Sudan University of Science and Technology
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Assessment of Serum Level of Triglycerides to High Density Lipoprotein (HDL-C) Ratio among Metabolic Syndrome Patients in Khartoum State

تقييم مستوى نسبه الدهون الثلاثيه للكلسترول الدهني عالي الكثافه عند مرضي متلازمة التمثيل الغذائي في ولاية الخرطوم

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بسم الله الرحمن الرحيم

{واتقو يوما ترجعون فيه الي الله ثم توفى كل نفس ما كسبت و هم لايظلمون}

صدق الله العظيم

سورة البقرة281

Dedication

To my parent for their love and support throughout my life to my sister who have always loved me unconditionally and whose good examples have taught me to work hard for the things that aspire to achieve

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Abstract

Metabolic syndrome represents a cluster of metabolic abnormalities that include hypertension central obesity, insulin resistance, and atherogenic dyslipidemia, this cross sectional study was carried out to investigate the level of triglycerides, HDL-C and triglycerides to HDL-C ratio among Sudanese metabolic syndrome patients in Khartoum State 2019.

A total of 80 participants were included in this study, forty blood samples were randomly collected from metabolic syndrome patients as case group and forty blood samples were collected from patently healthy individual as control group during the period from April to August. The estimation of serum triglycerides and HDL-C was done by using biosystems BTS-305, and then results were analyzed by using SPSS computer program.

Statistical analysis showed a significant increase of body mass index (BMI) in metabolic syndrome patients (mean±SD: 30.80±6.2) when compared to control (24.1±3.5) *p*- value = 0.000, and a significant increase in waist circumference(WC) in metabolic syndrome patients (mean±SD: 110±11) when compared to control (83.2±11.5) *p*-value = 0.00, and a significant increase in triglycerides levels in metabolic syndrome patients (mean±SD: 119.8±78) when compared to control (83.9±38.2) *p*- value = 0.011,and Insignificant difference HDL-C levels in metabolic syndrome patients (mean±SD: 51.1±26.9) when compared to control (52.4±14.4) *p*-value = 0.78 and significant increase in TG/HDL-C ratio in metabolic syndrome patients (mean±SD: 2.9±2.9) when compared to control (1.6±.84) *p*-Value = 0.026. Statistical analysis also showed insignificant difference in BMI, WC, systolic blood pressure (SBP), diastolic blood pressure (DBP), triglycerides, HDL-C and TG/HDL-C ratio in males of metabolic syndrome compared to females

Statistical analysis also showed insignificant difference in BMI, WC, SBP, DBP, triglycerides, HDL-C and TG/HDL-C ratio according to duration of metabolic syndrome from (< 1) (1-5), (>5) year respectively, and according to physical activity (In active) (<100), (100-150) minute respectively.

Statistical analysis also showed the associate between odd ratios of weight reduction for TG, HDL-C, TG/HDL-C ratio in metabolic syndrome patients, the odd ratios and *p*-values respectively as follow: for triglycerides (0.5, *p*-value=0.216) for HDL-C (1.1, *p*-value=0.437) for TG/HDL-C (0.89, *p*-value =0.430).

In conclusion: Metabolic syndrome patients had higher level of serum triglycerides, triglycerides to HDL-C ratio, the value of BMI, WC, while the level of HDL-C is had no difference, and level of triglycerides, HDL-C and triglycerides to HDL-C ratio, the value of BMI WC, SBP , and DBP were no difference in males compered to females in metabolic syndrome patients, also were no according to physical activity and duration in metabolic syndrome patients ,moreover level of triglycerides and triglycerides to HDL-C ratio is not associated by weight reduction, while the level of HDL-C was associated by weight reduction.

المستخلص

متلازمة التمثيل الغذائي هي مجموعة من التشوهات الأيضية التي تشمل السمنة المركزية ,لارتفاع ضغط الدم ، ومقاومة الأنسولين ، وداء خلل الدهون وتصلب الشراين ، وقد أجريت هذه الدراسة المستعرضية لفحص مستويات الدهون الثلاثية ,للكلسترول الدهني عالي الكثافه و نسبه الدهون الثلاثيه للكلسترول الدهني عالي الكثافه لمرضي متلازمة التمثيل الغذائي في ولاية الخرطوم

تم اخذ 80 مشاركا في هذه الدراسة تم جمع أربعين عينة دم من مريض متلازمة التمثيل الغذائي كمجموعة حالة وتم جمع أربعين عينة دم من بالغين أصحاء كمجموعة مراقبة من ولاية الخرطوم خلال الفترة من أبريل إلى أغسطس. تم تقدير الدهون الثلاثية وللكلسترول الدهني عالي الكثافة في االمصلل وتحليل النتائج احصائيا ببرنامج التحليل الاحصائي.

أظهر التحليل الإحصائي زيادة كبيرة ذات دلالة احصائية في مؤشر كتلة الجسم في مرضي متلازمة التمثيل الغذائي (30.80 ± 6.2) بالمقارنة مع بالفئة الضابطة (24.1 ± 3.5) القيمة الاحتمالية(0.00) ,وزيادة كبيرة ذات دلالة احصائية في محيط البطن في مرضي متلازمة التمثيل الغذائي(110 ± 11) بالمقارنة مع الفئة الضابطه (83.2 ± 11.5). القيمة الاحتمالية (0.00) ,زيادة كبيرة ذات دلالة احصائية في مستوى الدهون الثلاثية في مرضي متلازمة التمثيل الغذائي (119.8 ± 78) بالمقارنة مع بالفئة الضابطه (83.9 ± 38.2). القيمة الاحتمالية (0.011) وفرق ضئيل في الكلسترول عالي الكثافة في مرضي متلازمة التمثيل الغذائي(51.1 ± 26.9) بالمقارنة مع الفئة الضابطة(52.4 ± 14.4) القيمة الاحتمالية (0.78), وزيادة كبيرة في نسبة الدهون الثلاثية الي للكلسترول عالي الكثافة في مرضي متلازمة التمثيل الغذائي (2.9± 2.9) بالمقارنة مع الفئة الضابطة (1.6 ± .84) القيمة الاحتمالية 0.026. اظهر التحليل الاحصائي اختلاف ضئيل في مؤشر كلتة الجسم ,محيط البطن,الضغط الدم الانقباضي,ضغط الدم الانبساطي,الدهون الثلاثية,الكلسترول عالي الكثافة ونسبة الدهون الثلاثية للكلسترول عالي الكثافة في الذكور من مرضي متلازمة التمثيل الغذائي مقارنة مع الإناث

واظهر التحليل الاحصائي اختلاف ضئيل في مؤشر كلتة الجسم ,محيط البطن,الضغط الدم الانقباضي,ضغط الدم الانبساطي,الدهون الثلاثية,الكلسترول عالي الكثافة ونسبة الدهون الثلاثية للكلسترول عالي الكثافة وفقا لمدة متلازمة التمثيل الغذائي) وفقا لمدة متلازمة التمثيل الغذائي من (> 1) (1−5) ، (> 5) سنة على التوالي. و ايضاحسب النشاط البدني للمرضي النشاط البدني لمتلازمة التمثيل الغذائي (غير نشيط) (>100) ، (100−150) دقيقة على التوالي:.

اظهر التحليل الإحصائي نسبة الارجحية من تخفيض الوزن على الدهون الاثلاثية,للكلسترول عالي الكثافة ونسبة الدهون الثلاثية الي للكلسترول عالي الكثافة, النسب الارجحية والقيم الاحتمالية على التوالي على النحو التالي: لدهون الاثلاثية(0.5 ، القيمةالاحتمالية 0.216) الكلسترول عالي الكثافة(1.1 ، القيمة الاحتمالية 0.437) ونسبةالدهون الثلاثية للكلسترول عالي(0.89 ، القيمةالاحتمالية 0.430) .

خلصت هذة الدراسة علي ان مرضي متلازمة التمثيل الغذائي لدية زيادة في مستوى الدهون الثلاثية ، ونسبة الدهون الثلاثية للكلسترول عالي الكثافة ,مؤشر كتلة الجسم ومحيط البطن, في حين أن مستوى الكلسترول عالي الكثافة يشكل الفرق ضئيل , الدهون الاثلاثية,اللكلسترول عالي الكثافة ونسبة الدهون الثلاثية للكلسترول عالي الكثافة مؤشر كتلة الجسم,محيط البطن,الضغط الانقباضي و الضغط الانبساطي علي اختلاف ضئيل في الذكور بالمقارنة مع الإناث في مرضي متلازمة التمثيل الغذائي,، أيضا اختلاف ضئيل وفقا للنشاط البدني والمدة في مرضي متلازمة التمثيل الغذائي أيضا اختلاف ضئيل وفقا للنشاط البدني والمدة في مرضي متلازمة التمثيل الغذائي علاوة على ذلك ، لاتوجد علاقه بين مستوى الدهون الثلاثية ونسبة الدهون الثلاثية إلى الكلسترول عالي الكثافة بتخفيض الوزن ، بينماتوجد علاقه بين مستوى الكلسترول عالي الكثافة بتخفيض الوزن.

