Renal Function Assessment for CKD in Type 2 Diabetic Patients of Bangladesh: A Cross-Sectional Study

Submitted By
Mohammod Ferdaus Kamal
ID: 23376011

A thesis submitted to the Department of Mathematics and Natural Sciences (MNS) in partial fulfillment of the requirements for the degree of Masters of Science in Biotechnology

Department of Mathematics and Natural sciences
BRAC University
November 2024

Declaration

It is hereby declared that

1. The thesis submitted is my/our original work while completing my degree at BRAC University.

2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.

3. The thesis does not contain material that has been accepted, or submitted, for any other degree or diploma at a university or other institution.

4. I have acknowledged all main sources of help.

Student's Full Name & Signature:

Mohammod Ferdaus Kamal

Name: Mohammod Ferdaus Kamal
ID: 23376011

Approval

The thesis/project titled "Renal Function Assessment for CDK in Type 2 Diabetic Patients of Bangladesh" submitted by

1. Mohammod Ferdaus Kamal (23376011)

of July 2023 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Masters of Science in Biotechnology in November 2024.

Examining Committee:

Supervisor
(Member)

_____

Dr. Munima Haque
Associate Professor
Department of Mathematics and Natural Sciences
Brac University

Program Director
(Member)

_____

Dr. Munima Haque
Biotechnology Program Director & Associate Professor
Department of Mathematics and Natural Sciences
Brac University

Chairperson
(Member)

_____

Dr. Md. Firoze H. Haque
Chairperson and Professor
Department of Mathematics and Natural Sciences
Brac University

Abstract

Chronic Kidney Disease (CKD) is a major long-term complication of Type 2 diabetes mellitus. The aim of this study was to determine the prevalence of CKD among patients with Type 2 diabetes (T2D) and its associated parameters in Bangladesh.

A cross-sectional descriptive study design was chosen for data collection; data was collected from clinical laboratory test reports from A tertiary hospital in Bangladesh. The inclusion criteria were male and female patients from 30-90 years, diagnosed with type 2 diabetes mellitus. The data was analyzed using the SPSS version 26.

Males show the highest prevalence of CKD in the age group of 51-60 (18.1%). The renal profile assessment revealed significant gender-based differences in several biochemical parameters, a higher percentage of males having abnormal levels compared to females in serum urea ($p=0.02$), creatinine ($p=0.01$), sodium plasma ($p=0.05$), and plasma bicarbonates ($p= 0.001$). The distribution of the estimated glomerular filtration rate showed that males had a higher representation in stages II (18.6%), suggesting delayed diagnosis. As CKD progressed, females appeared to catch up and surpass males in later stages, particularly Stage III (9.5%). This might suggest that they might have different risk factors that accelerate the progression of CKD. This study highlights that renal function declines with age.

This study found substantial gender disparities in renal function among T2D patients, with males having a higher prevalence of aberrant renal parameters and more severe renal illness. These findings have significant implications for clinical care, indicating the need for gender-specific methods to preventing and treating renal problems.

Dedication

First of all, I would like to express my gratitude to the All-mighty, without His blessings, this opportunity never would have come true. I also remember my parents, the Late Mr. Abul Kashem and Mrs. Anowara Begum, for their untold sacrifice and devotion, without them it would never have happened to become a Physician in my life. Particularly my father late Mr. Abul Kashem, an ex-government official, with his limitation, patronized me in every possible way. Last but not least, I am grateful to my wife Dr Nadia Nawshin, an Associate Professor, at the Department of Anatomy, Delta Medical College, and my three beloved children Farzad, Faiza, Farnaz who used to inspire me in every aspect of this long journey.

Mohammod Ferdaus Kamal

October, 2024

Acknowledgement

The first thing I want to say is that I am grateful to the highest God for granting me the opportunity to do this research.

I would like to convey my profound appreciation to Professor A F M Yusuf Haider, Ph.D. Chairperson, Department of Mathematics and Natural Sciences for permitting me to pursue my studies in this department.

I would like to express my deepest gratitude to my supervisor Dr. Munima Haque, MS and BS Biotechnology Program Director & Associate Professor, Department of Mathematics and Natural Sciences (MNS), School of Data and Sciences (SDS), BRAC University, for all of her time, effort, understanding, encouragement, inspiration, insight, and expertise throughout my research work.

I want to thank my parents from the bottom of my heart for always believing in me, always encouraging me to follow my dreams, and always being there for me, even when things were bleakest.

Mohammod Ferdaus Kamal

October, 2024

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List of Acronyms

- DM- Diabetes Mellitus
- T2D- Type 2 Diabetes
- DKD-Diabetic Kidney Disease
- CKD- Chronic Kidney Disease
- DN- Diabetic Nephropathy
- MDRD - Modification of Diet in Renal Disease
- eGFR- estimating Glomerular Filtration Rate
- End-stage renal disease (ESRD).

Chapter 1: Introduction

Diabetes mellitus (DM) is a metabolic disorder that emerges when the pancreas does not produce adequate insulin, or the body's cells become insensitive to insulin actions, resulting in abnormally raised blood glucose levels (hyperglycemia) [1,2]. DM is becoming increasingly prevalent globally, but there is no single cause. Diabetic individuals are becoming more knowledgeable about their illness, contributing to this growth [3]. As the number of diabetic individuals increases, type 2 diabetes (T2D) accounts for the majority of the ratio due to its higher prevalence [4]. Due to the increase in its dominance each year this syndrome is considered as a heavy load on the medical field, while predicting the same pattern in developing countries [5]. With T2D some patients develop complications in the early stages and the recovery becomes much harder, but complications will happen eventually still we aim to delay these events as much as possible while controlling patients' condition under any circumstances. Concerning renal complications, diabetes alone has a lesser effect on health than if present with kidney disease, more than one factor acts on the pathophysiology of developing kidney disease with diabetic patients when patients are diagnosed at the start of diabetic kidney disease (DKD) the development will progress through stages, from reversible glomerular hyperplasia to renal dysfunction or Diabetic nephropathy or Chronic kidney disease (CKD). DKD unfortunately is not always early identified but with continuous monitoring of a diabetic patient's signs of albuminuria (ratio of albumin to creatinine in urine above 30 mg/g) are considered as a start of this condition [6-8]. Genuinely the health status is different from one patient to another, due to the differences in age, gender, co-morbidities, genetics, and many others.

According to a study Diabetic nephropathy (DN) now accounts for 46% of chronic kidney disease in the elderly [9]. A recent systematic review found that the overall pooled prevalence of CKD among Bangladeshi adults was 17.3%, ranging from 12.8% to 26.0% [10]. Another study reported that people with type 2 diabetes in Bangladesh had a high proportion of self-reported kidney disease [11]. A number of studies in Bangladesh have also reported the

prevalence of kidney disease in different population groups [12,13,14]. A few studies have reported on CKD in patients with T2D and its determinants in Bangladesh at community levels [15], in slums [16], in the rural population [17], or during screening [18]. However, information on renal function that leads to CKD in type 2 diabetic patients in tertiary care hospitals is limited. Understanding the parameters associated with CKD among people with T2D in Bangladesh is essential to developing preventive strategies and improving management practices. Therefore, this study aimed to determine the prevalence of CKD among patients with T2D and its associated parameters in Bangladesh.

Aim of the Study

- To assess the renal function that leads to CKD in type 2 diabetic patients.

Chapter 2: Type 2 Diabetic and Renal Function

2.1 Type -2 DM: Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose, which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves. The most common is type 2 diabetes, usually in adults, which occurs when the body becomes resistant to insulin or doesn't make enough insulin. Type 2 diabetes mellitus (T2DM) accounts for around 90% of all cases of diabetes. In T2DM, the response to insulin is diminished, and this is defined as insulin resistance. During this state, insulin is ineffective and is initially countered by an increase in insulin production to maintain glucose homeostasis, but over time, insulin production decreases, resulting in T2DM. T2DM is most commonly seen in persons older than 45 years. Still, it is increasingly seen in children, adolescents, and younger adults due to rising levels of obesity, physical inactivity, and energy-dense diets. Type 2 DM (formerly known as non-insulin dependent DM) is characterized by hyperglycemia, insulin resistance, and relative insulin deficiency [19]. Type 2 DM results from interaction between genetic, environmental and behavioral risk factors [20]. It is characterized by insulin insensitivity as a result of insulin resistance, declining insulin production, and eventual pancreatic beta-cell failure [21]. This leads to a decrease in glucose transport into the liver, muscle cells, and fat cells. There is an increase in the breakdown of fat with hyperglycemia. The involvement of impaired alpha-cell function has been recognized in the pathophysiology of type 2 DM [22]. As a result of this dysfunction, glucagon and hepatic glucose levels that rise during fasting are not suppressed with a meal. Given inadequate levels of insulin and increased insulin resistance, hyperglycemia results.

Patients with type 2 diabetes often have associated disorders including hypertension, dyslipidaemia (characterised by elevated levels of small dense low-density lipoprotein (LDL) cholesterol and triglycerides, and a low level of high-density lipoprotein (HDL) cholesterol), non-alcoholic fatty liver and, in women, polycystic ovarian syndrome. This cluster has been termed the ‘insulin resistance syndrome’ or ‘metabolic syndrome’ and is much more common in patients who are obese [23].

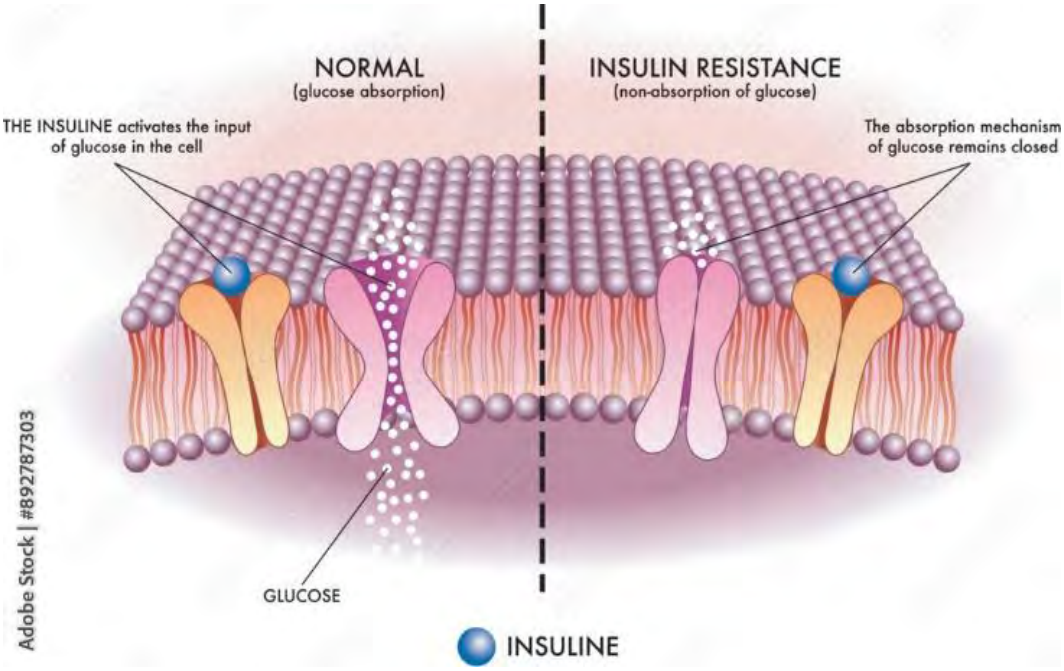

Figure 1: Mechanism of insulin resistance (Adobe stock, 892793805). [24]

2.2 Pathogenesis: T2DM is a multifactorial disease involving genetic and environmental factors. The pathophysiological changes are characterized by β-cell dysfunction, insulin resistance and chronic inflammation, all of which progressively hamper control of blood glucose levels and lead to the development of micro- and macro vascular complications. With respect to hyperglycemia, at least eight distinct pathophysiological abnormalities contribute to impaired glucose homeostasis, and these factors are already well established early in the natural history of T2DM [25,26].

Initially, there is a compensatory increase in insulin secretion, which maintains glucose levels in the normal range. As the disease progresses, beta cells change, and insulin secretion is unable to maintain glucose homeostasis, producing hyperglycemia. Most of the patients with T2DM are obese or have a higher body fat percentage, distributed predominantly in the abdominal region. This adipose tissue itself promotes insulin resistance through various inflammatory mechanisms, including increased FFA release and adipokine dysregulation. Lack of physical activity, prior GDM in those with hypertension or dyslipidemia also increases the risk of developing T2DM. Evolving data suggest a role for adipokine dysregulation, inflammation, abnormal incretin biology with decreased incretins such as glucagon-like peptide-1 (GLP-I) or incretin resistance, hyperglucagonemia, increased renal glucose reabsorption, and abnormalities in gut microbiota.

The primary cause of insulin resistance remains unclear; it is likely that there are multiple defects in insulin signalling, affecting several tissues. One theory is centred around the

adipocyte; this is particularly appealing, as obesity is a major cause of increased insulin resistance. Intra-abdominal 'central' adipose tissue is metabolically active, and releases large quantities of FFAs, which may induce insulin resistance because they compete with glucose as a fuel supply for oxidation in peripheral tissues such as muscle. In addition, adipose tissue releases several hormones (including a variety of peptides, called 'adipokines' because they are structurally similar to immunological 'cytokines') which act on specific receptors to influence sensitivity to insulin in other tissues. Because the venous drainage of visceral adipose tissue is into the portal vein, central obesity may have a particularly potent influence on insulin sensitivity in the liver, and thereby adversely affect gluconeogenesis and hepatic lipid metabolism. Physical activity is another important determinant of insulin sensitivity. Inactivity is associated with the downregulation of insulin-sensitive kinases and may promote the accumulation of FFAs within skeletal muscle. Sedentary people are therefore more insulin-resistant than active people with the same degree of obesity. Moreover, physical activity allows non-insulin-dependent glucose uptake into muscle, reducing the 'demand' on the pancreatic β cells to produce insulin. Deposition of fat in the liver is a common association with central obesity and is exacerbated by insulin resistance and/or deficiency. Many patients with type 2 diabetes have evidence of fatty infiltration of the liver (non-alcoholic fatty liver disease (NAFLD)). This condition may improve with effective treatment of the diabetes and dyslipidemia, but despite this, a few patients progress to non-alcoholic steatohepatitis (NASH) and cirrhosis.

