بسم الله الرحمن الرحيم

Sudan University of Science and Technology

College of Graduate Studies

Atherogenic Lipids Profile among Sudanese Females with Skin Tags in Khartoum State

مستوي دهون تصلب الشرايين لدي النساء السودانيات ذوات النخل في ولاية الخرطوم

A thesis submitted for partial fulfillment for the requirement of M.Sc. degree in Medical Laboratory Science (clinical chemistry).

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بسم الله الرحمن الرحيم

قال الله تعالى:

﴿وَيَسْأَلُونَكَ عَنِ الرُّوحِ ۖ قُلِ الرُّوحُ مِنْ أَمْرِ رَبِّي وَمَا أُوتِيتُم مِّنَ الْعِلْمِ إِلَّا قَلِيلًا﴾

صدق الله العظيم

الإسراء : الآية 85

Dedication

This work is dedicated

To

My parents, family and friends

Acknowledgement

All thank to **ALMIGHTY ALLAH** for giving me strength and courage to complete this work and made all things possible. Then thanks to my supervisor Dr. Mariam Abbas Ibrahim who encouraged me to complete this work.

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Finally, I must express my very profound gratitude to my parents, my sisters, my brothers, and my friends for providing me with unfailing support and continuous encouragement throughout my study and through the process of researching and writing this thesis. This accomplishment would not have been possible without them.

Abstract

Skin tag is one of the most common skin disorders that affect different populations and it associate with atherogenic lipid profile, dyslipidemia, insulin resistance, hypertension and atherosclerosis. This case control study was done in Khartoum state during March to December 2017 among Sudanese females with skin tags to evaluate the relationship between skin tags and lipids.

Eighty Sudanese females were included in this study (40 with skin tags were selected as test group and 40 without skin tags as control group (age was matched)), blood specimen was collected from both groups and cholesterol, low density lipoprotein cholesterol and high density lipoprotein cholesterol were analyzed spectrophotometrically; and BMI, LDL-C/HDL-C ratio and cholesterol/ HDL-C ratio were calculated.

Statistical analysis was done by using SPSS computer program. The study results revealed that there was significant elevation of cholesterol, LDL-C, cholesterol/ HDL-C ratio, LDL-C/HDL-C ratio and BMI with P. value (0.003), (0.024), (0.000), (0.000) and (0.000) respectively. The means± SD for skin tag group were (186.98± 31.79), (122.88± 31.29), (4.12± 1.12), (2.71± 0.91), (30.72± 5.11) respectively while in control group were (165.40± 31.52), (107.05± 30.29), (3.08± 0.88), (2.01± 0.76), (25.61± 4.98) respectively.

The result showed a significant decrease in HDL-C with (P. value 0.003), mean ±SD was (47.62± 11.24) in females with skin tags and (56.60±14.75) in control group. The results showed no correlation between BMI and cholesterol (r= 0.052, p. value 0.752), and no correlation between BMI and LDL-C (r= 0.038, p. value 0.817), while there is a significant negative correlation between BMI and HDL-C (r= -0.42, p. value= 0.006).

In conclusion: The study showed that skin tags are related to dyslipidemia and obesity.

المستخلص

علامة الجلد (النخل) هي واحدة من اضطرابات الجلد الأكثر شيوعا التي تؤثر على مختلف السكان ولها ارتباط بارتفاع مستوي دهون تصلب الشرايين والضغط والسكري ومقاومة الجسم لهرمون الانسيولين.

أجريت هذه الدراسة في ولاية الخرطوم خلال الفترة من مارس إلى ديسمبر 2017 بين الإناث السودانيات التي يعانين من علامات الجلد (النخل) لتحديد مستوي الدهون المرتبطة بتصلب الشرايين.

شملت هذه الدراسة 40 إمراة مصابة بالنخل و 40 إمراة غير مصابة بالنخل كمجموعة ضابطة, تم جمع عينات الدم من كلا المجموعتين وقياس مستوي الكوليسترول والكوليسترول في البروتين الدهني منخفض الكثافة (LDL-C) والكوليسترول في البروتين الدهني مرتفع الكثافة (HDL-C) وتم حساب مؤشر كتلة الجسم (BMI) و نسبة الكوليسترول الكلي إلى الكوليسترول في البروتين الدهني عالي الكثافة (Cholesterol/HDL-C ratio) ونسبة الكوليسترول في البروتين الدهني منخفض الكثافة الي الكوليسترول في البروتين الدهني عالي الكثافة (LDL-C/HDL-C ratio).

أجري التحليل الإحصائي بإستخدام SPSS واظهرت النتائج ان هناك زيادة ذات دلالة احصائية في متوسط تركيز الكوليسترول وLDL-C و cholesterol/LDL-C ratio وLDL-C/HDL-C ratio ومستوي مؤشر كتلة الجسم حيث كانت القيمة المعنوية (0.003) , (0.024) , (0.000) , (0.000) , (0.000) علي التوالي وكان المتوسط ± الانحراف المعياري يساوي (186.98± 31.79) , (122.88± 31.29) , (4.12± 1.12) , (2.71± 0.91) , (30.72± 5.11) علي التوالي لدي النساء المصابات بالنخل بينما كان لدي المجموعة الضابطة (165.40± 31.52) , (107.05± 30.29) , (3.08± 0.88) , (2.01± 0.76) , (25.61± 4.98) علي التوالي.

وكان هناك نقصان ذو دلالة احصائية في متوسط تركيز HDL القيمة المعنوية (0.003).بينما المتوسط ± الانحراف المعياري يساوي (47.62± 11.24) لدي مجموعة النساء المصابات بالنخل و (56.60±14.75) ادي المجموعة الضابطة.

ايضا اظهرت النتائج عدم وجود علاقة بين مؤشر كتلة الجسم ومستوي الكوليسترول (معامل بيرسون للارتباط = 0.052 , مستوي المعنوية = 0.752). ايضا لاتوجد علاقة بين مؤشر كتة الجسم ومستوي البروتين الدهني منخفض الكثافة (LDL) (معامل بيرسون للارتباط = 0.038 , مستوي المعنوية = 0.817). بينما توجد علاقة سلبية ذات دلالة معنوية بين مؤشر كتلة الجسم والبروتين الدهني عالي الكثافة (HDL) (معامل بيرسون للارتباط = -0.42 , مستوي المعنوية = 0.006).