List of Contents

Title	Page no.
الاية	I
Dedication	II
Acknowledgments	III
Abstract in English	IV
Abstract in Arabic	VI
List of Contents	VIII
List of tables	X
List of Abbreviations	XI
Chapter one	
1.1 Introduction	1
1.2 Rationale	3
1.3 Objective	4
Chapter two	
2.1. Metabolic syndrome	6
2.1.1Classification of metabolic syndrome	6
2.1.2 Etiology of metabolic syndrome	7
2.1.3 Risk Factors for metabolic Syndrome	8
2.1.4 Markers of metabolic Syndrome	8
2.1.5 Pathogenesis of metabolic syndrome	9
2.1.6 Complications of metabolic syndrome	11
2.1.7 Management of metabolic syndrome	13
2.1.8 Prevention from metabolic syndrome	14
2.2 High density lipoprotein (HDL-C)	15
2.3 Triglycerides	18
Chapter three	
3.1. Materials	22
3.2. Methods	23

Chapter four	
4. Results	25
Chapter five	
5.1. Discussion	33
5.2. Conclusions	36
5.3. Recommendations	37
References	39
Appendices	
Appendix I (Informed consent).	43
Appendix II (Questionnaire)	44
Appendix III (triglycerides)	45
Appendix IV(HDL-C)	46

List of tables

Table No.	Title	Page no.
(4.1)	Comparison of variable (Age. BMI, WC), TG, HDL-C and TG/HDL-C ratio in metabolic syndrome patients versus healthy individual	27
(4. 2)	Comparison of variables (Age. BMI, WC, SBP, DBP), TG, HDL-C and TG/HDL-C ratio of metabolic syndrome males versus females	28
(4. 3)	Comparison of variable (BMI, WC SBP, and DBP), TG, HDL-C and TG/HDL-C ratio according to duration of metabolic syndrome.	29
(4. 4)	Comparison of variable (BMI, WC SBP, and DBP), TG, HDL-C and TG/HDL-C ratio according to physical activity in metabolic syndrome patients	30
(4. 5)	the odd ratios of weight reduction on TG, HDL-C, and TG/HDL-C ratio in metabolic syndrome patients	31

List of abbreviations

ADP	Adenosine diphosphosphate
AGPAI	Acylglycerol phosphate acyltransferase
ATGL	Adipose triglycerides lipase
ATP	Adenosine triphosphosphate
BMI	Body mass index
CHD	Coronary heart disease
CKD	Chronic kidney disease
CPP32	Cysteine protease p32
CRP	C reactive protein
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DGAT	Diacylglycerol acltransferase
e NOS	Endothelial nitric oxide synthase
ER	Endoplasmic reticulum
FFA	Free fatty acids
FTO	Fat mass and obesity association
GLP-1R	Glucagon like peptide-1receptor
G3P	Glycerol-3 phosphate
GWAS	Genome wide association studies
HDL-C	High density lipoprotein cholesterol
HPA	Hypothalamic reticulum
HSL	Hormone sensitive lipase
IDF	International diabetes federation
IL	Interleukin
IRS-1	Insulin receptor substrate
LCAT	Lecithin cholesterol acytransferase
LDL-C	Low density lipoprotein cholesterol
LOX-1	Low density lipoprotein receptor-1
MGAT	Mono acylglycerol acltransferase

NCEP	National cholesterol education program
NHANE	National health and nutrition examination survey
NSFFA	Non sterified Free fatty acids
PAP	Phosphatidic acid phosphatase
PPAR	Peroxisome proliferator activated receptor
RA	Rheumatoid arthritis
RAS	Renin angiotensin system
RCT	Reverse cholesterol transport
ROS	Reactive oxygen species
SBP	Systolic blood pressure
SNP	Single nucleotide polymorphism
S-1P	Sphingosine-1phosphate
SPSS	Statistical package for social sciences
SR-BI	Scavenger receptor class B type I
TG	Triglycerides
TNF α	Tumor necrosis factor alpha
VAM-1	Vascular adhesion molecule
VLDL	very Low density lipoprotein
WHO	Word health organization

Chapter one

1. Introduction, Rationale and Objectives

Incidence of metabolic syndrome has recently increased in developing countries. It has been estimated that almost 10 % to 30 % of the world's adult population suffer from metabolic syndrome. previous studies approved that the prevalence of the metabolic syndrome is highly age dependent and the highest prevalence among women compare to men, In Sudan the prevalence rates of metabolic syndrome using WHO criteria was 6.1 % among adolescences (Ismail et al., 2018).

studies have advised that metabolic syndrome might be the end result of various, however interrelated, pathophysiological mechanisms which includes endothelial dysfunction, low-intensity inflammatory process, visceral obesity, oxidative stress, genetic factors, and changes in insulin sensitivity (Blanca , 2017).

Individuals with metabolic syndrome have greater risk to develop cardiac disease, stroke and disease associated to fat deposition in artery walls., The prevalence of metabolic syndrome rises through age, region, population and differs broadly dependent on the definition used aimed at medicine approach (Singh, 2018).

Accordance to national health and nutrition examination survey (NHANES), incidence of metabolic syndrome in the US adults aged 18 years or elder, rise with the aid of more than 35% from 1988-1994 to 2007-2012, increasing from 25.3% to 34.2%. About 7% of this population contains adolescents, of which almost 7% had been obese and 29% had been over weight adolescences. As well nearly 40% of individuals over age 60 meet the criteria of getting metabolic syndrome (Singh,2018).

Most those with metabolic syndrome also show atherogenic dyslipidemia and is characterized by raised triglycerides levels more than 185 mg/dL and decreased HDL-C levels in men, less than40 mg/dL and in women, less than50 mg/ dL because of impaired insulin signaling. Moreover, due to impaired signaling, lipid start deposition within the artery and leads to plaque formation, that is typically has a cholesterol-rich core. As soon as this plaque is rupture, individual suffers from acute cardiovascular events similar to myocardial infarction or stroke (Singh, 2018).

There are several previous studies assessing triglycerides, HDL-C and triglycerides to HDL-C ratio, in study on 72 India males patients with metabolic syndrome, High triglycerides was the most common dyslipidemia followed by low levels of HDL-C(Onkar Singh etal; 2015).

In another study in Kenya it was established that elevated triglycerides was the most predominant defining criteria for metabolic syndrome with 24.8% of the subjects diagnosed with the symptom. HDL-C was the second most predominant defining criteria for metabolic syndrome (Mbugua etal; 2017). Other study done in sudan among the patients having metabolic syndrome raised serum triglycerides levels were found in(80.43%) patients, decreased serum HDL-C levels were found in (65%) participants(Alawad and Makeen 2018).

1.2. Rationale:

Dyslipidemia is a part of metabolic syndrome, as well as a significant risk issue for CVD, triglycerides and HDL-C aren't only the constituents of metabolic syndrome but however conjointly as autonomous risk factors of CVD. Evidence spectacles that lipid ratios make better than singular lipids in predicting cardiac risk hence, it has been advised that ratios of lipid-lipoproteins can be measured as different way for recognizing individuals with metabolic syndrome (Bhagyashree, 2018).

Hyperlipidemia is correlated with metabolic syndrome form the main basis for progress of secondary complications. metabolic syndrome prompted oxidative stress may performance significant role in progress of cognitive impairment, neuropathy and depressive disorders whereas its effect on cell proliferation, angiogenesis and apoptosis may participate to the pathogenesis of colorectal cancer (Damini et al.,2015).

To the greatest of our knowledge few published data were found in Sudan assessing the level of serum triglycerides, HDL-C and triglycerides to HDL-C ratio in metabolic syndrome patients, that's why we attempt to do this study to highlights the risks of cardiovascular disease as complication of metabolic syndrome and provide knowledge of prevention and prevention protocol.

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1.3. Objectives

1.3.1. General Objective

To assess serum levels triglycerides to HDL-C ratio in Sudanese metabolic syndrome patients in Khartoum State.

