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BIOCHEMICAL COMPARATIVE STUDY FOR THE ROLE OF SELENIUM AND CHROMIUM IN METABOLIC SYNDROME

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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AZHAR KADHIM ABBOOD ALHAMEED

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BIOCHEMICAL COMPARATIVE STUDY FOR THE ROLE OF SELENIUM AND CHROMIUM IN METABOLIC SYNDROME

By Azhar Kadhim Abbood ALHAMEED

January 2022

We certify that we have read this thesis and that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science

Advisor **:** Assoc. Prof. Dr. Ebru KILIÇAY
Co-Advisor **:** Prof. Dr. Raid M. H. ALSALIH

Examining Committee Members:

Chairman **:** Assoc. Prof. Dr. Abdülkadir ALLI
Department of Chemistry
Düzce University

Member **:** Assoc. Prof. Dr. Ebru KILIÇAY
Department of Medical Services and Techniques
Çankırı Karatekin University

Member **:** Asst. Prof. Dr. Muhammed ALTUN
Department of Medical Services and Techniques
Çankırı Karatekin University

Approved for the Graduate School of Natural and Applied Sciences

Prof. Dr. İbrahim ÇİFTÇİ
Director of Graduate School

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Azhar Kadhim Abbood ALHAMEED

ABSTRACT

BIOCHEMICAL COMPARATIVE STUDY FOR THE ROLE OF SELENIUM AND CHROMIUM IN METABOLIC SYNDROME

Azhar Kadhim Abbood ALHAMEED

Master of Science in Biochemistry

Advisor: Assoc. Prof. Dr. Ebru KILIÇAY

Co-Advisor: Prof. Dr. Raid M. H. ALSALIH

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This study aimed to mark the role of selenium and chromium in MetS and their association with components and to know the effect of age, sex, and BMI on the studied parameters. Samples were collected from 140 participants, and 70 of them met the syndrome criteria used in this study. The other 70 were as a control group. Participants were divided by age, sex, and BMI. The target ages ranged from 20-75 years. The concentrations of Se, Cr, FBG, F. Insulin, HOMA-IR, TG, HDL, UA, and fibrinogen were examined. In addition to measuring systolic and diastolic blood pressure, waist circumference, weight, and height were also investigated. The results showed an inverse correlation between selenium and chromium with MetS. Age, sex, and BMI had a clear effect on the concentration of the studied parameters. The results showed a significant increase in the concentration of FBG, F. Insulin, HOMA-IR, TG, UA, fibrinogen, WC, SBP, and DBP. While it recorded a decrease in the concentration of HDL, Se, and Cr. Through the ROC Curve procedure, Se and Cr recorded a distinctive ability between non-diabetic MetS and control subjects. The concentrations of Se and Cr decreased with the occurrence of MetS, which may be useful in the future as diagnostic parameters of the syndrome or conduct studies to prove their therapeutic usefulness in improving MetS.

2022, 99 pages

Keywords: Metabolic syndrome, Selenium and chromium, Insulin resistance, Dyslipidemia, Hyperuricemia, Hypertension

ÖZET

METABOLİK SENDROMDA SELENYUM VE KROMUN ROLÜ İÇİN BİYOKİMYASAL KARŞILAŞTIRMALI ÇALIŞMA

Azhar Kadhim Abbood ALHAMEED

Biokimya, Yüksek Lisans

Tez Danışmanı: Doç. Dr. Ebru KILIÇAY

Eş Danışman: Prof. Dr. Raid M. H. ALSALIH

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Sunulan tez çalışmasının amacı, selenyum ve kromun MetS'deki rolünü ve bileşenlerle ilişkisini belirlemek ve yaş, cinsiyet ve VKİ'nin çalışılan parametreler üzerindeki etkisini tayin etmektir. 140 katılımcıdan örnekler toplanmış ve bunların 70'i bu çalışmada kullanılan sendrom kriterlerini karşılamıştır. Diğer 70 kişi ise kontrol grubunu oluşturmuştur. Katılımcılar yaş, cinsiyet ve VKİ'ye göre ayrılmış ve hedeflenen yaş aralığı 20 ila 75 yaş arasında olmuştur. Se, Cr, FBG, F. insülin, HOMA-IR, TG, HDL, UA ve fibrinojen konsantrasyonları incelenmiş buna ek olarak sistolik ve diyastolik kan basıncı, bel çevresi, kilosu ve boyu ölçülmüştür. Sonuçlar, selenyum ve krom arasında MetS ile ters bir korelasyon olduğunu göstermiştir. Yaş, cinsiyet ve VKİ'nin, çalışılan parametrelerin konsantrasyonu üzerinde açık bir etkiye sahip olduğu görülmüştür. FBG, F. insülin, HOMA-IR, TG, UA, fibrinojen, WC, SBP ve DBP konsantrasyonunda önemli bir artış görülürken, HDL, Se ve Cr konsantrasyonunda bir düşüş kaydedilmiştir. ROC eğrisi gözününde bulundurulduğunda Se ve Cr, diyabetik olmayan MetS ve kontrol denekleri arasında ayırt edici bir farklılık gözlenmiştir. Sonuçlar gözününe alındığında Se ve Cr konsantrasyonları, gelecekte sendromun tanısal parametrelerinin belirlenmesinde veya MetS'nin iyileştirilmesinde terapötik etkinlikleri açısından umut vaad etmektedir.

2022, 99 sayfa

Anahtar Kelimeler: Metabolik sendrom, Selenyum ve krom, İnsülin direnci, Dislipidemi, Hiperürisemi, Hipertansiyon

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LIST OF SYMBOLS

%	Percent
µg	Microgram
µL	Microliter
µU	Microunits
kg/m^2	Kilogram per meter squared
mg/dL	Milli grams per deci liter
mg/L	Microgram per liter
mL	Milliliter
mmHg	Millimeters of mercury
mmol/L	Millimoles per liter
pmol/L	Picomoles per liter
U/L	Units per liter

LIST OF ABBREVIATIONS

ADA	American diabetes association
AHA	American heart association
apo B	Apolipoprotein B
AT II	Angiotensin II
ATP III	Adult treatment panel III
AUC	Area under curve
BMI	Body mass index
BMI-N	Body mass index-normal weight
BMI-Ob	Body mass index-obese
BMI-OW	Body mass index-over weight
BP	Blood pressure
CI	Confidence interval
Cr	Chromium
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DM	Diabetes mellitus
EGIR	European group for the study of insulin resistance
ET-1	Endothelin-1
FBG	Fasting blood glucose
FFA	Free fatty acids
G1	Age group 1
G2	Age group 2
G3	Age group 3
GOD	Glucose oxidase
GPx	Glutathione peroxidase
HDL-C	High density lipoprotein- cholesterol
HOMA-IR	Homeostasis model assessment of insulin resistance
IAS	International atherosclerosis society
IASO	International association for the study of obesity
IDF	International diabetes foundation
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
IL-6	Interleukin-6
LDL	Low-density lipoproteins
LSD	Least significant difference
MAP	Mitogen activated protein
MetS	Metabolic syndrome
NAFLD	Non-alcoholic fatty liver disease
NCEP	National cholesterol education program

NHLBI	National heart, lung, and blood institute
nm	Nanometer
OSA	Obstructive sleep apnea
PCOS	Polycystic ovary syndrome
PI3K	Phosphoinositide 3-kinase
r	Pearson correlation coefficient
RAS	Renin-angiotensin system
ROC curve	Receiver operating characteristic curve
Rx	Pharmacologic treatment
SBP	Systolic blood pressure
SD	Standard deviation
Se	Selenium
SE	Standard error
SNS	Sympathetic nervous system
T2DM	Type 2 diabetes mellitus
TG	Triglycerides
TNFα	Tumor necrosis factor alpha
VLDL	Very low-density lipoproteins
WC	Waist circumference
WHF	World heart federation
β-cell	Beta cell

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1. INTRODUCTION

Metabolic syndrome (MetS) is important for identifying people at risk of developing type 2 diabetes (T2DM) and cardiovascular diseases (CVD), as it represents a collection of risk variables that includes high blood pressure, dyslipidemia, obesity, insulin resistance or hyperglycemia. MetS began with a concept introduced by the Swedish physician Kylin in 1923 when he explained the relationship between high blood sugar, gout and hypertension (Kylin 1923). Vague (1947) linked visceral obesity to abnormal metabolic parameters in patients with T2DM and CVD (Vague 1947). Avogaro and Crepaldi (1965) presented a summary of a syndrome that includes obesity, hyperglycemia and hypertension (Avogaro and Crepaldi 1965).

The concept of insulin resistance was introduced when a lecture was given by Gerry Reaven in 1988 in which he described a syndrome called "syndrome x" (Reaven 1988) that included a set of risk factors for CVD and diabetes (DM). But its definition lacks obesity or visceral obesity which is now considered a basic criterion (Emanuela *et al.* 2012). Kaplan (1989) called it “The Deadly Quartet”, which refers to a combination of obesity, high triglycerides, hypertension and glucose intolerance (Kaplan 1989). Then it was renamed to Insulin Resistance Syndrome (Haffner *et al.* 1992).

Despite the fact that the name "Metabolic Syndrome" is still the most widely used and agreed upon term, there are many groups that have attempted to develop the criteria and through which many synonyms have been given to MetS such as: Atherothrombogenic syndrome, metabolic cardiovascular syndrome, obesity syndrome, reaven syndrome, dysmetabolic syndrome X, wohlstands syndrome, plurimetabolic syndrome, syndrome of affluence and android obesity syndrome (Peters 2007)

The development of modern technologies that led to an increase in physical inactivity and with the increased demand for fast food with high calories in addition to genetic predisposition All factors interact to produce obesity, which is the most important risk factor for diabetes mellitus and heart disease. According to the International Diabetes

Foundation IDF more than 463 million adults suffered from diabetes until 2019, as half of this number were undiagnosed and suffering from T2DM, and it caused the death of 4.2 million people until that year. The prevalence of diabetes is expected to double by 2030 to 578 million (Diabetes Federation International 2019).

The increasing prevalence of MetS worldwide is a serious health problem, as it is thought to be a key element in the emergence of the two most common causes of mortality, T2DM and CVD. This increased prevalence is consistent with the prevalence of obesity worldwide, which according to the Centers for Disease Control and Prevention (CDC). One-third of adults were obese in the United States for the period 2011-2014 (Xu *et al.* 2019). As a result of a sedentary life and over nourishment, in 2035, the prevalence of MetS is predicted to have risen to almost 53% (Engin 2017). This leads to high blood pressure, dyslipidemia, hypoglycemia and clotting states that are collectively known as metabolic syndrome (Jiménez and Vidal 2016).

There is a clear interest in trace elements because of their essential role in the process of metabolic balance, and that imbalance in their leads to metabolic disorders that are the cause of many diseases (Shi *et al.* 2020). The (WHO) has classified trace elements into three categories: essential elements, possible essential elements and potentially toxic elements which, despite their toxicity, cannot be dispensed with in low quantities (Qin 2011). It should be noted that selenium and chromium are in the first group. According to (WHO) it is certain that the characteristics of MetS can be present for up to 10 years before blood glucose disorders are detected (Alberti and Zimmet 1998).

Studies indicate that we are currently in the era of a global MetS pandemic(Unnikrishnan *et al.* 2017, Puente *et al.* 2019). Therefore, it is important that studies focus on new prevention and treatment mechanisms. In this study, it was founded the possible relationship between serum selenium and chromium levels and to learn more about the significance effects of these trace elements on MetS parameters such as TG, HDL, HOMA and uric acid in metabolic syndrome.

2. LITERATURE REVIEW

2.1 Definitions of Metabolic Syndrome

An international definition of MetS has not been agreed upon. Just as there are multiple terms for metabolic syndrome, there are multiple definitions as well (Table 2.1). Among these definitions:

2.1.1 World health organization definition

Obesity, insulin resistance, hypertension, and dyslipidemia were all linked together for the first time in the WHO definition. WHO has stipulated that insulin resistance and / or diabetes or impaired glucose tolerance be a required component for diagnosing MetS with two or more of other factors including BP >140/90 mmHg, TG levels >150 mg/dL and / or HDL-C levels <35 mg/dL for men; <39 mg/dL for women, central obesity (men: waist : hip ratio > 0.90; women: waist :hip ratio > 0.85) and/or BMI > 30 kg/m^2, albumin to creatinine ratio ≥ 20 mg/g or the rate of urinary albumin excretion ≥ 20 μg/min (Alberti and Zimmet 1998). According to the definition of WHO, a patient does not suffer from MetS even if he fulfills all criteria unless insulin resistance is present.

2.1.2 European group for the study of insulin resistance definition

This definition included a slight change in the definition of WHO (Balkau and Charles 1999). Insulin resistance is required in this definition; however, it is determined by a fasting plasma insulin level greater than the 75th percentile, which simplifies the definition further. Fasting insulin is not useful for T2DM patients, which makes this definition for people without diabetes. As in the WHO definition, EGIR requires two additional contents of the following: Waist circumference: ≥ 94 cm for male; ≥ 80cm for female, BP >140/90 mmHg, TG levels ≥177 mg/dL and / or HDL-C levels <39 mg/dL or taking medicine for dyslipidemia. EGIR doesn't make Microalbuminuria among its criteria.

2.1.3 Adult treatment panel III definition

Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP) is one of the most extensively used definitions, this definition was introduced in 2001 and has been updated by the National Heart, Lung and Blood Institute and the American Heart Association in 2005 (Grundy *et al.* 2005), it necessitates the presence of three or more of the five components listed below: FBG > 110 mg/dL or Rx, BP≥ 130/85 mmHg or Rx, WC≥102cm in male; ≥ 88cm in female, TG levels ≥ 150 mg/dL or Rx, and HDL-C < 40 mg/dL for male; 50 mg/dL for female or Rx.

2.1.4 International diabetes foundation definition

In 2005 (IDF) introduced a definition of MetS that emphasizes abdominal obesity as a major feature and a required component for diagnosing the syndrome (Zimmet *et al.* 2005). The IDF was used to calculate the WC based on the population, so the value of the waist circumference for Middle Eastern men was ≥ 94 cm and ≥ 80 cm for women(Alberti *et al.* 2009), while there were different values for other populations. Plus, any two of the following: TG levels ≥ 150 mg/dL or Rx, HDL-C < 40 mg/dL for male; 50 mg/dL for female or Rx, FBG > 100 mg/dL or Rx, and SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or Rx.

2.1.5 American heart association definition

In 2020, AHA presented an update to its report that contained a definition of MetS (Virani *et al.* 2020). AHA relied on its definition of its meeting with other important organizations in an attempt to collect and unify criteria. These organizations were: The International Diabetes Federation (IDF); World Heart Federation (WHF); National Heart, Lung, and Blood Institute (NHLBI); International Association for the Study of Obesity (IASO); and International Atherosclerosis Society (IAS). They agreed that there should not be a mandatory component of the syndrome criteria(Alberti *et al.* 2009). The entity of any three of the five abnormal components is sufficient for the diagnosis, but waist

circumference can be used as a useful primary tool for selection. With the exception of waist circumference, single values were used for all components. SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg or taking medicine for Hypertension, or antihypertensive medications in a patient with a previous history of Hypertension, FBG ≥ 100 mg/dL or taking medicine for elevated glucose, TG levels ≥ 150 mg/dL or taking medicine for elevated triglycerides, High density lipoprotein- cholesterol levels < 40 mg/dL for males or < 50 mg/dL for females or taking medicine for reduced HDL-C, and waist circumference (population specific) for Middle Eastern males was ≥ 94 cm and for Middle Eastern females≥ 80 cm.

2.1.6 Criticism of some definitions

The American Diabetes Association (ADA) and the European Association for the Study of Diabetes presented a report that included their thoughts on MetS and shortage of precision in defining the syndrome, noting that risk factors such as age, smoking, gender and family history were not included in the previous definitions. Also not included are the signs of pro-thrombosis, inflammation and lack of physical activity, which are risk factors for insulin resistance and which consider more closely related to insulin resistance than high blood pressure (Kahn *et al.* 2005). Dr. Reaven criticized IDF for making obesity a prerequisite for diagnosing MetS rather than insulin resistance (Gerald 2006).

In this study, factors such as age, smoking, and family history, as well as pro-coagulation and inflammatory markers were taken into consideration because they improve the predictive vision of diabetes and cardiovascular disease.

2.2 Epidemiology

The global prevalence of MetS cannot be accurately assessed due to the different definitions, as well as the race, age and sex of the studied population. Nevertheless, an estimated 40% of the world's population meets the criteria for MetS due to the obesity

epidemic (Kassi *et al.* 2011). The prevalence rate ranges from less than 10% to 84% according to the criteria used and the population studied (Rozendaal 2018).

