بسم الله الرحمن الرحيم

Sudan University of Science and Technology

College of Graduate Studies

Determination of Lipids Profile of Sudanese Chronic Renal Failure Patients - Khartoum State

قياس مجموعة الدهون لدى المرضى السودانيين المصابين بالفشل الكلوي بولاية الخرطوم

(A desertation submitted in a partial fulfillment of the requirement for the master degree in clinical chemistry)

By:

Sadia Alamin Yousuf Yahia

B.Sc Clinical Chemistry – College of Medical Laboratories Science (SUST 2013)

Supervisor:

Dr. Nuha Elgaily Abobaker

Assistant Professor of Clinical Biochemistry

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بسم الله الرحمن الرحيم

قال الله تعالى :

(ويسألونك عن الروح قل الروح من أمر ربي وما أوتيتم من العلم إلا قليلا)

صدق الله العظيم

سورة الإسراء (الآية رقم 85)

Dedication

إلى من أكن لها كل مودتي ولشكرها بات الكلام يحول

كل حروفي ترجلت متنحية واحتار فكري .... ماذا أقول؟

لسعادتك سأسعى جاهدة حتى أنال رضاك المأمول

أمي الحبيبة

إليك يا من أعطيتني منذ الصغر حبا وعطفا وحنان

وتواصل بذلك المدرار لي وبفضلك اليوم صرت إنسان

فالآن كامل احترامي وتقديري لك وسيكون دوما على مر الزمان

أبي الحبيب

إليك يا من علمتني معنى المحبة والهوى

وزرعت في قلبي شتولا لا ترى,,, شتول حبك وعلى أوراقها قطر الندى

فرويتها من حبنا حتى أزهرت وبات لها أحلى شذى

حبيبي نور

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Firstly all thanks to ...

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For his gifts which never ends .

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For their encouraging and supporting me .

MY FRIENDS AND COLLEAGUS

For their honesty and lovely time we spend together .

PATIENTS AND HEALTHY CONTROLS

For their cooperation .

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Abstract

This study was conducted to measure serum levels of plasma lipids (TG, TC, HDL-c and LDL-c) in patients with chronic renal failure. Seventy fife random samples were collected from patients were alredy attended ALnaw Teaching Hospital during the period between January to march 2015 chosen randomly and seventy fife apparently healthy individuals were selected as controls.

Enzymatic method was used to estimate serum lipid profile levels manually using Biosystem kits and by using Mindary, and results were analyzed using (SPSS) computer program (T- test and ANova test).

The results showed that serum levels of TG,TC, and LDL were significantly increased (p-value = .000) (p-value = .001) (p-value = .000) respectively and the serum levels of HDL were significantly decreased (p-value = .000) in the Sudanese patients group.

TG serum level increasd between (101.5±35.8) in control to (132.2±56.3) in patients, TC also increased to (138.0±42.0) compared to control (121.6±23.0). LDL showed the same pattern and significantly increased to (133.8±43.1) in compare to control (92.8±37.8). HDL of patients decreased to (31.8±4.0) while in control was (37.0±5.4).

According to causes of renal failure the results of this study showed that; hypertension, diabetes and family history are the most common causes in Sudan.

The results of this study showed that there is a weak correlation between TG levels and duration of hemodialysis at (r = .223, p-value=.054). No correlation between TC (r=.166, p-value =.154), HDL-c (r=.166, p-value =.156) and LDL-c (r=.133, p-value =.254) levels and duration of dialysis was observed.

In conclution: the serum levels of TG,TC, and LDL significantly increased in Sudanese all patients, but serum levels of HDL significantly decreased in all patients subjected them to risk of many complications.

المستخلص

أجريت هذه الدراسة لمعرفة مستوى الدهون في بلازما مرضى الفشل الكلوى الذين يخضعون للغسيل الدموي. تم جمع 75 عينة دم من المرضى في الفترة ما بين يناير وحتى نهاية مارس 2015, تم إختيارهم بطريقة عشوائية من مستشفى النو مع 75 عينة من الأشخاص الأصحاء كمجموعة ضابطة أو تحكم لقياس مدى تأثير الغسيل الدموي على مستويات الدهون المصلية.

تم قياس مستويات الدهون بإستخدام طريقة إنزيمية بإستخدام جهاز ميندري , وتم تحليل البيانات بواسطة برنامج الحزمة الإحصائية للعلوم الإجتماعية.

توصلت النتائج الى ان هناك إرتفاع ملحوظ في مستويات كل من الكولسترول والجليسريدات الثلاثية و كولسترول الدهون البروتينية منخفضة الكثافة في المرضى الذين يخضعون للغسيل الدموي وكان الإحتمال الإحصائي للمقارنة (001, 0) (000, 0) و (000, 0) على التوالي . كما أوضحت النتائج أن هناك إنخفاض ملحوظ في مستوى كولسترول الدهون البروتينية مرتفعة الكثافة وكان الإحتمال الإحصائي للمقارنة (000, 0) وكانت النتائج كالآتي:

ارتفع مستوى الجليسريدات الثلاثية بين 101,5±35,8 لدى مجموعة التحكم الى132,2±56,3 لدى المرضى, وايضا ارتفع مستوى الكولسترول الى0, 138±42,0 مقارنة بمجموعة التحكم 121,6±23,0, كما اظهرت مستويات كولسترول الدهون البروتينية منخفضة الكثافة نتائج مشابهة حيث ارتفعت الى133,8± 43,1 مقارنة بمجموعة التحكم92,8±37,8 بينما انخفض مستوى كولسترول الدهون البروتينية مرتفعة الكثافة لدى المرضى31,8±4,0 مقارنة بمجموعة التحكم 37,0±5,4

وفقا لأمراض الكلى المزمنة, نتائج هذه الدراسة خلصت الى ان أمراض الضغط والسكري والعامل الجيني هما من اكثر الأسباب شيوعا في السودان.

