SERUM AMYLASE AND LIPASE IN TYPE 2 DIABETIC MELLITUS PATIENT ON DIFFERENT ANTIGLYCEMIC DRUGS IN BENIN CITY

BY

OLOGUNYE, OLORUNKEMI ADESEWA

BMS2001193

DEPARTMENT OF MEDICAL LABORATORY SCIENCE

SCHOOL OF BASIC MEDICAL SCIENCES

COLLEGE OF MEDICAL SCIENCES

UNIVERSITY OF BENIN,

BENIN CITY

SEPTEMBER, 2025.

SERUM AMYLASE AND LIPASE IN TYPE 2 DIABETIC MELLITUS PATIENT ON DIFFERENT ANTIGLYCEMIC DRUGS IN BENIN CITY

BY

OLOGUNYE, OLORUNKEMI ADESEWA

BMS2001193

A PROJECT SUBMITTED TO THE DEPARTMENT OF MEDICAL LABORATORY SCIENCE
SCHOOL OF BASIC MEDICAL SCIENCES,
COLLEGE OF MEDICAL SCIENCES,
UNIVERSITY OF BENIN,
BENIN CITY.

IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF BACHELOR OF MEDICAL LABORATORY SCIENCE (BMLS) DEGREE.

SUPERVISOR:
PROF.M.A. EMOPKAE

SEPTEMBER, 2025.

CERTIFICATION

This is to certify that this project work"**SERUM AMYLASE AND LIPASE IN TYPE 2 DIABETES MELLITUS PATIENT ON DIFFERENT ANTIGLYCEMIC DRUGS"** was carried out by **OLOGUNYE OLORUNKEMI ADESEWA,** bearing the matriculation number **BMS2001193**,in the Department of Medical Laboratory Science,School of Basic Medical Science, University of Benin,Benin City,Edo State , Nigeria.This project was completed under the supervision ,in partial fulfillment of the requirements for the Bachelor of Medical Laboratory Science Degree.

PROF. M.A EMOKPAE **DATE**
Supervisor

Dr. (Mrs.) ZAINAB OMORUYI **DATE**
Head of Department

EXTERNAL EXAMINER **DATE**

DEDICATION

This project aid dedicated to Almighty God,whose boundless love and guidance has made this project a reality.

Furthermore,I would like to dedicate this to my parents,Mr. and Mrs.OLOGUNYE,for their unwavering support.

ACKNOWLEDGEMENT

I express my gratitude to God for providing me with strength, insight,solace and guidance and enabled me to complete this work

A heartfelt expression of gratitude goes to my esteemed supervisor, Professor M.A Emokpae, for generously dedicating his valuable time to oversee and evaluate my work despite his busy schedule .His care, guidance and insightful suggestions have significantly contributed to the progress and success of this research project.

I extend my deepest appreciation to Dr.(Mrs.) Zainab Omoruyi, the head of the Department of Medical Laboratory Science,for her invaluable support to our class throughout the process.

I am immensely grateful for my parents, Mr.and Mrs.Ologunye ,for their unwavering trust, encouragement and financial support throughout this project.Your boundless support has been instrument in my journey ,and u deeply appreciate it.And to my brothers, Benjamin and Inioluwa, thank you for your support.

My sincere gratitude goes to my Aunties, Mrs. Ogunwale Oluwanisola Ayodele and Mrs. Opayele Blessing also to my friends Omotayo and Ayobami for their encouragement and unwavering support.

TABLE OF CONTENT

Title Page	i
Certification	ii
Dedication	iii
Acknowledgement	iv
Table of Content	v
List of Tables	ix
Abstract	x
CHAPTER ONE: INTRODUCTION	**1**
1.1 Background of study	1
1.2 Statement of problem	2
1.3 Justification of study	4
1.4 Aim of study	5
1.4.1 Specific Objectives	5
1.5 Research Questions	5
1.6 Research Hypothesis	6
1.6.1 Null Hypothesis	6

1.6.2 Alternative Hypothesis 6

CHAPTER TWO: LITERATURE REVIEW 7

2.1 Overview of Diabetes Mellitus 7

2.1.1 Types 1 Diabetes Mellitus 7

2.1.2 Type 2 Diabetes Mellitus 8

2.1.3 Gestational Diabetes 8

2.1.4 Other types of Diabetes 8

2.2 Epidemiology of Diabetes Mellitus 9

2.2.1 Pathophysiology of Diabetes Mellitus 10

2.3 Pancreatic function and Enzymes 11

2.3.1 structure and ole of pancreas 11

2.4 Amylase; Synthesis, function and pathology Role 16

2.4.1 Extra Digestive role and Gut Health 16

2.4.2 Amylase in Glucose Homeostasis 17

2.4.3 Lipase and Type 2 Diabetes Mellitus 17

2.5 Antiglycemic Drug Classes 18

2.6 Relationship between Antiglycemic Drugs and Pancreatic Enzyme Activity 23

2.7 Compartive Findings across Different Populations 24

2.7.1 Population and Ethnic Variability 25

2.7.2 Gaps and Future Directions 26

CHAPTER THREE: MATERIALS AND METHODS 28

3.1 Study Area 28

3.2 Study design 28

3.3 Study participants 28

3.4 Inclusion criteria 28

3.5 Sample size determination 29

3.6 Ethical Approval 30

3.7 Data Collection 30

3.8 Sample collection 30

3.9.1 Serum Amylase CNPG3 method (D'souza etc *et al.,*2011) 31

3.9.2 Pancreatic Lipase Methyl Resorufin method (panteghinib *et al.,*2001) 32

3.10 Statistical Analysis 33

CHAPTER FOUR: RESULT 34

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATION 45

5.1 Discussion 45

5.2 Conclusion 47

5.3 Recommdation 48

REFERENCES **50**

APPENDIX I: **53**

APPENDIX II: **57**

APPENDIX III: **58**

LIST OF TABLES

4.1 Socio_Demographic characteristics and study partipants 36

4 2 Body Mass Index category of study participants 37

4.3 Duration of Diabetes Among Subject 38

4.4 Antiglycemic medications used by subject 39

4.5 Serum Amylase and Lipase levels between Control and subject 40

4.6 Serum Amylase and Lipase across Antiglycemic Drugs 41

4.7 Serum Amylase and Lipase across Gender,BMI categories and duration of diagnosis 42

4.8 Serum Amylase and Lipase levels by Age group 43

4.9 Correlation of serum Amylase and Lipase with BMI, duration of diabetes and Antiglycemic medications. 44

ABSTRACT

Both endocrine and exocrine pancreatic functions are impacted by type 2 diabetes mellitus (T2DM), a chronic metabolic disease. Important indicators of pancreatic health, serum lipase and amylase, are frequently changed in type 2 diabetes, but little is known about how anti-diabetic medications affect these enzymes, especially in African populations. In Benin City, Nigeria, this study examined the serum levels of lipase and amylase in T2DM patients taking various antiglycemic medication classes. 50 T2DM patients and 50 age-matched non-diabetic controls were enlisted. Standard enzymatic assays were used to measure the concentrations of serum lipase and amylase, and correlation statistics and one-way ANOVA were used to analyse the data. The mean levels of lipase (67.03 ± 6.96 U/L) and amylase (93.19 ± 4.49 U/L) were significantly higher in T2DM patients than in controls (59.56 ± 4.81 U/L and 39.52 ± 3.19 U/L, respectively; $p < 0.001$). Although these differences were not statistically significant, variation was seen across antiglycemic drug classes, with patients on metformin plus sulfonylureas having the highest amylase levels and those on DPP-4 inhibitors having the highest lipase levels. Exocrine function gradually declined over time, as evidenced by the significant negative correlation between lipase activity and the length of diabetes ($r = –0.347$, $p = 0.014$). While lipase was lower in overweight people, demographic factors like age, sex, and BMI had no discernible impact on amylase. In conclusion, this study shows that T2DM is linked to increased pancreatic enzyme levels, with patterns impacted by the length of the disease and, to a lesser degree, anti-glycemic medication. These results emphasise the value of tracking exocrine pancreatic function in the treatment of diabetes and demand more extensive, long-term, population-based research to elucidate the clinical consequences of these changes.

CHAPTER ONE

INTRODUCTION

1.1 Background of Study

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from insulin resistance, impaired insulin secretion, or both. Beyond its well-established effects on glucose metabolism, T2DM can also impact pancreatic exocrine function, leading to conditions like exocrine pancreatic insufficiency (EPI). The pancreas, a vital organ, has both endocrine (insulin and glucagon production) and exocrine (digestive enzyme production, including amylase and lipase) functions. There is increasing evidence suggesting a close interplay between these two functions, often referred to as the "endocrine-exocrine axis" of the pancreas.

Serum amylase and lipase are key pancreatic enzymes, and their levels are often used as markers for pancreatic health. While elevated levels are typically indicative of acute pancreatitis, recent research suggests that altered (often lower) baseline levels of these enzymes are common in T2DM patients, even in the absence of overt pancreatic disease (Ko *et al.,* 2020; Kumar *et al.,* 2022). This alteration is believed to be linked to the derangement of the endocrine-exocrine axis in T2DM, potentially due to factors like insulin resistance and atrophy of exocrine acinar cells (Bhadarge *et al.,* 2021).

The management of T2DM involves various classes of antiglycemic drugs, each with distinct mechanisms of action. These include:

Metformin: Primarily reduces hepatic glucose production and increases insulin sensitivity.

Sulfonylureas and Meglitinides: Stimulate insulin secretion from pancreatic beta cells.

Thiazolidinediones (TZDs): Improve insulin sensitivity in peripheral tissues.

Dipeptidyl Peptidase-4 (DPP-4) Inhibitors (Gliptins): Enhance the action of incretin hormones (GLP-1 and GIP) by preventing their degradation, thereby increasing insulin secretion and suppressing glucagon.

Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RAs): Mimic the effects of GLP-1, leading to glucose-dependent insulin secretion, glucagon suppression, delayed gastric emptying, and increased satiety.

Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitors: Promote glucose excretion in urine by inhibiting glucose reabsorption in the kidneys.

While the primary focus of these drugs is glycemic control, their potential impact on pancreatic exocrine function, specifically on serum amylase and lipase levels, is a growing area of interest. Some studies have suggested that certain antiglycemic drugs, particularly incretin-based therapies (GLP-1 RAs and DPP-4 inhibitors), might influence pancreatic enzyme levels, although the clinical significance and long-term implications are still under investigation (Steinberg *et al.*, 2014; Sivertsen *et al.,* 2017). Understanding these effects is crucial for comprehensive patient management, especially considering the prevalence of gastrointestinal symptoms in T2DM patients, which could sometimes be linked to subtle exocrine pancreatic dysfunction.