Table 2.1 Diagnostic criteria for MetS by different organizations definitions

Organization / Criteria	WHO[1] 1998	EGIR[2] 1999	NCEP/ ATP III[3] 2001	IDF[4] 2005	AHA[5] 2009
Insulin resistance	IFG, T2DM, IGT or reduced insulin sensitivity, in addition to any two of the following	Plasma insulin > 75th percentile In addition to any two of the following	None, but any three of the following	None	None, but any three of the following
Obesity	Male: waist to hip ratio > 0.90; Female: WHR > 0.85 and/or BMI > 30 kg/m^2	WC ≥ 94 cm in male or ≥ 80 cm in female	WC in male ≥ 102 cm or ≥ 88 cm in female	Increased WC (population specific) In addition to any two of the following	WC (Population specific)
Triglycerides (TG)	TG≥ 150 mg/dL	TG≥ 150 mg/dL	TG≥ 150 mg/dL	TG≥ 150 mg/dL or on Rx	TG≥ 150 mg/dL or on Rx
High density lipoprotein – cholesterol (HDL-C)	Male: < 35 mg/dL Female: <39mg/dL	< 39 mg/dL in males or females	Male: < 40 mg/dL Female: <50mg/dL	Male: < 40 mg/dL Female: <50mg/dL or on Rx	Male: < 40 mg/dL Female: <50mg/dL or on Rx
Glucose	IFG, T2DM, IGT	IFG, or IGT but not diabetes	> 110 mg/dL including diabetes	≥ 100 mg/dL including diabetes	FBG ≥ 100 mg/dL or taking medicine for elevated glucose
Blood pressure	≥ 140/90 mmHg	≥ 140/90 mmHg or on HT Rx	≥ 130/85 mmHg	SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or on HT Rx.	SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or on HT Rx.
Other	Albumin: creatinine ratio ≥ 20 mg/g or the rate of urinary albumin excretion ≥ 20 μg/min				

The rate of prevalence of MetS among patients with diabetes in the African population is 80% (Okafor 2012). In Europe, the rate was 24.6%, with a slight difference between men and women (Scuteri *et al.* 2015). In the United States, a study of 12047 participants from 20-85 years old, classified into three groups based on BMI. The AHA criteria was applied. The prevalence of MetS was 33.2% in BMI group 25.0 to <30.0 kg/m^2, 61.6% in BMI group ≥30.0 kg/m^2, and 8.6% with BMI 18.5 to <25.0 kg/m^2(Shi *et al.* 2020). According to the National Health and Nutrition Examination Survey (NHANES), 35% of adults in

[1] World health organization
[2] European group for the study of insulin resistance
[3] National cholesterol education program/Adult treatment panel III
[4] International diabetes foundation
[5] American heart association

the US meet the advantages of MetS, and the percentage increases to 50% for individuals above the age of 60.The NCEP ATP III criteria was used (McCracken *et al.* 2018).

In a systematic study of the Middle East using ATP III criteria, the predominance of MetS was 32.1 - 42.7% in females and 20.7 - 37.2% in males (Mabry *et al.* 2010). In a Turkish study that included seven regions of Turkey with 2108 men and 2151 women from urban and rural areas for ages from 20 to 90 years, ATP III criteria was used in this study. The prevalence of MetS was 28% in men and 39.6% in women(Kozan *et al.* 2007).

In a study conducted in Baghdad / Iraq that included 440 obese participants, the results of MetS were 40.6%. (SALEH *et al.* 2017), while the study, which included 482 participants living in Erbil / Iraq(Ismael *et al.* 2016). The prevalence of MetS was 30.6%. The rate among women was higher than that of men in both studies.

2.3 Pathophysiology

There are mechanisms that humans walk to obtain energy and store excess of it in the form of fat, protein and glycogen. Obesity occurs when the expenditures are less than energy intake (Ahima 2016). Abdominal fat is commonly linked with insulin resistance, which is a major feature of MetS (Petersen and Shulman 2006). Some individuals who are not obese and suffer from insulin resistance often have fat in the liver, ectopic, or muscles (Lim and Meigs 2014). Hyperinsulinemia and high blood glucose contribute to high blood pressure (Sasaki *et al.* 2020). The summary shown in (Figure 2.1).

2.3.1 Insulin resistance

MetS is defined as insulin resistance syndrome as a result of the role of insulin resistance in the syndrome (Guo 2014). Insulin is the main regulator of glucose metabolism by inhibiting its production in the liver and enhancing its absorption into the peripheral tissues (Samuel and Shulman 2016). Insulin resistance is defined as lack of biological action expected from a certain concentration of insulin, which leads to MetS, obesity and

diabetes(Wang *et al.* 2019). Obesity reduces the receptors, which mainly causes insulin resistance, but it does not necessarily occur together (Lee *et al.* 2010). When insulin resistance and after a while, the beta cells in the pancreas is unable to make sufficient insulin to treat insulin resistance, which results in a person developing T2DM (Petersen and Shulman 2006).

When insulin binds to the receptor with a ligand-activated tyrosine kinase, it activates two pathways: the mitogen activated protein (MAP) kinase pathway and the phosphoinositide 3-kinase (PI3K) pathway. While the first maintains its function on insulin resistance, PI3K is affected, leading to a reduction in GLUT4 translocation, which results in a decrease in glucose absorption. On the other hand, there is continuous secretion of endothelin-1 (ET-1) with smooth muscle cells animating due to the unaffected MAP pathway. This change in the balance of the two pathways and a complex mechanism predisposes to atherosclerosis due to vascular abnormalities resulting from insulin resistance (Kaur 2014).

2.3.1.1 Homeostasis model assessment of insulin resistance

HOMA-IR is the most common assessment of insulin resistance (Chang *et al.* 2019) based on the link between fasting insulin and fasting glucose (Shashaj *et al.* 2016). Its levels are inversely related to physical activity (Balkau *et al.* 2008). HOMA-IR was developed by (Matthews *et al.* 1985):

$$HOMA - IR = Fasting\ glucose\ mg/dL \times Fasting\ insulin\ uU/mL\ /405 \quad (2.1)$$

HOMA-IR values depend on many factors, but as a general average, values less than 1.15 are optimal values, while those ≥ 1.9 are the early stages of insulin resistance, and values ≥ 2.9 indicate insulin resistance (Lu *et al.* 2020).

2.3.2 Dyslipidemia

The fatty acids in the liver promote the production of TG, glucose, and very low-density lipoproteins (VLDL). During the lipolysis process, by action of cyclic adenosine monophosphate, free fatty acids (FFA) are derived from TG stores in adipose tissue. Insulin reduces the activity of cyclic adenosine monophosphate, which inhibits this process. Lipolysis increases when the effect of insulin decreases in the setting of insulin resistance, and thus the production of fatty acids increases (McCracken *et al.* 2018). High levels of TG, fatty acids and increased fat storage resulting from insulin resistance lead to excess of VLDL by the liver, which contributes to atherosclerosis (Halpern *et al.* 2010). Insulin controls lipoprotein lipase activity, and also contributes to the degradation of apolipoprotein B (apo B) that free fatty acids increase their production, when there is insulin resistance, the level of VLDL will increase (Bokhari *et al.* 2018).

2.3.3 Hypertension

All other MetS indicators are linked to hypertension. Insulin resistance and obesity activate the sympathetic nervous system (SNS), sodium is reabsorbed by the kidneys as a result of this. Following then, due to an increase in cardiac output, blood arteries narrow, resulting in elevated blood pressure (Morse *et al.* 2005). Hyperinsulinemia and sodium retention in obesity increase renin-angiotensin system (RAS) activity. In adipose tissue there are angiotensinogen, angiotensin type 1 receptors and angiotensin II (AT II) that regulate metabolism, blood flow and growth in adipose tissue, and thus RAS contributes to hypertension in patients with insulin resistance and obesity (Malhotra *et al.* 2001, Prasad and Quyyumi 2004).

2.3.4 Obesity

The components of MetS do not happen by chance, but are related to some, and some cause the occurrence of others. It is believed that obesity is the key reason of the expansion of MetS, so studies suggest that to prevent MetS, a person should reduce

weight because obesity precedes the occurrence of other components.(Grundy *et al.* 2005). Visceral fat has a significant impact in MetS due to its connection with insulin sensitivity, and has an effect on the development of CVD (Canale *et al.* 2013).

Adipose tissue is a heterogeneous mixture of immune cells, adipocytes and endothelium that respond to increased nutrition (Halberg *et al.* 2008). The blood supply decreases due to the enlargement of adipocytes, which causes hypoxia. Studies suggest that hypoxia causes increased adipocytokines that include free fatty acids (FFA), TNFα, glycerol, C-reactive protein (CRP) and interleukin-6 (IL-6). It results in inflammation of the adipose tissue linked with the development of diseases related to obesity (Trayhurn and Wood 2004).

TNF-α exerts multiple activities including reducing anti-inflammatory cytokines such as adiponectin, secretion of inflammatory stimulant, and enhancing insulin resistance (Emanuela *et al.* 2012). Adiponectin protects against chronic inflammation and regulates body weight, glucose and lipid metabolism. Its levels decrease in the case of insulin resistance (Liu and Liu 2010).

C-reactive protein (CRP) is provided by hepatocytes and regulated by IL-6 and other cytokines. CRP is associated with MetS, T2DM, CVD, hypertriglyceridemia, HTN, and hypercholesterolemia (Den Engelsen *et al.* 2012, Jeong *et al.* 2019)

2.3.5 Prothrombotic state

In MetS patients, the increased risk of CVD is related to a hypercoagulable and hypofibrinolytic condition (Palomo *et al.* 2006). In this context, MetS has been linked with increased plasma levels of numerous variables involved in clotting and fibrinolysis (Dentali *et al.* 2007). Patients with MetS and IR have an increased cardiovascular risk associated with elevated fibrinogen plasma levels (Lansbury *et al.* 2002).

MetS is a hypercoagulable condition (Khunger *et al.* 2020), with its pathophysiology based on adipose tissue. Adipose tissue dysfunction could play a causative role in the prothrombotic condition found in obesity by influencing hemostasis, coagulation, and fibrinolysis directly and indirectly (Faber *et al.* 2009). Adipose tissue is an endocrine active organ and paracrine secretes adipokines and proinflammatory agents such as plasminogen activator inhibitor-1 (PAI-1). In individuals with metabolic complications of obesity, PAI-1 is elevated and is expressed in the adipose tissue stromal fraction, including endothelial cells(Kanaya *et al.* 2006). Through its serine protease inhibitor action, PAI-1 inhibits both tissue-type plasminogen activator and urokinase-type plasminogen activator, and thus contributes to a prothrombotic condition (Vykoukal and Davies 2011).

Endothelial dysfunction has been connected to visceral adipose tissue secretion of proatherosclerotic adipokines and proinflammatory in MetS patients (Berg and Scherer 2005). Endothelial dysfunction characterized by a deficit in the development of nitric oxide (NO) in response to physiological stimuli, increased expression of adhesion molecules on the surface of the endothelial cell (EC) and inflammatory changes underlying early atherosclerosis and CVD processes is a common feature of MetS (Palomo *et al.* 2010).

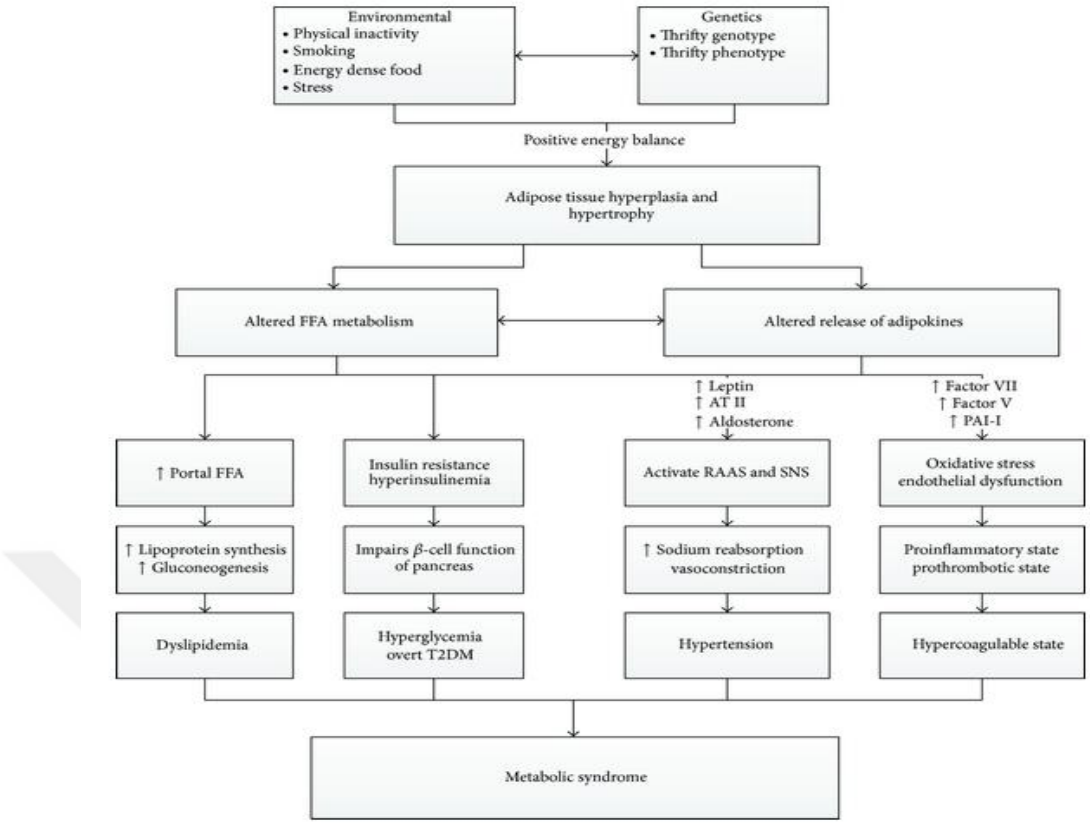

Figure 2.1 MetS schematic presentation (Kaur 2014)

2.3.6 Hyperuricemia

Recent studies indicate that hyperuricemia is an independent and important risk factor for cardiovascular disease, in addition to being a risk factor for blood pressure disease, kidney failure and type 2 diabetes as shown in Figure 2.2 (Nashar and Fried 2012, Gustafsson and Unwin 2013). It is well established that MetS is responsible for cardiovascular disease (Liu *et al.* 2014). The similar effect of the MetS and hyperuricemia has led to the suggestion that the MetS may include hyperuricemia (Klein *et al.* 2002).

Although the relationship is not yet clear, many authors have discussed the potential relationship between hyperuricemia and the prevalence of MetS. Some studies like (Liou *et al.* 2006) and many others suggest that there is no direct relationship and do not consider hyperuricemia as a major factor in metabolic syndrome, but its common

association with individual factors such as dyslipidemia, obesity, high blood pressure, glucose intolerance or cardiovascular disease. While (Sui *et al.* 2008, Huang *et al.* 2020, Jeong *et al.* 2020) and others see there is a direct correlation between hyperuricemia and the prevalence of metabolic syndrome. Despite these years of discussions, EGIR; ATP III; IDF and AHA did not include hyperuricemia in the final versions of its definitions as a major component.

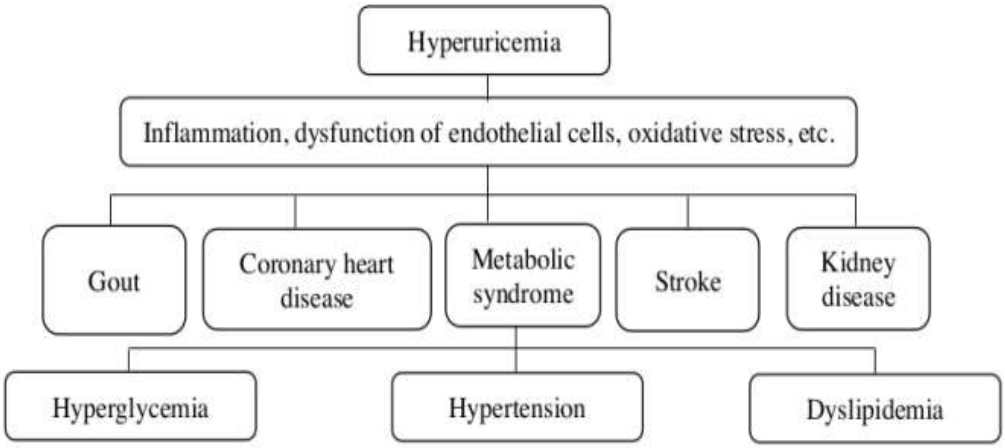

Figure 2.2 Hyperuricemia and its associated diseases (Wang *et al.* 2018)

2.4 Risk Factors for Developing Metabolic Syndrome

The main risk factor for developing MetS is lack of physical activity(Wilsgaard and Jacobsen 2007). Unhealthy Dietary habits including soft drinks, energy-high beverages, sugar-sweetened drink (Shin *et al.* 2018), carbohydrates (Kwon *et al.* 2018), skipping breakfast (Deshmukh *et al.* 2013), red meat (Kim and Je 2018), fried foods (Lutsey *et al.* 2008). Smoking (Sun *et al.* 2012), Increasing age (Hanna and Neary 2004), Excessive alcohol consumption (Fan *et al.* 2008). Another important factor that has bidirectional relationship in causing MetS is depression (Pan *et al.* 2012). Childhood obesity, pediatric MetS, BMI or obesity and parental history of DM, all of these factors increase the risk of developing MetS (Koskinen *et al.* 2017).

2.5 Complications of Metabolic Syndrome

MetS is not a disease by itself, but is a cluster of individual disease risk factors. It is considered risk factors for type 2 diabetes (Lee *et al.* 2020), cardiovascular disease (Yadav *et al.* 2020) and premature mortality (Shi *et al.* 2020). There are some diseases associated with metabolic syndrome, although it is not part of the definition, including non-alcoholic fatty liver disease(Pardhe *et al.* 2018), kidney diseases (Hu *et al.* 2019), some types of cancers (Mendonça *et al.* 2015), polycystic ovaries in females (Chandrasekaran and Sagili 2018) and erectile dysfunction in males (Wang *et al.* 2011), obstructive sleep apnea (Castaneda *et al.* 2018), the condition causing coagulation and inflammation, and osteoarthritis (Mendrick *et al.* 2018)

2.6 Prevention and Treatment of Metabolic Syndrome

For the treatment of MetS short and long-term goals. The short ones are controlling comorbidities such as hypertension and dyslipidemia, as well as achieving a healthy lifestyle and lose excess weight among the short-term goals. While prevention of CVD, T2DM and other complications expected to occur in the long term are among the long-term goals of treating MetS. Figure 2.3 shown the managment of MetS. The highest percentage of people with MetS suffer from obesity (BMI$\geq$30 kg/m^2), so improving the quality of food and controlling calories with regular physical activity are among the most important ideal steps for controlling the development of MetS (Grundy 2016).

