CHAPTER ONE
1. Introduction

1.1 Introduction:

Diabetes mellitus is group of metabolic disease characterized by high blood sugar (glucose) that result from defects in insulin secretions or its action, or both. (William, et al. 2012). The term diabetes mellitus describes metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion or its actions or both (WHO Expert Committee On Diabetes Mellitus 1985).

Diabetes mellitus classified in to four board categories type 1, type 2, gestational diabetes and other specific types. The term type 1 diabetes has replaced several former terms including childhood onset-diabetes, juvenile diabetes, and insulin dependent diabetes mellitus (IDDM), the term type 2 diabetes has replaced several former terms including adult-onset diabetes, obesity diabetes and non-insulin dependent diabetes mellitus (Gardner, 2011).

The classic symptoms of untreated diabetes are loss of weight, polyuria, polydipsia and polyphagia. Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes. (Cooke and Plotnick, 2008).

The major long term complication relate to damage to blood vessels including cardiovascular disease, atherosclerosis, ischemic heart disease, myocardial infarction, stroke and peripheral vascular disease (Boussageon, et al. 2011).

Nearly 16 million Americans are affected with the disease, and one-third of this number remains undiagnosed and untreated. In 1999, 800,000 new cases were reported, and the cost to the nation in medical expenses, disability, work loss, and premature mortality was more than 100 billion dollars. A survey published by the Santa Barbara County Health Assessment Task Force in April 2000, indicated that almost 5% of the County's adult population has been diagnosed with diabetes. Chinese medical association reported that, diabetes is fast becoming a major health problem in china with close to 40 million currently suffering from the disease (Carr and Gabbe, 1998). Ministry Health, In Sudan about 8 million cases are report as diabetic (Last report, of October 2008). There is another study showed a high prevalence of diabetes in the adult population of Sudan, with a wide difference among the different areas.
The high ratio of newly discovered to previously known diabetic cases may reflect poor public awareness and medical services. These findings will certainly have far-reaching implications for diabetes care delivery in this country (American Diabetes Association, 1996)
1.2 Rationale:

The diabetes mellitus represents as major health problem among non infectious diseases. In this study we would like to evaluate the renal status of type2 diabetic patients. We would measure the microalbuminuria, glycated hemoglobin and serum creatinine among type 2 diabetic. This study was conducted on-Type 2 diabetes and healthy people as control. This study was the lack of data sufficient local about the existence of micro albumin urea in patients with diabetes in Sudan, we have conducted this study to add more information about diabetes and its complications on the kidneys by measuring the micro albuminurea level which gives strong indications in the assessment of complications that occur due to the long duration of diabetes. The presence of microalbuminuria by exceeding the normal range indicates the presence of the beginning of kidney failure and do this examinations regularly has been reduces the development of these complications, also used in this study measured creatinine, which gives us evaluate the renal condition. Also we measured hemoglobin A1C to see if there was a relationship between heamoglobin A1c and the result of microalbuminuria. The present of hemoglobinA1C in high present gives a clear indication to assess whether adiabetic patient, is subject under control and diet program or not. And also the purpose of this study is to provide information and data on these cases in Sudan in order to help in other studies.
1.3 Objectives:

1.3.1 General Objective:

To evaluate microalbuminuria and creatinine level among Sudanese patients with type-2 diabetes mellitus in white Nile state.

1.3.2 Specific Objectives:

- To estimate microalbuminuria and creatinine level among type-2 diabetes mellitus patients in comparison with control group.

- To compare the mean of microalbuminuria, serum creatinine, glycated hemoglobin and fasting blood glucose in type2 diabetes in comparison with healthy Sudanese volunteer.

- To correlate between creatinine and duration of the disease among study group.

- To correlate between the level of microalbuminuria and serum creatinine in type2 diabetes.

- To correlate between microalbuminuria and duration of the disease among study group.
CHAPTER TWO
2. Literature Review

2.1 Diabetes Mellitus:

2.1.1 Definition of Diabetes Mellitus:

Diabetes mellitus is a heterogeneous group of syndromes characterized by an elevation of fasting blood glucose that caused by relative or absolute deficiency of insulin, which enables cells to absorb glucose in order to turn it into energy (Pamela et al., 2008). In diabetes, the body either fails to properly respond to its own insulin, does not make enough insulin, or both. This causes glucose to accumulate in the blood, often leading to various complications (Rother, 2007, Tierney et al., 2002). Many types of diabetes are recognized: The principal three are: Type 1: Results from the body's failure to produce insulin. It is estimated that 5%-10% of Americans who are diagnosed with diabetes have type 1 diabetes. Almost all persons with type 1 diabetes must take insulin injections. Type 2: Results from Insulin resistance, a condition in which cells fail to use insulin properly, sometimes combined with relative insulin deficiency. Most people who are diagnosed with diabetes have type 2 diabetes. Many people destined to develop type 2 diabetes spend many years in a state of Pre-diabetes: Termed "America's largest healthcare epidemic,"pre-diabetes indicates a condition that occurs when a person’s blood glucose levels are higher than normal but not high enough for a diagnosis of type 2 diabetes. In 2009 there are 57 million Americans who have pre-diabetes (Handelsman and Yehuda, 2009).

All forms of diabetes have been treatable since insulin became medically available in 1921, but there is no cure for the common types except a pancreas transplant; gestational diabetes usually resolves after delivery. Diabetes and its treatments can cause many complications. Acute complications including hypoglycemia, diabetic ketoacidosis, or nonketotic hyperosmolar coma may occur if the disease is not adequately controlled. Serious long-term complications include cardiovascular disease, chronic renal failure, retinal damage that can lead to blindness, several types of nerve damage, and micro vascular damage that may cause erectile dysfunction and poor wound healing. Poor healing of wounds, particularly of the feet, can lead to gangrene possibly requiring amputation (Mailbox and Lionel, 2007). Once considered primarily as a risk factor for heart disease, diabetes has now become a high profile
public health concern on its own right, due to the escalating epidemic of diabetes in older people, and the emergence of type 2 diabetes in children.

The number of people with diabetes worldwide is set to double in the next 20 years as a result of increasing obesity and longevity. While some of this increase will be observed in Europe and North America, it’s clear that bulk of epidemic will be observed in non-European origin population in countries undergoing rapid westernization. If anything, the European origin population are normally, being substantially protected from type 2 diabetes compared to other world population. This is reflecting in our current understanding of the epidemiology of diabetes derived mainly from the study of non-European population, such as the Pima Indians and neurons. But it is clear that diabetes risk, manifestation, natural history and even the criteria for the definition of diabetes itself, may vary considerably by population (Mekoe et al., 2001).

2.1.2 Classification of Diabetes Mellitus:

The first widely accepted classification of diabetes mellitus was published by WHO expert committee on diabetes mellitus, 1980). And modified in 1985(WHO study group diabetes mellitus, 1985).

