (35.2)	81 (64.8)	0.258
Rural	136	55 (40.4)	81 (59.6)		39 (28.7)	97 (71.3)	
WHO global recommendations on physical activity ^a							
Optimal	212	75 (35.4)	137 (64.6)	0.365	68 (32.1)	144 (67.9)	0.843
Suboptimal	49	14 (28.6)	35 (71.4)		15 (30.6)	34 (69.4)	
BMI ^b							
Non-obese	168	64 (38.1)	104 (61.9)	0.065	55 (32.7)	113 (67.3)	0.525
Obese	90	24 (26.7)	66 (73.3)		26 (8.9)	64 (71.1)	
Waist circumference ^c							
Normal risk	126	49 (38.9)	77 (61.1)	0.265	42 (33.3)	84 (66.7)	0.594
Increased risk	47	15 (31.9)	32 (68.1)		12 (25.5)	35 (74.5)	
Substantially increased risk	88	25 (28.4)	63 (71.6)		29 (33.0)	59 (67.0)	
Raised BP							
Yes	107	41 (38.3)	66 (61.7)	0.231	33 (30.8)	74 (69.2)	0.781
No	154	48 (31.2)	106 (68.8)		50 (32.5)	104 (67.5)	

^aAccording to WHO global recommendations on physical activity for health optimal physical activity is 150 minutes of moderate-intensity physical activity; or 75 minutes of vigorous-intensity physical activity; or an equivalent combination of moderate- and vigorous-intensity physical activity achieving at least 600 MET-minutes.

^bobese is based on WHO BMI classification (BMI ≥ 30 kg/m²).

^cWaist circumference classification is based on WHO recommendation where normal risk is ≤ 94 cm for men and ≤ 80 cm for women; increased risk is $>94 - 102$ cm for men and $>80 - 88$ cm for women; and substantial increased risk is >102 cm for men and >88 cm for women.

BP, blood pressure; FPG, fasting plasma glucose; 2-h PG, 2-hour plasma glucose; BMI, body mass index.

and 2-h PG was shown to be inconsistent, implicating the call for comprehensive studies across diverse populations to improve guidelines for the diagnosis of diabetes.

Most importantly, with the current study FPG was able to correctly identify 99.3% of individuals with no diabetes as measured by the 2-h PG. Several community-based studies also reported FPG is highly specific to rule-out diabetes. In an Iranian study from diabetes screening program, the specificity of FBG was comparable to the current study reported at 95.7%, indicating its reliability in screening in the community (25). The DECODE study compared the diagnostic performance of FPG and 2-h PG in large European populations. The study found that FPG had high specificity for identifying individuals without diabetes, with a low rate of misclassification when compared to the 2-h PG (26). The ADA guidelines indicated that FPG is a reliable screening method for identifying individuals without diabetes (4). Hence, results of the

current and previous studies indicate that the usefulness of FPG for screening of diabetes and prediabetes in this and other populations.

Although FPG is reported to have higher specificity and lower intra-individual coefficients of variation compared to 2-h PG (27), it was found to identify a smaller number of individuals with diabetes (28, 29). This study showed that a significant number of individuals with diabetes would have been missed if the screening relied only on FPG. Moreover, while about three-fourth (72.5%) of individuals screened to be diabetes through FPG were also detected by 2-h PG, the latter disclosed an additional 2.1% prevalence of diabetes. These findings were consistent with results from earlier studies (30–32). In addition, studies in Africa have consistently reported that the use of FPG alone identified fewer diabetes cases and IGT compared to 2-h PG (33, 34). The percentage of individuals missed by FPG in our study was similar to findings from Cape Town, South Africa, where about 44% of those with OGTT-detected diabetes missed (34). But

this percentage was higher than the DECODE report (30%) in Europe (35) and much lower than the percentage recorded in France, where 71% of the diabetes diagnoses would have gone undetected if the measurement was FPG alone (30). Moreover, as indicated in the report of WHO and IDF meeting, false negative and false positive results are inevitable given that any initial screening test is not a full diagnostic test (36). The study's findings emphasize the need for complementary tests, such as 2-h PG, to mitigate the limitations of a single screening method. By using multiple tests, healthcare providers can reduce the likelihood of missing true cases (false negatives) and improve the overall reliability of diabetes diagnosis.

As recommended by the 2019 European Society of Cardiology (ESC) guidelines on diabetes, pre-diabetes, and CVDs developed in collaboration with the European Association for the Study of Diabetes (EASD), it may be wise to implement a sequential screening framework (17). In this strategy, the FPG test serves as the initial blood glucose test. An FPG $\geq 105\%$ is diagnostic for diabetes, whereas an additional 2-h PG test is recommended in individuals who did not fulfil FPG criteria but can be considered at high risk of developing diabetes. When this sequential approach would have been used in this population, about two-third of the diabetes cases would have been identified by FPG alone. Screening in this manner is less laborious with a reasonable cost and thus might be a better patient care practice by prioritizing those individuals with a genuine need for 2-h PG, thereby mitigating the risk of overdiagnosis.

Screening in an apparently healthy population with lower FPG cut-off point may enhance the early detection of individuals with IGT. The current study has determined the optimal FPG cut-off values for identifying individuals with prediabetes and diabetes. This emphasizes the need to reassess screening thresholds for identifying diabetes and prediabetes in the African populations, given their significant importance for public health. The FPG cut-off value of 126 mg/dL had a very high specificity (99.3%) for identifying diabetes cases but had a relatively lower sensitivity (47.5%). Variations in sensitivity ranging from 40% to 94% and specificity from 83% to 100% for FPG 126 mg/dL was reported in a systematic review and meta-analysis (10). Once the cut-off value was lowered furthermore it improved the sensitivity at the expense of a minor lowering of specificity. We identified an FPG level of 99 mg/dL and 105 mg/dL as the optimal cut-off values for our population in screening pre-diabetes and diabetes cases, respectively. Our finding of the optimal cut-off for FPG is consistent with the 104 mg/dL cut-off reported in a systematic review and meta-analysis for detecting diabetes (10). But our finding of optimal threshold for FPG differs from that estimated by Hoyer, et al., 2018 (37).

Studies from Asian countries have also suggested reduced threshold values for FPG in the range of 95.0–113.4 mg/dL for screening diabetes (38–40). Similar to our results for screening pre-diabetes, other studies recommended a threshold value of 100 mg/dL as a good cut-off with acceptable sensitivity and specificity (13, 40).

In this research, FPG showed a higher rate of missing diabetes cases in women compared to men. This was in line with the NHANES study in the US where there were more women with isolated 2-h PG ≥ 200 mg/dL, while there were more men with isolated FPG ≥ 126 mg/dL (24). A study by Kim et al. found that FPG had lower sensitivity for detecting diabetes in women, particularly those with a history of gestational diabetes mellitus (GDM), who often have high level of postprandial plasma glucose rather than elevated FPG levels (41). Previous researches have also reported that women have lower FPG and higher 2-h PG levels (42–44). This confirms that the SSA women face a higher risk of developing diabetes following GDM, which often goes undetected due to scarce resources for screening. The combination of undetected GDM and the lower sensitivity of FPG in women creates a significant public health challenge for SSA women. Without effective screening and diagnostic tools, many women at risk of T2DM remain undiagnosed until complications arise (4).

While FPG exhibited a peak in the 45–59 age group, 2-h PG demonstrated a linear increase with advancing age. Likewise, research in other countries have also demonstrated a significant increase in both FPG and 2-h PG after OGTT with aging, as highlighted by Chia (45) and Kalyani (46). In the present study, the 2-h PG criterion was better in identifying older adult individuals with IGT than younger participants as older individuals (≥ 70 yrs) had higher percentages of missed IFG than the middle-aged and young individuals. The NHANES survey also reported that diabetes cases with isolated 2-h PG ≥ 200 mg/dL were older than the diabetes cases with isolated FPG ≥ 126 mg/dL (24). This may partly attribute to decreased muscle mass and reduced physical activity with aging. This underscores the significance of including post-OGTT PG levels to enhance sensitivity in identifying diabetes among older adult individuals in our population.

It is necessary to keep in mind that the importance of an early screening of IFG or IGT lies in its ability to predict diabetes in the future. In this context, while reducing the IFG threshold to 100 mg/dL enhances the predictive capacity of IFG for identifying IGT, it concurrently increases the number of false positive cases. This finding has triggered discussions on the public health merits of lowering the threshold for normal FPG (47, 48). It can be established that with an increasing threshold, the sensitivity of FPG test decreases while the specificity increases. In cases where a higher level of sensitivity is required, such as in screening for type 2 diabetes, a lower threshold may be preferable. It is important to note that establishing a diagnostic threshold for screening involves considerations of cost-effectiveness. Therefore, setting a screening threshold should not solely rely on estimated sensitivities and specificities; clinical and health-economic parameters shall also be taken into account. On the other hand, if the intention is to utilize highly specific tests for confirming a diagnosis, then higher thresholds should be considered.

The European Society of Cardiology (ESC) guidelines emphasized that while screening for diabetes is critical, it alone does not address the broader public health challenges in resource-limited settings such as SSA (17). Instead, it should be targeting

cost-effective and accessible screening methods, even if they are invasive, to ensure accurate identification of at-risk individuals. More accurate diagnostic methods are in demand for individuals who do not test negative, ensuring that resources are used efficiently to tackle the growing burden of diabetes and its complications. Therefore, clinicians need to consider moving beyond reliance on Western guidelines and advocate for locally tailored screening guidelines. Specifically, practitioners in SSA are recommended to develop locally validated FPG thresholds and confirm with subsequent diagnostic tests like 2-h PG or HbA1c, particularly for individuals at high-risk or with borderline test results. Women, who are more likely to be missed by FPG, should be screened more cautiously, with additional tests considered if clinical suspicion remains significant. By adapting practices to the local context, SSA can improve diabetes detection and reduce underdiagnosis, addressing the region's unique challenges more effectively.

5 Strength and limitation

The study employed a community-based, multi-center design on 1550 study participants from Sub-Sahara Africa. The diagnostic capacity of FPG was evaluated against the reference 2-h PG test, to our knowledge, one of the first such studies in the SSA population. Furthermore, setting the FPG cut-off level corresponding to a 2-h PG of 200 mg/dL, the gold standard for diabetes diagnosis, substantially adds to the novelty of this study in the SSA setting. Nevertheless, a single FPG or 2-h PG measurement was utilized to identify individuals with pre-diabetes or diabetes while the criteria for the diagnosis of diabetes requires repeated measurement in asymptomatic individuals. However, given the large study population, the consequences of this limitation are expected to be negligible.

6 Conclusion

FPG was able to correctly identify 99.3% of individuals with no diabetes indicating its usefulness for screening of diabetes. But, a significant percentage (44.4%) of diabetes cases would have remained undetected if only FPG had been utilized instead of the 2-h PG. The use of a lower FPG cut-off value at 105 mg/dL enhanced the detection of individuals with diabetes. Likewise, an FPG cut-off at 99 mg/d, comparable to that of ADA and IDF, can improve early detection of individuals at risk of type 2 diabetes. The use of 2-h PG test is recommended to identify older individuals, females and non-obese persons with diabetes who would be missed by measuring only FPG. In all cases implementing a sequential screening model has the potential to enhance patient care, minimize unnecessary over-diagnosis, and optimize efficient resource use.

Overall, re-evaluation of screening thresholds for FPG for the early identification of individuals with diabetes and prediabetes has pivotal public health implications. Our study emphasizes the need for a thorough and careful revision of diabetes screening guidelines tailored to demographic, clinical, and lifestyle factors influencing the screening and diagnosis of diabetes.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving humans were approved by Institutional Review Board of the College of Health Sciences, Addis Ababa University; The National Research Ethics Review Board (NRERB), Ethiopian Ministry of Education; and University of Nigeria Teaching Hospital, Health Research Ethics Committee. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in these studies.

Author contributions

AB: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. TF: Conceptualization, Project administration, Resources, Supervision, Writing – review & editing. SK: Methodology, Validation, Writing – review & editing. IN: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Writing – review & editing. EY: Investigation, Methodology, Resources, Validation, Writing – review & editing. CP: Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Supervision, Writing – review & editing. EP: Conceptualization, Funding acquisition, Project administration, Resources, Supervision, Writing – review & editing. IU: Conceptualization, Investigation, Methodology, Project administration, Resources, Supervision, Visualization, Writing – review & editing. AD: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. The Diabetes Epidemiologists' Network in Sub-Saharan Africa (DENSSA) collaborative research project involving the University of Dundee in United Kingdom, Addis Ababa University in Ethiopia and University of Nigeria in Nigeria funded by National Institute for Health Research provided financial support for this research (grant number 34558a_CRT). The authors alone are responsible for interpretation of the data, and any views or opinions presented are solely those of the authors and do not necessarily represent that of the funder.

Acknowledgments

We are grateful to all the staff of International Clinical Laboratories in Ethiopia and Chemical Pathology Laboratory of the University of Nigeria Teaching Hospital, which includes laboratory technicians, managers and sample transporters.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

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Manuscript – III

Delayed Treatment Intensification as a Barrier to Glycemic Control among Adults with Type 2 Diabetes: Retrospective Cohort Study at a Tertiary Hospital in Ethiopia

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24 **Abstract**

25 **Aims:** This study aimed to investigate the extent of clinical inertia, evaluated time to treatment
26 intensification and its association with glycemic control among individuals with type 2 diabetes.