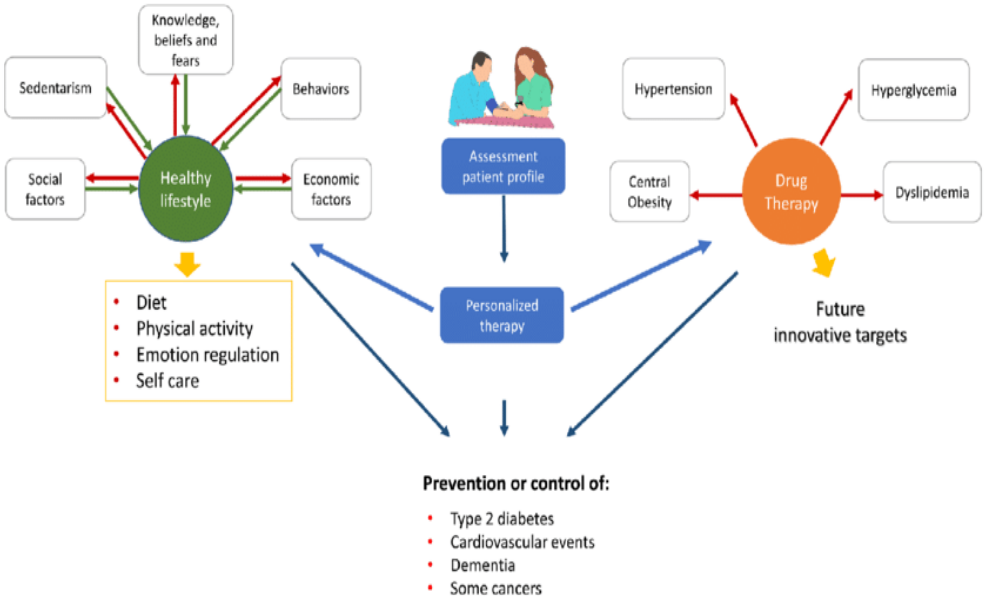

Figure 2.3 Management of MetS (Aguilar and Viveros 2019)

2.7 Trace Elements

Trace elements including selenium, chromium, and others are micronutrients that contribute to number of biological processes, such as oxidative stress, metabolism of lipids, and inflammation (Lei *et al.* 2017). The percentage of these elements is low (less than 0.01% of total body weight) (Shi *et al.* 2020). There are 20 important trace elements for maintaining human homeostasis (Squadrone *et al.* 2015).

2.7.1 Selenium

Selenium element 34 was initially discovered by Berzelius, a Swedish chemist, in 1818 in residues of sulfuric acid. Selenium, like arsenic, was considered highly toxic or carcinogenic until the 1930s (Köhrle 1999), this appraisal has changed throughout the 20th century and the evidence has been recorded for the essentiality of selenium. The treatment function of selenium was not established as a micronutrient until 1957 observed that low-dose selenium supplementation could prevent necrosis of the rat liver (Wrobel *et al.* 2016). In 1973, Se was discovered to be an integral component needed for the action

of glutathione peroxidase (GPx) (Hatfield *et al.* 2014). It is now considered important for human health, primarily due to it is present in the active sites of certain enzymes such as (GPx) (Qazi *et al.* 2019), these enzymes play basic roles in reproduction, tumors prevention, antioxidants, and muscle function (Mehdi *et al.* 2013), and its presence in selenoproteins that have a broad variety of protective functions (Zhang *et al.* 2020). Selenium has been shown in epidemiological studies to be a preventive factor against cardiovascular disease. (Tajaddini *et al.* 2015), and has antioxidant and anti-inflammatory properties(Steinbrenner and Sies 2009).

The main source for Se is through the diet: meat, eggs, fish, mushrooms, cereals, soyabeans, black tea, bamboo shoots, broccoli, nuts, and milk/dairy products (López *et al.* 2018). There are four oxidation states of selenium: 0, -2, +4, and +6. The oxidation states +4 and +6 have water solubility, so they are the most bioavailable (Barceloux 1999).

2.7.2 Chromium

Chromium (Cr) is a naturally occurring metal that can be found in water, soil and biological systems. It has three more stable forms: 0, +3, and +6 valence state. Trivalent chromium is essential for human nutrition (Lewicki *et al.* 2014). It plays a major role in the metabolism of fats and carbohydrates in humans (Vincent 2010). Cr has been suggested as a possible treatment for diabetes, lipid disorders and insulin resistance, but the effect on MetS remains controversial (Chen *et al.* 2020). However, there is a shortage of data relating specifically to the risk of MetS and chromium levels (Bai *et al.* 2015).

Interest in chromium dates back to the 1950s, when it was suggested that there is a glucose tolerance factor in brewer's yeast that prevents diabetes (Schwarz and Mertz 1959). In 1996, Cr was introduced as the basic trace element for the functions of living organisms (World Health Organization 1996). According to ADA (Cefalu and Hu 2004), many studies conducted on animals as well as humans have proven the benefits of chromium in preventing and treating diabetes.

3. MATERIALS AND METHODS

3.1 Design of Study

The study included separate areas of Thi-Qar governorate, which has a population of 2095172 people, and Al-Muthanna governorates, which has a population of 814371 people in Iraq, from urban and rural, and the target ages were from 20 to 75 years. The AHA criteria were used to diagnose MetS, and waist circumference was used as the primary guideline. Samples were collected from October 2020 to February 2021. 140 participants participated in this study, divided into 70 participants who meet the criteria for MetS, including 39 males, and 31 females; and 70 controls, including 33 males, and 37 females. The participants were divided into groups according to age, sex, and BMI (Table 3.1, Figure 3.1). Pregnant women and people suffering from other diseases, especially diabetes, were excluded. The information was taken from patients as shown in (Table 3.2). The study obtained written approval of the Director of the Health Directorate in Al-Muthanna Governorate, and a no-objection statement from the Training and Human Development Department to facilitate the completion of research requirements in the laboratories of Al-Hussein Teaching Hospital (350 bed), and the Specialized Center for Diabetes and Endocrinology. The bed capacity of Al-Hussein Teaching Hospital in Thi-Qar Governorate was 425 beds, and in Al-Muthanna Governorate 350 beds.

Table 3.1 Characteristics of the study participants

According to: / Participants type	Age			Sex		BMI[6] (kg/m^2)		
	G1[7] 20-34 Year	G2[8] 35-54 Year	G3[9] 55-75 Year	Male	Female	Normal weight 18.5-24.9	Overweight 25-29.9	Obese ≥ 30
Patients	21	32	17	39	31	11	18	41
Controls	21	32	17	33	37	11	18	41

[6] Body mass index
[7] Age group one
[8] Age group two
[9] Age group three

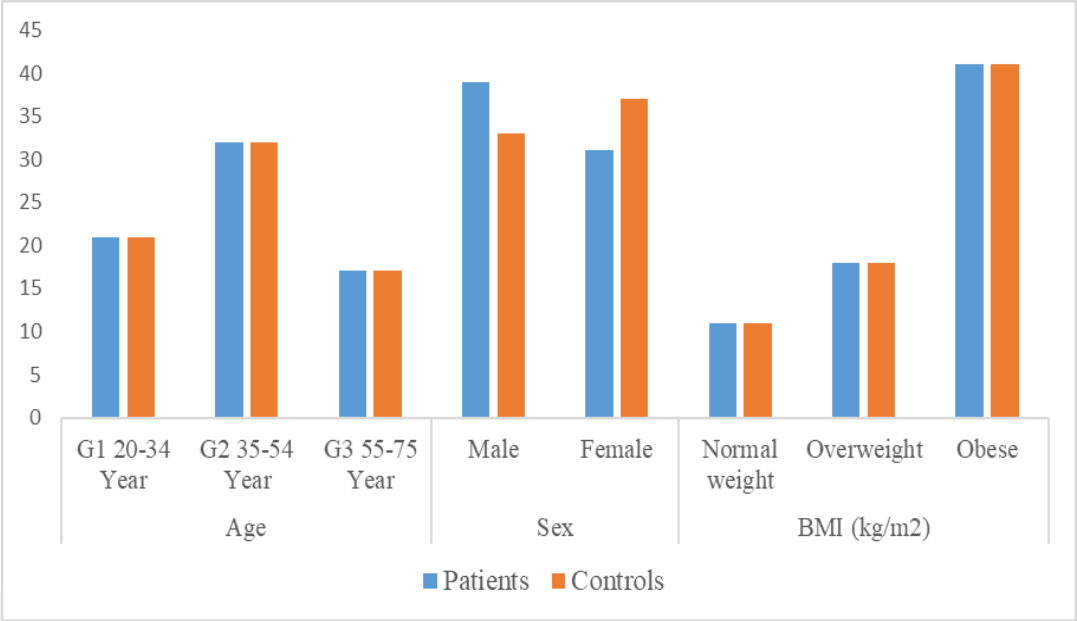

Figure 3.1 Characteristics of the study participants

3.2 Sample Collection

Blood was collected in the morning after fasting for at least 12 hours. 10 mL was taken from the veins of the participants. The blood was divided into two test tubes, the first vacuum tube contains sodium citrate to obtain plasma for the fibrinogen test, which was performed immediately after obtaining the plasma. The second vacuum tube contains a clot activator with gel to obtain serum to perform other biochemical tests. After allowing the blood to coagulate, it was centrifuged for 15 minutes at 2000 rpm. The separated serum was distributed into three Eppendorf tubes of 1.5 mL per participant. Then the serum was frozen at -20 ° C, for later use in the study assays.

3.3 Blood Pressure Measurement

Blood pressure was determined by MDF sphygmomanometer with Littmann® stethoscope. SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg had been considered as a risk factor for MetS.

Table 3.2 Participant's information form

Participant profile			
Name:		Sample ID:	
Age:	Gender:	Address:	
Job:	Smoking:	Drinking:	Pregnant:
Weight:	Length:	BMI:	Waist C.:
Past medical history:		Past drug history:	
Biochemical parameters			
Fasting serum triglycerides (TG)			
Fasting serum high density lipoprotein (HDL)			
Fasting blood glucose (FBG)			
Fasting insulin (F. Insulin)			
Plasma fibrinogen (Fib)			
Serum uric acid (S.UA)			
Serum selenium (Se)			
Serum chromium (Cr)			

3.4 Anthropometric Measurements

After fasting for at least 12 hours, measurements were obtained in the morning. Participants were encouraged to dress comfortably and remove their shoes. The weight was measured by a digital scale, and the length was measured with a scale of the category (DETECTO-MEDIC, BROOKLYN, USA) in a straight position and the horizontal scale cover was placed over the head, and the final reading was recorded. BMI was determined from dividing the participant's weight by the square of height (kg/m^2). The waist circumference was measured after exhalation with a non-elastic tape measure in a tight, non-compressive form on the skin, horizontal in the distance between the hip bone's top and the lowest floating rib, at the level of the belly button.

3.5 Chemicals

The chemicals utilized in this investigation are listed in the table below (Table 3.3).

Table 3.3 Chemicals used in the study

Chemicals	LOT	Company
Triglyceride kit	072032A	Biolabo, France
High density lipoprotein kit	091859B	Biolabo, France
Glucose kit	520149	Randox, UK
Insulin	43022302	Roche, Germany
Fibrinogen kit	256443	STAGO, US
Uric acid kit	061913A	Biolabo, France
Nitric acid	050114	General Drug House, India
Hydrogen peroxide	13016202	Scharlau, Spain

3.6 Instruments

The instruments used in this study and shown in Table 3.4 below were obtainable in the clinical biochemistry laboratories at Al-Hussein Teaching Hospital and the Specialized Center for Diabetes and Endocrinology/Al-Muthanna Health Directorate, some others available in Faculty of Pharmacy/Al-Muthanna University and the Department of Chemistry at the Faculty of Science / Thi- Qar University.

Table 3.4 Instrumentals used in the study

Instruments	Manufacturers
Centrifuge	Kokusan H-103n, Japan
Centrifuge	Kokusan H-19F, Japan
UV/VIS spectrophotometer	APEL PD-303, Japan
UV/VIS spectrophotometer	CECIL CE7200, England
Water bath	HH-S2, China
Water bath	LEICA HI 1210, China
Hot plate	MS-300HS, Korea
Fume Hood	China
Cobas e411	Roche, Germany
AA500 Atomic Absorption spectroscopy	England
Start Max	US

3.7 Diagnostic Criteria of Metabolic Syndrome

According to AHA/IDF/NHLBI/ WHF/IASO/IAS 2009 the presence of any three of the five risk factors listed in Table 3.5 was used to diagnose MetS:

Table 3.5 The criteria used in this study for the diagnosis of MetS

Variables	Values
Fasting blood glucose	≥ 100 mg/dL or taking medicine for elevated glucose
High density lipoprotein- cholesterol levels	< 40 mg/dL for males or < 50 mg/dL for females or taking medicine for reduced HDL-C
Triglycerides	≥ 150 mg/dL or taking medicine for elevated triglycerides
Waist Circumference	≥ 94 cm for males or 80 cm for females
Blood pressure	Systolic ≥ 130 mmHg and/or diastolic ≥ 85 mmHg or taking medicine for Hypertension, or antihypertensive medications in a patient with a past history of Hypertension

3.8 Determination of Fasting Serum Glucose Concentration

Principle

In the presence of glucose oxidase (GOD), glucose was oxidized to gluconic acid ($C_6H_{12}O_7$) and hydrogen peroxide (H_2O_2) Equation (3.1) that reacted with phenol and 4-aminophenazone Equation (3.2) to produce quinoneimine (red –violet dye) as indicator (Trinder 1969a, Lott and Turner 1975).

$$Glucose + O_2 + H_2O \xrightarrow{GOD} Gluconic\ acid + H_2O_2 \quad (3.1)$$

$$H_2O_2 + phenol + 4 - aminophenazone \xrightarrow{Peroxidase} quinoneimine + 4H_2O \quad (3.2)$$

Reagent compositions

Vial R1a Buffer Solution: Phosphate Buffer 0.1mol/L, pH 7.0; Phenol 11 mmol/L.
Vial R1b GOD-PAP Reagent: 4-aminophenazone 0.77 mmol/L, Glucose oxidase ≥1.5 kU/L, Peroxidase ≥1.5 kU/L.
CAL. Standard: Glucose 5.55 mmol/L (100 mg/dL).

Procedure

The contents of vial R1b were transferred to vial R1a and were mixed well to form a working reagent, which would remain stable for 5 days at +15 to +25 °C or for 3 months at +2 to +8 °C. The summary of the procedure was shown in (Table 3.6).

Table 3.6 Addition steps of procedure of fasting blood glucose

Pipette Into the Selected Test Tubes	**Blank**	**Standard**	**Assay**
Reagent	1 mL	1 mL	1 mL
Standard	—	10 µL	—
Serum	—	—	10 µL

They were incubated for 25 minutes at 15–25 °C or 10 minutes at 37 °C after mixing. At 500 nm, the absorbance was measured against a reagent blank.

Calculation

The result was calculated according to the Equation (3.3).

$$Glucose\ concentration = \frac{Absorbance\ (Assay)}{Absorbance\ (Standard)} \times Standard\ concentration\ (100) \qquad (3.3)$$

3.9 Determination of Fasting Insulin Concentration

Serum insulin concentration was determined with Elecsys Insulin Assay (cobas e411 analyzer, Roche Diagnostics GmbH, Germany). Elecsys Insulin Assay is based on the ECLIA technology (electro chemiluminescent immunoassay).

Principle

In 1st incubation, insulin availabled in the 20 µL sample, monoclonal insulin-specific antibody labeled with ruthenium complex (Tris(2,2'-bipyridyl) ruthenium (II)-complex ($Ru(bpy)_3^{+2}$), and biotinylated monoclonal insulin-specific antibody form the sandwich complex. The complex was attached to the solid phase by the interaction of streptavidin and biotin in the second incubation after streptavidin-coated microparticles had been added. The reaction mixture was delivered into the measurement cell, where the microparticles were magnetically trapped on the electrode surface. With ProCell/ProCell M, unbound materials were then extracted. The implementation of a voltage to the electrode then caused chemiluminescent emission that was weighted by a photomultiplier. The value of light created is proportional to the insulin value in the sample. The results were calculated via an instrument-specific calibration curve created by 2-point calibration and a master curve supplied via the barcode of the reagent.

Reagents

Vial M: Streptavidin-coated microparticles 0.72 mg/mL, preservative.
Vial R1: Biotinylated monoclonal anti-insulin antibody (mouse) 1 mg/L; MESb) buffer 50 mmol/L, pH 6.0; preservative.
b: MES = 2-morpholino-ethane sulfonic acid
Vial R2: Monoclonal anti-insulin antibody (mouse) labeled with ruthenium complex 1.75 mg/L; MES buffer 50 mmol/L, pH 6.0; preservative.

Calculation

The analyzer calculated the insulin concentration of each sample automatically (either in pmol/L or µU/mL).
Conversion factors: pmol/L x 0.144 = µU/mL, µU/mL x 6.945 = pmol/L

3.10 Determination of Fasting Serum Triglyceride

Principle

Fossati and Prencipe procedure (Fossati and Prencipe 1982) correlated with Trinder reaction (Trinder 1969b), as in the following reaction:

$$Triglycerides \xrightarrow{Lipase} Glycerol + free\ fatty\ acides \quad (3.4)$$

$$Glycerol + ATP \overset{Glycerol\ kinase}{\leftrightarrows} Glycerol\text{-}3\text{-}phosphate + ADP \quad (3.5)$$

$$Glycerol\text{-}3\text{-}phosphate + O_2 \overset{Glycerol\text{-}3\text{-}phosphate\ oxidase}{\leftrightarrows} Dihydroxyacetone\ phosphate + H_2O \quad (3.6)$$

$$H_2O_2 + 4 - Chlorophenol + PAP \xrightarrow{Peroxidase} Quinoneimine\ (pink) + H_2O \quad (3.7)$$

The absorbance of the (Quinoneimine) is proportional to triglycerides concentration in the specimen.

Reagent compositions

Vial R1 BUFFER: PIPES 100 mmol/L, Magnesium chloride 9.8 mmol/L, Chloro-4-phenol 3.5 mmol/L, and preservative.

Vial R2 ENZYMES: Lipase ≥ 1000 IU/L, Peroxidase (POD) ≥ 1700 IU/L, Glycerol-3-phosphate oxidase (GPO) ≥ 3000 IU/L, Glycerol kinase (GK) ≥ 660 IU/L, 4-Amino-antipyrine (PAP) 0.5 mmol/L, and Adenosine triphosphate Na (ATP) 1.3 mmol/L.
Vial R3 STANDARD: Glycerol 2.28 mmol/L, equivalent to triglycerides 200 mg/dL

Procedure

The working solution was prepared by adding vial R2 (Enzymes) to vial R1 (Buffer) and mixed well. Then the following procedure was followed (Table 3.7).

