بسم الله الرحمن الرحيم

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Assessment of Serum Levels of Total Cholesterol and LDL-C in Metabolic Syndrome Patients in Khartoum State

تقييم مستوى الكوليسترول الكلي والكوليسترول منخفض الكثافة البروتينية الدهنية في مرضى متلازمة التمثيل الغذائي في ولاية الخرطوم

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قَالَ تَعَالَىٰ:

﴿لَا يُكَلِّفُ ٱللَّهُ نَفْسًا إِلَّا وُسْعَهَا ۚ لَهَا مَا كَسَبَتْ وَعَلَيْهَا مَا ٱكْتَسَبَتْ ۗ رَبَّنَا لَا تُؤَاخِذْنَآ إِن نَّسِينَآ أَوْ أَخْطَأْنَا ۚ رَبَّنَا وَلَا تَحْمِلْ عَلَيْنَآ إِصْرًا كَمَا حَمَلْتَهُۥ عَلَى ٱلَّذِينَ مِن قَبْلِنَا ۚ رَبَّنَا وَلَا تُحَمِّلْنَا مَا لَا طَاقَةَ لَنَا بِهِۦ ۖ وَٱعْفُ عَنَّا وَٱغْفِرْ لَنَا وَٱرْحَمْنَآ ۚ أَنتَ مَوْلَىٰنَا فَٱنصُرْنَا عَلَى ٱلْقَوْمِ ٱلْكَٰفِرِينَ ﴿٢٨٦﴾﴾

صدق الله العظيم

البقرة الآية (٢٨٦)

Dedication

For my parents .....

My brothers .....

My sister .....

My friends.....

And off curse for my teachers.....

I dedicate my humble effort ..... .

With my love .....

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Firstly I thank Allah for his blessing and for giving me the ability for patience, believe, and withstand the hard work. I thank him for being here with me, for my life and for everything.

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Abstract

Metabolic syndrome is a group of metabolic abnormalities that predispose individual to cardiovascular disease hence dyslipidemia is major feature of it, so we aimed to estimate total cholesterol and LDL-C which are the main atheroscholaritc lipids .

This cross sectional study was carried out to estimate the level of serum total cholesterol and LDL-C in metabolic syndrome patients who had already diagnosed by the doctors according to WHO definition which require the presence of insulin resistance diabetes mellitus together with tow risk factors or more. Data about the Metabolic syndrome patients and the disease were collected such as (height, weight, waist circumference, blood pressure, duration of disease and physical exercise). Fourty blood sample were collected from metabolic syndrome patient as case group and fourty blood sample were collected from normal individuals as control group in Khartoum state during the period from June to November 2019.

The estimation of serum total cholesterol and low density lipoprotein cholesterol was done by using bio systems BTS-305 then the results were analyzed by using SPSS computer program. Statistical analysis showed an insignificant difference in total cholesterol level in cases (mean±SD: 166.7±33.1) when compared to control (159.9±20.2) p- value= 0.27, and insignificant difference in LDL-C level in cases (mean±SD: 61.7±29.3) when compared to control (54.6±16.1) p- value: 0.87, a significant increase in body mass index (BMI) in cases (mean±SD: 30.8±6.2) when compared to control (24.1±3.5) p- value =0.000, a significant increase in waist circumference (WC) in cases (mean±SD: 110±11) when compared to control (83.3±11.5) p- value = 0.000,. Also the Statistical analysis showed an insignificant difference of BMI in females when compared to

males p- value= 0.30, an insignificant difference of WC in females when compared to males p- value = 0.085, an insignificant difference of total cholesterol level in females when compared to males p- value=0 .435, an insignificant difference of LDL-C level in females when compared to males p- value = 0.295, insignificant difference of systolic blood pressure (SBP) in females when compared to males p- value = .265, an insignificant difference in diastolic blood pressure (DBP) in females when compared to males p- value = .524. Statistical analysis showed an insignificant difference in the BMI,W.C, SBP, DBP, Total cholesterol and LDL-C, According to duration (duration of metabolic syndrome <1Years, 1-5Years, >5Years respectively) P- values as follow respectively: 0.731, 0.610, 0.894, 0.440, 0.556, 0.196. Statistical analysis showed an insignificant difference in the BMI, W.C, SBP, DBP, Total cholesterol and LDL-C According to duration (no physical exercise, <100 minute a week, 100-150 minute a week respectively) of physical exercise, p-value as follow respectively: 0.723, 0.587, 0.779, 0.775, 0.203, 0.332. Statistical analysis showed no association between physical exercise and total cholesterol and LDL-C levels P-value: 0.7, 0.5, ODD ratio. : 0.6, 2 respectively.

In conclusion : metabolic syndrome patient had increased body mass index and waist circumference, with normal level of serum total cholesterol and LDL-C, and there was no difference in metabolic syndrome markers(BMI,WC, SBP, DBP, LDL-C and Total cholesterol) between females and males, and between periods of the disease , and metabolic syndrome markers did not affected by physical exercise.

ملخص الدراسة

متلازمة التمثيل الغذائي هي مجموعة من علل الأيضية التي تجعل الفرد عرضة لمرض القلب والأوعية الدموية وبما أنّ زيادة الدهون الضارة ونقصان الدهون النافعة هو سمة رئيسية في ذلك، لذلك نحن نهدف إلى تقويم الكوليسترول الكلي و الكوليسترول والكوليسترول منخفض الكثافة البروتينية الدهنية التي تمثل الدهون الرئيسية التي تسبب الترسبات الدهنية في الشرايين. أجريت هذه الدراسة لتقدير مستوى الكوليسترول الكلي في الدم والكوليسترول الدهني منخفض الكثافة في مرضى متلازمة التمثيل الغذائي في ولاية الخرطوم الذين تم تشخيصهم مسبقا بواسطة الاطباء تبعا لتعريف منظمة الصحة العالمية الذي يشترط وجود داء السكري المقاوم للاسولين مع وجود اثنين او اكثر من عوامل الخطر الاخرى. تم جمع معلومات عن مرضى متلازمة التمثيل الغذائي وعن المرض مثل (الطول ، الوزن ، محيط الخصر ، ضغط الدم ، فترة المرض والتمارين الرياضية). أربعين عينة دم من مرضى متلازمة التمثيل الغذائي وتم جمع أربعين عينة دم من أفراد صحيحين للمقارنة , في ولاية الخرطوم خلال الفترة من يونيو إلى نوفمبر 2019. تم تقدير الكوليسترول الكلي في الدم والكوليسترول الدهني منخفض الكثافة في الدم باستخدام BTS-305 bio systems ثم تم تحليل النتيجة باستخدام برنامج الكمبيوتر SPSS. أظهر التحليل الإحصائي فرق ضئيل في مستوى الكوليسترول الكلي في الحالات: (33.1 ± 166.7) عند مقارنتها بالافراد الصحيحين (20.2 ± 159.9) p=value 0. 27 ، و فرق ضئيل في مستوى LDL-C في الحالات (متوسط ± 29.3 ± 61.7 :SD) بالمقارنة مع الافراد الصحيحين (16.1 ± 54.6) P-value =0.87. زيادة كبيرة في مؤشر كتلة الجسم في الحالات (6.2±30.8) بالمقارنة مع الافراد الصحيحين (3.5±24.1) P-value=0.000، زيادة كبيرة في محيط الخصر في الحالات (11 ± 110) عند مقارنتها بالاشخاص الصحيحين (11.5±83.3) P-value =0.000. أظهر التحليل الإحصائي اختلافًا ضئيلًا في مؤشر كتلة