27 **Methods:** This is a retrospective cohort study on type 2 diabetes individuals from Tikur Anbessa
28 Specialized Hospital from January 2018 to June 2024. We used Pearson's chi-square tests to
29 compare the proportions of patients, independent t-test or ANOVA to compare the means; and
30 the Mann-Whitney test or Kruskal-Wallis test to compare the medians. Associations between
31 patient characteristics and the presence of clinical inertia were quantified in terms of adjusted
32 odds ratios and 95% confidence intervals.

33 **Results:** A total of 407 individuals were eligible for the analysis, of whom 52.6% were females.
34 Clinical inertia was observed in over half (57.0%) of the patients. Nearly half (48.9%) had
35 uncontrolled blood glucose and median time to treatment intensification was significantly longer
36 among patients with uncontrolled glycemia. Clinical inertia was significantly associated with the
37 duration of diabetes, HbA1c levels, and triglyceride levels.

38 **Conclusions:** Delays in treatment intensification were linked to higher rate of uncontrolled blood
39 glucose levels. Therefore, timely intensification of type 2 diabetes treatment is recommended to
40 enhance better glycemic control and reduce complications.

41 **Keywords:** clinical inertia, type 2 diabetes, treatment intensification

42 **1. Introduction**

43 Effective glycemic control is crucial in individuals with type 2 diabetes is well established[1]. While
44 clinical practice guidelines recommend regular monitoring of HbA1c and timely treatment
45 intensification (TI) to attain glycemic targets, suboptimal glycemic control remains suboptimal [2,
46 3]. Notably Sub-Saharan Africa reports a high prevalence of poor glycemic control with 74%
47 exhibiting HbA1c levels >7.0% (53 mmol/mol), of which 41% have HbA1c levels >10.0%(86
48 mmol/mol)[4]. In Ethiopia, a low-income country, a systematic review of 23 studies revealed that
49 only 38.9% achieved the desired glycemic target[5].

50 If blood glycemic level is not strictly controlled, there can be serious diabetes related
51 complications, such as retinopathy, nephropathy, cardiovascular diseases (CVD), diabetic
52 ketoacidosis (DKA), and a hyperglycemic hyperosmolar state (HHS)[6]. Non-adherence to
53 treatment and clinical inertia are the two primary reasons for suboptimal glycemic control[7, 8].

54 Clinical inertia defined as the 'failure of healthcare providers to initiate or intensify therapy when
55 indicated, plays a significant role in therapeutic management [9].

56 The causes of clinical inertia are complex, multifactorial, and can be identified at three levels: the
57 provider's level, the patient's level, and the system barriers level, counting for about 50%, 30%,
58 and 20% of clinical inertia causes, respectively [ref]. Provider-level barriers include time
59 constraints, competing demands, lack of knowledge. variations in guideline recommendations,
60 perceptions to side effects and inexperience in the management of the condition[10]. Patient level
61 barriers encompass, concerns over drug side effects, misunderstanding treatment regimens,
62 comorbidities, terminal illnesses, fear of needles, limited provider-patient relationship, low literacy
63 levels, and socioeconomic status[11]. System level barriers involve, high healthcare costs,
64 ineffective communication and coordination between departments, lack of healthcare
65 technologies or insurance coverage [12].

66 Clinical inertia contributes to various challenges leading to poor management of diabetes, higher
67 levels of HbA1c and therefore increased complications and a reduction in life expectancy.
68 Prolonged elevation of HbA1c is associated with retinopathy, neuropathy, and nephropathy, and
69 eventually macrovascular complications [13].

70 Research has shown that early tight control leads to the sustained maintenance of glycemic
71 control over the long term. The Efficacy and Durability of Initial Combination Therapy of Type 2
72 Diabetes (EDICT) study showed that early intensive therapy in newly diagnosed individuals with
73 type 2 diabetes was more effective compared to conventional therapy[14].

74 Clinical inertia has been associated with a poor quality of life for the patient, along with increased
75 risks of morbidity and mortality. Osataphan and colleagues demonstrated a significantly reduced
76 time to progression of diabetic retinopathy in a population without clinical inertia compared to
77 those with clinical inertia [15]. Persistent clinical inertia can eventually lead to macrovascular
78 complications [16]. In addition, a major consequence of inertia is the added cost on healthcare
79 systems and public health due to the deterioration of patients who suffer from additional
80 complications[17].

81 While several studies have reported on the level of glycemic control in Ethiopia, there is a lack of
82 evidences regarding the root causes of poor glycemic control including clinical inertia in real world
83 diabetes management. Therefore, this study aims to investigate the extent of clinical inertia
84 among type 2 patients. Additionally, we aim to evaluate the time to TI and its association with
85 glycemic control in this population.

86 **3. Methods**

87 **3.1 Study design**

88 The study was a six-and-half year retrospective open cohort study including data from January
89 2018 to June 2024.

90 **3.2 Study area and period**

91 The study setting was Tikur Anbessa Specialized Hospital (TASH), a tertiary hospital in Addis
92 Ababa. The cohort consisted of individuals with type 2 diabetes who were on OAD treatment in
93 the period between 1st January, 2018 and 31st December, 2023, with end of follow-up on 31st of
94 June, 2024.

95 **3.3 Participants**

96 Patients diagnosed with type 2 diabetes and prescribed OADs as the first treatment of diabetes,
97 and aged ≥ 18 years were included. In this study, the index date is defined as the first date of
98 HbA1c $\geq 7.0\%$ (53 mmol/mol) and/or FBS ≥ 130 mg/dL after three months of the first OAD
99 prescription. Patients diagnosed with type 1 diabetes, received insulin before the index date, on
100 hemodialysis or erythropoietin-stimulating agents after the first OAD prescription, hospitalization
101 for treatment of type 2 diabetes before the index date were excluded.

102 **3.4 Sample size determination**

103 Given that the prevalence of clinical inertia was undetermined in the study site, we determined a
104 sample of 422 participants using the single population proportion formula with a proportion (p) of
105 50% (or 0.5) and after a 10% contingency for incomplete data.

106 **3.5 Data sources and procedures**

107 Data were extracted from electronic medical record (EMR) of the hospital (formerly I-Care and
108 currently Ewket-care at TASH) by trained clinical pharmacists. The information extracted from the
109 records included sociodemographic and clinical characteristics such as age, sex, age at
110 diagnosis, duration of follow-up, clinical events during follow-up, including cardiovascular
111 diseases, diabetic neuropathy, and renal complications, along with dates of events. Detailed
112 information on OADs and insulin along with other medications were obtained from the data bases
113 along with dates. Laboratory test results with respective dates were recorded from the EMR.

114 3.6 Outcome measures

115 The primary outcome of interest was clinical inertia (CI). Clinical inertia is defined as failure of
116 healthcare providers to initiate or intensify therapy when indicated[9, 18, 19] such as increasing
117 the dose of the current OAD, adding other OADs and switching to other OADs within 180 days of
118 index date. Individuals whose HbA1c is maintained <7.0% (53 mmol/mol) after the index date
119 were not considered to have clinical inertia, even without TI. Secondary outcomes of interest were
120 time to TI and glycemic control. TI is defined as: (1) increasing the dose of the current OAD; (2)
121 adding a second OAD or (3) adding insulin to the first OAD (OAD + INS) or switching to a different
122 OAD. Time to TI was calculated by subtracting the index date from the first date of TI. The subjects
123 who do not have increased dose of the current OAD, adding a second OAD or adding insulin to
124 the first OAD were defined as “never intensified” category. According to ADA good glycemic
125 control is defined as A1C less than 7.0% (53 mmol/mol) and fasting plasma glucose (FPG) of 80-
126 130 mg/dL[20].

127 3.7 Statistical analyses

128 Baseline characteristics were described for the total population by clinical inertia status. These
129 were presented as number (%) for the categorical variables and mean (standard deviation, SD)
130 or median (interquartile range, IQR) for the continuous variables. We used Pearson’s chi-square
131 tests to compare the proportions of patients with and without clinical inertia. Independent t-test
132 and ANOVA were used to compare the means while the Mann-Whitney test and Kruskal-Wallis
133 test were used to compare the medians between patients with and without clinical inertia. The
134 proportion of the study population with TI was presented as number (%) with a 95% confidence
135 interval. Associations between patient characteristics and the presence of clinical inertia were
136 quantified in terms of adjusted odds ratios (AOR) and 95% confidence intervals (CIs); p values a
137 priori α value of 0.05 were considered significant to determine statistical significance.

138 3.8 Ethics approval

139 Ethical approval was granted from School of Pharmacy Research Ethics Committee (Ref. No.
140 ERB/SoP/0224/17/2024). Permission to collect the data was obtained from the hospital. To
141 protect the privacy and confidentiality of patient data in this study, strict data security measures
142 were implemented. Access to the electronic medical records was granted through authorized data
143 collectors only via password protected ID. All data was de-identified, and patient identifiers were
144 removed to ensure anonymity. Regular audits and compliance checks were also conducted to
145 safeguard against unauthorized access or data breaches.

146 4. Result

147 4.1. Baseline characteristics

148 Table 1 shows the characteristics of all type 2 diabetes patients and by clinical inertia. A total of
149 407 patients were identified as eligible for the study. Overall, more than half (57.0%) of the
150 patients had clinical inertia. Among the total cohort, 214 (52.6%) were younger adults (<60 years),
151 and 214 (52.6%) females. The majority of patients (57.0%) had follow-ups every three months,
152 with this pattern being similar among those with clinical inertia (59.1%) and those without it
153 (54.3%). Community-based health insurance (CBHI) was the most common payment modality,
154 accounting for 54.3% of the cohort, followed by out-of-pocket payments (43.0%) and free services
155 (2.7%).

156 The mean age of the study participants at diagnosis was 48.7 years which was slightly lower
157 among patients with clinical inertia compared to those without it, 47.4 years and 50.4 years,
158 respectively, suggesting that younger patients at diagnosis might experience higher rates of
159 clinical inertia.

160 The median duration of diabetes in the total cohort was 8.0 years (IQR: 5.3–13.0), with patients
161 in the clinical inertia group having a significantly longer median duration (9.5 years, IQR: 6.0–
162 14.0) compared to those without clinical inertia (7.0 years, IQR: 4.0–13.0; $P = 0.002$).

163 Patients with clinical inertia exhibited significantly higher median HbA1c, 8.0% (64 mmol/mol) vs.
164 6.7% (50 mmol/mol) and fasting blood sugar levels, 145 mg/dL vs. 124 mg/dL; $P < 0.001$, as
165 compared to those without clinical inertia. They also had elevated triglyceride levels compared to
166 those without clinical inertia (127.0 mg/dL vs. 113.0 mg/dL; $P = 0.032$), although other lipid
167 parameters and blood pressure levels showed no significant differences between the two groups.

168 Comorbidities were prevalent across the cohort (89.4%), with hypertension (64.9%) being the
169 most common. One-third of patients (32.2%) experienced diabetes-related complications, with
170 neuropathy being the most common (13.3%).

171 Half of the patients (51.1%) were initiated with dual therapy at the health facility, and this was
172 more frequent in patients with clinical inertia (57.3%) compared to those without clinical inertia
173 (42.9%). In contrast, monotherapy was more common in non-clinical inertia patients (56.0%) than
174 in clinical inertia patients (41.4%; $P = 0.014$).

175 4.2. Time to Treatment intensification

176 As shown in Table 2, among all patients who require TI (n=352) with index HbA1c $\geq 7.0\%$ (53
177 mmol/mol), slightly more than half (58.5%) were intensified in less than 6 months, and 18.5%
178 were intensified within 6 - 12 months, while nearly a quarter of patients (23.0%) were not
179 intensified within 12 months. TI was not deemed necessary for the remaining 55 cases as their
180 HbA1c was $< 7.0\%$ (53 mmol/mol) throughout the follow-up period,

181 Over all, the median time to TI was 6 months (95% CI: 4.3 – 7.7). Men experienced shorter median
182 times to TI (4.0 months, 95% CI: 2.3–5.7) compared to women, whose median time to TI was
183 more than double (9.0 months, 95% CI: 3.8–14.2). Inline to this, a higher proportion of men
184 (61.5%) had TI within 6 months compared to women (55.7%).

185 Individuals with DM complications experienced longer delay in TI, with a median time of 8 months
186 (95% CI, 2.6-13.4) compared to 4 months (95% CI, 2.4-5.6) for those without complications. A
187 lower proportion of participants with complications (50.9%) had TI within 6 months, compared to
188 those without complications (62.1%) ($p = 0.093$).

189 Patients on index monotherapy had a shorter median time to TI at 4.0 months (95% CI: 1.9–6.1)
190 compared to those on dual index treatment at 7.8 months (95% CI: 1.8-13.8). Similarly, nearly
191 two-third (64.9%) of DM cases on index monotherapy were intensified in less than six months as
192 compared to 53.5% of DM cases with dual index treatment.