كما أوضحت الدراسة أنه هناك علاقة ضعيفة بين إستمرارية الغسيل الدموي لفترة طويلة وتركيز الجليسريدات الثلاثية (معامل بيرسون للإرتباط= 0,223 ومستوى المعنوية= 0,054) وأنه لا علاقة بين إستمرارية الغسيل الدموي لفترة طويلة وتركيز الكولسترول (معامل بيرسون للإرتباط= 0,154 ومستوى المعنوية= 0,166), كولسترول الدهون البروتينية منخفضة الكثافة (معامل بيرسون للإرتباط= 0,156 ومستوى المعنوية= 0,166) و كولسترول الدهون البروتينية منخفضة الكثافة (معامل بيرسون للإرتباط= 0,254 ومستوى المعنوية= 0,133)

الخلاصة: تركيز مستويات الجليسريدات الثلاثية والكولسترول وكولسترول الدهون البروتينية منخفضة الكثافة يحدث بهم زيادة ملحوظة في مرضى الفشل الكلوي بينما يعانون من إنخفاض ملحوظ في مستوى كولسترول الدهون البروتينية مرتفعة الكثافة مما يعرضهم لخطر الاصابة بالعديد من المضاعفات.

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List of abbreviations

Abbreviation	Name
ARF	Acute renal failure
BMI	Body mass index
BP	Blood pressure
BUN	Blood urea nitrogen
CHD	Chronic heart disease
CRD	Chronic renal disease
CRF	Chronic renal failure
FCH	Familial compined hyperlipidemia
FH	Familial hypercholesterolemia
GFR	Glomerular filtration rate
HDL-c	High density lipoprotein cholesterol
IDL	Intermediate density lipoprotein
LDL-c	low density lipoprotein cholesterol
LPL	Lipoprotein lipase
TC	Total Cholesterol
TG	Triglycerides
VLDL	Very low density lipoprotein

Chapter I

Introduction

1.1. Introduction

Kidneys are paired, bean shaped organs located retro-peritoneally on either side of spinal column (Porveen and Michael 2000). Macroscopically each kidney is enclosed by fibrous capsule of connective tissue, when dissected longitudinally; two region can be clearly discerned: the outer region called the cortex and the inner one is named medulla. The pelvis of the kidney is a basin like cavity at the upper end of the ureter into which newly formed urine passes (Bishop *et al:,* 1982).

Acute renal failure is a sudden sharp decline in renal functions due to acute toxic or hypoxic insults to the kidneys (Bishop *et al:,* 1982).

Chronic renal failure is a clinical syndrome that occurs when there is gradual decline in renal functions over time (Porveen and Michael 2000).

The major forms of plasma lipids are: Fatty acids which are straight chain carbon compounds of variety lengths, they are be saturated, mono unsaturated or poly unsaturated (Williams and Braun 1995).

Triglycerides are molecules consist of one molecule of glycerol with three fatty acid molecules (Williams and Braun 1995)**.**

Phospholipids are polar , ionic lipids composed of 1.2 diacylglycerol and phosphodiester bridge link the glycerol back bone to some base usually nitrogenous such as choline, serine or ethanol amine (Williams and Braun 1995).

Cholesterol is saturated steroid of high molecular weight in it is esterifies form , it contain one fatty acid molecule (Williams and Braun 1995).

Lipoprotein are core of insoluble (non polar) cholesterol ester and triglycerides, surrounded by shell of protein, phospholipids and free cholesterol with their soluble (polar) group (Norbet and Tietz 1986).

Dyslipidemia is a very common complication of choronic renal failure (CRF) and are actively participate in the deterioration of renal function (Dipika *et al:,* 2013).

In Sudan feeding products which constitutes high amounts of calories beside low physical exercise are main factors which subjects Sudanese individuals to diseases as CRF.

1.2. Rationale:

Renal failure is a devastating medical, social and economic problem in Sudan and it is fatal unless treated properly. Recent studies were done in Sudan to determine the mortality rate causes of morbidity, they found that the mortality rate was 7.4% per year and the leading causes of death was infections (45%) and cardiovascular (22%) diseases.

According to the latest WHO data (2011) kidney disease deaths in Sudan reached 8.7% of total deaths, ranked the renal failure in 7^{th} top 20 causes of death in Sudan.

Patients with renal failure under hemodialysis are impairment in plasma lipids levels which raises the question of whether the impairment are related to chronic kidney disease or to the hemodialysis treatment.

This study was conducted to high light the effect of hemodialysis on TG, TC, HDL-c and LDL-c in Sudanese patients with renal failure under hemodialysis scince few published data concerned this lipid profile state of Sudanese patients with CRF are available.

1.3. Objectives :

1.3.1. General objectives:

To estimate the plasma lipids levels in renal failure patients under hemodialysis.

1.3.2. Specific objectives:

1- To assess the concentration of plasma lipids (TG,TC, HDL and LDL) in renal failure patients compared to control group.

2- To correlate the levels of plasma lipids with duration of dialysis.

Chapter II

Literature Review

2. Literature Review

2.1. The kidneys:

2.1.1. Renal anatomy:

The kidneys are paired, bean shaped organs located retroperitoneally on either side of spinal column (Porveen and Michael 2000). Macroscopically each kidney is enclosed by fibrous capsule of connective tissue, when dissected longitudinally; two region can be clearly discerned: the outer region called the cortex and the inner one is named medulla. The pelvis of the kidney is a basin like cavity at the upper end of the ureter into which newly formed urine passes (Bishop *et al:,* 1982).

2.1.2. Renal function:

The kidneys are the body filtering system, they remove waste materials and every day the two kidneys processes approximately 190 liters of blood by passing it around 225 kilometers of tubes and millions of mini-filters. The kidneys also help to maintain the body's balance of chemicals, including sodium and potassium, and produce some hormones and the active of vitamin D in addition to maintenance of water and acid-base balance (Bishop *et al:,*1982).

2.1.3. Renal failure:

2.1.3.1. Acute renal failure (ARF):

Acute renal failure is a sudden sharp decline in renal functions due to acute toxic or hypoxic insults to the kidneys. This has been defined as occurring when the GFR reduced to less than 10ml-min. this syndrome is subdivided into three types depending on the location of precipitation defect. In pre renal failure the defected lies in the blood supply before it reach the kidney (Porveen and Michael 2000). causes can include cardiovascular system failure, sever dehydration and consequent hypovolemia (Porveen and Michael 2000).