الجسم في الإناث مقارنة بالذكور P-value = 0.30 ، والفارق ضئيل من الخصر في الإناث بالمقارنة للذكور P-value=0.85، فرق ضئيل في مستوى الكوليسترول الكلي في الإناث عند مقارنتها بالذكو P-value=0.435، الفرق ضئيل من مستوى الكوليسترول منخفض الكثافة البروتينية الدهنية في الإناث عند مقارنتها بالذكور p-value =0.29, فرق ضئيل في ضغط الدم الإنقباضي في الإناث بالمقارنة مع الذكور P-value =0.265 ، فرق ضئيل في ضغط الدم الانبساطي في الإناث بالمقارنة مع الذكور P-value=0.524. أظهر التحليل الإحصائي اختلافًا ضئيلًا في مؤشر كتلة الجسم ومحيط الخصر و ضغط الدم الانيساطي وضغط الدم الانقباضي والكوليسترول الكلي و الكوليسترول منخفض الكثافة البروتينيةالدهنية وفقًا لمدةالمرض (<1سنة,1-5 سنوات, <5 سنوات) القيم الاحتمالية كالاتي تباعا: 0.731، 0.610، 0.894، 0.440، 0.556، 0.196. أظهر التحليل الاحصائي اختلافا ضئيلا في مؤشر كتلة الجسم, محيط الخصر و ضغط الدم الانيساطي وضغط الدم الانقباضي والكوليسترول الكلي و الكوليسترول منخفض الكثافة البروتينيةالدهنية وفقا لفترة التمارين الفيزيائية (لايوجد,<100دقيقة في الاسبوع, 100-150دقيقة في الاسبوع تباعا) القيم الاحتمالية كالاتي تباعا: 0.723، 0.587، 0.779، 0.775، 0.203، 0.332. اظهر التحليل الاحصائي انه لا يوجد ارتباط بين التمارين الرياضية و مستوى الكوليسترول الكلي والكوليسترول منخفض الكثافة البروتينية الدهنية p-value=0.7, 0.5, ODD ratio=0.6, 2 تباعا .

في الختام: مريض متلازمة الأيض لديهم زيادة في مؤشر كتلة الجسم ومحيط الخصر ، مستوى الكوليسترول الكلي والكوليسترول منخفض الكثافة البروتينية الدهنية ، ولم يكن هناك اختلاف في متغيرات متلازمة التمثيل الغذائي بين الإناث والذكور ، وبين فترات المرض ، ولم تتأثر متغيرات متلازمة التمثيل الغذائي من خلال ممارسة الرياضة البدنية.

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List of Abbreviations

AMP	Adenosine monophosphate
AT	Adipose tissue
ATPIII	Adult treatment panel III
ANOVA	Analysis of variance
BMI	Body mass index
C-H	Carbon-hydrogen
CHD	Coronary heart disease
CVD	Coronary vascular disease
CRP	c-reactive protein
DBP	Diastolic blood pressure
EDTA	Ethylenediamine tetraacetic acid
FH	Familial hypercholesterolemia
FFA	Free fatty acid
HDL	High density lipoprotein
HOMA.IR	Homeostatic model assessment of insulin resistance
IR	Insulin resistance
IL	Interleukin
IDF	International diabetes federation
LP	Lipoprotein
LDL-C	Low density lipoprotein cholesterol
m RNA	Messenger ribonucleic acid
MetS	Metabolic syndrome
NCEP	National cholesterol education program
NCD	Non communicable disease
PAI-1	Plasminogen activator inhibitor-1
P.value	Probability value
RPM	Rotate per minute

SAA	Serum amyloid A
SD	Standard deviation
SPSS	Statistical package for social sciences
SAT	Subcutaneous adipose tissue
SBP	Systolic blood pressure
TG	Triglyceride
TNF	Tumor necrosis facter
VAT	Vascular adipose tissue
VLDL	Very low density lipoprotein
WC	Waist circumference
WHO	World health organization

CHAPTER ONE

Introduction-objectives-rationale

1. Introduction, objectives and rationale

1.1. Introduction:

Metabolic syndrome is a group of metabolic abnormalities associated with insulin resistance diabetes mellitus and cardiovascular disease, and all reasons of mortality (Gasevic *et al*., 2014.). It is combined of cardiovascular risk factors including impaired glucose tolerance, hypertension, central obesity and dyslipidemia. Metabolic syndrome predispose patients with high risk of developing type 2 diabetes mellitus, non-alcoholic fatty liver disease, and vascular disease including stroke and cardiovascular disease (McNamara, 2019.). The prevalence of metabolic syndrome has raised at an alarming rate all over the world over the last cobbled decades. In china the prevalence has raised nearly by 20% from 2001 to 2010 (9.8% in 2001 vs 31.0% in 2010) according to the definition of National Cholesterol Education Program (NCEP)-the Adult Treatment Panel III (ATP III) (Fan *et al*.,2019) . The prevalence of metabolic syndrome by WHO criteria in adult with no diabetes Europeans is 15%. In USA the prevalence through those aged 20-29 years was 7%. In Thailand and china the prevalence was between 10-15% (Sabir *et al.,2016*). In a study conducted by Sabir ,Hassan and Elamin in Sudan they were reported that, the prevalence of metabolic syndrome was the highest by using international diabetes federation (IDF) definition (8.4%),then NCEP (7.5%) and finally WHO (6.7%) (Sabir *et al.,2016)*. Low-density lipoprotein is important carrier of cholesterol in the circulation. Raised level of LDL cholesterol adherent with increased risk of developing cardiovascular disease and common feature of metabolic syndrome (Fan *et al*., 2019).

1.2. Rationale:

Metabolic syndrome became very common now a days in Sudan, the incidence increase among people above age fourty, there is a very bad outcome and complication of the syndrome which maybe fatal such as cardiovascular disease and type 2-dibetes. Here in Sudan as general and Khartoum specifically our life style is very unhealthy almost in all aspects eating habits, the absence of physical activity and fitness moreover there is shortage in awareness in early diagnose of the disease and in its controlling . According to the fact that there is no enough data and information about the syndrome here; So this study may provide data to be directed to the Ministry of health and people who are in charge to take decisions and good steps in order to help minimizing the risk and the complications of the syndrome and change people lifestyle to be more healthier. I aimed to estimate the serum level of total cholesterol and LDL-C because they are the main risk factors of CHD which is a serious complication of metabolic syndrome. Total cholesterol and LDL-C believed to be elevated in metabolic syndrome patients this agreed by study conducted at 2013 which showed a significant increase of them (Rooki *et al*., 2013).

1.3. Objectives:

General objective:

To estimate the serum level of total cholesterol and low-density lipoprotein cholesterol among metabolic syndrome patients.

Specific objectives:

- To estimate serum levels of total cholesterol and LDL-C among metabolic syndrome patients and control group.
- To compare the serum levels of cholesterol and LDL-C between metabolic syndrome patient and control group and between females and males.
- To study the effect of physical exercise and duration of disease on cholesterol and LDL-C levels, BMI, WC, SBP and DBP among patients.

CHAPTER TWO

Literature Review

2. literature review

2.1. Metabolic syndrome:

Metabolic syndrome, also called syndrome X, insulin resistance, etc., is defined by WHO as a pathologic condition, characterized by abdominal obesity, insulin resistance, hypertension, and hyperlipidemia . Though there is some differences in the definition by other health care organization, the differences are minor. This new non-communicable disease (NCD) represent the major health hazard of modern world (Saklayen, 2018).

WHO 1999 defined metabolic syndrome as: Presence of insulin resistance or glucose more than 6.1 mmol/L (110 mg/dl), 2 h glucose more than 7.8 mmol (140 mg/dl) (required)

with any two or more of the following **:**

HDL cholesterol less than 0.9 mmol/L (35 mg/dl) in males, less than1.0 mmol/L (40 mg/dl) in females. Triglycerides more than 1.7 mmol/L (150 mg/dl) . Waist/hip ratio more than 0.9 (males) or more than 0.85 (females) or BMI more than 30 kg/m2. Blood pressure more than 140/90 mmHg (Saklayen, 2018).

National Cholesterol Education Program (NCEP) defined metabolic syndrome which does not require demonstration of insulin resistance, but the presence of at least three out of five risk factors for the diagnosis (abdominal obesity, raised blood pressure, raised triglycerides, decreased HDL-cholesterol, and raised fasting glucose) (Cavallari, 2018).