اظهرت الدراسة ارتباط النخل بعسر شحيمات الدم (dyslipidemia) والسمنة (ارتفاع مؤشر كتلة الجسم)

List of Contents

List of tables

List of figures

List of abbreviations

BMI	Body mass index
CVD	Cardiovascular disease
DM	Diabetes mellitus
FA	Fatty acyl
GL	Glycerolipids
GP	Glycerophospholipids
HDL	High density lipoprotein
HDL-C	High density lipoprotein- cholesterol
IR	Insulin resistance
LDL	Low density lipoprotein
LDL-C	Low density lipoprotein- cholesterol
Lp (a)	Lipoprotein a
LPL	lipoprotein lipase
SP	Sphengolipids
SREBP	Sterol regulatory element-binding protein
ST	Sterol lipids
TC	Total cholesterol
TG	Triglyceride
VLDL	Very low density lipoprotein

Chapter one

Introduction and literature review

1. Introduction and literature review

1.1 Introduction

Skin tag is soft fibromas, fibroepithelial polyps, consider as benign skin tumor with soft consistency, which commonly appears on the neck, axillary, groin, and inframammary regions (Fig1.1) and often found in individuals with middle and old age and incidence increase with age and during pregnancy. They are painless but can become painful secondary to irritation or torsion and infarction (El Safoury and Ibrahim, 2011; Jusuf *et al.*, 2017).

Skin tags are strongly associated with insulin resistance (Tamega *et al.*, 2010), impaired carbohydrate metabolism and obesity. Obesity and impaired glucose tolerance (IGT) are high risk factors for developing diabetes mellitus (Rasi *et al.*, 2007; Sari *et al.*, 2010; El Safoury and Ibrahim, 2011).

Skin tags also associated with atherogenic lipid profile, hypertension and atherosclerosis (Rasi *et al.*, 2007; Sari *et al.*, 2010).

Dyslipidemia is anther frequent disorder among people with skin tags, which characterized by elevated plasma concentration of lipid (Rasi *et al.*, 2014).

Dysipidemia and atherogenic lipid profile are associated with increased risk of cardiovascular disease (CVD) which is the cause of one third of deaths worldwide, and further more they related to insulin resistance, and type 2 diabetes mellitus (Crook, 2000 ; Niroumand *et al.*, 2015).

A study presented by Gorpelioglu *et al* amied to investigate the association between serum leptin, atherogenic lipid and glucose levels in patients with skin tags and healthy controls, they conclude that skin tags group showed significantly higher levels of total cholesterol and LDL-C, when compared with the healthy controls groups ($P < 0.01$) (Gorpelioglu *et al.*, 2009).

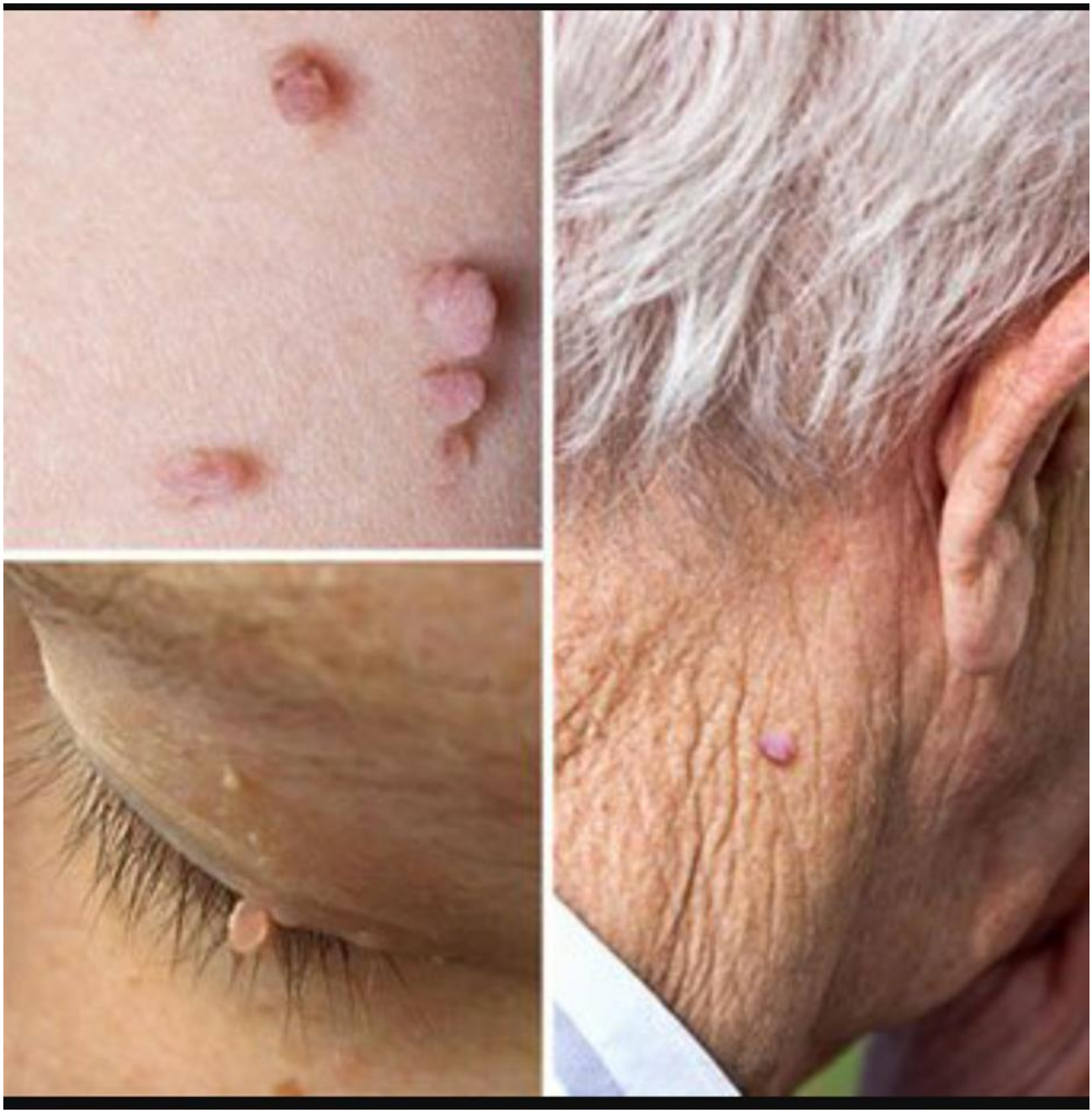

Fig 1.1: Show the appearance of skin tags

1.2. Literature review

1.2.1. Skin tags

Skin tags or Acrochordons are benign benign connective tissue tumors of the dermis that affect large portion of general population; they are soft, asymptomatic tan or skin colored papules range from normochromic to hyperchromic lesions(Fig1.1). They can become painful secondary to irritation or torsion and infarction.

