سم الله الرحمن الرحيم

Hypercholesterolemia due to chronic renal failure in diabetic Sudanese patients

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Dedication

To my family ...

To my father and my mother special dedication ..

To my friends and To all people who participated in this Work .

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Abstract

This study was conducted to compare the concentration of serum cholesterol in CRF patients due to diabetes with CRF due to other causes and making general assessment for the chance of developing atheroscleroatic cardiovascular disease .The study was performed in 80 Sudanese patients on hemodialysis and peirtoneal dialysis 40 of them had CRF due to D.M and others had CRF due to other causes. Health Sudanese served as control .

Serum samples were analyzed using colorimetric methods

Serum concentration of the total cholesterol showed significant increase and decrease in high density lipoprotein in CRF patients due to diabetes. This group has more chance for developing atherosclerotic cardiovascular disease when compaired with CRF group due to other causes and with the health subjects.

The mean of total cholesterol was 255mg/dl in the first group and in the second was 183mg/dl, triacylglycerols was 177mg/dl for the first group and for the second was 163mg/dl, low density lipoprotein was187mg/dl for the first group and for the second was113mg/dl, high density lipoprotein cholesterol was 27mg/dl for the first group and for the second is 31mg/dl.

There was no effect of sex, age, and the duration of renal failure.

This study evaluate the effect of diabetes mellitus on lipoproteins in patients with CRF as atherosclerotic risk factor.

ا لخلاصة

أجريت هذه الدراسة بهدف مقارنة تركيز و مكونات الكوليسترول في مصل الدم لمرضى الفشل الكلوي الناتج عن مرض السكري (المجموعة الاولى) والفشل الكلوي الناتج عن أمراض أخرى (المجموعة ا لثانيه) وذلك بغرض تقييم إ حتمالات حدوث أمراض القلب وتصلب الشرايين في عينة تتكون من أربعين مريضا " سودانيا من المجموعة الاولى وأربعيين عينه من المجموعة الثانية لمرضى الفشل الكلوي بدون سكري يترددون على مركز الغسيل الكلوي وتم مقارنتهم بأربعين عينه أخرى من الأصحاء (المجموعه الثالثة) .

تم تحليل مصل الدم بإستخدام القياس اللوني آخذيين في الإعتبار عوامل الجنس، العمرو فتره مرض الكلىحيث لم يكن هناك تأثير ملحوظ لهذه العوامل على تركيز الكوليسترول في مصل الدم .

كما إستبان أن هناك زيادة ملحوظة في تركيز الكولسترول الكلي وإنخفاض ملحوظ في تركيز كولسترول البروتينات الدهنيه عالية الكثافة عند مرضى الفشل الكلوي و السكري بالمقارنه بمرضى الفشل الكلوي حيث وجد أن المجموعة الأولى أكثر عرضه من المجموعه الثانية للإصابه بأمراض القلب وتصلب الشرايين حيث أن متوسط تركيز الكولسترول الكلي للمجموعه الأولى ٢٥٥ملجرام/ليتر وللمجموعة التانية ١٨٣ملجرام/ليتر ومتوسط تركيز ثلاثي إسيل الجليسرول للمجموعه الأولى ١٧٧ملجرام/ليتر وللمجموعة التانية ١٦٣ملجرام/ليتر ، كولسترول البروتينات الدهنيه عالية الكثافة الكلي للمجموعه الأولى ٢٧ملجرام/ليتر وللمجموعة التانية ٣١ملجرام/ليتر و كولسترول البروتينات الدهنيه ذات الكثافة المنخفضة للمجموعه الأولى ١٨٧ملجرام/ليتر وللمجموعة التانية ١١٣ملجرام /ليتر.

هذة الدراسه تعكس بوضوح تأثير مرض السكري في إرتفاع البروتينات الدهنيه كعامل من العوامل المسببة لأمراض القلب وتصلب الشرايين في مرضى الفشل الكلوي .

Introduction

Renal disease and dysfunction causes world wide medical problem,Renal insufficiency and renal failure are considered on the top of illnesses with Specific needs ,Different couses and Commplication.

Patients with chronic renal disease suffer from a secondary form of complex dyslipidemia. The most important abnormalities are an increase in serum triglyceride levels and increased plasma LDL cholesterol which is the first lipid abnormality to appear in nephrotic patient. Some patient exhibit evidence of decreased lipoprotein lipase activity and develop hypertriglyceridemia from over production of VLDL, chronic renal disease also promote its progression and the development of atherosclerosis. Therefore renal patients with dyslipidemia should be subjected to lipid-lowering therapy .

Patients with diabetes mellitus are at increased risk of coronary, cerebral, and peripheral vascular disease, and frequently have abnormal plasma lipid levels. Patient with diabetes may develop sever triglycerideemia and chylomicronemia syndrome becouse of possible presence of structural and functional abnormalities that may impair the lipid metabolism transport system in diabetic patients, Coronary heart disease may be increased in diabetic patients with poor glycaemic control or with microproteinuria. Treatment for diabetic patients would reduce the current rates of morbidity and mortality from vascular disease. For all that patient who have chronic renal failure due to diabetes are expected to have higher level of cholesterol and other lipids than patient with chronic renal failure due to other causes.

Objectives

To compare lipid profile in chronic renal failure due to diabetes (group A) to the lipid profile in patients with renal failure due to other causes (group B)and normal people as control group (group C)

In all groups the following will be determined:

1. Estimation of serum total cholesterol concentration (mg/dl).
2. Estimation of serum triglyceride TG concentration (mg/dl).
3. Estimation of serum low-density lipoprotein cholesterol concentration (LDL-C) (mg/dl).
4. Estimation of serum high-density lipoprotien (HDL-C) cholesterol concentration (mg/dl).

Chapter 1

1. literature review

1.1. Hyperlipidemia

The term hyperlipidemia is applied when the plasma cholesterol or triglyceride levels are increased. The degree of cholesterol or triglyceride elevation is a reflection of altered lipoprotein levels, which are often classified as lipoprotein phenotypes.

Hyperlipidemia is caused by a variety of disorders, which identifies specific lipoprotein disorders that are associated with a varitey of clinical features, the most prominent are atherosclerosis, pancreatitis, and xanthoma formation. These disorders are usually identified by measuring the plasma cholesterol and triglyceride level after a 12-to14-hour fast.

Lipoprotein disorders can be primary or secondary to some other disease process.The disorders have been classified in various ways one of these classification is based on lipoprotein phenotypes (Kelly,etal 2000).

There are four major lipid classes that are present in lipoproteins when extracted with a suitable lipid solvent, cholesterol, phospholipids, triacylglycerols, and cholesterol esters and the existence of amuch smaller fraction of unesterified long chain fatty acids (free fatty acids).

Cholesterol is present in tissues and plasma lipoproteins either as free cholesterol or combined with long chain fatty acid, as cholesterol ester, It is synthesized in many tissues from acetyl-COA and ultimately eliminated from the body in the bile as cholesterol or bile salt. It is an amphipathic lipid and is an essential structural component of membranes and of outer layer of plasma lipoprotein (Murray,etal, 2000)

1.1.1. Lipoproteins classes

There are four major subtypes of lipoproteins which vary in size, density, protein and fat content. Chylomicrons and very low density lipoproteins (VLDL) are the least dense lipoproteins and are comprised

primarily of a triglyceride rich core. low density lipoprotein (LDL) and high density lipoprotein (HDL) are the smallest and most dense lipoproteins and contain a core comprised primarily of cholesterol (Franklin,and Murphy,1999)

1.1.1.1. Low density lipoprotein (LDL)

Refers to a class and range of lipoprptein particles that is vary in their size and content, carry cholesterol in the blood and around the body for use by various cells. It is commonly referred to as bad cholesterol due to link between LDL levels and cardiovascular disease

1.1.1.2. High density lipoproteins (HDL)

Form a class of lipoproteins varying in their size and contents, that carry cholesterol from the body's tissues to the liver. Because HDL can remove cholesterol from atheroma within arteries, and transport it back to the liver for excretion, they are seen as "good" lipoproteins. HDL are the smallest lipoproteins, they are the most dense because they contain the highest proportion of protein. Epidemiologic studies have shown that high concentration of HDL(over 60mg/dl) have protective value against cardiovascular diseaese and low concentrations of HDL (below 40mg/dl) are a positive risk factor for atherosclerotic(Franklin,and Murphy,1999)

1.1.1.3. Chylomicrons and very low density lipoproteins (VLDL)

While circulating through the peripheral tissues, both the chylomicrons and VLDL are acted upon by the adipose tissue and muscle by the enzyme lipoprotein lipase which removes triglyceride from these particles for storage as fat or energy production in muscle. In this manner, the chylomicron is transformed into a cholesterol rich remnant particle that is removed from the circulation by the liver through the action of a specific remnant receptor.