IDF (International Diabetes Federation) 2006 defined metabolic syndrome as: Waist more than 94 cm (males) or more than 80 cm (females) along with the presence of two or more of the following:

Blood glucose more than 5.6 mmol/L (100 mg/dl) or diagnosed diabetes.

HDL cholesterol less than 1.0 mmol/L (40 mg/dl) in males, < 1.3 mmol/L (50 mg/dl) in females or drug treatment for low HDL-C. Blood triglycerides

more than 1.7 mmol/L (150 mg/dl) or drug treatment for elevated triglycerides. Blood pressure more than 130/85 mmHg or drug treatment for hypertension (Saklayen, 2018).

2.1.1. Biology of metabolic syndrome

Subcutaneous adipose tissue (SAT) represent around 80% of the adipose tissue (AT) and is the major supplier of free fatty acids to the liver. increased adipose-insulin resistance in MetS independent of adiposity was documented. Furthermore, adiposeIR correlated significantly and positively with leptin and chemerin and negativly with adiponectin and omentin1. Also, there was a 2.4-fold increase in plasma free fatty acids in the patients with MetS against controls. Adiponectin is a classical adipokine and is the most abundant adipokine secreted exclusively by the AT. Its anti-inflammatory and cardioprotective roles are mediated by the receptors, adiponectin receptor 1 and adiponectin receptor 2. Adiponectin has been shown to be reduced in chronic obesity and/or insulin resistant states in animal models and human subjects and has been shown to decrease atherosclerotic vascular lesions in vivo. Adiponectin is an insulin-sensitizing adipokine, it has a role in glucose and lipid homeostasis, through the activation of adenosine monophosphate (AMP)-activated protein kinase. In addition, it suppresses tumor necrosis factor (TNF)α, decreases oxidative stress, prevents cell apoptosis and decreases foam cell creation . A strong association between low levels of adiponectin and raised insulin resistance has been well established both in vivo and in vitro in animal models and humans. Adiponectin levels are significantly decreased in MetS patients compared to controls (Jialal and Devaraj, 2018).

Leptin Aids Restrict Abdominal Fat Deposition, Leptin levels firstly rise with increasing fat cell mass and deliver feedback to the hypothalamus of adequate “adiposity” or energy reserves. The hypothalamus then suppresses appetite, motivates physical activity, and promotes thermogenesis to

consume excess calories. So, leptin plays a critical role in directing fat deposition and control of body weight. Leptin normally directs deposition of fat to preexisting subcutaneous fat cells, while limiting ectopic TG deposition and expansion of deposition within VAT. Rapid or extreme weight gain leads to dyslipidemia and leptin resistance, causing the unresponsiveness of the hypothalamus, no longer suppressing hyperphagia. Infusion of leptin into leptindeficient animals adjusts diet-induced steatosis and dyslipidemia (Grade, 2010).

Serum amyloid A (SAA) as well as CRP circulating levels are significantly higher in obese subject than normal weight subjects. Numerous studies report that SAA is a reliable marker of low-grade inflammation in human obesity. It was reported that a significant rise in both plasma and SAT-secreted CRP and SAA in MetS assuring further that CRP derives from extra-hepatic sources also . with reference to the AT, the amount of SAT in subjects with MetS positively associates with increasing MetS factor scores and negatively associates with circulating adiponectin levels and positively with CRP levels (Jialal and Devaraj, 2018).

Chemerin Produced by both the liver and AT, is a chemoattractant for macrophages and appears to stimlate insulin resistance in skeletal muscle. furthermore levels are increased in diabetes and obesity. In patients with some criteria of MetS, chemerin levels are also increased. It was reported that plasma and SAT-secreted chemerin in nascent MetS levels were significantly increased independent of adiposity, and that both plasma and SAT-secreted levels correlated significantly. Moreover, chemerin associated significantly with high sensitivity CRP, homeostatic model assessment of insulin resistance (HOMA-IR), hypertriglyceridemia, systolic blood pressure and inversely with HDL-cholesterol. Therefore, SAT-secreted chemerin is an adipokine that could participate in both the pro-inflammatory state and insulin resistance of MetS (Jialal and Devaraj, 2018).

Omentin-1 appears to be derived predominately from vascular adipose tissue (VAT) and is reported to have insulin sensitizer actions (which induce glucose uptake stimulated by insulin in adipocytes). Lesser levels have been found in both obesity and diabetes. It was documented that both lower plasma and SAT secreted omentin-1 independent of adiposity. Importantly, decrease levels of omentin in patients with MetS have been related with increased severity of coronary artery disease (Jialal and Devaraj, 2018).

2.1.2. Etiology of Metabolic syndrome:

Development of metabolic syndrome count on two elements: firstly adult weight earning, with body fat accumulation and secondly a tendency to locate fat in intra-abdominal sites, including ectopic fat in liver, pancreas and heart. The metabolic syndrome is highly linked to a lifestyle described by a facile access to unlimited supply of high caloric, low nutrient-dense, foods and physical inactivity. This exposure is most effective during early period of life resulting in childhood obesity which is a main risk for metabolic syndrome in adulthood. Psychosocial stress has been suggested to contribute too, with most metabolic components are more predominant in socioeconomically deprived populations. Not all individuals develop metabolic syndrome because of the high individual differences and genetic/epigenetic factors for both the components of the syndrome, for example insulin resistance and dyslipidemia and body composition and their expression varies with alteration in external environment. It is estimated that genetic factors represent about 30% of the observed difference in BMI but about 70% of the difference in fat distribution that relates more to the metabolic syndrome. The lifestyle factors that rise intra-abdominal fat and metabolic risk factors are weight gain, a diet rich in saturated fat, smoking, inactivity and excess alcohol intake. Over 40 genetic differences since have been identified to associate with BMI, fat distribution or risk of obesity and metabolic syndrome. While certain excessively uncommon single gene

mutations (e.g. leptin deficiency, leptin-receptor defects) can cause vast obesity, usually expressed in early childhood, genetic factors which influence BMI appear to contribute little to the very substantial weight gain needed to generate obesity (Han and Lean, 2015).

2.1.3. Risk factors for metabolic syndrome:

Clinicians have historically evaluated each of the main risk factors contributing to metabolic syndrome on an individual basis. One of the major factors thought to accelerate the pathway is insulin resistance. It is the presence of specifically a high waist circumference that seems to contribute to the process. The visceral fat element of abdominal obesity ends up in not solely insulin resistance but additionally the release of nonesterified free fatty acids from adipose tissue. Thus, lipids accumulate in different sites like liver and muscle, and predisposing to insulin resistance and dyslipidemia. In addition, adipose tissue may produce different adipokines that may individually impact insulin resistance and CVD risk factors. These characteristics coupled with elevated blood pressure and dyslipidemia tend to be usually manifested as prothrombotic and proinflammatory states. The overlap of these factors in each disease state, leading to increased atherogenic risks (Sherling *et al*., 2017).

2.1.4. Criteria of Metabolic syndrome

The most widely used feature for the metabolic syndrome are those of the National Cholesterol Education Program ATP III. They combine cut-offs of blood pressure, HDL cholesterol, fasting triglycerides and fasting glucose e all set at levels beneath their individual treatment thresholds but which in combination greatly rise the risks of type 2 diabetes also the premature CHD. These feature also included a cut-off of waist circumference and the presence of three of the components is required for ‘diagnosis’. More recently, a group from the International Diabetes Federation (IDF) has

suggested a simpler set of feature, which requires a large waist circumference (set at a slightly lower level than ATP III) plus two other criteria. The IDF criteria are pointed at diabetes prevention as well as CVD prevention, and so use lower cut-offs of waist circumference and fasting blood glucose. The aim of applying these diagnostic criteria, apart from epidemiological surveys, is to start preventive interventions for an individual patient's weight management to prevent diabetes and CVD. A number of other metabolic abnormalities may co-exist, such as the presence of inflammation (e.g. elevated serum C-reactive protein (CRP), uric acid and cytokines) and a prothrombotic state (e.g. plasminogen activator inhibitor 1 (PAI-1)). A variety of obesity, and metabolic syndrome. Although only a small proportion of the difference in obesity (<2%) is observed to be attributable to common allelic differences, these risk alleles are considered likely to participate to obesity in a polygenic manner such that people who carry a higher number of risk alleles (>10) will gain extra body weight more than people who carry lower number (Han and Lean., 2015).