Skin tags can be classified into three types: Small (1-2 mm in width and height), furrowed papules, commonly located on the neck and the axillae. Single or multiple filiform lesions, with 2 mm in width and 5 mm in length, appear elsewhere on the body. And large, pedunculated tumor or nevoid, baglike, soft fibromas, usually appear on the lower part of the trunk. The Small lesions called skin tag while the large one called broepithelial polyps (Edwards and Lynch, 2010; Tamega *et al.,* 2010; Maluki and Abdullah, 2016).

Skin tags usually appear on the neck, eyelids, axillary, inframammary regions and groin where appear as soft pedunculated growths. Also skin tag may occur at unusual sites of the body. (Maluki and Abdullah, 2016; National Cancer Institute dictionary, 2017).

Skin tag are more common in the adult population over 40 years (46%), and increase incidence in the elderly, reaching 59% at 70 years of age, also skin tags occurrence increase with weight gain and pregnancy.

There is a familial component; however, the genetic segregation pattern and ethnic characteristics have yet to be defined. There is no difference in incidence between males and females (Tamega *et al.,* 2010; Rasi *et al.,* 2014).

The prevalence of skin tag not constant, it varies depending on the studied population, e.g. 46 % in Germany or 0.7 % in India. Also it is common in middle-aged individual and elder more than in younger, but there is no difference incidence of skin tag between male and female (Jusuf *et al.,* 2017).

The genesis and development of skin tag may be due to imbalance of the level of some hormones including estrogen level and trophic hormones level such as insulin, IGF-1 (insulin-like growth factor-1), TGF (transforming growth factor-) and epidermal growth factor (EGF) (Tamega *et al.*, 2010), Irritation in areas of skin friction and aging with other factor help in their development (Maluki and Abdullah, 2016).

Skin tags appear most common on obese population and people with disturbances on insulin and glucose metabolism and during pregnancy and some literature report skin tags as a cutaneous sign for impaired carbohydrate or lipid metabolism (Edwards and Lynch 2010; Jusuf *et al.*, 2017; Maluki and Abdullah, 2016).

An association between many diseases and skin tag was suggested and reported, including insulin resistance, hyperinsulinemia, hyperglymia, lipid profile abnormality (dyslipidemia), hypertension and hyperleptinemia, all of these condtion consider as metabolic abnormalities (Rasi *et al.*, 2014).

Metabolic abnormalities such as dyslipidemia, hypercholesterolemia and insulin resistance are well-known risk factors for atherosclerosis and cardiovascular disease (Rasi *et al.*, 2014).

Beyond the metabolic abnormalities also skin tag associate with different systemic disorders like acromegaly, colonic polyps, and Birt-Hogg-Dube syndrome and in children with nevoid basal cell carcinoma syndrome as a presenting sign was reported (Rasi *et al.*, 2014).

1.2.1.1. Skin tag metabolic disorders

A. insulin resistance

Insulin resistance (IR) defines as diminished ability of cells to respond to the action of a known quantity of exogenous or endogenous insulin. Normally insulin promotes glucose uptake in muscle, fat, and liver cells and can influence lipolysis and the production of glucose by hepatocytes ,

IR result in abnormality in transporting of glucose (sugar) from the bloodstream into muscle and other tissues resulting in decrease glucose uptake and utilization, also result in abnormalities in

insulin secretion and insulin receptor signaling, impaired glucose disposal, and pro inflammatory cytokines. (Lebovitz, 2001; Maluki and Abdullah, 2016; medicinenet, 2017). There for insulin resistance appears to be the primary mediator of metabolic syndrome (syndrome X). Also result in a systemic metabolic abnormality including cardiovascular events and certain malignant neoplasias. And consider as a risk factor for atherosclerosis, type II DM, systemic arterial hypertension, abdominal obesity and dyslipidemia. (Tamega *et al.,* 2010).

hyperinsulinemia is a hypersecretion of insulin. Occur as compensatory hyperinsulinemia to maintain normal glucose and lipid homeostasis. When hyperinsulinemia companied with hyperglycemia is considered a sign of insulin resistance, in which hyperinsulinemia due to pancreatic hypersecretion (Ibrahim *et al.*, 1996; Maluki and Abdullah, 2016).

The presence of multiple skin tags is strongly associated with insulin resistance irrespective of other risk factors. So skin tag consider as a skin sign for IR (Tamega *et al.,* 2010).

B. Type 2 diabetes mellitus

The possible association of skin tag with diabetes mellitus was first mentioned in 1951(Maluki and Abdullah, 2016). Then many studies done to approve this association and some show an increased risk of diabetes mellitus in patients with multiple skin tags (Rasi *et al.*, 2007).

Type2 diabetes referred to as non–insulin-dependent diabetes or adult-onset diabetes. It is chronic metabolic condition characterized by insulin resistance resulting in insulin insensitivity and insufficient pancreatic insulin production, resulting in high blood glucose levels (hyperglycaemia).

Type 2 DM caused by a combination of genetic factors related to impaired insulin secretion and insulin resistance, obesity and environmental factors such as physical inactivity, sedentary lifestyle, cigarette smoking, alcohol consumption, stress and aging. So it consider as multifactorial disease.

Type2 diabetes is commonly associated with obesity, raised blood pressure, disturbed blood lipid levels and a tendency to develop thrombosis, long-term microvascular and macrovascular

complications, so it tend to increase cardiovascular risk and reduced quality of life and life expectancy (NICE guideline, 2015; Kaku, 2010; American Diabetes Association, 2010; Olokoba *et al.*, 2012).

C. Dyslipidemia

Dyslipidemia is one of disease suggested to associate with skin tags, this association studded by Rasi and his team in 2014 and show evidence of dyslipidemia in skin tag populations (Rasi *et al.*, 2014*).*

Dyslipidemia defined as elevated plasma concentration of lipid (hyperlipidemia) including triglyceride (TG), total cholesterol (TC) and their blood transporting lipoproteins; HDL-Cholesterol, LDL-Cholesterol, VLDL-Cholesterol (Niroumand *et al.,* 2015).

High level of LDL-C and low level of HDL-C are strongly associated with high incidence of CVD and; therefore the LDL-C/HDL-C ratio is often calculated to estimate cardiovascular risk.