In the early stages of type 2 diabetes, reduction in the total mass of pancreatic islet tissue is modest. At the time of diagnosis, around 50% of β-cell function has been lost and this declines progressively. Some pathological changes are typical of type 2 diabetes, the most consistent of which is deposition of amyloid in the islets. In addition, elevated plasma glucose and FFAs exert toxic effects on pancreatic β cells to impair insulin secretion. However, while β-cell numbers are reduced, β-cell mass is unchanged and glucagon secretion is increased, which may contribute to hyperglycemia.

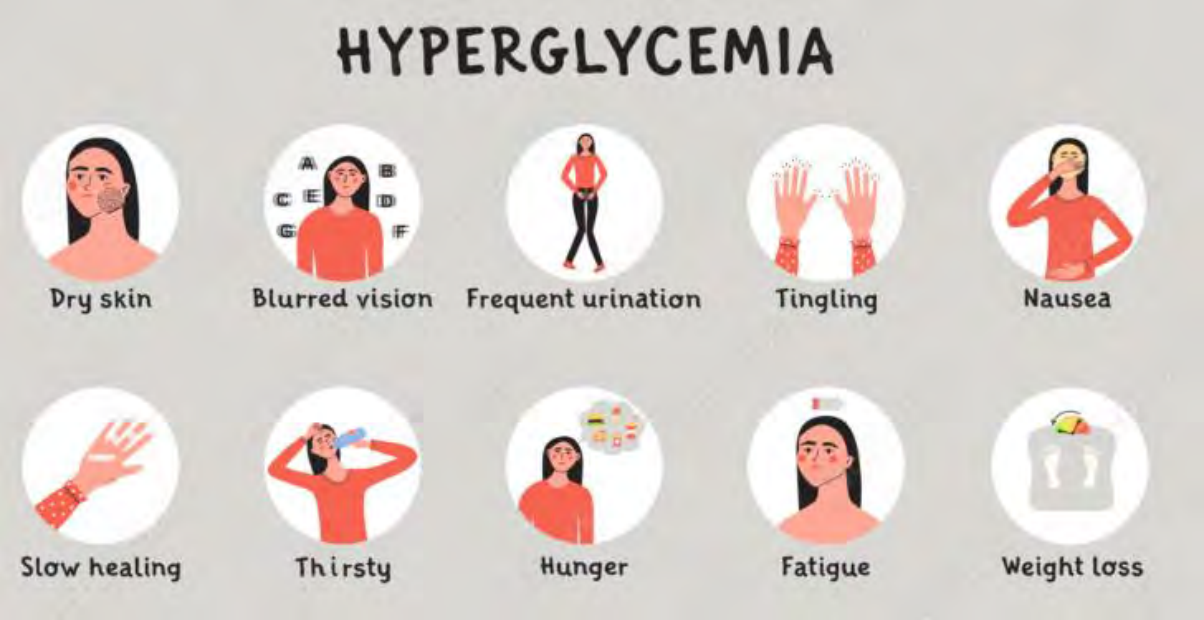

Figure 2: Hyperglycemic symptoms (Adobe Stock). [27]

2.3 Epidemiology: DM is now one of the most common no communicable diseases globally. It is an epidemic in many developing and industrializing countries. At present, the total number of diabetic persons globally are nearly 537 million with a prevalence of 10.5% in the adult population (20 to 79 years). China and India hold the first and second positions respectively having 140.9 and 74.2 million of total cases of diabetes. It is estimated that this current number of diabetic persons is projected to reach 643 million by 2030, and 783 million by 2045 [28]. In addition to diabetes, prediabetes also constitutes a major public health problem because of its association with an increased risk of DM and cardiovascular diseases (CVD). A total of 541 million (1 in 9) people are estimated to have impaired glucose tolerance (IGT) and 319 million (1 in 18) people have impaired fasting glucose (IFG). A pronounced rise in the prevalence of type 2 diabetes occurs in migrant populations to industrialized countries, as in Asian and Afro-Caribbean immigrants to the UK or USA. Type 2 diabetes is now being observed in children and adolescents, particularly in some ethnic groups, such as Hispanics and Afro-Americans.

2.4 Symptoms: The common mode of presentation in T2DM is atypical manifestations which are non-specific including non-healing infection, infertility or repeated pregnancy loss, pruritus vulvae, and undue fatigability according to national guidelines of diabetic mellitus Bangladesh. Symptoms of type 2 diabetes often develop slowly. People can be living with type 2 diabetes for years and not know it. When symptoms are present, they may include, increased thirst, frequent urination, increased hunger, unintended weight loss, fatigue, blurred vision, slow-

healing sores, frequent infections, numbness or tingling in the hands or feet, areas of darkened skin, usually in the armpits and neck.

2.5 Metabolic disturbances in type 2 diabetes: Patients with type 2 diabetes have a slow onset of 'relative' insulin deficiency. Relatively small amounts of insulin are required to suppress lipolysis, and some glucose uptake is maintained in muscle, so that, in contrast with type 1 diabetes, lipolysis and proteolysis are not unrestrained and weight loss and ketoacidosis seldom occur. The pathogenesis and progression of T2D is ascribed to four mechanisms; increased advanced glycation end product (AGE) formation, increased polyol pathway flux, activation of protein kinase C (PKC) isoforms, and increased hexosamine pathway flux.
In type 2 diabetes, hyperglycemia tends to develop slowly over months or years; because of this insidious onset many cases of type 2 diabetes are discovered coincidentally, and a large number are undetected. At diagnosis, patients are often asymptomatic or give a long history (typically many months) of fatigue, with or without 'osmotic symptoms' (thirst and polyuria). In some patients with type 2 diabetes, presentation is late, and pancreatic β-cell failure has reached an advanced stage of insulin deficiency. Islet tissue sections of T2D subjects show well-defined fibrosis, which is a hallmark of the late stage of a chronic inflammatory process. These patients may present with weight loss but ketoacidosis is uncommon. However, in some ethnic groups, such as African Americans, half of those whose first presentation is with diabetic ketoacidosis have type 2 diabetes. Intercurrent illness, e.g. with infections, increases the production of stress hormones that oppose insulin action, such as cortisol, growth hormone, and catecholamines. This can precipitate an acute exacerbation of insulin resistance and insulin deficiency, and result in more severe hyperglycemia and dehydration.

2.6 Risk factors: Medical conditions including obesity, hypertension, hyperlipidemia, and metabolic syndrome can give rise to Type 2 DM. Additional factors found to increase the risk of type 2 DM include aging, high-fat diets, and a less active lifestyle. There is a strong inheritable genetic connection in type 2 DM, having relatives (especially first-degree) with type 2 DM increases the risks of developing type 2 DM substantially. Concordance among monozygotic twins is close to 100%, and about 25% of those with the disease have a family history of DM [29].
Recently, genes discovered to be significantly associated with developing type 2 DM, include TCF7L2, PPARG, FTO, KCNJ11, NOTCH2, WFS1, CDKAL1, IGF2BP2, SLC30A8, JAZF1,

and HHEX. KCNJ11 (potassium inwardly-rectifying channel, subfamily J, member 11), encodes the islet ATP-sensitive potassium channel Kir6.2, and TCF7L2 (transcription factor 7-like 2) regulates proglucagon gene expression, and thus the production of glucagon-like peptide-1[30].

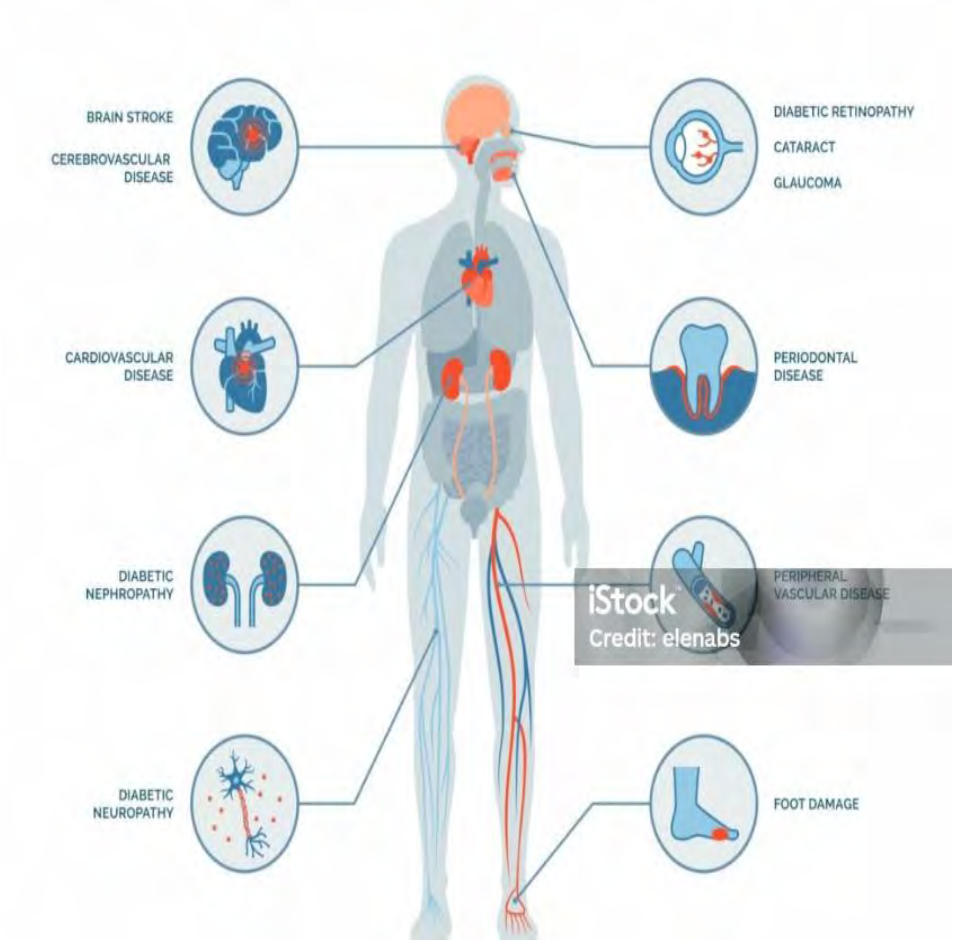

Figure 3: Risk factor of T2D. (Istock) [31]

2.7 Diagnosis: Persons older than 40 years of age should be screened annually. More frequent screening is recommended for individuals with additional risk factors for diabetes.

- Certain races/ethnicities (Native American, African American, Hispanics, Asian American, Pacific Islander),
- Overweight or obese persons with a BMI greater than or equal to 25 kg/m2 or 23 kg/m2 in Asian Americans,
- First-degree relative with diabetes mellitus
- History of cardiovascular disease or hypertension
- Low HDL-cholesterol or hypertriglyceridemia,
- Women with polycystic ovarian syndrome
- Physical inactivity

- Conditions associated with insulin resistance, for example, Acanthosis nigricans.

Women diagnosed with gestational diabetes mellitus (GDM) should have lifelong testing at least every three years. For all other patients, testing should begin at age 45 years, and if results are normal, patients should be tested at a minimum of every 3 years.

In asymptomatic individuals, the timing and frequency of testing for prediabetes or T2DM are based on the presence or absence of risk factors. Screening in at-risk individuals is important because prediabetes is common and ~30% of individuals with T2DM are undiagnosed.

- **Glycated Hemoglobin (Hb) A1C**

Type 2 diabetes is usually diagnosed using the glycated hemoglobin (A1C) test. This blood test indicates the average blood sugar level for the past two to three months [32]. Results are interpreted as follows:
Below 5.7% is normal.
5.7% to 6.4% is diagnosed as prediabetes.
6.5% or higher on two separate tests indicates diabetes.
If the A1C test isn't available, or people have certain conditions that interfere with an A1C test, the following tests may be used to diagnose diabetes.

This test gives an average of blood glucose over the last 2 to 3 months. Patients with a Hb A1C greater than 6.5% (48 mmol/mol) are diagnosed as having DM. Hb A1C is a convenient, rapid, standardized test and shows less variation due to pre-analytical variables. It is not much affected by acute illness or stress.

Hb A1C is costly and has many issues, including lower sensitivity. Hb A1C should be measured using the National Glycohemoglobin Standardization Program (NGSP) certified method standardized to Diabetes Control and Complications Trial (DCCT) assay. It is affected by numerous conditions such as sickle cell disease, pregnancy, hemodialysis, blood loss or transfusion, or erythropoietin therapy. It has not been well validated in non-white populations.

Anemia due to deficiency of iron or vitamin B12 leads to spurious elevation of Hb A1C, limiting its use in countries with a high prevalence of anemia. Also, in children and the elderly, the relation between Hb A1C and FPG is suboptimal.

For all of the above tests, if the person is asymptomatic, testing should be repeated later to make a diagnosis of diabetes mellitus.

- **Random blood sugar test**: Blood sugar values are expressed in milligrams of sugar per deciliter (mg/dL) or millimoles of sugar per liter (mmol/L) of blood. Regardless of last ate, a level of 200 mg/dL (11.1 mmol/L) or higher suggests diabetes including symptoms.
- **Fasting blood sugar test:** A blood sample is taken after overnight fasting (8-10 hours). Results are interpreted as follows:

Less than 100 mg/dL (5.6 mmol/L) is considered healthy.
100 to 125 mg/dL (5.6 to 6.9 mmol/L) is diagnosed as prediabetes.
126 mg/dL (7 mmol/L) or higher on two separate tests is diagnosed as diabetes.

In T2DM presentations may remain asymptomatic for quite a long period resulting in late diagnosis and intervention. So a significant proportion of T2DM cases present with one or more chronic complications.

2.7 Management: Management of T2DM is complicated by multiple pathophysiological disturbances and the 'ABCDE' of diabetes management (Age, Body weight, Complications, Duration, Education and Expense, and Etiology). Prevention of microvascular complications focuses on glycemic control, whereas prevention of macrovascular complications requires correction of classic cardiovascular risk factors that comprise the insulin resistance (metabolic) syndrome.

The majority of type 2 DM can be prevented by lifestyle modification. A diet low in saturated fat, refined carbohydrates, high fructose corn syrup, and high on fiber and monounsaturated fats needs to be encouraged. Aerobic exercise for a duration of 90 to 150 minutes per week is also beneficial. The major target in T2DM patients, who are obese, is weight loss. The incidence of type 2 DM can be significantly reduced with a combination of maintenance of body mass index of 25 kg/m2, eating high fiber and unsaturated fat and diet low in saturated and trans-fats and glycemic index, regular exercise, abstinence from smoking and moderate consumption of alcohol [33,34]. Patients with type 2 DM should receive a medical nutrition evaluation; lifestyle recommendations should be tailored according to physical and functional ability.