In primary renal failure the defect involves the kidney itself, the most common cause is acute tubular necrosis; other etiologies include vascular obstruction,

inflammation, glomerulonephrities. In post-renal failure the defect lies in the urinary tract after it exist the kidneys (Porveen and Michael 2000).

Toxic insult to the kidney may initiate acute renal failure. This include hemolytic transfusion reaction, heavy metals, solvent poisonings and analgesic and amino glycoside toxicities (Bishop *et al:,* 1982).

These conditions directly damage the renal tubules. Hypoxic insults include conditions that severely compromise renal blood flow, such as septic and hemorrhagic shocks, burns and cardiac failure (Bishop *et al:,*1982).

The outcome of acute renal failure is either recovery or, in the case of irreversible renal damage, progression to chronic renal failure (Bishop *et al:,*1982).

2.1.3.2. Chronic renal failure (CRF):

Chronic renal failure is a clinical syndrome that occurs when there is a gradual decline in renal functions over time (Porveen and Michael 2000).

Chronic renal failure is classified into four progressive stages. The first stage is marked by a period of silent deterioration in renal status (kidney function decrease but BUN and creatinine values stay within normal limits) (Porveen and Michael 2000).

The second stage is characterized by development of slight renal impairment (Bishop *et al:,*1982). a 50% reduction in normal function is necessary before BUN and creatinine values reflect the pathologic changes by increasing above reference ranges. The third stage is typified by impeding renal failure. Anemia begin to develop (due to the constant deficient in erythropiotin production), and systemic acidosis commences (due to the faulty clearance of endogenous metabolic acids) (Willand *et al;* 2000). The fourth and the last stage commences with the onset of the classic symptoms of the uremic syndrome (Bishop *et al:,*1982).

- **Signs and symptoms of chronic renal failure:**

Chronic renal failure (CRF) usually produces symptoms when renal function which measured as glomerular filtration rate (GFR) fall below 30 millimeters per minute (<30 ml/min). this is approximately 30% of the normal value. When glomerular filtration rate (GFR) drop to below 30 ml/min , signs of uremia may become noticeable. When the GFR falls below 15 ml/min most people become increasingly symptomatic (Willand and Ganong 2000).

Uremic symptoms can affect every organ system, most noticeably are the following:

- Neurological system: cognitive impairment, personality changes, and seizures.
- Gastrointestinal system: nausea, vomiting and food distase.
- Blood forming system: anemia due to erythropoietin deficiency, easy bruising and bleeding due to abnormal platelets.
- Pulmonary system: fluids in the lungs, with breathing difficulties.
- Cardiovascular system: chest pain due to inflammation of the sac surrounding the heart and pericardial effusion.
- Skin: generalized itching (Willand and Ganong 2000).

- **Stages of Chronic renal failure (according to GFR):**

1- Renal impairment (GFR falls to 30-70 ml/min).

2- Chronic renal failure (GFR less than 30 ml/min).

3- End stage renal (GFR less than 5 ml/min). (usually associated with signs and symptoms of ureamia (Chesley 1938).

- **Laboratory diagnosis of chronic renal failure:**

Chronic renal failure is diagnosed by the observation of combination of symptoms and elevated blood urea and creatinine levels in addition to other biochemical abnormalities; these abnormalities include:

Anemia, high level of parathyroid hormone, hypocalcaemia, hyperphosphatemia, hyperkalemia, hyponatraemia, low levelof bicarbonate and low blood plasma pH , with low creatinine clearance (Bleiler and Scredl 1972).

2.1.4. Dialysis:

Dialysis cleans the body of waste products in the body by use of filter system (Benjamin and longo 2015).

2.1.4.1. Types of dialysis:

There are two types of dialysis; 1) hemodialysis and 2) peritoneal dialysis. (Benjamin and longo 2015).

A- Hemodialysis:

Uses a machine filter called a dialyzer or artificial kidney to remove excess water and salts, to balance the other electrolytes in the body, and to remove waste products of metabolism. Blood is removed from the body and flows through tubing into the machine, where it passes next to a filter membrane .

A specialized chemical solution (dialysate) flows on the other side of the membrane. The dialysate is formulate to draw impurities from the blood through the filter membrane. Blood and dialysate never touch in the artificial kidney machine (Benjamin and longo 2015).

For this type of dialysis access to the blood vessels needs to be surgically created so that large amount of blood can flow into the machine and back to the body. Surgeons can build a fistula, a connection between a large artery and vein in the body, usually in the arm that allow a large amount of blood flow into the vein. This makes the vein swell or dilate, and its walls become thicker so that it can tolerate repeated needle sticks to attach tubing from the body to the machine. Since it takes many weeks or months for a fistula to mature enough to be used, significant palnning is required if hemodialysis is to considerd as an option (Benjamin and longo 2015).

If the kidney failure happens acutely and there is no time to build a fistula, special catheters may be inserted into the larger blood vessels of the arm, leg or chest. These catheter may be left in place for weeks. In some diseases the need for dialysis will be temporary, but if the expectation is that dialysis will continue for a prolonged period of time these catheters act as a bridge until a fistula can be planned, placed and mature. (Benjamin and longo 2015)

B- Peritoneal dialysis:

Uses the lining of the abdominal cavity as the dialysis filter to rid the body of waste and to balance electrolyte levels. A catheter is placed in the abdominal cavity through the abdominal wall by a surgeon and it is expected to remain in place for the long term. The dialysis solution is then dripped in through the catheter and left the abdominal cavity for a few hours and then is drained out. In that time waste products leech from the blood flowing through the lining of the abdomen (peritoneum) and attach themselves to the fluid that has been instilled by the catheters. Often patients instill the dialysis fluid before bedtime and drain it in the morning (Benjamin and longo 2015).