VLDL is likewise transformed into a cholesterol rich remnant particle which can be removed by the liver or further metabolized to the more cholesterol rich LDL particle by the action of hepatic lipase. A specific LDL receptor is responsible for the uptake of both the VLDL remnants and LDL particles. As VLDL is metabolized by lipoprotein lipase it is left with excess surface coat as its core diminishes in size. In exchange for surface coat, HDL transfers cholesterol esters to VLDL by the action of cholesterol ester transfer protein (CETP). The exchanged surface coat allows the HDL particle to continue to absorb cholesterol and grow in size while the exchanged cholesterol ester can then be taken up by the liver as the VLDL remnant particles are metabolized. This represents one of the two mechanisms by which HDL can remove cholesterol from tissues (Franklin,and Murphy,1999) .

1.2 Lipoprotein disorder

1.2.1 Primary lipoprotein disorder

The phenotypic classification of the hyperlipoproteinemias is based upon serum electrophoresis are: Type I, IIA, IIB, III, IV and V(Franklin,and Murphy,1999) .

1.2.2 Type I hyperlipidemia

Characterized by severe elevations of chylomicrons with resultant elevations of triglycerides in the plasma. This condition results from either a congenital deficiency of lipoprotein lipase or apo C-II, the apolipoprotein required to activate lipoprotein lipase. Eruptive xanthomas and pancreatitis represent the clinical manifestations of the disorder (Franklin,and Murphy,1999).

1.2.3 Type IIA hyperlipidemia

Characterized by elevation of only LDL cholesterol. Genetic conditions which can cause this are familial hypercholesterolemia,

Polygenic hypercholesterolemia, familial combined hyperlipidemia and familial defective apolipoprotein B-100. These individuals are at high risk for developing premature coronary heart disease(Franklin,and Murphy,1999) .

1.2.4 Type IIB hyperlipidemia

Characterized by elevation of both LDL cholesterol and triglycerides. Familial combined hyperlipidemia is the most common genetic cause of this disorder where both VLDL and LDL are elevated. This disorder affects approximately 1-2% of the American population. Approximately 10% of patients with (Franklin,and Murphy,1999) .

1.2.5 Type III hyperlipidemia

Develops due to a defect in VLDL remnant clearance. Also known as Familial Dysbetalipoproteinemia, these individuals have difficulty in removing triglyceride rich VLDL remnant particles and consequently have elevations of cholesterol and triglycerides that are equivalent. Tuberous and planar xanthomas are common. Premature coronary heart disease is frequent (Franklin,and Murphy,1999) .

1.2.6 Type IV hyperlipidemia

Characterized by Hypertriglyceridemia. Individuals with Type IV Hyperlipidemia have triglyceride levels generally between 250 and 500 mg/dl. Causes are genetic, other diseases such as Diabetes or Nephrosis, medications, and in some cases dietary factors particularly high sugar and alcohol intake(Franklin, L; Murphy, M.D).

1.2.7 Type V hyperlipidemia

Have elevated levels of chylomicrons and VLDL, defective lipolysis and an overproduction of VLDL are responsible. Eruptive Xanthomas and pancreatitis can occur and causes can be genetic or

secondary to diabetes mellitus, obesity or alcohol consumption ((Franklin,and Murphy,1999) .

Table 1: Definition and selected characteristics of plasma lipoprotein phenotypes.

Phenotype	Lipoprotein elevation	Plasma lipid elevation
١	Chylomicron	Triglycerides↑↑
2a	LDL	Cholesterol↑
2b	LDL andVLDL	Cholesterol↑ Triglycerides↑
3	Chylomicron and VLDL remnants	Cholesterol↑ Triglycerrides↑or↑↑
4	VLDL	Triglyceride↑↑
5	Chylomicrons and VLDL	Triglyceride↑ Cholesterol↑

1.3 Secondary forms of hyperlipidemia

The most comon forms of hyperlipidemia seen in clinical practice are not the primary (familial) types, but those secondary to other disorders, such as alcohol consumption, chronic severe uncontrolled diabetes mellitus (diabetic lipemia), nephrosis, and glycogenosis, drugs, nephrotic syndrome and obstructive liver disease (Franklin,and Murphy,1999) .

Secondary forms of hyperlipidemia are produced by diverse group of disorders. Usually the lipid abnormality is relatively mild, and hypertriglyceridemia is more common than hypercholesterolemia(Kelly, etal 2000).

13.1 Dietary influences

High cholesterol level relates directly to greater consumption of dietary fat and cholesterol. Studies indicated that these kind of diets

suppress hepatic LDL receptor activity and thereby rise the LDL cholesterol level by long term of ingestion.

Another factor contributing to hyperlipidemia is excess calories increase fat consumption that promotes obesity and increases VLDL production by the liver and that may lead to increased LDL production especially if LDL receptor activity is suppressed by excess fat and cholesterol in the diet (Kelly, etal 2000).

1.3.7 Alcohol

Excess alcohol intake is a common cause of hyperlipidemia. Regular alcohol consumption increases lipid level in most people, but the response is highly variable. The plasma cholesterol may increase slightly due to an increase in the HDL fraction.

The greatest effects of alcohol appear on VLDL level. Alcohol consumption stimulates hepatic secretion of VLDL because hepatic metabolism of ethanol by alcohol dehydrogenase increases level of nicotine amide adenine dinucleotide, which inhibits oxidation of free fatty acids as the free fatty acids accumulate(Kelly, etal 2000).

1.3.3 Estrogen therapy

Estrogen containing medications generally cause mild increase in cholesterol and triglyceride level HDL cholesterol level are particularly increased. In patient of either sex with genetic predisposition to develop hypertriglyceridemia, estrogens may promote increased VLDL synthesis and secretion from the liver and cause massive hyperlipidemia(Kelly, etal 2000).

Table 2: Common causes of secondary hyperlipidemia

Disease	**Dominated lipid and lipoprotein abnormality**

Diabetes mellitus Chronic renal failure	Raised in TG,VLDL, Low HDL
Drug E.g. Thiazides B-adrenoceptor Antagonists Estrogen replacement Therapy	Raised TG,VLDL,lowHDL Raised TG, raised HDL
Alcohol excess	Raised TG,VLDL, raised HDL
Hypothyroidisms Nephrotic syndrome	Raised cholesterol, LDL

1.4 Definition of Diabetes

Diabetes is any disorder characterized by excessive urine excretion. The most common form of diabetes is diabetes mellitus a metabolic disorder in which there is an inability to oxidize carbohydrate due to disturbances in insulin function. Diabetes mellitus is characterized by elevated glucose in the plasma and episodic ketoacidosis. Additional symptoms of diabetes mellitus include excessive thirst, glucosuria, polyuria, lipemia and hunger. If left untreated the disease can lead to fatal ketoacidosis. Other forms of diabetes include diabetes insipidus and brittle diabetes. Diabetes insipidus is the result of a deficiency of antidiuretic hormone. The major symptom of diabetes insipidus (excessive urine output) results from an inability of the kidneys to resorb water. Brittle diabetes is a form that is very difficult to control. It is characterized by unexplained oscillations between hypoglycemia and acidosis(King ,2005).