1.2 Statement of Problem

It is becoming more widely acknowledged that type 2 diabetes mellitus (T2DM) impacts both exocrine and endocrine pancreatic functions. Although results are still mixed, there is evidence

that people with type 2 diabetes may have changed serum levels of lipase and amylase. While some studies show that people with type 2 diabetes have lower levels of pancreatic enzymes than people without the disease, which may indicate exocrine insufficiency, other studies show that some patients have higher levels of enzyme activity, particularly after starting some antiglycemic drugs (Regasa, 2022; Nauck, 2021). Elevations in serum lipase and, to a lesser extent, amylase have been repeatedly linked to incretin-based medications, such as dipeptidyl peptidase-4 inhibitors (DPP-4i) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) (Sayiner et al., 2020; Czaplicka, 2024). Despite the fact that these enzyme increases are frequently asymptomatic, their documented correlations with severe pancreatitis have sparked concerns. The therapeutic importance of these biochemical changes is the subject of current controversy in diabetes treatment and safety guidelines due to inconsistent findings found in meta-analyses and pharmacovigilance reports released between 2020 and 2025 (Czaplicka, 2024; Kamrul-Hasan, 2024).The comparability of existing studies is limited by a number of methodological problems. These include discrepancies in assay techniques and diagnostic thresholds, variations in the timing and frequency of enzyme assessments, and heterogeneity in the antiglycemic medication classes under study. Furthermore, confounding variables that affect serum enzyme levels independently, like obesity, gallstone disease, alcohol consumption, and renal dysfunction, are frequently not well controlled for (Regasa, 2022). Therefore, it is still unknown if detected increases in pancreatic enzymes are real markers of pancreatitis risk, drug-specific side effects, or temporary laboratory results. The majority of the research that are now accessible are either retrospective pharmacovigilance evaluations, small randomized trials, or observational. Prospective, well-powered, head-to-head comparison studies that measure blood lipase and amylase across time across various antiglycemic treatments are scarce. Clinicians are unable to

provide evidence-based pancreatic safety counseling and develop suitable monitoring plans for patients receiving antiglycemic medication because of this information gap (Sayiner *et al.,* 2020; Czaplicka, 2024). Therefore, more study is required to properly account for confounding variables, correlate enzyme changes with clinical outcomes, and comprehensively compare serum amylase and lipase levels in T2DM patients across routinely used antiglycemic medication classes. Closing this gap will yield more precise data to support safe prescription and monitoring procedures in the treatment of diabetes.

1.3 Justification of the Study

This study is justified on the following grounds:

I. Patient Safety: Understanding how different antiglycemic drugs affect pancreatic enzymes can alert clinicians to subclinical pancreatic stress before it progresses to acute complications.
II. Evidence-Based Practice: There is insufficient comparative data or similar populations regarding serum lipase and amylase levels in patients on various antiglycemic regimens.
III. Guidance for Clinical Decision-Making: This research may help in tailoring antiglycemic therapies for individual patients based on safety, especially for those with a predisposition to pancreatic disorders.
IV. Scientific Contribution: The findings will contribute to the body of knowledge on the biochemical impact of antiglycemic agents and may prompt further longitudinal studies.

1.4 Aim of Study

This study aims to investigate the levels of serum amylase and lipase in T2DM patients on different classes of antiglycemic drugs, thereby contributing to a better understanding of the multifaceted effects of these medications and the overall pancreatic health in T2DM.

1.4.1 Specific Objectives

The specific objectives of the are to:

1. determine the levels of serum amylase and lipase in T2DM patients
2. correlate the serum levels of amylase and lipase with antiglycemic agents
3. correlate the serum amylase and lipase levels with duration of antiglyceamic usage.
4. determine the influence of demographic and clinical factors (e.g., age, sex,BMI, duration of diabetes) on the levels of serum amylase and lipase.

1.5 Research Questions

1. Are there significant differences in serum amylase and lipase levels among Type 2 Diabetes Mellitus patients receiving different classes of antiglycemic drugs?
2. Do specific classes of antiglycemic drugs (e.g., GLP-1 RAs, DPP-4 inhibitors, Metformin) have a distinct impact on serum amylase and lipase levels compared to other classes or to T2DM patients not on medication?
3. Is there a correlation between the duration of antiglycemic drug use and changes in serum amylase and lipase levels?
4. Is there any influence of demographic and clinical factors (e.g., age, sex,BMI, duration of diabetes) on the levels of serum amylase and lipase.

1.6 Hypothesis:

1.6.1 Null Hypothesis

1. There is no significant difference in serum amylase and lipase levels among Type 2 Diabetes Mellitus patients receiving different classes of antiglycemic drugs
2. The specific classes of antiglycemic drugs (e.g., GLP-1 RAs, DPP-4 inhibitors, Metformin) have no distinct impact on serum amylase and lipase levels compared to other classes or to T2DM patients not on medication
3. There is no correlation between the duration of antiglycemic drug use and changes in serum amylase and lipase levels?
4. There is no influence of demographic and clinical factors (e.g., age, sex,BMI, duration of diabetes) on the levels of serum amylase and lipase.

1.6.2 Alternate Hypothesis

1. There is a significant difference in serum amylase and lipase levels among Type 2 Diabetes Mellitus patients receiving different classes of antiglycemic drugs
2. The specific classes of antiglycemic drugs (e.g., GLP-1 RAs, DPP-4 inhibitors, Metformin) have distinct impact on serum amylase and lipase levels compared to other classes or to T2DM patients not on medication
3. There is a correlation between the duration of antiglycemic drug use and changes in serum amylase and lipase levels?
4. There is an influence of demographic and clinical factors (e.g., age, sex, BMI duration of diabetes) on the levels of serum amylase and lipase.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Overview of Diabetes Mellitus

Diabetes Mellitus (DM) is a chronic, progressive metabolic disorder characterized by persistent hyperglycemia (elevated blood glucose levels). This condition arises due to defects in insulin secretion, insulin action, or a combination of both. Insulin is a hormone produced by the pancreas that regulates blood glucose levels. Diabetes impairs the body's ability to use or produce insulin effectively, leading to a range of short-term and long-term complications. DM is one of the most common endocrine (hormone-related) disorders globally and represents a significant public health challenge contributing to substantial morbidity, mortality, and economic burden. (Yameny, 2024).

Diabetes mellitus is broadly classified into three major types: Type 1 diabetes, Type 2 diabetes, and gestational diabetes. Each category is distinguished by its underlying pathophysiology, clinical features, and natural course of progression.

2.1.1 Type 1 Diabetes

Type 1 diabetes is characterized by autoimmune destruction of pancreatic beta cells, leading to an absolute deficiency of insulin. In this form, the body is unable to synthesize insulin, and as a result, glucose derived from carbohydrate metabolism cannot enter cells for energy utilization. This results in persistent hyperglycemia with the classical symptoms of polyuria, polydipsia, polyphagia, and unexplained weight loss despite increased appetite (Yameny, 2025).

2.1.2. Type 2 Diabetes

Type 2 diabetes is the most prevalent form globally and has a multifactorial pathophysiology. It involves both peripheral insulin resistance and progressive beta-cell dysfunction, leading to inadequate insulin secretion. Although insulin production continues, its effectiveness in regulating blood glucose becomes increasingly impaired. The condition typically develops gradually and is often preceded by a prediabetic stage, such as impaired glucose tolerance or impaired fasting glucose. Type 2 diabetes is now increasingly recognized as a core component of the metabolic syndrome, also referred to as metabolic dysfunction syndrome (MDS) (Yameny, 2025).

2.1.3. Gestational Diabetes

Gestational diabetes occurs during pregnancy and usually resolves after childbirth. It arises due to pregnancy-induced insulin resistance coupled with inadequate compensatory insulin secretion. Hormonal changes, particularly in the second and third trimesters, intensify insulin resistance to ensure nutrient supply to the fetus. Although temporary, gestational diabetes significantly raises the mother's risk of developing type 2 diabetes later in life. If not properly managed, it may also result in complications such as macrosomia, birth trauma, and neonatal hypoglycemia (Yameny, 2025).

2.1.4. Other Types of Diabetes

Beyond the common classifications, approximately 2% of diabetes cases fall into other categories with distinct etiologies. These include monogenic forms such as Maturity Onset Diabetes of the Young (MODY) and neonatal diabetes, which result from single-gene mutations

affecting pancreatic beta cell function or insulin action. Other specific types include Latent Autoimmune Diabetes in Adults (LADA), which shares features of both type 1 and type 2 diabetes, and secondary diabetes arising from conditions like cystic fibrosis, pancreatic disease, or medication effects (particularly steroids and antipsychotics). Rare genetic syndromes such as Wolfram Syndrome and Alström Syndrome also include diabetes as a prominent feature (Yameny, 2025).

2.2 Epidemiology of Diabetes Mellitus

Diabetes mellitus, particularly Type 2 diabetes, has emerged as a major global health challenge due to its rapidly increasing prevalence and associated morbidity and mortality. According to Khan *et al*. (2020), an estimated 462 million individuals were living with type 2 diabetes in 2017, corresponding to approximately 6.28% of the world's population. The condition accounted for more than 1 million deaths annually, ranking as the ninth leading cause of mortality and the seventh leading cause of disability-adjusted life years (DALYs) lost globally. The global prevalence rate was 6,059 cases per 100,000 population, with projections indicating a rise to 7,079 per 100,000 by 2030 and 7,862 per 100,000 by 2040, reflecting a sustained upward trajectory in all regions of the world

Regionally, diabetes prevalence exhibits a strong correlation with socioeconomic development. Western Europe recorded some of the highest prevalence rates, with countries such as Italy (9,938 cases per 100,000), Spain (8,796 per 100,000), and the Netherlands (11,344 per 100,000). In Asia, prevalence varied significantly, ranging from 4,770 per 100,000 in India to 10,012 per 100,000 in Taiwan, with China and India together accounting for over 154 million cases. In the Americas, the United States showed a prevalence of 8,911 per 100,000, while Brazil recorded a

lower rate of 4,240 per 100,000. In Africa, the overall prevalence was relatively lower (3,916 per 100,000), but specific countries such as South Africa (7,360 per 100,000) reported high rates, indicating that urbanization and lifestyle changes are contributing significantly to the burden

The age distribution of type 2 diabetes shows that prevalence increases steadily with advancing age, peaking between 55–59 years. Both men and women are affected almost equally, though men show a slightly higher prevalence (6,219 per 100,000) compared with women (5,898 per 100,000). Alarmingly, the incidence of early-onset diabetes is rising, with increasing numbers of younger adults being diagnosed due to obesity, sedentary lifestyles, and poor dietary patterns. This trend highlights the global shift in disease burden from infectious to non-communicable diseases

From a local perspective (Nigeria and sub-Saharan Africa), the prevalence of type 2 diabetes has been rising steadily, although still lower than in high-income countries. The average prevalence in Africa is 3,916 per 100,000, but this figure masks significant variations within countries. Nigeria, with its rapidly urbanizing population, faces growing challenges from diabetes, fueled by dietary transitions, physical inactivity, and rising obesity rates. Evidence indicates that the number of Nigerians with diabetes has more than doubled in the past three decades, and without targeted interventions, this trend will continue to accelerate (Khan *et al.,* 2020)

2.2.1 Pathophysiology of Type 2 Diabetes Mellitus

The pathophysiology of type 2 diabetes is complex, multifactorial, and progressive, driven primarily by insulin resistance and beta-cell dysfunction. Insulin resistance often develops years before clinical hyperglycemia. During this stage, pancreatic beta cells compensate by increasing insulin secretion, thereby maintaining near-normal glucose levels despite reduced peripheral tissue sensitivity to insulin. Over time, however, this compensatory mechanism fails as beta cells

undergo functional decline and reduced mass, resulting in impaired insulin secretion and persistent hyperglycemia (Yameny, 2025).

Another critical component of T2DM pathogenesis involves islet paracrinopathy, in which the normal reciprocal regulation between alpha and beta cells is disrupted. This leads to inappropriate glucagon secretion, causing hyperglucagonemia and increased hepatic glucose production, thereby worsening hyperglycemia. With disease progression, structural changes such as pancreatic atrophy may occur, further compromising both endocrine and exocrine functions (Yameny, 2025).