The 1980 and 1985 classification of diabetes mellitus classes and two statistical risk classes. And they proposed two major classes of diabetes mellitus and named them, IDDM or type 1, and NIDDM or type 2. In both the 1980 and 1985 report other classes of diabetes included other types and impaired glucose tolerance (IGT) as well as Gestational Diabetes Mellitus (GDM) these were reflected in the subsequent International Nomenclature of Disease (IND) in 1991. The 1985 classification was widely accepted and is use internationally. It represented comprise between clinical and etiological classification of individual subjects and patient (WHO study group diabetes mellitus, 1985).

2.1.2.1 Type 1 Diabetes Mellitus:

Is characterized by inappropriate hyperglycemia primarily result of pancreatic islets β-cell destruction and a tendency to ketoacidosis. Type 2 diabetes, in contrast, includes hyperglycemia cases that result from insulin resistance with an insulin secretory defect. An intermediate stage, in which the fasting glucose increased above-normal limits but not to the level of diabetes, has been named impaired fasting glucose. The term impaired glucose tolerance to indicate glucose tolerance values above normal but below diabetes levels was
retained. Also, the term gestational diabetes mellitus was retained for women who develop glucose intolerance during pregnancy (Michael et al., 2010).

Type 1 diabetes mellitus is a result of cellular-mediated autoimmune destruction of β cells of the pancreas, causing an absolute deficiency of insulin secretion. Upper limit 110 mg/dl on the fasting plasma glucose is designated as the upper limit of normal blood glucose. Type1 constitutes only 10-20% of all diabetes and commonly occur in childhood and adolescence. This disease is usually initiated by an environmental factor or infection (usually a virus) in individuals with a genetic predisposition and causes the immune destruction of the β cells of the pancreas, and therefore, a decreased production of insulin. Characteristic of type 1 diabetes include abrupt onset, insulin dependence, and ketosis tendency. This diabetic type is genetically related. One or more of the following markers are found in 85-90% of individuals with fasting hyperglycemia: islet cell auto antibodies, insulin auto antibodies, glutamic acid decarboxylase, auto antibodies, and tyrosine phosphate 1A-2 and 1A-2B auto antibodies (Michael et al., 2010).

Sign and symptoms include polydipsia, polyphagia, polyuria, rapid weight loss, hyperventilation, mental confusion, and possible loss of consciousness (due to increase glucose to brain). Complications include micro vascular problems such as nephropathy, neuropathy, and retinopathy. Increased heart disease is also found in patients with diabetes. Idiopathic type 1 diabetes is a form of type 1 diabetes that's has no known etiology, is strongly inherited, and does not have β cell autoimmunity. Individuals with this form of diabetes have episodic requirements for insulin replacement (Michael et al., 2010).

2.1.2.2 Type 2 diabetes Mellitus:

In type 2 diabetes patient can still produce insulin, but do so relatively in adequately for their body's needs particularly in the face of insulin resistance. A major feature of type 2 diabetes is lack of sensitivity to insulin by the cells of the body (particularly fat and muscle cells) (William et al., 2012).

Type 2 characterized by hyperglycemia as result of individual resistance to insulin with insulin secretary defect. This resistance results in a relative, not an absolute, insulin deficiency. Type 2 constitutes the majority of the diabetes cases. Most patients in this type are obese or have an increased percentage of body fat distribution in the abdominal region. This type of diabetes often goes undiagnosed for many years and is associated with a strong
genetic predisposition, with patients at increased risk with an in age, obesity, and lack of physical exercise. Characteristics usually include adult onset of the disease and milder symptoms than in type 1, with ketoacidosis seldom occurring. However, these patients are more likely to go into a hyperosmolar coma and are at an increased risk of developing macrovascular and microvascular complications (Michael et al., 2010).

2.1.2.3 Gestational diabetes mellitus:

Gestational diabetes mellitus or (GDM) is a condition in which women without previously diagnosed exhibit high blood glucose level during pregnancy (especially during third trimester). Gestational diabetes caused when the insulin receptors do not function properly. This likely due to pregnancy. Related factor such as presence of human placental lactogen that interferes with susceptible insulin receptors. This in turn causes inappropriately elevated blood sugar levels. Gestational diabetes generally has few symptoms and its most commonly diagnosed by screening during pregnancy. Gestational diabetes affect 3-10% of pregnancies, depending on the populations studied so may be a natural phenomenon (Thomas et al., 2005).

As with diabetes mellitus in pregnancy in general, babies born to mother with untreated gestational diabetes are typically at increased risk of problems such as being for gestational age (which may lead to delivery complication), low blood sugar, and jaundice. If untreated, it can also cause seizures or still birth. Gestational diabetes is a treatable condition and women who have adequate control of glucose level can effectively decrease this risk. Women with unmanaged gestational diabetes are at increased risk developing type 2 diabetes mellitus or very rarely latent autoimmune diabetes or type 1 after pregnancy as well as having a high incidence of pre-eclampsia and caesarean section (Donovan, 2010).

2.1.2.4 Other Specific Types of Diabetes:

Several hormones oppose the action of insulin and are there for diabetagenic if secreted in excess include cortisol (Cushing’s syndrome), growth hormones (acromegaly), glucagon (pancreatic glucagonoma), and epinephrine (pheochromocytoma), many of this hormones lead to hyperglycemia by increase hepatic glucose production or decreasing insulin sensitivity. (Leibowitz et al., 1996)

Several monogenetic defects in B-cell function have been described. they are collectively referred to as maturity – onset diabetes of young (MODY) typically they manifest themselves
in infancy or childhood, cause impaired insulin secretion with relatively normal insulin action, and an inherited in autosomal–dominant fashion (American Diabetes Association, 2007).

2.1.3 Complication of diabetes mellitus:

Type 2 diabetes is typically chronic disease associated with a ten years shorter life expectancy. This is partly due to a number of complications with which it is associated, include two to four times the risk of cardiovascular disease, include ischemic heart disease and stroke. A 20 fold increase in lower limb amputation and increase risk of hospitalization. In the developed world, and increasingly elsewhere, type 2 diabetes is the largest case of non-traumatic blindness and kidney failure (Ripsin et al., 2009). It has also been associated with an increase risk of congestive dysfunction and dementia through disease processes such as Alzheimer’s disease and vascular dementia (Pasquier, 2010). Other complications include acanthosis Nigerians, sexual dysfunction, and frequent infections (Vijan, 2010). The importance of protecting the body from hyperglycemia cannot be overstated; the direct and indirect effects on the human vascular tree are the major source of morbidity and mortality in both type 1 and type 2 diabetes. Generally, the injurious effects of hyperglycemia are separated into macro vascular complications (coronary artery disease, peripheral arterial disease, and stroke) and micro vascular complications (diabetic nephropathy, neuropathy, and retinopathy). It is important for physicians to understand the relationship between diabetes and vascular disease because the prevalence of diabetes continues to increase in the United States, and the clinical armamentarium for primary and secondary prevention of these complications is also expanding (Fong et al., 2004).