2.8 Complications: Type 2 diabetes affects many major organs, including the heart, blood vessels, nerves, eyes and kidneys. It is associated with an increased risk of heart disease, irregular heart rhythms, stroke, high blood pressure and atherosclerosis, peripheral neuropathy, tingling, numbness, burning, pain, or eventual loss of feeling that usually begins at the tips of the toes or fingers and gradually spreads upward. Nerve damage in the digestive system can cause problems with nausea, vomiting, diarrhea, or constipation. Nerve damage also may cause erectile dysfunction. Diabetes may lead to chronic kidney disease or end-stage kidney disease and may require dialysis or a kidney transplant. Diabetes increases the risk of cataracts and glaucoma leading to blindness, bacterial and fungal skin infections, poor wound healing, hearing problems, and Obstructive sleep apnea, and increases the risk of Alzheimer's disease results in dementia [35].

2.9 Prevention: Healthy lifestyle choices can help prevent type 2 diabetes. lifestyle changes may slow or stop the progression to diabetes. A healthy lifestyle includes eating healthy foods, lower in fat and calories and higher in fiber, fruits, vegetables, and whole grains. Moderate to vigorous aerobic activity and losing weight.

Patients must be educated about the importance of blood glucose management to avoid complications associated with DM. Stress must be given to lifestyle management, including diet control and physical exercise. Self-monitoring of blood glucose is an important means for patients to take responsibility for their diabetes management. Regular estimation of glucose, glycated hemoglobin, and lipid levels is necessary.

Healthcare professionals should educate patients about the symptoms of hypoglycemia (such as tachycardia, sweating, and confusion) and the required action (ingestion of 15 to 20 gm of carbohydrates).

Patients should be motivated to stop smoking. Emphasis is required on regular eye check-ups and foot care.

For people with prediabetes, metformin (Fortamet, Glumetza, others), a diabetes medication, may be prescribed to reduce the risk of type 2 diabetes. This is usually prescribed for older adults who are obese and unable to lower blood sugar levels with lifestyle changes.

2.10 Renal Dysfunction: Diabetic nephropathy is a specific form of microangiopathy of the kidney which is characterized by: Persistent albuminuria Progressive renal insufficiency (declining eGFR) with or without hypertension. Albumin-to-creatinine ratio (ACR) is the preferred method to detect elevated protein in urine. The recommended method to evaluate albuminuria is to measure urinary ACR in a spot urine sample (preferably a morning fasting sample before exercise). ACR is calculated by dividing albumin concentration in milligrams by creatinine concentration in grams.

Normal: ACR <30 mg/g, normal to mildly increased albuminuria.

Microalbuminuria: ACR 30-<300 mg/g, moderately increased albuminuria.

Macroalbuminuria: ACR >300 mg/g, severely increased albuminuria.

2.11 How diabetes affects renal function: Markers of renal damage (one or more) include Albuminuria (AER ≥30 mg/24 hours; ACR ≥30 mg/g [≥3 mg/mmol]), Urine sediment abnormalities, Electrolyte and other abnormalities due to tubular disorders, Abnormalities detected by histology, structural abnormalities detected by imaging [36].

2.12 Prognosis: DM is associated with increased atherosclerotic cardiovascular disease (ASCVD) and treating blood pressure, statin use, regular exercise, and smoking cessation are of great importance in ameliorating risk. The overall excess mortality in those with T2DM is around 15% higher but varies widely. The prevalence of vision-threatening diabetic retinopathy in the United States is about 4.4% among adults with diabetes, while it is 1% for end-stage renal disease. Today, with pharmacotherapy for hyperglycemia, as well as lowering LDL cholesterol and managing blood pressure with ACE/ARB therapy, with other antihypertensive medications and aspirin in secondary prevention, vascular complications can be managed adequately, resulting in a reduction in morbidity and mortality.

2.13 Worldwide situation of renal dysfunction by diabetes: The rising burden of type 2 diabetes is a major concern in healthcare worldwide. Over 1 million deaths per year can be attributed to diabetes alone, making it the ninth leading cause of mortality [37]. Global prevalence of type 2 diabetes is projected to increase to 7079 individuals per 100,000 by 2030 4, reflecting a continued rise across all regions of the world. Diabetes caused the majority of new cases and patients with CKD in all regions. Diabetes type 2 became the second leading cause of CKD and CKD-related death and the third leading cause of CKD-related DALYs in

2019. Type 2 diabetes–related CKD accounted for most of the CKD-DM disease burden. There were 2.62 million incident cases, 134.58 million patients, 405.99 thousand deaths, and 13.09 million disability-adjusted life-years (DALYs) of CKD-DM worldwide in 2019 [38].

Chapter 3: Literature review

3.1 Introduction

The objective of this literature review is to provide context for the research publications linked to the topic of this study. Endometriosis is a common condition among women all over the world.

It can be difficult to diagnose and carries several complications. As an added note, the following academic publications serve as secondary references and provide recommendations for the methods used in the research. These sources also helped with the development of data-gathering strategies, the selection of focus groups, and the formulation of questionnaire questions. Also, the research papers increased my comprehension of the topic of this thesis. Each paper's summary review is provided below:

The article **"Evaluation of kidney function and risk factors of retinopathy in Type 2 diabetes mellitus people in South Africa" 2017** is a study done by F.A. Ganjifrockwala et al. Diabetic retinopathy (DR) is a disease of the retina and an important microvascular complication of diabetes, frequently causing blindness in adults. The study aims to evaluate kidney function and risk factors for the development of retinopathy in Type 2 diabetes mellitus (DM) patients. A total of 140 participants (54 Type 2 DM without retinopathy, 44 with DR, and 42 with normal, healthy controls) consented to participate in the study. Fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), lipid profile, and renal function tests were measured using routine laboratory methods. A significant increase in FPG, HbA1c, serum triglycerides (TG), serum urea, urine albumin, the urine albumin/creatinine ratio (UACR), and, a significant decrease in high-density lipoprotein cholesterol (HDL-C) was observed in DR patients, compared to controls. In multivariate logistic analysis, FPG, insulin treatment, and UACR were the risk factors found to be significantly associated with the presence of retinopathy. A mild alteration in renal function was observed in DR patients and UACR is found to be an important risk factor and can be a valuable marker for predicting DR.

The article titled **"Assessment of kidney function and associated risk factors among type 2 diabetic patients in United Arab Emirates in 2019"** in this study diabetic patients are required for continuous monitoring programs hence continuous assessment of kidney function parameters is crucial. So, we aimed to determine the prevalence of Chronic Kidney Disease (CKD) and abnormal renal parameters, with poorly controlled type 2 diabetes mellitus patients

Materials and methods: A cross-sectional study was carried out at a private health care center. A total of 300 diabetic patients aged 18 years and above attended the clinic from February 2018 to Dec 2018 were included. Socio-demographic, clinical, and laboratory data were obtained from the medical records of patients. Statistical analysis was carried out using (SPSS, version 23). Out of the 300 diabetes patients recruited 42% of patients with type 2 diabetes had abnormal Creatinine Serum levels and 22.3% had abnormal glomerular filtration rate (GFR). Abnormal albumin urine levels were found in 28.3% and 11.3% had abnormal creatinine in urine. Abnormal Albumin: Creatinine Ratios (Alb/Cr) were found in 23%. Of the total, 77% (n ¼ 231) had normal Alb: Cr Ratio, 20% had a risk of nephropathy and 9% had nephropathy. The current study revealed a high prevalence of abnormal renal parameters in patients with type 2 diabetes Mellitus. This necessitates the need for early and universal screening of renal functions. There is also an urgent demand for measures that target tight glycaemic, Vitamin D levels and lifestyle modifications are also required for all diabetic patients to achieve the target value of HbA1C≤ 7.

The article titled **"Liraglutide as Add-on to Oral Antidiabetic Agents or Insulin in Routine Practice of Patients with Type 2 Diabetes"** in 2014 a retrospective study from 3 outpatient clinics in Copenhagen, Denmark, (n = 534) initiating treatment with liraglutide. In 149 patients liraglutide was add-on to oral antidiabetic agents. The results show baseline insulin dose of 83 ± 59 U/day was reduced by 28 ± 36 U/day. Insulin therapy could be stopped in 19% of these patients. It concluded that effects on HbA1c and weight of liraglutide as add-on to oral antidiabetic agents were not different from results previously published in randomised trials. Adding liraglutide to existing insulin regimens is an attractive treatment strategy in obese type 2 diabetic patients.

"Active Smoking and the Risk of Type 2 Diabetes A Systematic Review and Meta-analysis" in 2007, yielded 25 prospective cohort studies (N=1.2 million participants) that reported 45 844 incident cases of diabetes during a study follow-up period ranging from 5 to 30 years. Of the 25 studies, 24 reported adjusted RRs greater than 1 (range for all studies, 0.82-3.74). The pooled adjusted RR was 1.44 (95% confidence interval [CI], 1.31-1.58). Results were consistent and statistically significant in all subgroups. The risk of diabetes was greater for heavy smokers (20 cigarettes/ day; RR, 1.61; 95% CI, 1.43-1.80) than for lighter smokers (RR,1.29; 95% CI, 1.13- 1.48) and lower for former smokers (RR, 1.23; 95% CI, 1.14-1.33) compared with active smokers, consistent with a dose-response phenomenon. It concluded that active smoking is associated with an increased risk of type 2 diabetes.

Authors in the article **"Epidemiology of Type 2 diabetes - Global burden of disease and forecasted trends"** in 2020 analyze the global epidemiology of type 2 diabetes- the incidence, prevalence, and burden of suffering of diabetes mellitus. Based on epidemiological data from the Global Burden of Disease (GBD) current dataset from the Institute of Health Metrics, Seattle. Global and regional trends from 1990 to 2017 of type 2 diabetes for all ages were compiled. Forecast estimates were obtained using the SPSS Time Series Modeler. In 2017, approximately 462 million individuals were affected by type 2 diabetes corresponding to 6.28% of the world's population (4.4% of those aged 15-49 years, 15% of those aged 50-69, and 22% of those aged 70+), or a prevalence rate of 6059 cases per 100,000. Over 1 million deaths per year can be attributed to diabetes alone, making it the ninth leading cause of mortality. The burden of diabetes mellitus is rising globally, and at a much faster rate in developed regions, such as Western Europe. The gender distribution is equal, and the incidence peaks at around 55 years of age. Global prevalence of type 2 diabetes is projected to increase to 7079 individuals per 100,000 by 2030, reflecting a continued rise across all regions of the world. There are concerning trends of rising prevalence in lower-income countries.

In the article **"Global, Regional, and National Burden of Diabetes-Related Chronic Kidney Disease From 1990 to 2019"** Yujiao Deng et al derived data from the GBD 2019 study, including four measures and age-standardized rates (ASRs). Estimated annual percentage changes and 95% CIs were calculated to evaluate the variation trend of ASRs. The results showed that ASRs for type 2 diabetes–related CKD increased over 30 years. Asia and Middle socio-demographic index (SDI) quintile always carried the heaviest burden of CKD-DM. Diabetes type 2 became the second leading cause of CKD and CKD-related death and the third leading cause of CKD-related DALYs in 2019. Type 2 diabetes–related CKD accounted for most of the CKD-DM disease burden. There were 2.62 million incident cases, 134.58 million patients, 405.99 thousand deaths, and 13.09 million disability-adjusted life-years (DALYs) of CKD-DM worldwide in 2019. Age-standardized incidence (ASIR) and prevalence rate (ASPR) of type 1 diabetes–related CKD increased, whereas age-standardized death rate (ASDR) and DALY rate decreased for females and increased for males. In high SDI quintile, ASIR and ASPR of type 1 diabetes–related CKD remained the highest, with the slowest increase, whereas the ASDR and age-standardized DALY rate remained the lowest there. In high SDI quintile, ASIR of type 2 diabetes–related CKD was the highest, with the lowest increasing rate. In addition, type 2 diabetes–related CKD occurred most in people aged 80-plus years worldwide.

The main age of type 2 diabetes–related CKD patients was 55–64 years in Asia and Africa. The prevalence, mortality, and DALY rate of type 2 diabetes–related CKD increased with age. As for incidence, there was a peak at 80 years, and after age of 80, the incidence declined. CKD-DM-related anemia was mainly in mild to moderate grade.

Author Kristina I. Rother in the article **"Diabetes Treatment — Bridging the Divide"** in 2007 clearly stated that the effectors of beta-cell failure are similar in the two main types of diabetes, regardless of the inciting event. Glucotoxicity and lipotoxicity induce oxidative stress and up-regulate inflammatory cytokines, thereby leading to cellular damage and promoting apoptosis in all beta cells, regardless of the type of diabetes. Abnormal islet innervation has been described as another common contributing element in animal models of type 1 and type 2 diabetes. Thus, alleviating beta-cell stress opens the door to therapeutic approaches that would probably be useful in all types of diabetes. none of the currently available medications are successful as long-term monotherapy, and none of them have effectively halted the continuous decline in beta-cell mass. Although the findings regarding anakinra break new ground by demonstrating that inhibition of cytokine function can restore insulin secretion, the ultimate goal is the improvement of blood-glucose control without the need for triple- and quadruple-combination therapies, as well as the prevention of beta-cell death.\

In the article **"Incidence of type 2 diabetes using proposed HbA1c diagnostic criteria in the European prospective investigation of cancer-nor folk cohort: implications for preventive strategies"** by Parinya Chamnan et al, evaluate the incidence and relative risk of type 2 diabetes defined by the newly proposed HbA(1c) diagnostic criteria in groups categorized by different baseline HbA(1c) levels. Data used from the European Prospective Investigation of Cancer (EPIC)-Norfolk cohort with repeat HbA(1c) measurements, They also examined the incidence and corresponding odds ratios (ORs) by different levels of baseline HbA(1c). Results showed that the overall prevalence of diabetes was 4.7%; 41% of prevalent cases were previously undiagnosed. Among 5,735 participants without diabetes at baseline (identified clinically or using HbA(1c) criteria, or both), 72 developed diabetes over 3 years (1.3% [95% CI 1.0-1.5]), of which 49% were identified using the HbA(1c) criteria. In 6% of the total population, the baseline HbA(1c) was 6.0-6.4%; 36% of incident cases arose in this group. The incidence of diabetes in this

group was 15 times higher than in those with a baseline HbA(1c) of <5.0% (OR 15.5 [95% CI 7.2-33.3]).