193 4.3. Glycemic control

194 Table 3 shows TI by the status of glycemic control. Among the total 407 participants, nearly half
195 (48.9%) had uncontrolled blood glucose levels as determined by their latest HbA1c or FBS. More
196 than half of the patients, 206 (58.2%), underwent TI in less than 6 months. Early TI was
197 significantly associated with glycaemic control as half (51.9%) of individuals intensified with less
198 than 6 months achieved glycaemic control while only a third of non-intensified cases achieved
199 glycaemic control ($p = 0.003$). In line to this, the median time to TI was significantly longer among
200 patients with uncontrolled glycemia (9 months, 95% CI: 4.1-13.9) than patients with controlled
201 blood glucose level (3 months, 95% CI: 2.9 -3.3) ($p < 0.001$). More importantly, participants with
202 clinical inertia had a larger proportion of uncontrolled glycemia (65.1%) compared to participants
203 without clinical inertia (27.4%) ($p < 0.001$).

204 About half (52.3%) of patients experienced treatment de-escalation, and this group had a lower
205 proportion of glycemic control (45.1%) compared to those without de-escalation (57.7%)

206 (p=0.011). Among the types of treatment de-escalation, the removal of antidiabetics was the most
207 common (66.2%), with only 39.0% achieving glycemic control.

208 **Factors associated with clinical inertia**

209 In the univariate analysis variables significantly associated with clinical inertia include age at
210 diagnosis (COR = 0.98, 95% CI: 0.96–0.99, p = 0.006), duration of DM (COR = 1.04, 95% CI:
211 1.01–1.07, p = 0.016), duration of follow-up at TASH of 5 years or more (COR = 3.18, 95% CI:
212 2.08–4.85, p < 0.001), FBS levels (COR = 1.01, 95% CI: 1.005–1.014, p < 0.001), and HbA1c
213 levels (COR = 1.61, 95% CI: 1.36–1.92, p < 0.001). In the multivariable analysis, clinical inertia
214 was significantly associated with the duration of diabetes, HbA1c levels, and triglyceride levels.
215 Specifically, each additional year of diabetes duration increased the odds of clinical inertia by 16%
216 (AOR = 1.16, 95% CI: 1.02–1.31, p = 0.022). For every 1% rise in HbA1c, the odds of clinical
217 inertia increased by 91% (AOR = 1.91, 95% CI: 1.17–3.14, p = 0.010). Furthermore, each unit
218 increase in triglyceride levels (mg/dL) was associated with a 2% increase in the odds of clinical
219 inertia (AOR = 1.02, 95% CI: 1.01–1.23, p = 0.048) (Table 4).

220 **Discussion**

221 Clinical inertia among type 2 diabetes patients on OADs, characterized by delays in treatment
222 intensification (TI) despite poor glycemic control [9], is an important reason for suboptimal
223 glycemic control [7, 8]. The result of this study shows that more than half of the cohort had clinical
224 inertia. A systematic review revealed that over 50% of individuals with T2D globally experienced
225 clinical inertia, with notably higher rates (68%) reported in developing countries such as Brazil
226 and Thailand[19]. This inertia can lead to prolonged periods of inadequate glycemic management,
227 thereby increasing the risk of complications[21].

228 Several studies have shown that timely intensification of antidiabetic therapy can significantly
229 improve glycemic control in type 2 diabetes. Furthermore, it has demonstrated a significant
230 reduction in diabetes related complications [22, 23]. In the current study, the median time for TI
231 among individuals with type 2 diabetes on OAD treatment varies significantly. In comparison to
232 the median time to TI observed in our study (6 months), previous studies have reported longer
233 duration. A Malaysian study reported a median time to TI of 1.29 years (15.5 months) [6] while a
234 Japanese cohort study found median times of 6.7 months for insulin intensification, 8.1 months
235 for OAD and 9.1 months for GLP-1 receptor agonists [24].

236 Delays in TI may contribute to a higher risk of DM-related complications, potentially due to
 237 prolonged periods of suboptimal glycemic control. In this study timely intensified cases had better
 238 glycemic outcome. Conversely, delays in TI were associated with prolonged periods of suboptimal
 239 glycemic control, this increasing the risk of complications [24, 25]. Concern of hypoglycemia and
 240 limited therapeutic options are often cited as reasons for longer delays in TI among individuals
 241 with DM complications[21]. Our findings also revealed a significant gender disparity in the timing
 242 of TI among individuals with diabetes. Consistent with our study, a report by Oktora *et al* in the
 243 Netherlands indicated that men are more likely to have TI earlier than women, often at higher
 244 HbA1c levels, indicating a greater perceived need for intensification by healthcare providers [26].
 245 This difference in treatment intensification practice based on gender needs further study.

246 Individuals on index monotherapy at the index date had shorter median time to TI compared to
 247 those on dual therapy. Patients on initial monotherapy, such as metformin or sulfonylureas, often
 248 show a clear need for intensification when glycemic targets are not met, prompting quicker
 249 adjustments in treatment [27], whereas those on dual therapy may have more complex treatment
 250 regimens, leading to a slower recognition of inadequate control and a subsequent delay in
 251 intensification [25].

252 During the course of their follow-up, over half of patients experienced treatment de-escalation.
 253 The combination of delayed TI and frequent de-escalation represents a critical clinical challenge
 254 where patients not only miss timely interventions but are also subjected to regressive treatment
 255 practices. Physicians may reduce treatment intensity to mitigate risks associated with
 256 hypoglycaemia, which can lead to adverse outcomes [21, 28]. Frequent de-escalation can result
 257 in inadequate glycemic control, further complicating diabetes management and increasing long-
 258 term health risks[8].

259 Our findings also revealed that individuals with early treatment intensification had better control
 260 glycemia experienced earlier and more frequent TI compared to those with uncontrolled glycemia.
 261 Researches indicated that patients who experienced delays in intensifying their treatment are at
 262 a higher risk of poor glycemic control and related complications. Patients with delayed TI (≥ 5
 263 years) had higher HbA1c levels compared to those with early intensification, indicating poorer
 264 glycemic control [29, 30]. The findings support the recommendation of early intervention through
 265 TI to optimizing glycemic outcomes. Early TI was linked to a significant decrease in both
 266 microvascular and macrovascular complications, with studies showing a 56% higher risk of
 267 complications for those with delayed TIs [21, 29]. Initiating insulin or other therapies early can
 268 reduce HbA1c levels by approximately 1.4%, leading to better overall glycemic control [21].

269 In the current study clinical inertia among individuals with type 2 diabetes was found to be
270 significantly associated with the duration of diabetes, HbA1c levels, and triglyceride levels Over
271 time, because of insulin resistance in the peripheral tissues[31], chronic metabolic stress,
272 inflammation and oxidative stress[32, 33], type 2 diabetes is characterized by a progressive
273 decline in beta-cell function, leading to worsening glycemic control. This often necessitates TI,
274 but due to clinical inertia, healthcare providers may delay adjustments, particularly in longstanding
275 cases. Patients with a longer history of diabetes are more likely to have developed complications
276 and be on multiple therapies, that may result in hesitancy among physicians to intensify treatment
277 due to concerns of polypharmacy, side effects, or challenges with patient adherence [34].
278 Physicians frequently cite fear of hypoglycaemia as a primary reason for delaying insulin initiation
279 or intensification[35].

280 We also found that the odds of clinical inertia increased by 91% for each 1% increase in HbA1c.
281 Elevated HbA1c indicates suboptimal glycemic control, which should have triggered TI. Studies
282 showed a strong correlation between elevated HbA1c and the severity of diabetes related
283 complications, reinforcing the need for proactive management[36, 37]. However, higher HbA1c
284 levels may reflect a pattern of delayed decision-making where adjustments are only considered
285 after prolonged poor control, perpetuating the cycle of inertia.

286 In summary, using recent electronic medical record data from January 2018 to June 2024 in a
287 real-world type 2 diabetes population, we observed that more than half of them had clinical inertia
288 and nearly a half had uncontrolled blood glucose levels. Delayed TI by six or more months was
289 associated with an increase in uncontrolled blood glucose levels. Identified patient characteristics
290 associated with clinical inertia shall be targeted for better clinical care of patients who experienced
291 clinical inertia and improve glycemic control. We also recommend healthcare providers to intensify
292 DM treatment to enhance better glycemic control and reduce complications.

293 **Authors Contributions**

294 A.M.B., A.Y.D., M.T. and T.G.F contributed to the conceptualization of this study. A.M.B., A.Y.D.,
295 M.T. and T.G.F designed the study. A.M.B. and M.T. contributed to the analyses data. A.Y.D and
296 T.G.F contributed to the supervision of the research. A.M.B. wrote the initial draft of manuscript.
297 A.Y.D., M.T., and T.G.F. contributed with a critical revision of the first and subsequent manuscript
298 versions. All the authors approved the final manuscript.

299 Funding

300 The authors received no funding from an external source.

301 Declaration of competing interest

302 The authors declare that they have no known competing financial interests or personal
303 relationships that could have appeared to influence the work reported in this article.

304 Acknowledgements

305 The authors wish to thank all the staff in Diabetes Center, Tikur Anbessa Specialized Hospital,
306 for accessing electronic medical records.

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Manuscript – IV

Accuracy of fasting capillary blood glucose test in type 2 diabetes screening in Butajira, Central Ethiopia: a community-based study [submitted]

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Abstract

Introduction: Although screening type 2 diabetes with fasting capillary blood glucose (FCG) is convenient and feasible, it can result in inconsistent findings when compared to venous glucose tests, especially in hypoglycemic or hyperglycemic ranges. This study was carried out to evaluate the screening performance of FCG against the standard 2-hour plasma glucose (2-h PG) after 75 gm oral glucose.

Methods: Data from a community-based, cross-sectional diabetes screening survey involving 619 participants in Butajira, central Ethiopia were analyzed between August, 2020 to October, 2021. FCG and 2-h PG were utilized for diabetes screening. We determined and plotted the receiver operating characteristic curve for FCG against the reference standard 2-h PG to evaluate the screening tool's sensitivity and specificity.

Results: The mean (SD) age of the participants was 40.8 ($\pm$ 13.5) years, with women comprising 63.7% of the cohort. With the FCG test, 2.1%, 12.8% and 78.5% of the study participants had diabetes, prediabetes and normal glucose tolerance, respectively. The FCG test exhibited nearly fair accuracy in identifying individuals with diabetes (AUC = 0.69) and prediabetes (AUC of 0.77). the optimal cut point of FCG for detecting newly diagnosed diabetes was 119 mg/dL with a sensitivity of 44.4% and specificity of 97.7% while the optimal cut-off-point of FCG in detecting prediabetes 99.5 mg/dL with a sensitivity of 62.5% and specificity of 88.4%. FCG missed 14.1% of all prediabetes and 48.0% of all diabetes cases identified by the 2-h PG test.

Conclusion: FCG test was able to correctly identify 99.0% of individuals with no diabetes but a significant percentage of diabetes cases would have remained undiagnosed if only FCG had been utilized instead of the 2-h PG. While FCG offers a feasible and fairly accurate method for detecting type 2 diabetes and prediabetes, its low sensitivity requires additional diagnostic methods, particularly in high-risk individuals. Lowering the cut-off value for FPG to 119 mg/dL substantially increases the identification of individuals with diabetes.

Keywords: Diabetes, Fasting Capillary Blood Glucose, 2-h Plasma Glucose, Ethiopia, Sensitivity, Specificity

1 Introduction

Based on the World Health Organization (WHO) diagnostic and screening strategies, clinical questionnaires, urine glucose, fasting plasma glucose (FPG), fasting capillary blood glucose (FCG), 2-h plasma glucose (2-h PG) after 75 gm oral glucose, glycated hemoglobin (HbA1C) and combinations of these tests can be used for screening diabetes(1). The most common test strategy for community-based screening is the FPG test. But there are several limitations with FPG test, such as professional venipuncture is required, the test should be conducted in health facilities, and it has high rate of false negative. Instead, FCG test is a preferred method to address the community. The FCG test avoids venipuncture, can be tested at every health facility, and can deliver immediate results for timely diagnosis of type 2 diabetes. Studies indicated that the level of glucose in capillary and venous are almost similar in the fasting state (2). As a consequence, FCG test may be a suitable alternative screening strategy for detecting undiagnosed type 2 diabetes in resource limited settings and in community-based screening programs. FCG tests are easy-to-use and feasible that makes them ideal for point-of-care testing (POCT) in different setting. This is mainly advantageous in setting with limited-resources where availability of laboratory facilities is inadequate(3).

Although it is convenient and feasible, screening type 2 diabetes with FCG can result in inconsistent findings when compared to FPG, especially in hypoglycemic or hyperglycemic ranges. Studies show that glucometer results may vary by 15–20% from reference values, which can result in wrong clinical interpretations(4). Moreover, hematocrit variations such as in anemia or polycythemia can inappropriately increase or decrease findings(5). More importantly, the thresholds for identifying diabetes and the optimal diagnostic and screening test to use are not defined for populations in SSA(6).