2.1.3.1 Micro vascular complication of diabetes

2.1.3.1.1 Diabetic retinopathy:

Diabetic retinopathy may be the most common micro vascular complication of diabetes. It is responsible for ~ 10,000 new cases of blindness every year in the United States alone (Fong, et al. 2004). The risk of developing diabetic retinopathy or other micro vascular complications of diabetes depends on both the duration and the severity of hyperglycemia. Development of diabetic retinopathy in patients with type 2 diabetes was found to be related to both severity of hyperglycemia and presence of hypertension in the U.K. Prospective Diabetes Study (UKPDS), and most patients with type 1 diabetes develop evidence of
retinopathy within 20 years of diagnosis (UK Prospective Diabetes Study Group, 2004). (Keenan, 2007).

2.1.3.1.2 Diabetic neuropathy:

Diabetic neuropathy is recognized by the American Diabetes Association (ADA) as “the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes. (American Diabetes Association). As with other microvascular complications, risk of developing diabetic neuropathy is proportional to both the magnitude and duration of hyperglycemia, and some individuals may possess genetic attributes that affect their predisposition to developing such complications. The precise nature of injury to the peripheral nerves from hyperglycemia is not known but likely is related to mechanisms such as polyol accumulation, injury from AGEs, and oxidative stress. Peripheral neuropathy in diabetes may manifest in several different forms, including sensory, focal/multifocal, and autonomic neuropathies. More than 80% of amputations occur after foot ulceration or injury, which can result from diabetic neuropathy. (Boulton et al., 2007)

2.1.3.1.3 Diabetic nephropathy:

Diabetes is the most common cause of end-stage renal disease in the United States today (American Diabetes Association, 1999). Approximately 40% of patients with type 1 diabetes and 5 - 15% of patients with type 2 diabetes eventually develop ESRD, although the incidence is substantially higher in certain ethnic groups (DeFronzo, 1995).

This is thought to be a potentially preventable calamity. Sensitive tests are available to identify patients with renal involvement early in the clinical course, when preventive measures may have greatest impact. For these reasons, it is imperative that clinicians who care for patients with diabetes be knowledgeable about diabetic nephropathy and attentive to its prevention, onset, progression, and treatment in their patients. The pathophysiologic mechanisms of diabetic nephropathy are incompletely understood but include glycosylation of circulating and intrarenal proteins, hypertension, and abnormal intrarenal hemodynamic. The earliest demonstrable abnormalities include intrarenal hypertension, hyper filtration increased glomerular filtration rate, and microalbuminuria. Clinically, the most important screening tool for identifying early nephropathy is detection of microalbuminuria. Risk factors for development of diabetic nephropathy include hyperglycemia, hypertension, positive family history of nephropathy and hypertension, and smoking. Key elements in the
primary care of diabetes include glycemic control, blood pressure control, and screening for microalbuminuria. In general, the goal for glycemic control is a blood glucose level as close to normal (HbA1c <7%) as possible without causing dangerous hypoglycemia. Blood pressure control is at least as important as glucose control, especially after the onset of renal damage, and blood pressure should be consistently <130/85. Screening for diabetic nephropathy involves monitoring at least yearly for urinary albumin excretion >30 mg per day (Timothy et al., 2000).

Diabetic nephropathy is the leading cause of renal failure in the United States. It is defined by proteinuria > 500 mg in 24 hours in the setting of diabetes, but this is preceded by lower degrees of proteinuria, or “microalbuminuria.” Microalbuminuria is defined as albumin excretion of 30-299 mg/24 hours. Without intervention, diabetic patients with microalbuminuria typically progress to proteinuria and overt diabetic nephropathy. This progression occurs in both type 1 and type 2 diabetes. As many as 7% of patients with type2 diabetes may already have microalbuminuria at the time they are diagnosed with diabetes. In the European Diabetes Prospective Complications Study, the cumulative incidence of microalbuminuria in patients with type 1 diabetes was ~ 12% during a period of 7 years.(Gross, et al. 2005) .(Chaturvedi et al., 2001). In the UKPDS, the incidence of microalbuminuria was 2% per year in patients with type2 diabetes, and the 10-year prevalence after diagnosis was 25%. ( Adler et al., 2003). The pathological changes to the kidney include increased glomerular basement membrane thickness, micro aneurysm formation, mesangial nodule formation (Kimmelsteil-Wilson bodies), and other changes. The underlying mechanism of injury may also involve some or all of the same mechanisms as diabetic retinopathy. Screening for diabetic nephropathy or microalbuminuria may be accomplished by either a 24-hour urine collection or a spot urine measurement of micro albumin. Measurement of the micro albumin-to-creatinine ratio may help account for concentration or dilution of urine, and spot measurements are more convenient for patients than 24-hour urine collections. It is important to note that falsely elevated urine protein levels may be produced by conditions such as urinary tract infections, exercise, and hematouria. Initial treatment of diabetic nephropathy, as of other complications of diabetes, is prevention.

Like other micro vascular complications of diabetes, there are strong associations between glucose control (as measured by hemoglobin A1c ) and the risk of developing diabetic nephropathy. Patients should be treated to the lowest safe glucose level that can be obtained to prevent or control diabetic nephropathy (Gross et al., 2005). ( Adler et al., 2003 ). Treatment with angiotensin-converting enzyme inhibitors has not been shown to prevent the
development of microalbuminuria in patients with type 1 diabetes but has been shown to decrease the risk of developing nephropathy and cardiovascular events in patients with type 2 diabetes (Heart Outcomes Prevention Evaluation Study Investigators, 2000).

In addition to aggressive treatment of elevated blood glucose, patients with diabetic nephropathy benefit from treatment with antihypertensive drugs. Rennin-angiotensin system blockade has additional benefits beyond the simple blood pressure-lowering effect in patients with diabetic nephropathy. Several studies have demonstrated renoprotective effects of treatment with ACE inhibitors and angiotensin receptor blockers, which appear to be present independent of their blood pressure-lowering effects, possibly because of decreasing intraglomerular pressure. Both ACE inhibitors and ARBs have been shown to decrease the risk of progression to microalbuminuria in patients with microalbuminuria by as much as 60-70%. These drugs are recommended as the first-line pharmacological treatment of microalbuminuria, even in patients without hypertension (Gross et al., 2005).

Similarly, patients with microalbuminuria benefit from control of hypertension. Hypertension control in patients with microalbuminuria from diabetic kidney disease slows decline in glomerular filtration rate. Treatment with ACE inhibitors or ARBs has been shown to further decrease the risk of progression of kidney disease, also independent of the blood pressure-lowering effect. Combination treatment with an ACE inhibitor and an ARB has been shown to have additional renoprotective effects. It should be noted that patients treated with these drugs (especially in combination) may experience an initial increase in creatinine and must be monitored for hyperkalemia. Considerable increase in creatinine after initiation of these agents should prompt an evaluation for renal artery stenosis (Rossing et al., 2003).

