بسم الله الرحمن الرحيم

Shendi University

Faculty of Graduate Studies and Scientific Research

Evaluation of the Serum Lipid Profile in Patients with Cholecystectomy in Almatama Locality

A thesis submitted for partial fulfillment for the requirement of M.Sc Degree in Medical Laboratory Sciences (Clinical Chemistry)

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الآيـــة

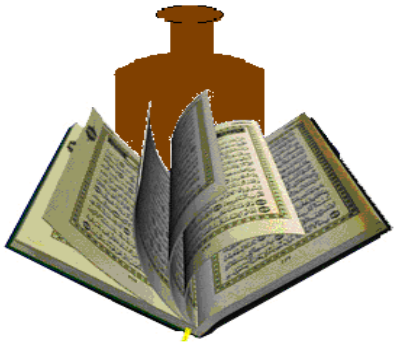
بسم الله الرحمن الرحيم

قـال تعالــي :

﴿ قَالُوا سُبْحَانَكَ لا عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ ﴾

صدق الله العظيم

سورة البقرة الآية (32)



Dedication

I dedicated this study to

My kind parents for their patience, helping and encouragement

My brothers for their patience and endless support

My dear husband who stand behind me

A family of academic medical laboratory at University of Shendi for their helping and endless patience.

The dearest people in my life with my respect.

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Firstly my deeply thanks for Allah liege lord who helped me to present this study

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I would like to express my thanks

Us .Aya mammon My great thanks also to

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List of Abbreviations

Abbreviations	Meaning
BAs	Bile Acids
CA	Colic Acid
Ca^{+}	Calcium
CCK	Cholecystokinin
CDCA	Chenodeoxy colic acid
C-H	Carbone-Hydrogen
CHD	Coronary Heart Disease
CL	Chloride
ESWL	Extra Corporal Shock-Wave Lithotripsy
FH	Familial Hypercholesterolemia
HCO_3	Bicarbonate
HDL	High Density Lipoprotein
K^{+}	Potassium
LACT	Lecithin Acyl Transferase
LDL	Low Density Lipoprotein
LPL	Lipoprotein Lipase
Na	Sodium
PUFAS	Poly Unsaturated Fatty Acid
SPSS	Statistical Package of Social Sciences
TC	Total Cholesterol
TG	Triglycerides
VLDL	Very Low Density Lipoprotein

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المستخلص

هذه دراسة وصفية تحليلية أجريت بين مجموعة اختبار ومجموعة ضابطة في محليةالمتمةخلال الفترة من مارس 2018 إلى اغسطس 2018 م ، والتي تهدف الي التحقيق من آثار استئصال الحويصلة الصفراوية على مستوى الدهون في المصل. لإجراء هذه الدراسة تم اختيار (40) من الذين اجريت لهم عمليات استئصال للحويصلة للصفراوية (مجموعة الاختبار) ، و (20) (مجموعة الضابطة) من الرجال والنساء الاصحاء.

وقد تم قياس الدهون الثلاثية الجلسرول والكوليستيرول والدهون ذات الكثافة العالية والدهون ذات الكثافة المنخفضة في المصل عن طريق وسيلة مقياس الالوان (كلوريميتر).

وقد تم تحليل النتائج التي تم الحصول عليها بواسطة الطرق الإحصائية باستخدام اختبار T. ولوحظ أنه يوجد فرق معنوي في متوسط مستوى الدهون الثلاثية الجلسرول، الكوليستيرول ، الدهون ذات الكثافة المنخفضة مع متوسط 163و 201 و 132 ملغم/ديسيلتر على التوالي ، مقارنة مع المجموعة الضابطة 111و 123و54 ملغم/ديسيلتر على التوالي. وخلصت الدراسة بأنّ استئصال الحويصلة الصفراوية له تأثير معنوي على مستوى الدهون. وايضاً اوضحت الدراسة ان ليس هناك فرق معنوي في متوسط الدهون ذات الكثافة العالية.

أيضاً اوضحت الدراسة أن ليس هناك تأثير معنوي للعمر و الجنس وتاريخ وطريقة الاستئصال على مستوى الدهون الدم.

Abstract

This is a cross sectional, descripitive study was conducted in Almatama town during period from March 2018 to August 2018. Aim to evaluate the effects of cholecystectomy on serum lipid profile. (40) Subject of cholecystectomy (test group), and (20) subject (control group) were enrolled in the study. Serum cholesterol ,triglycerides, HDL and LDL were measured in Blood sample collected from test and control groups using colorimeter.

Results were analyzed by statistical methods using T. test, It is noticed that there was significant difference in mean concentration of serum triglyceride , cholesterol, LDL among cholecystectomy (201.7mg/dl),(163.6 mg/dl) and (132.3 mg/dl) respectively in comparison with control group (123 mg/dl), (111.3 mg /dl) and(54.1 mg/dl) respectively with *p*.value values (0.000),(0.000), (0.000) respectively and insignificant difference in mean of HDL-c concentration in case and control(45.7mg/dl)and(51.3mg/dl) respectively with p.value(0.08).

The study concluded that cholecystectomy has significant effect on serum lipid TC, and LDL.

There was no significant effect of gender, age, procedure and history of cholecystectomy on lipid profile.

1.1 Introduction

Biological lipids are a chemically diverse group of compounds, the common and defining feature of which is their insolubility in water. The biological functions of the lipids are as diverse as their chemistry. Fats and oils are the principal stored forms of energy in many organisms. Phospholipids and sterols are major structural elements of biological membranes. Other lipids, although present in relatively small quantities, play crucial roles as enzyme cofactors, electron carriers, light absorbing pigments, hydrophobic anchors for proteins, “chaperones” to help membrane proteins fold, emulsifying agents in the digestive tract, hormones, and intracellular messengers. {1}

Lipoproteins constitute the body’s “petroleum industry and are divided depend on ultracentrifugation in to: Chylomicron are large, lipid-rich transport vessels that ferry dietary triglycerides, throughout the circulatory system to cells, finally docking at the liver as chylomicron remnants. The very low density lipoproteins (VLDL) are carrying triglycerides assembled in the liver to cells for energy needs or storage as fat. {2}

The low-density lipoproteins (LDL), rich in cholesterol, are deliver cholesterol to peripheral cells and liver after the triglycerides have been off-loaded. The high-density lipoproteins (HDL) are gathering up excess cholesterol for transport back to the liver. {2}

Lipids and lipoproteins, which are central to the energy metabolism of the body, have become increasingly important in clinical practice, primarily because of their association with coronary heart disease (CHD). {2}

Bile is a fluid-like substance that aids in fat digestion and absorption. The gallbladder stores about 50 ml of bile, which is released into the duodenum after cholecystokinin (CCK) secretion when fatty foods enter the digestive tract. After being stored in the gallbladder, the bile becomes more concentrated when compared to when it left the liver, thus increasing its potency and intensifying its effect on fats. Digestion occurs mostly in the upper intestine (the duodenum), where the bile is released. The compounds in bile may crystallize in the gallbladder, leading to gallstone formation. Gallstones may be excreted spontaneously. If they become lodged in the cystic duct, the stones cause severe abdominal pain. These small, hard stones are most commonly observed in individuals older than 40 years, especially women and the obese.