Therefore, this study was carried out in Butajira town, a representative area in central Ethiopia to evaluate the screening performance of FCG against the standard 2-h PG after 75 gm oral glucose. This is the first research ever carried out in Ethiopia to identify the diagnostic performance of FCG test for type 2 diabetes screening.

2 Materials and Methods

2.1 Study design and setting

The Diabetes Epidemiologists' Network in Sub-Saharan Africa (DENSSA): represents collaborative research initiative involving the University of Dundee in United Kingdom, Addis Ababa University in Ethiopia and University of Nigeria in Nigeria. Within this framework, a community-based, cross-sectional study was conducted at the Butajira Rural Health Program (BRHP) in central Ethiopia Data was collected between August, 2020 to October, 2021.

2.2 Study participants

The study participants comprised individuals from six villages in Butajira, Ethiopia. As describe by Baye et al(7) in detail, a multi-stage random cluster sampling technique was utilized to select study participants.

2.3 Data collection

After study participants were interviewed on the first day, they were requested to visit health centers on the subsequent day, between 7:30 a.m. and 9:00 a.m. following an overnight fast of 10–12 hours. The methodological details of this study is mention on a previously published paper.(7)

2.4 Diagnostic criteria

As stated on the published article of this study(7), the ADA's and IDF's diagnostic definitions were utilized to identify diabetes and pre-diabetes cases (8, 9).

2.5 Data analysis

We utilized Stata V.17 software program (StataCorp. Stata Statistical Software: Release 17. College Station, TX: Stata Corp LP) and R version 4.3.2, (R Core Team, 2023) for data analysis. Variables with continuous outcome were reported as mean $\pm$ standard deviation (SD). Categorical differences were expressed in proportions and assessed using a Chi-square test. Receiver operating characteristic (ROC) curves were computed and plotted, with the FCG compared to the reference standard 2-h PG to ascertain its diagnostic capacity as a diabetes and prediabetes screening tool.

Evaluation metrics such as sensitivity, specificity, and Youden's Index were employed to assess the performance of FCG tests (10). We considered $P < 0.05$ to declare statistically significant

3. Results

3.1 Prevalence of diabetes and prediabetes by FCG

Among the cohort of the DENSA study in Ethiopia and Nigeria (previously published)(7), the Ethiopian cohorts had the fasting capillary blood glucose test, so that were included for this analysis. Among the total of 730 Ethiopian participants, 619 individuals were included in the analysis after the exclusion of 30 previously diagnosed with diabetes and 81 who were not tested by 2-h PG. Majority were women (63.7%) and less than 45 years of age (63.5%) with mean age of 40.8 (± 13.5) years.

Of the 619 individuals analyzed, 79 participants (12.8%) demonstrated to have prediabetes detected by FCG, while 13 individuals (2.1%) were detected to have diabetes, and 527 individuals (78.5%) exhibited normal glucose tolerance. Both the prevalence of diabetes and prediabetes were significantly higher among 45 years and above than less than 45 years of age. Similarly, obese individuals had significantly higher diabetes and prediabetes prevalence than non-obese individuals.

Table 1. Diabetes status as measured by FCG among study participants in Butajira, Ethiopia, 2021

Variables	Frequency (%)	Normal	Impaired FCG	Diabetes	P-value
All	619	527 (85.1)	79 (12.8)	13 (2.1)	-
Sex					
Male	225 (36.3)	189 (84.0)	28 (12.4)	8 (3.6)	0.161
Female	394 (63.7)	338 (85.8)	51 (12.9)	5 (1.3)	
Age					
<45 years	393 (63.5)	346 (88.0)	40 (10.2)	7 (1.8)	0.027
≥45 years	226 (36.5)	181 (80.1)	39 (17.3)	6 (2.7)	
Residence					
Urban	354 (57.2)	302 (85.3)	44 (12.4)	8 (2.3)	0.916
Rural	255 (41.2)	225 (84.9)	35 (13.2)	5 (1.9)	
WHO global recommendation on physical activity					
Optimal	488 (78.8)	412 (85.1)	67 (13.7)	9 (1.8)	0.270
Suboptimal	131 (21.2)	115 (87.8)	12 (9.2)	4 (3.1)	
Current smoker					
Smoker	32 (5.2)	26 (81.3)	6 (18.8)	0	0.321
Non-smoker	587 (94.8)	501 (85.3)	73 (12.4)	13 (2.2)	
Current alcohol drinker					
Yes	98 (15.8)	79 (79.6)	16 (16.3)	4 (4.10)	0.191
No	521 (84.2)	449 (86.2)	63 (12.1)	9 (1.7)	
Current khat chewer					
Yes	375	321 (85.6)	47 (12.5)	7 (1.9)	0.856
No	244	206 (84.4)	32 (13.1)	6 (2.5)	
BMI					
Non-obese	575 (92.9)	497 (86.4)	67 (11.7)	11 (1.9)	0.005
Obese	44 (7.1)	30 (68.2)	12 (27.3)	2 (4.5)	
Waist circumference					
Normal	505 (81.6)	438 (86.7)	58 (11.50)	9 (1.8)	0.056
Increased risk	68 (11.0)	55 (80.9)	12 (17.6)	1 (1.5)	
Substantially increased risk	46 (7.40)	34 (73.90)	9 (19.6)	3 (6.50)	
Raised BP					
Normal	107 (17.3)	89 (83.2)	14 (13.1)	4 (3.7)	0.477
Raised	512 (82.70)	438 (85.5)	85 (12.7)	9 (1.8)	

3.2 Agreement between FCG and 2-h PG

The Bland–Altman plot (Figure 1) was developed to explore the limits of agreement between the FCG and 2-h PG tests. The mean bias predicted for these tests was 0.03 and the 1.96 SD ranged from -67.2 to +67.3. Mean differences were found to be larger at higher glucose values. Overall, there is **good agreement** between the two tests.

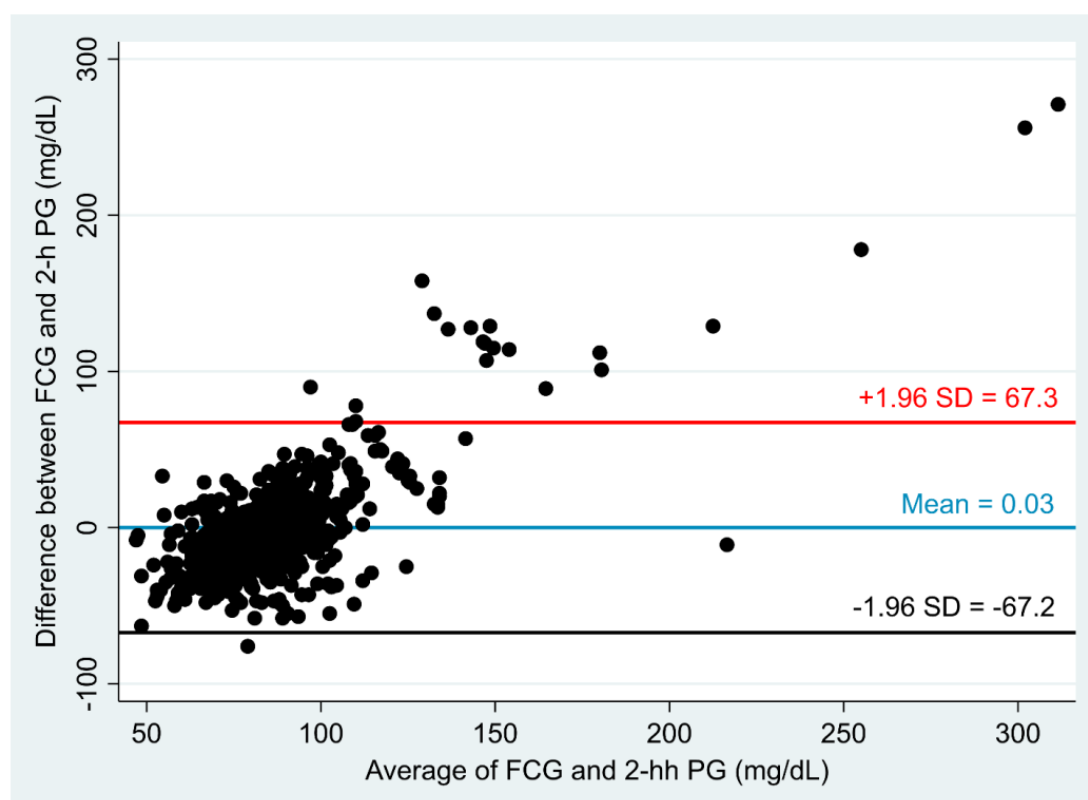


Figure 1. Bland–Altman plot of fasting capillary blood glucose concentration and 2-hour plasma glucose concentration after 75 gm oral glucose load.

3.3 Performance of FCG test

The ROC curve was plotted for FCG test with cut-off points to identify cases with diabetes and prediabetes as outlined in Figure 1. The FCG test exhibited nearly fair accuracy in identifying individuals with diabetes, with an overall AUC of 0.69 (95% CI: 0.52-.0.85) (Figure 1 and Table 2). The AUC for men, 0.79 (95% CI: 0.51-1.0), was higher than that for women, 0.63 (95% CI: 0.43-0.82), but this difference was statistically insignificant ($P=0.353$). In addition, the FCG test

also exhibited a fair accuracy in identifying individuals with prediabetes, with an overall AUC of 0.77 (95% CI: 0.68.-0.86).

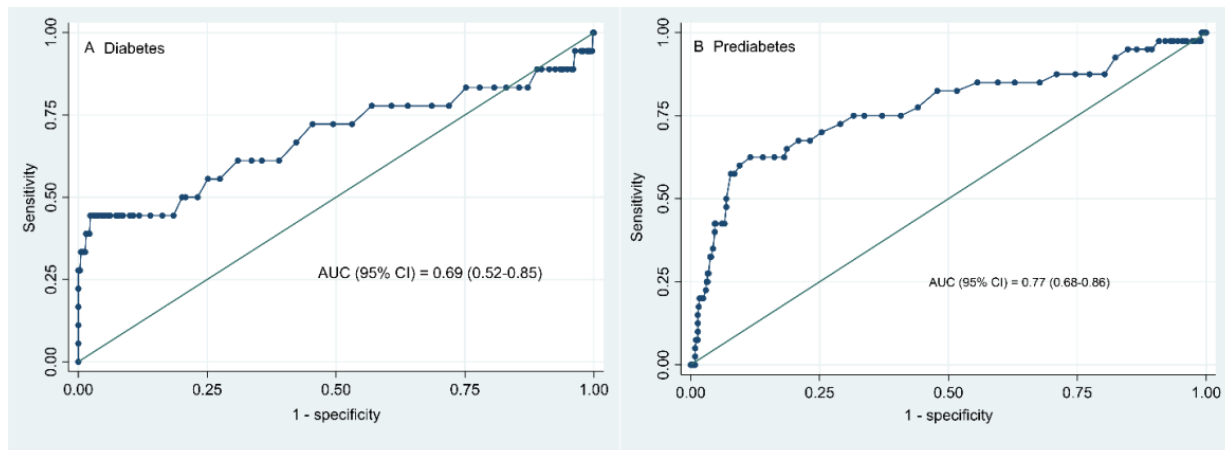


Figure 2. Receiver operating characteristic (ROC) curve for fasting capillary blood glucose (FCG) test to assess the presence of undiagnosed diabetes and prediabetes.

Similarly, the FCG test had good and acceptable performance in identifying individuals with prediabetes, with an overall AUC of 0.77 (95% CI: (0.68.-0.86)) (Figure 1B and Table 2). The performance of the FCG test to identify people with prediabetes revealed higher AUC among the females, 0.82 (95% CI: 0.72-0.92), compared to the men, 0.69 (95% CI: 0.51-0.87), although this is also statistically insignificant (Table 2).

Table 2. Performance of FCG test to identify diabetes and prediabetes, Butajira, Ethiopia, 2021

Variables	Diabetes		Prediabetes	
	AUC (95% CI)	P-value	AUC (95% CI)	P-value
All	0.69 (0.52-.086)		0.77 (0.68-.086)	
Sex				
Male	0.79 (0.51-1.0)	0.353	0.69 (0.51- 0.87)	0.223
Female	0.63 (0.43-0.82)		0.82 (0.72-0.92)	
Residence				
Urban	0.71 (0.50-0.92)	0.623	0.82 (0.72-0.91)	0.225
Rural	0.62 (0.36-0.89)		0.69 (0.51-0.87)	

3.4 FPG cut-off points for pre-diabetes and diabetes screening

Based on the ROC curve analysis, the optimal cut point of FCG for detecting newly diagnosed diabetes by 2-h PG was determined to be 119 mg/dL, associated with a sensitivity of 44.4% and specificity of 97.7% (AUC 0.69, 95% CI: 0.52-0.85) (Table 3). Applying this cut-off point, an additional 9 undiagnosed cases of diabetes could be identified, making the prevalence of diabetes 3.6% in the study population.