Table 3.7 Addition steps of procedure of fasting triglyceride

Pipette Into the Selected Test Tubes	**Blank**	**Standard**	**Assay**
Working reagent	1 mL	1 mL	1 mL
Demineralized water	10 µL	—	—
Standard	—	10 µL	—
Serum	—	—	10 µL

They mixed well and then allowed to stand for 10 minutes at room temperature or 5 minutes at 37 °C. Absorbance against reagent blank was recorded at 500 nm.

Calculation

The result was calculated according to the Equation (3.8).

$$Result = \frac{Absorbance\ (Assay)}{Absorbance\ (Standard)} \times Standard\ concentration\ (\mathbf{2}00) \quad (3.8)$$

3.11 Determination of High-Density Lipoprotein

Principle

This reagent was used to treat samples before measuring HDL cholesterol with a total cholesterol reagent.By magnesium chloride and phosphotungstic acid (PTA), very low-density lipoproteins (VLDL) and low-density lipoproteins (LDL) were precipitated. After centrifugation, the supernatant was obtained and the high-density lipoprotein (HDL) was measured using the total cholesterol reagent (Burtis *et al.* 1999).

Reagent compositions

Vial R1 PRECIPITANT: phosphotungstic acid (PTA) 13.9 mmol/L, magnesium chloride 570 mmol/L.
Vial R2 STANDARD: cholesterol 100 mg/dL (2.58 mmol/L)

Procedure

Specimen: 0.5 mL
Precipitant: 50 µL
It was allowed to the mixture to settle at room temperature for 10 minutes and centrifuged at 3550-400 RPM for 15 minutes and then proceeded to the next step (Table 3.8).

Table 3.8 Addition steps of procedure of high-density lipoprotein

Pipette Into the Selected Test Tubes	Blank	Standard	Assay
Reagent	1 mL	1 mL	1 mL
Demineralized water	25 µL	—	—
Standard 100 mg/dL	—	25 µL	—
Supernatant	—	—	25 µL

They were mixed thoroughly and set aside for 10 minutes at room temperature or 5 minutes at 37 °C. At 500 nm, the absorbance was measured against to reagent blank.

Calculation

The result was calculated according to the Equation (3.9).

$$Result = \frac{\boldsymbol{Absorbance\ (Assay)}}{\boldsymbol{Absorbance\ (Standard)}} \times Standard\ concentration\ \times 1.1 \quad (3.9)$$

3.12 Determination of Serum Uric Acid

Principle

The action of uricase on uric acid produced carbon dioxide, allantoin and hydrogen peroxide that reacted with chromogen (dichlorohydroxybenzene sulfonate and amino-antipyrine) to produce a red complex (quinoneimine) (Fossati *et al.* 1980, Burtis *et al.* 1999). The sample's abssorbance at 505 nm (495-505) was proportional to the amount of uric acid present.

Reagent composition

Vial R1 Enzymes: Potassium hexacyanoferrate (II) 42 µmol/L, Peroxidase ≥ 450 U/L, Amino-antipyrine 0,150 mmol/L, and Uricase ≥ 120 U/L.
Vial R2 Buffer: Dichlorohydroxybenzene Sulfonate 2 mmol/L, Tris pH 8.0 at 25°C 50 mmol/L, and Preservative.
Vial R3 Standard: Uric acid 595 µmol/L (10 mg/dL).

Procedure

The contents of vial R1 added promptly into vial R2 and mixed gently until completely dissolved. The summary of the procedure was shown in (Table 3.9).

Table 3.9 Addition steps of procedure of uric acid

Pipette Into the Selected Test Tubes	Blank	Standard	Assay
Reagent	1 mL	1 mL	1 mL
Standard	—	25 µL	—
Serum	—	—	25 µL

They were mixed and let stands for 5 min at 25°C.The absorbance against to reagent blank was recorded at 505 (495-505) nm.

Calculation

The result was calculated according to the Equation (3.10).

$$Result = \frac{Absorbance\ (Assay)}{Absorbance\ (Standard)} \times Standard\ concentration \quad (3.10)$$

3.13 Determination of Plasma Fibrinogen

The Clauss method (Clauss 1957, Mackie *et al.* 2003), which has been proved to be fast, sensitive, and exact, evaluates the rate of fibrinogen to fibrin conversion in the presence of excess thrombin. When diluted plasma clotted with an excess of thrombin, the fibrinogen level was negatively proportional to the clotting time.

The plasma sample was diluted 1:20 in Owren-Koller buffer, and then 100 µL of the diluted sample was incubated at 37°C for 240 seconds before adding thrombin to start the clotting process. The samples were measured by STA-Liquid Fib. STart Max.

3.14 Determination of Trace Elements Concentrations

The concentrations of chromium and selenium were measured by using the following procedure (Simeonov *et al.* 2010). 3 ml of serum was putted into a 50 ml glass beaker. 15 ml of the digester was added (a mixture of nitric acid and perchloric acid in a ratio of 1:3), and 6 ml of hydrogen peroxide. These additions were in three steps:

Step 1: Add 5 mL of the digester was added into the serum containing flask. The flask was placed on a hot plate at a temperature of 100 °C, after 15 minutes had passed and the volume of the solution had decreased and the color of the rising steam had begun to disappear, 2 mL of hydrogen peroxide was carefully added with stirring.

Step 2: After decreasing the volume of the previous solution until it becomes approximately 1 mL, 5 mL of the digester was added and left on the hot plate until it decreased, then 2 mL of hydrogen peroxide was added.

Step 3: Repeat the above in Step 2. After the solution was reduced to 1 mL and its color had disappeared, the flask was removed from the hot plate and cooled. Then it was added to the cylinder and the flask was washed with deionized water and the volume was completed to 20 mL. Then it was distributed into numbered tubes, covered, and kept at -20°C to measure later.

The concentrations of trace elements (Se and Cr) were measured by using AA500 Atomic Absorption Spectrometer.

3.15 Statistical Analysis

A statistical analysis of the data was performed by using SPSS version 26. The statistical significance criterion was set at a P value of less than 0.05. For each parameter, descriptive statistics were produced, which included mean and standard deviation (SD). Comparisons between MetS and Control were done by independent t-test. ANOVA

performed for age and BMI groups. The correlation between Se, Cr with other studies parameters of MetS cases was calculated via Pearson correlation (r= −1 to 1). Receiver operating characteristic (ROC) curve was formed to check the distinctive ability of the Se, Cr levels and all other parameters among control individuals and MetS cases.

4. RESULTS

4.1 Characteristic Features for the Studied Parameters

This study included 140 participants, 70 of whom met the criteria for diagnosing MetS adopted in the current study, and the other 70 were control subjects. Control subjects were selected with the same age groups and BMI as well as similar approximate numbers of sex for patients with MetS to study the exact effect of MetS only. Both patient and control categories were divided into groups according to age, sex and BMI, and their effect on all parameters was discussed.

4.2 General Comparison for the Studied Parameters

The results was shown in Table 4.1, Figure 4.1 indicated a significant decrease in the concentrations of Se ($P < 0.01$), Cr ($P < 0.01$), and HDL ($P < 0.01$) for the non-diabetic MetS cases when compared with the control group. While a significant increasing in the concentration of TG ($P < 0.01$), FBG ($P < 0.01$), HOMA-IR ($P < 0.01$), F. INSULIN ($P < 0.01$), UA ($P = 0.05$) and Fib ($P < 0.01$) was observed when the results were compared to the control. However, SBP ($P < 0.01$), DBP ($P < 0.01$) and WC ($P < 0.01$) levels showed a significant increase compared to control. There was no significant difference ($P > 0.05$) in the means of age and BMI between MetS and control subjects due to the selection of a control group similar in age and BMI, but control individuals did not meet the criteria of the syndrome studied.

4.3 The Effect of Age on Studied Parameters

The current study considered the impact of age on the factors under consideration. The participants in this study were divided into three age groups as shown in (Table 3.1, Figure 3.1). The results of each group were compared with the corresponding control group to find the significant difference.

Table 4.1 General comparison for all studied parameters

Groups / Parameters	Control Mean ± SD[1]	N[2]	MetS[3] Mean ± SD	N	P Value
Age years	43.60 ±14.95	70	44.14 ± 13.22	70	0.68
BMI kg/m^2	31.81 ± 5.12	70	32.41 ± 6.63	70	0.57
WC cm	98.78 ± 9.51	70	105.78 ± 13.38	70	0.001
SBP mmHg	121.14 ± 6.87	70	131.57 ± 10.05	70	< 0.001
DBP mmHg	77.78 ± 5.68	70	85.00 ± 6.86	70	< 0.001
TG mg/dL	105.28 ± 27.56	70	191.47 ± 80.74	70	< 0.001
HDL mg/dL	55.44 ± 12.53	70	39.67 ± 9.74	70	< 0.001
FBG mg/dL	87.68 ± 10.73	70	101.1 5 ± 11.65	70	< 0.001
Insulin uU/ml	10.07 ± 4.83	70	18.95 ± 11.48	70	< 0.001
HOMA-IR	2.17 ± 1.03	70	4.71 ± 2.86	70	< 0.001
Se µg/dL	103.79 ± 19.86	70	92.09 ± 19.09	70	0.001
Cr µg/dL	0.1095 ± 0.0318	70	0.0819 ± 0.0364	70	< 0.001
Fib. mg/dL	280.91 ± 28.95	70	306.57 ± 36.00	70	< 0.001
UA mg/dL	5.27 ± 1.25	70	5.72 ± 1.45	70	0.05

4.3.1 The effect of age on fasting blood glucose

The results indicated a significant increase in the FBG concentration for all age groups of patients with MetS when compared with the control. In Table 4.2 a significant increased was observed in G1 ($P < 0.01$), G2 ($P < 0.01$), and G3 ($P < 0.01$) when compared with the control subjects. In the same table, there was a clear significant increase among the three age groups of patients ($P < 0.01$) and control ($P < 0.01$). When performing LSD test, it was observed that there was a significant increased between G2 and G1 for patients ($P < 0.01$), and a significant increased between G3 and G1 ($P < 0.01$), While no significant difference was observed between age G3 and G2 ($P > 0.05$). However, Age-G3 mean was higher than Age-G2 and these values were higher than Age-G1.

[1] Standard deviation
[2] Number of patients
[3] Metabolic syndrome

Table 4.2 The effect of age on the fasting blood glucose concentration

Age groups	FBG[1] mg/dL				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	82.61±5.94	21	93.14±8.59	21	< 0.001
G2	87.75±10.37	32	103.25±9.74	32	< 0.001
G3	93.82±13.06	17	107.11±13.35	17	< 0.001
P Value Between groups	0.005		< 0.001		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
G2 vs. G1	0.074		0.001		
G3 vs. G1	0.001		< 0.001		
G3 vs. G2	0.048		0.220		

4.3.2 The effect of age on homeostasis model assessment

Table 4.3 revealed a significant increased in HOMA-IR concentration in patients with MetS compared to controls in all age groups ($P < 0.05$). However, no significant differences were observed within the age groups of patients ($P > 0.05$), while significant differences were observed for control ($P > 0.05$). The mean of HOMA-IR was higher at Age-G2 and we noticed a decrease at Age-G3.

Table 4.3 The effect of age on the HOMA-IR concentration

Age groups	HOMA-IR				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	1.73±0.86	21	4.91±3.56	21	< 0.001
G2	2.50±1.16	32	5.05±2.46	32	< 0.001
G3	2.08±0.77	17	3.82±2.58	17	0.012
P Value Between groups	0.024		0.632		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
G2 vs. G1	0.007		0.418		
G3 vs. G1	0.279		0.388		
G3 vs. G2	0.164		0.798		

[1] Fasting blood glucose

4.3.3 The effect of age on fasting insulin

Table 4.4 shows a significant rise in the three age categories of MetS patients compared to the control group ($P < 0.05$). Our study observed a decrease in fasting insulin concentrations with age.

Table 4.4 The effect of age on the fasting insulin concentration

Age groups	**Fasting Insulin (uU/ml)**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	8.51±4.31	21	21.02±14.10	21	< 0.001
G2	11.58±5.44	32	19.99±10.04	32	< 0.001
G3	9.14±3.38	17	14.45±9.77	17	0.042
P Value Between groups	0.049		0.170		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
G2 vs. G1	0.023		0.746		
G3 vs. G1	0.682		0.081		
G3 vs. G2	0.088		0.109		

4.3.4 The effect of age on serum triglycerides

It was noted in Table 4.5 a high significant increased in triglyceride concentration in patients with MetS compared with the control in all age groups ($P < 0.05$). Our results showed a substantial increase in the mean of TG with age in the same table.

Table 4.5 The effect of age on the serum triglycerides concentration

Age groups	**TG[1] mg/dL**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	108.33±26.70	21	169.52±86.54	21	0.004
G2	98.68±28.01	32	196.46±78.73	32	< 0.001
G3	113.94±26.19	17	209.17±75.70	17	< 0.001

[1] Triglycerides

Table 4.5 (continue)

P Value Between groups	0.153		0.292		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
G2 vs. G1	0.211		0.237		
G3 vs. G1	0.530		0.136		
G3 vs. G2	0.066		0.600		

4.3.5 The effect of age on high density lipoproteins

When comparing patients with MetS to controls, the results in Table 4.6 demonstrated a substantial decrease in HDL concentration in all age categories ($P < 0.05$). Depending on the mean value, the HDL concentration recorded a decrease with age.

Table 4.6 The effect of age on the high-density lipoprotein concentration

Age groups	**HDL[1] mg/dL**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	47.66±7.03	21	40.90±12.98	21	0.042
G2	58.21±14.96	32	40.18±6.30	32	< 0.001
G3	59.82±8.16	17	37.17±10.61	17	< 0.001
P Value Between groups	0.002		0.469		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
G2 vs. G1	0.002		0.795		
G3 vs. G1	0.002		0.247		
G3 vs. G2	0.646		0.308		

[1] High density lipoproteins

4.3.6 The effect of age on uric acid

In the results presented in Table 4.7 no significant differences (P > 0.05) were observed in the concentration of uric acid in patients with MetS compared to control in all the studied age groups. The level of uric acid decreased with age.

Table 4.7 The effect of age on the uric acid concentration

Age groups	Uric Acid mg/dL				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	5.39±0.98	21	6.16±1.68	21	0.077
G2	5.43±1.02	32	5.76±1.29	32	0.266
G3	4.80±1.79	17	5.09±1.30	17	0.588
P Value Between groups	0.207		0.075		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
G2 vs. G1	0.904		0.319		
G3 vs. G1	0.147		0.024		
G3 vs. G2	0.092		0.120		

4.3.7 The effect of age on fibrinogen

The current study's findings in Table 4.8 revealed a significant increased in fibrinogen concentration in patients with metabolic syndrome in all age groups when compared to the control group (P < 0.05). However, no significant difference was observed within the age groups (P > 0.05).

Table 4.8 The effect of age on the fibrinogen concentration

Age groups	Fibrinogen mg/dL				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	278.90±31.27	21	300.66±37.83	21	0.049
G2	284.50±26.54	32	312.34±34.91	32	0.001
G3	276.64±31.24	17	303.00±36.22	17	0.030
P Value Between groups	0.625		0.466		

Table 4.8 (continue)

Multiple Comparisons		
Groups	Significant (control)	Significant (MetS)
G2 vs. G1	0.497	0.254
G3 vs. G1	0.813	0.844
G3 vs. G2	0.373	0.392

4.3.8 The effect of age on selenium

In comparison to the control, there was a significant decrease in selenium levels at ages G1 and G3 ($P<0.05$) in the data of (Table 4.9). While no significant difference was observed in the age G2 ($P > 0.05$). A decrease in the level of selenium was observed at Age-G3.

Table 4.9 The effect of age on the selenium concentration

Age groups	**Selenium (Se µg/L)**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	107.29±21.68	21	93.73±20.48	21	0.044
G2	100.18±18.25	32	93.35±17.01	32	0.127
G3	106.27±20.26	17	87.69±21.45	17	0.015
P Value Between groups	0.379		0.556		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
G2 vs. G1	0.207		0.945		
G3 vs. G1	0.876		0.339		
G3 vs. G2	0.311		0.329		

4.3.9 The effect of age on chromium

In Table 4.10 the significant decrease ($P < 0.05$) in chromium concentration was observed for all age groups in patients with MetS when comparing the results with control. Cr concentration was decreased at Age-G3 while it was higher in Age-G2 than Age-G1.

Table 4.10 The effect of age on the chromium concentration

Age groups	Chromium (Cr µg/L)				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	0.1106±0.035	21	0.0792±0.046	21	0.018
G2	0.1088±0.032	32	0.0891±0.031	32	0.016
G3	0.1095±0.028	17	0.0717±0.030	17	0.001
P Value Between groups	0.981		0.264		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
G2 vs. G1	0.847		0.322		
G3 vs. G1	0.919		0.532		
G3 vs. G2	0.943		0.115		

4.3.10 The effect of age on waist circumference

In the age G1, there was a significant rise ($P < 0.01$) in waist circumference values for patients with MetS when compared to controls (Table 4.11). While no significant difference was noted in G2 and G3 ($P > 0.05$). It was also observed in the same table there was significant differences within age groups for MetS patients ($P < 0.01$). When the LSD test was performed, there was no significant difference between G2 vs G1 ($P > 0.05$), with a higher mean of waist circumference at Age-G1 than at G2. while observed a significant increase between G1 vs G3 ($P < 0.01$) as well as between G2 vs G3 ($P= 0.05$). While within the age groups of the control did not notice a significant difference ($P > 0.05$).