2.2. Plasma lipids:

The major forms of plasma lipids are:

2.2.1. Fatty acids:

Are straight chain carbon compounds of variety lengths, they are be saturated containing no double bonds , mono unsaturated with one double bond or poly unsaturated with more than one double bond. may be esterifies with glycerol to form triglycerides or non esterifies or free (Williams and Broun 1995)**.**

plasma free fatty acids liberated from adipose tissue are transported mainly bound to albumin to the liver and muscle where they are metabolized . they provide a significant proportion of energy requirement of the body (Williams and Broun 1995).

2.2.2. Triglycerides :

Triglycerides are molecules consist of one molecule of glycerol with three fatty acid molecules , it contain saturated fatty acids without bend, pack together closely and tend to solid at room temperature . The source to triglycerides in the body either exogenous (triglyceride molecule which constitutes 95% of fats stored in dietary) or endogenous (synthesized in the liver and other tissues). Triglyceride molecules allow the body to compactly store long carbon chain fatty acids for energy that can be used during fasting status between meals (Williams and Broun 1995).

The high energy tissue are transported in plasma mostly in the form of large triglyceride rich lipoprotein called chylomicrons and very low density lipoprotein (VLDL) when triglycerides are metabolized their fatty acids are released to the cells and converted into energy.The breakdown of triglycerides is facilitated by hormone sensitive lipoprotein lipase (LPL) as the triglycerides rich protein (chylomicrones and VLDL) are carried through circulation , the triglycerides are hydrolyzed as they come in contract with LPL hormones sensitive lipase which acts inside adipose (fat) cell to release free fatty acids from triglyceride stores for energy when dietary sources are unavailable or are insufficient for the body energy needs . Epinephrine and cortisol promotes triglycerides breakdown when the cell needs energy and glucose stored have been depleted (Williams and Broun 1995).

2.2.3.Phospholipids:

Phospholipids are polar , ionic lipids composed of 1.2 diacylglycerol and phosphodiester bridge link the glycerol back bone to some base usually nitrogenous such as choline , serine or ethanol amine . The most abundant phospholipids in human tissue are lecithin , phosphatidly-ethanol amine and phosphatidly serine . Phospholipids are important of cell membrane and also in lipoprotein (Williams and Broun 1995).

2.2.4.Cholesterol:

Cholesterol is saturated steroid of high moleculer weight in it is esteriffied form, it contain one fatty acid molecule . cholesterol is found almost exclusively in animals virtually all living cells and body fluids contain some cholesterol is used for manufacture and repair of cell membrane , for synthesis of bile acids and vitamin D , and the precursor of five major classes of steroid hormones . as with triglycerides there are both exogenous (dietary) and endogenous (primary) source of cholesterol, in the body about 70% of cholesterol is located in stationary pools located in the skin . adipose tissue and muscles cells , the remaining 30% or so forms a mobile pool that is transported in the form of lipoprotein and circulated through the liver . in the blood circulation two thirds of cholesterol is through the liver . in the blood circulation two thirds of cholesterol is esterified and one third is in a free form . (Williams and Broun 1995)

The risk factors for the blood vessels disease are strongly related to the fats (lipids) in the blood made up mainly of cholesterol and triglycerides individuals with abnormally high levels of the blood fats are at high risk for developing atherosclerosis (hardening of the arteries that supply blood to the heart or brain are narrowed) these organs are potentially deprived blood and hence deprived of oxygen , this will lead to serious defect in heart , the patient may be develop abnormal rhythms that may become lethal . inadequate blood supply to the brain causes stroke. (Williams and Broun 1995)

2.2.5. Plasma lipoprotein:

Lipoprotein are core of insoluble (non polar) cholesterol ester and triglycerides are surrounded by shell of protein , phospholipids and free cholesterol with their soluble (polar) group.

Lipids is relatively water insoluble , so they carried in body fluids as soluble protein complex , known as lipoprotein.

Lipoprotein is classified by their density which turn reflect the size. There are five major classes :

2.2.5.1. Chylomicron : Chylomicrons are the largest of the lipoproteins particles which transport exogenous lipid from intestine to all cells. They are rich in triglycerides and it's clearance time from the body is about 6 hours. (Bishop *et al;* 2000)

2.2.5.2. VLDL (very low density lipoprotein) : Like chylomicrons they rich in triglycerides which transport endogenous lipid, elevation in VLDL are evidenced by increased serum triglyceride concentration. (Bishop *et al:,* 2000)

2.2.5.3. IDL-c (intermediate density lipoprotein cholesterol) : Are usually un detectable in plasma it normally transient intermediate lipoprotein, forming conversion of VLDL to LDL-c (Norbet and Tietz 1986).

2.2.5.4. LDL-c (low density lipoprotein cholesterol) : LDL-c often called the bad cholesterol because it sticks to the walls of the blood vessels (Norbet and Tietz 1986).

Serum LDL-c is characterized by their high cholesterol , particularly in the form of cholesterol ester , this class of molecule is derived mainly from the breakdown of VLDL (Norbet and Tietz 1986).

The chemical composition of LDL-c is approximately 25%protein, 10%triglycerides , 8% unesterified cholesterol , 37% cholesterol ester and 22% phospholipids . LDL-c is small cholesterol rich lipoprotein containing only apoB , it has a longer life than its precursors . VLDL and IDL-c account for about 70% of the total cholesterol in plasma , it is taken up by specific receptors located on cell surface (LDL-c receptors or apoB/E receptors) (Norbet and Tietz 1986).

Although these are present on all cells , they are most abundant in the liver ,they recognize apoB and apoE and so can take up either LDL-c or IDL, after

entering cells IDL particles are broken down by lysosomes . Much of the released cholesterol contributes to membrane formation or in the adrenal cortex and gonads to steroid synthesis , most cells can synthesis cholesterol but several feedback mechanisms prevent its intracellular accumulation . If plasma LDL-c concentration are high some may also enter cells by a passive unregulated route, because of their small size LDL-c particles can infiltrate tissues such as those of the arterial wall and cause damage (Norbet and Tietz 1986).