Bile acids (BAs) travel to the gallbladder during the interdigestive phase for storage, and to the descending part of the duodenum via the common bile duct through the major duodenal papilla during digestion. About 95% of the BAs that are delivered to the duodenum will be recycled by enterohepatic circulation. The presence of biliary acids in the intestines helps in the digestion of fats and other substances. When gallstones become symptomatic, they should be managed by surgical removal of the gallbladder, called cholecystectomy. If the gallbladder is removed, the bile in the liver will directly enter the upper part of the intestine. As a result, BA circulates faster, thus exposing the enterohepatic system to a greater BA flux. Lipid and BA metabolisms are functionally interrelated {3}.

Even though lipid and BA metabolisms are functionally related, how gallbladder removal affects lipids is not well understood. Therefore, the goal of this study was to determine the changes in serum lipid levels (serum TG, total cholesterol, HDL, and LDL) in patients after cholcystectomy.{3}

1.2 Rationale

The steps of lipid metabolism started by absorption in the intestine, and the absorption of lipid depends on bile salt from gall bladders, the end steps of cholesterol metabolism formation of bile salt and stored in gallbladder, according to these information; we want to evaluate the lipid status in cholecystectomy by measuring lipid profile.

1.3 Objectives

1.3.1 General objective:

Evaluation of the serum lipid profile in patient with Cholecystectomy.

1.3.2 Specific objective:

1. To estimation serum cholesterol levels in cholecystectomy and compare it with control group .
2. To evaluation of triglyceride levels in cholecystectomy and compare it with control group.
3. To detect of LDL cholesterol levels in cholecystectomy and compare it with control group .
4. To estimation of HDL cholesterol levels in cholecystectomy and compare it with control group.
5. To evaluate the effect of history of cholecystectomy on lipid profile.

2. Literature Review

2.1 Lipid

The term lipid is used to classify a large number of substances having very different physical - chemical characteristics, being its solubility in organic non-polar solvents the common property for their classification. Lipids are composed of carbon, hydrogen and oxygen atoms, and in some cases contain phosphorus, nitrogen ،sulfur and other elements. Fat and oils are the main exponents of lipids present in foods and in nutritional processes, being diverse fatty acids and cholesterol the most representative molecules due their important metabolic and nutritional function. The lipid having important role in the growth ،development and maintenance of tissues .A clear example of this important is the elevated fatty acid concentration present in nerve tissue, especially very long-chain polyunsaturated fatty acids.[4]

2.1.1 Lipids chemistry

Lipids commonly referred to as fat, have a dual role. They are composed of mostly Carbone-hydrogen (C-H) bonds؛ they are rich source of energy and an efficient way for the body to store excess calories. Lipids are also an integral part of cell membrane and there for also play an important structural role in cells. The lipids transported by lipoproteins, namely fatty acids, phospholipids, cholesterol esters. [2]

2.1.2 Biological Roles of Lipid

They are efficient energy sources, serve as thermal insulators, they are structural components of the cell membrane, serve as precursors for hormones (steroid hormones) and They also dissolve the vitamins, which are fat-soluble and assist their absorption . [5]

2.1.3 Lipid classification

2.1.3.1 Fatty Acids

Fatty acids, both free and as part of complex lipids, play a number of key roles in metabolism – major metabolic fuel (storage and transport of energy), as essential components of all membranes, and as gene regulators. In addition, dietary lipids provide polyunsaturated fatty acids (PUFAs) that are precursors of powerful locally acting metabolites. As part of complex lipids, fatty acids are also important for thermal and electrical insulation, and for mechanical protection. Moreover, free fatty acids and their salts may function as detergents and soaps owing to their amphipathic properties and the formation of micelles.[6]

Fatty acids are classified either: Saturated fatty acids are 'filled'(saturated)with hydrogen. Most saturated fatty acids are straight hydrocarbon chains with an even number of carbon atoms. The most common fatty acids contain 12–22 carbon atoms and unsaturated fatty acids either: Monounsaturated fatty acids have one carbon–carbon double bond, which can occur in different positions. The most common monoenes have a chain length of 16–22 and a double bond with the cis configuration. This means that the hydrogen atoms on either side of the double bond are oriented in the same direction. Tran's isomers may be produced during industrial processing (hydrogenation) of unsaturated oils and in the gastrointestinal tract of ruminants. The cis fatty acids have lower melting points than the trans fatty acids or their saturated counterparts. In polyunsaturated fatty acids (PUFAs) the first double bond may be found between the third and the fourth carbon atom from the omega carbon; these are called omega-3 fatty acids. If the first double bond is between the sixth and seventh carbon atom, then they are called omega-6 fatty acids. The double bonds in PUFAs are separated from each other by methylene grouping.[6]

2.1.3.2 Triglycerides

Triglycerides contain three fatty acids molecules attached to one molecules of glycerol by ester bonds. Because of large number of possible form of fatty acids ,each fatty acid in the triglyceride molecule can potentially be different in structure ,so produce many triglycerides form.[2]

Because the polar of hydroxyls of glycerol and the polar carboxylates of the fatty acids are bound in ester linkage, triglycerides are non-polar, hydrophobic molecules, essentially insoluble in water. [1]

2.1.3.3 Phospholipids

Phospholipids are complex lipids, similar in structure to triglycerides but containing phosphate and a nitrogenous base in place of one of the fatty acids. They fulfill an important structural role in cell membranes, and the phosphate group confers solubility on non polar lipids and cholesterol in lipoproteins. [7]

2.1.3.4 Cholesterol

Cholesterol is important in membrane structure and is the precursor of steroid hormones and bile acids. Cholesterol is present in dietary fat, and can be synthesized in the liver by a mechanism that is under close metabolic regulation. [8]Cholesterol synthesis located intracellular(cytosol) and the liver is the major site of cholesterol synthesis, other tissues: intestine, adrenal cortex, gonads and skin, it synthesis begin by the formation of acetoacetyle CoA by condensation of two molecules of Acetyl CoA, then the acetoacetyle CoA is Converted to mevalonate and the later converted to cholesterol. [9]