Table 4.11 The effect of age on the waist circumference

Age groups	WC[1] (cm)				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	95.14±12.50	21	111.76±13.68	21	< 0.001
G2	101.40±7.61	32	105.84±12.35	32	0.089
G3	98.35±7.15	17	98.29±11.68	17	0.986
P Value Between groups	0.06		0.007		

[1] Waist circumference

Table 4.11 (continue)

Multiple Comparisons		
Groups	Significant (control)	Significant (MetS)
G1 vs. G2	0.019	0.100
G1 vs. G3	0.292	0.002
G2 vs. G3	0.276	0.05

4.3.11 The effect of age on systolic blood pressure

There was a substantial increase in systolic blood pressure values in patients with MetS when compared to controls in all age groups ($P < 0.01$), as shown in (Table 4.12). In both patients and controls, there was a significant difference in age groups ($P < 0.01$). After testing LSD, there were no significant difference between G1 vs. G2 in both patients and control ($P > 0.05$), while there was a significant difference between G3 vs. G1 as well as between G3 vs. G2 ($P < 0.05$).

Table 4.12 The effect of age on the systolic blood pressure

Age groups	**SBP[1] mmHg**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	117.85±4.05	21	130.71±7.95	21	< 0.001
G2	120.15±5.74	32	127.34±9.06	32	< 0.001
G3	127.05±8.11	17	140.58±8.63	17	< 0.001
P Value Between groups	< 0.001		< 0.001		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
G1 vs. G2	0.176		0.170		
G3 vs. G1	< 0.001		0.001		
G3 vs. G2	< 0.001		< 0.001		

[1] Systolic blood pressure

4.3.12 The effect of age on diastolic blood pressure

Table 4.13 revealed a substantial rise in diastolic blood pressure readings for MetS patients in all age groups when compared to controls ($P < 0.05$). Through the results in the same table there had been no significant difference within age groups to control ($P > 0.05$), while there had been significant difference in patients ($P < 0.05$), and after conducting LSD found that the significant difference between G3 vs. G2 only ($P < 0.01$), and there was no significant difference between G1 vs. G2 and G3 vs. G1 ($P > 0.05$).

Table 4.13 The effect of age on the diastolic blood pressure

Age groups	**DBP[1] mmHg**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
G1	76.19±4.44	21	85.00±5.24	21	< 0.001
G2	77.81±5.37	32	83.12±7.04	32	0.001
G3	79.70±7.17	17	88.52±7.23	17	0.001
P Value Between groups	0.167		0.030		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
G1 vs. G2	0.308		0.316		
G3 vs. G1	0.059		0.106		
G3 vs. G2	0.266		0.008		

4.4 The Effect of Sex on Studied Parameters

There was a significant rise in the concentrations of FBG, HOMA-IR, and F. Insulin in male and female MetS patients as compared to control ($P<0.01$) in the results presented in (Table 4.14). In the same table, male and female patients had a significant rise in TG concentration when compared to control ($P<0.01$), but a significant drop was observed in HDL concentration when compared to control ($P<0.01$). The results showed that the concentration of uric acid in males was substantially higher than in controls ($P<0.05$), but there was no significant difference in females ($P>0.05$). When compared to the control,

[1] Diastolic blood pressure

there was a substantial rise in fibrinogen concentration in both male and female patients ($P < 0.05$). There were no significant alterations in selenium concentration in males ($P > 0.05$), while a significant decrease was observed in females ($P < 0.01$). In the same table, a significant decrease in chromium concentration was observed in male and female patients compared to control ($P < 0.05$). Patients of both sexes had significantly were higher waist circumference and systolic and diastolic blood pressure outcomes ($P < 0.05$).

Table 4.14 The effect of sex on studied parameters

Parameters	Sex	Control Mean± SD	N	MetS Mean± SD	N	P value	P value within	
							M vs F Control	M vs F Patients
FBG	Male	90.66±11.94	33	99.84±11.84	39	0.002	0.027	0.294
	Female	85.02±8.86	37	102.80±11.37	31	< 0.001		
HOMA-IR	Male	2.31±1.30	33	5.08±3.24	39	< 0.001	0.277	0.228
	Female	2.04±0.71	37	4.24±2.27	31	< 0.001		
F. Insulin	Male	10.49±6.31	33	20.83±13.26	39	< 0.001	0.493	0.125
	Female	9.69±3.01	37	16.59±8.38	31	< 0.001		
TG	Male	107.60±29.13	33	198.28±85.16	39	< 0.001	0.510	0.433
	Female	103.21±26.31	37	182.90±75.32	31	< 0.001		
HDL	Male	51.12±11.42	33	37.71±8.25	39	< 0.001	0.006	0.059
	Female	59.29±12.36	37	42.12±10.98	31	< 0.001		
UA	Male	5.29±1.11	33	6.01±1.38	39	0.019	0.896	0.061
	Female	5.25±1.38	37	5.35±1.48	31	0.760		
Fib	Male	287.69±32.69	33	306.17±32.51	39	0.019	0.064	0.920
	Female	274.86±24.01	37	307.06±40.51	31	< 0.001		
Se	Male	100.87±19.07	33	92.85±20.44	39	0.092	0.248	0.713
	Female	106.40±20.44	37	91.14±17.54	31	0.002		
Cr	Male	0.1079±0.031	33	0.0791±0.036	39	0.001	0.693	0.470
	Female	0.1109±0.032	37	0.0855±0.037	31	0.004		
WC	Male	99.87±9.88	33	108.07±13.73	39	0.006	0.368	0.109
	Female	97.81±9.19	37	102.90±12.56	31	0.05		
SBP	Male	119.84±5.07	33	129.87±9.56	39	< 0.001	0.138	0.113
	Female	122.29±8.04	37	133.70±10.40	31	< 0.001		
DBP	Male	78.33±3.67	33	84.10±6.47	39	< 0.001	0.451	0.222
	Female	77.29±7.03	37	86.12±7.26	31	< 0.001		

4.5 The Effect of Body Mass Index on Studied Parameters

4.5.1 The effect of body mass index on fasting blood glucose

Table 4.15 revealed a substantial increase in FBG concentration in patients compared to controls for all BMI groups ($P < 0.01$). Within the BMI groups, no significant differences were found ($P > 0.05$).

Table 4.15 The effect of BMI on fasting blood glucose

BMI groups	**FBG (mg/dL)**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
BMI-N[1]	82.81±5.13	11	101.90±11.31	11	< 0.001
BMI-OW[2]	91.00±12.30	18	104.50±10.16	18	0.001
BMI-Ob[3]	87.53±10.78	41	99.48±12.25	41	< 0.001
P Value Between groups	0.136		0.310		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-N vs. BMI-OW	0.047		0.562		
BMI-N vs. BMI-Ob	0.193		0.541		
BMI-OW vs. BMI-Ob	0.251		0.132		

4.5.2 The effect of body mass index on homeostasis model assessment

It was noted in Table 4.16 that there was a substantial increase in all BMI groups of patients when compared with control ($P < 0.05$). However, the values of HOMA-IR in BMI-OW and BMI-Ob more than this in BMI-N.

[1] Body mass index normal weight
[2] Body mass index over weight
[3] Body mass index obesity

Table 4.16 The effect of BMI on HOMA-IR

BMI groups	HOMA-IR				
	Control Mean± SD	N	MetS Mean± SD	N	P value
BMI-N	1.20±0.40	11	4.16±3.15	11	0.006
BMI-OW	1.66±0.54	18	5.60±3.89	18	< 0.001
BMI-Ob	2.65±1.03	41	4.47±2.17	41	< 0.001
P Value Between groups	< 0.001		0.303		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-N vs. BMI-OW	0.162		0.194		
BMI-N vs. BMI-Ob	< 0.001		0.751		
BMI-OW vs. BMI-Ob	< 0.001		0.168		

4.5.3 The effect of body mass index on fasting insulin

It was observed in Table 4.17 that there was a significant increase in all BMI groups in the fasting insulin concentration of the patients when compared with the control ($P < 0.05$). However, no significant differences were seen across the patient groups ($P > 0.05$). Furthermore, higher levels were observed in overweight and obese subjects than normal weight. while a significant difference was observed within the control groups. The fasting insulin levels of the control subjects increased with the increase in body mass index.

Table 4.17 The effect of BMI on fasting insulin concentration

BMI groups	Fasting Insulin (uU/ml)				
	Control Mean± SD	N	MetS Mean± SD	N	P value
BMI-N	5.84±1.87	11	16.07±11.77	11	0.01
BMI-OW	7.56±2.70	18	22.07±15.65	18	< 0.001
BMI-Ob	12.31±4.84	41	18.36±9.04	41	< 0.001
P Value Between groups	< 0.001		0.350		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-N vs. BMI-OW	0.272		0.177		
BMI-Ob vs. BMI-N	< 0.001		0.56		
BMI-Ob vs. BMI-OW	< 0.001		0.256		

4.5.4 The effect of body mass index on serum triglycerides

Patients in all BMI groups had a considerable rise ($P < 0.05$) in triglyceride concentrations, as shown in (Table 4.18). But it did not show a significant difference within the groups for both patients and control ($P > 0.05$).

Table 4.18 The effect of BMI on serum triglycerides concentration

BMI groups	**TG (mg/dL)**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
BMI-N	120.00±17.46	11	194.00±64.90	11	0.002
BMI-OW	101.11±26.65	18	201.66±78.66	18	< 0.001
BMI-Ob	103.17±29.33	41	186.31±86.53	41	< 0.001
P Value Between groups	0.151		0.797		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-N vs. BMI-OW	0.074		0.807		
BMI-N vs. BMI-Ob	0.073		0.783		
BMI-OW vs. BMI-Ob	0.790		0.508		

4.5.5 The effect of body mass index on high density lipoproteins

The results of Table 4.19 showed that the concentration of HDL in the patients has decreased significantly compared with the control ($P <0.05$), but in the same table there was no significant difference within the groups ($P >0.05$).

Table 4.19 The effect of BMI on the high-density lipoprotein concentration

BMI groups	**HDL (mg/dL)**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
BMI-N	49.27±5.00	11	39.09±9.06	11	0.004
BMI-OW	54.83±9.66	18	39.11±9.39	18	< 0.001
BMI-Ob	57.36±14.51	41	40.07±10.26	41	< 0.001
P Value Between groups	0.160		0.921		

Table 4.19 (continue)

Multiple Comparisons		
Groups	Significant (control)	Significant (MetS)
BMI-N vs. BMI-OW	0.245	0.996
BMI-N vs. BMI-Ob	0.058	0.770
BMI-OW vs. BMI-Ob	0.472	0.732

4.5.6 The effect of body mass index on uric acid

In Table 4.20 the concentration of uric acid did not show any significant differences for patients when compared with control in all BMI groups (P > 0.05), and within these groups, no significant differences were seen (P > 0.05). However, the overweight people recorded the highest level of uric acid among the other groups.

Table 4.20 The effect of BMI on uric acid concentration

BMI groups	**Uric Acid (mg/dL)**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
BMI-N	5.21±0.96	11	5.44±1.23	11	0.635
BMI-OW	5.22±1.60	18	6.17±1.26	18	0.057
BMI-Ob	5.30±1.17	41	5.60±1.57	41	0.339
P Value Between groups	0.963		0.305		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-N vs. BMI-OW	0.993		0.196		
BMI-N vs. BMI-Ob	0.842		0.755		
BMI-OW vs. BMI-Ob	0.819		0.168		

4.5.7 The effect of body mass index on fibrinogen

Table 4.21 there was no significant difference in patients' fibrinogen concentration in BMI-N (P > 0.05) and BMI-OW (P > 0.05) when comparing results with control, but a significant increase in BMI-Ob was found when compared with control (P < 0.01). Within the groups there was no significant difference (P> 0.05).

Table 4.21 The effect of BMI on the fibrinogen concentration

BMI groups	Fibrinogen (Fib mg/dL)				
	Control Mean± SD	N	MetS Mean± SD	N	P value
BMI-N	276.00±33.78	11	302.09±31.82	11	0.077
BMI-OW	269.00±30.23	18	293.00±44.71	18	0.068
BMI-Ob	287.46±25.64	41	313.73±31.49	41	< 0.001
P Value Between groups	0.063		0.113		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-N vs. BMI-OW	0.519		0.504		
BMI-N vs. BMI-Ob	0.235		0.336		
BMI-OW vs. BMI-Ob	0.024		0.042		

4.5.8 The effect of body mass index on selenium

According to the results was shown in Table 4.22 in the BMI-N group, no significant difference (P >0.05) in selenium concentration was observed between patients and control. However, there was a significant decrease in selenium concentration in patients compared to the control in the BMI-OW and BMI-Ob groups (P < 0.05). Within the groups, there were no significant differences (P > 0.05). But BMI-OW and BMI-Ob people have lower means than BMI-N.

Table 4.22. The effect of BMI on the selenium concentration

BMI groups	Selenium (Se µg/l)				
	Control Mean± SD	N	MetS Mean± SD	N	P value
BMI-N	112.16±23.44	11	95.23±16.17	11	0.063
BMI-OW	101.78±17.78	18	90.48±14.81	18	0.046
BMI-Ob	102.43±19.63	41	91.95±21.59	41	0.024
P Value Between groups	0.317		0.812		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-N vs. BMI-OW	0.176		0.522		
BMI-N vs. BMI-Ob	0.153		0.619		
BMI-OW vs. BMI-Ob	0.908		0.788		

4.5.9 The effect of body mass index on chromium

Table 4.23 showed a significant decrease ($P < 0.05$) in chromium concentration for patients when compared with control in all BMI groups. No significant difference ($P > 0.05$) was found within the groups. The chromium concentration increased in the BMI-Ob group.

Table 4.23 The effect of BMI on the chromium concentration

BMI groups	**Chromium (Cr µg/l)**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
BMI-N	0.1194±0.030	11	0.0751±0.024	11	0.001
BMI-OW	0.1098±0.034	18	0.0765±0.026	18	0.003
BMI-Ob	0.1067±0.031	41	0.0861±0.042	41	0.014
P Value Between groups	0.510		0.522		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-N vs. BMI-OW	0.435		0.925		
BMI-N vs. BMI-Ob	0.248		0.381		
BMI-OW vs. BMI-Ob	0.736		0.354		

4.5.10 The effect of body mass index on waist circumference

No significant difference was observed in Table 4.24 in the waist circumference values of patients when compared with the control in the BMI-N and BMI-OW groups ($P > 0.05$), while the table showed a significant increase in the BMI-Ob group ($P < 0.01$). In the same table, the results showed that there was a significant difference within the groups for both patients and control ($P < 0.01$). LSD was determined, and a significant difference was found between BMI-OW vs. BMI-N ($P < 0.05$) and BMI-Ob vs. BMI-N ($P < 0.01$) as well as BMI-Ob vs. BMI-OW ($P < 0.01$).

Table 4.24 The effect of BMI on the waist circumference

BMI groups	WC (cm)				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
BMI-N	85.90±5.24	11	91.18±8.26	11	0.089
BMI-OW	96.83±3.32	18	99.66±5.40	18	0.067
BMI-Ob	103.09±8.83	41	112.39±12.62	41	< 0.001
P Value Between groups	< 0.001		< 0.001		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-OW vs. BMI-N	< 0.001		0.041		
BMI-Ob vs. BMI-N	< 0.001		< 0.001		
BMI-Ob vs. BMI-OW	0.004		< 0.001		

4.5.11 The effect of body mass index on systolic blood pressure

In the BMI-N and BMI-Ob groups, the SBP values of the patients increased significantly ($P < 0.01$) when compared to the control, as shown in (Table 4.25). But no significant difference ($P > 0.05$) was found in the BMI-OW group. In the same table it was shown that there was a significant difference ($P < 0.05$) within the groups of patients, and after checking the LSD test, it was found that the significant difference between the two groups BMI-Ob vs. BMI-OW only ($P < 0.05$), and no significant difference was observed between the other groups ($P > 0.05$).

Table 4.25 The effect of BMI on the systolic blood pressure

BMI groups	SBP (mmHg)				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
BMI-N	116.81±3.37	11	130.45±10.35	11	< 0.001
BMI-OW	123.05±7.88	18	126.94±10.86	18	0.228
BMI-Ob	121.46±6.73	41	133.90±9.04	41	< 0.001
P Value Between groups	0.052		0.044		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-OW vs. BMI-N	0.017		0.350		
BMI-Ob vs. BMI-N	0.044		0.301		
BMI-Ob vs. BMI-OW	0.402		0.014		

4.5.12 The effect of body mass index on diastolic blood pressure

In Table 4.26 there was a significant increase in the DBP values of the patients compared with the control in the BMI-N and BMI-Ob groups ($P < 0.01$), but no significant difference was recorded in the BMI-OW group ($P > 0.05$). In the same table, a significant difference ($P < 0.05$) was observed within the groups of patients, then the LSD statistical test was performed, and it was found that there was a significant difference between the two BMI-Ob vs BMI-OW groups ($P < 0.01$), and no significant differences were recorded between the other groups ($P > 0.05$).

Table 4.26 The effect of BMI on the diastolic blood pressure

BMI groups	**DBP (mmHg)**				
	Control Mean± SD	**N**	**MetS Mean± SD**	**N**	**P value**
BMI-N	75.90±4.36	11	84.54±7.56	11	0.004
BMI-OW	78.05±5.72	18	81.11±7.77	18	0.188
BMI-Ob	78.17±5.99	41	86.82±5.56	41	< 0.001
P Value Between groups	0.497		0.011		
Multiple Comparisons					
Groups	Significant (control)		Significant (MetS)		
BMI-OW vs. BMI-N	0.330		0.173		
BMI-Ob vs. BMI-N	0.248		0.305		
BMI-Ob vs. BMI-OW	0.943		0.003		

4.6 Pearson Correlation Analysis

4.6.1 The correlation of selenium with studied parameters

The results in Table 4.27 showed that there was a significant positive correlation between Se and Cr levels ($r = 0.228$) (Figure 4.2). It was also noted that there was a negative correlation between the levels of Se and FBG ($r = - 0.197$) (Figure 4.3). While there was a weak positive correlation between levels of Se and each of the HOMA-IR in Figure 4.4 and F. Insulin ($r = 0.053$ and 0.066 respectively) (Figure 4.5). In the same table, our study

found a negative correlation between the levels of Se and TG (r = - 0.212) (Figure 4.6). However, there was a positive correlation between the levels of Se and HDL (r = 0.109) (Figure 4.7). It was observed in the same table that there was a positive correlation between levels of Se and UA (r = 0.141) (Figure 4.8). While the correlation was negative between Se and Fibrinogen levels (r = - 0.116) (Figure 4.9). Our study detected a weak negative correlation between Se level and SBP (r = - 0.021) Figure 4.10 as well as DBP (r = - 0.078) (Figure 4.11). Also, the data showed positive correlation between Se and WC (r = 0.141) (Figure 4.12). Furthermore, weak positive correlation was observed between Se and BMI (r = 0.011) (Figure 4.13). Finally, Se showed a negative association with age (r = - 138) (Figure 4.14).