Criteria which clinically establish an individual as suffering from diabetes mellitus, include:

1-Having a fasting plasma glucose level in excess of 126mg/dL (7mmol/L). (Normal levels should be less than 110 mg/dL (<5.6mmol/L)).

2-having plasma glucose levels in excess of 200 mg/dL (11mmol/L) at two points during aglucose tolerance test (GTT), one of which must be within 2 hrs of ingestion of glucose(King ,2005).

1.4.1. Types of Diabetes Mellitus

Diabetes mellitus is a heterogeneous clinical disorder with numerous causes, two main classifications of diabetes mellitus exist, Idiopathic and secondary.

Idiopathic diabetes is divided into two main types; insulin dependent and non-insulin-depenedent. Insulin-dependent diabetes mellitus(IDDM), also called Type 1diabetes is defined by the development of ketoacidosis in the absence of insulin therapy. Type 1 diabetes most often manifests in childhood (hence also called juvenile onset diabetes) and is the result of an autoimmune destruction of the B-cells of the pancreas. Non-insulin-dependent diabetes mellitus (NIDDM) or Type 2 diabetes is characterized by persistent hyperglycemia but rarely leads to ketoacidosis. Type 2 diabetes generally manifests after age 40 and therefore has the obsolete name of adult onset-type diabetes. Type 2 diabetes can result from genetic defects that cause both insulin resistance and insulin deficiency. There are two main forms of type 2 diabetes:

Late onset associated with obesity and Late onset not associated with obesity.

There is a strong correlation between obesity and the onset of type 2 diabetes with its associated insulin resistance (King ,2005).

Secondary or other specific types of diabetes mellitus are the result of many causes including:

Pancreatic disease: Pancreatectomy leads to the clearest example of secondary diabetes.

Cystic fibrosis and pancreatitis can also lead to destruction of the pancreas.

Endocrine disease: Some tumors can produce counter-regulatory hormones that oppose the action of insulin or inhibit insulin secretion. These counter-regulatory hormones are glucagon, epinephrine, growth hormone and cortisol.

Drug-induced diabetes; treatment with glucocorticoids and diuretics can interfere with insulin function.

Anti-insulin receptor autoantibodies: Maturity onset type diabetes of the young (MODY) was previously considered to be a third form of type 2 diabetes. However, with the discovery of specific mutations leading to MODY, it is now classified under secondary or other specific types of diabetes. MODY is characterized by onset prior to age 25. All cases to date have shown impaired B-cell function. Patients may also exhibit insulin resistance and late B-cell failure.

Mutations in the insulin gene and mutation in insulin receptor gene.

Gestational diabetes: this syndrome sets in during pregnancy and usually resolves itself following child birth.

Many other genetic syndromes have either diabetes or impaired glucose tolerance associated with them (King ,2005).

1.4.2 Role of insulin in lipid metabolism

One major role of insulin is to stimulate the storage of food energy following the consumption of a meal. This energy storage is in the form of glycogen in hepatocytes and skeletal muscle. Additionally, insulin

stimulates hepatocytes to synthesize triglycerides and storage of triglycerides in adipose tissue. In opposition to increased adipocyte storage of triglycerides is insulin-mediated inhibition of lipolysis. In uncontrolled IDDM, there is a rapid mobilization of triglycerides leading to increased levels of plasma free fatty acids. The free fatty acids are taken up by numerous tissues (however, not the brain) and metablized to provide energy. Free fatty acids are also taken up by the liver.

Normally, the level of malonyl-CoA is high in the presence of insulin. These high levels of malonyl-CoA inhibit carnitine palmitoyltransferase I, the enzyme required for the transport of fatty acyl-CoA's into the mitochondria where they are subject to oxidation for energy production. Thus, in the absence of insulin, malonyl-CoA levels fall and transport of fatty acyl-CoA's into the mitochondria increases. Mitochondrial oxidation of fatty acids generates acetyl-CoA which can be further oxidized in theTCA cycle. However in hepatocytes the majority of the acetyl-CoA is not oxidized by the TCA cycle but is metabolized into the ketone bodies, acetoacetate and B-hydroxybutyrate. These ketone bodies leave the liver and are used for energy production by the brain, heart and skeletal muscle. In IDDM, the increased availability of free fatty acids and ketone bodies exacerbates the reduced utilization of glucose furthering the ensuing hyperglycemia. Production of ketone bodies in excess of the bodies ability to utilize them leads to ketoacidosis. In diabetics, this can be easily diagnosed by smelling the breath. A spontaneous breakdown product of acetoacetate is acetone which is volatilized by the lungs producing a distinctive odor.

Normally, plasma triglycerides are acted upon by lipoprotein lipase (LPL), an enzyme on the surface of the endothelial cells lining the vessels. In particular, LPL activity allows fatty acids to be taken from

circulating triglycerides for storage in adipocytes. The activity of LPL requires insulin and in its absence a hypertriglyceridemia results (King ,2005).

1.4.3 Complications of diabetes mellitus:

Several major types of complications occur in patients with type 2 diabetes. These include infectious complications; complications related to the premature development of macrovascular atherosclerotic disease, complications related to development of diabetic microvascular disease, acute metabolic complications; and complications related to drug therapy. Type 2 diabetes has long been known as a potent risk factor for premature development of coronary artery disease and lower extremity atherosclerosis. This is probably independent of the hyperlipidemia that often accompanies type 2 diabetes and associated obesity.The coronary artery disease is often indistinguishable from that seen in non diabetic people. In addition to these complications, patients with type 2 diabetes develop the classic microangiopathic consequences of diabetes. It is a common misconception that patients with type 2 diabetes do not get these complications, or that they occur with a much lower frequency than patient with type 1 diabetes. A large prospective study of newly diagnosed diabetes in Belgium demonstrated that the prevalence rates for the three major microangiopathic consequences of diabetes retinopathy, neuropathy,and nephropathy were similar in patients roughly divided into type 2 and type1 .This study showed that after 25 years of diabetes , about 60% of patient had clinically significant retinopathy, 40% had neuropathy, and 20% had nephropathy.In an individual patient, complications may develop at different times; there also may be racial or ethnic difference in the incidence or prevalence rates of these complications. For example, there is evidence showed that black patients

with diabetes are more likely to develop end stage renal disease as a result of long term diabetes than white patients; most of the black patients developing renal failure had type 2 disease and these commplications account for much of the morbidity(Macsween,and Whaley , 1992) .

In addition to the long term consequences of diabetes patients with type 2 disease are subgject to several types of acute complications. One form of metabolic decomposition in these patients is hyperosmolar nonketotic diabetic coma. This a syndrome of acute relative insulin deficiency in which severe hyperglycemia developse, followed by profound osmotic diuresis, fluid and electrolyte depletion, hyperosmolality, neurologic dysfunction and ultimately death in the untreated patients.

Patients with type 2 diabetes can also experience classic ketoacidosis. Other acute syndromes that occur in type 2 diabetes, include consequences of drug over dose. (Macsween,and Whaley , 1992)

1.4.4 Diabetes mellitus and hyperlipidemia:

Hyperlipididaemia in diabetic patient is due to overproduction of carbohydrate and decreased metabolism of VLDL. There is hypertriglyceridaemia and low HDL levels (Franklin,and Murphy,1999). Several forms of hyperlipidemia are recognized clinically in patients with diabetes mellitus. Patients with acute insulin deficiency and diabetic ketoacidosis have diminished lipoprotein lipase (LPL) activity and may develop severe hypertriglyceridemia with type 4 and 5 pattern. The hypertriglyceridemia is aggravated initially by enhanced release of free faty acids from adipose tissue, followed by their conversion to VLDL in the liver(Kelly, etal 2000).