1.3.2. Specific Objective

- To estimate and compare the level of serum triglycerides, HDL-C level, triglycerides to HDL-C ratio level in metabolic syndrome patients and healthy Individuals.
- To compare the level of serum triglycerides, HDL-C level, triglycerides to HDL-C ratio level according to duration of metabolic syndrome and physical activity in metabolic syndrome patients.
- To identify the associate of weight reduction for triglycerides level, HDL-C level, triglycerides to HDL-C ratio level in metabolic syndrome patients.

Chapter two

2. Literature review

2.1. Metabolic syndrome

Metabolic syndrome is a most important public health problem that has been regarded to be an international epidemic by the world health organization (WHO). It is a combination of clinical marks and suboptimal laboratory findings including five main features: central obesity, elevated blood pressure, hypertriglyceridemia, low serum levels of high-density lipoprotein (HDL) cholesterol and high serum levels of fasting glucose. In general agreed the occurrence of at least three of these components is required before a patient can be characterized as having metabolic syndrome. However the most broadly used definitions of the syndrome focus primarily on either waist circumference or insulin resistance criteria that apply in a different way to various ethnic groups (Ho et al.,2014).

2.1.1 Classification of metabolic syndrome

Metabolic syndrome, also variously known as syndrome X, Insulin resistance, etc. in the literature, is actually not a Single disease but a group of cardiovascular disease risk factors and had been well defined to some extent in a different way by various organizations. Three most prevalent definitions (Saklayen, 2018) used for surveys and health care strategies are:

WHO:

Presence of insulin resistance or glucose > (110 mg/dl), 2 hour glucose > (140 mg/dl) beside with any two or more of the following:

HDL -C < (35 mg/dl) in males, < (40 mg/dl) in females, Triglycerides > (150 mg/dl)., Waist/hip percentage > 0.9 males or > 0.85 females or BMI > 30 kg/m2.And Blood pressure > 140/90 mmHg (Saklayen, 2018).

NCEP (National Cholesterol Education Program):

Presence of any three or more of the following:

Blood glucose more than 100 mg/dlor drug usage for raised blood glucose level, HDL -C < 40 mg/dl in males, < 50 mg/dl in females or drug usage for low HDL-C level, Blood triglycerides > 150 mg/dl or drug usage for raised triglycerides level, Waist > 102 cm (male) or >88 cm (females), and blood pressure > 130/85 mmHg or drug usage for hypertension (Saklayen, 2018).

IDF (International Diabetes Federation):

Waist > 94 cm (males) or > 80 cm (females) beside with the Presence of two or more of the following:

Blood glucose more than 100 mg/dl or Identified diabetes, HDL -C < 40 mg/dl in males, < 50 mg/dl in females or drug usage for low HDL-C level, Blood triglycerides > 150 mg/dl or drug Usage for raised triglycerides level ,and Blood pressure > 130/85 mmHg or drug usage for hypertension (Saklayen, 2018).

2.1.2 Etiology of metabolic syndrome

The metabolic syndrome is intensely related to a westernized regime characterized by physical inactivity and a vast source of excessive fat meals. Juvenile obesity is a risk factor for the metabolic syndrome in adults. A title role for psychosocial stress has been suggested, and numerous constituents are more predominant in deprived populations. Not all individuals get the metabolic syndrome, however, and the presence of genetic factors is currently well recognized for both the constituents of the syndrome (like type 2 diabetes, dyslipidemia) and body composition .It is assessed that genetic factors contribute around 30-40% of the detected variance in BMI and around 70% of the variance in fat dissemination that relates more to the metabolic syndrome, In current years, genome-wide association studies (GWAS) have providing new visions into the genetic basis of obesity (Han, 2015).

Single nucleotide polymorphism (SNP) related with raised BMI was diagramed to a gene currently recognized as FTO (fat mass and obesity associated). The FTO gene influences obesity by regulating desire for food and energy expenditure. The usage of SNPs has later recognized above 40 genetic variants that are linked with BMI, fat dissemination or risk of obesity, and metabolic syndrome. Even though only a minor percentage of the variance in obesity is detected to be attributable to common allelic variants, these risk alleles are considered likely to contribute to obesity in a polygenic way such that individuals who carry a greater number of risk alleles will gain additional body weight than those who carry lower number. It has become clear that the underlying genetic reason of obesity needs interaction with the environment. The lifestyle factors that raise intra-abdominal fat and metabolic risk factors are weight gain, a diet high in saturated fat, smoking, inactivity and excess alcohol drinking (Han, 2015)

2.1.3 Risk Factors for metabolic syndrome

National Cholesterol Education Program guiding principle recommends that, there are several factors that raise the probability of getting metabolic syndrome. These factors were categorized into underlying, major, and emerging risk factors. Underlying risk factors for CVD are obesity (specifically abdominal obesity), physical inactivity, and atherogenic diet; the major risk factors are cigarette smoking, hypertension, raised LDL -C, low HDL-C, family history of premature coronary heart disease (CHD), and aging; and the emerging risk factors consist of raised triglycerides, small LDL-C particles, insulin resistance, glucose intolerance, pro-inflammatory state, and pro-thrombotic state (Singh, 2018).

The above-mentioned risk factors can be also categorized on the basis of - Non-modifiable, behavioral and physiological risk factors:

• **Non-modifiable risk factors** consist of age, sex, race, and family history of CVD, which can recognize high-risk individuals (Singh, 2018).

• **Behavioral risk factors** consist of inactive lifestyle, unhealthy diet, heavy alcohol or cigarette intake (Singh, 2018).

• **Physiological risk factors** consist of hypertension, obesity, lipid problems, and diabetes, which may be a result of behavioral risk factors(Singh, 2018).

2.1.4 Markers of metabolic syndrome

Constructed on the risk factors multiple biological markers are recommended for diagnosis of metabolic syndrome like those associated to adipose tissue such as percentage of abdominal fat by digital tomography, blood levels of leptin, adiponectin, another markers of dyslipidemia such as apolipoprotein B or LDL-C/HDL-C, insulin resistance like (oral glucose tolerance test) endothelial dysfunction which measured via the vasodilatory response in the humeral artery, inflammation markers like C-reactive protein, TNF-a, IL-6, IL-8 or thrombosis markers such as high fibrinogen or plasminogen activator inhibitor-1 (Singh, 2018).

2.1.5 Pathogenesis of metabolic syndrome role of inflammation

The huge variant in geographical distribution of metabolic syndrome and the current within developing world give emphasis to the significance of environmental and Lifestyle factors such as the eating of excess calories and absence of physical activity as being main contributors (Yogita et al., 2017).

Visceral adiposity has been established to be a primary stimulate for most of the pathways involved in metabolic syndrome, therefore stressing the importance of a high caloric consumption as a major causal factor. Of the whole thing the recommended mechanisms, insulin resistance, neurohormonal activation, and chronic inflammation seem to be the main performers in the initiation, progression, and transition of metabolic syndrome to CVD (Yogita et al., 2017).

2.1.5.1 Insulin resistance

Insulin resistance-mediated rising in circulating free fatty acids (FFAs) is thought to play critical role in the pathogenesis of metabolic syndrome. Insulin raises glucose uptake in muscle and liver, and prevents lipolysis and hepatic gluconeogenesis. Insulin resistance in adipose tissue impairs insulin- mediated inhibition of lipolysis, directing to a rise in circulating FFAs that otherwise prevent the antilipolytic effluence of insulin. FFAs prevent protein kinase activation in the muscle directing to decrease glucose uptake. They raise protein kinase activation in the liver that enhances gluconeogenesis and lipogenesis. The net effect is the formation of a hyperinsulinemic state to maintain euglycemia (Yogita et al., 2017).

Finally, the compensation fails and insulin secretion reductions. FFAs are as well lipotropic to beta cells of the pancreas causing reduced insulin secretion. Insulin resistance as well participates to the progress of hypertension due to lack of the vasodilator impact of insulin and vasoconstriction make by FFAs. Other mechanisms contain raised sympathetic activation and sodium reabsorption in the kidneys (Yogita et al., 2017).