Table 2.1 : Criteria used in the diagnosis of metabolic syndrome according to NCEP and IDF definitions (Han and Lean, 2016).

Large waist circumference	**1**	**2**
Male	>102 cm (40 in)	>94 cm (37 in)
Female	>88 cm (35 in)	>80 cm (32 in)
High triglycerides	> 1.7 mmol/L (150 mg/dL)	> 1.7 mmol/L (150 mg/dL)
Decreased HDL cholesterol		
Male	<1.03 mmol/L (40 mg/dL)	<1.03 mmol/L (40mg/dL)
Female	<1.29 mmol/L (50 mg/dL)	<1.29 mmol/L (50 mg/dL)
High blood pressure	> 130/ 85 mmHg	130/ 85 mmHg
High fasting plasma glucose	>6.1 mmol/L (110 mg/dL)	5.6 mmol/L (100 mg/dL)

1. NCEP proposals: any three features
2. IDF proposals: large waist plus two other features

2.1.5. Pathophysiology of metabolic syndrome

High glucose and insulin resistance: some of the links between components of the metabolic syndrome attached to insulin resistance, although about 30% of cases with the metabolic syndrome have normal insulin sensitivity. Insulin resistance is characterized by an elevated plasma insulin concentration that fails to reduce plasma glucose normally. The participating factors are complex ; a central feature is unresponsiveness to insulin at the cellular level because of alteration in receptor binding or post-receptor mechanisms. high free fatty acid (FFA) concentrations as a common mediator is suggested, attached to an expanded intra-abdominal fat mass. Insulin resistance differ between tissues and organs (e.g. subcutaneous/white and intra-abdominal/brown adipose tissues, muscle, liver, skin); this might be important in the clinical manifestation of insulin resistance, pancreatic b-cell defects and impaired insulin secretion. Insulin resistance is closely attached to deteriorated glucose tolerance, diabetes and risk of CHD (Han and Lean, 2015).

Hypertension and insulin resistance: The relationship between insulin resistance and hypertension has been recognized and relates to numerous possibly different mechanisms. First, it is important to record that insulin is a vasodilator when given iv to individuals of normal weight, with secondary impact on sodium reabsorption in the kidney. Evidence indicates that sodium reabsorption is raised in whites but not Africans or Asians with the MetS. In the setting of insulin resistance, the vasodilatory influence of insulin can be lost , but the renal influence on sodium reabsorption kept. Fatty acids can mediate proportional vasoconstriction. Also, the infusion of fatty acids into the portal vein triggers the sympathetic nervous system and elevates blood pressure in rodents. Insulin also raises the activity of the sympathetic nervous system, an influence that might also be preserved in the setting of insulin resistance. Since adipose tissue is a source of angiotensinogen, the

association of hyperaldosteronism with hypertension and the MetS is not a surprise. Recent evidence also proposes that raises in adipocyte-derived resistin and leptin may contribute to the pathogenesis of hypertension in insulin resistance patients (Cornier, 2008).

Dyslipidemia refers to a poor lipid profile, involving increased TGs level, increased total cholesterol level, and a reduced HDL-to- LDL ratio. This state is typically found in obese patients with insulin and leptin resistance, and often results in lipotoxicity and atherosclerosis. High FFAs contribute significantly to lipotoxicity and athero-sclerosis, but their levels are rarely measured (grade, 2010).

Inflammation: activation of various pro-atherogenic pathways in MetS ends in a final common pathway of inflammation that finally leads to clinical manifestations of MetS. Inflammation has important contribution in the pathogenesis of CVD and numerous inflammatory markers have been shown to be raised in patients with MetS. Tumor necrosis factor alpha: Macrophages within the adipose tissue secrete tumor necrosis factor alpha (TNF- α) and its production rises with rise in adipose tissue mass. TNF- α causes phosphorylation and alter the activity of insulin receptors in the adipose tissue and in smooth muscle cells, the induction of lipolysis increasing FFA load, and inhibits adiponectin release. Raised serum TNF- α levels are linked with obesity and insulin resistance, both of which are chief components of MetS. Interleukin-6 and C-reactive protein*:* Interleukin-6 (IL-6) is a cytokine formed by adipocytes and immune cells and has complex regulatory mechanisms. Production of IL-6 rises with elevation in body fat and insulin resistance. It acts on the liver, bone marrow, and endothelium, leading to increased production of acute phase reactants in the liver, including C-reactive protein (CRP). Several studies have demonstrated a association between high CRP levels and the development of MetS, diabetes, and CVD. IL-6 also rises fibrinogen levels causing a prothrombotic state.

IL6 also encourages adhesion molecule expression by endothelial cells (Rochlani, 2017).

Polycystic ovaries and depression: females with the metabolic syndrome are predisposed to have polycystic ovary syndrome and depression, which may be partly explained by disturbances in insulin, cortisol and sex hormones, with decreased sex hormone binding globulin (Han and Lean, 2015).

Large waist circumference and intra-abdominal fat accumulation:

The structure and function of adipose tissues differ between anatomical sites.s Intra-abdominal fat (mostly omental and retroperitoneal) displays higher rates of lipolysis and glycolysis than subcutaneous fat, and greater mitochondrial density (reflecting its origin as brown adipose tissue). It appears to be largely involved, not in fat storage, but in high-turnover fatty acid provision to the liver and elsewhere. Problems seem to happen when intra-abdominal fat becomes used as fat storage. Increased abdominal fat mass (mainly the intra-abdominal fat depot) is readily recognized as an 'apple-shaped' torso and might have a direct intermediary role in the development of the metabolic syndrome. It has been proposed that the great amounts of FFAs secreted via the portal system into the liver by the highly metabolically active intra-abdominal (visceral) fat mass might interfere with insulin clearance by the liver. Intra-abdominal fat is now recognized as an active endocrine organ secreting a number of cytokines (adipokines), including leptin, adiponectin, resistin, interleukins (IL) such as IL-1 and IL-6, and tumour necrosis factor alpha (TNF-a), which are important substances in energy regulation. Extreme amounts of these substances released by an expanded intra-abdominal fat mass are related with increased metabolic disorders. It is not easy to interpret the relation between visceral fat and risk factors for CVD because there are many confounding factors (e.g. subcutaneous fat and skeletal muscle mass, lifestyle and hormonal factors). Specific subcompartments of intraabdominal fat (e.g. intraperitoneal and

retroperitoneal, because of their closeness to the portal system) may be serious but it is difficult to study these depots separately from the total intra-abdominal fat mass, or even entire abdominal fat. However, surveillance of high incidence of the metabolic syndrome, in individuals with partial lipodystrophy or those with spinal cord damage, have brought to light the important roles of subcutaneous adipose tissue and skeletal muscle in the development of metabolic disturbances (Han and Lean, 2015).

2.1.6. Management of the metabolic syndrome

MetS doubles the risk of CVD consequences and rises all causes of mortality by 1.5 times. Management of MetS involves a dual system that combines lifestyle changes and pharmacological interventions in an effort to reduce CVD. Lifestyle modification: MetS results from increased calorie intake disproportionate to metabolic requirements. Lifestyle modification is essential in the management of underlying risk factors. Weight reduction and conservation of ideal body weight are essential preventive and management strategies. Pharmacotherapy is another option for prevention of CVD such as statin for the management of dyslipidemia and antiplatelet drugs for decreasing prothrombotic risk. Moreover there are dietary supplements that provide health benefits as management of MetS (Rochlani, 2017).