In 2010, R A DeFronzo in the article "**Insulin resistance, lipotoxicity, type 2 diabetes and atherosclerosis: the missing links."** stated that insulin resistance is a hallmark of type 2 diabetes mellitus and is associated with a metabolic and cardiovascular cluster of disorders (dyslipidaemia, hypertension, obesity [especially visceral], glucose intolerance, endothelial dysfunction), each of which is an independent risk factor for cardiovascular disease (CVD). Multiple prospective studies have documented an association between insulin resistance and accelerated CVD in patients with type 2 diabetes, as well as in non-diabetic individuals. The molecular causes of insulin resistance, i.e. impaired insulin signalling through the phosphoinositol-3 kinase pathway with intact signalling through the mitogen-activated protein kinase pathway, are responsible for the impairment in insulin-stimulated glucose metabolism and contribute to the accelerated rate of CVD in type 2 diabetes patients. The current epidemic of diabetes is being driven by the obesity epidemic, which represents a state of tissue fat overload. Accumulation of toxic lipid metabolites (fatty acyl CoA, diacylglycerol, ceramide) in muscle, liver, adipocytes, beta cells and arterial tissues contributes to insulin resistance, beta cell dysfunction and accelerated atherosclerosis, respectively, in type 2 diabetes. Treatment with thiazolidinediones mobilises fat out of tissues, leading to enhanced insulin sensitivity, improved beta cell function and decreased atherogenesis. Insulin resistance and lipotoxicity represent the missing links (beyond the classical cardiovascular risk factors) that help explain the accelerated rate of CVD in type 2 diabetic patients.

In the study "**Correlation of Diabetes Related Factors with Vitamin D and Immunological Parameters in T2DM Kashmiri Population**" by Najeebul Tarfeen et al, the role of inflammatory biomarkers and vitamin D in Type 2 diabetes mellitus (T2DM) and their correlation with diabetes related factors (HbA1c, FPG, and insulin) was analysed. In this study, Kashmiri patients with T2DM and healthy individuals were considered as cases (n = 100) and controls (n = 100) respectively. Blood samples from both groups were collected, inflammatory biomarkers (TNF-α, CRP), as well as serum vitamin D levels, were estimated by ELISA. From our results it was revealed that patients with T2DM had significantly lower serum vitamin D levels than control groups (p<0.05). Pro-inflammatory cytokine levels, including TNF-α and CRP, were seen to be elevated reaching a level of statistical significance (p<0.05). On correlating the HbA1c, FPG and insulin with TNF-α, CRP and vitamin D, significant positive

correlation (p<0.05) was found between TNF-α and CRP with HbA1c and FPG in patients, non-significant positive correlation (p>0.05) was observed between insulin with TNF-α, and vitamin D and weak negative correlation with CRP in case study group. On correlating the impact of vitamin D on HbA1c and FPG levels, non-significant weak negative correlation was observed in patient group than controls, indicating that patients with lower vitamin D levels have higher HbA1c, showing that lower vitamin D have some role in etiology of T2DM.

In the review article " Epidemic obesity and type 2 diabetes in Asia" by Kun Ho Yoon et al it was observed that the proportions of people with type 2 diabetes and obesity have increased throughout Asia, and the rate of increase shows no sign of slowing. People in Asia tend to develop diabetes with a lesser degree of obesity at younger ages, suffer longer with complications of diabetes, and die sooner than people in other regions. Childhood obesity has increased substantially and the prevalence of type 2 diabetes has now reached epidemic levels in Asia. The health consequences of this epidemic threaten to overwhelm health-care systems in the region. Urgent action is needed, and advocacy for lifestyle changes is the first step. Countries should review and implement interventions, and take a comprehensive and integrated public-health approach. At the level of primary prevention, such programmes can be linked to other non-communicable disease prevention programmes that target lifestyle-related issues.

Paolo Boffetta et al in the article "**Body Mass Index and Diabetes in Asia: A Cross-Sectional Pooled Analysis of 900,000 Individuals in the Asia Cohort Consortium"** in 2011, evaluate the association between baseline body mass index (BMI, measured as weight in kg divided by the square of height in m) and self-reported diabetes status in over 900,000 individuals recruited in 18 cohorts from Bangladesh, China, India, Japan, Korea, Singapore and Taiwan. Logistic regression models were fitted to calculate cohort-specific odds ratios (OR) of diabetes for categories of increasing BMI, after adjustment for potential confounding factors. OR were pooled across cohorts using a random-effects meta-analysis. The sex- and age-adjusted prevalence of diabetes was 4.3% in the overall population, ranging from 0.5% to 8.2% across participating cohorts. Using the category 22.5–24.9 Kg/m^2 as reference, the OR for diabetes spanned from 0.58 (95% confidence interval [CI] 0.31, 0.76) for BMI lower than 15.0 kg/m^2 to 2.23 (95% CI 1.86, 2.67) for BMI higher than 34.9 kg/m^2. The positive association between BMI and diabetes prevalence was present in all cohorts and in all subgroups of the study population, although the association was stronger in individuals below age 50 at baseline (p-value of interaction<0.001), in cohorts from India and Bangladesh (p<0.001), in individuals

with low education (p-value 0.02), and in smokers (p-value 0.03); no differences were observed by gender, urban residence, or alcohol drinking.

The article **"Global estimates of the prevalence of diabetes for 2010 and 2030"** by J E Shaw et al in 2010 estimated the number of people worldwide with diabetes for the years 2010 and 2030. Studies from 91 countries were used to calculate age- and sex-specific diabetes prevalences, which were applied to national population estimates, to determine national diabetes prevalences for all 216 countries for 2010 and 2030. Studies were identified using Medline, and contact with all national and regional International Diabetes Federation offices. Studies were included if diabetes prevalence was assessed using a population-based methodology, and was based on World Health Organization or American Diabetes Association diagnostic criteria for at least three separate age-groups within the 20-79 year range. Self-report or registry data were used if blood glucose assessment was not available. Results the world prevalence of diabetes among adults (aged 20-79 years) will be 6.4%, affecting 285 million adults, in 2010, and will increase to 7.7%, and 439 million adults by 2030. Between 2010 and 2030, there will be a 69% increase in numbers of adults with diabetes in developing countries and a 20% increase in developed countries.

Chapter 4: Methodology

4.1 Introduction

"Research methodology" refers to the process of collecting data, evaluating it, and drawing conclusions about the subject being studied. A research technique is an essential component of any study plan. Developing and refining a methodology is crucial in achieving a study's objectives.

A valid and reliable research technique ensures that the conclusions drawn are based on solid scientific evidence. Furthermore, the specific details of the plan help researchers stay on track, resulting in a more efficient and less overwhelming process overall. The methodology used by a researcher provides insight into the thought process and procedures that led to the study's findings

4.2 Aim of the study

- To assess the renal function that leads to CKD in type to diabetic patients.

4.3 Research Methodology

A cross-sectional methodology to analyze the data, which is a form of descriptive study. For a cross-sectional study, a sizable sample of participants is collected at a specific time and location. These studies are non-invasive, gathering information without any attempt at modifying observable variables.

4.4 Subject, material, and methods

A cross-sectional descriptive study design was chosen for data collection; data was collected from clinical laboratory test reports from A tertiary hospital in Bangladesh. A total of 210 patients enrolled in this study. The inclusion criteria of the study were male and female patients from 30-90 years, diagnosed with type 2 diabetes mellitus, having laboratory tests assessing kidney function such as Modification of Diet in Renal Disease (MDRD). The exclusion criteria were male and female patients with type 1 diabetes, patients with gestational diabetes or pregnant females, non-diabetic patients and patients not having recent data specifically laboratory kidney function data. The duration of the study was from July 2023 to September 2024. Ethical approval for the study was secured from the BRAC University Institutional Review Board (IRB) under the IRB number BRACUIRB_220240006, and all the participants gave their informed consent following the Declaration of Helsinki [38].

4.5 Statistical analysis

The data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 26. Qualitative variables were summarized using frequencies and percentages. The Chi-square and Fischer Exact tests were used to compare differences in proportions of qualitative variables. A p-value < 0.05 was chosen as the criteria to make decisions regarding statistical significance.

Chapter 5: Results

Data from patient interviews was summarized and analyzed. The goal of this data analysis is to identify the prevalence of certain features among patients and to compare these frequencies among patients with different factors.

The total number of participants was 210 diagnosed with type 2 diabetes mellitus and patients with type 1 diabetes, patients with gestational diabetes or pregnant females, non-diabetic patients and patients not having recent data specifically laboratory kidney function data were excluded from the study.

5.1 Distribution of T2D Patients Based on Socio-Demographic Factor:

5.1.1. Distribution of T2D Patients Based on Gender:

Table 1: Frequency Table Distribution of Age Among T2D patients

Age	Frequency	Percent	Valid Percent	Cumulative Percent
30-40	47	22.4	22.4	22.4
41-50	41	19.5	19.5	41.9
51-60	54	25.7	25.7	67.6
61-70	45	21.4	21.4	89.0
71-80	16	7.6	7.6	96.7
81-90	7	3.3	3.3	100.0
Total	210	100.0	100.0	

Table 1 presents the distribution of a sample population across different age groups. The age group with the highest frequency is 51-60 years, comprising 54 individuals, which represents 25.7% of the total sample. The 30-40 age group follows with 47 individuals (22.4%), and the 61-70 age group includes 45 individuals (21.4%). The 41-50 age group contains 41 individuals (19.5%). The 71-80 and 81-90 age groups have lower frequencies, with 16 (7.6%) and 7 (3.3%) individuals, respectively.

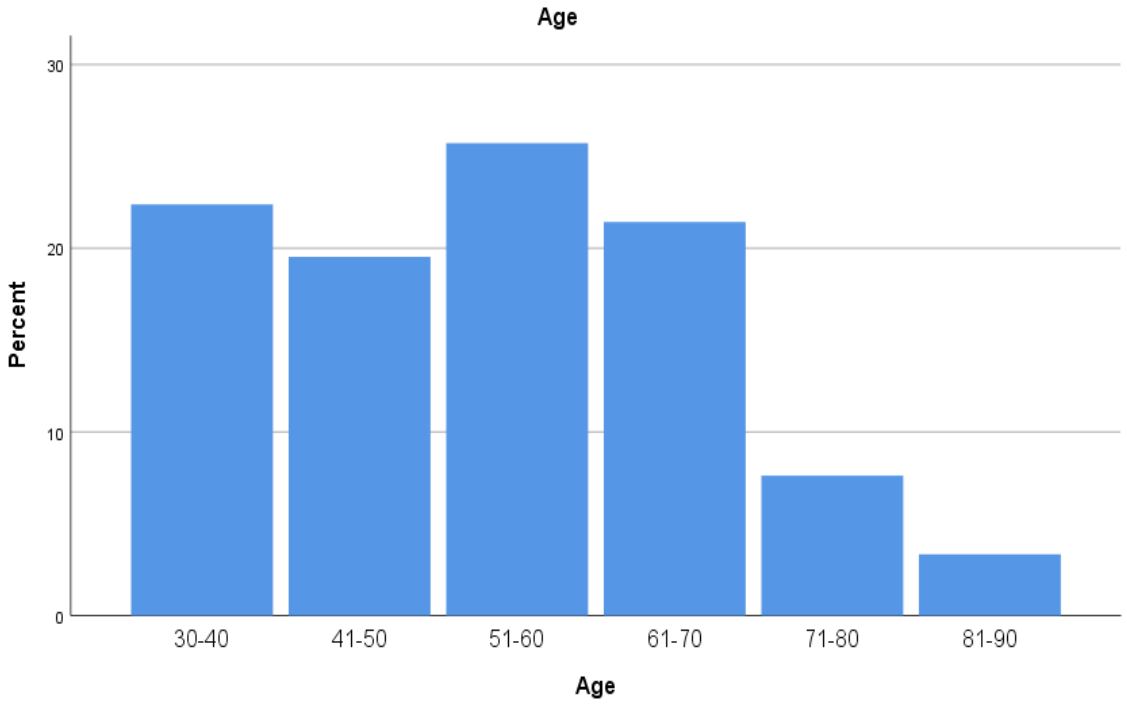

Figure 4 : Distribution of T2D Patients Based on Age.

5.1.2 Distribution of T2D Patients Based on Gender:

Table 2: Frequency Table Distribution of Gender Among T2D patients

Gander	Frequency	Percent	Valid Percent	Cumulative Percent
Male	136	64.8	64.8	64.8
Female	74	35.2	35.2	100.0
Total	210	100.0	100.0	

Table 2 illustrates the gender distribution within a sample population of 210 individuals. Males constitute the majority, with 136 individuals, representing 64.8% of the total sample. Females, on the other hand, comprise 74 individuals, accounting for 35.2% of the sample.

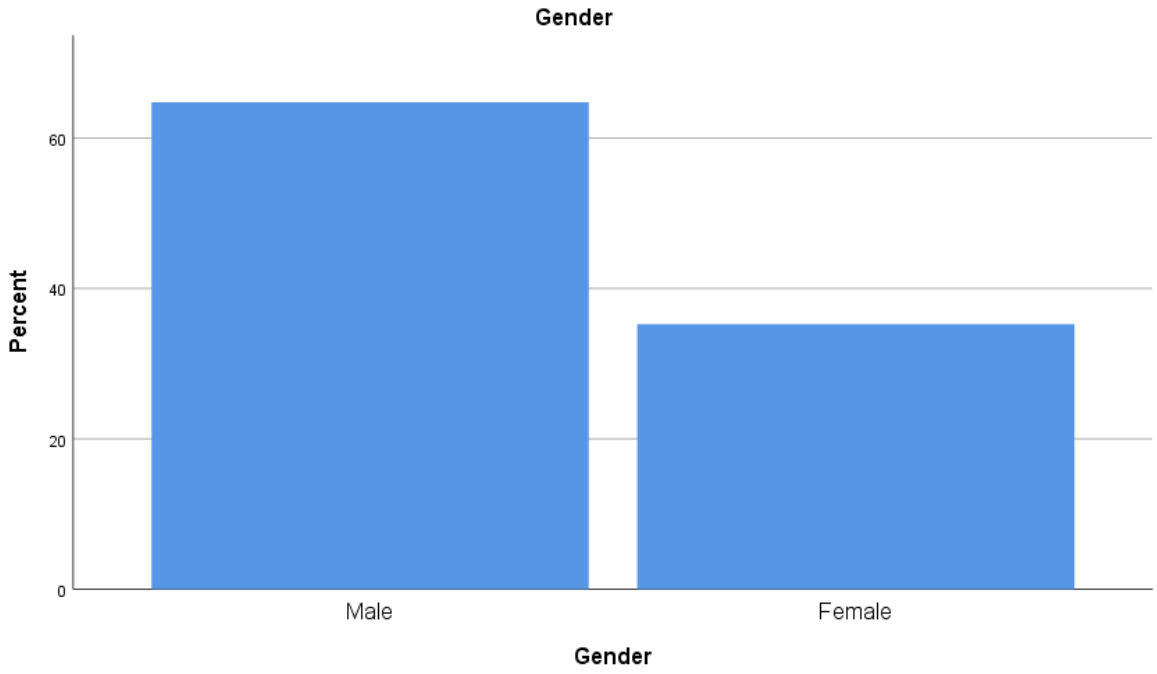

Figure 5: Distribution of T2D Patients Based on Gender

5.2 Distribution of T2D Patients Based on Renal Function

5.2.1 Distribution of T2D Patients Based on Urea Serum

Table 3: Frequency Table Distribution of Urea Serum Among T2D patients

Urea Serum	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	127	60.5	60.5	60.5
Abnormal	83	39.5	39.5	100.0
Total	210	100.0	100.0	

Table 3 presents the distribution of serum urea levels among a sample of 210 individuals. Out of the total participants, 127 individuals (60.5%) had normal serum urea levels, while 83 individuals (39.5%) exhibited abnormal levels.