2.1.3.2 Macro vascular Complications of Diabetes:

The central pathological mechanism in macro vascular disease is the process of atherosclerosis, which leads to narrowing of arterial walls throughout the body. Atherosclerosis is thought to result from chronic inflammation and injury to the arterial wall in the peripheral or coronary vascular system. In response to endothelial injury and inflammation, oxidized lipids from LDL particles accumulate in the endothelial wall of arteries. Angiotensin II may promote the oxidation of such particles. Monocytes then infiltrate the arterial wall and differentiate into macrophages, which accumulate oxidized lipids to form foam cells. Once formed, foam cells stimulate macrophage proliferation and attraction of T-lymphocytes. T-lymphocytes, in turn, induce smooth muscle proliferation in
the arterial walls and collagen accumulation. The net result of the process is the formation of a lipid-rich atherosclerotic lesion with a fibrous cap. Rupture of this lesion leads to acute vascular infarction (Boyle et al., 2007).

In addition to atheroma formation, there is strong evidence of increased platelet adhesion and hypercoagulability in type 2 diabetes. Impaired nitric oxide generation and increased free radical formation in platelets, as well as altered calcium regulation, may promote platelet aggregation. Elevated levels of plasminogen activator inhibitor type 1 may also impair fibrinolysis in patients with diabetes. The combination of increased coagulability and impaired fibrinolysis likely further increases the risk of vascular occlusion and cardiovascular events in type 2 diabetes (Beckman et al., 2002).

Diabetes increases the risk that an individual will develop cardiovascular disease. Although the precise mechanisms through which diabetes increases the likelihood of atherosclerotic plaque formation are not completely defined, the association between the two is profound. CVD is the primary cause of death in people with either type 1 or type 2 diabetes (Laing, 2003). (In fact, CVD accounts for the greatest component of health care expenditures in people with diabetes (Paterson et al., 2003). Among macro vascular diabetes complications, coronary heart disease has been associated with diabetes in numerous studies beginning with the Framingham study (Kannel et al., 1997).

Type 2 diabetes typically occurs in the setting of the metabolic syndrome, which also includes abdominal obesity, hypertension, hyperlipidemia, and increased coagulability. These other factors can also act to promote CVD. Even in this setting of multiple risk factors, type 2 diabetes acts as an independent risk factor for the development of ischemic disease, stroke, and death (Almdal et al., 2004). among people with type 2 diabetes, women may be at higher risk for coronary heart disease than men. The presence of micro vascular disease is also a predictor of coronary heart events (Avogadro et al., 2007).

Diabetes is also a strong independent predictor of risk of stroke and cerebrovascular disease, as in coronary artery disease (Lehto et al., 1996). Patients with type 2 diabetes have a much higher risk of stroke, with an increased risk of 150-400%. Risk of stroke-related dementia and recurrence, as well as stroke-related mortality, is elevated in patients with diabetes (Beckman et al., 2002).
2.1.4 Medical conditions of Type 2 diabetes mellitus:

There are many factors which can potentially give rise to or exacerbate type 2 diabetes. These include obesity, hypertension, elevated cholesterol (combined hyperlipidemia), and with the condition often termed metabolic syndrome (it is also known as Syndrome X, Reavan's syndrome) (Hu, 2003). Other causes include acromegaly, Cushing's syndrome, thyrotoxicosis, pheochromocytoma, chronic pancreatitis, cancer and drugs. Additional factors found to increase the risk of type 2 diabetes include aging, high-fat diets and a less active lifestyle (Iwasaki et al., 2008).

2.1.5 Path physiology of Diabetes Mellitus:

In diabetic person, there is an abnormal of insulin metabolism, the actual reason of this malfunction differ according to type of diabetes. Whatever the cause is the body cells and tissues do not make use glucose from the blood resulting elevates blood glucose (a typically symptom of diabetes called hyperglycemia). This condition also exacerbated by the conversion of glycogen to glucose i.e. increase hepatic glucose production (Ningthoujam, 2011). In both type 1 and type 2 diabetes, the individual will be hyperglycemic, which can be sever. Glucosuria can also occur after the renal tubular transporter system for glucose becomes saturated. This happens when the glucose concentration of plasma exceeds roughly 180mg/dl in an individual with normal renal function and urine output. As hepatic glucose overproduction continues, the plasma glucose concentration reaches a plateau around 300-500mg/dl (17-28mmoL/L). Provided renal output is maintained, glucose excretion will match the overproduction, causing the plateau. The individual with type 1 diabetes has a higher tendency to produce ketones, patient with type 2 diabetes seldom generate ketones, but instead have a greater tendency to develop hyperosmolar nonketotic states. The difference in glucagon’s and insulin concentrations in these two groups appear to be responsible for the generation of ketones through increased β- oxidation. In type 1, there is an absence of insulin with an excess of glucagons. This permits gluconeogenesis and lipolysis to occur. In type 2, insulin is present as is (at times) hyperinsulinemia; therefore, glucagon's is attenuated. Fatty acid oxidation is inhibited in type 2. This causes fatty acid to be incorporated into triglycerides for release as very-low density lipoproteins (Michael et al., 2010).

The laboratory findings of a patient with diabetes with ketoacidosis tend to reflect dehydration, electrolyte disturbances, and acidosis. Acetoacetate, β- hydroxybutyrate, and acetone are produced form the oxidation of fatty acids. The two former ketone bodies
contribute to the acidosis. Lactate, fatty acid, and other organic acid can also contribute to a lesser degree. Bicarbonate and total carbon dioxide are usually decreased due to kussmaul-kien respiration (deep respiration). This compensatory mechanism to blow off carbon dioxide and remove hydrogen ions in the process. The anion gap in this acidosis can exceed 16 mmol/L. Serum osmolality is high as a result of hyperglycemia; sodium concentrations tend to be lower due in part to losses (polyuria) and in part to a shift of water from cells because of the hyperglycemia. The sodium value should not be falsely underestimated because of hypertriglyceridemia. Grossly elevated triglycerides will displace plasma volume and give the appearance of decreased electrolytes when flame photometry or pre diluted, ion-specific electrodes are used for sodium determinations. Hyperkalemia is almost always present as a result of the displacement of potassium from cells in acidosis. This somewhat misleading because the patient's total body potassium is usually decreased (Michael et al., 2010).

More typical of untreated patient with type 2 diabetes is a nonketotic hyperosmolar state. The individual presenting with this syndrome has an overproduction of glucose; however, there appears to be an imbalance between production and elimination in urine. Often, this state is precipitated by heart disease, stroke, or pancreatitis. Glucose concentrations exceed 300-500 mg/dL (17-28mmol/L) and severe dehydration is present. The severe dehydration contributes to the inability to excrete glucose in the urine. Mortality is high with this condition. Ketones are not observed because the severe hyperosmolar state inhibits the ability of glucagon's to stimulate lipolysis. The laboratory findings of nonketotic hyperosmolar coma include plasma glucose values exceeding 1000 mg/dL (55 mmol/L), normal or elevated plasma sodium or potassium, slightly decreased bicarbonate, elevated blood urea nitrogen and creatinine, and an elevated osmolality. The gross elevation in glucose and osmolality, the elevation in BUN, and the absence of ketones distinguish this condition from diabetic ketoacidosis. Other form of impaired glucose metabolism that does not meet the criteria for diabetes mellitus includes impaired fasting glucose and impaired glucose tolerance (Michael, et al. 2010).