Another type of problem in diabetics relates to inadequate insulin therapy and poor diabetic control over long periods of time. The patients are usually obese type 2 diabetics with moderate or severe hypertriglyceridemia(Kelly, etal 2000).

There are at least two causes for their hyperlipidemia. The relative lack of insulin causes decrease LPL activity and reduced capacity to catabolize VLDL and chylomicrons. In addition the obesity and excess caloric intake stimulate excess VLDL production.

Such patients may exhibit type 4 or 5 patterns over prolonged periods, consequently they may have eruptive xanthomas and are at risk for experiencing pancreatitis (Kelly, etal 2000).

Improved diabetic control and weight loss ameliorate the hyperlipidemia.

Diabetes mellitus may aggravate the clinical features of the hyperlipidemia and produce the chylomicronemia syndrome with severe hypertriglyceridemia, a type 5 patttern, and increased risk for pancreatitis(Kelly, etal 2000).

1.4.5 Diabetes and the kidney:

Each year in the United States, nearly 80,000 people are diagnosed with kidney failure, a serious condition in which the kidneys fail to rid the body of wastes. Kidney failure is the final stage of a slow deterioration of the kidneys, a process known as nephropathy (Sharol ,2001).

Diabetes is the most common cause of kidney failure, accounting for more than 40 percent of new cases in USA. Even when drugs and diet are able to control diabetes, the disease can lead to nephropathy and kidney failure. Most people with diabetes do not develop nephropathy that is severe enough to cause kidney failure.

About 16 million people in the United States have diabetes, and about 100,000 people have kidney failure as a result of diabetes.

Scientists have not been able to explain this higher rate, nor can they explain fully the interplay of factors leading to diabetic nephropathy. Factors including heredity, diet, and other medical conditions, such as high blood pressure. They have found that high blood pressure and high levels of blood sugar increase the risk that a person with diabetes will progress to kidney failure .The deterioration that characterizes kidney disease of diabetes takes place in and around the glomeruli.

Early in the disease, the filtering efficiency diminishes, and important proteins in the blood are lost in the urine. Medical professionals know the presence of early kidney disease by measuring protein in the urine. Later in the disease the kidneys lose their ability to remove waste products, such as creatinine and urea, from the blood. Measuring these waste products in the blood gives an indication of how far kidney disease has progressed. Symptoms related to kidney failure usually occur only in late stages of the disease, when the kidney function has diminished to less than 10 to 25 percent of normal capacity. For many years before that point, kidney disease of diabetes exists as a silent process(Sharol ,2001).

1.4.5 Stages of progression to kidney failure in people with diabetes mellitus

Scientists have described five stages in the progression to kidney failure in people with diabetes. They are as follows:

Stage I. The flow of blood through the kidneys, and therefore through the glomeruli increases this is called hyperfiltration and the kidneys are larger than normal. Some people remain in stage I indefinitely; others advance to stage II after many years.

Stage II. The rate of filtration remains elevated or at near-normal levels, and the glomeruli begin to show damage. Small amounts of a blood protein known as albumin leak into the urine a condition known as

microalbuminuria. In its earliest stages, microalbuminuria may not be detected on each evaluation. But as the rate of albumin loss increases from 20 to 200 micrograms per minute, the finding of microalbuminuria becomes more constant (Normal losses of albumin are less than 5 micrograms per minute.) A special test similar to a urine dipstick is required to detect microalbuminuria. People with type 1 and type 2 diabetes may remain in stage II for many years, especially if they have good control of their blood pressure and blood sugar levels(Sharol ,2001).

Stage III. The loss of albumin and other proteins in the urine exceeds 200 micrograms per minute. It now can be detected during routine urine tests. Because such tests often involve dipping indicator strips into the urine, they are referred to as "dipstick methods." Stage III sometimes is referred to as "dipstick-positive proteinurea" (or "clinical albuminuria" or "overt diabetic nephropathy"). Some patients develop high blood pressure. The glomeruli suffer increased damage. The kidneys progressively lose the ability to filter waste, and blood levels of creatinine and urea-nitrogen rise. People with type 1 and type 2 diabetes may remain at stage III for many years.

Stage IV. This is referred to as "advanced clinical nephropathy." The glomerular filtration rate decreases to less than 75 milliliters per minute, large amounts of protein pass into the urine, and high blood pressure almost always occurs. Levels of creatinine and urea-nitrogen in the blood rise further.

Stage V. The final stage is kidney failure. The glomerular filtration rate drops to less than 10 milliliters per minute. Symptoms of kidney failure become apparent.

These stages describe the progression of kidney disease for most people with type 1 diabetes who develop kidney failure. For people with type 1,

the average length of time required to progress from onset of kidney disease to stage IV is 17 years. The average length of time to progress to kidney failure is 23 years. Progression to kidney failure may occur more rapidly (5-10 years) in people with untreated high blood pressure. If proteinuria does not develop within 25 years, the risk of developing advanced kidney disease begins to decrease. Type 1 diabetes accounts for only 5 to 10 percent of all diagnosed cases of diabetes, but type 1 accounts for 30 percent of the cases of kidney failure caused by diabetes(Sharol ,2001).

1.5 Renal functions:

Renal functions include the excretion of waste material from the bloodstream, secretion of hormones particularly erythropoietin and renin and maintaining serum electrolyte, acid-base balance and osmolality. Nephropathy is the condition in which small arteries in the kidneys become hardened and the glomeruli become damaged, in much the same way that the small vessels of the eye become damaged during retinopathy. The kidneys ultimately fail in their job of filtering out wastes. People with kidney failure must go on dialysis (the use of a machine to filter blood) or have a kidney transplant; otherwise, lethal levels of wastes and toxins build up in their bodies (Wadhwa,2003). Nephropathy is caused by high blood-sugar levels Also, high blood pressure, arteriosclerosis, smoking, and high cholesterol increase the likelihood of kidney complications. Frequent urinary tract infections add to the problem because an infection can easily spread to the kidneys and damage them. Early warning signs of nephropathy include problems emptying the bladder, blood in the urine, and urinary tract infections. The disease can be confirmed through simple urine and blood tests. Just as the kidneys lose their ability to discharge wastes, they also lose their ability

to keep protein and glucose in circulation. Sugar and protein begin to show up in the urine tests in larger amounts. Blood tests also detect high levels of urea nitrogen and creatinine, another indication of kidney damage(Wadhaw,2003).

1.5.1 Renal failure

This term is used to primarily denote failure of the excretory function of the kidney, leading to retention of nitrogenous waste products of metabolism. Various other aspects of renal function may fail at the same time, including the regulation of fluid and electrolyte status and the endocrine function of the kidney.

1.5.1.1 Acute renal failure

Acute renal failure (ARF) refers to as sudden and usually reversible loss of renal function, which develops over period of days or weeks. An increase in plasma creatinine concentration to greater than 200μmol/l is often used as the biochemical definition.Chinese data suggests that patients with acute renal failure who are treated right away, have an 89.6% - 92.1% chance of recovering normal kidney function. There are many causes of acute kidney failure but a common cause which can be prevented, or treated in conjunction with dialysis, is acute failure due to acute nephritic syndrome(Wadhaw,2003).

1.5.1.2 Chronic renal failure

Chronic renal failure (CRF) is an irreversible deterioration in renal function which classically develops over period of years. Initially it is manifest only as biochemical abnormality. Eventually, loss of the excretory, metabolic and endocrine function of the kidney leads to the development of the clinical symptoms and Signs of renal failure (Wadhaw,2003).

Chronic renal failure is due to irreversible loss of large numbers of functioning nephrons. Clinical symptoms occur when there are less than 30% normal functioning nephrons.