Cholesterol have two source either Endogenous cholesterol is formed in the body almost in all nucleated cells from Acetyl-CoA, or Exogenous cholesterol occurs only in food animal origin such as egg yolk, meat, liver and brain. [9]

Cholesterol is hydrophobic molecule so it is transported in plasma in the more soluble lipoprotein forms: LDL-C, VLDL and HDL-C and free cholesterol is removed from tissues by HDL-C and transported to be excreted by the liver. {9}

2.1.3.4.1 Function of cholesterol

Cholesterol can ,however be converted in the liver to primary bile acids such as cholic acid and chenodeoxycholic acid, which promote fat absorption in the intestine by acting as detergents A small amount of cholesterol can also be converted by some tissue, such as the adrenal gland, testis, and ovary to steroid hormones such as glucocorticoids, mineralocorticoids, and estrogens .Finally a small amount of cholesterol after first being converted to 7-dehtdrocholesterol, can also be transformed to vitamin D3 on irradiation of the skin by sunlight. {2}

2.1.4 Lipoprotein

Lipoproteins are typically spherical in shape and range in size from 10 to1200 nm. As the name implies lipoproteins are composed of both lipids and proteins, called apolipoproteins{2}.

2.1.4.1Chylomicrons

Chylomicrons are very large particles that carry dietary lipid. They are associated with a variety of apolipoproteins, including A-I, A-II,A-IV,B-48, C-I,C-II,C-III and E. {10}

2.1.4.2 Very Low Density Lipoproteins (VLDL)

VLDL is synthesis in the liver and carries lipids from liver to the blood to the peripheral tissues. It composed from lipids (Triacylglycerol, TG main component and Cholesterol esters and phospholipids.) and 10% Proteins (Apo B100, Apo E and Apo C (C11)). {9}

2.1.4.3 Intermediate Low Density Lipoproteins (IDL)

Carries cholesterol ester and triglycerides. It associated with Apo lipoprotein B-100, C-III and E. {10}

2.1.4.4 Low Density Lipoproteins cholesterol (LDL-C)

LDL-C is synthesized from VLDL. It consists of lipids (Cholesterol, cholesteryl esters, and phospholipids) and22% Apo proteins include apo B100, the primary function of LDL-C particles is to provide cholesterol to the peripheral tissues. They do so through:

- Deposition of free cholesterol on cell membranes.
- By binding to receptors on cell membranes that recognize Apo B100.{9}

2.1.4.5 High Density Lipoprotein cholesterol (HDL-C)

HDL-C also carries cholesterol ester. It is associated with Apolipoproteins A-I, A-II, C-I, C-II, C-III, D and E. {10}

2.1.5 Lipoprotein Physiology and Metabolism

The four major pathways involved in lipoprotein metabolism. The lipid absorption pathway, the exogenous pathway, and the endogenous pathway, which all depend on Apo B–containing lipoprotein particles, can be viewed as means to transport dietary lipid and hepatic-derived lipid to peripheral cells. {2}

2.1.5.1 Lipids absorption

Because fats are water insoluble, special mechanisms are required to facilitate the intestinal absorption of the 60to 130 g of fat per day. During digestion, pancreatic lipase, converts dietary lipids into more polar compounds with amphipathic properties. Thus triglycerides are transformed into monoglycerides and diglycerides; cholesterol esters are transformed into free cholesterol; and phospholipids are transformed into lysophospholipids. Short chain free fatty acids, with 10 or fewer carbon atoms, can readily pass directly into the portal circulation and are carried by albumin to the liver. The absorbed long chain fatty acids,

monoglycerides, and diglycerides are reesterified in intestinal cells to form triglycerides and cholesteryl esters. The newly formed triglycerides and cholesteryl esters are then packaged into Chylomicron, along with Apo B-48. {2}

2.1.5.1.2 Exogenous pathway

The synthesized Chylomicron in the intestine are secreted into the lymphatic ducts and enter the circulation by thoracic duct. After entering the circulation, Chylomicron inter act with proteoglycans, such as heparan sulfate, on the surface of capillaries in various tissues. The proteoglycans also promote the binding of lipoprotein lipase (LPL) which hydrolyzes triglycerides on Chylomicron in to fatty acid and glycerol are used for energy and excess fatty acids, particularly in fat cells, are re-esterified into triglycerides for long term storage in intracellular lipid drops. Hormone can release free fatty acids from triglycerides in stored fat when energy sources from carbohydrates are insufficient for the body's energy needs. The hormones epinephrine and cortisol play a key role in the mobilization and hydrolysis of triglycerides from adipocytes, whereas insulin prevents lipolysis by adipocytes and promotes fat storage and glucose utilization. During lipolysis of Chylomicron, there is a transfer of lipid and apolipoproteins onto HDL-C, and chylomicron are converted within a few hours after a meal into chylomicron remnant particles, these particles rapidly taken up by the liver through interaction of Apo E with specific remnant receptors on the surface of liver cells, then lysosomal enzymes break down the remnant particles to release free fatty acids, free cholesterol, and amino acids. Some cholesterol is converted to bile acids. Both bile acids and free cholesterol are directly excreted into the bile but not all of the excreted cholesterol and bile salt exit the body. As previously described, approximately half of the excreted biliary cholesterol is reabsorbed by the intestine, with the remainder appearing in the stool, as fecal neutral steroids. In the

case of bile acids, almost all of the bile acids are reabsorbed and reused by the liver for bile production**.** {2}

2.1.5.1.3 Endogenous pathway

Most triglycerides in the liver that are packaged into VLDL are derived from the diet after recirculation from adipose tissue. Only a small fraction is synthesized in the liver from dietary carbohydrate. VLDL particles, once secreted into the circulation, undergo a lipolytic process similar to that of Chylomicron. VLDL loses core lipids causing dissociation and transfer of apolipoproteins and phospholipids to other lipoprotein particles, primarily by the action of LPL. During this process, VLDL is converted to VLDL remnants, which can be further transformed by lipolysis into LDL-C. About half of VLDL is eventually completely converted to LDL-C, and the remainder is taken up as VLDL remnants by the liver remnant receptors. LDL-C particles are the major lipoproteins responsible for the delivery of exogenous cholesterol to peripheral cells due to the efficient uptake of LDL-C by the LDL-C receptors. Once bound to LDL-C receptors, they are endocytosed by cells and transported to the lysosome, where they are degraded. The triglycerides in LDL-C are converted by acid lipase into free fatty acids and glycerol and further metabolized by the cell for energy or are re-esterified and stored in lipid drops for later use. Free cholesterol derived from degraded LDL-C can be used for membrane biosynthesis, and excess cholesterol is converted by Acyl-CoA: cholesterol acyl transferase (ACAT) into cholesteryl esters and stored in intracellular lipid drops. {2}