2.1.7. Prevention of metabolic syndrome

Whereas there are encouraging developments in the management of the metabolic syndrome, the superior need is for prevention. Although metabolic disorders naturally develop with age, numerous changeable factors can be removed in order to prevent acceleration of this process. At-risk individuals can be recognized from their family history and large waist circumference. Serious tissue damage has already happened by the time diabetes has developed. Regular physical exersice (brisk walking for 24 hoursper week) is possible to prevent most instances of metabolic syndrome and, even after

it has developed, modest weight loss (about 5 kg) can inverse all its components, thus decreasing its occurrence and its future incidence, as well as preventing about 60% of new cases of diabetes. Modest weight loss with orlistat has beenshown to decrease the incidence of metabolic syndrome and of diabetes by 30-40%. Metformin can prevent progression of pre-diabetes, it opposites metabolic syndrome in only 5% of cases (Han and Lean, 2015). .

2.2. Lipids

The term lipid applies to a class of compounds that are soluble in organic solvents, but not soluble in water. lipids contain primarily nonpolar carbon-hydrogen (C-H) bonds and yield fatty acids and or complex alcohols after hydrolysis. Some lipids also contain charged or polar groups, such as sialic, phosphoryl, amino, sulfuryl or hydroxyl groups. The existence of these chemical groups gives lipid molecules an affinity for both water and organic solvents (amphipathic). This allows them to exist at the aqueous interface of biological membranes. Overall, lipids are approximately subdivided into six groups based on their chemical structure, namely (1) cholesterol, (2) fatty acids, (3) acylglycerols, (4) sphingolipids, (5) prostaglandins, and (6) terpen (Burits *et al.*, 2001).

Lipids, commonly referred to as fats, have a dual function. First, because they are composed of mostly carbon-hydrogen (C-H) bonds, so they are a rich source of energy and an effective way for the body to store excess calories. Because of their unique physical characteristic, lipids are also an essential part of cell membranes and, thus, also play an important structural role in cells. The lipids transported by lipoproteins, are triglycerides, phospholipids, cholesterol, and cholesteryl esters, are also the main lipids found in cells (Bishop, *et al.*, 2010).

2.2.1. Cholesterol

Cholesterol is found almost solely in animals and is a key membrane constituent of all cells. It is a steroid alcohol with 27 carbon atoms that are organized in a tetracyclical sterane ring system, with a C-H side chain. Cholesterol is mainly composed of C-H bonds, and hence it is fairly water insoluble. It does, though, have a polar hydroxyl (OH) group on its A-ring. Therefore, it is both a polar and nonpolar molecule (amphipathic) (Burits *et al*., 2001).

2.2.1.1. Cholesterol Absorption

The average American diet is assessed to contain around 300 to 450 mg of cholesterol per day, which mostly comes from the ingestion of animal products. A similar quantity of cholesterol arrives the gut from biliary secretions and the turnover and release of intestinal mucosal cells. Nearly all cholesterol in the intestine is present in the unesterified (free) form. Esterified cholesterol, which comprises a fatty acid attached to the hydroxyl group on the A-ring, is rapidly hydrolyzed, in the intestine by cholesterol esterases which secreted from the pancreas and small Intestine to free cholesterol and fatv acids , Before absorbetion, cholesterol is first solubilized through a procedure named emulsification. Emulsification happens by the creation of mixed micelles that contain (1) unesterified cholesterol, (2) fatty acids, (3) monoglycerides, (4) phospholipids, and (5) conjugated bile acids. Bile acids, by acting as detergents, are the utmost critical factor in micelle formation. In their absence, digestion and absorption of both cholesterol and triglyceride are severely reduced. The capability of cholesterol to form micelles is also influenced by the amount of dietary fat hut not its degree of saturation. Increased quantities of fat in the diet results in the rise of mixed micelles, which in turn allows for more cholesterol absorption. Most cholesterol absorption happens in

the middle jejunum and terminal ileum parts of the small intestine and is mediated by the enterocyte surface protein. This protein is the target for the drug ezetimibe that blocks cholesterol absorption. Once cholesterol enters the intestinal mucosal cell, it is wrapped with triglycerides, phospholipids, and a large protein called apolipoprotein B-48 into large lipoprotein particles named chylomicrons. Chylomicrons are secreted into the lymph and finally enter the circulation where they carry the absorbed dietary lipid to the liver and peripheral tissues (Burits *et al*., 2001).

2.2.1.2. Cholesterol synthesis

Cholesterol is synthesized from its precursor unit acetyl-CoA through a complex metabolic pathway. Eighteen acetyl CoA units having 36 carbon (C) atoms are consumed to synthesize one molecule of cholesterol; which contains 27 C atoms and 46 hydrogen (H) atoms. Seven H atoms are incorporated into the cholesterol molecule directly from water while another 15 atoms are implanted from nicotinamide adenine dinucleotide phosphate-oxidase (NADPH). H atoms from water may also become combined to substrates that later generate cytosolic acetyl CoA used for cholesterol biosynthesis. HMG-CoA reductase is the rate-limiting enzyme in cholesterol synthesis. Recently squalene monooxygenase, which catalyzes the first oxygenation step in cholesterol synthesis, was proposed to represent a possible second control point in cholesterol synthesis beyond HMG-CoA reductase. The importances of cholesterol synthesis for survival is demonstrated by the fact that faults in the cholesterol synthesis pathway are generally lethal in mice. Complete loss of function of early cholesterogenic enzymes is seldom described in humans and deficiencies of these enzymes lead to severe malformations and disease (Van der Wulp, 2013).

2.2.2. General lipoprotein structure

.Lipoproteins are typically round in shape and range in size from 10 to 1200 nm. Lipoproteins are composed of both lipids and proteins, called apolipoproteins. The amphipathic cholesterol and phospholipid molecules are mainly found on the surface of lipoproteins as a single monolayer, while the hydrophobic and neutral triglyceride and cholesteryl ester molecules are found in the core region. Because the chief role of lipoproteins is the transfer of fuel to peripheral cells, the core of the lipoprotein particle essentially represents the load that is being transported by lipoproteins. The size of the lipoprotein particle associates with its lipid content. The larger lipoprotein particles have correspondingly larger core regions and, thus, consist of relatively more triglyceride and cholesteryl ester. The larger lipoprotein particles also consist of more lipid relative to protein and thus are lighter in density The numerous lipoprotein particles were originally separated by ultracentrifugation into different density fractions (chylomicrons [chylos], VLDL, LDL, and HDL). Apolipoproteins are mainly situated on the surface of lipoprotein particles. They help preserve the structural integrity of lipoproteins and also work as ligands for cell receptors and as activators and inhibitors of the various enzymes that modify lipoprotein particles. Apolipoproteins consist of a structural motif called an amphipathic helix, which accounts for the capability of these proteins to bind to lipids . Amphipathic helices are protein segments organized in coils so that the hydrophobic amino acids residues interact with lipids, whereas the part of the helix containing hydrophilic amino acids faces away from the lipids and in the direction of the aqueous environment (Bishop *et al*., 2010).

Apo B Is a large protein with a molecular weight of approximately 500 kD and the main protein on LDL, VLDL, and chylomicrons. Apo B

exists in two forms: apo B-100 and apo B-48. Apo B-100 is found on LDL and VLDL and is a ligand for the LDL receptor, and it is, therefore, very important in the uptake of LDL by cells. Apo B-48, solely found in chylomicrons, is essentially the first 48% or half of the apo B molecule and is produced by posttranscriptional editing of the apo B-100 mRNA. Apo B-100 can also be found covalently linked to apo (a), a plasminogen- like protein that is found in a proatherogenic lipoprotein particle called lipoprotein (a) (Lp(a)). Apo E, another important apolipoprotein found on many types of lipoproteins (LDL, VLDL, and HDL), also works as a ligand for the LDL receptor and the chylomicron remnant receptor. There are three major isoforms of apo E: apo E2, E3, and E4. The apo E isoforms affect lipoprotein metabolism because they vary in their capability to interact with the LDL receptor. The association with lipid metabolism is not fully understood, but individuals with the apo E4 isoform have been shown to have an increased risk for developing Alzheimer's disease (Bishop *et al*., 2010).