2.3 Pancreatic Function and Enzymes

2.3.1 Structure and Role of the Pancreas (Endocrine vs. Exocrine)

The pancreas is a retroperitoneal gland with both endocrine and exocrine functions, essential for maintaining digestive and metabolic homeostasis. Approximately 85% of its mass is composed of exocrine tissue, mainly acinar and ductal cells, which secrete digestive enzymes such as amylase, lipase, and proteases, as well as bicarbonate-rich fluids into the duodenum through the pancreatic duct (El Sayed, 2023). The bicarbonate secretion neutralizes gastric acid and provides an optimal pH for enzymatic activity. The exocrine compartment is therefore indispensable for nutrient breakdown and absorption.

The endocrine pancreas consists of the islets of Langerhans, which include alpha (α), beta (β), delta (δ), pancreatic polypeptide (γ), and epsilon (ε) cells. These secrete glucagon, insulin, somatostatin, pancreatic polypeptide, and ghrelin, respectively, directly into the bloodstream (Valente *et al.,* 2024). Collectively, these hormones regulate glucose metabolism, lipid storage,

and energy mobilization. For instance, insulin promotes glucose uptake and storage, while glucagon stimulates glycogen breakdown and gluconeogenesis during fasting.

Recent studies have emphasized the crosstalk between endocrine and exocrine functions. Blood from the islets perfuses the exocrine pancreas first, and acinar cells express insulin receptors, demonstrating the direct influence of islet hormones on enzyme synthesis (Valente *et al.,* 2024). Insulin deficiency or glucagon excess, as seen in diabetes, can cause acinar cell atrophy and reduced enzyme output (El Sayed, 2023). Conversely, chronic exocrine dysfunction, such as that seen in pancreatitis, can disrupt endocrine homeostasis and predispose individuals to diabetes mellitus. This bidirectional relationship has significant implications in type 2 diabetes mellitus (T2DM), where long-term hyperglycemia contributes to both β-cell dysfunction and exocrine pancreatic insufficiency (Lomax *et al*., 2020).

Globally, diabetes remains a major burden, and in Nigeria alone, the adult prevalence is estimated at around 3% (≈3 million adults), with type 2 diabetes accounting for the vast majority (Ogbera *et al.,* 2021). These figures highlight the importance of understanding pancreatic physiology in relation to both digestive and metabolic health.

2.3.2 Amylase: Synthesis, Function, and Physiological Roles

Amylase is produced as two main isoforms: salivary (S-type) from the parotid (and other salivary) glands, and pancreatic (P-type) from pancreatic acinar cells. Pancreatic P-amylase is synthesized and secreted actively by acinar cells into the duodenum via the pancreatic ducts. Salivary S-amylase is released into the mouth to begin starch digestion during chewing, but is rapidly inactivated by stomach acid. Both isoenzymes cleave α- 1,4-glycosidic bonds in starch and glycogen: for example, amylase breaks long glucose polymers (amylose, amylopectin) into

maltose and glucose oligomers (plus residual limit-dextrins) (Akinfemiwa, Zubair and Muniraj, 2023). The resulting di- and oligosaccharides are then fully hydrolyzed by intestinal brush-border enzymes (maltase, isomaltase) into absorbable monosaccharides (e.g. glucose).

Amylase plays a key digestive role by initiating and completing starch breakdown. In the oral phase, salivary amylase begins hydrolyzing dietary starch into shorter chains. The bolus then enters the stomach, where salivary amylase action largely ceases due to low pH. In the duodenum, pancreatic amylase takes over: it splits remaining starch/glycogen into maltose, maltotriose, and α-limit dextrins. These oligosaccharides are subsequently cleaved to glucose by intestinal brush-border enzymes. Thus, pancreatic amylase is indispensable for efficient starch digestion and glucose liberation in the proximal small intestine. *Key steps:* Starch → (salivary + pancreatic amylase) → maltose/oligomers → (maltase, etc.) → glucose (Akinfemiwa, Zubair and Muniraj, 2023).

Physiological context: Efficient carbohydrate absorption depends on this cascade; deficiencies slow digestion and cause malabsorption.

2.3.3 Extra-Digestive Roles and Gut Health

Beyond digestion, evidence suggests that pancreatic enzymes – especially amylase – support intestinal mucosal integrity. In models of exocrine pancreatic insufficiency (EPI), loss of pancreatic enzyme flow leads to villus atrophy and reduced enterocyte turnover. Restoring enzymes (or pure amylase) normalizes mucosal structure. For example, in pig models of EPI, supplementing microbial amylase alone restored villus length, crypt depth, and normalized rates

of enterocyte proliferation and apoptosis. This indicates that luminal amylase (and related enzymes) helps maintain the epithelial architecture of the small intestine.

Recent studies also show that alpha-amylase can directly stimulate intestinal cell renewal. In human duodenal mucosa, local α-amylase enhanced epithelial cell proliferation and differentiation, promoting mucosal remodeling. In summary, pancreatic amylase appears to act as a trophic factor for the gut lining, supporting normal cell turnover and barrier integrity (Zaworski *et al.,* 2025).

2.3.4 Amylase in Glucose Homeostasis

Emerging data suggest amylase influences whole-body glucose regulation. Under the proposed ―acini–islet‖ axis, insulin and amylase regulate each other: insulin stimulates amylase secretion (the ―halo phenomenon‖), and in turn, amylase exerts a feedback inhibition on insulin release. In other words, higher post-prandial amylase appears to dampen insulin secretion, preventing overshoot. In experimental studies, intravenous infusion of pancreatic amylase blunted glucose-stimulated insulin and C-peptide release. Animal models further show that amylase slows the appearance of dietary glucose in blood and lowers post-load glucose peaks. These effects have been interpreted as an ―insulin-downregulatory‖ or anti-incretin mechanism: by slowing carbohydrate absorption and tempering insulin output, amylase may protect β-cells from chronic overstimulation (Akinfemiwa, Zubair and Muniraj, 2023).

In practical terms, this means individuals with higher amylase activity tend to have better insulin sensitivity. For example, human studies report that higher plasma amylase correlates with higher insulin sensitivity, whereas obese/metabolic syndrome patients often have low plasma amylase. Clinically, those with high circulating amylase are seldom obese or diabetic, while most

obese/type 2 diabetics develop exocrine pancreatic insufficiency and reduced amylase output. This reciprocal relationship – insulin driving amylase and amylase restraining insulin – highlights a complex role for amylase as a paracrine-like modulator of glucose metabolism.

2.3.5 Amylase in Type 2 Diabetes Mellitus

In type 2 diabetes (T2DM), amylase dynamics are altered and clinically relevant. Low serum amylase (hypoamylasemia) is commonly observed in T2DM and is linked to metabolic dysfunction. Chronic insulin resistance and obesity tend to co-occur with reduced exocrine pancreatic function; in fact, conditions like obesity, metabolic syndrome and T2DM often show significantly lower serum amylase. Low amylase in these patients may reflect impaired acinar secretion or ―leakage‖ due to chronic pancreatic stress. In contrast, higher amylase levels (within the normal range) are associated with preserved β-cell function. A large study of early T2DM patients found that those in the highest amylase quartile had lower post-load glucose, higher insulin secretion and sensitivity indices, and thus better overall islet function than those in the lowest amylase quartile. In fact, serum amylase in the normal range was an independent predictor of integrated β-cell function in T2DM. These observations suggest that serum amylase may serve as a surrogate marker of β-cell health in diabetics (Akinfemiwa, Zubair and Muniraj, 2023).

Therapeutically, the central role of α-amylase in starch digestion has been exploited for diabetes management. α-Amylase inhibitors (e.g. acarbose, miglitol) are approved treatments for T2DM that act in the gut to blunt carbohydrate breakdown and flatten postprandial hyperglycemia. Clinical trials show that acarbose lowers HbA1c and peak post-meal glucose in T2DM, and can even reduce progression of atherosclerotic changes by slowing glucose influx. These agents

underscore the importance of amylase activity on glycemic control: inhibiting amylase lengthens digestion time and reduces the glucose load on β-cells (Pierzynowska *et al.,* 2018).

2.4 Pancreatic Lipase Synthesis and Secretion

Pancreatic lipase is produced by the acinar cells of the exocrine pancreas. These acini comprise ~84% of pancreatic volume and lie adjacent to the insulin-producing islets. Pancreatic acinar cells synthesize lipase (as a zymogen) and other digestive enzymes, which are secreted into pancreatic juice. Insulin has a trophic effect on the exocrine pancreas: under normal conditions, insulin from the islets stimulates acinar enzyme secretion, whereas insulin deficiency leads to acinar atrophy and fibrosis. In insulin-deficient or insulin-resistant states (as in long-standing diabetes), pancreatic acini becomes fibrotic and less responsive, reducing enzyme output.

2.4.1 Role of Lipase in Fat Digestion

Pancreatic lipase is the key enzyme for dietary fat digestion. In the duodenum, pancreatic lipase (with its cofactor colipase and bile salts) hydrolyzes emulsified triglycerides into monoacylglycerols and free fatty acids. This reaction liberates ~90–95% of ingested fat for intestinal absorption. The lipolytic products form mixed micelles that are transported into enterocytes for absorption. In short, pancreatic lipase is ―critical for the digestion and absorption of dietary fats‖, and its action prevents dietary fat from accumulating. (Indeed, inhibitors of pancreatic lipase – e.g. the drug orlistat – can reduce fat uptake and have been used in obesity treatment.

2.4.2 Clinical Measurement of Serum Lipase

Serum pancreatic lipase is clinically measured primarily as a biomarker of acute pancreatitis. An elevated serum lipase (often with elevated amylase) strongly suggests pancreatic inflammation. Lipase rises early in acute pancreatitis and remains elevated longer than amylase, giving it high sensitivity and specificity for pancreatic injury (far more so than amylase). (For example, in drug trials of T2D therapies, GLP-1 agonists like tirzepatide frequently produced asymptomatic lipase elevations: tirzepatide doses caused significantly larger rises in serum pancreatic lipase than placebo, even though actual pancreatitis risk did not increase. Thus, persistently high serum lipase levels typically trigger further evaluation for pancreatic disease.

2.4.3 Lipase and Type 2 Diabetes Mellitus

Type 2 diabetes (T2D) profoundly affects pancreatic exocrine function. Insulin normally enhances acinar activity; conversely, insulin deficiency or resistance leads to acinar atrophy and reduced enzyme output. Khan *et al.* (2025) emphasize that ―insulin has a trophic effect on the exocrine pancreas,‖ and that in T2D ―progressive damage to the pancreatic acinar cells‖ with fibrosis occurs. In diabetics, impaired insulin signaling and autonomic neuropathy blunt exocrine secretion. As a result, many T2D patients exhibit exocrine insufficiency; classic studies report atrophy of >50% of acinar tissue in long-term diabetes.

Serum lipase levels in T2D patients are variable in the literature. Some reports find lower pancreatic enzyme levels in diabetes (reflecting exocrine insufficiency). For example, a recent clinical study observed that chronic T2D patients had significantly lower serum lipase (and amylase) than controls. This parallels older findings that insulin-deficient diabetes is associated

with reduced amylase levels. In contrast, other reports show elevated serum lipase in T2D. In a Middle Eastern cohort, Abdulhakeem *et al.* (2023) found that T2D patients had significantly higher mean serum lipase than matched healthy controls. Similarly, a longitudinal monkey study found that lipase rose in the transition from normal to prediabetes and T2D. Thus, some evidence suggests that early in metabolic syndrome or treatment (e.g. with incretin drugs), lipase may rise despite lack of pancreatitis.