2.1.5.1.4 Reverse Cholesterol Transport Pathway

The major roles of HDL-C are to maintain the equilibrium of cholesterol in peripheral cells by the reverse cholesterol transport pathway. HDL-C is believed to remove excess cholesterol from cells by multiple pathways. In the aqueous diffusion pathway, HDL-C acts as a sink for the small amount of cholesterol that

can diffuse away from the cells. Although cholesterol is an amphipathic lipid, it is soluble in plasma in micro molar amounts and can spontaneously dissociate from the surface of cell membranes and enter the extracellular fluid. Some free cholesterol will then bind to HDL-C in the extracellular space, and it becomes trapped in lipoproteins after it is converted to cholesteryl ester by lecithin cholesterol acyl transferase (LCAT), which resides on HDL-C. HDL-C can then directly deliver cholesterol to the liver by the SR-BI receptor and other receptors. Approximately half of the cholesterol on HDL-C is returned to the liver by the LDL-C receptor, after first being transferred from HDL-C to LDL-C by the cholesteryl ester transfer protein (CETP), which connects the forward and reverse cholesterol transport pathways. Cholesterol that reaches the liver is then directly excreted into the bile or first converted to a bile acid before excretion. Another pathway in which HDL-C mediates the removal of cholesterol from cells, involves the ABCA1 transporter. The ABCA1 transporter is a member of the ATP-binding cassette transporter family that pumps various ligands across the plasma membrane. The exact mechanism of the ABCA1 transporter is not known, but it is believed that the transporter modifies the plasma membrane by transporting a lipid, which then enables Apo A-I that has dissociated from HDL-C to bind to the cell membrane. Apo A-I then removes excess cholesterol and phospholipids from the plasma membrane of cells to form a discoidal-shaped HDL-C particle. The newly formed HDL-C is then competent to accept additional cholesterol by the aqueous diffusion pathway and is eventually converted into spherical HDL-C by the action of LCAT. Recently, ABCG1, another ABC transporter, has been described to facilitate the efflux of cholesterol to lipid-rich spherical HDL-C via a mechanism that appears to be different than the ABCA1 transporter. {2}

2.1.6 Disorders of plasma lipid

Hyperlipidemia refers to elevated levels of lipids and cholesterol in the blood, and is also identified as dyslipidemia, to describe the manifestations of different disorders of lipoprotein metabolism. Although elevated low density lipoprotein cholesterol (LDL-C) is thought to be the best indicator of atherosclerosis risk, dyslipidemia can also describe elevated total cholesterol (TC) or triglycerides (TG), or low levels of high density lipoprotein cholesterol (HDL-C). {11}

2.1.6.1 Hyperlipidemia

On the basis of causing factors Hyperlipidemia can be designated as either primary or secondary. According to Fredrickson familial Hyperlipidemia is classified into five types on the basis of electrophoresis or ultracentrifugation pattern of lipoproteins.

• Type I–Raised cholesterol with high triglyceride levels.

• Type II–High cholesterol with normal triglyceride levels.

• Type III–Raised cholesterol and triglycerides.

• Type IV–Raised triglycerides, atheroma and uric acid.

• Type V–Raised triglycerides. {12}

2.1.6.1.1 Primary Hyperlipidemia

- **Familial Hypercholesterolemia**

One form of the disease, which is associated with genetic abnormalities that predispose affected individuals to elevated cholesterol levels, is called familial hypercholesterolemia (FH). Homozygote for FH are rare (1:1 million in the population) and can have total cholesterol concentrations as high as 800 to 1,000 mg/dL. Heterozygote for the disease are frequently (1:500 in the population) because it is an autosomal co-dominant disorder; a defect in just one of the two copies of the LDL-C receptor can adversely affect lipid levels. Heterozygote tend

to have total cholesterol concentrations in the range of 300–600 mg/dL. In both homozygote and Heterozygote, the cholesterol is elevated with an increase in LDL cholesterol. These individuals synthesize intracellular cholesterol normally but lack, or are deficient in, active LDL-C receptors. Consequently, LDL-C builds up in the circulation because there are insufficient receptors to bind the LDL-C and transfer the cholesterol into the cells. Cells, however, which require cholesterol for use in cell membrane and hormone production, synthesize cholesterol intracellularly at an increased rate to compensate for the lack of cholesterol from the receptor mediated mechanism. {2}

- **Familial hypertriglyceridemia**

This condition, which has a prevalence of approximately 1 in 600, is usually associated with an excess of VLDL in plasma. It is usually not manifest until adulthood. The molecular basis is uncertain; there is increased hepatic synthesis of VLDL. Inheritance is autosomal dominant. Triglyceride concentrations are not usually higher than 5 mmol/L, but in severe cases, in which other factors (e.g.
Obesity and alcohol) are often implicated, they can be much higher; chylomicronemia can occur and only then are physical signs (e.g. eruptive exanthemata and lipaemia retinalis) usually present. {8}

It is uncertain whether there is an increased risk of CHD in patients with familial Hypertriglyceridemia, although HDL-C concentration is often reduced; in severe cases, there is a risk of pancreatitis. {8}

- **Familial combined Hyperlipidemia**

In this case the plasma lipids may have elevated, The Fredrickson's phenotypes seen in this condition include IIa, IIb and IV. Familial combined Hyperlipidemia maybe inherited as an autosomal dominant trait. The metabolic defect is unclear, although plasma Apo is often elevated due to increased synthesis; LDL-C and

VLDL Apo concentration is increased. The synthesis of VLDL triglyceride is increased in FCH and there may also be a relationship with insulin resistance. {8}

Children with FCH usually show hypertriglyceridemia and not the type IIa phenotype (unlike the situation found in FH). Unlike familial hypertriglyceridemia, plasma VLDL particles are usually smaller in FCH. {8}

- **Hyperalphalipoproteinemia**

It results in elevated plasma HDL cholesterol concentration, and can be inherited as an autosomal dominant condition or, in some cases, may show polygenic features. The total plasma cholesterol concentration can be elevated, with normal LDL cholesterol concentration. There is no increased prevalence of cardiovascular disease in this condition; in fact, the contrary probably applies, with some individuals showing longevity. Plasma HDL-C concentration is thought to be cardio protective, and individuals displaying this should be reassured. {7}

- **Dysbetalipoproteinemia**

This form is due to high Chylomicron and IDL-C (intermediate density lipoprotein). Also known as broad beta disease or dysbetalipoproteinemia, the most common cause for this form is the presence of ApoE E2/E2 genotype. It is due to cholesterol-rich VLDL (β-VLDL). Its prevalence has been estimated to be approximately 1 in 10,000. {12}

2.1.6.1.2 Acquired (Secondary) Hyperlipidemia

Acquired Hyperlipidemia (also called secondary dyslipoproteinemias) may mimic primary forms of Hyperlipidemia and can have similar consequences. They may result in increased risk of premature atherosclerosis or, when associated with marked hypertriglyceridemia, may lead to pancreatitis and other complications of the chylomicronemia syndrome.