2.2.2.1. Low-Density Lipoproteins

LDL mainly contains apo B-100 and is more cholesterol rich than other apo B–containing lipoproteins. They produced as a consequence of the lipolysis of VLDL. LDL is readily taken up by cells via the LDL receptor in the liver and peripheral cells. In addition, because LDL particles are significantly smaller than VLDL particles and chylomicrons, they can penetrate into the extracellular space of the vessel wall, where they can be oxidized and taken up by macrophages through numerous scavenger receptors. Macrophages that take up too much lipid become filled with intracellular lipid drops and became foam cells, which are the main cell type of fatty streaks, an early precursor of atherosclerotic plaques. LDL particles can exist in numerous sizes and arrangements and have been separated into as many as eight subclasses Through density

ultracentrifugation or gradient gel electrophoresis. The LDL subclasses vary largely in their content of core lipids; the smaller particles are denser and have relatively more triglyceride than cholesteryl esters. Currently, there has been great interest in measuring LDL subfractions, because small, dense, LDL particles have been shown to be more proatherogenic and may be a better marker for coronary heart disease risk (Bishop *et al.*, 2010). LDL is believed to play a vital role in starting and promoting plaque formation. It is placed into the subendothelial space where it is taken up by different cells, including macrophages. This changes the gene and protein expression pattern of these cells and can promote an inflammatory response, particularly when LDL becomes oxidized. Injury signals from the developing plaque trigger the expression of adhesion proteins on endothelial cells and the production of soluble chemotactic proteins from resident macrophages, which encourages the attachment and infiltration of additional macrophages, lymphocytes, and platelets to the plaque. Continual injury and repair lead to additional narrowing of the vessel opening, or lumen, causing the blood to circulate in a nonlaminar manner under greater pressure, which further aggravates plaque formation. The final event leading to complete obstruction of blood flow occurs when there is a hemorrhage into the plaque, which results in the development of a thrombus that blocks blood flow and precipitates a myocardial infarction (Bishop *et al.*, 2010).

2.2.3. Clinical significance

Hypercholesterolemia

Hypercholesterolemia is the lipid abnormality most closely related to heart disease. One form of the disease, which is related with genetic abnormalities that predispose affected individuals to raised cholesterol levels, is named familial hypercholesterolemia (FH). Homozygotes for FH are luckily rare (1:1 million in the population) and can have total

cholesterol concentrations as high as 800 to 1,000 mg/dL (20–26 mmol/L). These patients frequently have their first heart attack while they still teenagers. Heterozygotes for the disease are seen much more commonly (1:500 in the population) because it is an autosomal codominant disorder; a defect in just one of the two copies of the LDL receptor can unfavorably affect lipid levels. Heterozygotes tend to have total cholesterol concentrations in the range of 300–600 mg/dL (8–15 mmol/L) and, if not treated, become symptomatic for heart disease in their 20s to 50s. Approximately 5% of patients younger than age 50 with CAD are FH heterozygotes. Other symptoms associated with FH include tendinous and tuberous xanthomas, which are cholesterol deposits under the skin, and arcus, which are cholesterol deposits in the cornea. In both homozygotes and heterozygotes, the cholesterol raise is primarily related with an rise in LDL cholesterol. These individuals synthesize intracellular cholesterol normally but lack active LDL receptors. So, LDL builds up in the circulation since there are inadequate receptors to bind the LDL and transfer the cholesterol into the cells. Most individuals with raised LDL cholesterol levels do not have FH but are still at high risk for premature CHD and should be preserved on a low-fat, low-cholesterol diet and receive statin treatment when needed. Regular physical activity should also be combined, with drug therapy (Bishop *et al*., 2010).

2.2.4.Association of lipids with coronary heart disease

Increased cholesterol is a factor in the cause of atherosclerotic diseases. As early as 1910, Windaus described cholesterol in the lesions of atherosclerotic diseased arteries. Numerous studies have established that when the total cholesterol and LDL cholesterol concentrations are high, the incidence and prevalence of CHD are also high. In contrast to LDL cholesterol, increased HDL cholesterol concentrations have been shown to be protective for CHD in both epidemiological and clinical trial

studies. Because atherosclerosis begins at an early age and can take decades to clinically manifest itself, the measurement of plasma lipids and lipoproteins is a valuable means to identify individuals at risk for CHD and determine the most appropriate therapy (Burits *et al*., 2001).

Other diseases include genetic disorder of lipoprotein metabolism, common genetic polymorphism of the many enzymes, structural proteins, and receptors involved in lipoprotein metabolism are supposed to have major effect on any individual predisposition for developing dyslipidemia. (Burits *et al*., 2001).

CHAPTER THREE

Material and methods

3. Materials and methods

3.1. Materials

3.1.1. Study design:

This is a cross sectional hospital based study.

3.1.2. Study area:

The study was conducted in Khartoum state-Sudan.

3.1.3. Study period:

The study was carried out over five months from June to November 2019 in Abdalla Khalil center for diabetes and prof Mahadi diabetes center.

3.1.4. Ethical consideration :

This study was approved by the scientific Committee of Clinical Chemistry Department in Sudan University of Science and Technology. A written informed consent was obtained from each participant (appendix I), data was collected by using questionnaire (appendix II).

3.1.5. Study population:

This study included 40 Sudanese metabolic syndrome patients who are already diagnosed by the doctors according to WHO criteria which require presence of insulin resistance diabetes mellitus and two or more of the risk factors (19 of them were males and the other 21 were females) and 40 healthy individuals as control group (19 of them were males and 21 of them were females), Age was matched in both groups, and ranged from 24 to 69 years. Females and males with metabolic syndrome were excluded from this study if they had chronic renal disease, thyroid disease or pregnant women.

3.1.6. Sampling:

Three ml of venous blood was collected from each participants and placed in plain containers and left till formation of clot at room temperature then serum was obtained after centrifugation for 3 minutes at 3000 RPM and kept until analysis.

3.2. Methods:

Estimation of serum total Cholesterol , LDL cholesterol concentrations was done by using Biosystem analyzer.

3.2.1. Cholesterol Estimation:

Principle of method:

Cholesterol ester is hydrolyzed by cholesterol esterase in the presence of water molecule which produces cholesterol and fatty acid, cholesterol is oxidized by cholesterol oxidase in the presence of oxygen and water molecule which produces cholestenone and H_2O_2 is measured quantitatively in peroxidase catalyzed reaction that produce a color in the presences of 4-aminoantipyrine and phenol, absorbance of the color is measured at 500 nm. The color intensity is proportional to cholesterol concentration (Appendix III).

3.2.2. LDL Cholesterol Estimation:

Principle of method:

Low density lipoprotein (LDL) in the precipitate with polyvinyl sulphate. Their concentration is calculated from the difference between the serum total cholesterol and the cholesterol in the supernatant after centrifugation by the same principle mentioned above in cholesterol estimation. The cholesterol is spectrophotometrically measured by means of the coupled reaction described below (appendix IV).

3.3. Quality Control:

Biochemistry control serum level I (cod. 18005, 18009 and 18042) and II (cod. 18007 ,18010 and 18043) were used to verify the performance of the measurement procedure and to assure the accuracy of results.

3.4. Statistical analysis:

Data was statistically analyzed by using SPSS computer program version 16, T test and ANOVA test were used for comparison of means and chi square test was used for calculation of odds ratio. p-value < 0.05 considered significant.

CHAPTER FOUR

Results

4. Results

In this study 80 individuals were enrolled, 40 metabolic syndrome patients as case group and 40 healthy individuals as control group to assess serum level of total cholesterol and LDL-C among both groups in Khartoum state, data were analyzed statistically using computer SPSS program and the results were as follow:

Table 4.1: shows significant increase in BMI in cases (mean±SD: 30.8±6.2) when compared to control (24.1±3.5) p- value =0.000, significant increase in W.C in cases (mean±SD: 110±11) when compared to control (83.3±11.5) p- value = 0.000, insignificant difference in total cholesterol level in cases (mean±SD: 166.7±33.1) when compared to control (159.9±20.2) p- value= 0.27, and insignificant difference in LDL-C level in cases (mean±SD: 61.7±29.3) when compared to control (54.6±16.1) p- value: 0.87.