The physiological function of LDL-c appears to be related to cholesterol transport , it has been suggested that the development of atherosclerosis , is significantly related to : increased LDL-c level, cigarette smoking , high blood pressure (PB above 140/90 mm/hg), low HDL-c cholesterol , family history of early heart disease , age men 45 or older (Norbet and Tietz 1986).

2.2.5.5. High density lipoprotein cholesterol (HDL-c) :

It is the smallest and most dense lipoprotein particle,it is important to transport cholesterol from cells to the liver . it is synthesized by both the liver and intestine it can exist as either disk shaped particles or more commonly spherical particles. Discoidal HDL-c typically contains two molecules of apo A-1 which form a ring around a central lipid bilayer of phospholipid and cholesterol. Discoidal HDL-c is represent nascent or newly secreted HDL-c and is the most active form in removing excess cholesterol from cells called reverse cholesterol transport, and is one of the main mechanisms proposed to explain the antiatherogenic property of HDL-c (Bishop and Edward 2005).

When discoidal HDL-c has acquired additional lipid, cholesteryle esterase and triglycerides form a core region between its phospholipids bilayer, which transforms discoidal HDL-c. HDL-c is highly heterogeneous separable into as many as 13 or 14 different subfractions. There are two major types of spherical HDL-c based on density differences: HDL_2 and HDL_3. HDL_2 particles are larger in size and richer in

lipid than HDL_3 and may reflect better efficiency in delivering lipids to the liver (Bishop *et al:,* 2000).

Table (2-1) shows the composition of the lipoprotein : (Philip *et al:,*1994)

Lipoprotein	Source	Protein	Cholesterol	TG	Phospholipids
Chylomicron	Intestine	1%	4%	90%	5%
VLDL	Liver	8%	25%	55%	12%
LDL	ViaVLDL	20%	55%	5%	20%
HDL	Liver	50%	20%	5%	25%

2.2.6. Lipid disease , prevention , diagnosis, and treatment:

Diseases associated with abnormal lipid concentration are referred to as dyslipidemia ,they can be caused directly by genetic abnormalities or through environmental/lifestyle imbalance or they can develop secondarily as a consequence of other disease . dyslipidemia are generally defined by clinical characteristic of the patient and the result of blood tests and do not necessarily defined the specific defect associated with the abnormality . many dyslipidemia however regardless of etiology are associated with chronic heart disease or arteriosclerosis (Bishop *et al;* 2000).

2.2.6.1. Arteriosclerosis :

The relationship between heart disease and lipid abnormality stems from the deposition of lipids , mainly in the form of esterified cholesterol in the walls of the arteries which starts with thin layers called fatty streaks , under certain condition the fatty streaks develop overtime into plaque which partially block blood flow (Bishop *et al:,*2000).

Deposits in vessele wall are frequently associated with increased serum concentration of LDL-c or decreased HDL-c cholesterol , high levels of cholesterol and triglycerides are caused by genetic abnormalities or due to

increased consumption of foods rich in fats and cholesterol , smoking , lack exercise or other disease that have effects on lipids metabolism such as diabetes , hypertension , obesity and others (Bishop *et al:,*2000).

2.2.6.2. Dyslipidemias :

Lipoprotiens are complex transported venicles for moving cholesterol , cholesterol esters , and triglycerides in the blood , disease starts associated with normal serum lipids are generally caused by malfunction in the synthesis , transport or catabolism of lipoprotein (Bishop *et al:,*2000). dyslipidemia can be divided into:

A- hyperlipoprotenemias :

which are diseases associated with elevated lipoprotein levels .

I- Hypercholesterolemia :

Is the lipid abnormality most closely linked to heart disease , one form of disease which is associated with genetic abnormalities that predispose affected individuals to elevated cholesterol levels is called familial hypercholesterolemia (FH) , homozygotes for FH patients can have total cholesterol concentration as high as 800 -1000mg/dl (20-26mmol/L) , while heterozygotes for FH tend to have total cholesterol concentration in the range of 300-600mg/dl (8-15mmol/L) (Bishop *et al:,* 2000).

II- Hypertriglyceridemia :

Hypertriglyceridemia can drive from a genetic abnormality and is then called familial hypertriglyceridemia or from secondary cause such as hormonal abnormality . hypertriglyceridemia is generally due to an imbalance between synthesis and clearance of VLDL in the circulation .

sever hypertriglyceridemia is generally caused by deficiency of LPL or by deficiency in lipoprotein c-II which is necessary cofactor for LPL activity (Bishop *et al:,* 2000).

III- Combined hyperlipidemia :

Combined hyperlipidemia is generally defined as the presence of elevated level of both serum total cholesterol and triglyceridemia , in the genetically derived form called familial combined hyperlipidemia (FCH), another rare genetic form of combined hyperlipidemia is called dysbetalipoproteinemia or type III hyperlipoproteinemia , the disease stems from an accumulation of cholesterol rich-VLDL and chylomicrons remnant due to defective catabolism of those particles . individual with type III will frequently have total cholesterol values of 200-300mg/dl (5-8mmol/L) and triglycerides of 300-600mg/dl (3-7mmol/L) (Bishop *et al:,* 2000).

B- Hypolipoproteinemias :

Hyplipoproteinemia are abnormalities marked by decreased lipoprotein concentration they fall into two major categories : hypoalphalipoproteinemia which associated with chronic heart disease (CHD),and hypobetalipoprotein-emia which associated associated with isolated low levels of LDL-c cholesterol and not associated with (CHD) (Bishop *et al:,* 2000).

2.3. Relationship between plasma lipids and renal failure:

Dyslipidemia (disturbances in lipoprotein metabolism) is a very common complication of choronic renal failure (CRF) and are evident even at the early stages of CRF and may actively participate in the deterioration of renal function. CRF Patients on hemodialysis have abnormalities in lipoprotein structure and metabolism and subsequently they associated with cardiovascular diseases which causes nearly 50% of all deaths in chronic hemodialysis patients. The underlying

pathophysiologic mechanisms of the relationship between dyslipidimia and progression of CRF are not yet fully understood but does not appear to be due to just one factor (Dipika *et al:,* 2013).