Dyslipidemia also lead to atherosclerosis of arteries (atherogenic dyslipidemia) in which the circulating lipid may form plague on vessels leading to decreasing of blood flow, and forming of intimal lesion in presence of foam cell (macrophage engulfing lipid), this lesions may progress to atheromatous plaque (atheroma).

Atherogenic dyslipidemia clinically presents as elevated serum triglyceride levels, increased small dense low-density lipoprotein particles, and decreased levels of high density lipoprotein – cholesterol. Also defined as high LDL-C/HDL-C ratio, it associated with high cardiovascular risk and powerful risk factor for coronary heart disease, defined as angina pectoris, unstable angina, myocardial infarction, or coronary death.

Furthermore dyslipidemia is strongly associated with hypertension as 60.7% to 64.3%of hypertensive individual found to hypercholeterolemic (Niroumand *et al.,* 2015; Kamal and Abdelkader, 2016; Maluki and Abdullah, 2016).

D. Cardiovascular disease (CVD)

CVD is a number of diseases that involve the heart (cardiac muscle) and vascular system supplying the heart, brain, and other vital organs. CVD includes coronary artery diseases (CAD)

such as angina and myocardial infarction (heart attack) , stroke, heart failure , hypertensive heart disease , rheumatic heart disease , cardiomyopathy , heart arrhythmia , congenital heart disease , valvular heart disease , carditis , aortic aneurysms , peripheral artery disease, thromboembolic disease and venous thrombosis. CVD consider as number one cause of death worldwide.

Risk factor of CVD include obesity, high blood pressure, high cholesterol, diabetes, smoking, family history, lack of physical activity, metabolic syndrome, mental stress and depression.

Dyslipidemia is recognized as a prominent risk factor for increasing cardiovascular (CV) disease, including high levels of total cholesterol and LDL-C, elevated triglycerides and low levels of HDL-C (Miller, 2009; Boudi *et al.*, 2016).

Most of the risk factors of CVD present in skin tag populations such as dyslipidemia, obesity, diabetes mellitus and metabolic syndrome.

1.2.2. Lipid and Lipid profile

1.2.2.1. Lipid profile

Lipid profile is a panel of blood tests that serves as an initial broad medical screening tool for abnormalities in lipids, such as cholesterol and triglycerides. The results of this test can identify certain genetic diseases and can determine approximate risks for cardiovascular disease, certain forms of pancreatitis, and other diseases

The lipid profile includes; total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C). Using these values, a laboratory may also calculate very low-density lipoprotein (VLDL), cholesterol:HDL-C ratio, LDL-C/HDL-C ratio and other. (Fischbach and Dunning , 2009)

1.2.2.2. Lipid

Lipid is a fatty or waxy organic compound including fats, oils, hormones, and certain components of membranes that is readily soluble in nonpolar solvent (e.g. ether) and insoluble in polar solvent (e.g water).

Its major biological functions of lipids involve energy storage molecules; as the cleavage of fatty acids they produce both energy and metabolic water which is a main component in almost all lipids. Structural function; lipids primarily involved in the formation of cell membranes which is a bi-lipid layer and present in all living things like bacteria and human. Also lipid serve as chemical messengers between cells, tissues, and organs, and others communicate signals between biochemical systems within a single cell, this chemical messengers including steroid hormones such as estrogens, testosterone, progesterone, and cortisol which enter cells and turn on specific chemical reactions. (Thompson, 2017; Biology on line dictionary, 2017; Tutorvista, 2017)

1.2.2.3 Type of lipid

Mainly lipids are classified in five types.

A. Fatty acyl (FA)

Fatty acyls a generic term are used for fatty acids and their derivatives, composed of one non-polar in nature and hydrophobic hydrocarbon chain which terminates with a carboxylic acid group which is polar and soluble in water (hydrophilic) (Wikibooks, 2016; Tutorvista, 2017).

B. Glycerolipids (GL)

Referred to as triglycerides also called as neutral fats, they composed of mono-, di- and tri-substituted glycerol. They formed by the esterification of glycerols with different fatty acids. Usually the three hydroxyl groups of glycerol are each esterified, different fatty acids. The triglycerides serve as energy-storage they considered as efficient energy storing for organisms and also provide thermal insulation (Wikibooks, 2016; Tutorvista, 2017).

During fat metabolism, glycerolipids releases glycerol and fatty acids from adipose tissue

Glycosylglycerols is a class of glycerolipids which composed of one or more sugar residues with glycerol through a glycosidic linkage and fatty acids (Wikibooks, 2016; Tutorvista, 2017).

C. Glycerophospholipids (GP)

Also called phospholipids, they composed of fatty acids, glycerol with phosphate groups, they are the main constituents of the lipid bilayer of cells and also are involved in metabolism and cell signaling (Wikibooks, 2016; Tutorvista, 2017).

D. Sphengolipids (SP)

They composed of a sphingoid base backbone which is synthesized from serine; an amino acid and a fatty acyl CoA long-chain. Further they converted into ceramides, glycosphingolipids, phosphosphingolipids and other compounds.

Some common examples of sphingolipids are Ceramides, sphingomyelins(a phosphosphingolipids) are found in mammals (Wikibooks, 2016; Tutorvista, 2017).

D. Sterol lipids (ST)

These lipids are the main components of the membrane lipids along with sphingomyelins and the glycerophospholipids.

Steroids are composed of fused four-ring core structure, but show different biological roles; such as hormones like estrogen, testosterone and androsterone.

The best common examples of sterol are cholesterol and its derivatives, some vitamins like vitamin-D which contain one sterol group, bile acids in mammals, and phytosterols in plants. (Wikibooks, 2016; Tutorvista, 2017).

Cholesterol:

Cholesterol is a waxy, fat-like chemical compound that the body requires as a building block for cell membranes and for hormones like estrogen and testosterone, cholesterol composes about 30% of all animal cell membranes and required to build and maintain membranes and modulates membrane fluidity over the range of physiological temperatures. The liver produces about 80% of the body's cholesterol other sites of higher synthesis rates include the intestines, adrenal glands, and reproductive organs. The rest comes from dietary sources like meat, poultry, eggs, fish, and dairy products. Foods derived from plants contain no cholesterol.

Cholesterol in the bloodstream is regulated by the liver. After a meal, cholesterol in the diet is absorbed from the small intestine and metabolized and stored in the liver. As the body requires cholesterol, it may be secreted by the liver. Biosynthesis of cholesterol is directly regulated by the cholesterol levels present the higher intake from food leads to a net decrease in endogenous production, whereas lower intake from food has the opposite effect. The main regulatory mechanism is the sensing of intracellular cholesterol in the endoplasmic reticulum by the protein SREBP (sterol regulatory element-binding protein 1 and 2).