2.1.6 Diagnosis of Diabetes Mellitus:

Diabetes mellitus is diagnosed on the basis of history (i.e. polyuria, polydipsia and unexplained weight loss.(CMOs update, 2000). The requirement for diagnostic confirmation for a person presenting with severe symptoms and gross hyperglycemia differ from those for a symptomatic person with blood glucose values found to be just above the diagnostic cut – off value (Mc Cance, 1998). Diabetes is often detected when a person suffers a problem that is frequently caused by diabetes, such as a heart attack, stroke, neuropathy, poor wound
healing or a foot ulcer, certain eye problems, certain fungal infections, or delivering a baby with macrosomia or hypoglycemia. Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the followings, fasting plasma glucose level at or above 126 mg/dL (7.0 mmol/L), plasma glucose at or above 200 mg/dL (11.1 mmol/L) two hours after a 75 g oral glucose load as in a glucose tolerance test. Symptoms of hyperglycemia and casual plasma glucose at or above 200 mg/dL (11.1 mmol/L). A positive result, in the absence of unequivocal hyperglycemia, should be confirmed by a repeat of any of the above-listed methods on a different day. Most physicians prefer to measure a fasting glucose level because of the ease of measurement and the considerable time commitment of formal glucose tolerance testing, which takes two hours to complete and offers no prognostic advantage over the fasting test. According to the current definition, two fasting glucose measurements above 126 mg/dL (7.0 mmol/L) are considered diagnostic for diabetes mellitus. Patients with fasting glucose levels from 100 to 125 mg/dL (6.1 and 7.0 mmol/L) are considered to have impaired fasting glucose. Patients with plasma glucose at or above 140 mg/dL or 7.8 mmol/L, but not over 200, two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance. Of these two pre-diabetic states, the latter in particular is a major risk factor for progression to full-blown diabetes mellitus as well as cardiovascular disease. (World Health Organization, 1999), (Saydah et al., 2001). While not used for diagnosis, an elevated level of glucose irreversibly bound to hemoglobin (termed glycated hemoglobin or HbA1c) of 6.0% or higher (the 2003 revised U.S. standard) is considered abnormal by most labs; HbA1c is primarily used as a treatment-tracking test reflecting average blood glucose levels over the preceding 90 days (approximately) which is the average lifetime of red blood cells which contain hemoglobin in most patients. However, some physicians may order this test at the time of diagnosis to track changes over time. The current recommended goal for HbA1c in patients with diabetes is 6.5% (Sniderman et al., 2007, Genuth, 2006)

2.2 Glycated hemoglobin (HbA1c):

2.2.1 Definition of Glycated Hemoglobin:

Also named as glucosylated hemoglobin, is formed by a post- translational, non-enzymatic, substrate-concentration dependent irreversible process of combination of aldehyde group of glucose and other hexoses with the amino-terminal valine of the alpha-chain of hemoglobin and the rate of combination is directly proportional to the plasma glucose concentration.
Because the average red blood cell lives approximately 120 days, the glyced hemoglobin level at any one time reflect the average blood glucose level over the previous 2-3 months (Michael et al., 2005).

Glycated hemoglobin or glycosylated hemoglobin is form of hemoglobin that is measured primary to identify the average plasma glucose concentration over prolonged periods of time. It's formed in a non–enzymatic glycation pathway by hemoglobin exposure to plasma glucose. Normal level of glucose produces a normal amount of glycated hemoglobin. As the average amount of plasma glucose increase, the fraction of glycated hemoglobin increases in the predictable way. This serves as a marker for average blood glucose levels over the previous months prior to the measurement. In diabetes mellitus, higher amount of glycated hemoglobin, indicating poorer control of blood glucose levels. Have been associated with cardiovascular disease, nephropathy and retinopathy. Monitoring of hba1c in type 2 diabetic patients may improve outcome (Larsen et al., 1990).

A number of techniques are used to measure hba1c, laboratories use, high performance liquid chromatography (HPLC), the hba1c result is calculated as a ratio to total hemoglobin by using chromatogram ,immunoassay, enzymatic and capillary electrophoresis ( Parry Plant , 2008 ).

2.3 Microalbuminuria:

2.3.1 Definition of microalbuminuria:

Is defined as excretion of between 30mg and 300mg of albumin a day in the urine , lees than 30mg is insignificant, over 300 mg is albuminuria or microalbuminuria. Microalbuminuria occur when the kidney leak small amounts of albumin in to the urine, in other words when there is an abnormally high permeability for albumin in the renal glomerulus (NICE clinical guideline, 2008).

2.3.2 Diagnosis of microalbuminuria:

The level of albumin protein produce by microalbuminuria can be detected by special albumin – specific dipstick. A micro albumin urine test determines the presence of the albumin in urine. In properly functioning body, albumin is not normally present in urine because it is retained in the blood stream by the kidneys .micro albumin can be diagnosed from a 24 hour urine collection (between 30-300mg/24h) or more commonly, from elevated
concentration in spot sample (30-300mg/l) both must be measured on at least two of three measurement over a two – to three month period (Person Micro albumin Level (measured), 2007). To compensate for variation in urine concentration in spot – check samples , it is helpful to compare the amount of albumin in sample against its concentration of creatinine , this is termed albumin / creatinine ratio (ACR ).(Bakker A , 1999 ).And microalbuminuria is defined as ACR >3.5 mg/mmol female or .2.5mg/mmol male .(Clinlabnavigator.com, 2010).

2.3.3 Significant of microalbuminuria:

An indication of subclinical cardiovascular disease , marker of vascular endothelial dysfunction , an important prognostic marker for kidney disease in (diabetes mellitus , hypertension ,and in post streptococcal glomerulonephritis), and increasing microalbuminuria during the first 48h after admission to an intensive care unit predicts elevated risk for acute respiratory failure , multiple organ failure and overall mortality and risk factor for venous thromboembolism (Mahmoodi et al., 2009).

There have been several studies examining the relationship between microalbuminuria and renal outcomes in type 2 diabetes (Monessen et al., 1984).