Insulin resistance as well causes a rise in serum viscosity, creation of a prothrombotic state, and liberation of pro-inflammatory cytokines of the adipose tissue that participated to raised risk of CVD visceral fat deposits participate to insulin resistance further than subcutaneous fat, as visceral lipolysis produce an increased supply of FFAs to the liver through the splanchnic circulation . Rise in FFAs produce increased triglycerides synthesis and the production of Apo lipoprotein B comprising triglyceride-rich very low-density lipoprotein in the liver. Rise in small dense LDL –C and decrease in HDL –C are indirect impact of insulin resistance produced by changed lipid metabolism in the liver. Visceral adipose tissue is as well considered further metabolically active and synthesizes significantly higher quantities of bioactive secretory proteins like plasminogen activator inhibitor, which supports a prothrombotic state, and heparin binding epidermal growth factor such as growth factor, which supports smooth muscle cell proliferation and vascular remodeling (Yogita et al., 2017)

2.1.5.2 Neurohormonal activation

The discovery of endocrine and immune properties of adipocytes has providing more mechanistic visions into the progress of metabolic syndrome. Adipocytes liberated from visceral adipose tissue have been shown to be linked with metabolic syndrome and CVD. Leptin is an adipocyte that controls energy homeostasis mediated by the hypothalamus and is known to trigger the immune cells activating the Th1 pathway. Adiponectin is an anti-inflammatory and antiatherogenicadipokine and its impact counter those of leptin. Adiponectin has anti-atherogenic Properties and it reduce both vascular reactivity and smooth muscle proliferation, and promote plaque stability. Adiponectin has been considered a protective factor against the progress of diabetes, hypertension, and acute myocardial infarction. A rise in adipose tissue mass links with decreased adiponectin and greater leptin levels, which finally improve CVD risk (Yogita et al., 2017).

Triggering of the renin-angiotensin system (RAS) Also serves as a significant neurohumoral pathway participating to the progress of metabolic syndrome. Angiotensin II (Ang II), made as a consequence of angiotensin-converting enzyme activation, is as well formed by adipose tissue. Obesity and insulin resistance are related with raised production of Ang II. Ang II, through triggering of the type 1 receptor, triggers nicotinamide adenine dinucleotide phosphate oxidase leading to the production of reactive oxygen species (ROS). ROS residue a great of effects involving oxidation of LDL, endothelial injury, platelet accumulation, expression of redox-sensitive transcription factor nuclear factor kappa-light-chainenhancer of activated B cells (NF-kB), and expression of lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1) on the endothelium and vascular smooth muscle cells. RAS, ROS, and LOX-1 have an interconnected positive feedback loop that begin a vicious cycle of inflammation, endothelial injury, and fibroblast proliferation that contributes to the progress of hypertension, dyslipidemia, and diabetes, cardiac hypertrophy, and CVD (Yogita et al., 2017).

2.1.5.3 Inflammation: final common pathway

Triggering of different pro-atherogenic pathways in metabolic syndrome ended in a final common pathway of inflammation that lastly leads to clinical appearances of metabolic syndrome. Systemic oxidant stress made by obesity and insulin resistance leads to raised activation of downstream signaling cascades that cause atherogenesis and tissue fibrosis (Yogita et al., 2017).

Inflammation manipulates an essential role in the pathogenesis of CVD and different inflammatory markers have been shown to be raised in patients with metabolic syndrome. Whether these markers performed a causative role or are just by standers of continuing inflammation remains controversial (Yogita et al., 2017).

Tumor necrosis factor alph: Macrophages in the adipose tissue excrete tumor necrosis factor alpha (TNF-α) and its product rises with rise in adipose tissue mass. TNF-α cause phosphorylation and inactivation of insulin receptors in the adipose tissue as well as in smooth muscle cells, the creation of lipolysis raising FFA load, and prevents adiponectin liberation Raised serum TNF-α level are related with obesity and insulin resistance, both of which are greatest important constituents of metabolic syndrome (Yogitaand et al., 2017).

Interleukin 6 and C-reactive protein: Interleukin 6 (IL-6) is a cytokine formed by adipocytes and immune cells and has complex regulatory mechanisms. Formation of IL-6 rises with rise in body fat and insulin resistance. It performed on the liver, bone marrow, and endothelium, leading to raised creation of acute phase reactants in the liver, involving C-reactive protein (CRP). Numerous studies have confirmed an association between high CRP levels and the progress of metabolic syndrome, diabetes, and CVD. IL-6 as well rises fibrinogen levels resulting in a prothrombotic state. IL6 also enhance adhesion molecule expression by endothelial cells and triggering of local RAS pathways (Yogita et al., 2017).

2.1.6 Complications of metabolic syndrome

Metabolic syndrome may give rise to number of secondary complications which primarily comprise atherosclerosis and other cardiovascular disorders. Dementia, neuropathy and arthritis occurred at late stage of disease (Damini, 2015).

2.1.6.1 Cognition impairment and metabolic syndrome

Metabolic syndrome and related factors such as visceral obesity, raised triglycerides, raised fasting blood glucose, high blood pressure and reduced HDL-C all have injurious effects on cognition. Biological toxicity occurs together with rise in plasma glucose levels producing protein glycation, modification of redox potential and production of reactive oxygen species. The ensuing oxidative stress may cause vascular damage. This microvascular dysfunction may demonstrate to be injurious to hippocampal neurons causing cognitive deficit. Liberation of excess glucocorticoides may increase natural fat and reason of insulin resistance (Damini, 2015).

Augmented cortisol level due to stress has been associated with signs of metabolic syndrome cortisol may also decrease the quantity of insulin transported across the blood–brain barrier. Glycemic control affects cognitive performance that depends on generally on hippocampal neurons (Damini, 2015).

2.1.6.2 Metabolic syndrome associated neuropathy

Mechanisms of injury comprise fatty deposition in nerves, extracellular protein glycation, mitochondrial dysfunction, and oxidative stress .Hyperglycemia and hyperlipidemia related with metabolic syndrome may cause cellular damage with generation of reactive oxygen species causing to mitochondrial dysfunction and endoplasmic reticulum (ER) stress .These alterations not only cause to direct neuronal injury but also enhance insulin-resistance facilitated by excess nutrient, originating tissue inflammation, which in turn may aggravate insulin resistance (Damini, 2015).

2.1.6.3 Metabolic syndrome associated depressive disorders

Metabolic syndrome have been related with depressive disorders, whereas others have presented women with depressive disorders are more probable to progress metabolic syndrome. Hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis which is critical to the stress response has main implications in depressive disorders. Raise of glucose uptake by insulin is disturbed by extreme increase in glucocorticoids causing to deposition of body fat. Individuals suffering from mood disorders because of cortisol dysregulation regularly display augmented occurrence of metabolic syndrome. Stimulation of immuno-inflammatory systems by change in insulin sensitivity may disturb the neuronal or glial cells by oxidative stress mechanisms (Damini, 2015).

2.1.6.4 Arthritis and metabolic syndrome

Metabolic syndrome with Insulin resistance and obesity has been individually correlated with psoriatic arthritis, which is identify via joint pain, rigidity and swelling, emphasized in a systemic inflammatory state .There is augmented evidence that chronic inflammation and immune dysregulation may contribute to augmented atherogenesis and may performance a main role in all phases of atherosclerosis. Studies recommend that patients with rheumatoid arthritis (RA) have augmented atherosclerosis. Therefore, inflammation correlated with RA may contribute to raise risk of metabolic syndrome and coronary-artery disease (Damini, 2015).

Pro-inflammatory cytokines such as IL-1β, TNF-α and C-reactive protein CRP have been displayed to be up regulated in RA. Whereas the healthy endothelium inhibits adhesion of mononuclear cells, through inflammation they express adhesion molecules ,Which encourages the adherence of monocytes to the endothelium, which is supposed to be the initial events during atherosclerogenesis ,Inflammatory cytokines such as TNF-α may itself prompt insulin resistance and inhibition of glucose transporter expression via preventing insulin receptor autophoshorylation or via prompting serine phosphorylation of insulin receptor substrate (IRS)-1(Damini, 2015).

Leptin formed via adipose tissues may also contribute to insulin resistance during phosphorylation of serine residues of IRS-1. The contribution of inflammatory cytokines in insulin resistance is mostly significant for the following causes. First, it associates adipose tissue, a main source of inflammatory cytokines in patients with abdominal obesity, insulin resistance and metabolic syndrome. Secondly, it provides a reasonable description for the interaction between chronic inflammatory diseases such as rheumatoid arthritis RA and metabolic syndrome (Damini, 2015).

2.1.7 Management of metabolic syndrome

Metabolic syndrome is related with a raise risk of both atherosclerotic and no atherosclerotic CVD. Management of metabolic syndrome includes a double approach that combines lifestyle alterations and pharmacological interventions in an attempt to decline CVD (Yogita et al., 2017).

2.1.7.1 Lifestyle modification

Metabolic syndrome result of raised calorie intake not propitiate to metabolic requirements. Lifestyle modification is vital in the management of underlying risk factors. Weight reduction and keeping of ideal body weight are important protective and management approaches. The aim of weight reduction is a loss of 7–10% in baseline body weight .Dietary alteration can as well control other metabolic syndrome constituents; low consumption of saturated fats, cholesterol, sodium, and simple sugars is recognized to aid with dyslipidemia, hyperglycemia and hypertension, for instance. Diets high or very low in fat contented aggravate atherogenic dyslipidemia, as such, 25– 35% of daily caloric consumption in the form of fat is frequently suggested.. Exercise helping weight loss and decreasing global CVD risk: about 30–60 min of reasonable strength exercise and responsive efforts to change a sedentary lifestyle can be useful for the management of metabolic syndrome (Yogita et al., 2017).