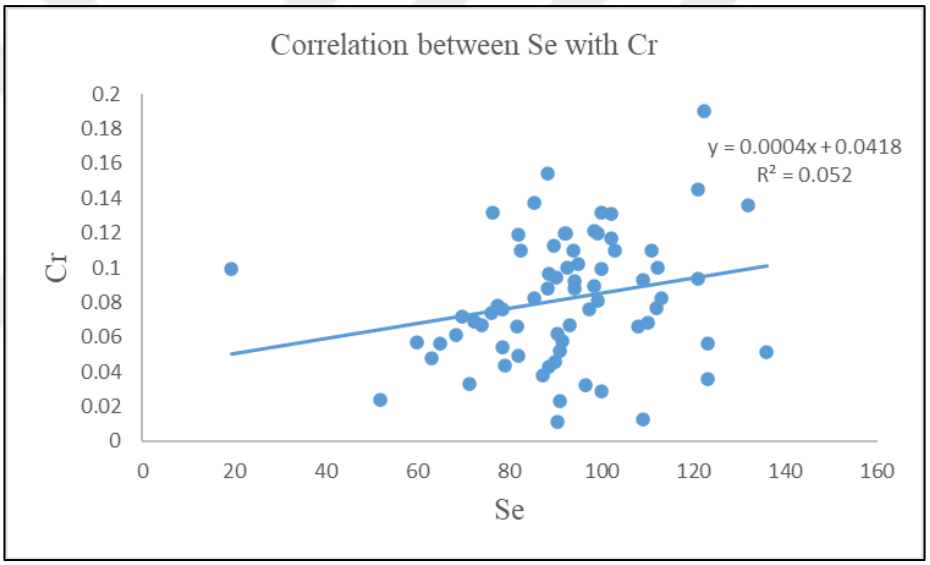

Figure 4.2 Correlation between Se with Cr

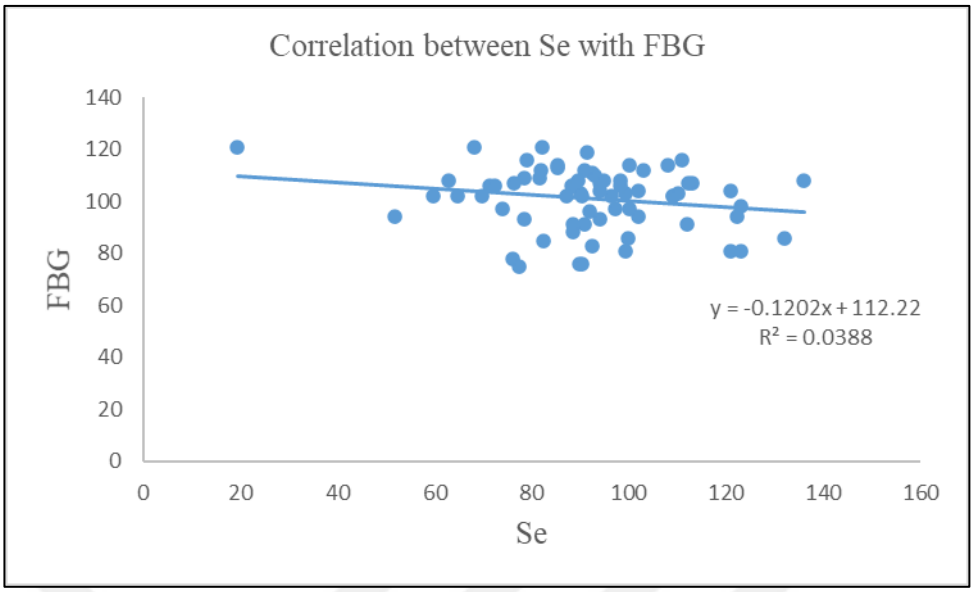

Figure 4.3 Correlation between Se with FBG

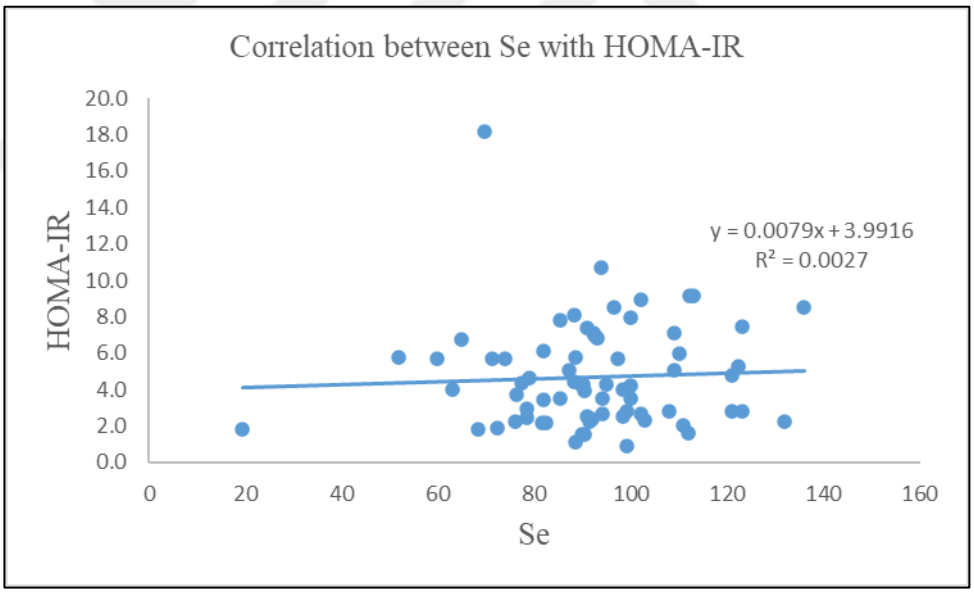

Figure 4.4 Correlation between Se with HOMA-IR

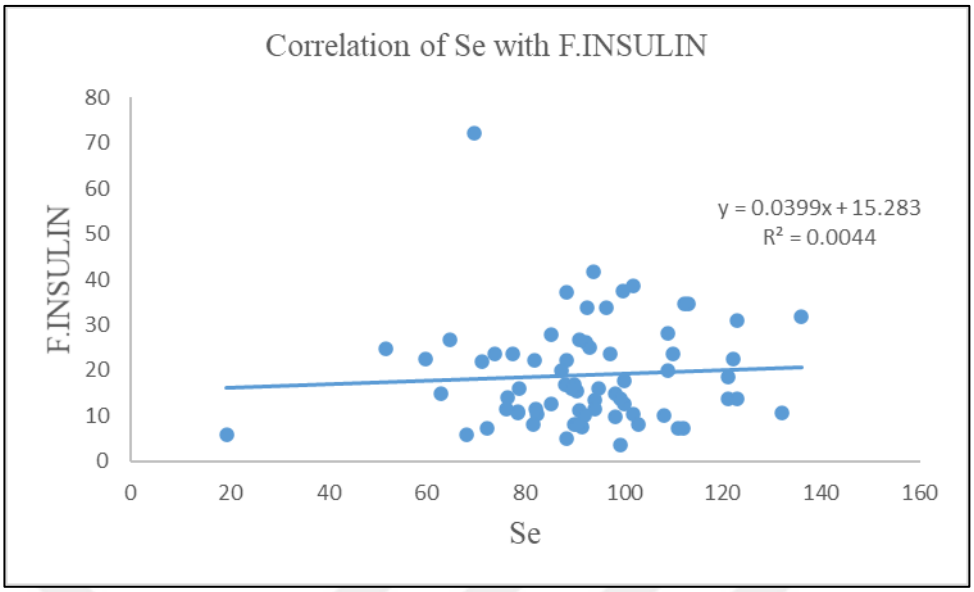

Figure 4.5 Correlation between Se with f. insulin

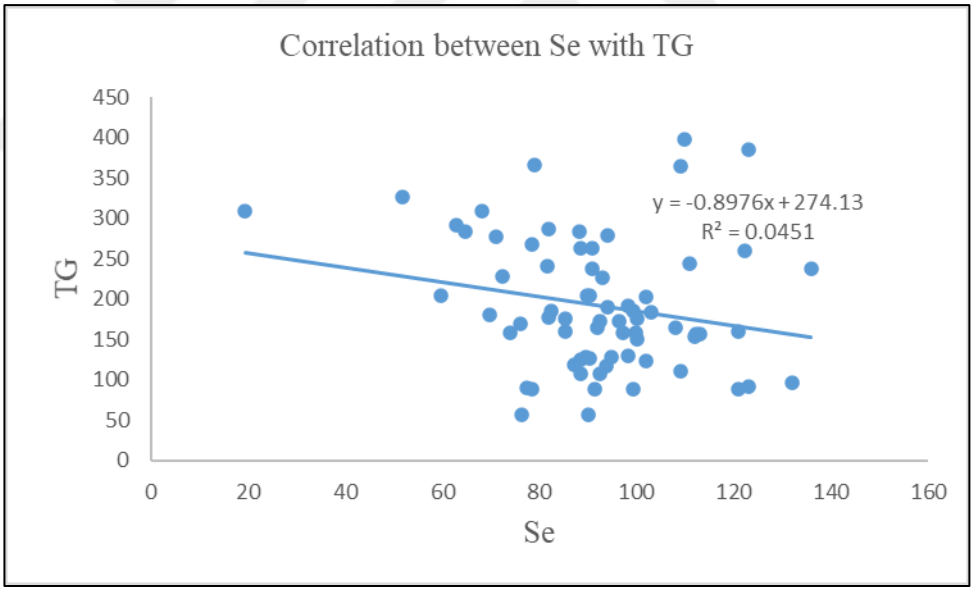

Figure 4.6 Correlation between Se with TG

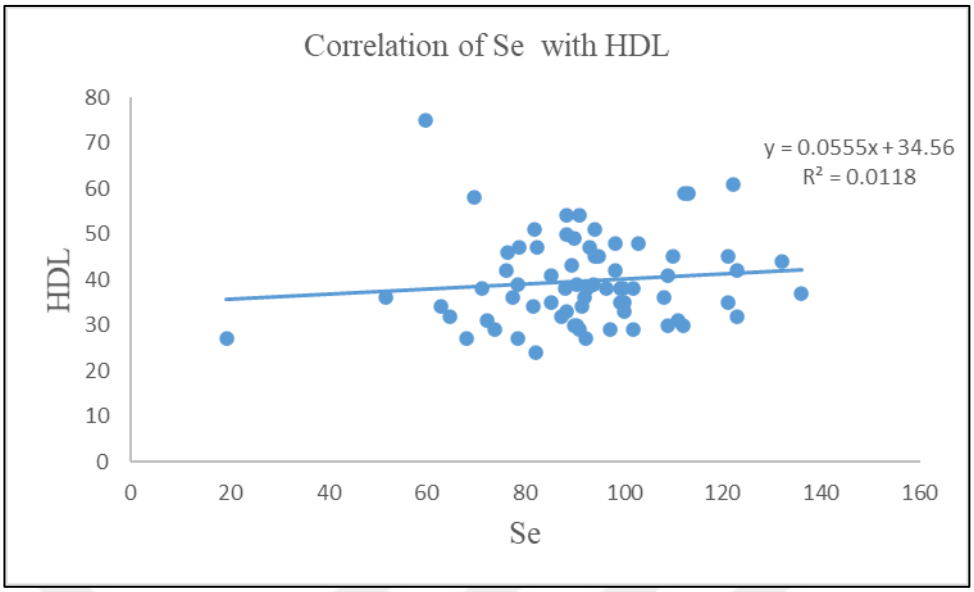

Figure 4.7 Correlation between Se with HDL

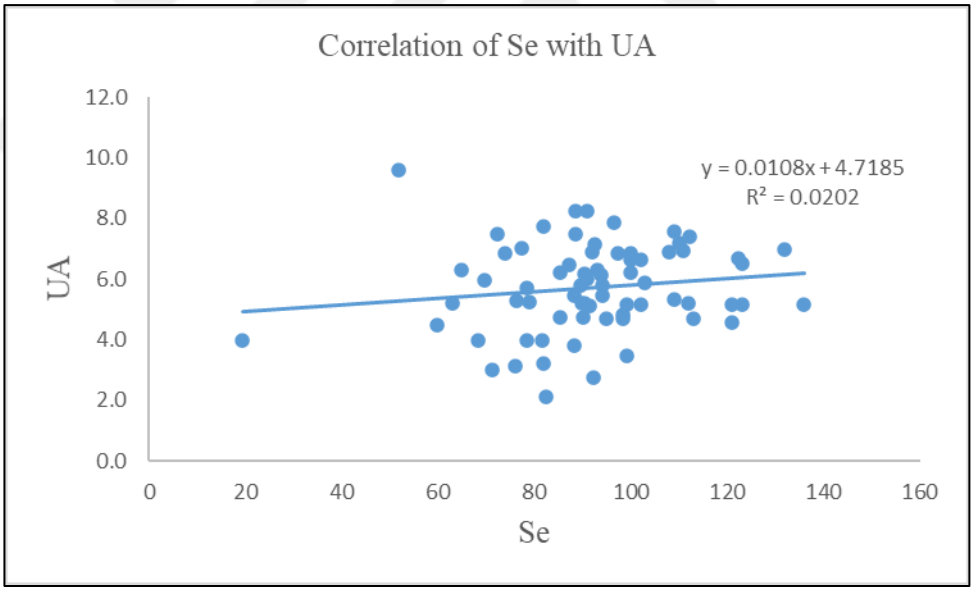

Figure 4.8 Correlation between Se with UA

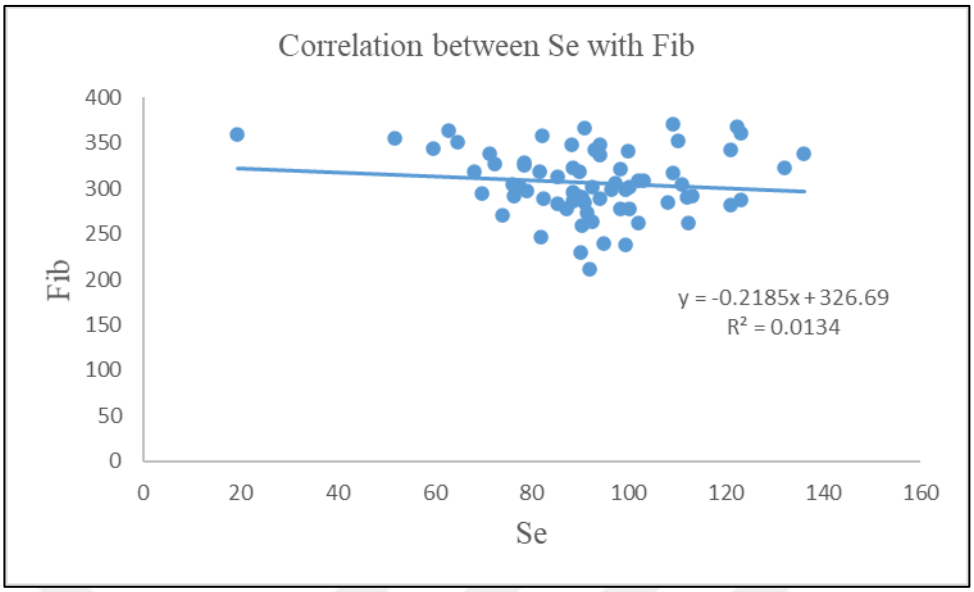

Figure 4.9 Correlation between Se with fibrinogen

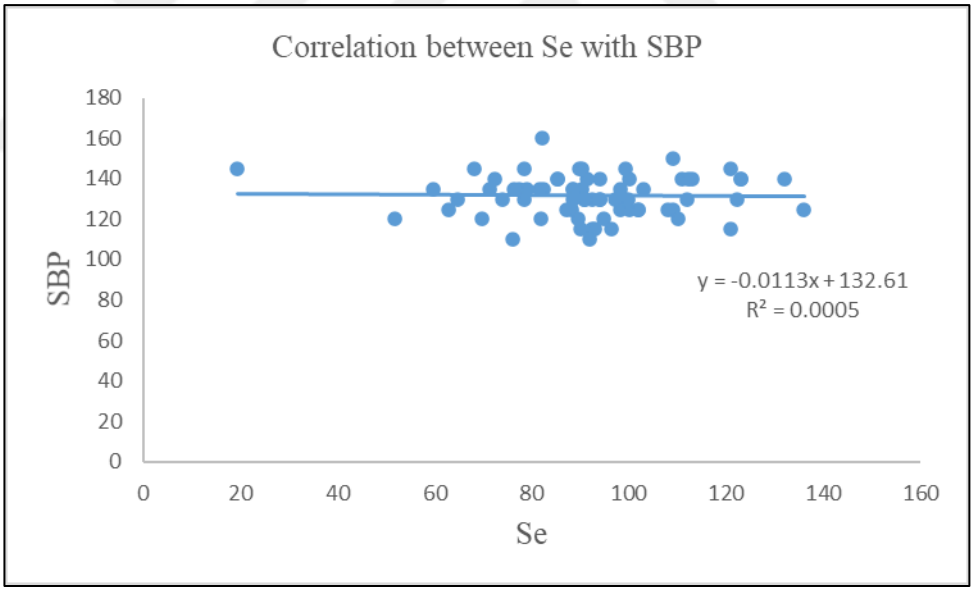

Figure 4.10 Correlation between Se with SBP

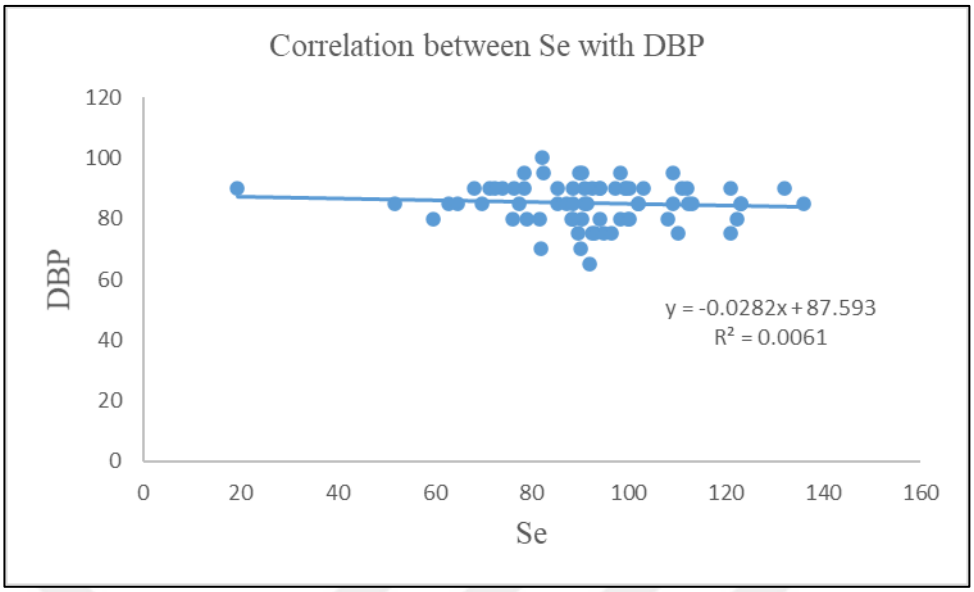

Figure 4.11 Correlation between Se with DBP

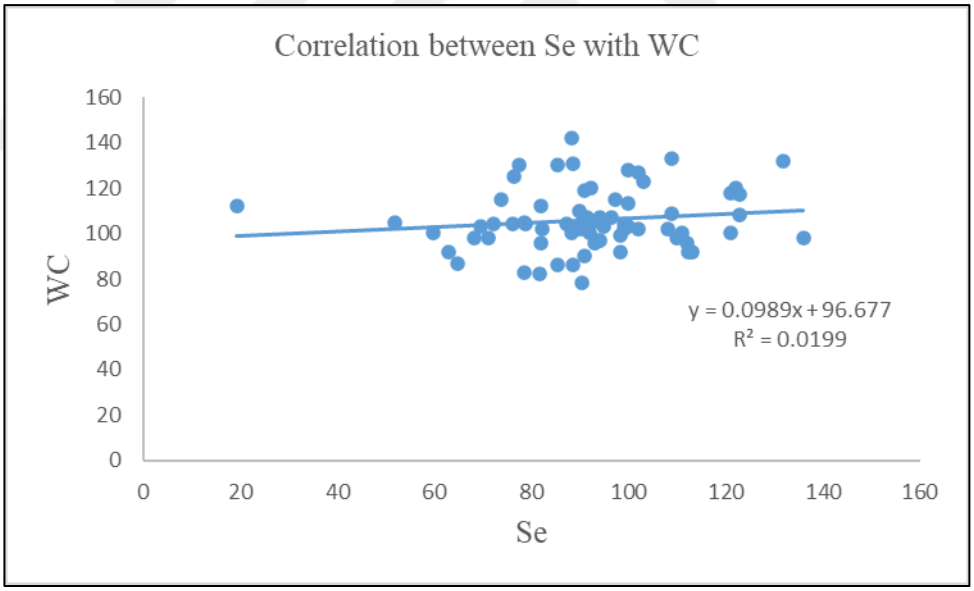

Figure 4.12 Correlation between Se with WC

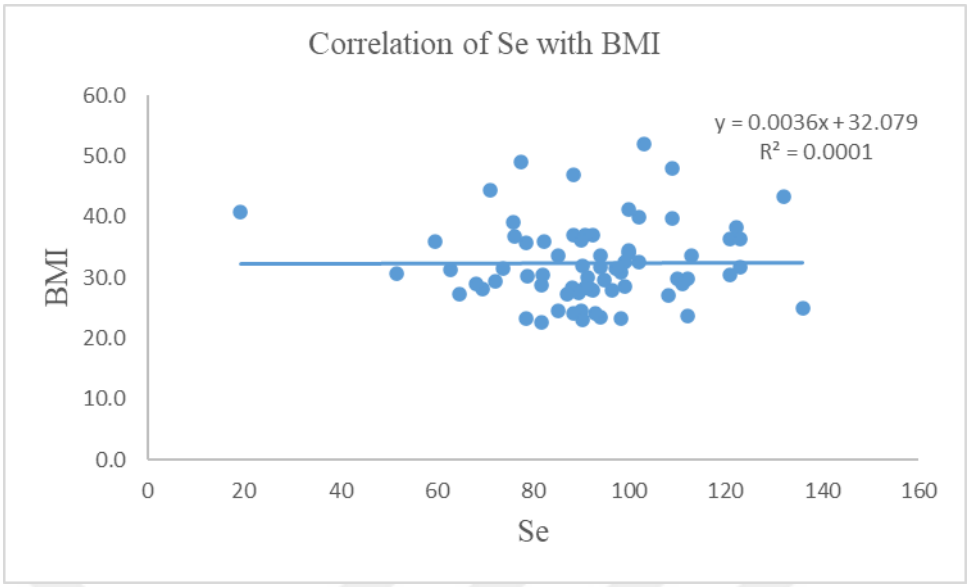

Figure 4.13 Correlation between Se with BMI

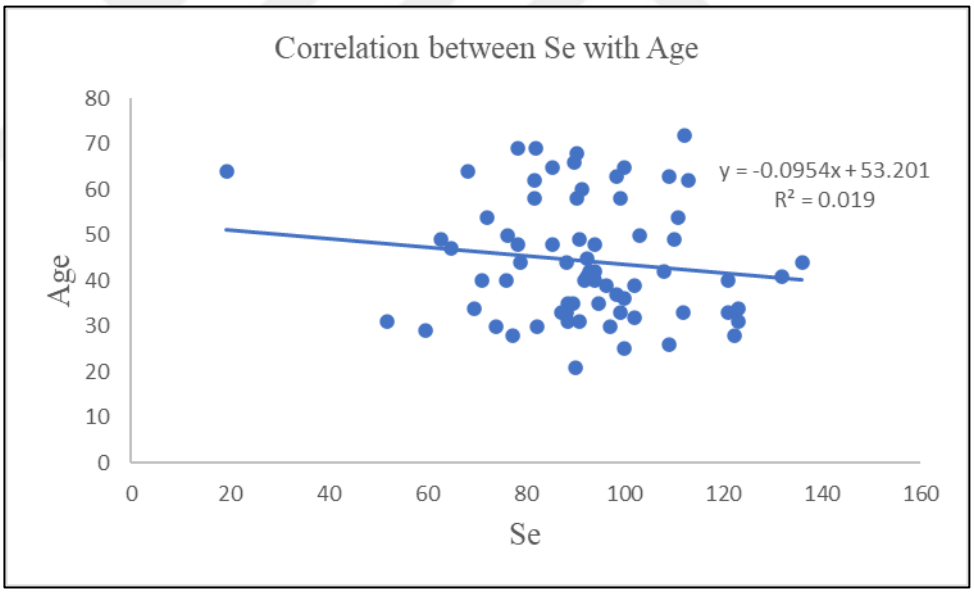

Figure 4.14 Correlation between Se with age

4.6.2 The correlation of chromium with studied parameters