When the level of cholesterol increase in the body, it can build up in deposits called plaque along the inside walls of arteries, causing them to narrow (Espenshade and Hughes, 2007; Medlineplus, 2016; Wedro and Davis, 2017)

High levels of cholesterol in the blood can increase risk of heart disease, stroke, and peripheral artery disease. The pathological mechanism of these three diseases involving cholesterol is similar; in which plaque buildup within arteries leading to decrease of the blood flow affecting the function of the cells and organs that these blood vessels supply (Medlineplus, 2016)

Types of cholesterol:

Cholesterol does not travel freely through the bloodstream. so it is attached or carried by lipoproteins (lipo = fat) in the blood

There are two main types of cholesterol:

- HDL stands for high-density lipoproteins "good" cholesterol
- LDL stands for low-density lipoproteins "bad" cholesterol (Medlineplus, 2016; Wedro and Davis, 2017).

1.2.2.4. Lipoproteins

Lipoproteins are complex particles with a central core containing cholesterol esters and triglycerides surrounded by free cholesterol outer shell, a single-layer phospholipids, and apolipoproteins which embedded in the membrane. They help in transport hydrophobic lipids molecules in water, as it occurs in blood and extracellular fluid. Also serve to emulsify the fats.

Many structural proteins,enzymes, antigens, adhesions, transporters , and toxins are lipoproteins. Lipoproteins classed into seven group based on size, lipid composition, and apolipoproteins; include chylomicrons, chylomicron remnants, VLDL, IDL, LDL, HDL, and Lp (a)).

Chylomicron remnants, VLDL, IDL, LDL, and Lp (a) are pro-atherogenic while HDL is anti-atherogenic (Gofman *et al.,* 1950; Feingold and Grunfeld, 2015).

1.2.2.5 Types of lipoproteins

The most important types include:

A. HDL-C (good cholesterol)

High-density lipoprotein made by Liver and small intestine, and Secreted into blood stream, rich in cholesterol and Contain Apo proteins A,C,E&D. It carries cholesterol from other parts of body back to your liver which removes the cholesterol from your body so it is called the "good" cholesterol because it reverse cholesterol transport back to the liver (reverse heart diseases).

Increasing concentrations of HDL-C particles are strongly associated with decreasing accumulation of atherosclerosis within the walls of arteries. This is important because atherosclerosis eventually results in sudden plaque ruptures, cardiovascular disease, stroke and other vascular diseases, so that high HDL-C to LDL-C ratio is good because it can be protective against heart disease, stroke, and peripheral artery disease (Zhang *et al.,* 2008; Kamal and Abdelkader, 2016; Wedro and Davis, 2017).

B. LDL-C (bad cholesterol)

Low-density lipoprotein made by losing a lot of TGs form VLDL through the action of lipoprotein lipase (LPL) and they become smaller and denser, containing a higher proportion of cholesterol esters so LDL-C Rich in cholesterol function to deliver cholesterol to all body, It is called the "bad" cholesterol because a high LDL-C level leads to a buildup of cholesterol in your arteries. Contain Apo proteins B100 (Kamal and Abdelkader, 2016; Medlineplus, 2016).

Elevated levels of LDL-C increase the risk of heart disease, stroke, and peripheral artery disease, by helping form cholesterol plaque in artery walls. Over timeplaque deposits increases and the artery narrows (atherosclerosis) and blood flow decreases. The plaque may rupture and lead to

blood clot formation. This clot is the cause of a heart attack or myocardial infarction if the clot occurs in one of the coronary arteries in the heart (Wedro and Davis, 2017).

C. VLDL

Very low density lipoprotein made by liver, Secreted into blood stream, rich in TGs. Function in delivering of TGs to body cells. Contain Apo proteins B100,C&E. VLDL has been associated with plaque deposits (Kamal and Abdelkader, 2016; Wedro and Davis, 2017).

D. Chylomicrons

Large triglyceride rich particles, made by Small intestine and secreted into lymph vessels then to blood stream, rich in TGs. Transport dietary triglycerides and cholesterol to peripheral tissues and liver. Contain Apo proteins A,B48,C&E (Feingold and Grunfeld, 2015; Kamal and Abdelkader, 2016).

1.3. Rationale

Skin tags is one of the common skin disorders affecting different people specially with increasing age, and it is associated with type 2 diabetes mellitus, obesity, insulin resistance, hypertension, and recently some studies report association of skin tags with dyslipidemia and atherogenic lipid profile.

A study done in Turkey by Terzi *et al* to assess the association of skin tag with serum leptin, lipid profile, glucose level ,insulin resistance and BMI. Their study results confirm that skin tags are associated with obesity and dyslipidemia (Terzi *et al.*, 2017*).*

A study done in Sudan to assess the atherogenic lipid Profile in skin tags population with diabetes mellitus Type2, their result showed that skin tags population with DM2 were found to have hyperlipidaemia in 60% of cases while 50% of control group with DM2 have hyperlipideamia (Mustafa *et al.*, 2017). Insipid of these serious disorders which associated with the skin tags, a little information about this association are available among Sudanese population. Also less Focus and attention are provided to these clinical disorders in comparison to that care provided to the dermatological procedures for removing of skin tags.

So this study represented to evaluate the atherogenic lipid profile among females with skin tags.

1.4. Objectives

1.4.1. General objective:

To assess the level of atherogenic lipid profile in Sudanese females with skin tags.

1.4.2. Specific objectives:

- To measure and compare mean levels of total cholesterol, HDL-C and LDL-C among study groups.
- To calculate and compare BMI and cholesterol/HDL-C ratio among study groups.
- To correlate levels of cholesterol, LDL-C, HDL-C levels and cholesterol/HDL-C ratio with BMI in females with skin tags.

Chapter two

Material and methods

2. Materials and methods

2.1. Materials

2.1.1. Study design: Descriptive case control study.

2.1.2. Study area and period: Khartoum State, from society, from March to December 2017.

2.1.3. Study population: This study included 40 females with skin tags their age range from (18-68) and 40 female without skin tag as control, their age was matched.

Inclusion criteria: Test group: Sudanese females with skin tag. Control group: Sudanese females without skin tags from the same age of test group.

Exclusion criteria: Females with hypertension, diabetes mellitus, cardiovascular disease, lipid abnormality, and women consuming lipid lowering drugs were excluded.