In general, chronic renal failure occurs due to the same reasons of acute renal failure occurs, but the progression is slower. Often the initial insult to the kidney leads to progressive deterioration of kidney function and increased loss of nephrons over time until the person reaches end-stage renal failure and is placed on dialysis or receives a kidney transplant. When nephrons are lost, other nephrons take on a larger load. They adapt and excrete normal amounts of water and solutes until the kidney is reduced to 20-30% normal nephron mass. Over the years, the glomeruli are injured. It is thought this injury is caused by the increased pressure and stretch from the increased blood pressure on the glomeruli. This eventually causes sclerosis and further destruction of the kidneys. The only method known by conventional medicine to slow the glomerular damage down is to lower blood pressure and glomerular hydrostatic pressure by using drugs such as angiotensin-converting enzyme inhibitors to block formation of angiotensin II. The most important tool you have for prevention of renal failure is recognition of the leading causes of renal failure. You can prevent or slow down renal failure only if you treat the early stages. Clinical symptoms show up when there is 70% destruction of functional nephrons(Wadhaw,2003).

1.5.1.2.1 Causes of Chronic Renal Failure

The most common causes of end stage renal failure are diabetes mellitus, hypertension and glomerulonephris. Diabetic nephropathy is the most common cause of renal failure in europe but glomerulonephris is the the most common cause in Sudan(Aboud,1998)

Almost all insulin-dependant diabetics have histological evidence of glomerulosclerosis. 35% will develop clinical nephropathy, usually about 15-20 years after diagnosis. The younger the age of onset of IDDM, the longer the duration, and the more frequent the episodes of ketoacidosis, the more likely the diabetic is to have diabetic nephropathy. Renal failure accounts for 48% of the diabetic deaths in those who acquire IDDM before age 20. Hypertension and atherocsclerosis can be a primary cause of renal damage. However, renal failure can also induce hypertension and lead to increased renal damage. Even in "normal" people benign nephrosclerosis takes place which diminishes normal kidney function to 40 or 50% by age 80.

Abnormal blood cholesterol may be the first and only sign for a few years. High cholesterol levels are seen in renal failure. The levels may be as high as 400 or 500 mg/dl (Wadhaw,2003).

1.5.2 HyperLipidemia in renal failure:

Hypercholesterolemia is almost universal in patients with significant proteinuria, and increased triglyceride levels are also common in patients with CRF, as well as influencing the development of vascular disease. Hyperlipidemia is common in patients with chronic renal disease, particularly those with the nephrotic syndrome. In addition to accelerating the development of systemic atherosclerosis, experimental studies suggest that high lipid levels also may promote progression of the renal disease. The major evidence in cholesterol loading enhances glomerular injury and that reducing lipid levels with a drug such as lovastatin slows the rate of progressive injury. The factors responsible for the lipid effects are incompletely understood leading to increased production of fibronectin (a component of the extracelluar matrix) and of a chemo-attractant for monocytes. Both of these changes could contribute to glomerular injury.

In addition, HMG CoA reductase inhibitors such as lovastatin may act independently of plasma lipid levels by directly inhibiting mesangial cell proliferation. In different animal models, a high cholesterol intake may be deleterious in the applicability of these findings to human disease is unproven, since there are no studies evaluating the possible protective effect of lowering lipid levels. However, both increased mesangial lipid deposition and enhanced expression of LDL-receptors on mesangial and epithelial cells have been demonstrated in patients with chronic glomerular diseases. Mesangial phagocytosis and increased traffic of macromolecules through the more permeable glomerular capillary wall could be responsible for the lipoprotein deposition; in addition, the increase in receptors could promote lipid accumulation even in the absence of hyperlipidemia.

People with kidney failure undergo either dialysis hemodialysis or protonial dialysis, which substitutes for some of the filtering functions of the kidneys, or transplantation to receive a healthy donor kidney

(Bellza 2003).

1.5.3 Hemodialysis

Hemodialysis involves exchanges between a patient's plasma and a dialysate bath through semipermeable membranes. Vascular access is achieved either through a temporary large intravenous double lumen catheter or repeated cannulation of a permanent, surgically constructed, arterio-venous fistula. Complications involve mechanical obstruction, infection, hemorrhage, and hemodynamic instability during or after dialysis therapy The objective of dialysis therapy is the removal of toxins, metabolic waste products, and excess volume from the vascular space.

Through the processes of ultrafiltration and diffusion, solutes and material pass from the vascular space to a dialysate solution by crossing semipermeable membranes(Bellza , 2003).

1.5.4 Peritoneal dialysis

Peritoneal dialysis involves the sterile introduction of dialysate fluid into the peritoneum through a surgically implanted catheter. The dialysate fluid is then allowed to equilibrate with the patient's plasma for a specific amount of time. By adjusting the dialysate material and the length of time, the consistency of a patient's plasma can be adjusted. The fluid is later withdrawn under sterile conditions. Although multiple modalities of peritoneal dialysis are available, the one most commonly used is continuous ambulatory peritoneal dialysis (CAPD). In this modality, the dwell time lasts from 4-6 hours and treatment is performed by the patient four times daily. Because of its ease of use, avoidance of hemodynamic instability from rapid volume shifts, and freedom from use of a dialysis center, CAPD is favored by younger patients, the elderly, and those with severe cardiovascular problems. Because CAPD is relatively stable, conditions such as hypotension, chest pain, and neurological deficits should not be attributed to the dialysis process(Bellza , 2003).

Chapter 2

2. Materials and Methods

2.1 Subjects

Subjects included in this study were 40 chronic renal failure diabetic patients (groupA), with age range between 20-80years,from patients attending Khartoum Dialysis Unit and Khartoum University Centre for kidney Dialysis &Transplantation. Other 40 Sudanese patients with chronic renal failure due to other causes (groupB) and 40 healthy Sudanese people (group C) from Alneelin University and from people who work in Khartoum University Centre for kidney Dialysis &Transplantation were taken as a control group.

SampleS were collected and analyzed in the period, 20\3\2005 to 28\5\2005.

2.2 Materials

2.2.1.Blood samples

Fasting venous blood sample from each patient (5ml) and control was obtained using disposable syringes. The blood was allowed to clot

for one hour at room temperature,and centrifuged at 5000 r.p.m .for 10 minutes to separate serum from blood cells. Sera were kept in a tightly covered containers at -20 º and used later for estimation of serum total cholesterol, serum triglycerol and serum HDL-C.

2.3 chemicals:

All chemicals used in this study were commercial kits obtained from Linear Chemicals, Spain

a.Cholesterol kit

a. Traicylglycerol kit
b. HDLcholesterol kit

2.4 Instruments

1-Minor centrifuge was used to separate serum from blood.
2-Minor centrifuge was used for separation of HDL fraction in the serum.
3-Corning colorimeter model 252 was used to estimate lipid profiles.

2. 4 Methods

2.4.1Estimation of serum total cholesterol concentration (mg/dl)

Serum total cholesterol concentration was estimated using enzymatic method.

A-Reagent composition:

Monoreagent pipes 200mmol/l ph 7.0,sodium cholate 1mmmol/l, cholesterol esterase>250U/L, peroxidase>1KU/L, 4amino antipyrine0.33mmol/l, ADPS0.4mmol/l, non-ionic tensiooactives 2g/l (w/v) biocides.

Cholesterol standard**:** Cholesterol 200mg/dl (5.18mmol/l) organic matrix based primary standard.

B- Principle:

This method used for the measurement of total cholesterol in serum involves the use of three enzymes: cholesterol esterase (CE), cholesterol

oxidase (CO) and peroxidase (POD) in the presence of the of the former the mixture of ADPS and 4-aminoantipyrine (4-AA) are condensed by hydrogen peroxide to from a quinoneimine dye proportional to cholesterol in the sample.

Cholesterol ester $\xrightarrow{CE}$ cholesterol + fatty acid

Cholesterol + O_2 $\xrightarrow{CO}$ cholestenone + H_2O_2

4-AA+ADPS $\xrightarrow{H202\ /POD}$ quinoeimine + $4H_20$

The absorbence of the dye was read at 520nm.

C- Procedure

A set of three test tubes was prepared, labeled as test, standard and blank.1ml of working solution was pipetted into each of the three test tubes using automatic pipette (1ml)

0.01ml of sample was pipetted into the test tube.