The most common causes of acquired Hyperlipidemia are :

- Diabetes Mellitus

- Use of drugs such as diuretics, beta blockers, and estrogens

Other conditions leading to acquired Hyperlipidemia include:

Hypothyroidism, renal failure, nephrotic syndrome, alcohol and some rare endocrine disorders and metabolic disorders. {13}

2.1.6.1.3 Signs and Symptoms of Hyperlipidemia

Hyperlipidemia usually has no noticeable symptoms and tends to be discovered during routine examination or evaluation for atherosclerotic cardiovascular disease. Xanthoma, xanthelasma of eyelid, chest pain, abdominal pain, enlarged spleen, liver enlarged, high cholesterol or triglyceride level, heart attacks, higher rate of obesity and glucose intolerance, pimple like lesions across body, atheromatous plaques in arteries and arcussenile. {13}

2.1.6.1.4 Causes of Hyperlipidemia

A diet rich in saturated fat and cholesterol, other disorders as obesity, diabetes mellitus and hypothyroidism increase the risk of Hyperlipidemia.

Smoking and not exercising, excessive use of alcohol, certain drugs (steroids and β–blockers), hereditary factor, lipoprotein lipase mutations and in some cases during pregnancy. {13}

2.1.6.2 Hypolipoproteinemia

Hypolipoproteinemia, or low levels of lipoproteins, exist in two forms: hypoalphalipoproteinemia and hypobetalipoproteinemia. {2}

- **Hypoalphalipoproteinemia**

It is indicating an isolated decrease in circulating HDL-C, currently defined as an HDL cholesterol concentration less than 40 mg/dL(1.0 mmol/L) without the presence of hypertriglyceridemia {2}.

The term alpha denotes the region in which HDL-C migrate on agarose electrophoresis. There are several defects, often genetically determined, that are

associated with hypoalphalipoproteinemia. Virtually all of these defects are associated with increased risk of premature CHD. {2}

- **Tangier disease**

In Tangier disease, plasma HDL-C concentrations are reduced; clinically, the condition is characterized by hyperplastic, orange tonsils and the accumulation of cholesteryl esters in other reticuloendothelial tissues. The condition is due to a loss of function mutation in the gene that codes for the protein ABCA1, which normally stimulates the uptake of cholesterol into HDL-C. {8}

- **Betalipoproteinaemia**

In abetalipoproteinemia, there is a defect in the synthesis of Apo B; CM, VLDL and LDL-C are absent from the plasma. Clinically, there is malabsorption of fat, acanthocytosis, retinitis pigmentosa and anataxic neuropathy. {8}

- **Hypobetalipoproteinemia**

In this condition, there is partial deficiency of Apo B; CM, VLDL and LDL-C are present, but in low concentrations. {8}

2.2 Liver

The liver is the largest solid organ, the largest gland and one of the most vital organs that functions as a center for metabolism of nutrients and excretion of waste metabolites. Its primary function is to control the flow and safety of substances absorbed from the digestive system before distribution of these substances to the systemic circulatory system. {14}

2.2.1 Gallbladder

The gallbladder is a thin-walled sac usually placed between both hepatic lobes consisting of three` anatomic parts: the fundus, corpus, and infundibulum Anatomically the human gallbladder is fairly similar to mammalian species that have been subjected to experimental studies in dogs, cats, opossums, guinea pigs, prairie dogs and mice. In some species, like the rat, the gallbladder is absent. The

gallbladder ends in the cystic duct that is a passive conduit that in humans has a diameter of about 7mmwitha mucosa containing spiral valves (valves of Heister).This duct drains into the common bile duct without a sphincteric structure. {15}The common bile duct courses through the head of the pancreas ending in the sphincter of Oddi, as it penetrates theduodenal wall where it forms the ampulla of Vater. The commonbile duct has few unorganized muscle fibers. Neither the cystic duct nor the common bile duct has peristaltic motility. {15}

2.2.1.1 Location and function of the gallbladder

The gallbladder is found in the upper right corner of the abdomen beneath the liver. Its function is very easy to explain: It collects and concentrates the bile that is produced in the liver cells and carried by the bile ducts to the gallbladder. The gallbladder also controls the release of bile into the duodenum (small bowel), where it assists in the digestion of our food.{16}

The liver assists intestinal digestion by secreting 700 to 1200 ml of bile per day. Bile is an alkaline, bitter-tasting, yellowish green fluid that contains bile salts (conjugated bile acids), cholesterol, bilirubin (a pigment), electrolytes and water. It is formed by hepatocytes and secreted into the canaliculi. Bile salts, which are conjugated bile acids, are required for the intestinal emulsification and absorption of fats. Having facilitated fat emulsification and absorption, most bile salts are actively absorbed in the terminal ileum and returned to the liver via the portal circulation for resecretion as follows:

Bile has two fractional components: the acid-dependent fraction and the acid-independent fraction. Hepatocytes secrete the bile acid-dependent fraction of the bile. This fraction consists of bile acids, cholesterol, lecithin (a phospholipid), and bilirubin (a bile pigment). The bile acid-independent fraction of the bile, which is secreted by the hepatocytes and epithelial cells of the bile canaliculi, is a bicarbonate-rich aqueous fluid that gives bile its alkaline pH{14}

Bile acids are important physiological agents required for disposal of cholesterol and absorption of vitamins and fats. Bile acids are synthesized from cholesterol in the liver. Enter hepatic circulation of bile acids are very efficient and plays an important physiological role in lipid absorption and secretion, and regulation of bile acid biosynthesis and cholesterol homeostasis. Conversion of cholesterol to bile acids requires 15 different enzymatic steps. Four cytochrome P450 enzymes play important roles in bile acid biosynthesis. The classic bile acid biosynthesis pathway starts with modification of the sterol ring and followed by side chain cleavage reactions to synthesize cholic acid (CA) and chenodeoxy cholic acid (CDCA), the primary bile acids in most species. {17}