Chapter III

Materials and methods

3. Materials and Methods

3.1. Materials:

3.1.1. Study design:

This is a cross-sectional, control, and hospital case based study.

3.1.2. Study area and Study population:

The study was conducted in Alnaw hospital in Khartoum State. The study included patients with renal failure (males and females) under hemodialtsis.

3.1.3. Sample size:

This study included 75 patient with chronic renal disease under hemodialysis as cases and 75 apparently healthy subjects serve as control with normal kidney function.

Inclusion criteria:

Sudanese patients with renal failure and apparently healthy volunteers were included in this study.

Exclusion criteria:

Patients with renal failure and other disease that may affect the parameters under study were excluded from this study.

3.1.4. Ethical consideration:

Consent was taken regarding acceptance to participate in the study and reassurance of confidentiality. Before the sample was collected, the donors knew that this specimen was collected for research and the purpose of the research was explaned to eachpatients.

3.1.5. Data collection:

The clinical data were obtained from history. Clinical examinations and hospital follow up records and were recorded on a questionnaire sheet.

3.1.6. Sample collection and processing:

About 2.5 ml of venous blood were collected from each participant (both cases and control). The samples collected under aseptic conditions and placed in sterile heparin containers, and after mixing centrifuged for 5 minutes at 3000 RPM to obtain plasma, then The obtained plasma were kept at $^{-}20^{o}C$ till the time of analysis.

3.1.7. Requirements:

- Colorimeter, model JENWAY.
- Centrifuge
- Sterile heparin containers
- Disposable syringes
- 70% alcohol
- Tourniquets
- Cotton
- Micropipettes (automatic pipettes)
- Graduated pipettes
- Test tubes with different sizes
- Mindary

3.2. Methods:

3.2.1. Estimation of total cholesterol level using Mindary (Appendix I)

3.2.2. Estimation of triglycerides level using Mindary (Appendix II)

3.2.3. Estimation of HDL cholesterol using BIOSYSTEM (Appendix III)**.**

3.2.4. Estimation of LDL-c using BIOSYSTEM (appendix V)**.**

3.3. Quality control:

The precision and accuracy of all methods used in this study were checked by commercially prepared control sample before its application for the measurement of test and control samples.

3.4. Statistical analysis:

Data obtained from this study was analyzed using statistical package for the social science (SPSS).

Chapter IV

Results

4. Results

Table(4-1): Illustrated the ages, sex and family history of patients with renal failure. The results showed that the patients whose ages over fifty years were more susceptible for renal failure with the percentage of 73% compared to those with age below fifty years (27%).

The number of males in patients was (60%) and females was (40%).

Patients were was with family history disease constitute 37% while those who has no family history of disease constitute 62%.

Table (4-2): Represents the mean of body mass index (BMI) in both the study groups. BMI indicated that most of patients under dialysis are obese (29±4.1Kg /m^2), while the mean of control group is (25±31Kgm^2).

Table (4-3): Show that Hypertension and diabetes were significantly related to chronic renal failure the frequencies were renal failure patients is (48%), while diabetes was found in (32%).

According to **Table (4-4)** the levels of TG,TC, and LDL-c were significantly increased (p-value = .000) (p-value = .001) (p-value =.000) respectively and the serum levels of HDL were significantly decreased (p-value =.000) in the Sudanese patients under hemodialysis group compared to control group.

TG serum level increasd between (101.5±35.8) in control to (132.2±56.3) in patients, TC also increased to (138.0±42.0) compared to control (121.6±23.0). LDL showed the same pattern and significantly increased to (133.8±43.1) in compare to control (92.8±37.8). HDL of patients decreased to (31.8±4.0) while in control was (37.0±5.4).

Figure (4-1): The scatter showed that there is a weak correlation between TG levels and duration of dialysis at (r=.223, p-value=.054).

Figure (4-2): The scatter showed that no correlation between TC levels and duration of dialysis at (r=.166, p-value=.154).

Figure (4-3): The scatter showed that no correlation between HDL levels and duration of dialysis at (r=.166, p-value=.156).

Figure (4-4): The scatter showed that no correlation between LDL levels and duration of dialysis at (r=.133, p-value=.254).

Table (4-1): Ages, gender and family history of patients with renal failure disease:

Age of patients			Gender			Family history disease		
	No	**%**		**No**	**%**		**No**	**%**
25 – 50	20	27	Male	45	60	Yes	28	37
51 – 80	55	73	Female	30	40	No	47	62

Table (4-2): Body mass index(BMI) of patients with renal failure group and control group:

Variable	**Patients group N=75**	**Control group N=75**	**p-value**
BMI(Kg/m^2)	29±4.1 Kg/m^2 (19-30)	25±3 Kg/m^2 (19-30)	=0.02

Table (4-3): Distribution of patients according to other Associated Disease:

Disease	**Frequency**	**Percentage**
Hypertension	36	48%
Diabetes	24	32%
Hepatitis	15	20%

Table (4-4): The mean of plasma TG, TC, HDL and LDL levels in study groups.

Variable	**Case** Mean ± SD	**Control** Mean ± SD	**P-value**
Triglyceride (mg/dl)	132.2±56.3	101.5±35.8	.000
Total cholesterol (mg/dl)	138.0±42.0	121.6±23.0	.001
HDL-cholesterol (mg/dl)	31.8±4.0	37.0±5.4	.000
LDL-cholesterol (mg/dl)	133.8±43.1	92.8±37.8	.000