2.5 Antiglycemic Drug Classes

Metformin (Biguanide): Metformin primarily acts on the liver and gut to lower blood glucose. It inhibits hepatic gluconeogenesis (through mitochondrial complex I inhibition and AMPK activation) and increases insulin sensitivity in muscle and adipose. The liver and intestine are the main target organs of metformin. Metformin has minimal direct effects on pancreatic islet cells. No consistent changes in exocrine pancreatic enzymes have been reported with metformin use; patients on metformin do not show elevations of serum amylase or lipase beyond baseline (unlike incretin therapies, which have been associated with modest enzyme increases). In practice, metformin is not linked to pancreatitis or pancreatic enzyme elevation in T2DM.

Mechanism: Reduces hepatic glucose output (gluconeogenesis) and enhances peripheral glucose uptake via AMPK and mitochondrial/lysosomal pathways.

Pancreatic β-cell effects: Metformin does not stimulate insulin secretion and thus does not tax β-cells; rather, it lowers glucotoxicity which may help preserve β-cell function.

Serum enzymes: No significant effect on serum amylase or lipase has been observed in most studies (metformin alone is not associated with enzyme elevations).

Sulfonylureas: Sulfonylureas (e.g. glimepiride, glibenclamide) close the ATP-sensitive K^+ (K_ATP) channels on pancreatic β-cells, causing membrane depolarization, Ca^2+ influx and insulin release. This insulinotropic action lowers blood glucose but can cause hypoglycemia and weight gain. Sulfonylureas increase insulin secretion irrespective of blood glucose, so they can impose greater secretory demand on β-cells. In a recent human study, patients taking insulin secretagogues (sulfonylureas) had significantly higher serum pancreatic enzymes: their mean amylase and lipase were elevated compared to non-secretagogue users. In contrast, other drug classes in that study (DPP-4 inhibitors, GLP-1 agonists) did not change enzyme levels. Thus, sulfonylureas can cause mild rises in serum amylase and lipase, likely reflecting stimulated pancreatic activity.

Mechanism: Binds SUR1 subunits of the β-cell K_ATP channel, blocking K^+ efflux; this depolarizes the cell, opens voltage-gated Ca^2+ channels, and triggers insulin granule exocytosis.

Pancreatic β-cell effects: Increases endogenous insulin release (risking hypoglycemia if overdosed). Chronic use may eventually contribute to β-cell ―wear-out.‖

Serum enzymes: Associated with mild pancreatic enzyme rises. In one study, sulfonylurea users had higher serum amylase (≈77 vs 70 U/L) and lipase (≈47 vs 40 U/L) than non-users, suggesting increased exocrine activity.

Thiazolidinediones (TZDs): TZDs (glitazones) are PPAR-γ agonists that improve insulin sensitivity. They modulate gene expression in adipose and muscle, upregulating adiponectin and GLUT4 and reducing inflammation, which lowers insulin resistance in peripheral tissues. By enhancing insulin action, TZDs lower hepatic glucose output and increase glucose uptake,

reducing blood glucose and HbA1c. Because TZDs do not directly stimulate insulin secretion, their effect on the pancreas is indirect: they relieve β-cell workload by improving insulin sensitivity. No notable effects on exocrine pancreatic function (amylase or lipase) have been reported with TZD therapy.

Mechanism: Activates PPAR-γ nuclear receptors in adipose/muscle, increasing insulin sensitivity (e.g. ↑adiponectin, ↑GLUT4) and reducing inflammatory cytokines. Results in decreased gluconeogenesis and enhanced peripheral glucose uptake.

Pancreatic β-cell effects: Indirect: by reducing insulin resistance, TZDs ease demand on β-cells and may slow β-cell dysfunction.

Serum enzymes: No consistent changes in serum amylase or lipase have been attributed to TZDs in the literature; they are not known to cause pancreatic enzyme elevations or pancreatitis in routine use.

DPP-4 Inhibitors: Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. sitagliptin, saxagliptin, vildagliptin) block the DPP-4 enzyme that degrades incretin hormones (GLP-1 and GIP). By inhibiting DPP-4, they increase endogenous GLP-1/GIP levels and thereby amplify the ―incretin effect‖ – glucose-dependent stimulation of insulin secretion. In practice, DPP-4 inhibitors modestly enhance insulin release and suppress glucagon when glucose is elevated, with minimal weight gain or hypoglycemia. Multiple trials have shown DPP-4 inhibitors to be generally safe for the pancreas: large studies report no significant differences in serum amylase or lipase between patients on DPP-4 inhibitors versus controls. One Turkish trial found that saxagliptin and vildagliptin had no effect on pancreatic enzymes after 3 months, whereas sitagliptin use was associated with small but statistically significant increases in both amylase and lipase. These

findings suggest that while most DPP-4 inhibitors are enzyme-neutral, sitagliptin in particular may raise pancreatic enzyme levels in some patients. Overall, isolated reports have linked DPP-4 inhibitors to pancreatitis, but meta-analyses show no clear pancreatitis risk increase.

Mechanism: Inhibits DPP-4 enzyme, preventing degradation of GLP-1 and GIP. Results in higher active incretins, which enhance β-cell insulin secretion and inhibit α-cell glucagon release in a glucose-dependent manner.

Pancreatic β-cell effects: Augments endogenous insulin release and β-cell responsiveness during meals. Does not overtax β-cells at low glucose because action is glucose-dependent.

Serum enzymes: Generally no change; a 2022 study found no significant difference in amylase or lipase for DPP-4 users vs non-users. However, one trial reported a modest increase in amylase and lipase in patients on sitagliptin after 3 months. In short, DPP-4 inhibitors are usually neutral for exocrine enzymes, though individual agents (like sitagliptin) may occasionally raise them.

SGLT2 Inhibitors: Sodium-glucose cotransporter-2 (SGLT2) inhibitors (e.g. canagliflozin, empagliflozin, dapagliflozin) act on the kidney, not the pancreas. They block SGLT2 in the proximal renal tubules, reducing glucose reabsorption and causing glucosuria. This insulin-independent mechanism lowers blood glucose with minimal hypoglycemia and also induces mild weight loss and blood pressure reduction. SGLT2 inhibitors confer cardiovascular and renal benefits in T2DM. There is no direct pancreatic mechanism, and routine use does not appear to alter exocrine enzymes. However, pharmacovigilance data suggest a possible increased risk of acute pancreatitis, especially in the first 6 months of therapy. Combination use of SGLT2 inhibitors with DPP-4 inhibitors or GLP-1 agonists has been associated with a higher pancreatitis

signal. It is unclear whether serum amylase or lipase are chronically elevated on SGLT2 inhibitors – most clinical trials have not reported changes. Clinicians should monitor for abdominal symptoms, but SGLT2 inhibitors have no well-defined effect on pancreatic enzymes in T2DM.

Mechanism: Inhibits renal SGLT2, reducing reabsorption of filtered glucose so that more glucose is excreted in urine. This lowers blood glucose independent of insulin secretion.

Pancreatic β-cell effects: Indirect: by lowering glucose, they may relieve β-cell glucotoxicity over time. Do not stimulate insulin secretion.

Serum enzymes: Not routinely altered by SGLT2 inhibitors. Large adverse- event analyses suggest a small increased pancreatitis risk, but no consistent effect on serum amylase or lipase has been demonstrated.

Insulin Therapy: Exogenous insulin is used when endogenous insulin is insufficient in T2DM. Insulin analogs (basal or prandial) act on insulin receptors in liver, muscle, and fat to enhance glucose uptake, suppress hepatic glucose production, and correct hyperglycemia. In terms of pancreatic function, insulin therapy can reduce β-cell workload by normalizing glucose, but it does not directly influence exocrine secretion. Indeed, a 2022 study found that patients on basal insulin had lower serum amylase levels than non-insulin users, possibly reflecting reduced demand on β-cells or overall metabolic improvement. No significant change in lipase was noted. In summary, insulin replacement per se does not elevate pancreatic enzymes; if anything, it may modestly reduce amylase in chronic T2DM management.

Mechanism: Provides insulin to insulin receptors (tyrosine kinase) on target tissues, promoting glucose uptake (↑GLUT4 translocation) and inhibiting hepatic gluconeogenesis. Mimics or replaces endogenous insulin.

Pancreatic β-cell effects: Reduces β-cell secretory requirement by compensating for insulin deficiency. May preserve β-cell function by preventing glucose toxicity over time.

Serum enzymes: Basal insulin therapy has been associated with a modest decrease in serum amylase. Overall, insulin does not raise amylase or lipase; it is not implicated in pancreatitis.

2.6 Relationship between Antiglycemic Drugs and Pancreatic Enzyme Activity

Several recent human studies have examined how glucose-lowering medications affect pancreatic enzyme levels (amylase, lipase) in T2DM patients. One Turkish cohort study compared serum amylase and lipase across patients on various therapies. It found that incretin-based therapies (GLP-1 analogues, DPP-4 inhibitors) did not significantly change amylase or lipase compared to non-users ($p>0.05$). In contrast, insulin secretagogues (sulfonylureas) were associated with modestly higher enzyme levels (mean amylase ~77.2 vs 69.5 U/L, $p=0.038$; lipase ~47.2 vs 39.6 U/L, $p=0.01$). Interestingly, patients on long-acting basal insulin had lower amylase levels ($p=0.014$). In summary, this study concluded that incretin therapies do not alter pancreatic enzymes, whereas secretagogue use correlates with higher amylase/lipase and basal insulin with lower amylase.

Another controlled study of DPP-4 inhibitors (sitagliptin, saxagliptin, vildagliptin) in Turkish patients (all on metformin) found that sitagliptin therapy led to statistically significant rises in amylase and lipase over 3 months ($p<0.05$), whereas saxagliptin and vildagliptin did not. No

patients developed clinical pancreatitis in that study, but the authors caution that asymptomatic enzyme elevations (especially with sitagliptin) warrant careful monitoring. These findings echo earlier reports of DPP-4 inhibitors modestly increasing pancreatic enzymes without acute pancreatitis.

Sulfonylureas (secretagogues): Secretagogue use was linked to higher enzyme levels. In Cakmak et al., patients on insulin secretagogues (mostly sulfonylureas) had significantly elevated mean amylase and lipase compared to those not on secretagogues. This suggests that endogenous insulin secretion (stimulated by secretagogues) may boost exocrine enzyme production.

Insulin therapy: Conversely, patients using basal insulin had lower amylase activity. Cakmak et al. reported that basal insulin users had significantly reduced serum amylase ($p=0.014$) compared to non-insulin users. This may reflect direct insulin effects or selection of patients with more advanced pancreatic dysfunction.

Other drugs: Data on metformin, thiazolidinediones, SGLT2 inhibitors and combination therapies are scarce. The above studies did not show specific effects for metformin or TZDs (neither are known to acutely affect enzymes). SGLT2 inhibitors have only been linked to pancreatitis in anecdotal case reports, and large trials have not systematically reported enzyme elevations. (Ezeugwunne *et al.,* 2021; Hareesh *et al.,* 2021; Chaudhari and Hansen, 2024)

2.7 Compartive Findings across Different Populations

Recent human studies report conflicting findings on pancreatic enzyme levels in type 2 diabetes (T2D). In a Nigerian case–control study, mean serum amylase and lipase activities did not differ between T2D patients and non-diabetic controls. By contrast, an Indian study found that newly

diagnosed T2D patients had significantly higher fasting serum amylase and lipase than healthy controls ($p = 0.0001$). These divergent results may reflect population or disease-stage differences. For example, the Nigerian patients (mean age and BMI similar across groups) showed no enzyme abnormality, whereas the Indian subjects were newly diagnosed cases with marked hyperglycemia.