0.01ml of the standard was pipetted into the standard tube

0.01ml of the working solution was pipetted in to the blank tube using automatic pipette (0.01ml).

The three test tubes were mixed, incubated for 5 minutes at 37ºc and the absorbence of the sample and the standard were measured against blank using the colorimeter at wavelength 520 nm.

D- Calculation

Serum total cholesterol concentration was calculated according to the following equation.

$$\text{Serum totalcholesterol concentration (mg/dl)} = \frac{\text{bsorbence of the sample} \times \text{Concentration of the standard}}{\text{Absorbence of the standard}}$$

2.4.2 Estimation of the serum triacylglycerol concentration (mg/dl)

Serum triacylglycerol concentration was measured using enzymatic method.

A- Reagent composition:

Monoreagent. PIPES buffer 50 mmoI/L pH 6.8 LPL>12 KU/L GK> 1KU/L GPO > 10 KU/L ATP 2.0 mmoI/L Mg2+ 40 mmoI/L POD > 2.5 KU/L 4-AA 0.5 mmoI/L phenol 3 mmoI/L non-ionic tensioactives 2 g/L (W/V) biocides.

Triglycerides standard: glycerol 2.26mmol/l equivalent to 200mg/dl of glycerol trioleate.secondary standard.

B- Principle

The method is based on the enzymatic hydrolysis of serum or plasma triglyceride to glycerol and free fatty acids (FFA) by lipoprotein lipase (LPL). The glycerol is phosphorylated by adenosine triphosphate (ATP) in the presence of glycerolkinase (GK) to form glycerol-3-phosphate G-3-Pis oxidized by glycerolphosphate oxidase (GPO) to form dihydroxyacetone phosphate (DHAP) and hydrogen peroxide.

A red chromogen is produced by the peroxidase (POD) catalyzed coupling of 4-aminoantipyrine (4-AA) and phenol with hydrogen peroxide (H_2O_2) proportional to the concentration of triglyceride in the sample.

Triglyceride + 3H2O $\xrightarrow{\text{LPL}}$ Glycerol +3FFA

Glycerol + ATP $\xrightarrow{\text{GK}}$ Glycerol-3-P +ADP

Glycerol-3P+O2 $\xrightarrow{\text{GPO}}$ DHAP+H_2O_2

4AA+4Phenol $\xrightarrow{H_2O_2/POD}$ Quinoeimine+H_2O

C- procedure

One ml of the working reagent was pipetted into three test tubes labeled as test, standard and plank tube.

0.01ml of the sample was pipetted in to test tube

0.01ml of the standard was pipetted into standard tube and 0.01ml of working reagent was pipetted into plank tube using automatic pipette (0.01ml).

All tubes were mixed, incubated at 37ºc for 5 minutes

Absorbences of the sample and that of the standard were measured against blank using the colorimeter at wavelength 520.

D- Calculation

Serum triacylglycerols concentration was calculated according to the following equation.

$$\frac{\text{Absorbence of the sample}}{\text{Absorbence of the standard}} \times \text{Concentration of the standard}$$

2.4.3 Estimation of serum high-density lipoprotein cholesterol concentration (mg/dl).

HDL –cholesterol concentration in serum was measured using phophotungestic acid precipitation method.

A-Reagent composition

Precipitating reagent: phosphotungestic acid 0.63 mmol/l, magnesium chloride 25 mol/l stabilizers.

Cholesterol standard: Cholesterol 50mg/dl (0.38) organic matrix based primary standard.

B- Principle

This technique uses a separation method based on the selective precipitation of apoliprotein B-containing lipoproteins (VLDL, LDL and (a) Lap by phosphotungestic acid/MgCl2, sedimentation of the precipitant by centrifugation, and subsequent enzymatic analysis of high density lipoprotein (HDL) as residual cholesterol remaining in the clear supernatant.

C- Procedure:

1. Precipitation:

Into a microcentirfuge tube 0.5 ml of the reagent and 0.2ml of the sample were pipetted using micro pipette, the tubes were mixed, allowed to stand for 10minutes at room temperature and centrifuged for 5 minutes at 5000 r.m.p.

2. Cholesterol assay

Cholesterol content of the HDLsupernatant was determined using linear commericial kit. Using micropipettes, 1ml of the reagent and 0.1ml of the sample were pipetted in to a test tube labeled as test into another test tube 1ml of the reagent and 0.1ml of working reagent were pipetted and this tube is labeled as blank

Both test and the blank one were incubated at 37ºc for 10 minutes. The absorbence of the sample was measured against the reagent blank using colorimeter at wavelength 540nm within 45 minutes

D-Calculation

HDL-cholesterol cocentration (mg/dl)=

$$\frac{\text{Absorbence of the sample}}{} \times \text{Concentration of the standard}$$

Absorbence of the standard

2.4.4 Calculation of the serum low-density lipoproteins cholesterol concentration (mg/dl)

A-Friedwald equation

serum low-density lipoproteins cholesterol concentration (mg/dl)=serum cholesterol concentration-serum HDL-cholesterol concentration - serum triacylglycerol concentration .

5

Chapter 3

3. Results

In this study, the lipid profile of forty Sudanese patient with chronic renal failure due to diabetes mellites (group A) has been compared to the lipid profile of forty Sudanese patients with renal failure due to other causes (group B) and forty heathy people used as control (group C).

Patients were randomly selected from Khartoum Dialysis Unit and Khartoum University Centre for kidney Dialysis &Transplantation.

The range of age was from 25 to 75 years for all groups and the mean of age was as follow:group A 54 years, group B 43 years and group C 46 years.

The distripution of sex among the study groups was as follows :group A 25 males and 15 females, group B 29 males and 11 females and group C 21 males and 19 females

The mean of serum level of total cholesterol concentration, triglyceride concentration, low-density lipoprotein cholesterol concentration, and high-density lipoprotein cholesterol concentration for both patients and control were presented as follows:

3.1 Serum total cholesterol

Table 3 and Figure 1 show that (group A) had the higest level of serum total cholesterol concentration in the study group,followed by (group B) while (group C) had a normal value.

There was statistically significant difference between group A and group B, also there was significant difference between group A and group C, No statistically significant difference between group B and group C was observed.

3. 2 Serum triglyceride concentration

Table 4 and Figure 2 showed that group A had the higest level of serum triglyceride concentration, followed by group B while group C had a normal value.

There was no statistically significant difference between group A and group B, and between group B and group C, There was significant difference between group A and group C.

3.3 Serum low-density liboprotein cholesterol concentration

Table 5 and Figure 3 showed that group A had the higest level of serum low-density lipoprotein cholesterol concentration in the study group, followed by group B but group C had normal value.

There was statistically significant difference between group A and group B and between group A and group C, but there was no significant difference between group B and group C.

3.4. Serum high-density lipoprotein cholesterol concentration

Table 6 and Figure 4 showed that group A has the lowest level of of serum high-density lipoprotein cholesterol concentration , followed by group B while group C had normal value.