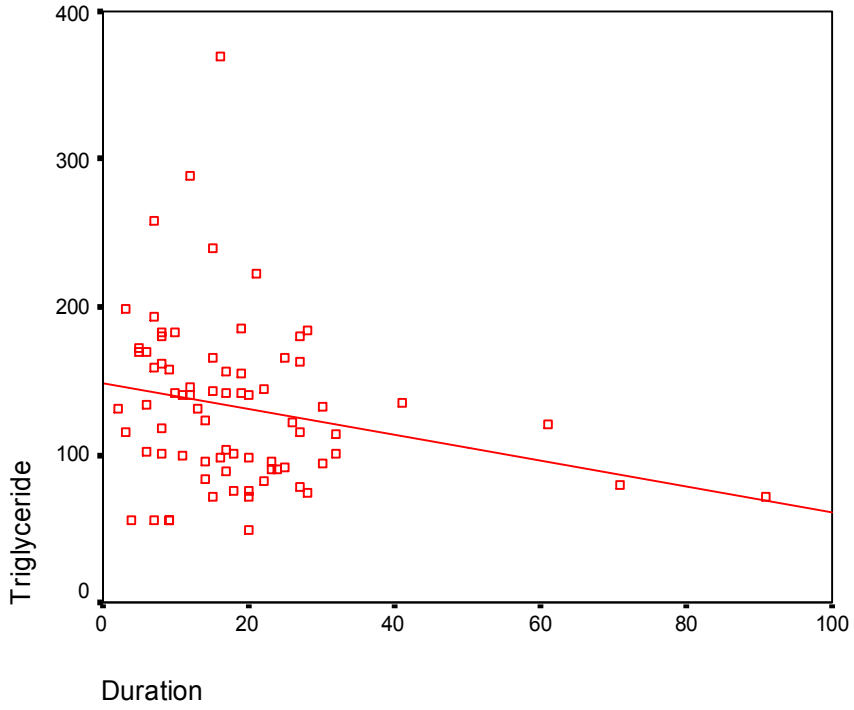

Figure (4-1): Scatter plot of correlation between TG level and duration of dialysis (r=.223, p-value=.054).

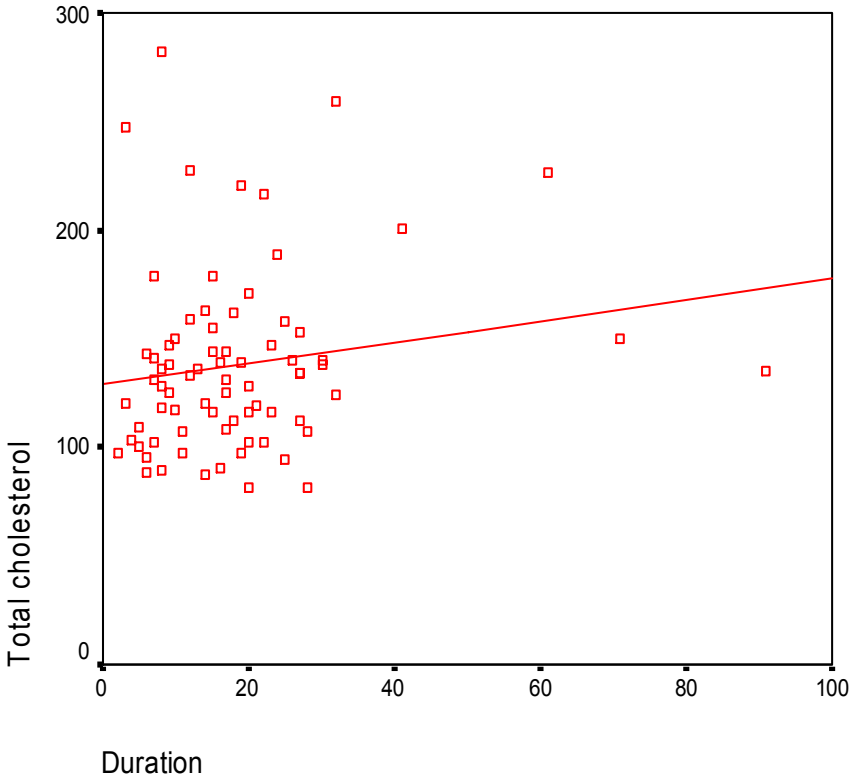

Figure (4-2): Scatter plot of correlation between TC level and duration of dialysis (r=.166, p-value=.154).

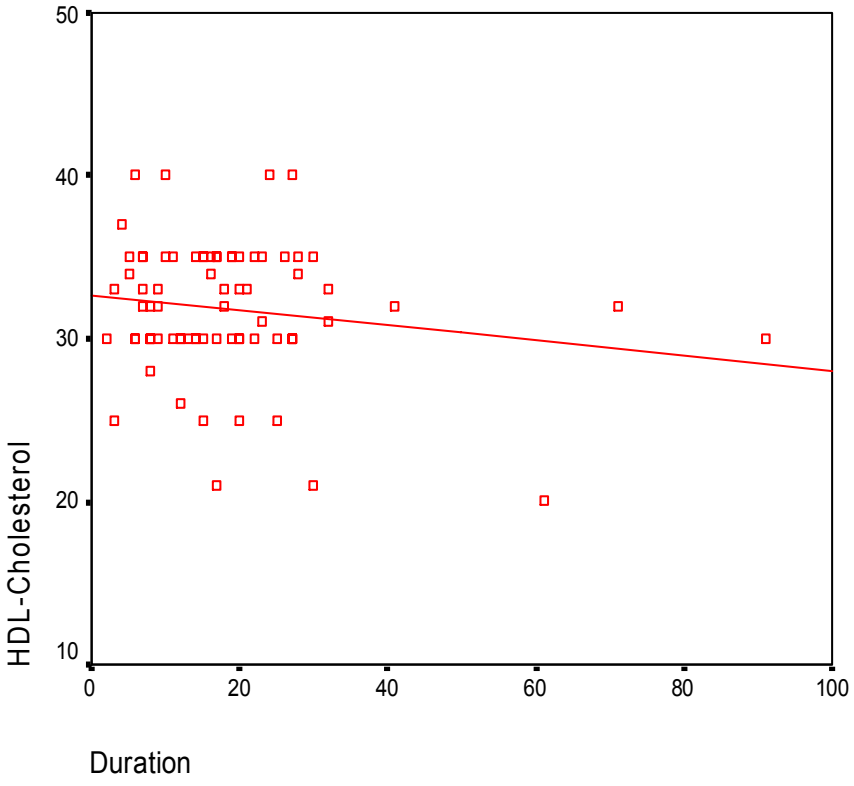

Figure (4-3): Scatter plot of correlation between HDL level and duration of dialysis. (r=.166, p-value=.156).