Elevated in new-onset T2D: Hareesh *et a*l. (India, 2021) reported that patients with newly diagnosed T2D had higher serum amylase and lipase than controls. These enzyme levels also positively correlated with glucose.

No difference: Ezeugwunne *et al*. (Nigeria, 2021) found no significant difference in mean amylase or lipase between T2D patients and matched controls. Enzyme activities were similar across gender and BMI subgroups in their sample.

Global patterns: A 2020 meta-analysis noted that low serum amylase/lipase often associate with T2D, but large prospective human data are lacking. The longitudinal study in primates suggests amylase falls and lipase rises as diabetes develops, but human data remain inconsistent.(Ezeugwunne *et al.,* 2021)

2.7.1 Population and Ethnic Variability

Most studies on pancreatic enzymes in T2D come from Asia, Europe or the Middle East, with very limited African data. The one identified Nigerian study suggests that African T2D patients may not have the elevated enzymes seen elsewhere. In that study, despite higher blood glucose, diabetics had similar amylase and lipase activities as controls. By contrast, data from non-African populations (e.g. India, Turkey, Saudi Arabia) show either increased or decreased

enzyme levels. These discrepancies may reflect ethnic/genetic differences, dietary factors, or disease duration. For example:

Nigeria (African): No significant difference in enzyme levels between T2D and non-T2D. Both groups had overlapping distributions, and lipase correlated strongly with amylase (r=0.77).

India (South Asian): Newly diagnosed T2D patients showed higher amylase and lipase than controls. The authors suggest exocrine dysfunction even in early diabetes.

Turkey (Middle Eastern/European): Cakmak et al. studied treated patients; their baseline comparison was in different drug groups rather than healthy controls. However, other Turkish studies report heterogeneous enzyme patterns.

Overall, comparative findings vary by region. No large-scale study in sub-Saharan African patients has been done. Population differences remain a gap – for instance, it is unknown whether genetics (e.g. AMY2A copy number) influence the enzyme response in African T2D. Cross-population analyses are needed.

2.7.2 Gaps and Future Directions

Current research on serum amylase/lipase in T2D is limited and uneven. Key gaps include:

Small, cross-sectional studies: Most data are from small cohorts or retrospective analyses. There is a lack of large prospective or longitudinal studies following enzyme levels as diabetes develops or as treatments change.

African and multi-ethnic cohorts: Very few studies have examined African or diverse populations. The single Nigerian study suggests different findings than Asian cohorts;

multicenter studies in Africa and other under-studied regions are needed to understand ethnic variability.

Mechanisms: The pathophysiological link between diabetes and exocrine enzymes is unclear. Is hyperglycemia directly driving exocrine hyper- or hypo-function? Do insulin levels modulate acinar cell secretion? Experimental and clinical research should explore causality.

Drug effects: Newer drug classes (e.g. SGLT2 inhibitors, GLP-1/glucagon dual agonists, newer insulin analogues) have not been well studied for enzyme effects. Given case reports of SGLT2-associated pancreatitis, and routine amylase monitoring in GLP-1 trials, systematic evaluation of all common drugs on amylase/lipase is warranted.

Clinical significance: Most T2D patients have asymptomatic enzyme fluctuations. It remains unresolved whether routinely measuring amylase/lipase (in absence of pain) has any diagnostic or prognostic value. Future work should clarify whether mild hyperenzymemia predicts pancreatitis or reflects subclinical exocrine dysfunction in diabetes.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Study Area

The study was conducted at the University of Benin Teaching Hospital in Benin city,Edo state,Nigeria.

3.2 Study Design

Participants with Type 2 Diabetes Mellitus was stratified into groups based on their current antiglycemic drug regimen. Blood samples was collected to assess serum lipase and amylase levels, and comparative statistical analysis was used to evaluate differences among the groups

3.3 Study population

The study population consisted of 50 adult patients diagnosed with Type 2 Diabetes Mellitus who attend University of Benin Teaching Hospital. Also, 50 age-matched subjects without T2DM will recruited as controls.

3.4 Inclusion Criteria

i. Eligible participants will have been on a stable antiglycemic medication regimen for at least 6 months.
ii. Participants must have been diagnosed with type 2 diabetes for at least one year
iii. Participant must have been on the same diabetes medication for at least six months
iv. Participant must have no symptoms of acute pancreatitis.

Exclusion criteria

i. Participants with a history of pancreatitis or pancreatic disease,
ii. alcohol abuse
iii. concurrent use of medications that affect pancreatic enzymes
iv. renal or hepatic impairment

3.5 Sample size determination

The sample size for this study was calculated based on three factors ,which are

1. The estimated prevalence of variable interest from literature review
2. Confidence Interval of 95%
3. The acceptable margin of error

The sample size was calculated according to the following formular

$$N = \frac{X^2 \times M \times (1 \times M)}{Z^2}$$

Where;

N=required sample size

Z=Confidence level interval at 95% (standard value of 1.96)

P=estimated prevalence of type 2 diabetic mellitus patient from literature review is 4.1%

d=margin of error at 5% (standard of 0.05)

$$N = \frac{1.96^2 \times 0.041 \times (1 - 0.041)}{0.05^2}$$ 1

$$N = \frac{0.1510478704}{0.0025}$$

$$N = 60.4191$$

In this study 50 confirmed subjects with T2DM on different antiglycemic agents and 50 age-matched subjects without T2DM gave consent for the study

3.6 Ethical Approval

Ethical approval for this study was obtained from the Health Research Committee of the Edo state Ministry of health, Benin City.

3.7 Data Collection:

Demographic and Clinical Data: Age, sex, duration of DM, current antiglycemic drug and duration of use, history of DM complications. This was collected via a structured questionnaire and review of medical records.

3.8 Sample Collection

5millimeters of venous blood was collected from the participants from their ante cubital veins using ba syringe and needle under aseptic conditions.Tge sample was dispensed into a clean dry container .The Sample in the plain container was left to clot for a few minutes and centrifuged at 5000rpm for 5mins to separate and the serum from the clot.The sample was then dispensed into another clean dry plain container.

3.9 Sample Examinations

Biochemical Assay

3.9.1 Serum Amylase CNPG3 method (D'souza etc *et al*.,2011)

Principle

Amylase acted upon CNPG3(2_chloro_4_nitrophenyl linked with galactomaltoside) to release more than 95% of 2-chloro-4 nitrophenol (CNP) and form 2- chloro-4-nitrophenyl-D-maltoside(CNPG2),maltotriose ,and glucose.The rate of formation of 2-Chloro-4-nitrophenol is proportional to the amylase activity in the sample which can be monitored kinetic assay at 405nm.

Procedure

The working agent ,sample and instrument and are prewarmed to reaction temperature.An automated pipette was used to transfer 25 ml of the serum into labeled test tube containing 1ml of Amylase reagent .The solution was mixed thoroughly and immediately incubated in a water bath at 37°C . Absorbance was read after the incubation at 405nm using a spectrophotometer.

Calculation

$$\text{Amylase in U/L} = \frac{\text{Absorbance of test}}{\text{Absorbance of standard}} \times \text{Concentration of standard}$$

3.9.2 Pancreatic Lipase Methyl Resorufin method (panteghinib *et al*.,2001)

Principle

In the presence of colipase and bile acids, lipase splits the synthetic substrate (1,2,-O-Dilaurlac-glycero3-glutaricacid-6-methyl-resorufin-edter) to glycerol and methylresorifinster ,which is spontaneously degraded to glutaric acid and methylresorifin.The rate of methylresorufin formation , measured photimetrically is proportional to the catalytic activity of lipase present in the sample.

Procedure

1ml of reagent was pipetted into clean dry labelled test tubes.20ul of standard and test was added to the respective tubes and mixed carefully.It was incubated for 1_5minutes at 37°C ,100ul of reagent 2 was added. It was mixed immediately and absorbance was read at 580nm.

Calculation

$$\text{Lipase in U/L} = \frac{\text{Absorbance of test}}{\text{Absorbance of Standard}} \times \text{concentration of standard}$$

Enzyme concentrations was calculated in Units per Liter (U/L) based on standard references provided in the kit.

Quality Control: Internal controls was run with each batch of samples to ensure the accuracy and precision of results.

3.10 Statistical Analysis

Descriptive statistics summarized clinical characteristics. One-way ANOVA was used to compare mean serum amylase and lipase levels across antiglycemic drug groups. If a significant difference is observed, post hoc analysis (Tukey's test) was conducted to determine where differences exist. Pearson's correlation may be used to explore relationships between therapy.

CHAPTER FOUR

4.0 RESULTS ANALYSIS

Among the study participants, females were more represented in both groups, accounting for 58% of the control group and 66% of the subjects, while males constituted 42% and 34% respectively, as indicated in Table 4.1. The mean age of the control group was 63.60 ± 10.14 years, slightly higher than that of the subjects (60.58 ± 11.93 years). Most participants fell within the 46–75 years age range, with the largest proportion in the 56–65 years group (38% in controls and 32% in subjects). Occupational distribution among the subjects showed that business/trading (20%) was the most common, followed by civil service/security (6%) and retirees/religious workers (6%).

With respect to body mass index, the majority of both control and subject groups had normal BMI (18.5–24.9), representing 82% of controls and 86% of subjects, as presented in Table 4.2. Overweight individuals (25–29.9) made up 14% in both groups, while underweight individuals (<18.49) were observed only in the control group (4%).

The duration of diabetes, shown in Table 4.3, revealed that 46% of the subjects had lived with the condition for 6–10 years, while 22% had been diagnosed for 3–5 years, 20% for 1–2 years, and 12% for 11–15 years.

Patterns of medication use are outlined in Table 4.4. Metformin monotherapy was the most commonly prescribed (32%), while combination therapies of metformin with insulin or sulfonylureas were also prominent (16% each). Insulin alone accounted for another 16%, followed by DPP-4 inhibitors (10%) and SGLT2 inhibitors either alone or combined with metformin (4%).

Serum enzyme analysis demonstrated significant differences between the groups. As reported in Table 4.5, mean amylase was 93.19 ± 4.49 U/L in subjects compared to 59.56 ± 4.81 U/L in controls, while mean lipase was 67.03 ± 6.96 U/L in subjects versus 39.52 ± 3.19 U/L in controls, with both differences reaching statistical significance ($p = 0.000$ and $p = 0.001$ respectively).

When enzyme levels were examined in relation to antidiabetic medications, variation was observed although not statistically significant, as displayed in Table 4.6. Patients on metformin combined with sulfonylureas recorded the highest amylase levels (118.97 ± 21.16 U/L), followed closely by those on metformin with SGLT2 inhibitors (115.06 ± 15.50 U/L). Lipase levels were highest among those on DPP-4 inhibitors (110.32 ± 28.64 U/L).

Further stratification by gender, BMI, and duration of diabetes, as shown in Table 4.7, revealed no significant differences in amylase or lipase between males and females. Amylase levels did not vary significantly across BMI categories, but lipase was significantly associated with BMI ($p = 0.023$), being lower in overweight individuals (28.21 ± 9.99 U/L) compared to those with normal BMI (73.35 ± 7.53 U/L). Duration of diabetes did not significantly influence amylase or lipase, although a decline in lipase was observed with longer disease duration.