As shown in Table 4.27, our study indicated that there was a weak negative correlation between Cr levels and each of FBG (r = - 0.071) in Figure 4.15 and Fibrinogen (r = - 0.01) in Figure 4.16 as well as negative correlation between Cr and TG (r = - 0.287) In Figure 4.17, UA levels (r = - 0.169) in Figure 4.18 and age (r = - 0.095) (Figure 4.26). In the same table, it was observed that there was a significant positive correlation between Cr and Se (r = 0.228) in Figure 4.2, HDL (r = 0.103) in Figure 4.19, WC (r = 0.365) in Figure 4.20, and BMI (r= 0.203) (Figure 4.21). Our study data found a weak positive correlation between Cr and HOMA-IR (r = 0.012) in Figure 4.22, Fasting Insulin (r = 0.042) in Figure 4.23, SBP (r = 0.063) in Figure 4.24 and DBP (r = 0.003) (Figure 4.25).

Table 4.27 The correlation of selenium and chromium with other studied parameters

Parameters	**r[1]**	**Parameters**	**r**
Cr / Se	0.228	Se / Cr	0.228
Cr / FBG	- 0.071	Se / FBG	- 0.197
Cr / HOMA-IR	0.012	Se / HOMA-IR	0.053
Cr / Fasting Insulin	0.042	Se / Fasting Insulin	0.066
Cr / TG	- 0.287	Se / TG	- 0.212
Cr / HDL	0.103	Se / HDL	0.109
Cr / UA	- 0.169	Se / UA	0.141
Cr / Fib	- 0.010	Se / Fib	- 0.116
Cr / WC	0.365	Se / WC	0.141
Cr / SBP	0.063	Se / SBP	- 0.021
Cr / DBP	0.003	Se / DBP	- 0.078
Cr / BMI	0.203	Se / BMI	0.011
Cr / Age	- 0.095	Se / Age	- 0.138