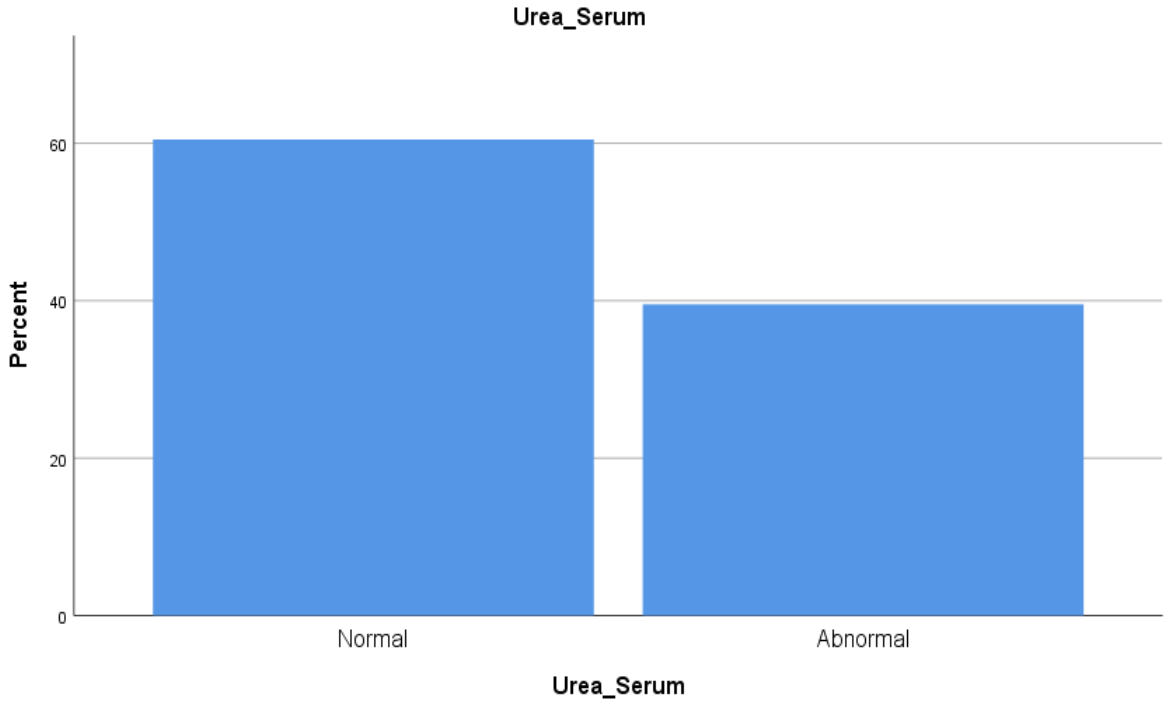

Figure 6: Distribution of T2D Patients Based on Urea Serum

5.2.2 Distribution of T2D Patients Based on Uric Acid Serum

Table 4: Frequency Table Distribution of Uric Acid Serum Among T2D patients

Uric acid serum	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	130	61.9	61.9	61.9
Abnormal	80	38.1	38.1	100.0
Total	210	100.0	100.0	

Table 4 provides a summary of serum uric acid levels in a group of 210 individuals. Among the participants, 130 individuals (61.9%) have normal serum uric acid levels, while 80 individuals (38.1%) exhibit abnormal levels.

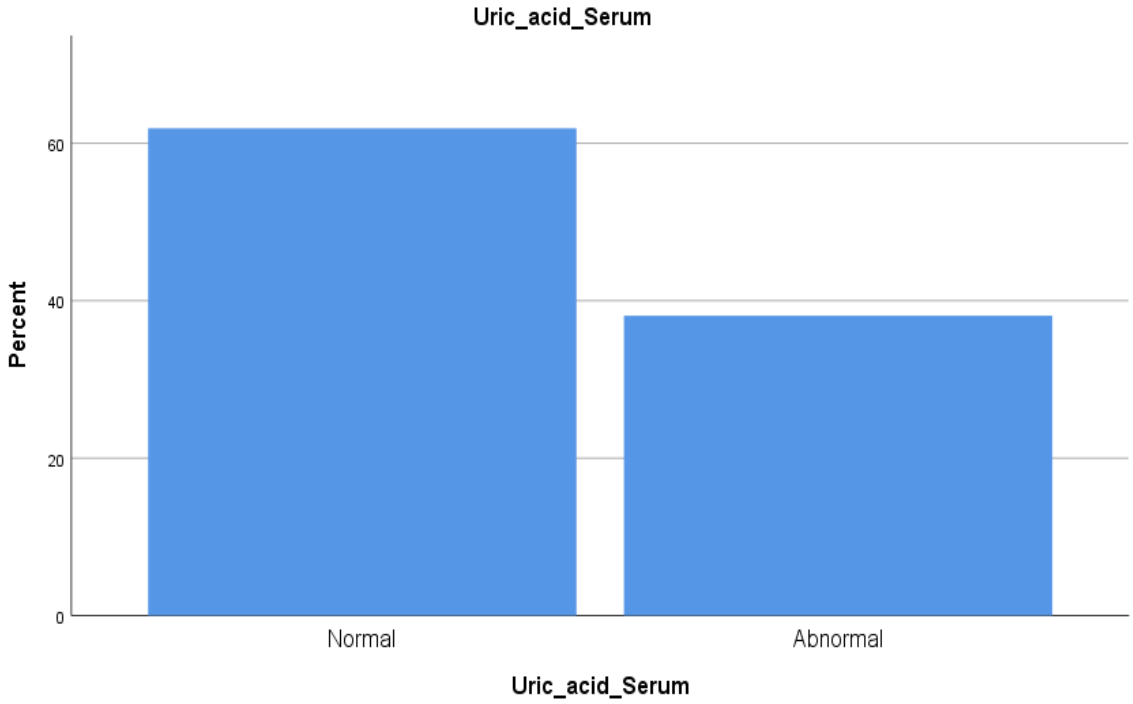

Figure 7: Distribution of T2D Patients Based on Uric Acid Serum

5.2.3 Distribution of T2D Patients Based on Total Calcium Serum

Table 5: Frequency Table Distribution of Total Calcium Serum Among T2D patients

Total calcium serum	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	190	90.5	90.5	90.5
Abnormal	20	9.5	9.5	100.0
Total	210	100.0	100.0	

Table 5 outlines the distribution of total calcium serum levels in a sample of 210 individuals. A substantial majority of participants, 190 individuals (90.5%), have normal total calcium serum levels. In contrast, only 20 individuals (9.5%) exhibit abnormal levels.

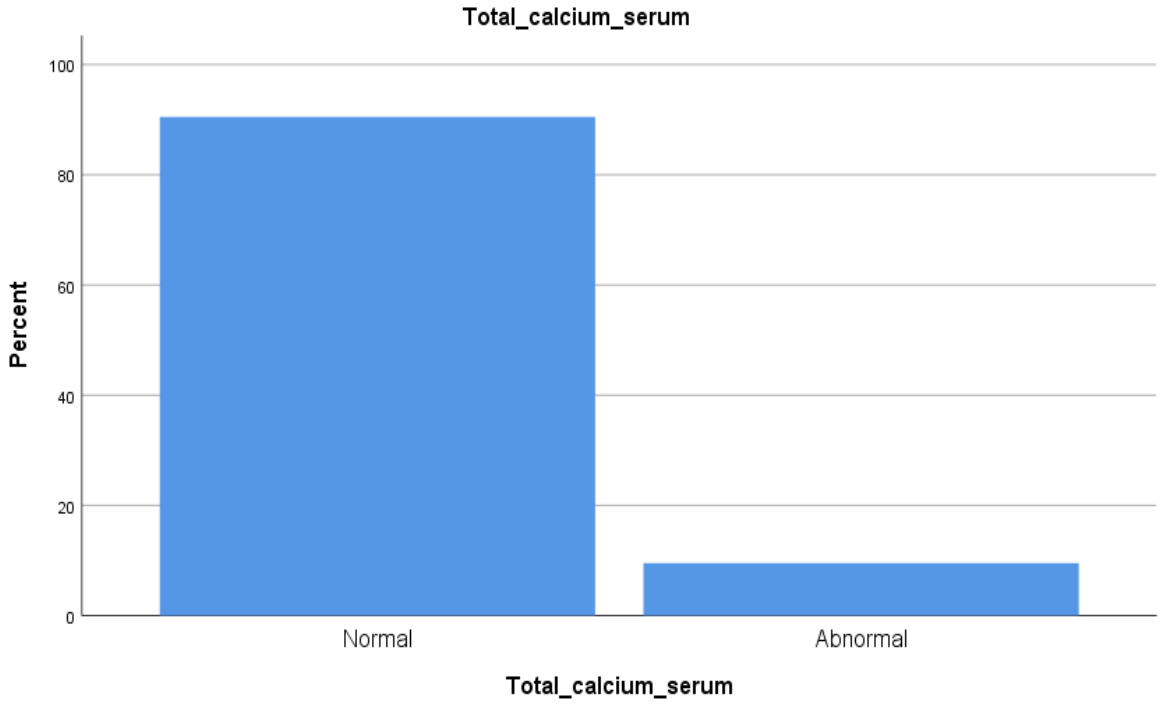

Figure 8: Distribution of T2D Patients Based on Total Calcium Serum

5.2.4 Distribution of T2D Patients Based on Albumin Serum

Table 6: Frequency Table Distribution of Albumin Serum Among T2D patients

Albumin Serum	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	193	91.9	91.9	91.9
Abnormal	17	8.1	8.1	100.0
Total	210	100.0	100.0	

Table 6 provides a summary of albumin serum levels among 210 individuals. The majority, 193 individuals (91.9%), have normal albumin serum levels, whereas 17 individuals (8.1%) have abnormal levels.

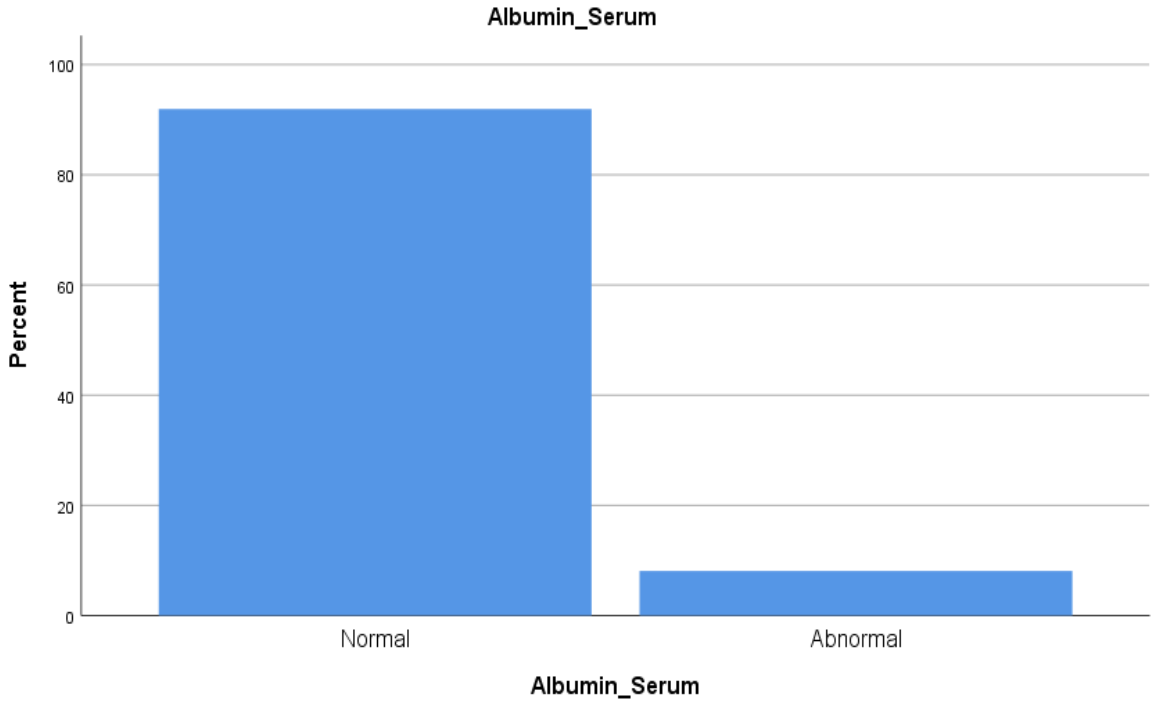

Figure 9: Distribution of T2D Patients Based on Albumin Serum

5.2.5 Distribution of T2D Patients Based on Inorganic Phosphorus Serum

Table 7: Frequency Table Distribution of Inorganic phosphorus serum Among T2D patients

Inorganic phosphorus serum	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	172	81.9	81.9	81.9
Abnormal	38	18.1	18.1	100.0
Total	210	100.0	100.0	

Table 7 summarizes the distribution of inorganic phosphorus serum levels in a sample of 210 individuals. Out of the total, 172 individuals (81.9%) have normal inorganic phosphorus levels, while 38 individuals (18.1%) exhibit abnormal levels.