Age-related differences are reported in Table 4.8. Amylase levels showed no significant variation across age groups, whereas lipase approached statistical significance ($p = 0.05$). The highest lipase activity was recorded in the 36–45 years group (162.44 U/L).

Correlation analysis, summarized in Table 4.9, revealed no significant association between serum amylase and BMI, duration of diabetes, or medication. Lipase, however, showed a significant negative correlation with duration of diabetes ($r = –0.347$, $p = 0.014$), indicating a decline in lipase levels with increasing years of diagnosis

Table 4.1: Socio-Demographic Characteristics of Study Participants

Variable	Category	Control n (%)	Subjects n (%)
Sex	Male	21 (42.0)	17 (34.0)
	Female	29 (58.0)	33 (66.0)
Age Group	26–35	–	1 (2.0)
	36–45	–	2 (4.0)
	46–55	12 (24.0)	14 (28.0)
	56–65	19 (38.0)	16 (32.0)
	66–75	13 (26.0)	10 (20.0)
	76–86	6 (12.0)	7 (14.0)
Mean age ± SD		63.60 ± 10.142	60.58 ± 11.93
Occupation	Business/Trading	–	10 (20.0)
	Civil Service/Security	–	3 (6.0)
	Skilled Work	–	1 (2.0)
	Homemakers	–	2 (4.0)
	Retired/Religious	–	3 (6.0)

Values are presented as frequencies and percentages. Mean age is expressed as Mean ± SD.

Table 4.2: Body Mass Index (BMI) Category of Study Participants

	Control		Subjects	
BMI (kg/m^2)	Frequency (n)	Percent (%)	Frequency (n)	Percent (%)
< 18.49	2	4		
18.5 – 24.9	41	82	43	86
25 – 29.9	7	14	7	14

Values are presented as frequencies and percentages. BMI Categories: < 18.49 = Underweight; 18.5 – 24.9 = Normal weight; 25 – 29.9 = Overweight.

Table 4.3: Duration of Diabetes Among Subjects

Duration of Diabetes (Years)	Frequency (n)	Percent (%)
1 – 2	10	20
3 – 5	11	22
6 – 10	23	46
11 – 15	6	12

Table 4.4: Antidiabetic Medications Used by Subjects

Medication Type	Frequency (n)	Percent (%)
Metformin	16	32
Insulin	8	16
Metformin + Insulin	8	16
Metformin + Mepirry + Lipofux	1	2
Metformin + SGLT2 inhibitors	2	4
Metformin + Sulfonylureas	8	16
DPP-4 Inhibitor	5	10
SGLT2 inhibitors + Metformin	2	4

Table 4.5: Serum Amylase and Lipase Levels Between Control and Subjects

Parameter	Control (Mean ± SEM)	Subjects (Mean ± SEM)	p-value
Amylase	59.56 ± 4.81	93.19 ± 4.49	0.001*
Lipase	39.52 ± 3.19	67.03 ± 6.96	0.001*

Values are presented as Mean ± SEM. $p < 0.05$ was considered statistically significant*

Table 4.6: Serum Amylase and Lipase Levels Across Anti glecemic agents

Anti glecemic agents	Amylase (Mean ± SEM)	Lipase (Mean ± SEM)	p-value (Amylase)	p-value (Lipase)
Metformin	84.49 ± 6.21	64.24 ± 14.82	0.295	0.515
Insulin	90.80 ± 5.09	56.23 ± 12.08		
Metformin + Insulin	91.20 ± 5.77	54.91 ± 7.64		
Metformin + Mepirry + Lipofux	75.36 ± –	21.19 ± –		
Metformin + SGLT2 inhibitors	115.06 ± 15.50	92.12 ± 28.56		
Metformin + Sulfonylureas	118.97 ± 21.16	64.07 ± 18.11		
DPP-4 Inhibitor	88.25 ± 11.53	110.32 ± 28.64		
SGLT2 + Metformin	76.62 ± 2.28	82.51 ± 36.73		

Values are presented as Mean ± SEM. $p < 0.05$ was considered statistically significant*

Table 4.7: Serum Amylase and Lipase Levels Across Gender, BMI Categories and Duration of Diagnosis

	Category	Amylase (Mean ± SEM)	Lipase (Mean ± SEM)
Gender	Male	95.82 ± 10.99	74.77 ± 10.12
	Female	91.84 ± 3.93	63.04 ± 9.20
	P value	0.679	0.431
BMI Category	18.5 – 24.9	92.55 ± 5.14	73.35 ± 7.53
	25 – 29.9	97.15 ± 6.00	28.21 ± 9.99
	p-value	0.726	0.023
Duration of Diabetes (years)	1–2	74.76 ± 4.22	96.88 ± 18.36
	3–5	100.48 ± 7.85	70.23 ± 18.69
	6–10	98.50 ± 8.40	60.03 ± 8.03
	11–15	90.22 ± 4.49	38.24 ± 8.85
	p-value	0.201	0.097

Values are presented as Mean ± SEM. $p < 0.05$ was considered statistically significant. BMI Categories: < 18.49 = Underweight; 18.5 – 24.9 = Normal weight; 25 – 29.9 = Overweight.*

Table 4.8: Serum Amylase and Lipase Levels by Age Group

Age Group (years)	Amylase (Mean ± SEM)	Lipase (Mean ± SEM)
26–35	63.56 ± –	63.56 ± –
36–45	95.34 ± 38.13	162.44 ± 0.00
46–55	85.99 ± 6.51	80.41 ± 18.12
56–65	107.36 ± 11.12	60.52 ± 10.72
66–75	83.62 ± 4.56	50.39 ± 4.18
76–86	92.51 ± 5.83	52.16 ± 10.02
p-value	0.344	0.05

Values are presented as Mean ± SEM. $p < 0.05$ was considered statistically significant*

Table 4.9: Correlation of Serum Amylase and Lipase with BMI, Duration of diabetes and Antigenemic production

Variable	BMI	Duration of Diabetes	Medication
Amylase	r = 0.027, p = 0.853	r = 0.016, p = 0.910	r = 0.196, p = 0.174
Lipase	r = –0.166, p = 0.249	r = –0.347, p = 0.014	r = 0.206, p = 0.151

*Values represent Pearson's correlation coefficients (r). Positive values indicate a direct relationship between variables, while negative values indicate an inverse relationship. *p < 0.05 is considered statistically significant.*

CHAPTER FIVE

5.0 DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion of Findings

This study investigated the levels of serum amylase and lipase in patients with Type 2 Diabetes Mellitus (T2DM) on different classes of antiglycemic drugs, as well as the influence of demographic and clinical variables on these enzyme activities. The findings provide insight into the interaction between diabetes, its management, and exocrine pancreatic function.

The socio-demographic data showed that females were more represented among subjects (patients with Type 2 Diabetes Mellitus (T2DM) than males, consistent with reports that women often constitute a greater proportion of patients accessing healthcare in Nigeria and sub-Saharan Africa (Khan *et al.,* 2020). The majority of participants were within the 46–65 years age bracket, a pattern aligning with the global observation that T2DM prevalence increases steadily with advancing age and peaks in middle to late adulthood (Yameny, 2025). This confirms that T2DM remains a disease predominantly of older adults, though earlier-onset cases are on the rise worldwide due to obesity and lifestyle transitions.

Body mass index analysis revealed that most participants had normal BMI, while overweight individuals accounted for 14% in both groups. This contrasts with literature reporting a strong association between T2DM and overweight/obesity (Yameny, 2025). One explanation may be the predominance of normal BMI in the study population, reflecting ethnic or dietary factors, or possible weight loss due to long-standing disease. In support of this, Ogbera *et al.* (2021) emphasized that African diabetics may not always present with obesity, highlighting population-specific differences.

Duration of diabetes among subjects showed that almost half had lived with the condition for 6–10 years. Prolonged duration of diabetes has been linked to progressive pancreatic dysfunction (Khan *et al*., 2025). This is relevant in interpreting the observed enzyme levels, since chronicity of disease may influence both endocrine and exocrine output.

Serum enzyme analysis revealed significantly higher mean amylase (93.19 ± 4.49 U/L) and lipase (67.03 ± 6.96 U/L) in T2DM subjects compared to controls (59.56 ± 4.81 U/L and 39.52 ± 3.19 U/L, respectively). These results support studies such as Hareesh *et al.* (2021), who reported elevated amylase and lipase in newly diagnosed Indian patients with T2DM. However, the findings contradict those of Ezeugwunne *et al*. (2021) in Nigeria, where no significant differences in enzyme levels were noted between diabetics and non-diabetics. This disparity highlights the variability in pancreatic enzyme activity across populations and supports the view that ethnicity, genetics, and disease stage contribute to divergent outcomes (Ezeugwunne *et al.,* 2021). It also suggests that in this cohort, T2DM was associated with hyperenzymemia rather than the hypoamylasemia often documented in chronic T2DM (Akinfemiwa, Zubair, and Muniraj, 2023).

When enzyme levels were compared across antiglycemic drug classes, variations were observed though not statistically significant. Patients on metformin plus sulfonylureas and metformin plus SGLT2 inhibitors had the highest mean amylase levels, while lipase was greatest in those on DPP-4 inhibitors. This is in line with earlier reports that sulfonylureas, by stimulating endogenous insulin secretion, may also enhance exocrine enzyme release (Cakmak *et al.,* 2021). Similarly, sitagliptin, a DPP-4 inhibitor, has been shown to modestly raise serum amylase and lipase (Chaudhari and Hansen, 2024). In contrast, metformin and thiazolidinediones are generally neutral with respect to pancreatic enzymes (Yameny, 2025), a trend also reflected in

this study. These observations underscore the potential of certain antiglycemic drugs to influence exocrine pancreatic markers, although the lack of statistical significance suggests that other confounders, such as sample size and disease duration, may have affected the results.

Gender, age, and BMI did not significantly affect amylase levels. However, lipase showed a significant relationship with BMI ($p = 0.023$), being lower in overweight individuals than in those with normal BMI. This pattern contrasts with the expectation that obesity, often linked to insulin resistance, would correspond to higher enzyme activity (Akinfemiwa, *et al.,* 2023). The finding may reflect exocrine insufficiency associated with long-standing obesity-related T2DM or reduced acinar responsiveness, a possibility supported by Khan *et al*. (2025), who described progressive acinar atrophy in insulin-resistant states. Furthermore, lipase negatively correlated with duration of diabetes ($r = –0.347$, $p = 0.014$), confirming that prolonged disease is associated with declining exocrine function. This agrees with studies showing that enzyme activity diminishes over time as pancreatic fibrosis progresses (Khan *et al.,* 2025).

Age-related differences showed no significant variation in amylase but lipase approached significance, with the highest levels observed among those aged 36–45 years. This could suggest that enzyme elevations are more pronounced in earlier or mid stages of the disease, while declining with chronicity, a trend echoed in primate longitudinal studies where lipase rose during early diabetes and declined with progression (Abdulhakeem *et al.,* 2023).

5.2 Conclusion

This study assessed the levels of serum amylase and lipase in patients with Type 2 Diabetes Mellitus (T2DM) receiving different classes of antiglycemic drugs, as well as the influence of demographic and clinical variables on these enzymes. The results demonstrated that serum amylase and lipase were significantly elevated in T2DM patients compared to non-diabetic

controls. Variation in enzyme levels was observed among patients on different medications, with sulfonylurea- and DPP-4–based therapies showing higher mean values, though these differences were not statistically significant. Lipase showed a significant negative correlation with the duration of diabetes, suggesting progressive decline in exocrine function with chronicity of the disease.