Table 3. Sensitivity and specificity for FCG in diagnosing diabetes and prediabetes, Butaira, Ethiopia, 2021

FCG cut-off	Diabetes			Prediabetes		
	Se (%)	Sp (%)	Youden J	Se (%)	Sp (%)	Youden J
70.5	88.9	8.7	-0.025	97.5	9.2	0.067
75.5	83.3	17.0	0.003	92.5	17.6	0.101
76.5	83.3	19.3	0.026	87.5	19.7	0.072
80.5	77.8	31.4	0.092	85.0	32.3	0.173
85.5	72.2	50.6	0.228	82.5	52.2	0.347
90.5	61.1	66.4	0.275	75.0	68.4	0.434
95.5	50.0	79.2	0.292	65.0	81.3	0.463
99.5	44.4	86.0	0.305	62.5	88.4	0.509
100.5	44.4	88.2	0.326	60.0	90.5	0.505
105.5	44.4	92.2	0.366	42.5	93.4	0.359
110.5	44.4	94.8	0.393	35.0	95.7	0.307
115.5	44.4	96.5	0.410	25.0	96.7	0.217
119.0	44.4	97.7	0.421	20.0	97.6	0.176
125.5	33.3	98.8	0.322	12.5	98.6	0.111
126.5	33.3	99.0	0.323	10.0	98.6	0.086
135.5	27.8	99.8	0.276	2.5	99.1	0.016
170.0	16.7	100.0	0.167	0.00	99.5	-0.005

Likewise, the optimal cut-off-point of FCG in detecting prediabetes diagnosed by 2-h PG was determined to be 99.5 mg/dL with a sensitivity of 62.5% and specificity of 88.4% (AUC 0.77, 95% CI:0.68-0.86). This cut-off was equivalent to the ADA recommended cut-off for prediabetes.

When utilizing the guideline recommended cut-off 126 mg/d, the sensitivity of FPG in identifying diabetes is 33.3%, with a specificity of 99.0%. A lower FCG cut-off value 119 mg/dL revealed an increased sensitivity (44.4%) and high specificity (97.7%) for identifying individuals with diabetes (Table 3).

3.5 Prediabetes and diabetes missed by FPG and 2-h PG

Table 4 highlight the percentages of prediabetes and diabetes cases missed by either FCG. Among the total 619 participants tested by both FCG and 2-h PG, FCG would miss 13 cases (14.1%) of all prediabetes and 13 cases (48.0%) of all diabetes cases.

Table 4. Percentages of diabetes and prediabetes missed by FCG, Butajira, Ethiopia, 2021

Characteristics	Diabetes			Prediabetes		
	All diabetes (%)	Diabetes missed by FCG		All prediabetes (%)	Prediabetes missed by FCG	
		Missed (%)	Not missed (%)		Missed (%)	Not missed (%)
All (N=619)	25 (4.0)	12 (1.9)	13 (98.1)	92 (14.9)	13 (2.1)	606 (97.9.0)
Sex						
Men	11 (4.9)	3 (1.3)	222 (98.7)	33 (14.7)	5 (2.2)	220 (97.8)
Women	14 (3.6)	9 (2.3)	385 (97.7)	59 (15.0)	8 (2.0)	386 (98.0)
Age						
< 45 years	14 (3.6)	7 (1.8)	386 (98.2)	51 (13.0)	11 (2.8)	382 (97.2)
≥ 45 years	11 (4.9)	5 (2.2)	221 (97.8)	41 (18.1)	2 (0.9)	224 (98.1)
Residence						
Urban	15 (4.2)	7 (2.0)	347 (98.0)	50 (14.1)	6 (1.7)	348 (98.3)
Rural	10 (3.8)	5 (1.9)	260 (98.1)	42 (15.8)	7 (2.6)	258 (97.4)
WHO global recommendations on physical activity ^a						
Optimal	19 (3.9)	10 (2.0)	478 (98.0)	78 (16.0)	2 (1.5)	129 (98.5)
Suboptimal	6 (4.6)	2 (1.5)	129 (98.5)	14 (10.7)	11 (2.3)	477 (97.7)
BMI ^b						
Non-obese	21 (3.7)	10 (1.7)	565 (98.3)	80 (13.9)	13 (2.3)	562 (97.7)
Obese	4 (9.1)	2 (4.5)	42 (95.5)	12 (27.3)	0	44 (100.0)
Waist circumference ^c						
Low risk	17 (3.4)	8 (1.6)	497 (98.4)	70 (13.9)	12 (2.4)	493 (97.8)
Increased risk	4 (5.9)	3 (4.4)	65 (95.6)	12 (17.6)	0	68 (100.0)
Substantially increased risk	4 (8.7)	1 (2.2)	45 (97.8)	10 (21.7)	1 (2.2)	45 (97.8)
Raised BP						
Yes	8 (7.5)	4 (3.7)	103 (96.3)	17 (15.9)	3 (2.8)	104 (97.2)
No	17 (3.3)	8 (1.6)	504 (98.4)	75 (14.6)	10 (2.0)	502 (98.0)

The rates of diabetes misdiagnosis were higher among women (2.3%) than men (1.3%) using FCG test, while the rate of misdiagnosis for prediabetes was higher among men (2.2%) compared to women (2.0%), despite these differences were not statistically significant. Moreover, the rate of missed cases of diabetes by FCG was higher among older individuals (2.2%) as compared to middle-aged and young study participants (1.8%). This difference is also statistically insignificant.

4 Discussion

The results from the DENSA study in Ethiopia provided valuable insights into the burden of type 2 diabetes and prediabetes identified by fasting plasma glucose (FPG), 2-hour plasma glucose (2-h PG) after 75 gm oral glucose tolerance test and fasting capillary glucose (FCG) testing, as well as the diagnostic performance of FPG and FCG compared to the 2-h PG test. This study has produced several important findings that shall be interpreted in the context of available scientific information on diabetes screening in resource constraint settings.

In the current study, individuals above the age of 45 and those who are obese had higher prevalence of diabetes and prediabetes detected by FCG tests compared to their younger and non-obese counterparts. These findings are consistent with the pattern of the global epidemiology, where increased age and obesity are well-defined predictors for abnormality of glucose metabolism that results in hyperglycemia(11). The high rate of type 2 diabetes among older individuals accounts for the need of targeted screening in this age group, particularly in SSA, where type 2 diabetes is often underdiagnosed due to limited access to healthcare and low health literacy level(6).

The Bland–Altman plot (12) showed a small mean bias (0.03) between FCG and 2-h PG tests tests, with 95% limits of agreement ranging from -67.2 to +67.3, with overall good agreement. This finding is similar to previous studies comparing FCG and 2-h PG. For example, a study found reasonable agreement between FCG and 2-h PG in screening for diabetes (13), though with notable discrepancies in some individuals, particularly at higher glucose levels.

The FCG test showed a fair accuracy in identifying diabetes (AUC = 0.69) and prediabetes cases (AUC = 0.77). While these levels of accuracy indicate that FCG is not a perfect screening tool, they are similar to results from other researches in low-income countries where laboratory-based FPG and 2-h PG tests are not always practically feasible(14). The slightly higher performance of FCG test in men (AUC = 0.79) compared to women (AUC = 0.63) for diabetes screening, though it is not statistically significant, may indicate biological and hormonal influences on blood glucose metabolism, as reported by previous study (15).

The study highlights that while the FCG test effectively identifies 99.0% of individuals with no diabetes (optimal specificity), its sensitivity is poor in identifying individuals with diabetes

compared to the 2-h PG test, leading to a high rate of missed cases if used alone. This limitation calls the importance of incorporating the 2-h PG or other more sensitive tests in diagnostic guidelines to enhance the accuracy of diabetes detection, as FCG alone may not adequately identify individuals with IGT or postprandial hyperglycemia (4, 16).

Based on the standard 2-h PG after 75 gm oral glucose test, this study established an optimal FCG cut-off of 119 mg/dL to screen type 2 diabetes with improved sensitivity (44.4%) while maintaining high specificity (97.7%) compared to the conventional WHO, IDF and ADA-recommended threshold of 126 mg/dL yielding a 33.3% sensitivity in the study population(1, 11, 17). This underscores that in screening type 2 diabetes, particularly in high-risk populations, a slightly lower threshold may help to identify more undiagnosed type 2 diabetes cases without substantially increasing false positives. Similarly, the FCG cut-off for prediabetes (99.5 mg/dL) closely matched the ADA guideline (100 mg/dL), reinforcing its validity in screening programs.

One of the critical findings with this study was FCG missed nearly half (48%) of type 2 diabetes cases and 14.1% of prediabetes cases that were detected by the 2-h PG test. This high rate of misdiagnosis (false negatives) corresponds to previous studies indicating that FCG test alone may underreport type 2 diabetes prevalence, particularly in the SSA populations where postprandial hyperglycemia is more common (18). The higher extent of false negative rates of FCG tests for type 2 diabetes among women and older adults further calls the need for additional diagnostic tests, such as HbA1c, FPG or OGTT, in high-risk groups (1).

Although FCG testing has practical and feasibility advantages in resource-limited settings, its fair level of accuracy and high rate of missed cases of type 2 diabetes indicate that its singular use as a diagnostic tool shall be discouraged. Integrating risk-based screening (e.g., advanced age, obesity and positive family history) with confirmatory diagnostic tests (2-h PG) could improve detection rates(1). Moreover, additional studies are required in the future to investigate the cost-effectiveness of different diagnostic test approaches in SSA, where healthcare access and resources remain a challenge.

5 Conclusion

This study investigated both the prevalence of diabetes and performance of FCG testing based on 2-h PG tests. While FCG offers a feasible and fairly accurate method for detecting type 2 diabetes and prediabetes, its low sensitivity requires additional diagnostic methods, particularly in high-risk individuals. Community health screening strategies should recommend multiple screening models to decrease the burden of undiagnosed diabetes (and its complications) and prediabetes in Ethiopia and similar settings.

Data availability

The datasets generated and/or analyzed during this study are available from the corresponding author on reasonable request.

Ethics statement

This study was approved by Institutional Review Board of the College of Health Sciences, Addis Ababa University and the National Research Ethics Review Board (NRERB), Ethiopian Ministry of Education. The study was conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Funding

This research was part of the Diabetes Epidemiologists' Network in Sub-Saharan Africa (DENSSA) collaborative research project, financially supported by National Institute for Health Research (grant number 34558a_CRT). The authors alone are responsible for interpretation of the data, and any views or opinions presented are solely those of the authors and do not necessarily represent that of the funder.

Acknowledgements

We are grateful to all the staff of International Clinical Laboratories in Ethiopia which includes laboratory technicians, managers and sample transporters.

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APPENDICES

Appendix I: Eligibility Criteria for Study Subjects in Diabetes Screening

Institute: Addis Ababa University, CHS, SOP	Principal Investigator: Assefa Mulu Baye
Project Title: Screening for Type 2 Diabetes in Ethiopia and Nigeria	

Adults above the age of 18 years are eligible if they:

- Report that they are not pregnant
- Report that they have no hemophilia
- Report that they have not received cancer chemotherapy in the last 3 weeks
- Report that they have fasted at least 8 hours
- Do not refuse in phlebotomy during the initial venipuncture

Appendix II: Procedures for Diabetes Screening

Institute: Addis Ababa University, CHS, SOP	Principal Investigator: Assefa Mulu Baye
Project Title: Screening for Type 2 Diabetes in Ethiopia and Nigeria	
1. Confirm the patient's details and that he/she has fasted for at least 8, and no more than 14 hours (water is permitted) and has not smoked on the morning of the test (or during the test). If the patient has eaten or smoked on the morning of the test, the test must be abandoned, and a repeat appointment arranged. 2. Explain the nature of the procedure to the participant. Two blood samples will be collected, 2 hours apart, 2mL before and 2 mL after the 75gm oral glucose drink. 3. Using a glucose meter, determine the patient's fasting blood glucose concentration with a capillary blood sample obtained by finger prick. 4. The result must be less than, or equal to 180 mg/dL to proceed the second test. If the result is greater, referral will be sent to the local health center, and we do not recommend continuing with the test. Instead, take a venous sample of blood for a fasting glucose concentration and send it to the laboratory to confirm the result obtained on the glucose meter. 5. Providing the glucose meter result is less than, or equal to 180 mg/dL, proceed with the test. Blood must be collected into a (2mL to fluoride oxalate tube (grey top). Record full patient details on the collection bottle including the test time (i.e. time zero/fasting). 6. The anhydrous glucose solution must be drunk over the course of 5 minutes. 7. When the test is complete, the patient may eat and drink normally again and is free to leave. 8. Send the blood samples to the laboratory for analysis as soon as possible on dry ice/cold packs to the laboratory.	