2.1.7.2 Pharmacotherapy for metabolic syndrome

Pharmacotherapy is other choice for the inhibition of CVD. Most important pharmacological interventions involve management of dyslipidemia with statins, reducing prothrombotic risk with antiplatelet treatments, and the usage of insulin to reduce the risk of diabetes. There is no single treatment therapy for metabolic syndrome and now accessible pharmacotherapy and related comorbidities require extended use of numerous treatments, which is challenging for patients due to polypharmacy and reduced compliance. Hence, there is increasing interest in the usage of naturally happening compounds in reducing the risk and development of metabolic syndrome however their influence on long-term cardiovascular results and long-term compliance is unidentified (Yogita et al., 2017).

2.1.8 Prevention from metabolic syndrome

Metabolic disorders naturally development with age, several modifiable factors can be removed in order to inhibit acceleration of this development. At-risk individuals can be recognized from their family history and large waist circumference severe tissue injury has previously happened by the time diabetes has established. Regular physical activity is probable to inhibit most occurrences of metabolic syndrome and, even after it has established, moderate weight loss can inverse all its constituents. Moderate weight loss with or list at has been presented to reduce the frequency of metabolic syndrome and of diabetes by 30-40%.Even though metformin can inhibit development of pre-diabetes, it converses metabolic syndrome .anther agents, such as PPAR agonists and GLP-1R agonists, might furthermore be considered: liraglutide can create a mean continued weight loss of 10 kg, related with reverse of pre-diabetes and metabolic syndrome (Han, 2015).

2.2. HDL-C:

2.2.1 HDL-C structure:

HDL-C are heterogeneous they vary in proteins, lipids, size, shape and charge. HDL-C can be different significantly in its protein content. The major proteins are apoA-I and apoA-II. HDL-C has a hydrophobic core of cholesterol es-ters and a number of triglycerides enclosed by a shell composed of phospholipids, free cholesterol, and proteins. HDL-C contains different proportions of different lipids: TG, cholesterol esters, free cholesterol, and phospholipids. Certain HDL-C particles are lipid poor or lipid-free (Katerina ,2017).

They range in size from 7.5 nm to 15 nm; they can range from size of albumin to size of LDL-C. They vary in shape. Much individuals have spherical HDL-C particles and certain have discoidal HDL-C particles. Density ranges from 1.063 g/mL to 1.25 g/mL. Depending on density, HDL-C can be split in two subftractions: HDL3 (small and dense particles) and HDL2 (large and less-dense particles) HDL-C particles have charge. Most of them have α electrophoretic migration, certain of them have pre-β migration, and a number of them have pre-α migration. Lipid poor apoA-I and discoidal particles have pre-β mobility, and spherical particles have α mobility on electrophoresis. Numerous plasma proteins, enzymes, and transfer proteins are include in HDL-C remodeling and metabolism, which results in HDL-C heterogeneity. Each constituent of HDL-C individually cross the plasma and HDL-C particle is collected in the plasma (Katerina ,2017).

2.2.2 HDL-C synthesis:

Synthesis and metabolism of HDL-C consist of the following steps:

Hepatic and intestinal synthesis of small nascent HDL-C particles composed of phospholipid and apolipoproteins.

Then, there is collecting of surface constituents (phospholipids, cholesterol and apolipoproteins) as of triglyceride-depleted chylomicron and VLDL residue, Gaining of free cholesterol from tissue location and different lipoproteins, as the initial HDL-C particles comprise comparatively little cholesterol, Apolipoprotein A-I on the surface of HDL-C perform an essential role in this process. It aids as a signal transduction protein to mobilize cholesterol esters from intracellular pools (Bhatt, 2017). After diffusion of free cholesterol onto HDL-C, the cholesterol is esterified to cholesterol esters via lecithin-cholesterol lecithin-cholesterol acyltransferase (LCAT), a plasma enzyme that is triggered mainly via apolipoprotein A-I. By an analogous mechanism, HDL-C cans performance as an acceptor for cholesterol liberation during lipolysis of triglyceride-containing lipoproteins. Cholesterol efflux regulatory protein also seems to perform a central role in the uptake of cellular cholesterol by HDL-C by encouraging the transfer of intracellular cholesterol to the cell membrane (Bhatt, 2017)

Mutations in the gene encoding for this protein, are related with low serum HDL-C concentrations in familial HDL-C deficiency and Tangier disease. Lipid transfer proteins, like cholesteryl ester transfer protein, simplify movement of these newly synthesized cholesterol esters to apolipoprotein B-containing lipoproteins (VLDL, IDL, and LDL). The cholesterol can then be transported to the tissues for steroid synthesis or storage (Bhatt, 2017).

2.2.3 Biological functionality of HDL -C:

HDL-C perform a major role in reverse cholesterol transport (RCT), by which excess cholesterol is eliminate from the peripheral vessels and is carry back to the liver for disposal . On the other hand, HDL-C has numerous other useful biological properties, which improve its protective effect against CVD. These contain antioxidative, anti-inflammatory, vasodilatory, antithrombotic and cytoprotective function. Further specifically, HDL-C may provide powerful protection of LDL-C in vivo from oxidative damage, made by free radicals in the arterial intima, with consequential inhibition of the generation of proinflammatory oxidized lipids, mostly lipid hydroperoxides but moreover short-chain oxidized phospholipids. HDL-C also block the expression of adhesion molecules in endothelial cells and hence it reductions the recruitment of blood monocytes to the arterial wall. HDL-C also raises the production of the atheroprotective signaling molecule nitric oxide by upregulation of the expression of endothelial NO synthase (eNOS), as well as via preserving the lipid environment in caveolae, where eNOS is co-localized with partner signaling molecules. In addition, HDL-C catalyzes eNOS as an end result of kinase cascade stimulation by the high-affinity HDL-C receptor, scavenger receptor class B type (Kosmas2 et al.,018).

The antithrombotic function of HDL-C may be used through the stimulation of prostacyclin synthesis, as well as through the weakening of the expression of tissue factor and selectins, with consequent downregulation of thrombin generation by the protein C pathway and direct and indirect dulling of platelet activation The direct cytoprotective impact of HDL-C on endothelial cells may be used through inhibition of the suicide pathway leading to apoptosis of endothelial cells by reducing the cysteine protease P32 (CPP32)-like protease activity. Therefore, HDL-C performs a protective role against injury (Kosmas et al.,2018).

2.2.4 Disorders with reduced HDL-C concentration

Contrast to genetically determined abnormalities in HDL-C metabolism, low HDL-C greatly more repeatedly arises in patients with metabolic syndrome or diabetes mellitus. Low HDL-C levels are as well related with systemic inflammation, like with cigarette smoking, chronic inflammatory diseases or chronic kidney disease. In cases of very low HDL-C, infrequent diagnosis may be considered, like. neoplasia or a raised risk for sepsis .In summary Low HDL-C is an sign that the affected individual should be inspected for metabolic and inflammatory pathology (Speer et al.,017)

2.2.5 HDL-C in metabolic syndrome

The concentration of HDL-C particles is reduced in metabolic syndrome. Also, they are triglycerides enriched and newly established abnormalities of their sphingophospholipidome, with, in specific, a decline in sphingosine- 1-phosphate (S1P). These abnormalities are detected at an initial stage of metabolic syndrome, before the appearance of hyperglycemia. They are probable to impair the functionality of HDL-C and, therefore, their antiatherogenic properties. The raised progress of atherosclerotic lesions in metabolic syndrome is multifactorial, but dyslipidemia, characterized by quantitative and qualitative abnormalities of apolipoprotein (apo) B–containing lipoproteins and HDL-C, plays a Major role (Damien, 2017).

2.3. Triglycerides

2.3.1 Triglycerides structure:

Triglycerides are composed of a glycerol backbone with three fatty acid chains. Difference in triglycerides structure emerges of the fatty acid chains, which can differ in extent, functionalization and grade of saturation. The location at which these fatty acids are joining to the glycerol backbone influence the physical and physiological properties of the triglycerides (Timothy et al., 2018).