2.1.4. Ethical consideration: Ethical clearance was obtained from Clinical Chemistry Department, College of Medical Laboratory Science in Sudan University for Science and Technology, and verbal informed consent was obtained from each participant in the study.

2.1.5. Sampling: Random blood samples were collected in lithium heparin containers then plasma separated into plain containers and stored till the time of measurement of total cholesterol, HDL-C and LDL-C.

2.1.6. Statistical analysis: data were analyzed by statistical package for social science (SPSS) version 16, by using independent T test for comparisons and Person's test was used for obtaining correlations ; *p* value less than 0.05 was considered significane for the difference between variables.

2.1.7. Quality control: Normal and pathological control sera were used, to assure the accuracy of results.

2.2. Methods

2.2.1. Total cholesterol estimation:

Free and esterified cholesterol in sample converted into a colored complex that can be measured by spectrophotomery by the following reaction:

Cholesterol + H_2O + cholesterol esterase ⟹ cholesterol + fatty acid

Cholesterol + ½O_2 + H_2O + cholesterol oxidase ⟹ cholestenone + H_2O

2H_2O+ 4- aminoantipyrine+ phenol. (Appendix II).

2.2.2. HDL-C estimation:

VLDL and LDL in the sample precipitate with phosphotungstate. The supernatant contains HDL-C which is spectrophotometrically measured by the coupled reaction of cholesterol mentioned above. (Appendix III).

2.2.3. LDL-C estimation:

LDL in sample precipitate with polyvinyl sulphate, and then the cholesterol in the supernatant are measured spectrophotometrically by the same coupled reaction of cholesterol. Then the LDL concentration is calculated from the difference between the total cholesterol and cholesterol in supernatant. (Appendix IV).

2.2.4. BMI calculation:

BMI was calculated using this formula:

BMI = weight (in kilograms) / height (in meters) ^2

2.2.5. Total cholesterol /HDL-C ratio calculation:

Cholesterol /HDL-C ratio= cholesterol concentration / HDL-C concentration.

LDL-C /HDL-C ratio= LDL-C concentration / HDL-C concentration.

Chapter three

Results

3. Results

Forty females with skin tags were enrolled in this study to assess the level of cholesterol, HDL-C, LDL-C in comparison to females without skin tags who served as control group. Spectrophotometer was used for estimation of cholesterol, HDL-C, LDL-C using biosystem kits.

Statistical analysis was done by using SPSS and the results were as follow:

Table 3.1 shows the general characteristic of study groups.

Table 3.2 shows the comparison of cholesterol, HDL-C, LDL-C level among case and control: there is a significant increase in total cholesterol level, LDL-C level, LDL-C/ HDL-C ratio, cholesterol/HDL-C ratio and BMI in females with skin tags when compared to females without skin tag, while the HDL-C level was significantly deceased.

Figure 3.1. A scatter plot shows no correlation between BMI and cholesterol level.

Figure 3.2. A scatter plot shows significant negative weak correlation between BMI and HDL-C level.

Figure 3.3. A scatter plot shows no correlation between BMI and LDL-C level.

Table 3.1 General Characteristics of Study groups

Parameters	mean± SD(case)	Mean± SD (control)
Age	43.88± 12.61	36.07± 11.69
Weight	79.30± 14.13	66.30± 13.85
Height	1.61± 0.6 (meter)	1.60± 0.65 (meter)

Table 3.2 Comparison between levels of total cholesterol, HDL-C, LDL-C, BMI, LDL-C/HDL-C ratio, cholesterol/HDL-C ratio among study groups.

Variable		mean± SD	p-value
Total cholesterol	Case	186.98± 31.79	0.003
	Control	165.40± 31.52	
HDL-C	Case	47.62± 11.24	0.003
	Control	56.60±14.75	
LDL-C	Case	122.88± 31.29	0.024
	Control	107.05± 30.29	
BMI	Case	30.72± 5.11	0.000
	Control	25.61± 4.98	
LDL-C/HDL-C ratio	Case	2.71± 0.91	0.000
	Control	2.01± 0.76	
Total cholesterol/HDL-C ratio	Case	4.12± 1.12	0.000
	Control	3.08± 0.88	

Independent sample T test was used, value consider significant at level ≤ 0.05.