2.2.1.2Bile composition:

Bile mainly consists of water, in which there are organic and inorganic substances in suspension, dissolved, or in equilibrium between both states. In bile samples, collected from the human common bile duct, the concentrations of the inorganic electrolytes sodium (Na^+), potassium (K^+), calcium (Ca^{2+}) and bicarbonate (HCO_3^-) are slightly higher than their plasmatic concentrations, whereas biliary chloride (Cl) concentrations are slightly lower than these found in plasma. BAs concentrations range between 2 and 45 mmol/L. The concentrations of biliary pigments range from 50 to 200 mg/100 mL. Proteins and peptides, such as glutathione, are also found in bile. [36] It is also possible to detect glucose and small amounts of endogenous substances such as thyroid and steroid hormones. {18}

Human bile is rich in lipids. Thus, phospholipids concentrations seem to range between 25 and 810 mg/100 mL, whereas these of cholesterol vary between 60 and 320 mg/100 mL, with average ratios of phospholipids to BA of 0.3 and cholesterol to BA {18}

2.2.1.3 Bile flow

The mean basal flow of bile in humans is approximately 620 mL/d. One portion of this flow (220 mL/d, 35%) is determined by the secretion of BAs and is called the BAs-dependent canalicular fraction -BADFc-[8]. In addition, there is a linear correlation between the amount of BAs secreted into bile and the amount of water that follows them (7-25ml/mmol) {17}

2.2.1.4Pathology of the gallbladder

2.2.1.4.1Gallstone

Gallstones are calculi formed in the gallbladder or less commonly in the biliarytree. The term cholelithiasis (derived from the Greek: chol-, "bile" + lith-,"stone" + iasis-, "process") describes the presence of gallstones, whilst cholecystolithiasis describes the presence of stones in the gallbladder and choledocholithiasis is stones in the bile ducts. Gallstones may cause symptoms, and hence gallstone disease, either within the gallbladder, or if they migrate, the biliary tree or small bowel {19}

2.2.1.4.2Gallstone development and pathophysiology

Depending on their composition, gallstones are often divided into three major types: cholesterol-, black pigment- and brown pigment stones. Black pigment stones are more common among patients with haemolytic diseases (hereditary spherocytosis, sickle cell anaemia, and Thalassemia) and liver cirrhosis {20}.

Brown stones are often caused by stasis and infection in the biliary system. In the Western world, the major constituent of gallstones is cholesterol, which comprises 50-98 % of the dried substance of the stone. Other constitues may include fatty acids, triglycerides, proteins, polysaccharides, as well as calcium bilirubinate, calcium carbonate and calcium bicarbonate. Gallbladder stones vary in size from less than a millimeter up to a few centimeters in diameter. Most patients only

harbour stones in the gallbladder, but in 10-15% the stones have migrated into the common bile duct.{21}

2.2.1.4.3Risk factors

The most common risk factors for developing gallstone disease are increasing age, female gender and ethnicity.{22}

- **Estrogen therapy**

In a large Danish study Jorgensen et al showed that differences in prevalence between men and women could be explained by estrogen therapy and childbirth {23}. Novacek in Austria reached the same conclusion.{24}

- **Obesity**

Several studies identify obesity as a major risk factor for developing gallstones gender disregarded, although the relationship is usually stronger in women than in Men .{23}

Biliary hypersecretion of cholesterol, which is an important determinant in gallstone formation, is profoundly exacerbated by obesity. Rapid weight loss is also associated with an increased risk of developing gallstones.{25}

- **Smoking**

Data in the literature is conflicting as to whether smoking is predisposing or protective. It has been suggested that smokers are protected against the development of gallstones through a mechanism which leads to a decrease in prostaglandin synthesis and mucus production in the gallbladder epithelium.{26}

- **Diabetes mellitus**

It has been suggested that gallstone development is associated with common metabolic disorders such as, obesity, diabetes mellitus and dyslipidemia which supports the hypothesis that gallstone disease is part of the metabolic syndrome {27}
Another pathophysiological link between insulin resistance and gallstone development is the increase of cholesterol saturation in gallbladder bile. This is

related to an increase in body cholesterol synthesis and hypersecretion of biliary cholesterol as observed in obesity.[28]This idea was supported by the findings in epidemiological studies, but the matter is controversial since other studies found no such correlation.[28]

- **Physical activity**

The exact role that physical activity plays in preventing the formation of gallstones is unknown. One suggested mechanism behind the protective effect of physical activity is a reduced colonic transit time associated with a reduced intestinal bile salt dehydroxylation and an increased gallbladder motility.[29]

2.2.1.4.3Complications of gallstone

Most studies show that approximately 20% of gallbladder stones are- or become symptomatic. In the symptomatic gallstone population complications to the disease are more common. [30]

- ✓ **Acute cholecystitis**

The cystic duct connects the gallbladder to the common bile duct. When it is obstructed for a longer time period by a gallstone, an acute inflammatory response occurs.

The patient usually presents with fever, pain and a localized tenderness in the upper right quadrant or epigastrium.[31]

- ✓ **Jaundice**

If gallstones migrate from the gallbladder to the common bile duct, they can cause an obstruction of the bile flow to the small intestine.[32]

- ✓ **Acute pancreatitis**

Small gallstones [33], or so called microlithiasis [34], are generally the cause of acute gallstone pancreatitis. [33]

- ✓ **Gallstone ileus**

In progressive acute cholecystitis, the inflammation, in combination with stones may lead to a fistula between the gallbladder and the small intestine or stomach. If they are large enough, the stones may become impacted in the small bowel causing obstruction.