2.3.2 Triglycerides synthesis:

The synthesis of triglycerides mainly takes place in adipose tissue and the liver, but is also observed in skeletal muscle, kidney, lung, heart and the brain. Triglycerides synthesis can take place by the glycerol-3-phosphate, or the monoacylglycerol pathway in both the ER and the mitochondria .In the glycerol-3- phosphate pathway, synthesis initiates with glucose, which is transformed into glycerol-3-phosphate via a multi-step metabolic reaction. Glycerol-3-phosphate, the rate-limiting step of triglycerides synthesis, is transformed to lysophosphatidic acid via glycerol- 3-phosphate acyltransferase. Lysophosphatidic acid is then transformed to phosphatidic acid via 1-acylglycerol-3- phosphate acyltransferase (AGPAT), phosphatidic acid into 1,2-diacylglycerol via phosphatidic acid phosphatase (PAP), and lastly 1,2-diacylglycerol to triglycerides via diacylglycerol acyltransferase (DGAT) (Timothy et al., 2018).

The monoacylglycerol pathway is analogous, but rather than starting with glucose, this pathway initiates with monoacylglycerol, which is transformed into 1,2-diacylgycerol via monoacylglycerol acyltransferase (MGAT) (Timothy et al., 2018).

The pathway then continues as for glycerol-3-phosphate. After synthesis, triglycerides are packed into lipid droplets Triglycerides breakdown; a process also identified as lipolysis, is vital for the performance of fatty acids to numerous tissue types. Lipolysis mainly occurs in the adipose tissue and is facilitated by a set of enzymes recognized as lipases. Lipolysis initiates with the transformation of triglycerides to diacylglycerol via adipose triglyceride lipase (ATGL), liberating one fatty acid molecule. This reaction can also be catalyzed to certain degree via hormone-sensitive lipase (HSL). Diacylglycerol is formerly more catabolized to monoacylglycerol via HSL, liberating a second fatty acid molecule. Lastly, monoacylglycerol is broken down to glycerol and the last fatty acid. Lipolysis can also take place in the bloodstream, as is required for the performance of fatty acids to the blood brain barrier. In such cases, LPL catalyzes the reaction (Timothy et al., 2018).

2.3.3 Biological functionality of triglycerides:

Contrast to the other lipid classes, triglycerides performs a minor role in neuronal lipid metabolism. But, they do action as the storage form of lipid precursors (Timothy et al., 2018). Triglycerides and its constituent fatty acids are the vital molecules in lipoprotein metabolism, major mediators of insulin actions, main sources of energy for heart function, and a main reason of heart dysfunction. Combination of triglycerides into circulating lipoproteins lets for the effective movement of calories from the gut and liver toward peripheral organs (Goldberg, 2018).

2.3.4. Hypertriglyceridemia

Hypertriglyceridemia is defined as an abnormal concentration of triglycerides in the blood. According to (NCEP ATP III) principles, a normal triglycerides level is 150 mg/dL. Hypertriglyceridemia may be primary or secondary in nature. Primary hypertriglyceridemia is the consequence of numerous genetic defects leading to disordered triglycerides metabolism. Secondary causes are acquired causes, such as, high fat diet, obesity, diabetes, hypothyroidism, and some treatments. More importantly nevertheless, hypertriglyceridemia is typically not an isolated abnormality. It is often linked with other lipid abnormalities and the metabolic syndrome which are associated to coronary artery disease (Alfhaid, 2018).

2.3.5 Disorders associated with hypertriglyceridemia:

Moderately raised in plasma triglycerides signalize raised risk for cardiovascular disease; extremely raised triglycerides signalize elevated risk for pancreatitis and lipemia retinalis. Numerous genetic and non-genetic factors are involved in regulation of triglycerides levels. Extremely raised triglycerides (concentration greater than 10 mmol/l) not provoked by Dietary factors, specifically via high alcohol consumption are more probable to have a monogenic cause. On the contrary, mildly to moderately raised triglycerides (concentration 2 to 10 mmol/l) have frequently polygenic origin and often exist with other metabolic disorders, mostly with central obesity, metabolic syndrome and diabetes mellitus (pitha et al.,2015).

2.3.6 Triglycerides in metabolic syndrome

Raised free fatty acids cause hypertriglyceridemia in individuals with insulin resistance and hyperinsulinemia. Hypertriglyceridemia is cooperated with alteration in HDL-C and LDL-C structure and metabolism .raised serum triglycerides levels are often detected in subjects with metabolic syndrome. Numerous studies presented that hypertriglyceridemia is powerfully cooperated with all constituents of metabolic syndrome. Patients with metabolic syndrome and elevation triglycerides in several cases display raised atherogenic level of triglyceride-rich lipoproteins. It has been showed that non-fasting triglycerides levels were linked with occurrence of CVD, raised risk of myocardial infarction, ischemic heart disease and death the incidence of triglycerides levels greater than 150 mg/dL is nearly twofold greater in subjects with metabolic syndrome compared to those deprived of metabolic syndrome. Elevation triglycerides level was the second greatest common among components of metabolic syndrome .Observation of high incidence of triglycerides levels have presented in patients with metabolic syndrome and CVD. Numerous risk factors such type 2 diabetes mellitus obesity, and infrared change lipoprotein metabolism, metabolic syndrome, frequently are seen in CKD patients (Marjani, 2015).

2.3.7 Triglyceride to HDL-C ratios

Elevated levels of triglycerides and low level of HDL-C are independent risk factors of cardiovascular diseases. Triglycerides and HDL-C are also components of metabolic syndrome. In practice, numerous clinicians focus primarily on LDL-C in high-risk cardiovascular patients (Hyun et al.,017).

The TG/HDL-C ratio was recommended as a compliment to LDL-C for predicting the risk of cardiovascular diseases. The TG/HDL-C ratio is significantly correlated to insulin resistance and also seems to be valuable in predicting the development of diabetes, coronary heart disease, and cardiovascular mortality. It would be clinically valuable to recognize insulin resistant individuals prior the appearance of cardiovascular diseases. One method has been to assess the number of criteria for metabolic syndrome existing in a patient. Numerous studies have recommended that the TG/HDL-C ratio can recognize insulin resistant individuals in an easy way. Moreover, the TG/HDL-C ratio has been displayed to be similar to of the use of metabolic syndrome criteria in recognizing insulin resistance in apparently healthy individuals (Hyun et al., 2017).

Chapter three

3. Materials and methods

3.1 Materials

3.1.1 Study design:

This was across- sectional hospital based study.

3.1.2 Study area and period:

The study was carried out over 5 months (April-August 2019).in Abdalla Khalil center and Mahdi center in Khartoum state in Sudan.

3.1.3 Ethical consideration

This study was approved by the ethical committee of Federal Ministry of Health Then a verbal informed consent was obtained from participants (Appendix I), data was collected using questionnaire (Appendix II).

3.1.4 Study population

This study included 40 Sudanese metabolic syndrome patients (19 of them were males and 21 were females) and 40 healthy individuals as control group, age was matched in both groups, ranged from 24 to 69 years, Sudanese males and females who were diagnosed with metabolic syndrome were excluded from this study if they had chronic renal disease, thyroid disease, pregnant women, and patient using drug lower level of TG and HDL-C were excluded carefully by clinical history.

3.1.5 Sampling

3ml of venous blood was collected from each participant after overnight fasting, placed in plane containers, Sample left clot at room temperature then serum was obtained after centrifuged for 3 Minutes at 3000 RPM and analyzed immediately or kept until analysis, the participants underwent routine examinations that included the measurement of Height, weight, BP, and overnight fasting blood sampling. Weight and height were measured without shoes; BP was measured on the right upper arm and maintained at the level of the heart with participants in sitting position. BP was measured by trained and certified nurse's working in Hospital.

.3.2 Methods

3.2.1 Estimation of triglycerides level

Principle of the method

Sample triglycerides incubated with lipoproteinlipase(lpl), liprate glycerol and free fatty acids. Glycerol is converted to glycerol-3-phosphate (G3P) and adenosine-5-diphosphate (ADP) by glycerol kinase and ATP.Glycerol-3-phosphate is then converted by glycerol phosphate dehydrogenase (GPO) to dehydroxyacetone phosphate (DAP) and hydrogen peroxide (H2O2).

In the last reaction hydrogen peroxide (H2O2) react with 4-aminophenazone (4-AP) and chlorophenol in the presence of peroxide (POD) to give red colored dye. The intensity of color formed is propotional to the triglycerides concentration in the sample (Appendix III).

Procedure of method

the reagent to room temperature was brined, 1ml of reagent to all test tubes were pipetted then10 uL of sample to test tubes was added to labeled as sample and 10 uL of standard to tube labeled as standard was added, The tube was mixed thoroughly and incubated for 15 minutes at room temperature, the absorbance of standard and sample were measured at 500 nm against the blank the colour is stable for at least 2 hours.