Overall, these findings indicate that pancreatic exocrine function is altered in T2DM and may be influenced by both disease duration and the class of antiglycemic drugs used. The pattern of elevated enzyme activity in this cohort differs from some previous reports that documented reduced levels, underscoring the variability across populations and the complex relationship between endocrine and exocrine pancreatic functions in diabetes.

5.3 Recommendations

1. **Clinical Monitoring:** Routine monitoring of serum amylase and lipase may be valuable in T2DM patients, especially those on incretin-based therapies or secretagogues, to identify subclinical pancreatic alterations.
2. **Longitudinal Studies:** Further prospective studies with larger cohorts are needed to establish causal relationships between antiglycemic drugs, duration of therapy, and changes in pancreatic enzyme levels.
3. **Population-Based Research:** More studies in African and other underrepresented populations should be conducted to better understand ethnic and regional variability in pancreatic enzyme responses in diabetes.

4. **Integrated Care Approach:** Clinicians should consider both endocrine and exocrine pancreatic health in the management of T2DM, recognizing that prolonged disease duration may predispose patients to progressive exocrine insufficiency.

5. **Patient Education:** Diabetic patients should be educated on the possible gastrointestinal and pancreatic implications of their treatment regimens, and encouraged to report persistent abdominal symptoms promptly.

REFERENCES

Abdulhakeem, Z. R., Odda, A. H., & Abdulsattar, S. A. (2023). Relationship of serum ghrelin, amylase and lipase with insulin level in type 2 diabetes mellitus patients. *Medical Journal of Babylon,* 20(1): 71–76.

Akinfemiwa, O., Zubair, M., and Muniraj, T. (2023). Amylase. In StatPearls [Internet]. StatPearls Publishing.

Bhadarge, G., Dawande, P., Bankar, N., and Kotecha, R. (2021). Study of serum pancreatic amylase and lipase enzyme in patients with type 2 diabetes. *Journal of Pharmaceutical Research International*, 33(37B): 197–201.

Cakmak, R., Caklili, O. T., Tekin, S., Hacisahinogullari, H., Tanrikulu, S., Koc, M. S., and Dincag, N. (2022). Comparison of amylase and lipase levels of patients with type 2 diabetes under different treatment modalities. Biomarkers in Medicine, 16(1): 5–10.

Chaudhari, U. K., and Hansen, B. C. (2024). Amylase and lipase levels in the metabolic syndrome and type 2 diabetes: A longitudinal study in rhesus monkeys. Physiological Reports: 12(13).

Çıkrıkçı Işık, G., Çinpolat, R., and Çevik, Y. (2021). The prevalence of simultaneously ordering amylase and lipase for diagnosing pancreatitis. *Eurasian Journal of Emergency Medicine,* 20(1): 35–38.

Czaplicka, A., And Kaleta, B. (2024). The effect of incretin-based drugs on the risk of acute pancreatitis: a review. *Journal of Diabetes & Metabolic Disorders*, 23(1): 487–495.

D'souza ,B.,and D' souza V.(2011). Hyperamylasemia in ovarian tumors serum amylase as a marker for ovarian cancers (?).*International journal of pharma and Bio sciences*, 2(1): 445-449.

El Sayed, S. A. (2023). Physiology, Pancreas. In StatPearls. StatPearls Publishing.

Ezeugwunne, I. P., Idris, S., Nnaemeka, W. S., Ejiogu, I. C., Elosuba, N. V., and Ibimere, O. D. (2021). Activities of pancreatic enzymes and anthropometric indices in type 2 diabetic patients attending Nnamdi Azikiwe University Teaching Hospital Nnewi, South Eastern Nigeria. *International Journal of Current Science Research and Review,* 4(8): 991–996.

Hareesh, R., Harish, K. V., And Savith, A. (2021). Association of serum amylase and lipase levels in newly diagnosed type 2 diabetes mellitus. I*nternational Journal of Advances in Medicine,* 8(2): 254–259.

Imamura, M., And Maeda, S. (2024). Perspectives on genetic studies of type 2 diabetes from the genome-wide association studies era to precision medicine. *Journal of Diabetes Investigation*, 15(4): 410–422.

Jalal, M., Gbadegesin, S. A., Tehami, N., Nakajima, K., and Challacombe, B. (2024). What is the clinical significance of low serum amylase? Systematic review of conditions associated with low serum amylase. Frontline Gastroenterology, 15(2): 154–161.

Kamrul-Hasan, A. B. M., Mondal, S., Dutta, D., Nagendra, L., Kabir, M. R., and Pappachan, J. M. (2024). Pancreatic safety of tirzepatide and its effects on islet cell function: A systematic review and meta-analysis. Obesity Science & Practice, 10(6): e70032.

Khan, M. A. B., Hashim, M. J., King, J. K., Govender, R. D., Mustafa, H., and Al Kaabi, J. (2020). Epidemiology of type 2 diabetes – Global burden of disease and forecasted trends. *Journal of Epidemiology and Global Health*, 10(1): 107–111.

Khan, M. R., Thivyahprabha, A. G., Sowmithri, K. D., and Kumaran, K. (2025). Serum amylase levels in T2DM patients: Surrogate biomarker of cardiometabolic status. *Journal of Medical Evidence,* 6(1): 24–28.

Ko, J., Cho, J., And Petrov, M. S. (2020). Low serum amylase, lipase, and trypsin as biomarkers of metabolic disorders: A systematic review and meta-analysis. Diabetes Research and Clinical Practice: 159.

Lomax, A. R., Karamanou, D., and Stamataki, N. S. (2020). Pancreatic exocrine–endocrine crosstalk: Physiology and pathophysiology. Nutrients, 12(9): 2685.

Młynarska, E., Czarnik, W., Dzieża, N., Jędraszak, W., Majchrowicz, G., Prusinowski, F., Stabrawa, M., Rysz, J., and Franczyk, B. (2025). Type 2 diabetes mellitus: New pathogenetic mechanisms, treatment and the most important complications. *International Journal of Molecular Sciences*: 26(3).

Nauck, M. A., Quast, D. R., Wefers, J., and Meier, J. J. (2021). GLP-1 receptor agonists in the treatment of type 2 diabetes — state-of-the-art. Molecular Metabolism: 46, 101102.

Odimegwu, C. L., Uwaezuoke, S. N., Chikani, U. N., Mbanefo, N. R., Adiele, K. D., Nwolisa, C. E., Eneh, C. I., Ndiokwelu, C. O., Okpala, S. C., Ogbuka, F. N., Odo, K. E., Ohuche, I. O., & Obiora-Izuka, C. E. (2024). Targeting the epigenetic marks in type 2 diabetes mellitus: Will epigenetic therapy be a valuable adjunct to pharmacotherapy? Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 17

Panteghini , M.,Bonita,R., and pagani, F .(2001). Measurement of pancreatic lipase activity in serum by a kinectic colorimetric assay using a new chromogenic substance. Annals of clinical biochemistry, 38(4): 365-370.

Pierzynowska, K. G., Lozinska, L., Woliński, J., And Pierzynowski, S. (2018). The inverse relationship between blood amylase and insulin levels in pigs during development, bariatric surgery, and intravenous infusion of amylase. PLoS ONE, 13(6): e0198672.

Regasa, T. (2022). The elevation of pancreatic enzymes in serum and their distribution at different stages of renal insufficiency among diabetic patients. *Journal of Clinical Laboratory Analysis,* 36(9): e24651.

Saini, J., Marino, D., Badalov, N., Vugelman, M., And Tenner, S. (2023). Drug-induced acute pancreatitis: An evidence-based classification (Revised). Clinical and Translational Gastroenterology, 14(8): e00621.

Sayiner, Z. A., Demiroglu, G. I., Akarsu, E., And Araz, M. (2020). The relationship between dipeptidyl peptidase-4 inhibitor usage and asymptomatic amylase lipase increment in type 2 diabetes mellitus patients. *Turkish Journal of Pharmaceutical Sciences*, 17(1): 68–73.

Valente, R., Coppola, A., Scandavini, C. M., Halimi, A., Magnusson, A., Lauro, A., Sotirova, I., Arnelo, U., And Franklin, O. (2024). Interactions between the exocrine and the endocrine pancreas. *Journal of Clinical Medicine,* 13(4): 1179.

Yameny, A. A. (2024). Diabetes mellitus overview. *Journal of Bioscience and Applied Research*, 10(3): 1–15.

Yameny, A. A. (2025). Diabetes mellitus: A comprehensive review of types, pathophysiology, complications, and standards of care in diabetes. *Journal of Modern Applied Life Sciences,* 9(1): 1–20.

Zaworski, K., Wychowański, P., Szkopek, D., Woliński, J., Donaldson, J., Pierzynowski, S., and Pierzynowska, K. (2025). The regulatory role of pancreatic enzymes in the maintenance of small intestinal structure and enterocyte turnover with special reference to alpha amylase. International Journal of Molecular Sciences, 26(1): 249.

Zhu, G., Fang, Q., Zhu, F., Huang, D., and Yang, C. (2021). Structure and function of pancreatic lipase-related protein 2 and its relationship with pathological states. Frontiers in Genetics, 12: 693538.

APPENDIX I

QUESTIONNAIRE

RESEARCH STUDY: SERUM AMYLASE AND LIPASE IN TYPE 2 DIABETES MELLITUS PATIENT ON DIFFERENT ANTIGLYCEMIC DRUGS

Dear Sir/Ma

The researcher is an undergraduate of the Medical Laboratory Science, School of Basic Medical Sciences, University of Benin, researching the topic stated above in partial fulfillment of the requirements for the award of the Bachelor of Medical Laboratory Science (B.MLS) degree.

Could you please spare your time to fill out this questionnaire? The information acquired from this research will be treated with utmost confidentiality.