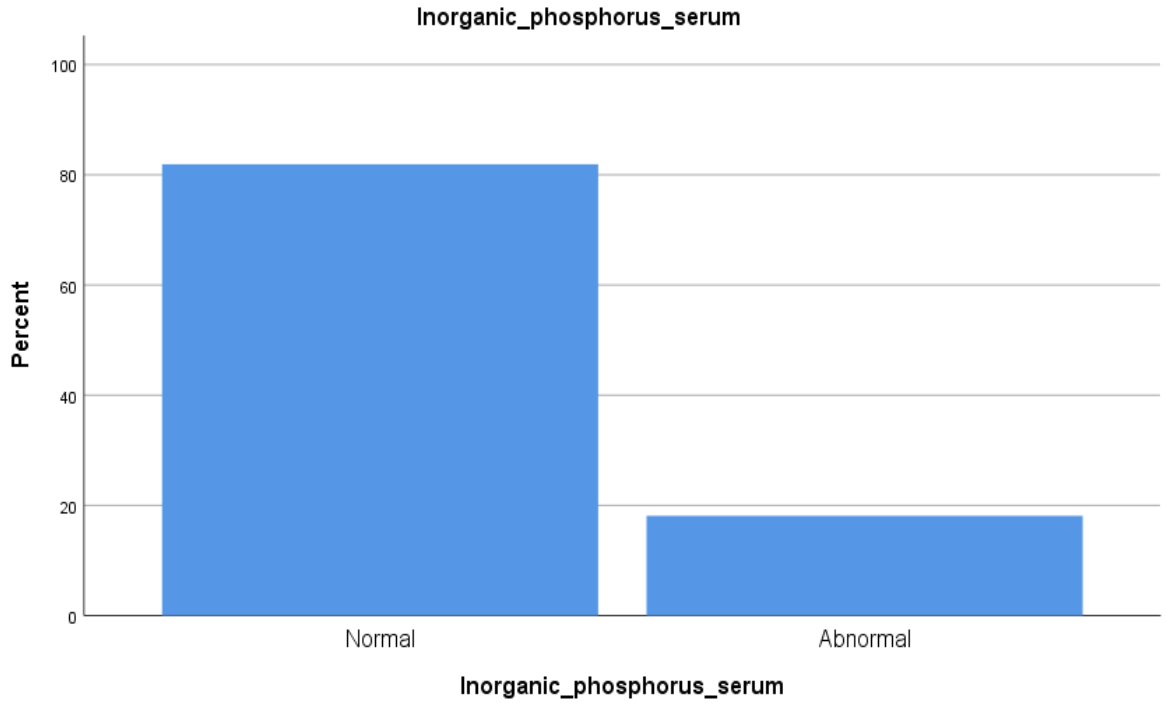

Figure 10: Distribution of T2D Patients Based on Inorganic phosphorus serum.

5.2.6 Distribution of T2D Patients Based on Sodium Plasma

Table 8: Frequency Table Distribution of Sodium plasma Among T2D patients

Sodium plasma	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	161	76.7	76.7	76.7
Abnormal	49	23.3	23.3	100.0
Total	210	100.0	100.0	

Table 8 provides a summary of sodium plasma levels in a sample of 210 individuals. The majority, 161 individuals (76.7%), have normal sodium plasma levels, while 49 individuals (23.3%) have abnormal levels.

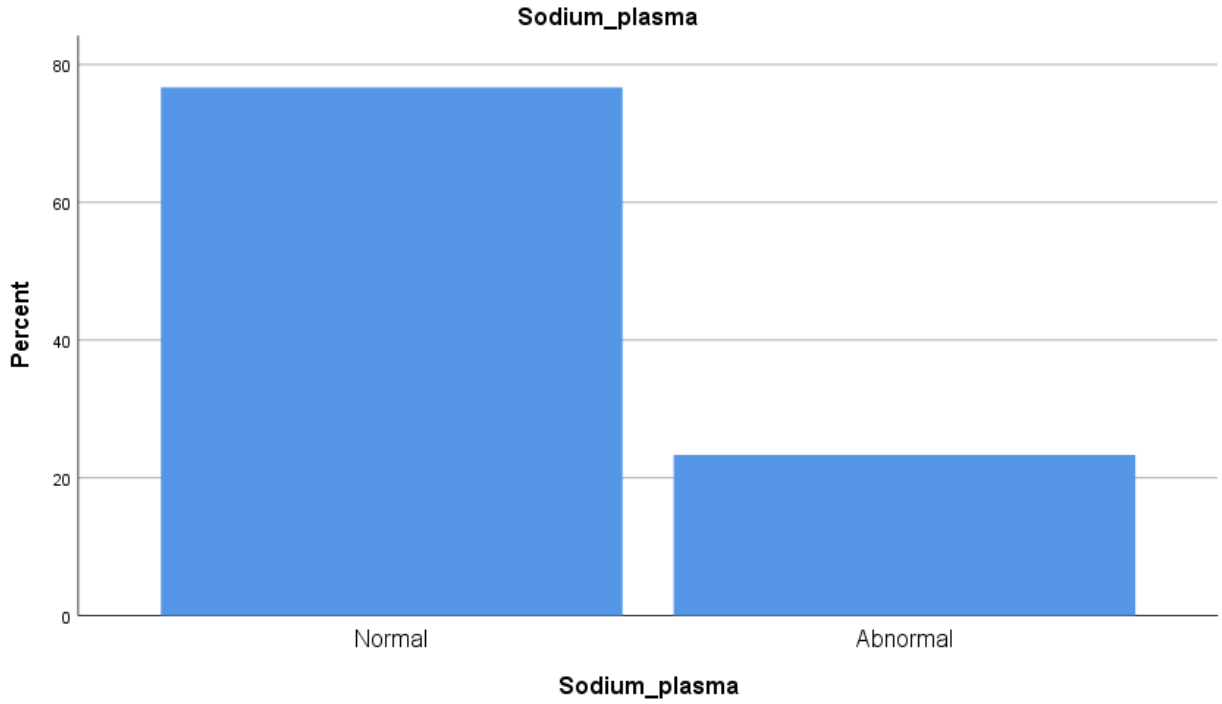

Figure 11: Distribution of T2D Patients Based on Sodium plasma

5.2.7 Distribution of T2D Patients Based on Potassium Plasma

Table 9: Frequency Table Distribution of Potassium Plasma Among T2D patients

Potassium plasma	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	165	78.6	78.6	78.6
Abnormal	45	21.4	21.4	100.0
Total	210	100.0	100.0	

The table 9 presents the distribution of potassium plasma levels in a sample of 210 individuals. Among these participants, 165 individuals (78.6%) have normal potassium plasma levels, while 45 individuals (21.4%) exhibit abnormal levels.

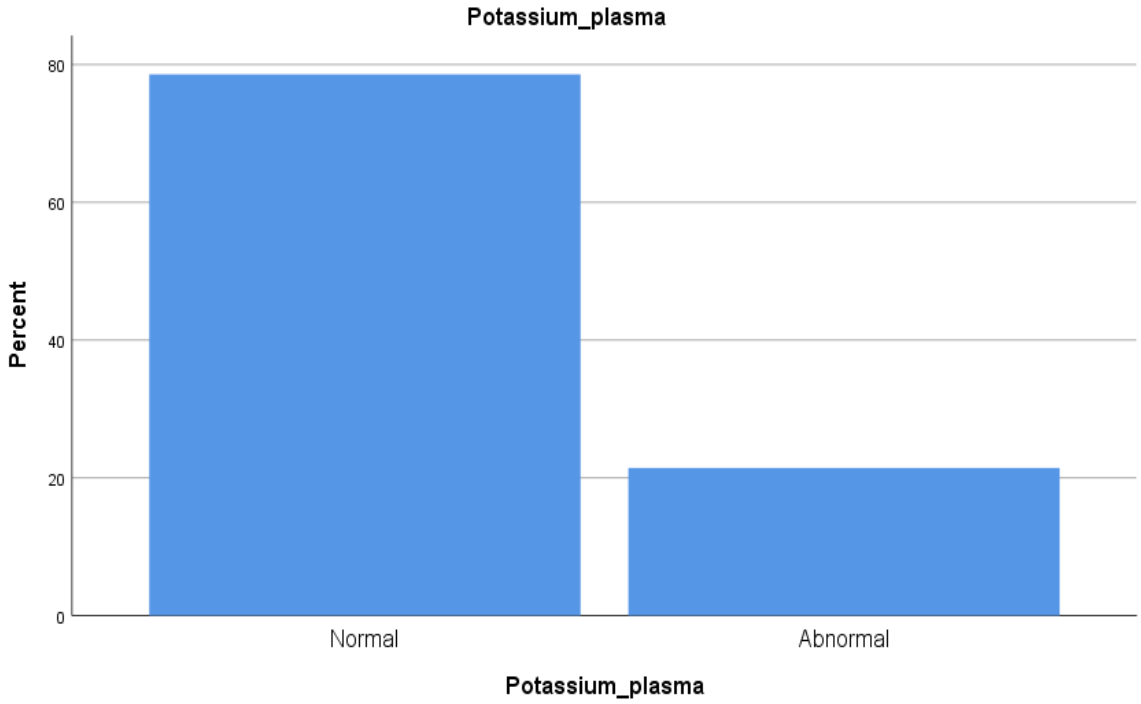

Figure 12: Distribution of T2D Patients Based on Potassium Plasma

5.2.8 Distribution of T2D Patients Based on Chloride Plasma

Table 10: Frequency Table Distribution of Chloride Plasma Among T2D patients

Chloride plasma	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	181	86.2	86.2	86.2
Abnormal	29	13.8	13.8	100.0
Total	210	100.0	100.0	

Table 10 summarizes chloride plasma levels in a sample of 210 individuals. A majority, 181 individuals (86.2%), have normal chloride plasma levels, while 29 individuals (13.8%) exhibit abnormal levels.

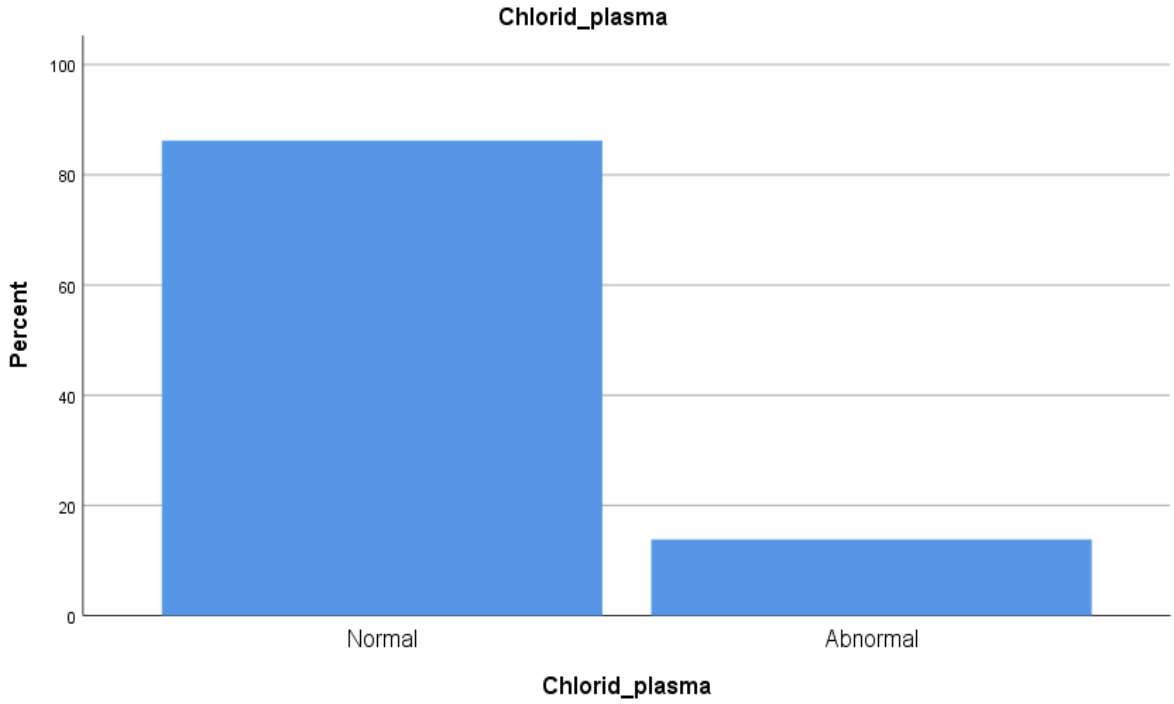

Figure 13: Distribution of T2D Patients Based on Chloride Plasma

5.2.9 Distribution of T2D Patients Based on Bicarbonates Plasma

Table 11: Frequency Table Distribution of Bicarbonates plasma Among T2D patients

Bicarbonates plasma	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	141	67.1	67.1	67.1
Abnormal	69	32.9	32.9	100.0
Total	210	100.0	100.0	

Table 11 provides a summary of bicarbonate plasma levels in a sample of 210 individuals. Among these participants, 141 individuals (67.1%) have normal bicarbonate plasma levels, while 69 individuals (32.9%) have abnormal levels.

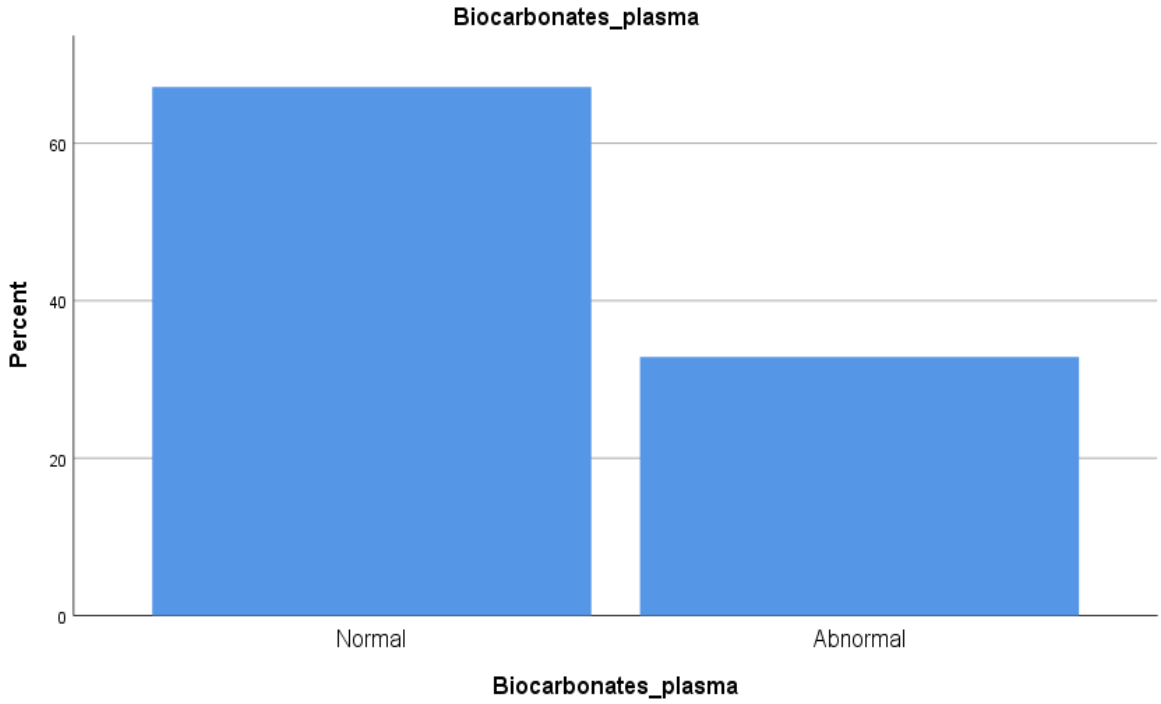

Figure 14: Distribution of T2D Patients Based on Bicarbonates plasma

5.2.10 Distribution of T2D Patients Based on Anion GAP

Table 12: Frequency Table Distribution of Anion GAP Among T2D patients

Anion GAP	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	173	82.4	82.4	82.4
Abnormal	37	17.6	17.6	100.0
Total	210	100.0	100.0	

Table 12 summarizes the anion gap levels in a sample of 210 individuals. The majority, 173 individuals (82.4%), have normal anion gap levels, while 37 individuals (17.6%) exhibit abnormal levels.