Table 4.2: shows insignificant difference of BMI in females (mean±SD: 31.8±6.6) when compared to males (29.7±5.8) p- value= 0.30, insignificant difference of W.C in females (mean±SD: 107±9.8) when compared to males (113.2±11.7) p- value = 0.085, insignificant difference of total cholesterol level in females (mean±SD: 170.6±25.5) when compared to males (162.3±40) p- value=0 .435, insignificant difference of LDL-C level in females (mean±SD: 57±19) when compared to males (66.8±37.6) p- value = 0.295, insignificant difference of SBP in females (mean±SD: 138.2±18.7) when compared to males (131.8±14.3) p- value = .265, insignificant difference in DBP in females (mean±SD: 84.2±10.3) when compared to males (86.2±7.6) p- value = .524.

Table4.3*:* shows insignificant difference in the BMI,W.C ,Total cholesterol, LDL-C,SBP and DBP According to duration (duration of metabolic

syndrome <1Years, 1-5Years, >5Years respectively) Mean±SD and P- values as follow: For BMI: 28.9±4.9, 31.3±7.9, 31.4±5.4, p-value 0.731.For W.C(cm) : 113±11.2, 106.9±10.7, 110.9±11.7, p- value 0.610. For SBP: 136.8±13.1, 132.3±20.6, 136.8±15.9, p- value 0.894. For DBP: 89.4±7.3, 83.8±12.1, 83.6±6, p- value 0.440.For total cholesterol (mg/dl): 175.4±35.6, 160±30.7, 167.5±34.4, p- value 0.556. For LDL-C(mg/dl): 48.6±19.2, 65.8±34.5, 65.2±28.6, p-value 0.196.

Table 4.4: shows insignificant difference in the BMI,W.C ,Total cholesterol, LDL-C,SBP and DBP According to duration (nil, <100 minute a week, 100-150 minute a week respectively) of physical exercise mean±SD and p-value as follow:

For BMI: 31.1±7.1, 29±4, 31.7±4.3, p-value 0.723. For W.C(cm): 109.7±10.9, 107.7±15, 114±6.5, p-value 0.587. For SBP: 135.4±17.8, 138±16.4, 130±11.5, p-value 0.779. For DBP: 85.7±9.3, 84±11.4, 82.5±5, p-value 0.775. For total cholesterol(mg/dl): 170±35.8, 173±23.7, 144.5±22.3, p-value 0.203. For LDL-C(mg/dl): 57±27.6, 68.3±26.2, 74.9±39.1, p-value 0.332.

Table 4.5: shows the association between odd ratios of physical exercise on total cholesterol and LDL-C levels in metabolic syndrome patients ODD ratios and p-value respectively as follow: for LDL-C (0.4, p-value=0.5), for total cholesterol (1.7, p-value=0.7).

Table 4.1: Comparison between BMI, W.C, Total cholesterol and LDL-C in metabolic syndrome patient and control group

Variable value	Case n=40 (Mean ± SD)	Control n=40 (Mean ± SD)	P. value
BMI	**30.8 ± 6.2**	**24.1 ± 3.5**	**0.000**
W.C (cm)	**110 ± 11**	**83.3 ± 11.5**	**0.000**
T.C (mg/dl)	**166.7 ± 33.1**	**159.9 ± 20.2**	**0.27**
LDL (mg/dl)	**61.7 ± 29.3**	**54.6 ± 16.1**	**0.87**

Independent sample T test used, p. value <0.05 considered significant.

Table 4.2: Comparison between mean of BMI, W.C, Total cholesterol, LDL-C, systolic blood pressure and diastolic blood pressure in female and male group.

Variable	FEMALE N=21	MALE N=19	P.VALUE
BMI	**31.8 ± 6.6**	**29.7 ± 5.8**	**0.30**
W.C (cm)	**107 ± 9.8**	**113.2 ± 11.7**	**0.085**
T.C (mg/dl)	**170.6 ± 25.5**	**162.3 ± 40**	**0.435**
LDL (mg/dl)	**57.0 ± 19.0**	**66.8 ± 37.6**	**0.295**
SBP (mmHg)	**138.2 ± 18.7**	**131.8 ± 14.3**	**0.265**
DBP (mmHg)	**84.2 ± 10.3**	**86.2 ±7.6**	**0.524**

Independent sample T test used, p. value <0.05 considered significant.

Table 4.3: Comparison between mean of BMI, W.C, SBP, DBP, Total cholesterol and LDL-C according to duration of metabolic syndrome.

Variable	Mean ± SD			P.VALUE
	< 1 year	1-5 years	> 5 years	
BMI	28.9 ± 4.9	31.3 ± 7.9	31.4 ± 5.4	0.731
W.C (cm)	113 ± 11.2	106.9 ± 10.7	110.9 ± 11.7	0.610
SBP(mmHg)	136.8 ± 13.1	132.3 ± 20.6	136.8 ± 15.9	0.894
DBP(mmHg)	89.4 ± 7.3	83.8 ±12.1	83.6 ± 6.0	0.440
TC (mg/dl)	175.4 ± 35.6	160.0 ± 30.7	167.5 ± 34.4	0.556
LDL(mg/dl)	48.6 ± 19.2	65.8 ± 34.5	65.2 ± 28.6	0.196

One way ANOVA was used for comparison of variable among duration of metabolic syndrome.

Table 4.4: Comparison between mean of BMI, W.C, SBP, DBP, Total cholesterol and LDL-C according to duration of physical exercise.

Variable	No physical exercise	< 100min	100-150min	P.VALUE
BMI	**31.1 ± 7.1**	**29.0 ± 4.0**	**31.7 ± 4.3**	**0.723**
W.C (cm)	**109.7 ± 10.9**	**107.7 ± 15.0**	**114.0 ± 6.5**	**0.587**
SBP(mmHg)	**135.4 ± 17.8**	**138.0 ± 16.4**	**130.0 ± 11.5**	**0.779**
DBP(mmHg)	**85.7 ± 9.3**	**84.0 ± 11.4**	**82.5 ± 5.0**	**0.775**
TC (mg/dl)	**170 ± 35.8**	**173 ± 23.7**	**144.5 ± 22.3**	**0.203**
LDL (mg/dl)	**57.0 ± 27.6**	**68.3 ± 26.2**	**74.9 ± 39.1**	**0.332**

One way ANOVA was used for comparison of variable among physical exercise periods.

Table 4.5: the association between the odd ratios of physical exercise for LDL-C and TC levels in metabolic syndrome patients

	Physical Exercise yes	**Physical Exercise No**	**Odd ratio**	**95% CI**	**p-value**
LDL-C normal	**11**	**27**	**0.4**	**0.023-7.108**	**0.5**
LDL-C abnormal	**1**	**1**			
TC normal	**13**	**23**	**1.7**	**0.159-18.015**	**0.7**
TC abnormal	**1**	**3**			

Chi-square test was used, p-value<0.05 considered significant

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CHAPTER FIVE

Discussion, conclusion and recommendations

5. Discussion, conclusion and recommendations

5.1 Discussion:

Metabolic syndrome is a group of risk factors (insulin resistance diabetes mellitus, hypertension, dyslipidemia and central obesity) that predispose patients to cardiovascular disease and type 2 diabetes mellitus (McNamara, 2019).

The present study aimed to assess serum level of total cholesterol and LDL-C in metabolic syndrome patients. 40 metabolic syndrome patients were enrolled as cases and 40 normal individuals were enrolled as control group, age is ranged from 24 to 69 years, the data analysis was done by using SPSS computer program. The result showed that body mass index and waist circumference were significantly increased in cases with metabolic syndrome, this result agreed with study done by Augusthy *et al*., 2017 that BMI was significantly increased in metabolic syndrome patients (Augusthy *et al*., 2017). Other study showed that mean of WC was increased in metabolic syndrome patients (Singh *et al*., 2015). The possible explanation is that metabolic syndrome patients have metabolic abnormalities resulting from insulin resistance state which contributes directly to obesity and increase levels of BMI and WC, also sedentary life style as consumption of highly processed, energy dense food of poor nutritional value, moreover metabolic syndrome patients have increased level of free fatty acid compared to normal individuals.