Appendix III: Questionnaire for Collection - English

Institute: Addis Ababa University, CHS, SOP

Principal Investigator: Assefa Mulu Baye

Project Title: Screening for Type 2 Diabetes in Ethiopia and Nigeria

Location and Date		Response	Code
Cluster/Centre/Village ID			I1
Cluster/Centre/Village name			I2
Interviewer ID			I3
Date of completion of the instrument		 dd mm year	I4
Consent, Interview language			
1	Informed consent has been obtained	Yes No	☐ 2 (If No, END)
2	(a) Interview language (b) Mother tongue of the individual	----- Code ----- Code (Please write in English)	
Migration details			
3	How long have you been living in this area?	Years: Months	:
4	Where did you spend most of your childhood? (from Birth to 12 years)	Urban area Rural area	1 2 ☐
5	How many years have you lived in urban / rural area?	Urban area Rural area	Years : Months : :
Demographic Information			
6	Sex	Male Female	1 2 ☐
7	Date of Birth	 Day Month Year	☐ Don't know

8	Age (completed)	Years	
9	Religion	Christian 1 Muslim 2 Traditional Religion 3 Others_____ / Unknown 4	
10	What is your current marital status?	Never married 1 Currently married 2 Widow/Widower 3 Divorced/Separated 4 Others, Specify 5 _____	☐
11	What is the highest grade of education you completed?	1.No Formal Education 1 2.Some Primary Education 2 3.Completed Primary Education 3 4.Junior Secondary Education 4 5.Senior Secondary Education 5 6.More than secondary education 6 96.Other (specify)..... 98.Refused to Say 99.Don't know	
12	What kind of work / occupation do you do? Specify the Job:	Professional/Executive/ Manager/Big business 1 Clerical / Medium business 2 Sales 3 Agriculture 4 Self-employed 5	

	----- (Please write in English)	Household & domestic work 6 Services 7 Skilled manual 8 Unskilled manual 9 Do not work/Unemployed 10 Others (Specify) ----- 11 (Please write in English)	
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Smokeless Tobacco Use

13	Do you use any smokeless tobacco such as chewing tobacco or putting in the nose?	Never 1 Past 2 Current 3	☐
14	On average, how many times a day do / did you use [RECORD FOR EACH TYPE] (Record 000, if any product is not used instead of leaving blank in the product categories).	Chewing tobacco Tobacco Snuff by mouth Snuff by nose Others	 Don't remember 999
15	How old were you at the time when you first started using smokeless tobacco regularly?	Age (in completed years)	 Don't remember 999

CORE: Tobacco Use

Now I am going to ask you some questions about tobacco use.

Question	Response	Code
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16	Do you currently smoke any tobacco products, such as cigarettes, cigars or pipes? (USE SHOWCARD)	Yes 1 No 2 <i>If No, go to T8</i>	T1
17	Do you currently smoke tobacco products daily ?	Yes 1 No 2	T2
18	How old were you when you first started smoking?	Age (years) Don't know 77 <i>If Known, go to T5a/T5aw</i>	T3
19	Do you remember how long ago it was? (RECORD ONLY 1, NOT ALL 3)	In Years <i>If Known, go to T5a/T5aw</i>	T4a
	OR in Months <i>If Known, go to T5a/T5aw</i>	T4b	
	Don't know 77 OR in Weeks	T4c	
20	On average, how many of the following products do you smoke each day/week ? (IF LESS THAN DAILY, RECORD WEEKLY) (RECORD FOR EACH TYPE, USE SHOWCARD) Don't Know 7777	DAILY↓ WEEKLY↓	
	Manufactured cigarettes		T5a/T5aw
	Hand-rolled cigarettes		T5b/T5bw
	Pipes full of tobacco		T5c/T5cw
	Cigars, cheroots, cigarillos		T5d/T5dw
	Number of Shisha sessions		T5e/T5ew
	Other	 <i>If Other, go to T5other, else go to T6</i>	T5f/T5fw

		Other (please specify): ☐ ☐ ☐ ☐ ☐ ☐ ☐	T5other/ T5otherw
21	During the past 12 months, have you tried to stop smoking ?	Yes 1 No 2	T6
22	During any visit to a doctor or other health worker in the past 12 months, were you advised to quit smoking tobacco?	Yes 1 No 2 No visit during the past 12 months 3	T7
23	In the past, did you eversmoke any tobacco products? (USE SHOWCARD)	Yes 1 No 2	T8
24	In the past, did you ever smoke daily ?	Yes 1 No 2	T9

CORE: Alcohol Consumption

The next questions ask about the consumption of alcohol.

Question		Response	Code
25	Have you ever consumed any alcohol such as beer, wine, spirits or <i>[add other local examples]</i> ? (USE SHOWCARD OR SHOW EXAMPLES)	Yes 1 No 2 <i>If No, go to A1 6</i>	A1
26	Have you consumed any alcohol within the past 12 months ?	Yes 1 <i>If Yes, go to A4</i> No 2	A2
27	Have you stopped drinking due to health reasons, such as a negative impact on your health or on the advice of your doctor or other health worker?	Yes 1 <i>If Yes, go to A1 6</i> No 2 <i>If No, go to A1 6</i>	A3
28	During the past 12 months, how frequently have you had at least one standard alcoholic drink?	Daily 1 5-6 days per week 2 3-4 days per week 3 1-2 days per week 4	A4

	(READ RESPONSES, USE SHOWCARD)	1-3 days per month 5 Less than once a month 6 Never 7	
29	Have you consumed any alcohol within the past 30 days ?	Yes 1 No 2	A5
30	During the past 30 days, on how many occasions did you have at least one standard alcoholic drink?	Number Don't know 77	A6
31	During the past 30 days, when you drank alcohol, how many standard drinks on average did you have during one drinking occasion? (USE SHOWCARD)	Number Don't know 77	A7
32	During the past 30 days, what was the largest number of standard drinks you had on a single occasion, counting all types of alcoholic drinks together?	Largest number Don't Know 77	A8
33	During the past 30 days, how many times did you have six or more standard drinks in a single drinking occasion?	Number of times Don't Know 77	A9
34	During each of the past 7 days , how many standard drinks did you have each day? (USE SHOWCARD) Don't Know 77	Monday	A10a
		Tuesday	A10b
		Wednesday	A10c
		Thursday	A10d
		Friday	A10e
		Saturday	A10f
		Sunday	A10g
CORE: Diet			

The next questions ask about the 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.

Question		Response		Code
35	In a typical week, on how many days do you eat fruit ? (USE SHOWCARD)	Number of days Don't Know 77	If Zero days, go to D3	D1
36	How many servings of fruit do you eat on one of those days? (USE SHOWCARD)	Number of servings		D2
37	In a typical week, on how many days do you eat vegetables ? (USE SHOWCARD)	Number of days Don't Know 77	If Zero days, go to D5	D3
38	How many servings of vegetables do you eat on one of those days? (USE SHOWCARD)	Number of servings		D4

Dietary salt

With the next questions, we would like to learn more about salt in your diet. Dietary salt includes ordinary table salt, unrefined salt such as sea salt, iodized salt, salty stock cubes and powders, and salty sauces such as soy sauce or fish sauce (see showcard). The following questions are on adding salt to the food right before you eat it, on how food is prepared in your home, on eating processed foods that are high in salt such as [insert country specific examples], and questions on controlling your salt intake. Please answer the questions even if you consider yourself to eat a diet low in salt.

39	How often do you add salt or a salty sauce such as soy sauce to your food right before you eat it or as you are eating it? (SELECT ONLY ONE)	Always 1 Often 2 Sometimes 3 Rarely 4 Never 5 Don't know 77	D5
40	How often is salt or a salty sauce added in cooking or preparing foods in your household?.	Always 1 Often 2 Sometimes 3 Rarely 4 Never 5 Don't know 77	D6

41	How often do you eat processed food high in salt ? By processed food high in salt, I mean foods that have been altered from their natural state, such as packaged salty snacks, such as chips, salted roast groundnuts or cashew nuts, salty food prepared at a fast food restaurant or salty grilled meat (USE SHOWCARD)	Always 1 Often 2 Sometimes 3 Rarely 4 Never 5 Don't know 77	D7
42	How much salt or salty sauce do you think you consume?	Far too much 1 Too much 2 Just the right 3 Too little 4 Far too little 5 Don't know 77	D8

CORE: 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.

Think first about the time you spend doing work. Think of work as the things that you have to do such as paid or unpaid work, study/training, household chores, harvesting food/crops, fishing or hunting for food, seeking employment. *[Insert other examples if needed]*. In answering the following questions 'vigorous-intensity activities' are activities that require hard physical effort and cause large increases in breathing or heart rate, 'moderate-intensity activities' are activities that require moderate physical effort and cause small increases in breathing or heart rate.

	Question	Response	Code
	Work		
43	Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like <i>[carrying or lifting heavy loads, digging or construction work]</i> for at least 10 minutes continuously? <i>[INSERT EXAMPLES] (USE SHOWCARD)</i>	Yes 1 No 2 <i>If No, go to P 4</i>	P1
44	In a typical week, on how many days do you do vigorous-intensity activities as part of your work?	Number of days	P2

45	How much time do you spend doing vigorous-intensity activities at work on a typical day?	Hours : minutes : hrs mins	P3 (a-b)
46	Does your work involve moderate-intensity activity, that causes small increases in breathing or heart rate such as brisk walking <i>[or carrying light loads]</i> for at least 10 minutes continuously? <i>[INSERT EXAMPLES] (USE SHOWCARD)</i>	Yes 1 No 2 <i>If No, go to P 7</i>	P4
47	In a typical week, on how many days do you do moderate-intensity activities as part of your work?	Number of days	P5
48	How much time do you spend doing moderate-intensity activities at work on a typical day?	Hours : minutes : hrs mins	P6 (a-b)

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]*

49	Do you walk or use a bicycle (<i>pedal cycle</i>) for at least 10 minutes continuously to get to and from places?	Yes 1 No 2 <i>If No, go to P 10</i>	P7
50	In a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?	Number of days	P8
51	How much time do you spend walking or bicycling for travel on a typical day?	Hours : minutes : hrs mins	P9 (a-b)

CORE: Physical Activity, Continued

Question		Response	Code
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), <i>[Insert relevant terms]</i>.			
52	Do you do any vigorous-intensity sports, fitness or recreational (<i>leisure</i>) activities that cause large increases in breathing or heart rate like <i>[running or football]</i> for at least 10 minutes continuously? (USE SHOWCARD)	Yes 1 No 2 <i>If No, go to P 13</i>	P10
53	In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational (<i>leisure</i>) activities?	Number of days	P11
54	How much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?	Hrs : minutes : hrs mins	P12 (a-b)
55	Do you do any moderate-intensity sports, fitness or recreational (<i>leisure</i>) activities that cause a small increase in breathing or heart rate such as brisk walking, <i>[cycling, swimming, volleyball]</i> for at least 10 minutes continuously? (USE SHOWCARD)	Yes 1 No 2 <i>If No, go to P16</i>	P13
56	In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational (<i>leisure</i>) activities?	Number of days	P14
57	How much time do you spend doing moderate-intensity sports, fitness or recreational (<i>leisure</i>) activities on a typical day?	Hrs : minutes : hrs mins	P15 (a-b)
CORE: History of Raised Blood Pressure			
Question		Response	Code
58	Have you ever had your blood pressure measured by a doctor or other health worker?	Yes 1 No 2 <i>If No, go to H6</i>	H1

59	Have you ever been told by a doctor or other health worker that you have raised blood pressure or hypertension?	Yes 1 No 2 <i>If No, go to H6</i>	H2a
60	Were you first told in the past 12 months?	Yes 1 No 2	H2b
61	In the past two weeks, have you taken any drugs (medication) for raised blood pressure prescribed by a doctor or other health worker?	Yes 1 No 2	H3
62	Have you ever seen a traditional healer for raised blood pressure or hypertension?	Yes 1 No 2	H4
63	Are you currently taking any herbal, supplements or traditional remedy for your raised blood pressure?	Yes 1 No 2	H5

CORE: History of Diabetes

64	Have you ever had your blood sugar measured by a doctor or other health worker?	Yes 1 No 2 <i>If No, go to H12</i>	H6
65	Have you ever been told by a doctor or other health worker that you have raised blood sugar or diabetes?	Yes 1 No 2 <i>If No, go to H12</i>	H7a
66	Were you first told in the past 12 months?	Yes 1 No 2	H7b
67	In the past two weeks, have you taken any drugs (medication) for diabetes prescribed by a doctor or other health worker?	Yes 1 No 2	H8
68	Are you currently taking insulin for diabetes prescribed by a doctor or other health worker?	Yes 1 No 2	H9
69	Have you ever seen a traditional healer for diabetes or raised blood sugar?	Yes 1 No 2	H10
70		Yes 1	

	Are you currently taking any herbal or traditional remedy for your diabetes?	No 2	H11
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CORE: History of Raised Total Cholesterol

Question		Response	Code
71	Have you ever had your cholesterol (fat levels in your blood) measured by a doctor or other health worker?	Yes 1 No 2 <i>If No, go to H17</i>	H12
72	Have you ever been told by a doctor or other health worker that you have raised cholesterol?	Yes 1 No 2 <i>If No, go to H17</i>	H13a
73	Were you first told in the past 12 months?	Yes 1 No 2	H13b
74	In the past two weeks, have you taken any oral treatment (medication) for raised total cholesterol prescribed by a doctor or other health worker?	Yes 1 No 2	H14
75	Have you ever seen a traditional healer for raised cholesterol?	Yes 1 No 2	H15
76	Are you currently taking any herbal or traditional remedy for your raised cholesterol?	Yes 1 No 2	H16