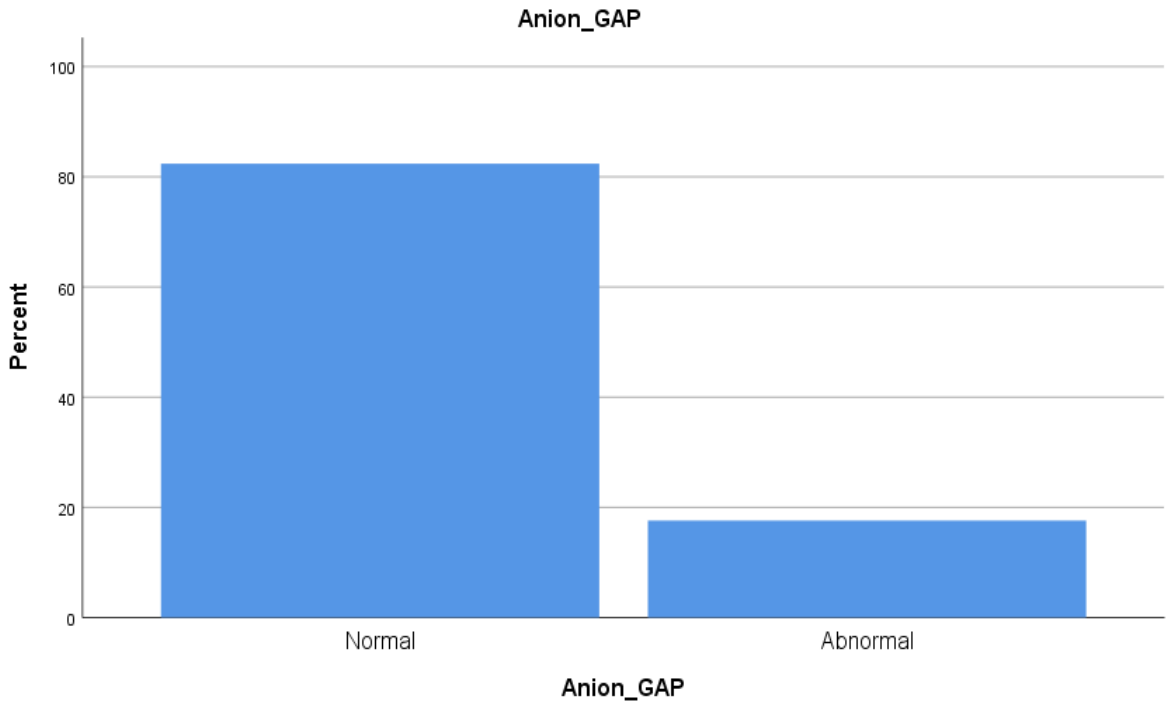

Figure 15: Distribution of T2D Patients Based on Anion GAP

5.2.11 Distribution of T2D Patients Based on Creatinine Serum

Table 13: Frequency Table Distribution of Creatinine Serum Among T2D patients

Creatinine Serum	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	111	52.9	52.9	52.9
Abnormal	99	47.1	47.1	100.0
Total	210	100.0	100.0	

Table 13 provides a summary of creatinine serum levels in a sample of 210 individuals. Of the total, 111 individuals (52.9%) have normal creatinine serum levels, while 99 individuals (47.1%) have abnormal levels

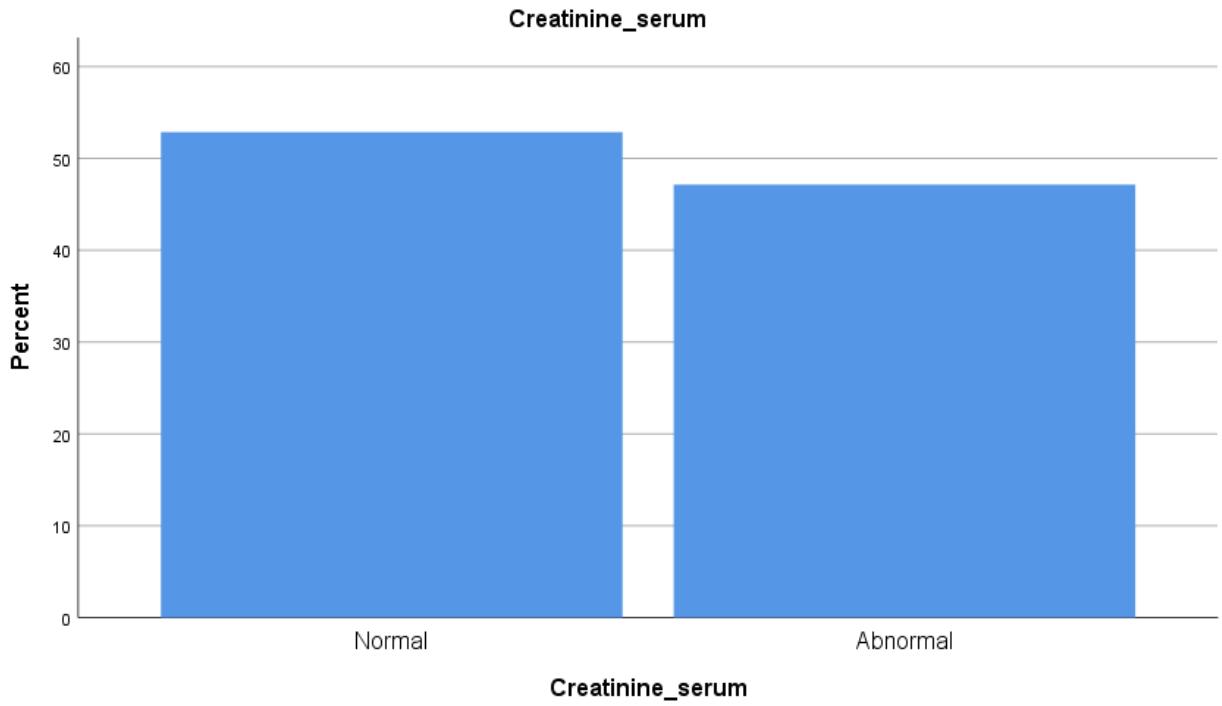

Figure 16: Distribution of T2D Patients Based on Creatinine Serum

5.2.12 Distribution of T2D Patients Based on eGFR

Table 14: ***Frequency Table Distribution of eGFR Among T2D patients***

eGFR	Frequency	Percent	Valid Percent	Cumulative Percent
Stage 1	50	23.8	23.8	23.8
Stage 2	48	22.9	22.9	46.7
Stage 3	55	26.2	26.2	72.9
Stage 4	26	12.4	12.4	85.2
Stage 5	31	14.8	14.8	100.0
Total	210	100.0	100.0	

The table categorizes the estimated Glomerular Filtration Rate (eGFR) levels into five stages for a sample of 210 individuals. The distribution is as follows: 50 individuals (23.8%) are classified in Stage 1, indicating normal kidney function, while 48 individuals (22.9%) are in Stage 2, showing mild reduction in kidney function. Stage 3, which represents moderate reduction, includes 55 individuals (26.2%). Stage 4, indicating severe reduction, comprises 26 individuals (12.4%), and Stage 5, which signifies end-stage kidney failure, includes 31 individuals (14.8%).

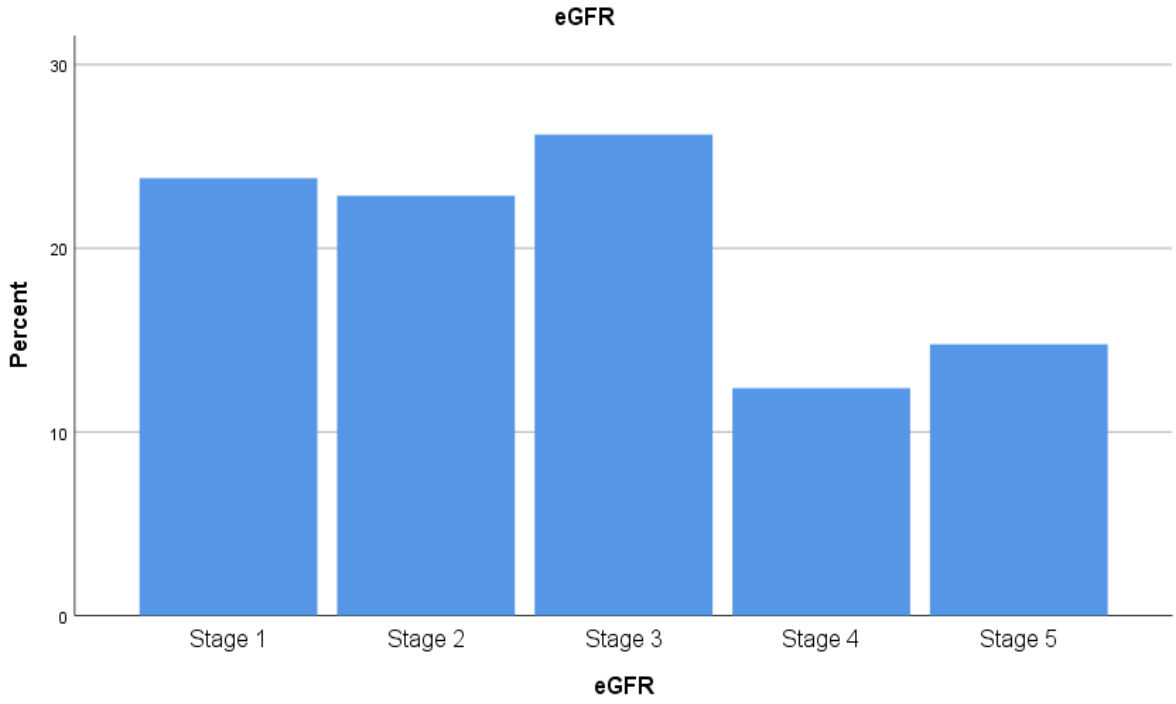

Figure 17: Distribution of T2D Patients Based on eGFR

5.3 Crosstab Analysis of participants' age with Gender

Table 15: Crosstab Analysis of participant's age with Gender

Gender		Age						P value
		30-40	41-50	51-60	61-70	71-80	81-90	0.04
Male	N	29	32	38	24	7	6	
	%	13.8	15.2	18.1	11.4	3.3	2.9%	
Female	N	18	9	16	21	9	1	
	%	8.6	4.3	7.6	10.0	4.3	0.5%	

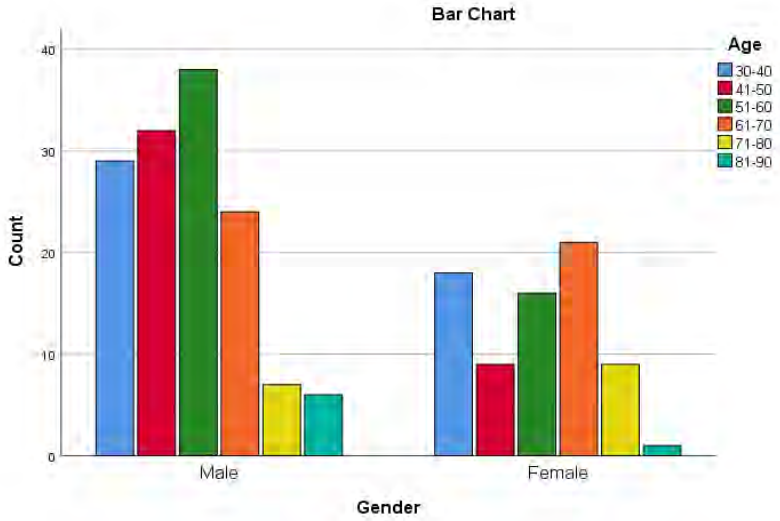

Figure 18: Crosstab Analysis of participants age with Gender

Table 15 represents the analysis of age distribution by gender revealing significant variations across different age groups, with a P value of 0.04 indicating statistical significance. Among males, the highest representation is in the 51-60 age group, accounting for 18.1% of the total, followed by the 41-50 age group at 15.2%, and the 30-40 age group at 13.8%. The numbers decline in older age groups, with 11.4% in the 61-70 age group, 3.3% in the 71-80 age group, and 2.9% in the 81-90 age group. In contrast, females show a different pattern, with the 61-70 age group having the highest representation at 10%, followed by the 30-40 age group at 8.6%, and the 51-60 age group at 7.6%. The 41-50 and 71-80 age groups show a lower representation at 4.3%, respectively. while the 81-90 age groups account for 0.5%. 5.4 Crosstab Analysis of Renal Function Parameters with Gender

Table 16: Crosstab analysis table of renal function parameters with gender

Parameters	Male N(%)	Female N(%)	P value
Urea Serum			0.02
Normal	90(42.9)	37(17.6)	
Abnormal	46(21.9)	37(17.6)	
Uric Acid Serum			NS
Normal	90(42.9)	40(19.0)	
Abnormal	46(21.9)	34(16.2)	
Total Calcium Serum			NS
Normal	125(59.0)	65(31.0)	
Abnormal	11(5.2)	9(4.3)	
Albumin Serum			NS
Normal	126(60.0)	67(31.9)	
Abnormal	10(4.8)	7(3.3)	
Inorganic Phosphorus Serum			NS
Normal	114(54.3)	58(27.6)	
Abnormal	22(10.5)	16(7.6)	
Sodium plasma			0.05
Normal	110(52.4)	51(24.3)	
Abnormal	26(12.4)	23(11.0)	
Potassium Plasma			NS
Normal	111(52.9)	54(25.7)	
Abnormal	25(11.9)	20(9.5)	
Chloride Plasma			NS
Normal	119(56.7)	62(29.5)	
Abnormal	17(8.1)	12(5.7)	
Bicarbonates plasma			0.001
Normal	102(48.6)	39(18.6)	
Abnormal	34(16.2)	35(16.7)	
Anion GAP			NS
Normal	112(53.3)	61(29.0)	

Abnormal	24(11.4)	13(6.2)	
Creatinine Serum			0.01
Normal	80(38.1)	31(14.8)	
Abnormal	56(26.7)	43(20.5)	

The table 15 presents a comparative analysis of various serum and plasma parameters between male and female individuals, including the distribution of normal and abnormal results for each parameter and the associated p-values indicating statistical significance. For urea serum levels, a significant difference is noted (p=0.02), with a higher percentage of males having abnormal levels compared to females. Uric acid serum levels show no significant difference (p=NS), with both genders having comparable proportions of normal and abnormal results. Total calcium serum levels also lack significant differences (p=NS), although males show a higher percentage of normal levels. Similarly, albumin serum-levels and inorganic phosphorus serum levels show no significant gender-based differences (p=NS). Sodium plasma levels approach significance (p=0.05), indicating a higher percentage of males with abnormal levels. Potassium plasma, chloride plasma, and anion gap levels do not show significant gender differences (p=NS). Bicarbonate plasma levels exhibit a significant gender difference (p=0.001), with a higher proportion of abnormal levels in males. Finally, creatinine serum levels reveal a significant difference (p=0.01), with a higher percentage of males showing abnormal levels compared to females.