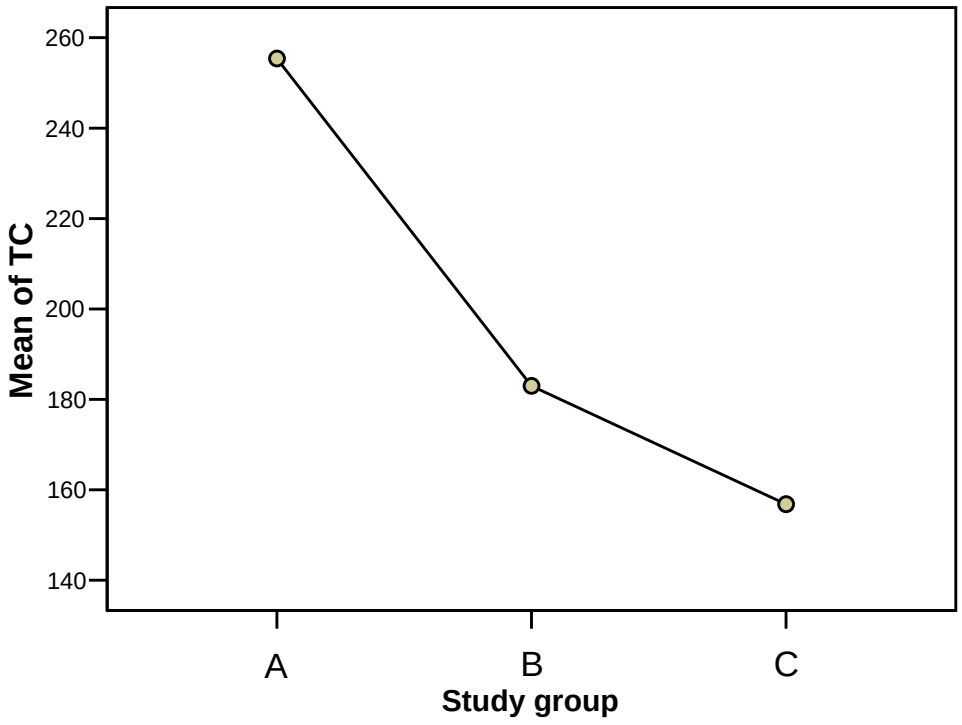
There was no statistically significant difference between group A and group B but there was statistically significant difference between group B and group C also there is significant difference between group A and group C was detected.

Table (3): Total cholesterol concentration among chronic renal failure patients due to diabetes, chronic renal failure due to other causes and control

Group	Frequency No/group	Mean ±SD Mg/dl	Groups comparative	p.value
A	40	255±91	A,B	0.00
B	40	183±53	A,C	0. 00
C	40	198±76	B,C	0.199

The mean difference is significant at the p.value <0.05

Figure (1): The mean of total cholesterol in chronic renal failure patients due to other causes due to diabetes, chronic renal failure and control



A: CRF associated with D.M.

B: CRF due to other causes

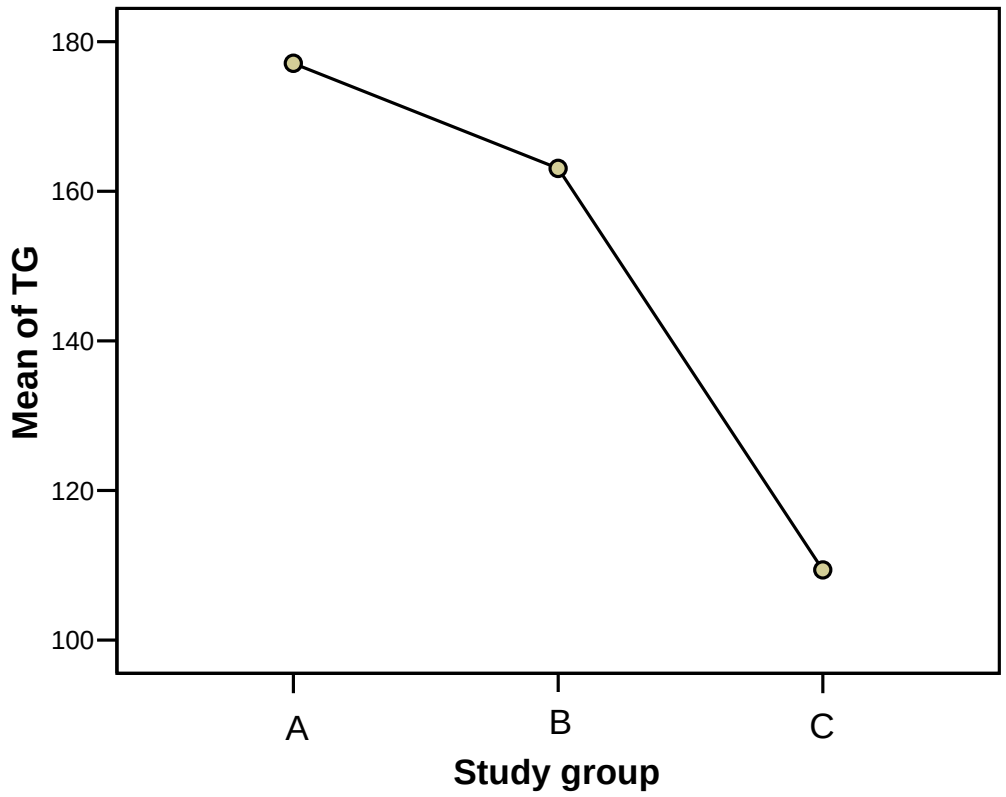
C: Control

Table (4): Triglyceride concentration among chronic renal failure patients due to diabetes, chronic renal failure due to other causes and control

Group	Frequency No/group	Mean ±SD Mg/dl	Groups comparative	p.value
A	40	177±82	A,B	0.682
B	40	163±77	A,C	0.00
C	40	109±50	B,C	0.05

The mean difference is significant at the p.value <0.05

Figure (2): The mean of triglyceride concentration in chronic renal failure patients due to diabetes, chronic renal failure due to other causes and control



A: CRF associated with D.M.

B: CRF due to other causes

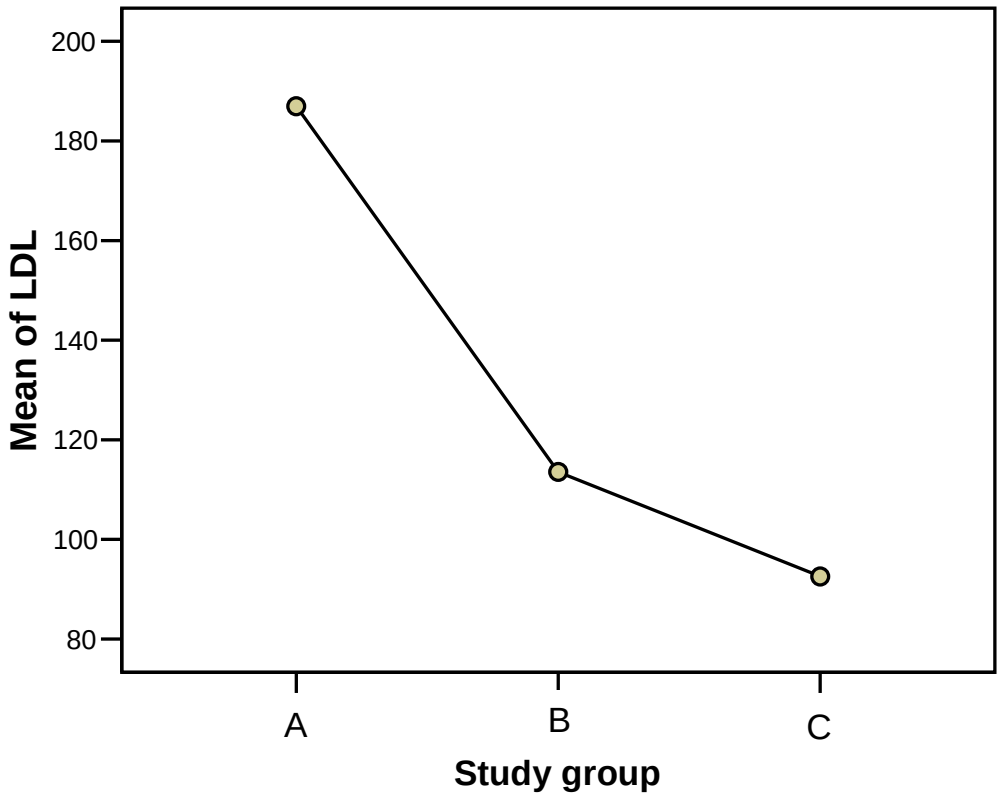
C: Control

Table(5) Low density lipoprotien concentration among chronic renal failure patients due to diabetes ,chronic renal failure due to other causes and control .