3.2.2 Estimation of HDL-C level

Principle of the method

VLDL and LDL-C in the sample precipitate with phosphotungstate and magnesium ions. The supernatant contain HDL-C. The HDL-C is then spectrophotometrically measured by means of the coupled reaction, Cholesterol esters react with H2Oin the presence of CHE to give cholesterol and fatty acids. then cholesterol react with O2 in the presence of CHOD to give 4-cholestenona and H2O2.2H2O2 react with phenol and 4-aminophenazone in the presence of POD to give quinonimine and 4H2O.the intensity of color formed is proportional to the cholesterol concentration in the sample (Appendix IV)

Procedure of method

0.5mL of precipitation reagent was pipetted into labelled centrifuge tubes and 0.2mL of sample was added, was mix thoroughly and lifted stand for 10 minutes at room temperature then centrifuged at minimum of 400 r.p.m. for 10minutes then carefully collected the supernatant, the cholesterol kit to room temperature was brined then into test tubes 1.0 mL of reagent to all test tubes were pipetted then 100 uL of sample supernatant to tube labelled as test tube was pipetted and 100Ul to tube labelled as standard tube was pipetted.

The tubes were mixed thoroughly and incubated the tube for 30 minutes at room temperate then the absorbance of standard and sample were measured at 500 nm against the blank the color is stable for at least 3o minutes.

3.2.3 Calculation

Calculation of BMI by formula:BMI =body mass divided by the suqure of body height.

Calculation of TG\HDL-C ratio by formula = triglycerides divided by HDL-C.

3.4 Quality control

Pathological and normal control sera were measured to verify the performance of the measurement procedure, for TG use control serum level I (cod.18040) and II(cod.18041) and for HDL-C use control serum level I (cod.18005,18009 and 18042).

3.5statistical analysis

Data was analyzed statistically by using the SPSS computer program the independent T test and Anova test were used for comparison and chi-square test was used for calculation odd ratios (*p*-value< 0.05) was consider significant.

Chapter four

4. Results

In this study 80 participant were enrolled,40 metabolic syndrome patients as case group and 40 healthy individuals as control group to Assess serum levels of triglycerides, HDL-C and TG/HDL-C ratio among Sudanese metabolic syndrome patients in Khartoum State**,** data were analyzed statistically using computer SPSS program and the result were as follow:

Table 4.1: shows a significant increase in BMI in metabolic syndrome patients (mean±SD: 30.80±6.2 cm) when compared to control (24.1±3.5) *p*-value =0.000 and a significant increase in WC in metabolic syndrome patients (mean±SD: 110±11) when compared to control (83.2±11.5) *p*- value =0.00and a significant increase in serum triglycerides level in metabolic syndrome patients (mean±SD: 119.8±78 mg/dl) when compared to control (83.9±38.2 mg/dl) *p*-value =0.011and Insignificant difference HDL-C level in metabolic syndrome patients (mean±SD: 51.1±26.9 mg/dl) When compared to control (52.4±14.4) *p*- value =0.78and significant increase in TG/HDL-C ratio in metabolic syndrome patients (mean±SD: 2.9±2.9) when compared to control (1.6±.84) *p*- Value=0.026.

Table 4.2: shows an insignificant difference in BMI, WC, SBP ,DBP ,triglycerides, HDL-C and TG/HDL-C ratio in males of metabolic syndrome compared to females mean ±SD and *p*-values is in table

Table 4.3: shows Insignificant difference in BMI, WC, SBP, DBP, TG, HDL-C and TG/HDLC ratio according to duration (duration of metabolic syndrome < 1year,1-5year,>5 year respectively) mean ±SD and *p*-values is in table.

Table 4.4: shows Insignificant difference BMI, WC, SBP ,DBP ,TG, HDL-C and TG/HDL-C ratio according to physical activity (physical activity of metabolic syndrome patients inactive, <100minate, 100-150minate respectively) Mean ±SD and *p*-values is in table:

Table 4.5: the associated between odd ratios of weight reduction for TG, HDL-C, TG/HDL-C ratio in metabolic syndrome patients, the odd ratios and *p*-values respectively as follow: for triglyceride (0.5, *p*-value=0.216) for HDL-C (1.1, *p*-value=0.437) for TG/HDL-C (TG/HDL-C (0.89,*p*-value=0.430).

Table (4.1): Comparison of variables (Age. BMI, WC), TG, HDL-C and TG/HDL-C ratio in metabolic syndrome patients versus healthy individuals

variables	Metabolic syndrome patients (mean±SD)	Healthy individuals (mean±SD)	*p*- value
BMI(kg/m2)	30.80±6.2	24.1±3.5	0.000
W C (cm)	110±11	83.2±11.5	0.000
TG(mg/dl)	119.8±78	83.9±38.2	0.011
HDL-C(mg/dl)	51.1±26.9	52.4±14.4	0.780
TG/HDL-C ratios	2.9±2.9	1.6±.84	0.026

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

Table (4. 2): Comparison of variables (Age. BMI, WC, SBP, DBP), TG, HDL-C and TG/HDL-C ratio of metabolic syndrome males versus females

variable	Males(n=19) (mean±SD)	Females(n=21) (mean±SD)	*p*-value
BMI(kg/m2)	29.7±5.7	31.8±6.5	0.30
WC(cm)	113.2±11.7	107.1±9.8	0.08
SBP(mmHg)	131.8±14.3	138±18.6	0.26
DBP(mmHg)	86.2±7.6	84.2±10.3	0.52
TG(mg/dl)	131.5±87.6	109±68.7	0.37
HDL-C(mg/dl)	50.6±35.9	51.6±15.8	0.90
TG/HDL-C ratio	3.7±4	2.1±.9	0.08

Independent sample T- test was used, *p*- value <0.05 considered significant

Table (4. 3): Comparison of variable (BMI, WC SBP, and DBP), TG, HDL-C and TG/HDL-C ratio according to duration of metabolic syndrome.

variable	< 1year n(9) (mean±SD)	1-5year n(14) (mean±SD)	>5year n(17) (mean±SD)	*p*-Value
BMI(kg/m2)	28.9±4.9	31.2±7.9	31.4±5.3	0.060
WC(cm)	113±11.2	106.9±10.7	110.9±11.2	0.403
SBP(mmHg)	136.7±13.2	132.3±20.6	136.8±15.8	0.264
DBP(mmHg)	89.4±7.3	83.8±12.1	83.5±6	0.756
TG(mg/dl)	105.7±55.5	102.5±61.9	141.4±96.9	0.330
HDL-C(mg/dl)	39.9±8.1	53.8±35.7	55.4±24.2	0.309
TG/HDL-C ratio	2.8±1.6	2±0.81	3.5±4.3	0.344

The table shows the mean± standard deviation and probability (P) One way Anova test was used for comparison.

Table (4. 4): Comparison of variable (BMI, WC, SBP, and DBP), TG, and HDL-C and TG/HDL-C ratio according to daily physical activity (walk) in metabolic syndrome patients.

variable	Inactive	<100minte	100-150minte	*p*-value
BMI(kg/m2)	31.1±7.1	29.1±4	31.6±4.3	0.72
WC(cm)	109.7±10.8	107.7±15	114±6.5	0.58
SBP(mmHg)	135.4±17.8	138±16.4	130±11.5	0.77
DBP(mmHg)	85.7±9.3	84±11.4	82.5±5	0.77
TG(mg/dl)	118.7±70.8	132.8±110	112.5±80.6	0.88
HDL-C(mg/dl)	50.9±28.5	60.6±22.7	40.9±23.3	0.43
TG/HDL-C ratio	2.7±2.82	2.3±1.6	3.9±4.6	0.59

The table shows the mean± standard deviation and probability (P) One way Anova test was used for comparison.

Table (4.5): the associated between odd ratios of weight reduction for TG, HDL-C, and TG/HDL-C ratio in metabolic syndrome patients

	Weight reduction (yes)	Weight reduction (no)	Odd ratios	95% CI	*p*-value
TG normal	3	5	0.5	0.108-2.598	0.21
TG abnormal	17	15			
HDL normal	4	4	1.1	0.241-5.340	0.43
HDL abnormal	15	17			
TG/HDL-C ratio			0.89	0.22-3,59	0.43
Normal	3	7			
Abnormal	10	20			

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

Chapter five

5. Discussion, conclusion and recommendations

5.1 Discussion:

Metabolic syndrome is a group of metabolic disorders and diagnosed with raised blood pressure, elevated blood sugar, excess body fat around the waist, and abnormal triglycerides levels. These metabolic disorders together or autonomously, increase the risk of an individual for developing cardiovascular disease, diabetes mellitus, and vascular or neurological complications (Singh, 2018).