5.4 Crosstab Analysis of eGFR with Gender

Table 17: Crosstab analysis table of eGFR with gender

eGRF	Stage	Male N(%)	Female N(%)
≥ 90	Stage I	33(15.7)	17(8.1)
60-89	Stage II	39(18.6)	9(4.3)
30-59	Stage III	35(16.7)	20(9.5)
15-29	Stage IV	12(5.7)	14(6.7)
< 15	Stage V	17(8.1)	14(6.7)

The table provides a breakdown of eGFR (estimated Glomerular Filtration Rate) stages by gender for a sample of individuals. In Stage I, indicating normal kidney function (eGFR ≥ 90), 33 males (15.7%) and 17 females (8.1%) are classified. For Stage II, representing mild kidney dysfunction (eGFR 60-89), 39 males (18.6%) and 9 females (4.3%) are observed. In Stage III, indicating moderate kidney dysfunction (eGFR 30-59), there are 35 males (16.7%) and 20 females (9.5%). Stage IV, denoting severe kidney dysfunction (eGFR 15-29), includes 12

males (5.7%) and 14 females (6.7%). Finally, in Stage V, reflecting end-stage kidney failure (eGFR < 15), 17 males (8.1%) and 14 females (6.7%) are classified. This distribution highlights that males generally have a higher proportion of individuals in the earlier stages of kidney dysfunction compared to females, particularly in Stage I and Stage II, while the proportions in the later stages (Stage IV and V) are more balanced between genders.

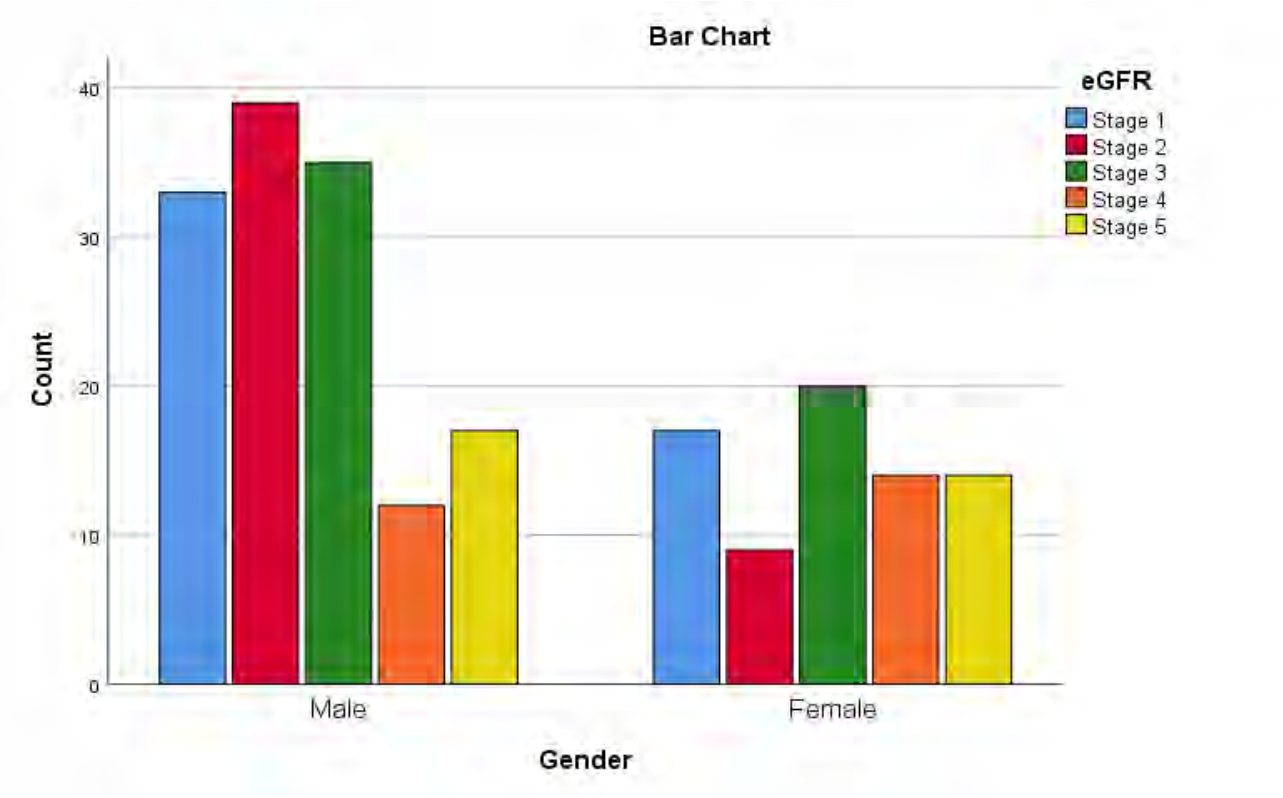

Figure 19: Crosstab Analysis of eGFR with Gender

5.5 Crosstab Analysis of eGFR with Age

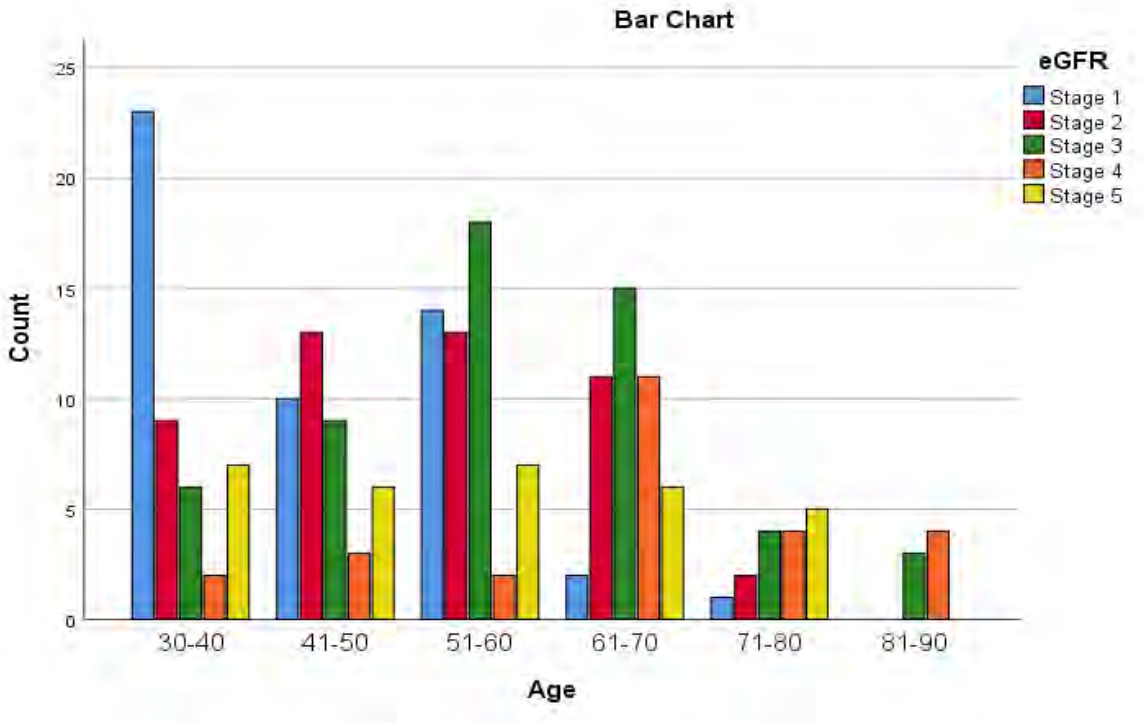

Figure 20: Crosstab Analysis of eGFR with Age

The bar chart in Figure 20 presents a crosstab analysis of eGFR (Estimated Glomerular Filtration Rate) across different age groups. The eGFR stages (1 through 5) are represented using different colors, showing the distribution of patients at various stages of renal function. The chart highlights that the 30-40 age group has the highest count in Stage 1, while Stage 3 is more prominent in older age groups, especially between 51-70 years. This graphical representation emphasizes how renal function tends to decline with age, with more advanced stages of kidney dysfunction appearing in older populations.

Chapter 6: Discussions

Among 210 T2D diabetes participants, the analysis of age distribution by gender reveals significant variations across different age groups, with a P value of 0.04 indicating statistical significance. Males show the highest representation in the age group of 51-60, accounting for 38 (18.1%) of the total. In contrast, females show a different pattern, with the 61-70 age group having the highest representation at 21(10%). Although there have been previous reports that women had a higher prevalence of CKD and that prevalence increased with age [39,40,41]. Our study revealed that the prevalence of CKD was higher in T2D males than females.

The renal profile assessment of patients with T2D reveals significant gender-based differences in several biochemical parameters. In the assessment of serum urea, abnormal levels were observed in 21.9% of males and 17.6% of females, demonstrating a significant difference (P = 0.02). The prevalence of CKD is heralded by abnormalities in serum urea [41]. Serum creatinine abnormality provides indications of kidney dysfunction [43]. Other studies had also examined serum creatinine in diabetic patients and was found to be abnormal, thus patients are recommended to consider caution for developing kidney disease in this condition [44]. Our study showed a notable gender disparity of 26.7% of males versus 20.5% of females displaying abnormal levels, resulting in a significant difference (P = 0.01). Correspondingly Sodium plasma levels indicated that abnormal levels were noted in 12.4% of males versus 11.0% of females, with this difference reaching borderline significance (P = 0.05). Furthermore, plasma bicarbonates exhibited a significant gender variation, with abnormal levels in 16.2% of males compared to 16.7% of females (P = 0.001). Previous studies have shown that having multiple abnormal parameters increases the risk of kidney disease progression. This risk begins with the occurrence of one abnormal renal value and increases as the disease progresses. Previous research suggests that as kidney disease progresses to advanced stages, several aberrant values may occur [44]. Other parameters, including serum uric acid, total calcium, albumin, inorganic phosphorus, potassium, chloride, and anion gap, did not demonstrate significant differences between males and females, these findings underscore the importance of considering gender differences in the renal profile assessment and management of T2D patients.

The estimated glomerular filtration rate highlights the distribution of male and female participants across five eGFR stages. Males have a higher representation in the earlier stages II, which might indicate delayed diagnosis in males. As CKD progresses, females appear to catch up and surpass males in the later stages, particularly Stage III. This might suggest that females have a steeper decline in kidney function once it starts deteriorating, or that they might have different risk factors that accelerate the progression of CKD. Another study investigated

that women were less likely to have a decline in estimated glomerular filtration rate [46,47]. This study emphasizes how renal function tends to decline with age, with more advanced stages of kidney dysfunction appearing in older populations. Several studies also found that GFR declines with normal aging [48,49,50]. This underscores the need for aggressive management and monitoring in both males and females as they approach end-stage renal disease (ESRD) with aging.

Chapter 7: Conclusions

This study aimed to assess renal function in patients with Type 2 diabetes in Bangladesh, focusing on the prevalence of chronic kidney disease (CKD). The findings highlight significant gender differences in renal function among T2D patients, with males showing a higher prevalence of abnormal renal parameters and more advanced CKD stages. Healthcare providers should be aware of the higher risk of renal deterioration in males and tailor treatment strategies accordingly.

Key renal function markers such as glomerular filtration rate (GFR) and serum creatinine levels were found to be adversely affected in a substantial number of participants. This calls for the integration of routine renal function assessments in diabetes management protocols in Bangladesh. Early screening and proper management of CKD in diabetic patients can reduce the progression of kidney damage and improve patient outcomes, underscoring the importance of targeted healthcare strategies.

This study has several limitations. First, the cross-sectional design limits the ability to establish causality between gender and renal function outcomes. Longitudinal studies are needed to track changes in renal function over time and to better understand the progression of CKD in T2D patients. Additionally, the study did not account for other confounding factors such as diet, medication, and comorbid conditions, which could influence the observed differences in renal function between males and females. The research data are insufficient to depict a global scenario. Patients with T2D were less likely to express or disclose their lifestyles, making it difficult to undertake appropriate lifestyle analyses.

Furthermore, convenience sampling was adopted, which reduced the variety of patients and raised the possibility of sample bias. The study had a small amount of data, which may have resulted in low statistical power, increased error rates, and less precise data. The study lasted one year, which may not be sufficient for this investigation. Furthermore, there were challenges in data collecting for this study because several hospital officials were reticent to give or share their personal information.

We took only the dry lab dataset. Did not use real samples for this research. Which could have given more insight into the issues.

Further research is needed to explore the underlying mechanisms driving these gender disparities and to investigate the potential role of hormonal influences on renal function in T2D patients.

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