This condition accounts for 1-4% of all cases with small bowel obstruction.[35]

- ✓ **Gallbladder carcinoma**

Gallstone disease is considered to be the most important risk factor in the development of gallbladder carcinoma. [36]

2.2.1.4.4Treatment

– Oral dissolution of gallstones using drugs

– Shock wave treatment

– Surgery

– Adjuvant dietary me .[16]

2.2.1.5Cholecystectomy

Surgical removal of the gallbladder is one of the most common and safest surgical procedures.[16]

More than a century after the introduction of the open cholecystectomy by Karl Langenbuch, the removal of the gallbladder is the optimal treatment of gallstone disease. However, alternative therapies do exist. These include oral dilution therapy and ESWL (Extra corporal shock-wave lithotripsy) alone or in combination.[37]

Post-Cholecystectomy syndrome

The most commonly used indication for cholecystectomy is abdominal pain, but unfortunately some patients still experience pain after an operation. Unchanged, worsened or even new symptoms after cholecystectomy are major problems. Persistent pain or the so called “Post-cholecystectomy syndrome” varies in

frequency between 6-47%15, even after excluding causal factors such as retained common bile duct or cystic duct stones, postoperative bile duct stenosis and sphincter Oddi dysfunction.[38]

2.3 Previous study

The study done by **Moazeni M**, to evaluate the effects of cholecystectomy on plasma lipids. The total serum cholesterol, HDL, and LDL level no significant differences after one year (P = 0.126, P =0. 063, and P =0.075, respectively). However, a significant increase in TG levels was observed during the study ($P \leq 0.001$). [39]

Other study done by.**Zahra Seaf**in Iran at 2017 to evaluate the lipid profile in cholecystectomy patients, and they found, there was no significant difference was found regarding serum concentration of triglycerides, total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) to LDL proportion, while, HDL concentration represented a significant reduction after the cholecystectomy.[40]

Study done by **Batajoo H, et al** In Nepal in 2013 to analyze of serum lipid profile in cholestasis patient, age group >40 years serum LDL of gallstone patients were statistically significantly raised (P<0.05) (95% CI -22.077; -850) compared with controls and serum total cholesterol and triglycerides were not statistically significantly high (P >0.05). Serum HDL and VLDL were lower in gallstone patients but not statistically significant (P >0.05) compared to control group .[41]

Study done by **Rasheed A**, to evaluate Lipid profile and hematological changes in gallstone patients, they found there was significant (p<0.05) elevation in total cholesterol, triglyceride and LDL levels in patients with cholelithiasis when compared to the healthy control persons. While the level of serum HDL was

significantly ($p<0.05$) decreased in gallstone patients as compared with healthy individuals. [42]

3. Material and methods

3.1 Study design:

This a descriptive, cross sectional study conducted in period of march to July 2018 and aimed to determine the association between cholecystectomy and serum lipid profile.

3.2 Study area:

This study was done in Almatama town which is located in river Nile state, 180 far away from Khartoum state.

3.3 Study population:

Patient with cholecystectomy in Almatama Locality

3.4 Sample size

A total of 40 patients with a cholecystectomy, males and females as a test group and 20 healthy individual's males and females as a control group their age vary from 27_55 years were enrolled in the study.

3.5 Sampling:

5 ml venous blood was collected from patients in a plan container (container without anticoagulant).

3.6 Ethical consideration:

Each cholecystectomy patient was told before taken sample and they all agree to participate in this study.

3.7 Tools of data collection:

Information from a cholecystectomy patient was collected in preformed questionnaire

3.8 Methodology:

Enzymatic, liquid, colorimetric test for total cholesterol, triglyceride, HDL and LDL

3.9Materials:

Syringe, 70% alcohol, plan container, centrifuge, pipettes, cholesterol reagent, triglyceride reagent, HDL precipitation cholesterol reagent, LDL precipitation reagent, tubes, and colorimeter.

Principle of methods:

Total cholesterol:

Cholesterol ester $+H_2O \xrightarrow{CHE}$ Cholesterol +fatty acid

Cholesterol $+O_2 \xrightarrow{CHO}$ Cholesterol-3-one $+H_2O_2$

H_2O_2 + chromogen $\xrightarrow{POD}$ H_2O + colour compound (pink colour).

See App (1)

Triglyceride :

TG + $H_2O \xrightarrow{lipase}$ fatty acid + glycerol

Glycerol + ATP $\xrightarrow{glycerol\ kinase}$ glycerol phosphate + ADP

Glycerol phosphate + $O_2 \xrightarrow{glycerol}$ Dihydroxy Acetone phosphate $+H_2O_2$

H_2O_2 + chromogen $\xrightarrow{peroxidase}$ colour compound + H_2O

See App (2)

HDL:

Lipoprotein rather than HDL is precipitated from sample by using polyanion and divalent cation (polyanion is bind to positive charge group of these lipoprotein and divalent cation bind to negative charge group) forming aggregation and precipitate which is sediment using centrifugation, then HDL in supernatant is measured using enzymatic T.C method.

See App (3)

LDL

Low density lipoproteins (LDL)in the sample precipitate with polyvinyl sulphate.

Their concentration is calculated from the difference between the serum total cholesterol and the cholesterol in the supernatant after centrifugation. The

cholesterol in spectrophotometrically measured by means of the coupled reaction described below.

Cholesterol esters + H_2O $\xrightarrow{\text{chol.estrasec}}$ cholesterol+ Fatty acid

Cholesterol+1/2 O_2+H_2O $\xrightarrow{\text{col.oxidase}}$ cholestenone +H_2O

$2H_2O$+4-Aminoantipyrine + phenol $\xrightarrow{\text{peroxidase}}$ quinoneimine +$4H_2O$

See App (4)

3.9 Data analysis:

Data was analyzed by using SPSS (statistical packaged for social science) computer program.

4. Results

Table (4.1):mean concentration of cholesterol, triglycerides, LDL, HDL among case and control

	Frequency	Cholesterol	Triglycerides	HDL	LDL
Case	40	201.7	163.6	45.7	132.3
Control	20	123.0	111.3	51.3	54.2
p. value		0.000*	0.000*	0.080	0.000*

*p. value ≤ 0.05

Table (4.2): mean concentration of cholesterol, triglycerides, LDL, HDL in case group according to sex

Gender	Frequency	Cholesterol	Triglycerides	HDL	LDL
Male	3	168.3	166.4	37.4	114.0
Female	37	204.4	163.3	46.4	133.8
p. value		0.293	0.929	0.137	0.490

p. value≤ 0.05

Table (4.3): mean concentration of cholesterol, triglycerides, LDL, HDL in case group according to age

	Frequency	cholesterol	triglycerides	HDL	LDL
Less than40	14	182.1	152.9	49.1	114.9
More than 40	26	211.8	169.8	43.9	141.7
P .value		0.123	0.344	0.119	0.086

p. value≤ 0.05

Table (4.4): mean concentration of cholesterol, triglycerides, LDL, HDL in case group according to history of Cholecystectomy

	Frequency	Cholesterol	Triglycerides	HDL	LDL
1-4	30	200.3	161.1	45.8	130.5
5-9	6	187.3	147.1	43.9	120.3
10-14	4	233.8	206.5	46.8	163.9
P value		0.438	0.232	0.886	0.333

p. value≤ 0.05

Table (4.5): mean concentration of cholesterol, triglycerides, LDL, HDL in case group according to procedure of cholecystectomy