CORE: History of Cardiovascular Diseases

77	Have you ever had a heart attack or chest pain from heart disease (angina) or a stroke (cerebrovascular accident or incident)?	Yes 1 No 2	H17
78	Are you currently taking aspirin regularly to prevent or treat heart disease?	Yes 1 No 2	H18
79	Are you currently taking statins (Lovastatin/Simvastatin/Atorvastatin or any other statin) regularly to prevent or treat heart disease?	Yes 1 No 2	H19

CORE: Lifestyle Advice

Question		Response	Code
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80	During the past 12 months, have you visited a doctor or other health worker?	Yes 1 No 2	H20
81	During any of your visits to a doctor or other health worker in the past 12 months, were you advised to do any of the following?(RECORD FOR EACH)		
	Quit using tobacco or don't start	Yes 1 No 2	H20a
	Reduce salt in your diet	Yes 1 No 2	H20b
	Eat at least five servings of fruit and/or vegetables each day	Yes 1 No 2	H20c
	Reduce fat in your diet	Yes 1 No 2	H20d
	Start or do more physical activity	Yes 1 No 2	H20e
	Maintain a healthy body weight or lose weight	Yes 1 No 2	H20f
	Reduce sugary beverages in your diet	Yes 1 No 2	H20g
CORE: Blood Pressure			
Question		Response	Code
83	Interviewer ID		M1
	Device ID for blood pressure		M2
	Cuff size used	Small 1 Medium 2 Large 3	M3

	Reading 1	Systolic (mmHg)	M4a
		Diastolic (mmHg)	M4b
	Reading 2	Systolic (mmHg)	M5a
		Diastolic (mmHg)	M5b
	Reading 3	Systolic (mmHg)	M6a
		Diastolic (mmHg)	M6b
	During the past two weeks, have you been treated for raised blood pressure with drugs (medication) prescribed by a doctor or other health worker?	Yes 1 No 2	M7
CORE: Height and Weight			
84	For women: Are you pregnant? (PREGNANT WOMEN ARE EXCLUDED FROM THE STUDY)	Yes 1 <i>If Yes, terminate</i> No 2	M8
	Interviewer ID		M9
	Device IDs for height and weight	Height	M10a
		Weight	M10b
	Height	in Centimetres (cm)	M11
	Weight <i>If too large for scale 666.6</i>	in Kilograms (kg)	M12
CORE: Waist			
85	Device ID for waist		M13
	Waist circumference	in Centimeters (cm)	M14

CORE: Blood Glucose		
Question	Response	Code
During the past 12 hours have you had anything to eat or drink, other than water?	Yes 1 No 2	B1
Technician ID		B2
Device ID		B3
Fasting blood glucose <i>[CHOOSE ACCORDINGLY: MMOL/L OR MG/DL]</i>	mmol/l	B5
	mg/dl	
	Time Measured	
2hr Blood glucose	mmol/l	
	Mg/dl	
Today, have you taken insulin or other drugs (medication) that have been prescribed by a doctor or other health worker for raised blood glucose?	Yes 1 No 2	

Appendix IV: Consent Form – English

Institute: Addis Ababa University, CHS, SOP	Principal Investigator: Assefa Mulu Baye Mobile: 251-910-980410
Project Title: Screening for Type 2 Diabetes in Ethiopia and Nigeria	

Information sheet

Taking part in this research is entirely voluntary. You may choose not take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled.

Purpose of the research: this information sheet explains the study and testing that we are planning to do. The data collector will read this information sheet, and ask questions about anything that you do not understand. We want you to understand the study before signing the consent form.

The main goals of the study are:

- To determine the prevalence of type 2 diabetes in the Ethiopian community screened by OGTT
- To identify risk factors for diabetes mellitus in Ethiopian community

Description of the study procedure: You will be asked to complete a questionnaire about basic demographic characteristics, health status and medical and family histories. Then, you will be given appointment to visit the nearby health centre/health post in a fasting state at least for 8 hours. Measurements like weight, height, waist circumference and hip will be obtained using standardized techniques for you. Your blood pressure will also be recorded twice (in 5 minutes interval) in the sitting position in your right arm.

4 mL of your blood sample (1 teaspoonfuls) will be collected by well-qualified field technicians in the fasting state and 2-hours after you take 75 gm oral glucose.

Risks of the study: you may feel some minor pain when the blood sample is collected. The risk involve will not be any different from what you experience during any normal blood test. The amount of blood taken is not enough to cause you any problem with anemia.

If you are diagnosed with diabetes at screening, you will be referred to a locally registered health care practitioner. If the fasting glucose test indicates that you are hyperglycemic the subsequent oral glucose tolerance test will not be done, rather you will be referred to a local healthcare practitioner.

Benefits to participating in the project: your participation will help medical researchers better understand about the disease and develop better treatments, which may help others like you in the future.

Although you may receive no direct benefit, your participation in this study may help medical researchers better understand the prevalence of type 2 diabetes and its complications. It is likely that you will learn something about your health through the initial screening procedure. It will be a great opportunity for you to get screened for diabetes before it is complicated. Referral for treatment will be facilitated based on the screening result.

Financial Reimbursement, Costs and Commercialization: by consenting to participate, you authorize the use of your samples and clinical information for this research. There are no costs to you for taking part in this study. You will be compensated 50 Birr for your time for taking part in this study. We will use your sample and data only for research and will not be sold or used directly for the production of commercial products.

Withdrawal from Research: participation in this study is voluntary. The decision to participate is up to you. You do not have to participate if you do not want to. You may withdraw from the study at any time. The care you receive now or in the future from the healthcare providers will not be affected, whether you participate in or withdraw from this study.

If you decide to withdraw from the study, your samples will be destroyed and your identity information will be purged from all the databases, so that your samples and data will not be included in any future analyses. However, there are limitations in our ability to exclude your information after it has already been used or shared. For example, it will be difficult or impossible to destroy your information after the analysis of your clinical information has been published in a research journal.

Confidentiality: all information gathered in this study will be kept confidential. When the results of this study are reported in medical journals or at medical meetings, you will not be identified. All medical records will be stored by the researcher in safe cabinets. All clinical information will be password protected.

Clinical information from this study will be identified with a code number instead of your name. The link connecting your personal information and your study code number will be kept in a locked file cabinet. The study investigators and the person managing the clinical information will be the only people with the access to the link.

Appendix V: Certificate of Consent – English

Institute: Addis Ababa University, CHS, SOP	Principal Investigator: Assefa Mulu Baye Mobile: 251-910-980410
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Project Title: Screening for Type 2 Diabetes in Ethiopia and Nigeria

COMPLETE APPROPRIATE ITEMS BELOW (<i>for the data collector</i>)		
I have read the explanation about this study and have been given the opportunity to discuss it and ask questions. Therefore,		
☐ I consent to take part in this study		
☐ I don't like to participate in this study		
_____	_____	_____
Name of the participant	Signature	Date
I have accurately read or witnessed the accurate reading of the consent form to the potential participant, who has had the opportunity to ask questions. I confirm that the participant has given consent freely.		
_____	_____	_____
Name of the investigator	Signature	Date

Address of Institutional Review Board (IRB): Addis Ababa University, College of Health Sciences, CHS Building (7th Floor)

Phone No.

Appendix VI: Consent Form - Amharic

ለስኳር ህመም ቅድመ-ምርመራ የፈቃደኝነት መግለጫ ቅፅ

<u>ተቋም:</u> አዲስ አበባ ዩኒቨርሲቲ የጤና ሳይንስ ኮሌጅ ፋርማሲ ትምህርት ቤት	<u>ዋና ተመራማሪ:</u> አሰፋ ሙሉ ባዬ ስልክ: 251-910-980410
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የጥናቱ ርዕስ: የስኳር ህመም መጠንና ስርጭት፣ በኢትዮጵያ እና ናይጄሪያ

ስለ ጥናቱ ማብራሪያ

በዚህ ጥናት መሳተፍ ሙሉ በሙሉ በፈቃደኝነት ላይ የተመሰረተ ነው። ፈቃደኛ ካልሆኑ በዚህ ጥናት አለመሳተፍ ወይም ጥናቱን አቋርጦ መውጣት ይችላሉ። በጥናቱ ባለመሳተፍ ወይም ስላቋረጡ ሊያገኙት የሚችሉት ማንኛውም አገልግሎት አይቋረጥም።

የጥናቱ ዓላማ: በዚህ የጥናት መረጃ ቅጽ ስለ ጥናቱ ምንነትና የጥናቱ ዓላማዎች በግልፅ ተቀምጧል። መረጃ ሰብሳቢዎች ካነበቡለዎ በኋላ ግልጽ ያልሆነልዎን ጥያቄ ይጠይቁ። በጥናቱ አለመሳተፍ በፊት የጥናቱን ዓላማ ሙሉ በሙሉ መረዳት ይኖርበዎታል።

የጥናቱ ዋና ዋና ዓላማዎች የሚከተሉት ናቸው፡

- አዋቂዎች ላይ የስኳር ስርጭት ምን እንደሚመስል ማጥናት
- ከስኳር ህመም ጋር ተያይዞ የሚከሰት የዓይን ችግር ያለበትን ስርጭትና አጋላጭ ሁኔታዎችን መለየት።

በጥናቱ የሚከናወኑ ተግባራት: ከማንነትዎ ጋር የተያያዙ መረጃዎች፣ የጤናዎ ሁኔታ፣ እንዲሁም ከቤተሰብዎ ጋር የተያያዙ የቆዩ የጤና ሁኔታዎች ምን እንደሚመስሉ ይጠየቃሉ። ከዚያም በሚቀጥለው ቀን ጧት ምንም ዓይነት ምግብ ሆነ ፈሳሽ ሳይወስዱ በቅርብ ወዳለ ጤና ተቋም ይመጣሉ። እንደ ክብደት፣ ቁመት፣ የወገብና የዳሌቅጥነት የመሳሰሉ ልኬቶች ደረጃቸውን በጠበቁ መለኪያዎች ይለካሉ። የደም ግፊትዎ መጠን በአምስት ደቂቃ ልዩነት በተቀመጡበት ሁለት ጊዜ ይለካል።

ምግብዎ ይሁን ፈሳሽ ከመውሰድዎ በፊት በሙያው በሰለጠኑ ባለሙያዎች ለናሙና የሚሆን 4 ሚሊ ደም (1 የሻይ ማንኪያ) ይወሰዳል። እንዲሁም ለዚሁ ጥናት ተብሎ የተዘጋጀ 75 ግራም ስኳር የያዘ ፈሳሽ ከወሰዱ ከሁለት ሰዓት በኋላ በድጋሜ አነስተኛ ደም ይወሰዳል።

ከጥናቱ ጋር የተያያዙ ስጋቶች: ከደምዎ ናሙና ሲወሰድ አነስተኛ የሆነ የህመም ስሜት ሊኖር ይችላል። ለማንኛውም አይነት የደም ምርመራ ሲደረግ ከሚሰማው የህመም ስሜት የተለየ ስሜት አይኖረውም። ለናሙናው የሚወሰደው የደም መጠን ያንያክል ለደም ማነስ የሚያጋልጥ አይሆንም። በምርመራው ሂደት በደምዎ ውስጥ ያለው የስኳር መጠን ከፍተኛ ያል ከሆነ (የስኳር ህመም እንዳለብዎ ከተረጋገጠ) ወደ ጤና ተቋም ሪፈር ይባላሉ።

በጥናቱ መሳተፍዎ የሚኖረው ጥቅም: በዚህ ጥናት መሳተፊዎ ተመራማሪዎችና ሁሉም የጤናው ማህረሰብ ስለስኳር ያላቸውን ግንዛቤ እንዲጨምር ያደርጋል፤ ስለበሽታው የሚደረጉ ምርምሮችና ህክምናዎች የበለጠ እንዲያድጉ ያደርጋል።

ምንም እንኳን ከጥናቱ በቀጠታ የተለየጥቅም ባያገኙም፤ የርስዎ በዚህ ጥናት መሳተፍ በህክምናው የሚደረገው ምርምር የስኳር ህመም ስርጭትና በሽታው የሚያስከትለውን ጉዳት በስፋት ግንዛቤ እንዲኖረን ያደርጋል። የስኳር ህመምን ከባድ ጉዳት ከማስከተሉ በፊት ቅድመ ምርመራ ማድረግ የሚያስገኘውን ጥቅም በዚህ ጥናት የበለጠ ማስገንዘብ ይቻላል። ለራስዎም ቢሆን የስኳር ህመም ቅድመ ምርመራ ማድረግዎ መልካም አጋጣሚ ይሆንለዎታል። የምርምራ ውጤቱ የስኳር ህመም እንዳለብዎካመላከተ አስፍላጊው ሪፈራል ይደርጋል።

ክፍያና ፋይናንስ: በጥናቱ ለመሳተፍ ከወሰኑ የሰጡት ናሙናና መረጃ ለዚህ ጥናት እንዲውል ሙሉ በሙሉ ፈቅደዋልማለት ነው። በጥናቱ ለሚያጠፉት ጊዜ 50 ብር ማካካሻ ይከፈልዎታል። ከእርስዎ የተወሰደው ናሙና ለምርምሩ ዓላማ እንጅ ለሽያጭ ወይም ለንግድ አገልግሎት አይውልም።