Comparison of means between cases and control showed insignificant differences in total cholesterol and LDL-C serum level disagreed with a study conducted at 2013 showed a significant increase in serum level of total cholesterol and LDL-C($p<0.05$) (Rooki *et al*., 2013), a good explanation of this study results is the effect of anti-lipids medication (18 out of 40 were

using anti-lipids medication) and/or our life style of Sudanese population, as a major contributor in the result.

Comparison of means between females and males showed insignificant differences in BMI, WC, blood pressure, duration of disease, physical activity. Also showed insignificant difference in the mean of total cholesterol and LDL-C levels this results supported by Natah and Mohammed study of who found no significant difference between females and males in lipid profile (Natah and Mohammed, 2014). The possible explanation of this study results are the difference in the pattern of obesity between men and women, hyperinsulinemia alter insulin alter estrogen related protective mechanism also low grade of inflammation may have greater role in disturbing insulin action in women or inflammatory factors may interact with female sex hormmons resulting in a decrease of protective effect of estrogen on body fat distribution and insulin action.

The study showed insignificant difference in the means of BMI, WC, SBP, DBP, Total cholesterol and LDL-C according to the duration of disease.

The study showed insignificant difference in the mean of BMI, WC, SBP, DBP, Total cholesterol and LDL-C according to physical exercise our study supported by study that showed insignificant difference in the means of BMI, WC and SBP but significant decrease in DBP but only after vigorous exercise (Wyldbore, 2016). The low level of physical exercise and sedentary life style represent a good explanation for the study results.

Eskandary and Rahimi showed that LDL-C levels changes was not significant in eight weeks aerobic training group (Eskandary and Rahimi, 2017).

In general here in Sudan we have different life style and most of the people lake of physical activity.

5.2. Conclusion

Patients with metabolic syndrome had increased BMI and WC, level of total cholesterol and LDL-C are normal in metabolic syndrome patients, BMI, WC, DBP, SBP, total cholesterol and LDL-C means are not different between females and males, finally BMI, WC, DBP, SBP, total cholesterol and LDL-C means are not different according to duration of disease and are not affected by physical exercise.

5.3. Recommendations:

1. For reliable results I recommend to assess more parameters such as small dense lipoprotein particles and other atherogenic lipid profile.

2. Interventional studies would be helpful to assess the effect of physical exercise on the serum level of lipids in metabolic syndrome patients.

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APPENDICES

Appendix I

Informed consent

الموافقة المستنيرة

أنا الباحث : امنية علي خلف الله الحاج , كلية الدراسات العليا ,جامعة السودان للعلوم والتكنولوجيا , أقوم ببحث لنيل درجة الماجستير وعنوان الدراسة هذه تقويم مستوى الكوليسترول الكلي والكوليسترول منخفض الكثافة البروتينية الدهنية في مرضى متلازمة التمثيل الغذائي في ولاية الخرطوم.

Assessment of serum Levels of Total cholesterol and LDL-C in metabolic syndrome patients in Khartoum state.

الكُولِسترول هو مادة دهنية شمعية أساسية في تكوين أغشية الخلايا في جميع أنسجة الكائنات الحية. بالإضافة إلى ذلك يلعب الكولسترول دورا أساسياً في الاستقلاب الحيوي (التمثيل الغذائي).

من الكوليسترول نوعان أحدهما طيب مفيد والأخر ضار للصحة إذا زاد عن الحد. النوع المفيد وهو بروتين دهني مرتفع الكثافة أو (HDL) ويجب أن تكون نسبته في الدم أعلى من 40 مليجرام/ديسيلتر. والنوع الضار يجب أن تكون نسبته في الدم أقل من 100 مليجرام/ديسيلتر، وهذا يسمى بروتين دهني منخفض الكثافة أو .(LDL) ويتزايد ضرر الكوليسترول السيء إذا زاد عن الحد واقترن بارتفاع ضغط الدم . فكلاهما يؤثر سلبا على القلب والكلى ، وعموما على الأوعية الدموية.

لقد تم اختيارك لتشارك في هذا البحث و معك عدد اخر من المشاركين ومشاركتك طواعية. نتوقع بمشاركتك وانت والمشاركين الاخرين أن نتحصل على نتائج تفيد فهم طبيعة هذا المرض وتشخيصه المبكر وقد يعود البحث بفوائد على كل من المشارك نفسه او المجتمع أو مقدمي الخدمات الصحية.

خلال هذه الدراسة سأقوم بأخذ معلومات عنك وعن المرض وأخذ عينة دم من الوريد حوالي 5 ملليتر, ثم اجراء قياس مستوى الكوليسترول والكوليسترول منخفض الكثافة البروتينية الدهنية من عينة الدم.

الاجراء الذي ساقوم به تجاهك ليس به أية مخاطر أو اعراض جانبية على المشارك سوى ألم بسيط أثناء اخذ العينة واحتمال ورم اخضرار يزول بعد ساعة على الاكثر وسنحاول تجنب

حدوث ذلك ونحن اذ نأمل في مشاركتك معنا في هذا البحث ,نؤكد لك على سرية المعلومات والوثائق الخاصة بك ,وأنه لن يطلع عليها إلا الباحث المعني ولجنة اخلاقيات البحوث الصحية القومية او المحلية .

وسوف نخبرك بنتيجة الفحوصات عن طريق طبيبك المعالج , لن نجمع منك اي عينات اخرى , اما العينات التي يتم جمعها سوف تستعل لغرض هذه الدراسه فقط والمتبقي من العينة يتم التخلص منة بطريقة آمنة .ونود ان نشير كذلك الى ان المشاركة في البحث طوعية وان رفضك للمشاركة في البحث او الانسحاب في اي وقت لا تفقدك الحق في اي فوائد من البحث , مع التاكيد علي انة لن يتم منحك اي قيمة نقدية مقابل المشاركة في هذا البحث وانة بي مشاركتك ستكون احد المتطوعين الذين يشملهم البحث .

إذا كان لديك اي سؤال او استفسار يخص البحث يمكنك الاتصال علي الباحث اعلاه في رقم جواله : **********

<u>فورم إقرار موافقة المشاركة فى البحث</u>

إقرار المشارك :

لقد إطلعت علي المعلومات الحالية التي تم شرحها لي واتيح لي طرح الاسئلة عنها كيفما شئت , وقد تلقيت الاجابة الوافية عن كل الاسئلة , وانا أقر بالموافقة علي المشاركة طواعية في هذه الدراسة واعلم بحقي في التوقف عن المشاركة في اي وقت دون ان يؤثر ذلك علي حوقي في تلقي العناية الطبية الازمة في اي وقت .

رمز المشارك :.....

اسم المشارك : .....

توقيع المشارك :.....

في حال عدم قدرة المشارك علي قراءه الاقرار ويحتاج الي من يشرح او يترجم له:

اسم الشارح(المترجم) : .....

عنوان الشارح (المترجم) :.....

توقيع الشارح (المترجم).....

توقيع الباحث :.....

التاريخ:.....

Appendix II

Questionnaire

Sudan University of Science and Technology

Assessment of serum Levels of Total cholesterol and LDL-C in metabolic syndrome patients in Khartoum state.

Name: …… No: ……..….....

Age/years: …….

Sex:…….….

Height/cm: ……..... Wight/

Kg……...

BMI: …….

Waist circumference/cm……..

Systolic blood pressure/mmHg: …….

Diastolic blood pressure/mmHg: …….

duration of metabolic syndrome:

<1 year …… 1-5 years…… >5 year……

How often do you take part in physical exercise?

No physical exercise …… <100minte…… 100-150minte…….