2.3.4 Albuminuria and renal outcomes in type2 diabetes:

Studied the predictive value of microalbuminuria in patients with type 2 diabetes. It was predictive of the development of overt proteinuria as well as mortality. Patients with type 2 diabetes and albumin concentrations of 30–140 μg/ml at baseline were more likely to develop clinically detectable proteinuria (>400 μg/ml) after 9 years of average follow-up than patients with baseline urinary albumin concentrations <30 μg/ml. These findings were supported (Berrut, et al. 1997), who examined patients with type 2 diabetes and hypertension. The GFR of patients with microalbuminuria declined more than the GFR of patients with normoalbuminuria over the average 22 months of follow-up (P < 0.01), There have also been several larger trials that have shown the association between albuminuria and renal outcomes in patients with type 2 diabetes. The Irbesartan Diabetic Nephropathy Trial (IDNT) examined 1,715 patients with hypertension, type 2 diabetes, and proteinuria. Patients enrolled in IDNT had urinary protein excretion of at least 900 mg/24 h and serum creatinine concentration between 1.0 and 3.0 mg/dl in women and 1.2 and 3.0 mg/dl in men at baseline (Lewis et al., 2002). The risk for the development of end-stage renal disease or doubling of serum creatinine during the average 4 years of follow-up doubled for each doubling of baseline
proteinuria level (hazard ratio [HR] 2.04, 95% CI 1.87–2.22). (Atkins et al., 2005). Similarly, the Reduction of Endpoints in Non-Insulin Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan (RENAAL) study followed 1,513 patients with type 2 diabetes. (Nephren Brenner, et al. 2001). And nephropathy was defined as a urinary ACR ≥300 mg/g with a serum creatinine level of 1.3–3.0 mg/dl. The presence of albuminuria was associated with an adjusted HR of 6.2 (95% CI 4.4–8.7; P < 0.001) for the outcome of doubling of serum creatinine or end-stage renal disease (Keane et al., 2003).

2.4 Creatinine:

2.4.1 Definition of creatinine:

Creatinine is synthesized primarily in the liver from arginine, glycine, and methionine. It is then transported to other tissue, such as muscle, where it converted to phosphocreatinine, which serves as a high-energy source, creatinine phosphate loses phosphoric acid and creatine loses water to form creatinine, which passes in to the plasma, elevated creatinine concentration is associated with abnormal renal function, especially as it relates to glomerular function. The glomerular filtration rate (GFR) is the volume of plasma filtrated (V) by the glomerulus per unit of time (t). (Michael et al., 2005).

2.5 Blood glucose:

The blood sugar concentration or blood glucose level is the amount of glucose present in the blood of a human or animal. The body naturally tightly regulates blood glucose levels as a part of metabolic homeostasis, Glucose is the primary source of energy for the body's cells, and blood lipids (in the form of fats and oils) are primarily a compact energy store. (There are exceptions. For example, because their dietary metabolizable carbohydrates tend to be used by rumen organisms, ruminants tend to be continuously gluconeogenic (Young, 1977). Consequently their hepatocytes must rely on such primary energy sources as volatile fatty acids, absorbed from the rumen, rather than glucose, glucose is transported from the intestines or liver to body cells via the bloodstream, and is made available for cell absorption via the hormone insulin, produced by the body primarily in the pancreas (Davidson et al., 2011). Glucose levels are usually lowest in the morning, before the first meal of the day (termed "the fasting level"), and rise after meals for an hour or two by a few mill molar. The normal blood glucose level (tested while fasting) for non-diabetics, should be between 70 and 100 milligrams per deciliter (mg/dL), blood sugar levels for those without diabetes and who
are not fasting should be below 125 mg/dL. Glucose test - blood. NIH – National Institutes of Health). The blood glucose target range for diabetics, according to the American Diabetes Association, should be 70–130 (mg/dL) before meals, and less than 180 mg/dL after meals (as measured by a blood glucose monitor). Davidson et al., 2011.

Blood sugar levels outside the normal range may be an indicator of a medical condition, a persistently high level is referred to as hyperglycemia, low levels are referred to as hypoglycemia, diabetes mellitus is characterized by persistent hyperglycemia from any of several causes, and is the most prominent disease related to failure of blood sugar regulation. Intake of alcohol causes an initial surge in blood sugar, and later tends to cause levels to fall. Also, certain drugs can increase or decrease glucose levels (Rosemary Walker & Jill Rodgers, 2006).

2.5.2 Abnormality in blood sugar levels:

If blood sugar levels remain too high the body suppresses appetite over the short term. Long-term hyperglycemia causes many of the long-term health problems including heart disease, eye, kidney, and nerve damage, the most common cause of hyperglycemia is diabetes, when diabetes is the cause, physicians typically recommend an anti-diabetic medication as treatment. From the perspective the majority of patients, treatment with an old, well-understood diabetes drug such as metformin will be the safest, most effective, least expensive, most comfortable route to managing the condition. (Consumer Reports Health Best Buy Drugs, 2012).

If blood sugar levels drop too low, a potentially fatal condition called hypoglycemia. Symptoms may include lethargy, impaired mental functioning; irritability; shaking, twitching, weakness in arm and leg muscles; pale complexion; sweating; paranoid or aggressive mentality and loss of consciousness. (Renschler et al., 1965).

Mechanisms that restore satisfactory blood glucose levels after extreme hypoglycemia (below 40 mg/dl) must be quick and effective to prevent extremely serious consequences of insufficient glucose: confusion or unsteadiness, and in the extreme (below 15 mg/dl) loss of consciousness and seizures. It is far more dangerous to have too little glucose in the blood than too much, at least temporarily. In healthy individuals, blood glucose-regulating mechanisms are generally quite effective, and symptomatic hypoglycemia is generally found only in diabetics using insulin or other pharmacological treatment, hypoglycemic episodes
can vary greatly between persons and from time to time, both in severity and swiftness of onset. For severe cases, prompt medical assistance is essential, as damage to brain and other tissues and even death will result from sufficiently low blood-glucose levels (Renschler et al., 1965).
3. Materials and methods

Approach

This study utilized the qualitative approach to estimate microalbuminuria and glycated hemoglobin in type 2 diabetic patient.

3.1 Materials

3.1.1 Study design:

Its cross-sectional study

3.1.2 Study area:

This study was carried out at Kosti diabetic center.

3.1.3 Study period:

This study was carried out during the period from March – August 2013.

3.1.4 Study people:

Fifty men and women patients with type 2 diabetes mellitus were enrolled in this study as a test group and forty apparently healthy (non diabetic) were included as a control group.

3.1.5 Inclusion criteria:

Men and women had type 2 diabetes mellitus.

3.1.6 Exclusion criteria:

Men and women had type 1 diabetes mellitus and children were excluded from this study.

3.1.7 Ethical consideration:

Permission of this study was obtained from the medical authorities in the area of the study. All individuals enrolled in this study were fully informed about the aim of the study. There
was full commitment precaution sample taken, privacy and confidentiality. The results of analysis have been used for clinical diagnosis and were offered free for charge to all patients participating in the study.

3.1.8 Study variables:

Microalbuminuria and glycated hemoglobin in type 2 diabetic was considered as independent variables and the following as dependent variables:

Age, Duration of disease, Type of treatment, Complication of disease and Associated illness

3.1.9 Sampling:

Blood sample was obtained by use of local anti septic for skin (70% ethanol) 5ml of venous blood had been collected from each men and women with type 2 diabetes and control individuals without diabetic using a disposable sterile plastic syringe. The blood was collected from cubical vein or the back of the hand. Plasma was separated from blood cells after centrifugation for 10 minutes at 5000 r.p.m (round per minute) at room temperature. The plasma was collected and investigated directly after separation.