In current result indicates that triglycerides to HDL-C ratio were significantly increased in metabolic syndrome patients than controls. A TG/HDL-C ratio is not only a strong independent predictor of myocardial infarction but also the extent of coronary disease; can be explained the TG/HDL-C ratio predicts insulin resistance. Insulin resistance promotes the accumulation of fat in the body, resulting in obesity. Insulin resistance also facilitates the progression to pre-diabetes or diabetes, and is related with hypertension. Also, insulin resistance induces endothelial dysfunction of the blood vessels and is associated with oxidant stress and hormone and cytokine secretion from fat cells, resulting in inflammation that promotes the progress of atherosclerosis (Hyun gyu shin, etal 2017).

According to results of this study; the value of BMI, WC, and the level of serum triglycerides and triglycerides to HDL-C ratio were significant increased in metabolic syndrome patients compared to healthy individuals. These results are in agreed with study done by (Dharunie etal., 2016) and (Onkar Singh etal; 2015). In fact increase in BMI and WC in metabolic syndrome patients. Lead to ascertain the risk of increased insulin resistance in obese individuals (Dharunie etal., 2016) In present result indicated that increase in serum levels of triglycerides due to impaired insulin action at the level of the adipocyte is thought to result in defective suppression of intracellular hydrolysis of triglycerides with the release of nonesterified (free) fatty acids (NEFAs) into the circulation. The increased influx of NEFAs to the liver stimulates triglycerides synthesis (Mohammed etal; 2014).

In this study results showed insignificant difference in serum HDL-C level in metabolic syndrome patients when compared to control. Result is disagreed with study done by (Dharuni R., 2016). The possible explanation is the used of anti-lipid treatment regulated HDL-C level in metabolic syndrome patients included in this study.

The results of study show an no difference in BMI, WC, SBP ,DBP ,triglycerides, HDL-C and TG/HDL-C ratio in males when compared to females in metabolic syndrome patients. Results are in agreed with study done by (Mohammed etal; 2014).

this study results shows an no difference in BMI ,WC, SBP ,DBP ,triglycerides, HDL-C and TG/HDL-C ratio in males when compared to females in metabolic syndrome patients , This was due to differences in the pattern of obesity between males and females and, low grade inflammation may have a greater role in disturbing insulin action in females, or inflammatory factors may interact with females sex hormones, resulting in a reduction of protective effects of estrogens on body fat distribution and insulin action (Mohammed etal; 2014).

In present study results showed no difference in BMI, WC, SBP, DBP, triglycerides, HDL-C and TG/HDL-C ratio according to physical activity in metabolic syndrome patients results were in agreed with study done by (Sedumedi, 2016), in fact the metabolic syndrome is not only being due to physical inactivity but also the increased circulating levels of insulin(Sedumedi, 2016).The study results showed weight reduction associated with the level of HDL-C in metabolic syndrome patients, these results was agreed with study done by (Rothberg etal; 2017).

In this study results showed weight reductions have no associated with level of triglycerides these result is disagreed with study done by (Hye Soon etal;2010) ,which used intervation study design to itdenty assioateation of weghit reducation on triglycride and HDL-C level, in contrast to our reslut we used questionnaire,which it inaccurateand lead to variation resluts of weghit reducation compare to intervation study.

According to results of our study the value of BMI, WC, SBP, DBP, triglycerides, HDL-C and TG/HDL-C ratio was no difference according to duration of metabolic syndrome. And this study also showed weight reductions have no associated with level of TG/HDL-C ratio in metabolic syndrome patients. To the best of our knowledge no pervious study found to support this result.

5.2 Conclusions

Metabolic syndrome patients had higher levels of serum triglycerides, triglycerides to HDL-C ratios levels, the value of BMI and WC, while the levels of HDL-C was no difference, levels of triglycerides, HDL-C and triglycerides to HDL-C ratio, the value of BMI, WC, SBP, and DBP had no difference in males compered to females in metabolic syndrome patients, also had no difference according to physical activity and duration in metabolic syndrome ,moreover levels of triglycerides and triglyceride to HDL-C ratio is not associated by weight reduction, while the levels of HDL-C was associated by weight reduction.

5.3 Recommendations

1. Further study to periodic and mentoring levels of serum triglycerides, triglyceride to HDL-C ratio and HDL-C are helpful to prevent cardiovascular diseases as complication of metabolic syndrome.
2. Further study based on measurement of small dense LDL-C as good marker for cardiovascular disease is recommended to study the mechanisms of metabolic syndrome.
3. Further study to see the intervention of effect with weight reduction on level of serum triglycerides, triglycerides to HDL-C ratios and HDL-C levels in metabolic syndrome patients.

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Appendices

Appendix I
Informed Consent
الموافقه المستنيرة

أنا الباحثة مآب مساعد عبد الله من كليه علوم المختبرات الطبية قسم الكمياء السريرية، جامعه السودان للعلوم والتكنولوجيا،اقوم بدراسة علميه بحثيه لنيل درجه الماجستير بعنوان تاثير متلازمه التمثيل الغذائي على مستوي الدهون الثلاثيه واللكلسترول الدهني عالي الكثافه لدي مرضي متلازمة التمثيل الغذائي في ولاية الخرطوم.

Assessment levels of serum Triglycerides to HDL-C ratio among Metabolic Syndrome Patients in Khartoum State

متلازمه التمثيل الغذائي هي مجموعة من الحالات المرضية – زياده ضغط الدم وارتفاع نسبه السكر في الدم والدهون الزائدة في الجسم حول منطقه الخصر وتغير مستويات الكلسترول او الدهون الثلاثيه بشكل غير طبيعي- التي تحدث معا لتزيد من خطر الاصابه بامراض القلب والسكته الدماغية والسكري. ان الاصابه بحالة واحدة فقط من هذه الحالات المرضيه لا تشير الي الاصابه بمتلازمه االتمثيل الغذائى.

لقد قمنا باختيارك لتشارك في هذا البحث العلمي لانك تنطبق عليك كل شروط الشخص الذي يمكن ان يكون ضمن المشمولين للدراسة (شخص بالغ مصاب بداء السكري، ضغط الدم، ليس مصاب بمرض الكبد و الغده الدرقية)

خلال الدراسة سوف نقوم باخذ 3 ملم من الدم لاجراء تحليل مستوي الدهون الثلاثية وللكلسترول الدهني عالي الكثافة و هذا يتطلب صيام 12-14 ساعه للحصول علي نتائج سليمة وايضا ساقوم باخذ معلومات عنك وعن المرض،علما بان سحب العينة قد يؤدي الي ظهور بعض الالم قد يؤدي ايضا ظهور ورم في منطقه الحقن قد يتفشي بمرور ساعات وظهور كدمات زرقاء وسوف نعمل علي تفادي كل هذة المضاعفات.

بعد الموافقة منك واخذ المعلومات الكافية والاجابه علي الاسئلة المطلوبة في البحث سوف يتم اخذ العينة والعمل علي تحليليها وسيتم اخبارك بنتائج التي حصلنا عليها خلال فتره من الزمن والتي سوف تكون في سرية تامة ولن يطلع عليها احد غير العاملين في بحث بدون التعرف علي محددات الهوية الشخصية ، علما بان اشتراكك سيكون طواعية ويمكنك الانسحاب من الإشتراك في أي وقت تشاء دون أي خسائر، ونحيطكم بإنه لن تكون هنالك أي عوائد مالية نتيجة الأشتراكك في البحث ويمكنك الإتصال علي الباحث في الرقم ..... في أي وقت للمزيد من المعلومات خلال فتره البحث.

إقرار المشارك في البحث:

لقد اطلعت علي المعلومات الحالية والتي تم شرحها لي واتيح لي طرح الا سئلة عنها كيفما شئت،وقد تلقيت الاجابات الوافية عن كل الاسئلة ،وانا اقر بالموافقة علي المشاركة طواعية في هذه الدراسه واعلم بحقي في التوقف عن المشاركه في اي وقت دون ان يؤثر ذالك علي حقوقي الاخري والاستفاده من نتائج الدراسة.

توقيع المشارك : .....

ت- المشارك : .....

توقيع الباحث:.....

التاريخ:.....

Appendix II

Questionnaire

Sudan University of Science and Technology

Assessment levels of serum Triglycerides to HDL-C ratio among 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?

inactive …… <100minte…… 100-150minte…….

Weight reduction:

Yes….. No….

Type of therapy:

Metformin……. other antidiabetic…….

Antihypertensive …… anti lipid ……..