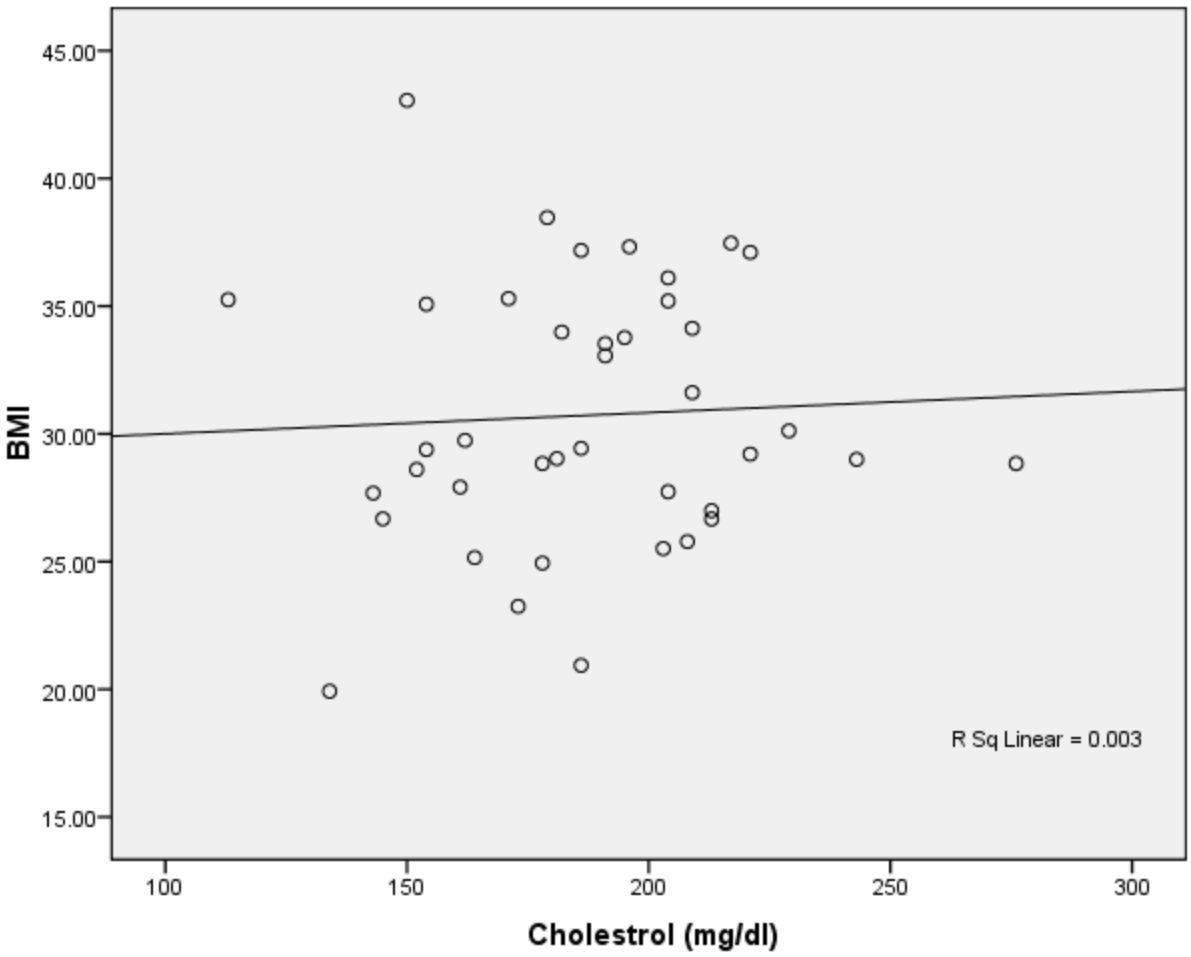

Figure 3.1 Correlation between BMI and cholesterol concentration (mg/dl) significant consider as p-value ≤0.05.

R= 0.052 p. value 0.75

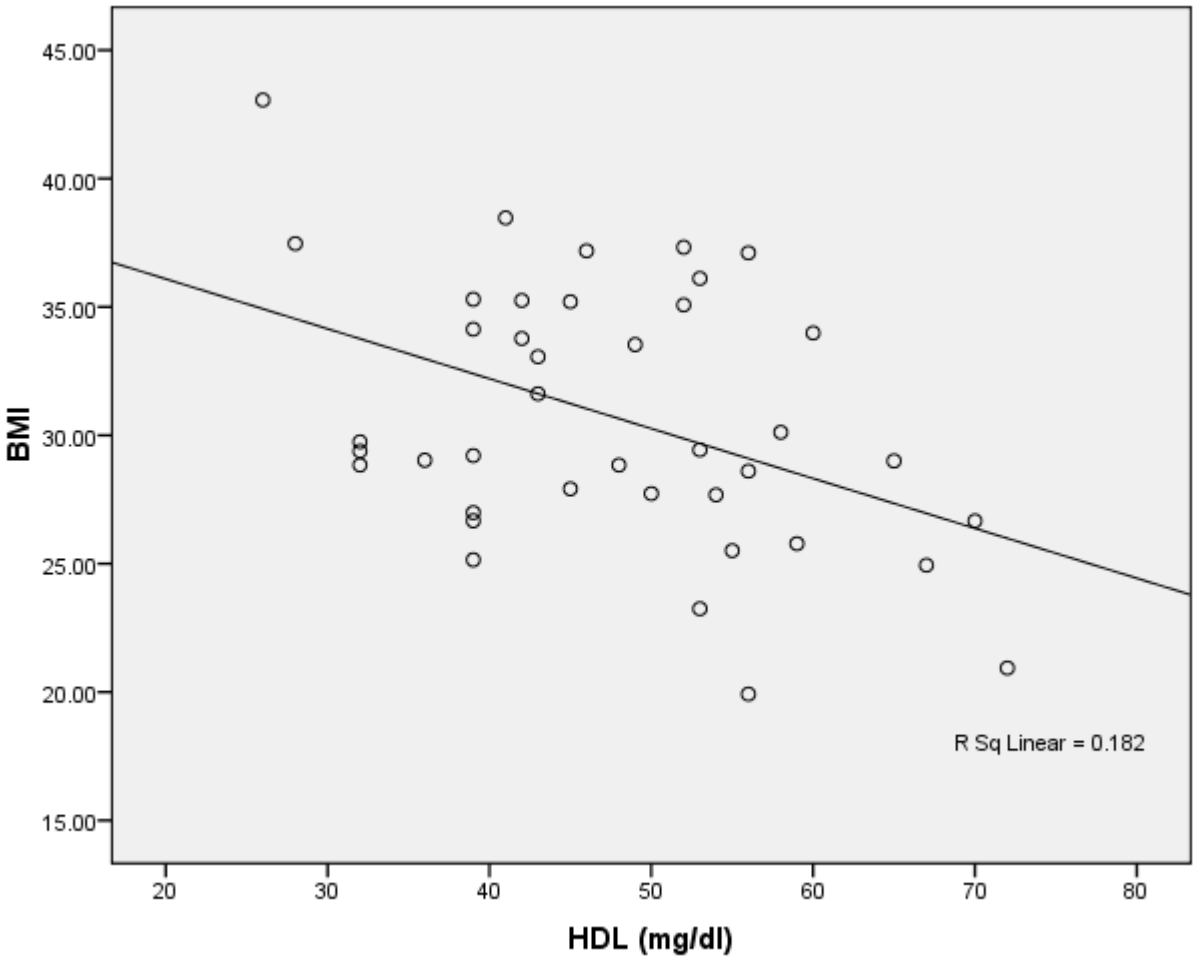

Figure 3.2 Correlation between BMI and HDL-C concentration (mg/dl) significant consider as p-value ≤0.05.