ጥናቱን አቋርጦ ስለመውጣት: በዚህ ጥናት መሳተፍ ሙሉ በሙሉ በፍቃደኝነት ላይ የተመሰረተ ነው፤ በጥናቱ ለመሳተፍም ሆነ ላለመሳተፍውሳኔው የእርስዎ ነው። በማንኛውም ጊዜ ጥናቱን አቋርጠው መውጣት ይችላሉ። በጥናቱ ተሳታፊ ባለመሆንዎ አሁንም ይሁን ወደፊት ከጤና ባለሙያዎች የሚያገኙት አገልግሎት አይቋረጥም።

ምናልባት የጥናቱን ተሳትፎዎትን ቢያቋርጡ፤ ከርስዎ የተወሰዱት ናሙናዎች ባግባቡ ይወገዳሉ፤ ማንኛውም ከእርስዎ ጋር የተያያዘ መረጃም ይሰረዛል። ስለሆነም ናሙናዎም ሆነ ሌላ መረጃ በጠናቱ አይካተትም። ነገር ግን መረጃው አንዴ ጥቅም ላይ ከዋለና ለሌሎች ከተጋራ-በጋላለማስወገድ አስችጋሪ ይሆናል።

ሚስጥራዊነት፡ ማንኛውም መረጃ ሚሥጢራዊነቱ የተጠበቀ ነው። የዚህ ምርምር ውጤት በታወቀ የምርምር ጆረናል ላይ ሲታተም ወይም የህክምና ኮንፈረንሶች ላይ ሲቀርብ የእርስዎ ማንነት አይገለጽም። ማንኛውም የዚህ ምርምር መረጃ ደህንነቱ በተጠበቀ ሳጥን ይቆላፋል። መረጃው ከምፒውተር ላይ ሲቀመጥም በሚሰጥር ቁልፍ የተጠበቀ ይሆናል። መረጃዎች የሚያዙት (የሚለዩት) በስምዎ ሳይሆን በሚሰጣቸው የኮድ ቁጥር ይሆናል። የመለያ ኮዶችን ከእያንዳንዱ የጥናቱ ተሳታፊ መረጃ ጋር ማገናዘብ የሚችሉት የጥናቱ ተመራማሪዎች ብቻ ይሆናሉ።

Appendix VII: Certificate of Consent - Amharic

የስኳር ህመም ቅድመ ምርምራ የፈቃደኝነት ማረጋገጫ ቅፅ

<u>ተቋም:</u> አዲስ አበባ ዩኒቨርሲቲ የጤና ሳይንስ ኮሌጅ ፋርማሲ ትምህርት ቤት	<u>ዋና ተመራማሪ:</u> አሰፋ ሙሉ ባዬ ስልክ: 251-910-980410
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የጥናቱ ርዕስ: የስኳር ህመም መጠንና ስርጭት በኢትዮጵያ እና ናይጄሪያ

ከታች ያሉትን መረጃዎች በትክክል ይሙሉ (ለመረጃ ሰብሳቢው)		
ስለ ጥናቱ በቂ የሆነ ማብራሪያ ተሰጥቶኝ ከመረጃ ሰብሳቢው ጋር በቂ የሆነ ውይይት በማድረግ ያልገቡኝን ጥያቄዎችን ጠይቄለሁ፤ ለጥያቄዎችም በቂ ምላሽ አግኝቻለሁ። ስለሆነም:		
☐ በጥናቱ ለመሳተፍ ሙሉ ፈቃደኛ ነኝ ☐ በጥናቱ ተሳታፊ ለመሆን ፈቃደኛ አይደለሁም።		
_____	_____	_____
የተሳታፊው ሙሉ ስም	ፊርማ	ቀን
የጥናቱ ተሳታፊ ይህ የፈቃደኝነት ውል ሙሉ በሙሉ እና በትክክል ተነበላቸዋል፤ በቂ የሆነ ውይይትም አድርገናል። ያልገባቸውን እንዲጠይቁ እድሉ ተሰጥቷቸዋል። ለጥያቄዎቻቸው በቂ ምላሽ ተሰጥቷቸዋል። : ይህን የፈቃደኝነት ቅፅ በነጻነት መመላታቸውን አረጋግጣለሁ።		
_____	_____	_____
የዋና ተመራማሪው ስም	ፊርማ	ቀን

የጥናት ስነ-ምግባር ተቆጣጣሪ አድራሻ: አዲስ አበባ ዩኒቨርሲቲ፣ ህክምናና ጤና ሳይንስ ኮሌጅ ህንፃ 7ኛ ፎቅ

ስልክ:

Appendix: VIII Client Referral Form

Institute: Addis Ababa University, CHS, SOP

Principal Investigator: Assefa Mulu

Project Title: Screening for type 2 Diabetes and Risk Factors in Ethiopia and Nigeria

Case number			Date: ____/____/____		
From (referring facility)					
Address of health facility					
Arrangements made	Yes ☐	No ☐	Tel No: _____	Fax No: _____	
To (receiving facility)					
Address of receiving facility					
Patient's Name					
Age: _____	Address: _____		Sex	M ☐	F ☐
History					
Findings					
Treatment given					
Reason for referral					
Name of referring health professional (and tel no.)				Signature: _____	
<i>Fill in two copies and send one copy with patient for the receiving health facility</i>					

Appendix IX – Data Abstraction Instrument from Iwket-Care Database

Section I: Sociodemographic Characteristics

SN	Items	Responses
1.1	Age	_____ years
1.2	Gender	☐ Male ☐ Female
1.3	Weight	_____ kg
1.4	BMI	_____ kg/m ²
1.5	Marital Status	☐ Married/living with partner ☐ Single ☐ Divorced ☐ Widower/widow
1.6	Working Status	☐ Temporary work ☐ Permanent work ☐ Unemployed ☐ Retired
1.7	Educational Level	☐ Can't read and write ☐ Can read and write ☐ Elementary school ☐ High/secondary school ☐ College and above
1.8	Smoking Status	☐ Never ☐ Current ☐ Former
1.9	Drinking Status	☐ Never ☐ Current ☐ Former
1.10	Availability of home glucometer	☐ Yes ☐ No
1.11	Availability of home BP monitoring	☐ Yes ☐ No
1.12	Payment modality	☐ Free ☐ CBHI ☐ Out of pocket

Section II: Clinical and laboratory characteristics

SN	Variables	Baseline	Current
----	-----------	----------	---------

2.1	Random blood sugar (RBS), mg/dL	_____	_____
2.2	Fasting Blood Sugar (FBS), mg/dL	_____	_____
2.3	HbA1c, %	_____	_____
2.4	Total Cholesterol, mg/dL	_____	_____
2.5	HDL Cholesterol, mg/dL	_____	_____
2.6	LDL Cholesterol, mg/dL	_____	_____
2.7	Triglycerides (TG), mg/dL	_____	_____
2.8	Serum Creatinine (SCr), mg/dL	_____	_____
2.9	Blood Urea Nitrogen (BUN), mg/dL	_____	_____
2.10	eGFR, mL/min/1.73m ²	_____	_____
2.11	Systolic Blood Pressure (SBP), mmHg	_____	_____
2.12	Diastolic Blood Pressure (DBP), mmHg	_____	_____
2.13	Family history of DM	☐ Yes ☐ No	
2.14	Duration of diabetes	_____ years	
2.15	Follow-up schedule	Every _____ month	
2.16	Type of antidiabetic agent	☐ OAD ☐ Insulin ☐ Both	
2.17	Current antidiabetic agent (s)	_____	
2.18	Other chronic disease	☐ Yes ☐ No	

2.1 9	Type of chronic disease	_____
2.2 0	Diabetes complication	☐ Yes ☐ No
2.2 1	Type of complication	☐ Retinopathy ☐ Nephropathy ☐ Neuropathy ☐ Diabetic foot ☐ Other ----- -
2.2 2	Other medication (s)	----- ----- ----- -----
2.2 3	Hypoglycemia within the last 12 months	☐ Yes ☐ No

Section III: Treatment intensification

SN	Treatment intensification items	Response
5.1	Index date	_____
5.2	Index treatment	_____
5.3	Serial HbA1c, %	3 months_____ 6 months _____ 1 year_____
5.4	Index HbA1c (HbA1c requiring TI)	_____
5.5	Treatment Intensification (TI)	☐ Yes ☐ No
5.6	Date of TI	_____
5.7	Method of TI at first visit*	☐ Addition of new OAD ☐ Increase dose of OAD ☐ Addition of insulin

		☐ Increase dose of OAD + addition of new OAD ☐ Increase dose of OAD + addition of new insulin ☐ Addition of new OAD + addition of new insulin ☐ Increase dose of OAD + addition of new OAD + addition of insulin ☐ Other _____
5.8	Type of TI at first visit*	☐ Addition new medication ☐ Increase dose of medication
5.9	Type of antidiabetic for TI at first visit*	☐ OAD ☐ Insulin ☐ Insulin + OAD
5.10	Specific medication(s) for TI at first visit*	_____
5.11	Number of medications for TI at first visit*	_____
5.12	Number of TI across study time frame	_____

*The first visit where treatment intensification occurred, following the index visit

Appendix X. IRB Letters



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FEDERAL DEMOCRATIC REPUBLIC OF ETHIOPIA
MINISTRY OF EDUCATION

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ቀን/DATE:

13 FEB 2023

ቁጥር/REF NO:

17/1521402/23

Addis Ababa University College of Health Sciences (AAU-CHS)

Addis Ababa

Subject: Letter of Approval

The Ministry of Education (MoE) via its National Research Ethics Review Committee has reviewed the "The Epidemiology of Type 2 Diabetes and Pathway to Preemptive Pharmacogenomics Study in Ethiopia" project protocol in an expedited manner. We are writing to advise you that MoE has granted full approval to the above named project, for a period of one year (February 09, 2023-February 08, 2024).

All your most recently submitted documents have been approved for use in this study. The study should comply with the international and national scientific and ethical standard guidelines. Any change to the approved protocol or consent material must be reviewed and approved through the amendment process prior to its implementation. In addition, any adverse or unanticipated events should be reported within 24-48 hours to MoE. Please ensure that you submit biannual progress report to MoE once in six months and annual renewal application 30 days prior to the expiry date.

We are confident that your esteemed organization and the PI (copied) of the project should monitor the ethical implication of the project as stipulated in the latest approved document.

Cc

- > State Minister for Higher Education Development Sector
- > CEO, Research and Community Engagement Affairs
- > Research Ethics Desk
- > Ministry of Education
- > Prof. Teferi Gedif (PI)
- > AAU-CHS



Sincerely


Solomon Benor Belay (PhD)
Chief Executive Officer
Research and Community
Engagement



ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES (IRB)
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Institutional Review Board

ANNEX 3
Form AAUMF 03-008

IRB's Decision

Meeting No: 09/2022

Meeting Date: August 23, 2022

Protocol number: 027/19/SoP

Protocol Title: The Epidemiology of Type 2 diabetes and pathway to preemptive pharmacogenomics study in Ethiopia	
Principal Investigator:	Prof. Teferi Gedif Fenta
Institute:	College of Health Sciences, AAU
Elements Reviewed (AAUMF 01-008)	☒ Attached ☐ Not attached
Review of Revised Application ☐ Yes ☐ No	Date of Previous review:
Decision of the meeting:	☒ Approved ☐ Approved with Recommendation ☐ Resubmission ☐ Disapproved

- I. Elements approved-
1. Protocol Version No: 03
 2. Protocol Version Date:
 3. Informed consent Version No. 03
 4. Informed Consent Version Date:

II. Obligations of the PI-

1. Should comply with the standard international & national scientific and ethical guidelines
2. All amendments and changes made in protocol and consent form need IRB approval
3. The PI should report SAE within 10 days of the event
4. End of the study, including manuscripts and thesis works should be reported to the IRB
5. The PI should report non-compliance and unanticipated events

III. TO NERC ☒

Institution Review Board (IRB) Approval: Period from September 30, 2022, to September 29, 2023

Follow up report expected in 3 Months ___ 6 months ☒ 9 months ___ one year ___

Chairperson, IRB
Dr. Adamu Adhiso

Signature

Date: September 10, 2022

Institutional Review Board Office
(IRB)
Faculty of Medicine
ADDIS ABABA UNIVERSITY

Director of Research & Technology Transfer, CHS
Dr. Wondwossen Amogne

Signature

Date

10/3/2022





Addis Ababa University

School of Pharmacy Research Ethics Review Committee

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Date November 17, 2024 GC

Ref. No. ERB/SoP/0224/17/2024

To: Assefa Mulu
School of Pharmacy

Re: Ethical Clearance

It is to be recalled that you submitted a research proposal titled "Clinical Course, Treatment Intensification, and Outcomes in Type 2 Diabetes Patients Attending Tikur Anbessa Specialized Hospital, Ethiopia". The committee thoroughly reviewed the proposal based on its operational guideline and found that, it fulfils all the ethical requirements stipulated in the guideline. This is, therefore, to inform you that the proposal is ethically approved for implementation.

With best regards,

A handwritten signature in black ink, appearing to be 'Zelalem'.

Zelalem Petros (PhD)

Chairperson, Ethical Review Committee

School of Pharmacy, College of Health Sciences