Group	Frequency No/group	Mean ±SD Mg/dl	Comparative between groups	P. value
A	40	187±84	A,B	0.00
B	40	113±49	A,C	0.00
C	40	92±34	B,C	0.296

The mean difference is significant at the p.value <0.05

Figure (3): The mean of low density lipoprotein concentration concentration in chronic renal failure patients due to diabetes, chronic renal failure and control



A: CRF associated with D.M.

B: CRF due to other causes

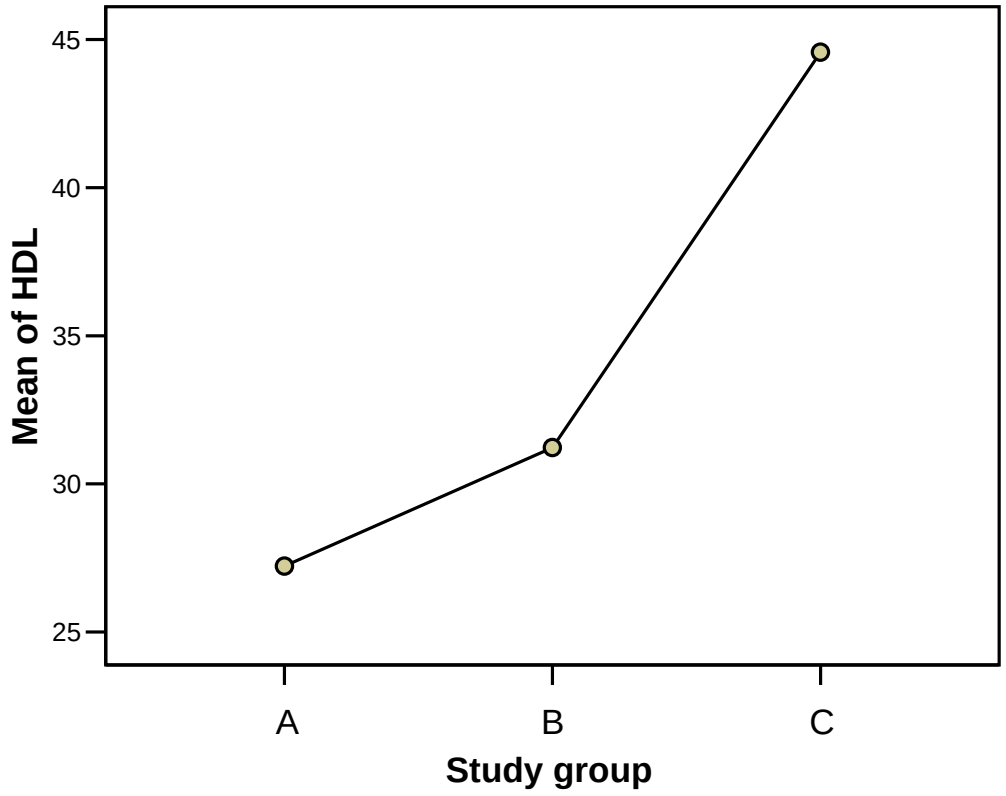
C: Control

Table (6): High density lipoprotein concentration among chronic renal failure patients due to diabetes, chronic renal failure due to other causes and control

Group	Frequency No/group	Comparative between groups	P. value	Mean ±SD Mg/dl
A	40	A,B	0.103	27±8
B	40	A,C	0.00	31±8
C	40	B,C	0.00	44±8

The mean difference is significant at the p.value <0.05

Figure (4): The mean of high density lipoprotien concentration in chronic renal failure patients due to diabetes, chronic renal failure due to other causes and control



A: CRF associated with D.M.

B: CRF due to other causes

C: Control

Chapter 4

4. Discussion

Patients with CRF due to any cause have hyperlipidemia mainly hypercholesterolemia (Attman,etal 1998). they suffer from a secondary form of complex dyslipidemia also hyperlipidemia promotes progrestion of CRF to end stages renal disease and the development of of atherosclerosis. Therefore, renal patients with dyslipidemia should be subjected to lipid lowering therapy(Wanner and Quaschning ,2001).

Patients with diabetes mellitus have abnormal plasma lipid levels and frequently may develop severe triglyceridemia chylomicronemia syndrome and they are at increased risk of coronary, cerebral and peripheral vascular disease because of possible presence of structural and functional abnormalities that may impair the lipid metabolism and transport system in diabetic patients(Guerci, etal 1994).

Patients who have chronic renal failure due to diabetes are expected to have higher levels of cholesterol and other lipids than patient with chronic renal failure without diabetes; this may be explained by the synergetic effect of both diabetes and renal failure on lipid metabolism(Attman ,etal 1998).

4.1 Serum total cholesterol concentration

Table 3 and figure 1 showed that group B has high level of serum total cholesterol compare to healthy people (group C); this agree with the previous studies(Attman, etal 1998) and (Attman,etal . 1996). this support idea that CRF is a cause of hyperlipidemic state.

Hyperlipidemia is a common finding in renal disease especially nephrotic syndrome in which hypercholesterolemia is one of the criteria for diagnosis of renal disease. Group A had significantly higher level of serum total cholesterol as shown in figure 1 and table 3. This could be

explained by the effect of both CRF and D.M on lipid metabolisem which may act synergetically to raise serum total cholesterol .The results agree previous studies(Attman, etal 1998).

The serum total cholesterol concentration in group A was significantly higher than normal (group C) and might indicate great risk for atherosclerosis and vascular disease.These patients need treatment of hyperlipidemia as well as protective measures.

4.2 Serum low-density lipoprotein cholesterol concentration

Table 5 and figure 3 show that the serum LDL cholesterol concentration is greatly increased in group A; this account for the significant increase of total cholesterol level in these patients and may indecate that the type of cholesterol increase in the blood of group A is bad cholesterol and that agree the previous studies (Hirano,etal. 1993) ,This indicate that these patients (group A) are at increased risk for atherosclerosis and vascular disease and may need management .Group B had also significant increases in LDL cholesterol, This also agree with the results of previous studies (Hirano ,etal .1993) and (Stewart ,etal . 1993) and need management

4.3 Serum high-density lipoprotein cholesterol concentration

Table 6 and figure 4 showed that group A had the lowest level of serum HDL cholesterol concentration .This high level of HDL is protective aganist atherosclerosis and vascular disease while the decrease in the level of HDL increases the risk factor for these conditions. (Attman, etal 1998) and (Joren ,etal .1993) .

It was notice that group A had significantly lower level of HDL than group B so this showed renal failure and diabetes severley affected the level of HDL .

4.4 Serum triacylglycerols concentration

Table 4 and figure 2 showed that both group A and B both had increased level of TG so renal failure due to any cause can lead to increased TG level as shown in the previous studies (Attman ,etal .1998). but no significant difference between group A and group B was observed

Lipoproteins disturbance in patients with CRF receiving haemodialysis appears to be independent of length of dialysis, also age and sex do not affected the concentration of lipid profile(Vaziri and Kaihui ,1997)and (Altahir, 1998).

4.5 Conclusion

1. Group A patients with CRF had hyperlipidemia mainly hypercholesterolemia.
2. Patients with CRF due to D.M had more severe hyperlipidemia than patients with CRF due to other causes.
3. The increase in total cholesterol level in patients with CRF was mainly due to elevation in LDL fraction which was high in group A.
4. Lipoproteins disturbance in patients with CRF receiving haemodialysis appears to be independent of length of dialysis, age and sex .

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Questionnaire

Date ---------- Serial no---------

Name---------- Age----------

Sex---------- Triple----------

History of present disease

Hypertension ( ) Heart disease ( )

Liver disease ( ) Jaundice ( )

Duration of diabetes----------

Duration of C.R.F ----------

Family history of diabetes ----------

Chronic medication ----------

Clinical examination

Body weight (Kg) --------

Blood pressure----------

Investigations

Total cholesterol---------

TG----------

LDL----------

HDL----------