R= -0.42 p. value 0.00

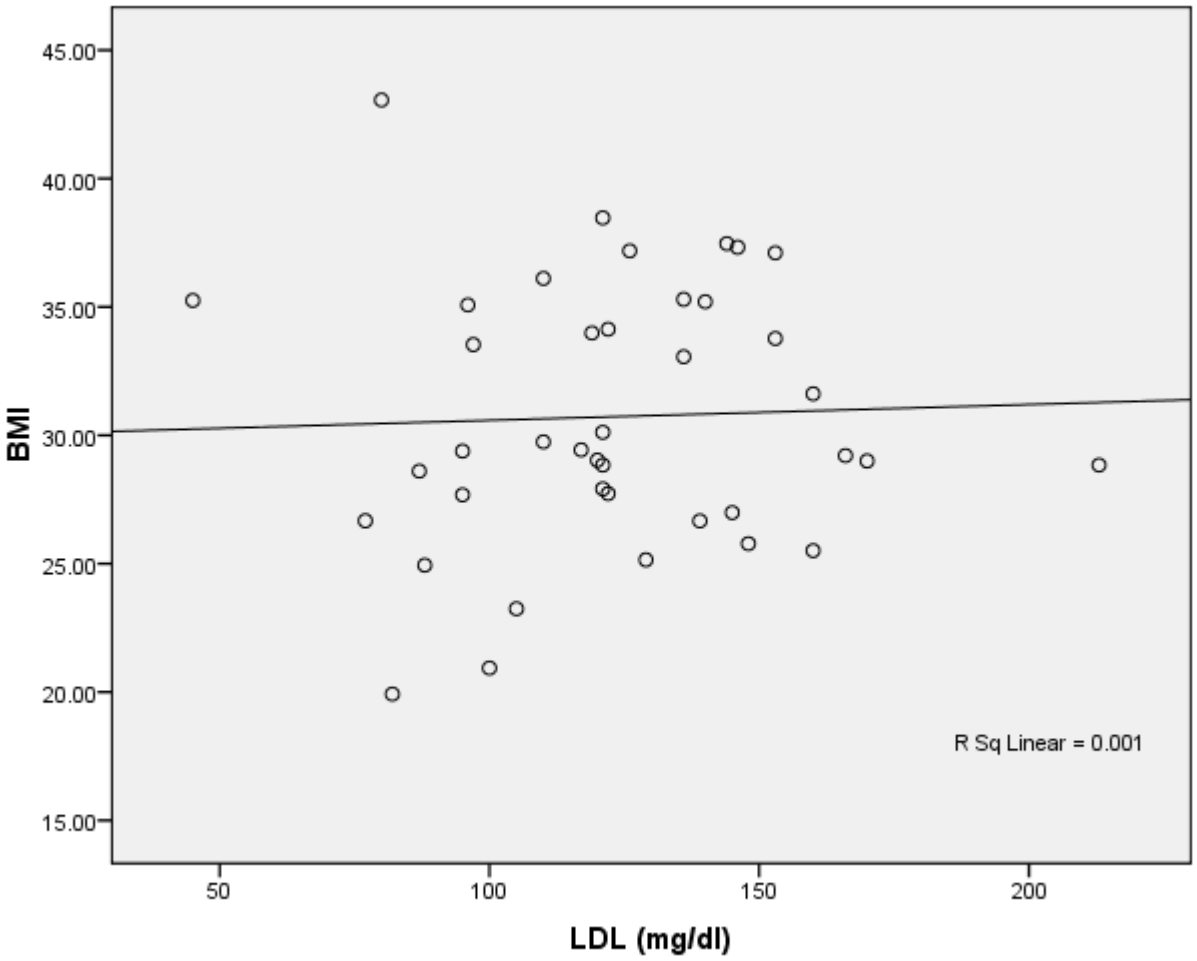

Figure 3.3 Correlation between BMI and LDL-C concentration (mg/dl) significant consider as p-value ≤0.05.

R= 0.038 p. value 0.81

Chapter four

Discussion, conclusion and Recommendations

4.1. Discussion

Many studies showed association between skin tag and abnormal lipid concentrations (Crook, 2000; Niroumand *et al.*, 2015).

This case control study amied to evaluate atherogenic lipid profile in females with skin tags in Khartoum state. 40 Sudanese females with skin tags and 40 without skin tags were enrolled in this study. After evaluation of levels of cholesterol, HDL-C, LDL-C, the statistical analysis was done and the results showed a significantly higher concentration of cholesterol and total cholesterol/HDL-C ratio, and increased BMI in female with Skin tags. This result agreed with study results done by Idris & Sunitha, they assessed the BMI, Serum Leptin Levels and Lipid Profile in Patients with Skin Tags, their results showed significantly higher values of BMI, total cholesterol (TC) and TC/HDL-C ratio with p. values (p=0.001), (p=0.001) and (p=0.019) respectively (Idris and Sunitha, 2014). The significant increase of BMI in Skin tags patients also concluded by Jusuf in study done to evaluate the Correlation between Body Mass Index with the Occurrence of Skin Tag with (p value = 0.00) (Jusuf *et al.*, 2017).

In the current study there was also significant increase in LDL-C, and significant decrease in HDL-C concentrations. This results agreed with study done by Vinod Wali and Vishal V. Wali, their results showed significant increase in LDL-C level and significant decrease in HDL-C level with p. value (0.01) (Wali V and Wali V V, 2016).

The increase of cholesterol level, LDL level, cholesterol/LDL ratio and BMI can be explained by insulin resistance that associated with skin tags population. Insulin resistance is linked to a wide array of pathophysiologic sequelae including hyperlipidemia and atherosclerosis. Also insulin resistance and hyperinsulinemia, in addition to being caused by obesity, can contribute to the development of obesity which associated with increasing of BMI. Furthermore insulin resistance affect carbohydrate metabolism leading to impaired glucose metabolism or hyperglycemia and there for affect lipid metabolism leading to hyperlipidemia (Kahn & Flier, 2000; Tamega *et al,* 2010).

On the other hand the results of this study disagreed with study done in Iran by Rasi A and his team who concluded that there were no significant differences in Cholesterol, LDL-C and HDL-

C between case (Skin tag group) and control (Skin tags free group), the p. values were (0.099) for Cholesterol, (0.096) for LDL-C and (0.078) for HDL-C (Rasi *et al.,* 2014)

Results of the present study revealed that there was no correlation between cholesterol and BMI, no correlation between LDL-C and BMI but HDL-C and BMI were inversely correlated**.**

4.2. Conclusion

From this study it is concluded that:

- The levels of cholesterol, LDL-C and cholesterol/HDL-C ratio are increased in skin tag females while the levels of HDL-C are decreased.
- The level of HDL-C was negatively correlated with BMI in skin tag females, and there was no correlation between cholesterol and LDL-C with BMI.

4.3. Recommendations

From the findings of this study it is recommended that:

- Lipid profile must be routinely evaluated in skin tag population to decrease the possibility of getting dyslipidemia and decrease its complication.
- Further studies should be done to evaluate C- reactive protein as a predective marker for CVD and Atherosclerosis among skin tag population.
- Estimation of atherogenic index of plasma (AIP) as marker of CVD is recommended to be done among skin tag population.

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Appendices

Appendix I

Sudan University of Science and Technology

College of Medical Laboratory Sciences

Department of Chemical chemistry

Questionnaire

Patient name ……..

Age…….

Weight……kg height……Cm

Body mass index…….

Results:

Cholesterol…….. (mg /dl)

HDL……..… (mg /dl)

LDL …….(mg /dl)

Cholesterol/HDL ratio…….

Signature……..