3.1.10 Data collection:

A questionnaire (see appendix 1) was specifically design to obtain information which helps in either including or excluding certain individuals in or from study.

3.1.11 Apparatus:

(NycoCard READER2), centrifuge, and colorimeter were used.

3.2 Methods:

3.2.1 Estimation of urine albumin:

NycoCard for urine albumin..
3.2.1.2 Intended use:

Nyco Card urine albumin is a rapid in vitro test for measurement of low albumin concentration in human urine.

3.2.1.3 Test Principle:

Nyco Card u – albumin is a solid phase, sandwich –format, immunometric assay. The test device contains a membrane coated with immobilized albumin specific monoclonal antibodies.

When the diluted sample is applied to the test device, the sample flows through the membrane, and immobilized antibodies on the membrane capture the albumin molecules. Albumin trapped on the membrane will bind the gold antibody conjugate then added, in a sandwich –type reaction. Unbound conjugate is removed from the membrane by washing solution. The paper layer underneath the membrane absorbs excess liquid. Due to the bound gold particles the membrane appears purple with color intensity proportional to the albumin concentration of the sample. The color intensity is measured quantitatively by using the color densitometer NycoCard READER 2 (Braz Biol, 1997).

3.2.1.4 Test procedure:

We add 50ml urine sample or C/Control to a test tube with R1/Dilution liquid. Mix well, then applied 50ml diluted urine or diluted control to a TD/Test Device. Allow the diluted sample to soak completely into the membrane (approximately 50 sec.), applied 50 ml of R2/conjugate to the test device. Allow the conjugate to soak completely into the membrane (approximately 50 sec).

Immediately applied 50ml of R3/washing solution to the test device. Allow the washing solution to soak completely in to the membrane (approximately 50 sec).

Finally read the result within 5 minutes using the NycoCard READER 2. Follow the instruction given in the NycoCard READER2 Instruction Manual.

3.2.1.5 Reference range:

3.2.2 Estimation of HbA1C:

NycoCard for HbA1C

3.2.2.1 Test principle:

HbA1C is a boronate affinity assay. The kit contains test devices with a porous membrane filter, test tube prefilled with reagent and a washing solution. The reagent contain agents that lyses erythrocyte and precipitate hemoglobin specifically, as well as a blue boronic acid conjugate that binds cis-diols of glycated hemoglobin. When blood is added to the reagent, the erythrocytes immediately lyses. All hemoglobin precipitates. The boronic acid conjugate binds to the cis-diol is added to the test device, and all the precipitated hemoglobin, conjugate–bound and unbound, remains on top of the filter. Any excess of colored conjugate is removed with washing solution. The precipitate is evaluated by measuring the blue (glycated hemoglobin) and the red (total hemoglobin) color intensity with the NycoCard READER2, the ratio between them being proportional to the percentage of HbA1C in the sample (Jeppsson, et al. 2002).

3.2.2.2 Test procedure:

We added 5ml whole blood to the test tube with R1/Reagent. Mixed well. Incubated the tube for minimum 2 minutes, maximum 3 minutes. Use a timer Remix to obtain a homogenous suspension. Then applied 25ml of the reaction mixture to a test device by holding the pipette approx. 0.5cm above the test well. Empty the pipette quickly in the middle of the test well. Allowed the reaction mixture to soak completely into the membrane (approx. 10 sec). Then applied 25ml R2/washing solution to the test device. Allowed the washing solution to soak completely into the membrane. Wait for minimum 10 sec.

Finally we readed the test result within 5 min using the NycoCard READER2.

3.2.3 Estimation of Blood glucose:

Glucose oxidase/peroxides method
3.2.3.1 Principle of the method:

Glucose in the sample originates, by means of the coupled reaction a colored complex that can be measured by spectrophotometer (Tinder, 1969).

3.2.3.2 Procedure of the test:

We brought the reagent to room temperature, pipetted into labeled test tubes 1ml from reagent and .1ml from sample, then mixed thoroughly and incubate the tubes for 10minutes at room temperature (16-25c) or for 5minutes at 37c, finally measured the absorbance (A) of the standard and the sample at 500nm against the blank. The color is stable for at least 2 hours.

3.2.3.3 Calculation:

\[
\frac{A_{\text{sample}}}{A_{\text{standard}}} \times C_{\text{standard}} = C_{\text{sample}}
\]

3.2.3.4 Reference value:

70-105 mg/dl.

3.89-5.83 mmol/l (Tietz textbook of Clinical Chemistry and Molecular Diagnostic, 2005).

3.2.4 Estimation of Serum creatinine:

Alkaline picrate

3.2.4.1 Principle of the method:

Creatinine in the sample reacts with picrate in alkaline medium forming a colored complex. The complex formation rate is measured in a short period to avoid interferences. (Bartels, et al .1971) (Fabiny, et al. 1971).

3.2.4.2 Test procedure:

Pinged the working reagent and photometer to 37c, Pipetted into a corvette, 1 ml from working reagent and .1ml from sample, mixed and inserted curette into the photometer. Started stopwatch, recorded the absorbance at 500nm after 30sec (A1) and after 90 sec (A2).

3.2.4.3 Calculation of result:
\[
\frac{(A_2 - A_1)_{\text{sample}}}{(A_2 - A_1)_{\text{standard}}} \times \text{sample dilution factor} = C_{\text{sample}}
\]

3.2.4.4 Reference values:

Serum and plasma

Men  
0.9 - 1.3 mg/dl  
80 - 115 µmol/l

Women  
0.6 - 1.1 mg/dl  

Quality Control and Statistical Analysis:

See Appendices.
CHAPTER FOUR

4. Results

The current study conducted on fifty (50) patients with type2 diabetes mellitus and forty (40) apparently healthy individuals matched age from (30-75), the frequency and percentage of sex (25 male and 25 female in study group) to measure levels of microalbuminuria, glycated hemoglobin, serum creatinine and fasting blood glucose.

Microalbuminuria:

Table (4.1) shows baseline characteristic of study group between mean of patients and control group, which present there is significant difference in microalbuminuria between case and control group (p-value = 0.002), and the mean of microalbuminuria in case and control (mean± SD) = (69±68 mg/l) (17±2.3 mg/l). And shows baseline characteristic of hemoglobin A1c in between mean of patients and control group, which present there is significant difference in hemoglobinA1C between case and control group (p-value = 0.000), and the mean of hemoglobinA1c in case and control (mean± SD) =(10±2.1 %) (5.5±0.5 %). Also shows baseline characteristic of serum creatinine between mean of patients and control group, which present there is significant difference in creatinine between case and control group (p-value = 0.005), and the mean of creatinine in case and control (mean± SD) =(0.6±2 mg/dl) (0.4±0.2 mg/dl). Also shows baseline characteristic of blood glucose between mean of patients and control group, which present there is significant difference in fasting blood glucose between case and control group (p-value = 0.000), and the mean of creatinine in case and control (mean± SD) = (196±50 mg/dl) (99±9 mg/dl).
Figure 4.1 Express percentage of age group of case study group (1) 30-45
Group (2) 45-60, group (3) 61-75 years.
Table (4.1) Comparison between means of Microalbuminuria (mg/l), HbA1c (%), Creatinine (mg/dl) and fasting blood sugar (mg/dl) in study and control group.