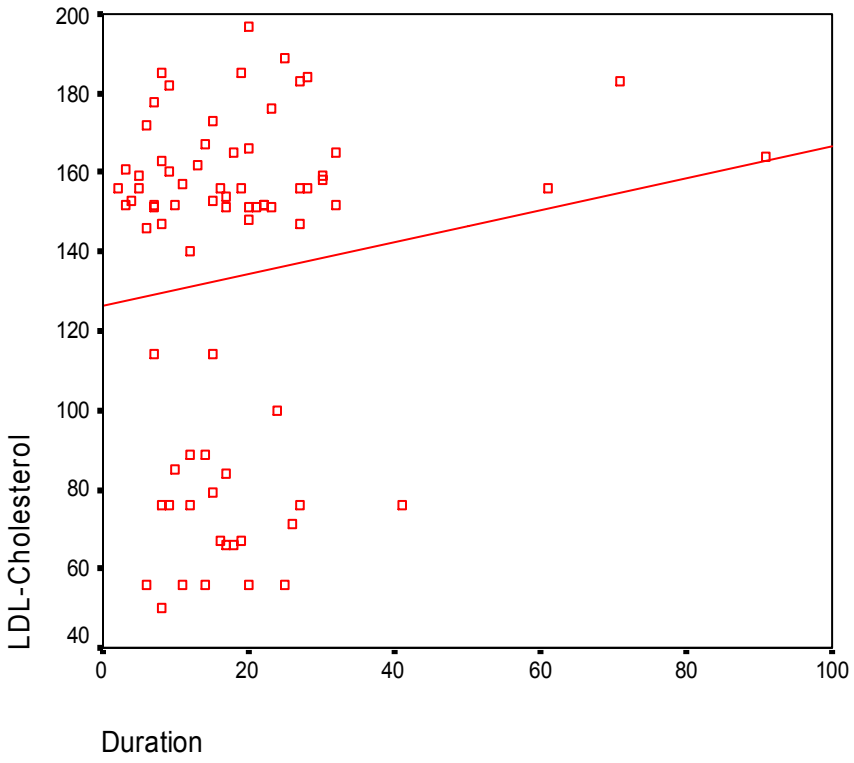

Figure (4-4): Scatter plot of correlation between LDL level and duration of dialysis (r=.133, p-value=.254).

Chapter V

Discussion, conclusion and recommendation

5.1. Discussion

From the finding of this study it appears that serum levels of TG,TC, and LDL were significantly increased and the serum levels of HDL were significantly decreased in patients under hemodialysis group in compare to control group.

This results agreed with a study carried by (Sathyian *et al:,* 2013) which showed that ; Plasma TG, TC and LDL concentration frequently elevated in patient with CRF under hemodialysis because heavy proteinuria alone or in combination with chronic renal insufficiency results in acquired LDL receptor deficiency, which play a central role in the genesis of the associated hypercholesterolemia (Sathyian *et al:,* 2013).

Also the results was in agreement with another studies carried by many authers (Dipika *et al;*2013), (Weam; 2008), (Nzere et ai; 2012) which finding confirmed that Chronic renal failure patients with hemodialysis are at greater risk of development of dyslipidemia characterized by hypertriglyceridemia, elevated TC and LDL-c levels and decreased HDL-c levels generated during the course of CRD which place them at risk of developing cardiovascular diseases.

According to figure (4-1) showed that, there was a weak correlation between TG levels and the duration of hemodialysis this result disagreed with another result, which showed that, there was a strong between TG levels and the duration of dialysis (Weam, 2008).

Also the findings of this study showed that there were no correlation between duration of dialysis and concentration of TC, HDL-c and LDL-c as appeared in figure (4-2) (4-3) (4-4). This results agreed with previous results which revealed that no significant correlation between serum lipid profile levels and the duration of hemodialysis (Weam, 2008).

5.1. Conclusion:

According to the results of this study it is concluded that:

1- Triglycerides, total cholesterol and LDL cholesterol concentration are significantly increased in patients with renal failure under hemodialysis.
2- HDL cholesterol concentration is significantly decreased in patients with renal failure under hemodialysis.

3- No significant correlation between serum lipid profile and duration of hemodialysis.

5.2. Recommendations:

From the findings of this study it is recommended that:

1- Hypertensive and diabetic patient should be monitored regularly to avoid complications of disease.

2- Overweight individuals should follow special diet to prevent themselves from the risk of diseases associated withobesity.

3- Chronic renal disease patients must monitor regularly their lipid profile to avoid developing of kidney disease

3- More studies should be carried out on the effect of hemodialysis on TG, TC, HDL-c and LDL-c Cholesterol concentration with large sample size and to cover area with high population.

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Appendices

Questionnaire

Sudan University of Sciences and Technology

Collage of graduate studies

Number ( )

Topic: The effect of hemodialysis on plasma lipids (TG, TC,HDL-c and LDL-c) in renal failure patients under hemodialysis.

A: General information:-

1- Name: …….. 3- Hospital: ……

2- Age: …….. 4- Sex: ……

B: Type of renal failure:-

1- Acute renal failure ( ) 2- Chronic renal failure ( )

C: Hemodialysis:-

1- Yes ( ) 2- No ( )

- If yes duration of dialysis: ……
- Body mass index (BMI): ……

D: Present history of disease:-

- Liver disease ( ) - Heart disease ( )

- Bone disease ( ) - Others ( )

E: Past history of disease:-

1- Hypertension ( ) 2- Liver disease ( )

3- Renal disease ( ) 4- Diabetes ( )

F: Family history of renal failure:-

1-Yes ( ) 2- No ( )

G: Investigations:-

1-Serum TG …… mg/dl.

2-Serum TC …… mg/dl.

3-Serum HDL …….. mg/dl.

4-Serum LDL ……... mg/dl.