	Frequency	Cholesterol	Triglycerides	HDL	LDL
Laparoscopy	2	222	182.5	53.3	139.7
Surgery	38	200.6	162.6	45.3	131.9
p. value		0.608	0.628	0.279	0.823

p. value≤ 0.05

Table (4.6) : mean concentration of cholesterol, triglycerides, LDL, HDL in hypertensive and non-hypertensive case subject

Hypertension	Frequency	Cholesterol	Triglycerides	HDL	LDL
Yes	9	245.9	192.3	48.1	166.6
No	31	188.8	155.2	44.9	122.4
p. value		0.006*	0.78	0.417	0.011*

*p. value≤ 0.05

Table (4.7): mean concentration of cholesterol, triglycerides, LDL, HDL in diabetes mellitus and non-diabetes case subject

Diabetes	Frequency	Cholesterol	Triglycerides	HDL	LDL
Yes	8	228.1	195.2	44.7	158.4
No	32	195.1	155.7	45.9	125.8
p. value		0.140	0.072	0.756	0.079

p. value≤ 0.05

5.1 Discussion

A cross sectional, descriptive study conducted during the period from March to July 2018 in Almatama locality, performed to evaluate TC, TG, HDL-C and LDL-C in both male and female cholecystectomy patients with age range from 27-60years in comparison with health individuals, (40) cholecystectomy patients and matched 20 healthy control were included in this study.

Study result shows there were significant differences in mean concentration of serum TC, TG and LDL-C levels among cholecystectomy patients (201.7 mg/dl),(1163.6 mg/dl) and (132.310 mg/dl) respectively when compared with controls (123.0mg/dl),(111.3 mg/dl) and (54.2 mg/dl) respectively with P. Value (0.000), (0.000) and (0.000) respectively. And there was no significant effect of cholecystectomy on HDL because the mean of HDL in test group was (45.7mg/dl) when compared with control group of (51.3mg/dl) with p.value of (0.08).

These results were agree with study conducted byRasheed A, [42] they found there was significant ($p<0.05$) elevation in total cholesterol, triglyceride and LDL levels, and agreement with Batajoo H, et al [41] In LDL of statistically significantly raised ($P<0.05$), and disagreement with Moazeni M,[39]The total serum cholesterol, HDL, and LDL level n ($P >0.05$),and Zahra Seaf [40]in no significant difference was found regarding serum concentration of triglycerides, total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL), p.value($p>0.05$).

And disagreement with Batajoo H, et al[41] in serum total cholesterol and triglycerides were ($P>0.05$).

The study showed that there was significant effect of hypertensive on serum TC, LDL-C level with p.value (0.006) and (0.011) respectively.

Our study results show there was no significant difference in mean concentration of serum TC, TG,HDL-C and LDL-C levels between male and female , among male (168.3mg/dl) , (166.43mg/dl) , HDL (37.43mg/dl) and LDL (1143mg/dl) respectively when compare with female (204.3mg/dl) ,(163mg/dl) ,(46.3mg/dl) ,(133.7mg/dl) respectively with p.value (0.293,0.929, 0.137and0.490) respectively. Also our result show there was no significant difference in mean concentration of serum TC, TG,HDL-C and LDL-C levels between age groups: less than (40 years)and more than (40 years) because the P.value were > 0.05.And there were no significant effects of history ,procedure of cholecystectomy , and diabetes p.value > 0.05.

5.2 Conclusion

On the basis of the study results we can conclude the following:

- ✓ There was statistical significant difference in mean concentration of total cholesterol, triglyceride, LDL-C in cholecystectomy patients when compare with health subjects, which indicate that serum lipid level is effected by cholecystectomy.
- ✓ There was statistical significant effect of hypertension on serum TC, LDL-C level
- ✓ No significant effects of gender, age, procedure and history of cholecystectomy on means of lipid profile.

5.3 Recommendations

After Cholecystectomy some people develop watery stools .in most cases, the diarrhea no more than a few week to a few month .there are a few things you might consider:

- ✓ Patients must help to understand why they having diarrhea
- ✓ Go easy on the fat avoid high-fat foods, fried and greasy foods.
- ✓ Increase the fiber in your fat. this can help normalize bowel movements
- ✓ Meals must be smaller and more frequent
- ✓ patients must be avoid foods that tend to worsen diarrhea such as caffeine, dairy products and very sweet food
- ✓ Patients must contacts their doctors if the diarrhea doesn't gradually go away or becomes more sever, or loss weight
- ✓ Other study must be conducted with large sample size with other parameters.
- ✓ Patients of Cholecystectomy must measure their lipid profile regularly.

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6.2 Appendixes

بسم الله الرحمن الرحيم

جامعة شندي

كلية الدراسات العليا والبحث العلمي

استبيان حول تأ ثير استئصال الحويصلة الصفراوية

على مستوى الدهون في المصل

الاسم : ..... السكن : .....

الجنس : ..... العمر : .....

الوزن : ..... الطول : .....

متي اجريت العملية : .....

طريقةالاستئصال : 1. جراحه ( ) 2. منظار ( )

الأمراض التي تعاني منها :

سكري : نعم : ( ) لا : ( )

ضغط الدم : نعم : ( ) لا : ( )

الغدة : نعم : ( ) لا : ( )

فشل كلوي : نعم : ( ) لا : ( )

متلازمة الكلائية : نعم : ( ) لا : ( )

نوع الأدوية المستخدم : .....

خاص بالباحث :

الكلسترول

الدهون الثلاثية

الدهن عالي الكثافة

الدهن منخفض الكثافة

Appendixes 11

بسم الله الرحمن الرحيم

إقـرار بالموافقـة

الاسم :----------

العمر:---------- العنوان :----------

أوافق بمحض ارادتى بالمشاركة فى البحث العلمى المتعلق بدراسة تأثير استئصال الحويصلة الصفراوية على مستوى الدهون في المصل .

الطالبة :هناء علي محمد سعد

بعد أن شرح لى بأنه لا يترتب عليه أى أذى جسدى واعلم أن المشاركة في هذا البحث لن تؤثر بأي حال من الأحوال في الرعاية الطبية التي يتلقاها مولودي كما أنه يحق لي بدون ابداء أسباب الإنسحاب من هذا البحث في أي مرحلة من مراحله.

البحث بإشراف :

د.عبد الوهاب عابدين سعيد

التوقيع : ---------- التاريخ :----------