<table>
<thead>
<tr>
<th></th>
<th>Groups</th>
<th>mean± SD</th>
<th>p- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microalbuminuria (mg/l)</td>
<td>Case</td>
<td>69±68 mg/l</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>17±2.3 mg/l</td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>Case</td>
<td>10±2.1 %</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>5.5±0.5 %</td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>Case</td>
<td>0.6±0.2 mg/dl</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>0.4±0.2 mg/dl</td>
<td></td>
</tr>
<tr>
<td>Fasting blood Sugar (mg/dl)</td>
<td>Case</td>
<td>196±50 mg/dl</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>99±9 mg/dl</td>
<td></td>
</tr>
</tbody>
</table>

The table shows the mean, standard deviation and probability value (P-value)

Independent t .test used for comparison

P -value≤ 0.05 is considered significant.
Table 4.2 Express frequency and percentage of sex in case study group.

<table>
<thead>
<tr>
<th></th>
<th>Frequency (n)</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>25</td>
<td>50%</td>
</tr>
<tr>
<td>Female</td>
<td>25</td>
<td>50%</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100%</td>
</tr>
</tbody>
</table>
Table (4.3) Comparison between means of fasting blood sugar (mg/dl) and sex in study group.

<table>
<thead>
<tr>
<th></th>
<th>Mean±SD</th>
<th>P.Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>198±59mg/dl</td>
<td>0.698</td>
</tr>
<tr>
<td>Female</td>
<td>192±40mg/dl</td>
<td></td>
</tr>
</tbody>
</table>
Figure (4.2)

A scatter blot of the correlation between creatinine and duration of the Disease among study group, \((r=0.495, \text{p-value}=0.00)\)
Figure (4.3)

A scatter blot of the correlation between microalbuminuria and duration of the disease among study group, ($r=.495$, p-value0.00).
Figure (4.4)

A scatter blot between Fasting Blood Glucose and HbA1c among Study group, \((r=0.280, \text{p-value } 0.49)\).
A scatter blots between Microalbuminuria and creatinine among study group, \( r = 0.246, \) \( p\)-value 0.085).
CHAPTER FIVE

5. Discussion, Conclusion, and Recommendation

5.1 Discussion:

This study was conducted on 50 diabetes patients as a test group and 40 healthy non diabetic as control group.

In this study there was significant increased of microalbuminuria in case study when compared with control group (p-value= 0.002), this agree with previous study done by (Afkhami) who stated that, A significant increased elevation of microalbuminuria in long term diabetes patients (P = 0.001).

In the current study there is highly significant elevation of glycated hemoglobin levels in test group when compared with control group (P-value= 0.000), this result agree with result done by (Goud), who stated that, the levels of glycated hemoglobin and fasting glucose were significantly increased in diabetic group when compared to normal subjects (p-value= 0.001).

In the present study there was significant increased in serum creatinine in test group compared with control group (P-value= 0.005), this result agree with study done by (Kassab), who stated that, Creatinine was significantly increased in type 2 diabetes when compared with controls.

Also in this study there was significant moderate positive correlation between long duration of diabetes mellitus and microalbuminuria in test group, (r=.495, p-value 0.00), these agree with study done by (Sean) who stated that Duration of NIDDM ranged from newly diagnosed to 13 years no significant increase it increase in more than 13years. Other study done by (Berrut), who stated that patients with type 2 diabetes and albumin concentrations of 30–140 μg/ml at baseline were more likely to develop clinically detectable proteinuria (>400 μg/ml) after 9 years of average follow-up than patients with baseline urinary albumin concentrations <30 μg/ml.

In current study there were no significant positive correlation between glyhemoglobin and fasting blood glucose in test group, (r=.280, p-value0.49), this result disagree with study
done by (Clark Perry) who stated that, in the subjects with OGTT-diagnosed diabetes and FPG levels between 5.5 and 8.0 mmol/l, detection of an elevated HbA₁c. Other study done by (Enzi) agrees with current study who stated The Correlations between HbA₁c and plasma/blood glucose at different times of the day ranged from 0.44 to 0.67. The strongest correlation was between HbA₁c and mean daily glucose (r = 0.57–0.69).

5.2 Conclusion:

1- The level of microalbuminuria was increased in type2 diabetes when compared with control group.

2- The level of glycated hemoglobin was increased in type2 diabetes when compared with control group.

3- There were increased in level of fasting blood glucose and moderate increase in serum creatinine in type2 diabetes.

4- There was positive correlation between microalbuminuria and duration of disease in study group and positive correlation between hemoglobinA1C and fasting blood glucose in study group and there was no increased in hemoglobinA1c, microalbuminuria, and serum creatinine in control group.
5.3 Recommendation:

From the results of this study, it is recommended that:

1. Microalbuminuria should be checked annually in type 2 diabetes patients to evaluate their renal status.
2. All patients with type 2 diabetes should measured HbA1c every six months at least.
3. Take the appropriate treatment and follow the right diet and exercise work leads to avoid complications of diabetes.
4. Increasing health education is important factor in the lowering of complication of diabetes.
5. Further studies are required to determine other parameters for the evaluation of nephropathy especially in type2 diabetes.
CHAPTER SIX

6. References


D Sean , MD, MSc, FRCPI; H Gerstein, MD, MSc, FRCPC, (1997), The Association of Microalbuminuria and Mortality in Non—Insulin-Dependent DiabeR. Clark Perry, DO1, R. Clark Perry, R. Ravi Shankar, , HbA1c Measurement Improves the Detection of Type 2 Diabetes in High-Risk Individuals With Nondiagnostic Levels of Fasting Plasma Glucose, Diabetes Mellitus JAMA Internal Medicine], Vole 157, No. 13


Allen K, Walker J, (2003), Microalbuminuria and mortality in long-duration type 1 diabetes, Diabetes Care, pages26(8):2389-91


Vijan S, (March 2010), Type 2diabetes" Annals of Internal Medicine,), 152 (5).


Allen, PJ ,(May 2012) "Creative metabolism and psychiatric disorders: Does creative supplementation have therapeutic value?". Neurosis' BiobehavRev, , 36 (5).


Davidson, Nancy Klobassa, and Moreland, (2011), Peggy living with diabetes blog .mayoclinic.com, July 26,.


Mailbox, Lionel."Up-to-date", 2007, 02-1315147


Paterson AD, Rutledge BN, Cleary PA, Lachin JM, Crow RS, The effect of intensive diabetes treatment on resting heart rate in type 1 diabetes: the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications study, 2007, Diabetes Care30:2107 -