SECTION A : **Consent and Demographics**

Do you voluntarily agree to participate in this study? (Yes/No)

1. Age: _____

2. Sex:

☐ Male ☐ Female

3. Marital Status:

☐ Single ☐ Married ☐ Widowed ☐ Divorced

4. Occupation: _____

5. Education level:

☐ No formal education ☐ Primary ☐ Secondary ☐ Tertiary

SECTION B: Clinical History

6. When were you diagnosed with Type 2 Diabetes Mellitus?

☐ <1 year ☐ 1–5 years ☐ 6–10 years ☐ >10 years

7. Do you have any history of acute or chronic pancreatitis?

☐ Yes ☐ No

8. Have you ever been diagnosed with any pancreatic disease (e.g., pancreatic cancer, cysts)?

☐ Yes ☐ No

9. Do you currently experience any of the following? (Check all that **apply**)

☐ Abdominal pain ☐ Nausea ☐ Vomiting ☐ Loss of appetite ☐ None

SECTION C :ANTHROPOMETRIC AND LIFESTYLE DATA

10. Do you consume alcohol?

☐ Never ☐ Occasionally ☐ Frequently

11. Do you smoke?

☐ Yes ☐ No

12. What is your current weight (kg)? _____

13. What is your height (cm)? _____

SECTION D: Antiglycemic Medication Use

14. . Which of the following antiglycemic drugs are you currently taking? (Check all that apply)

☐ Metformin

☐ Sulfonylureas (e.g., glibenclamide, gliclazide)

☐ DPP-4 Inhibitors (e.g., sitagliptin, vildagliptin)

☐ SGLT2 Inhibitors (e.g., empagliflozin, dapagliflozin)

☐ GLP-1 Receptor Agonists (e.g., liraglutide, exenatide)

☐ Insulin

☐ Others (specify): _____

15. How long have you been on your current antiglycemic drug(s)?

☐ <6 months ☐ 6–12 months ☐ 1–2 years ☐ >2 years

16. Do you take your medications consistently as prescribed?

☐ Yes ☐ No

17. Have you changed your antiglycemic medication in the past 6 months?

☐ Yes ☐ No

If yes, why? _____

18.. What is your current weight (kg)? _____

19. What is your height (cm)? _____

SECTION D: Laboratory and Screening

(To be filled by researcher based on lab results)

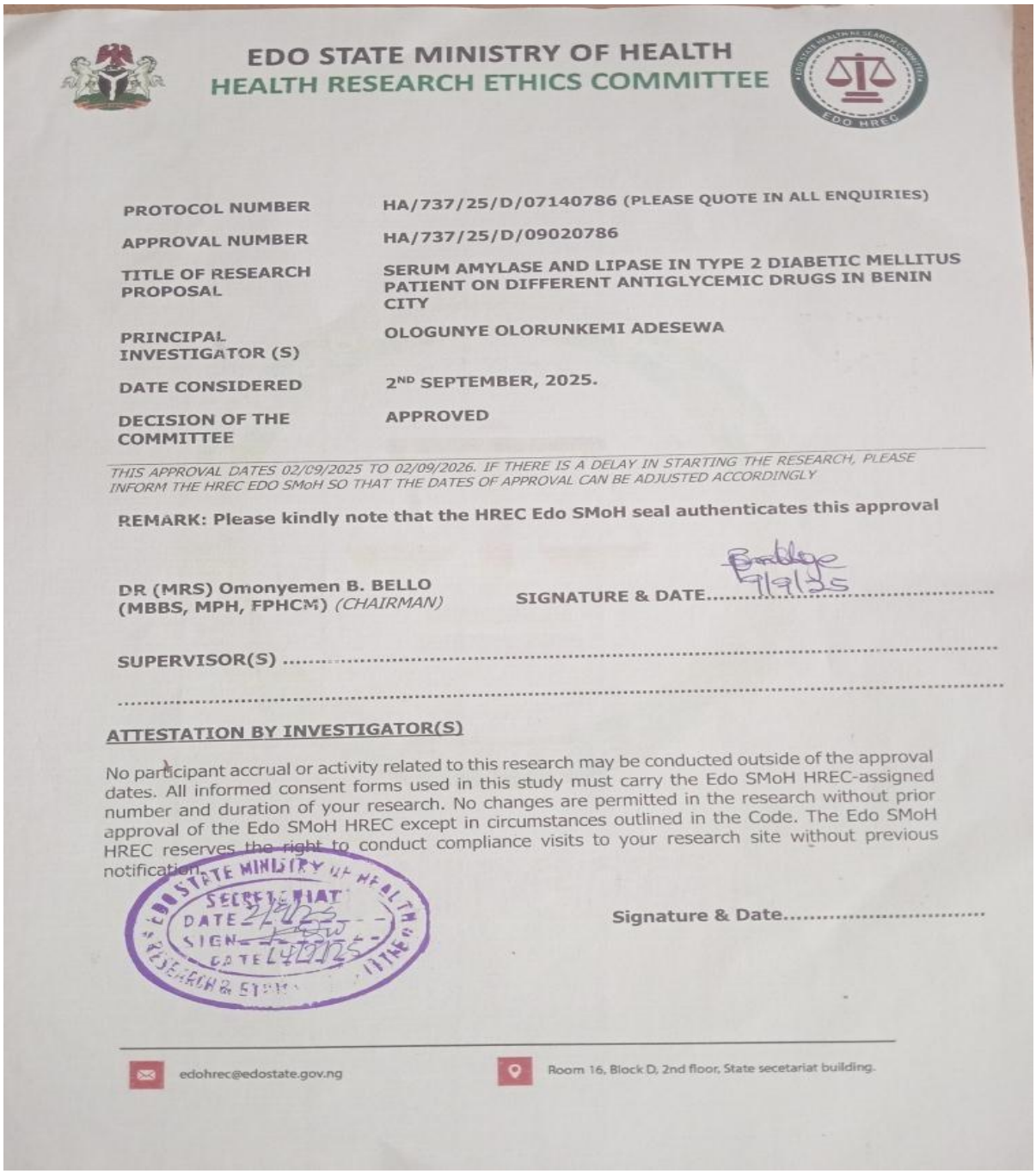
20. Date of blood sample collection: _____

21. Serum Amylase Level: _____U/L

22. Serum Lipase Level: _____U/L

APPENDIX LL

ETHICAL APPROVAL



EDO STATE MINISTRY OF HEALTH
HEALTH RESEARCH ETHICS COMMITTEE

PROTOCOL NUMBER	HA/737/25/D/07140786 (PLEASE QUOTE IN ALL ENQUIRIES)
APPROVAL NUMBER	HA/737/25/D/09020786
TITLE OF RESEARCH PROPOSAL	SERUM AMYLASE AND LIPASE IN TYPE 2 DIABETIC MELLITUS PATIENT ON DIFFERENT ANTIGLYCEMIC DRUGS IN BENIN CITY
PRINCIPAL INVESTIGATOR (S)	OLOGUNYE OLORUNKEMI ADESEWA
DATE CONSIDERED	2ND SEPTEMBER, 2025.
DECISION OF THE COMMITTEE	APPROVED

THIS APPROVAL DATES 02/09/2025 TO 02/09/2026. IF THERE IS A DELAY IN STARTING THE RESEARCH, PLEASE INFORM THE HREC EDO SMoH SO THAT THE DATES OF APPROVAL CAN BE ADJUSTED ACCORDINGLY

REMARK: Please kindly note that the HREC Edo SMoH seal authenticates this approval

DR (MRS) Omonyemen B. BELLO (MBBS, MPH, FPHCM) *(CHAIRMAN)* **SIGNATURE & DATE**..... 9/9/25

SUPERVISOR(S) .....

.....

ATTESTATION BY INVESTIGATOR(S)

No participant accrual or activity related to this research may be conducted outside of the approval dates. All informed consent forms used in this study must carry the Edo SMoH HREC-assigned number and duration of your research. No changes are permitted in the research without prior approval of the Edo SMoH HREC except in circumstances outlined in the Code. The Edo SMoH HREC reserves the right to conduct compliance visits to your research site without previous notification.

EDO STATE MINISTRY OF HEALTH SECRETARIAT DATE 2/9/25 SIGN DATE 4/09/25

Signature & Date.....

edohrec@edostate.gov.ng Room 16, Block D, 2nd floor, State secetariat building.

APPENDIX III

CONSENT FORM

Title of research: Serum Amylase and lipase in type 2 diabetes mellitus patient on different antiglycemic drugs in Benin city

Name of principal investigator:

OLOGUNYE OLORUNKEMI ADESEWA

Phone Number: 07063459814

Name of supervisor:

PROF. M.A. EMOKPAE

Phone Number: 08034511182

Institution and Contact Address: Department of Medical Laboratory Science, School of Basic Medical Sciences, University of Benin, Benin City.

Phone Number: 08171568527**.**

Email: ologunyeadesewa47@gmail.com.

Commencement Date of Research: July 2025

Proposed Duration of Research: 3months

Financial Sponsors: Parents and self

Conflict of Interest: None declared

Purpose of Research: The aim of this study is to investigate the level of serum amylase and lipase in type 2 diabetic mellitus patient on different antiglycemic drugs

Estimated Number of Participants: Sample size calculation was used to obtain the needed number of subjects whose samples shall be collected

Procedure Involved in the Study: Questionnaires and oral interview was used for data collection and while blood sample was used for biochemical investigation.

Research Design and Methods: The study is case control study.

Risks to Participants: No risk envisaged aside the slight discomfort while collecting blood sample from participant's antecubital vein.

Benefits to Participants: No benefit (voluntary participation), however, if there is any abnormality found after testing, the subjects will be assisted to consult a specialist at no cost.

Compensation/ Inducement: None

Statement of Voluntariness and Circumstances for Withdrawal: Participants are allowed to withdraw from the research at any stage, and the withdrawal will have no adverse effect on the sujects in any form.

Statement on Use of Personal Data: Personal data was stored permanently with the research coordinator / principal investigator for further research purposes and no more than such.

Statement on Confidentiality: Strict and absolute confidentiality is guaranteed. Information of the patients obtained from this study/research was stored in my personal pass worded computer.

Measures To Take Care of Research-Related Injuries: Full personal protective equipment (PPE) wears / kits was provided to present research related injuries and there was provision of a standby vehicle in cases of any emergency.

I Have Fully Explained This Research to The Participant(s) and Have Given Sufficient Information, Including information about the Risks and Benefits, to make an Informed Decision.

Signature /Date:

NAME: PROF. M.A. EMOKPAE

Witness' Name / Signature & Date (If any):

OLOGUNYE OLORUNKEMI ADESEWA

CONTACT (Any of the Researchers): PROFESSOR M.A. EMOKPAE (Supervisor)

If You have any Question about Your Participation in this Research, You can Contact the Principal Investigator. The Address is Department of Medical Laboratory Science (Chemical Pathology Unit), School of Basic Medical Sciences, College of Medical Sciences, University of Benin, Benin City; Edo State, Nigeria.

Email: mathias.emokpae@uniben.edu

Phone Number: 08034511182

STATEMENT FROM PARTICIPANT(S)

I have Read the Description of the Research or have had it Translated to my Understanding. I have also Talked it over with the Researcher to my Satisfaction. I Understand that my Participation is Voluntary. I know enough about the Purpose, Methods, Risks, and Benefits of the Research Study to Judge that I want to take Part in it. I also understand that I may freely stop being Part of this Study at any Time if I so wish for any Reasons Best known to me. I have Received a Copy of this Consent Form and Additional Information Sheet to keep for myself.

Participant's Signature / Thumb Print: _____ Date: _____

Participant's Name / Or Number (If Applicable):----------

Witness' Signature (if any): - - - - - - - - - - - - - - - Date: - - - - - - - - - - - - - - - - - -

Witness' Name (If Applicable): ----------

PLEASE KEEP A COPY OF OF THE SIGNED INFORMED CONSENT

For Official Use Only

Director, Edo State Ministry of Health Approval Number: _____

Commencement Date of Research (dd/mm/yy): _____

This Research has been approved by Director, Edo State Ministry of Health and the Chair of the

Committee can be contacted on:

Do you voluntarily agree to participate in this study? (Yes/No)

1. Age: _____

2. Sex:

☐ Male ☐ Female

3. Marital Status:

☐ Single ☐ Married ☐ Widowed ☐ Divorced

4. Occupation: _____

5. Education level:

☐ No formal education ☐ Primary ☐ Secondary ☐ Tertiary

SECTION B: Clinical History

6. When were you diagnosed with Type 2 Diabetes Mellitus?

☐ <1 year ☐ 1–5 years ☐ 6–10 years ☐ >10 years

7. Do you have any history of acute or chronic pancreatitis?

☐ Yes ☐ No

8. Have you ever been diagnosed with any pancreatic disease (e.g., pancreatic cancer, cysts)?

☐ Yes ☐ No