[1] Pearson correlation coefficient

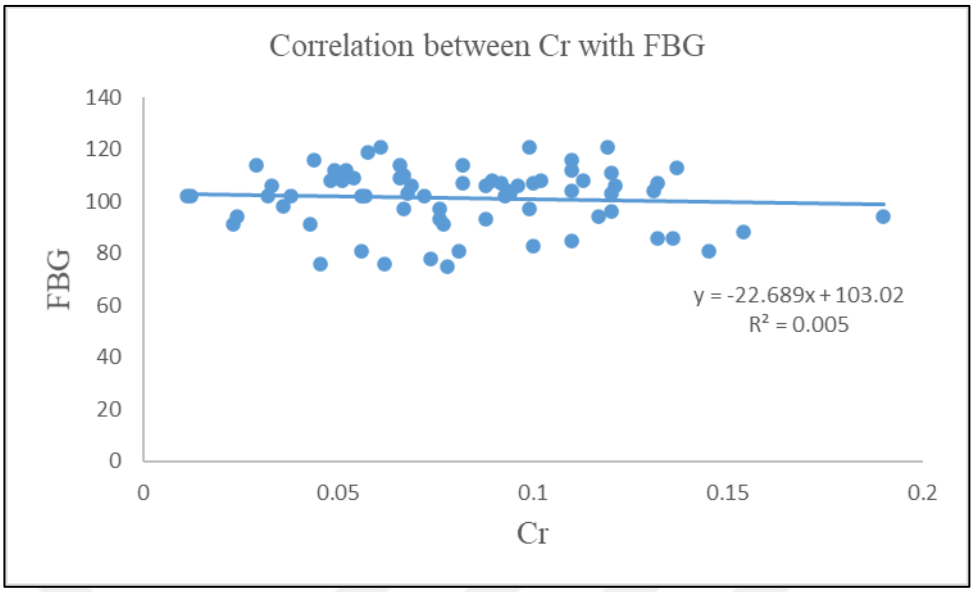

Figure 4.15 Correlation between Cr with FBG

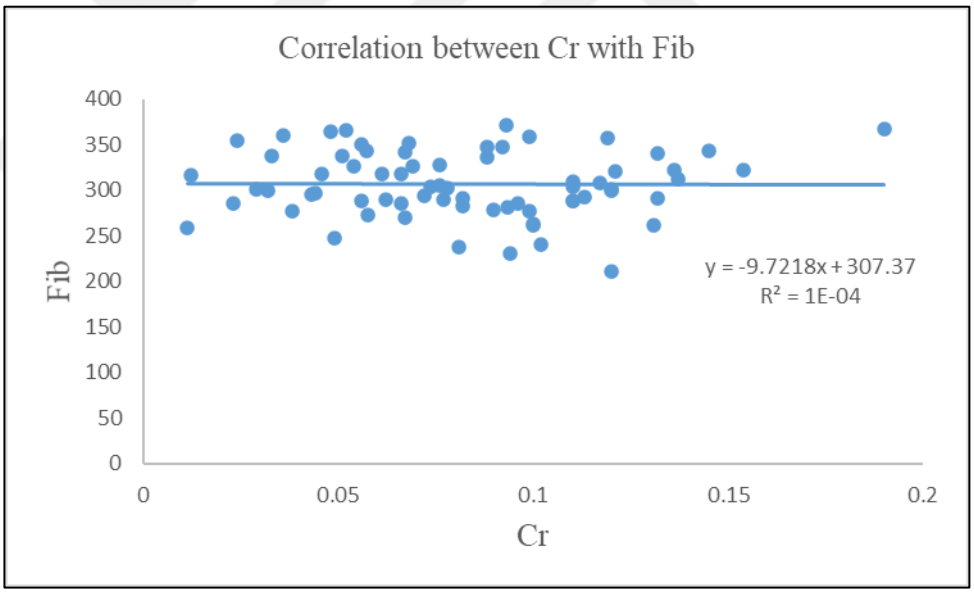

Figure 4.16 Correlation between Cr with Fib

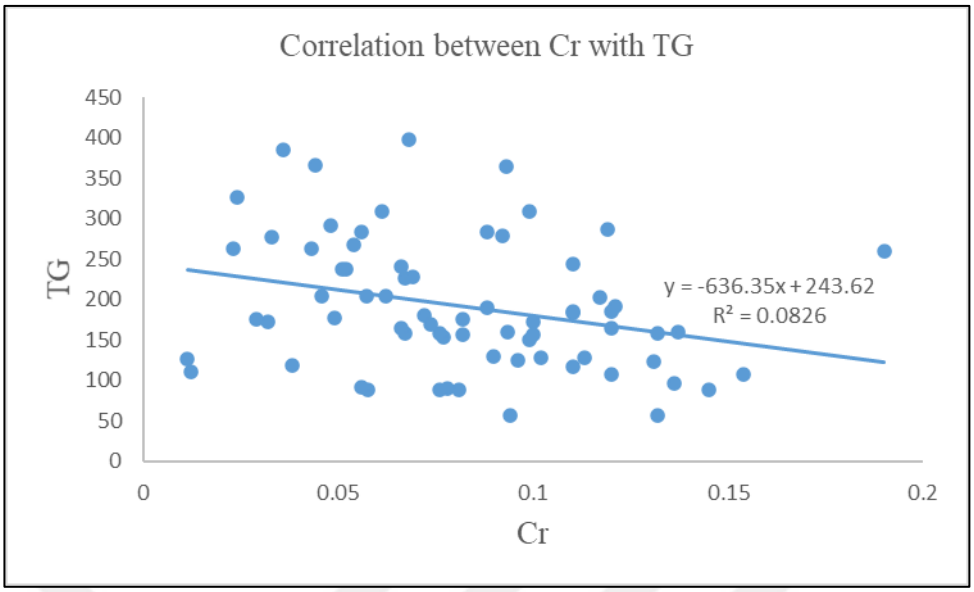

Figure 4.17 Correlation between Cr with TG

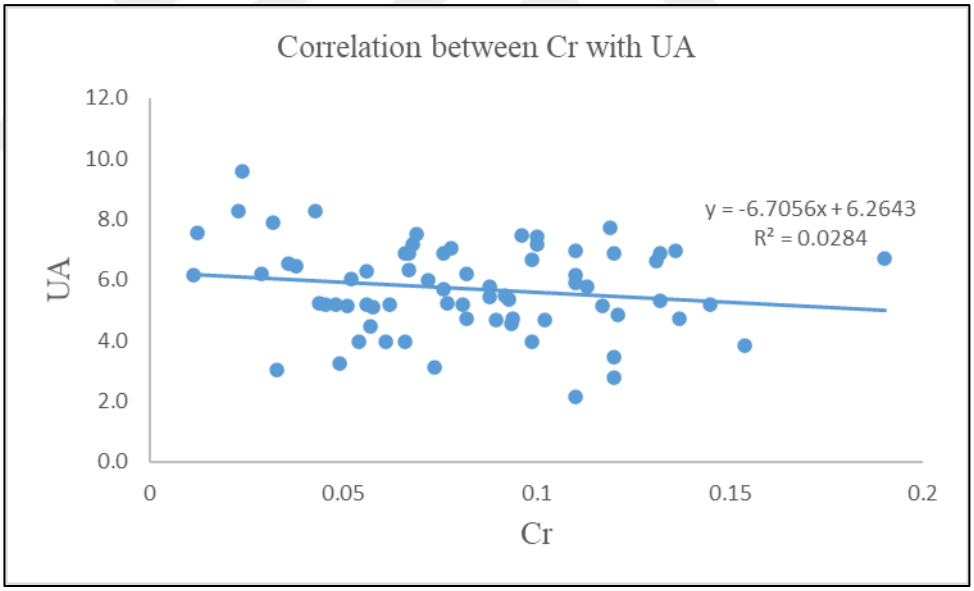

Figure 4.18 Correlation between Cr with UA

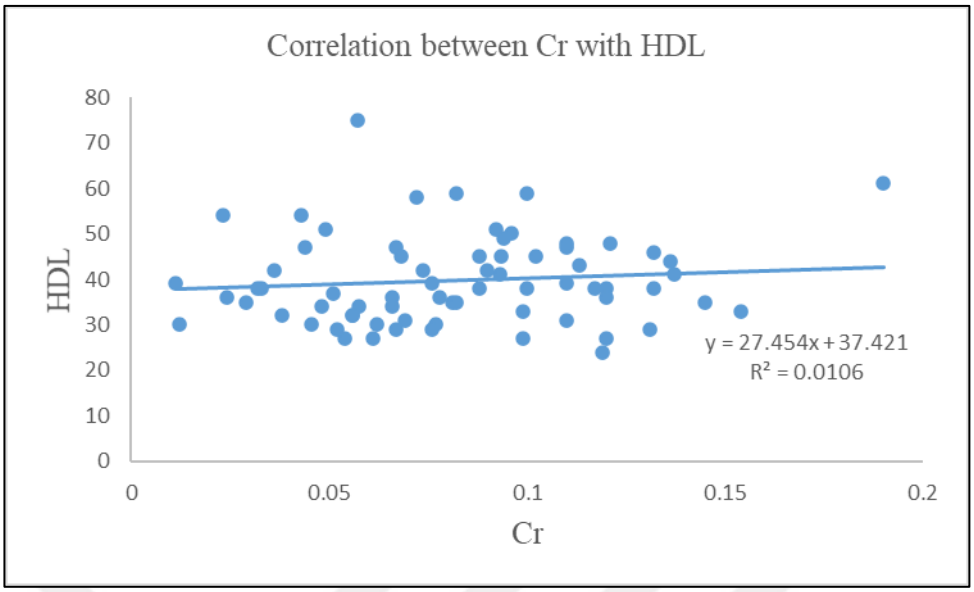

Figure 4.19 Correlation between Cr with HDL

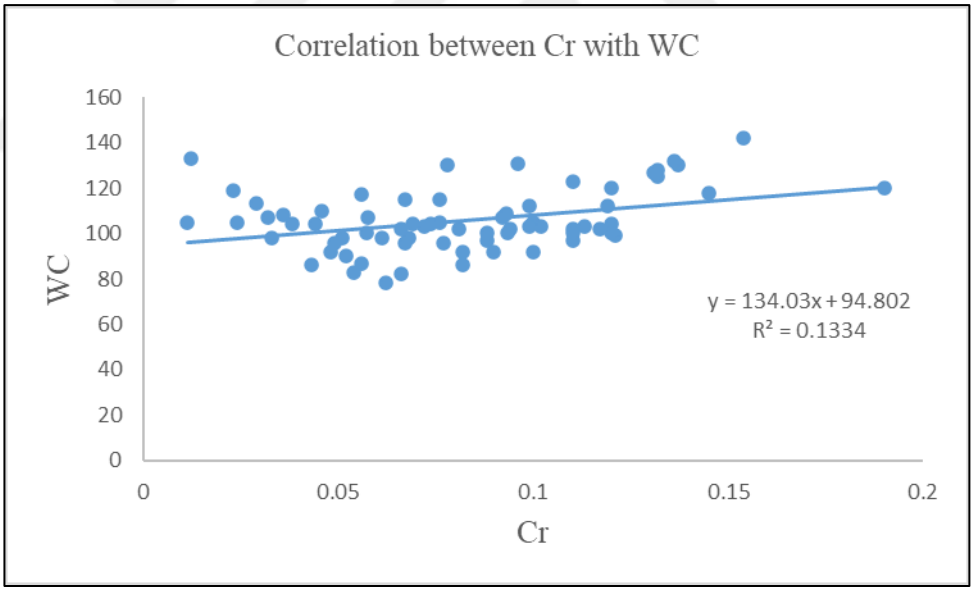

Figure 4.20 Correlation between Cr with WC

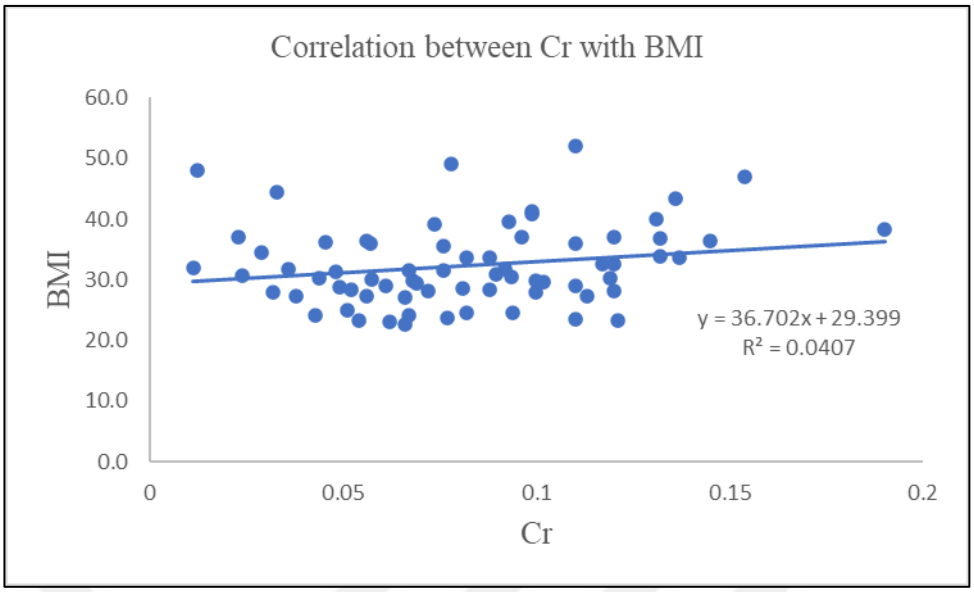

Figure 4.21 Correlation between Cr with BMI

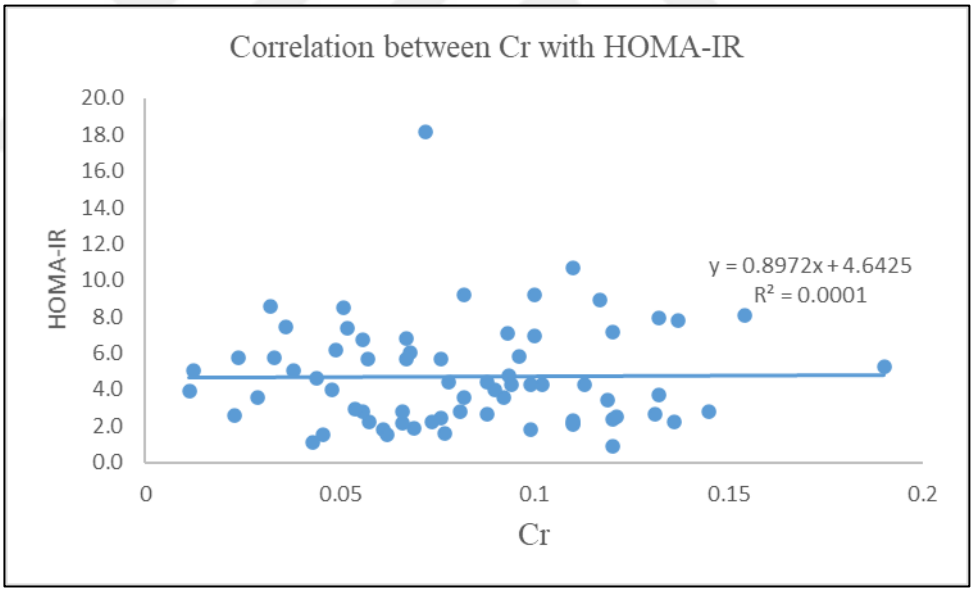

Figure 4.22 Correlation between Cr with HOMA-IR

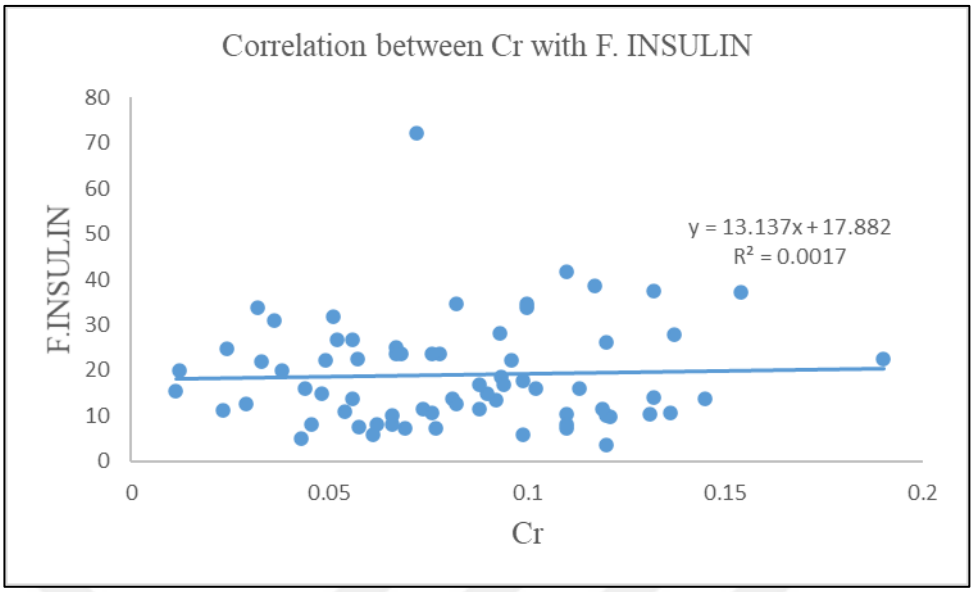

Figure 4.23 Correlation between Cr with F. INSULIN

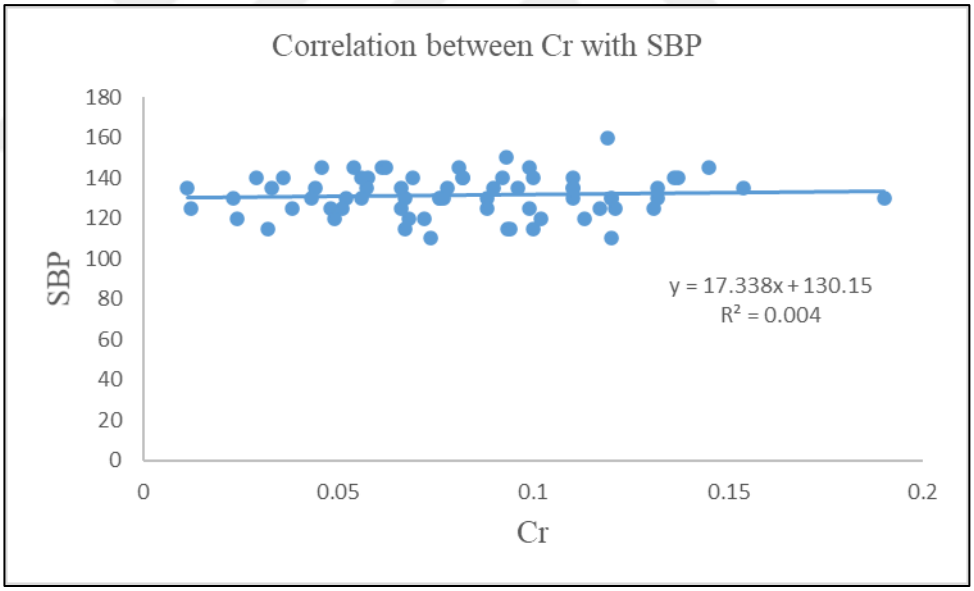

Figure 4.24 Correlation between Cr with SBP

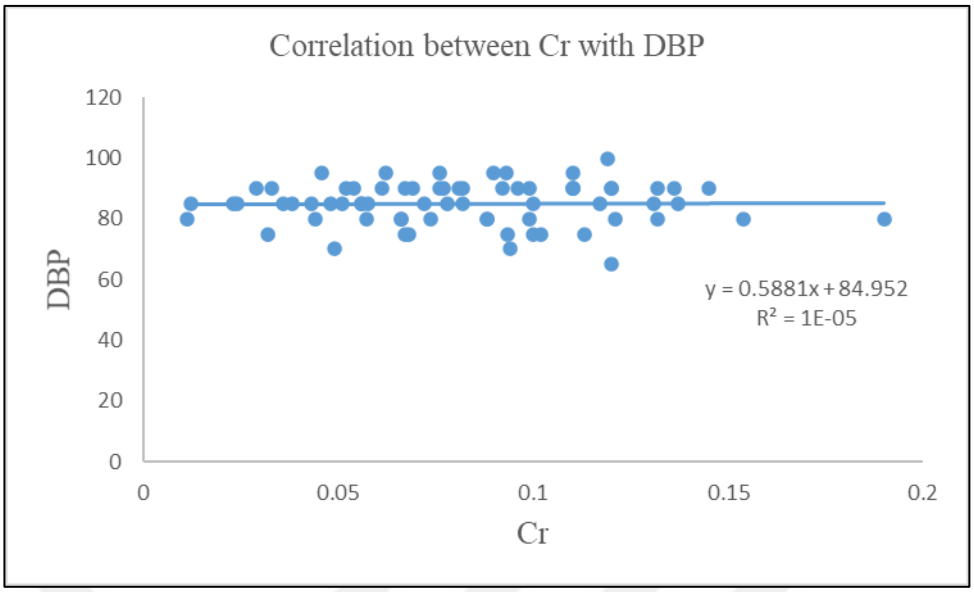

Figure 4.25 Correlation between Cr with DBP

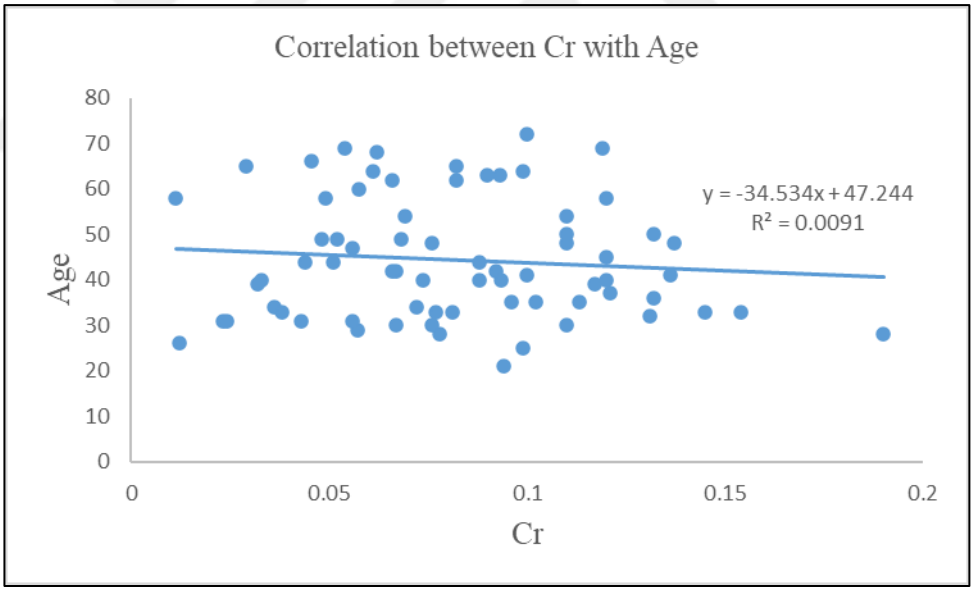

Figure 4.26 Correlation between Cr with Age

4.7 Receiver Operating Characteristic Curve

As in Table 4.28, the ROC curve showed that HDL levels demonstrated an excellent way to distinguish between subjects with MetS and those who did not meet the criteria [AUC = 0.851; P < 0.001; 95% Confidence Interval (CI): 0.789 to 0.914; Standard Error (SE): 0.032] (Figure 4.29). Also, the TG values showed very important levels of discrimination [AUC = 0.850; P < 0.001; 95% CI: 0.783 to 0.916; SE: 0.034] (Figure 4.30). So, it was possible to assert that HDL and TG were definitely useful for diagnosing MetS.

Our study found that HOMA-IR was a better predictor than FBG for diagnosing non-diabetic MetS cases [AUC = 0.830; P < 0.001; 95% CI: 0.763 to 0.897; SE: 0.034] vs [AUC = 0.802; P < 0.001; 95% CI: 0.727 to 0.876; SE: 0.038] respectively (Figure 4.30). Moreover, fasting insulin was considered as a good significant parameter for MetS risk [AUC = 0.775; P < 0.001; 95% CI: 0.698 to 0.853; SE: 0.040] (Figure 4.30).

SBP showed differential efficacy between subjects without MetS and those with MetS, more than DBP [AUC = 0.801; P < 0.001; 95% CI: 0.725 to 0.876; SE: 0.038] vs [AUC = 0.788; P < 0.001; 95% CI: 0.712 to 0.863; SE: 0.039] respectively (Figure 4.27). However, fibrinogen and chromium were reported similar levels of discrimination [AUC = 0.712; P < 0.001; 95% CI: 0.627 to 0.798; SE: 0.044] vs [AUC = 0.710; P < 0.001; 95% CI: 0.625 to 0.795; SE: 0.043] respectively (Figures 4.28, 4.29).

The current study demonstrated the values of WC and Se parameters have been appeared as a fair significant diagnostic tool between individuals without MetS and cases with MetS [AUC = 0.663; P = 0.001; 95% CI: 0.572 to 0.753; SE: 0.046] vs [AUC = 0.634; P = 0.006; 95% CI: 0.543 to 0.725; SE: 0.047] respectively (Figures 4.27, 4.29). While UA demonstrated low validity in predicting of MetS [AUC = 0.594; P = 0.055; 95% CI: 0.500 to 0.688; SE: 0.048] (Figure 4.28).

Table 4.28 Area under the curve for all studied parameters

Area Under the Curve (AUC)					
Parameters	**Area**	**SE[1]**	**Asymptotic Significant**	**Asymptotic 95% Confidence Interval**	
				Lower Bound	**Upper Bound**
HDL	0.851	0.032	< 0.001	0.789	0.914
TG	0.850	0.034	< 0.001	0.783	0.916
HOMA-IR	0.830	0.034	< 0.001	0.763	0.897
FBG	0.802	0.038	< 0.001	0.727	0.876
SBP	0.801	0.038	< 0.001	0.725	0.876
DBP	0.788	0.039	< 0.001	0.712	0.863
F. Insulin	0.775	0.040	< 0.001	0.698	0.853
Fib	0.712	0.044	< 0.001	0.627	0.798
Cr	0.710	0.043	< 0.001	0.625	0.795
WC	0.663	0.046	0.001	0.572	0.753
Se	0.634	0.047	0.006	0.543	0.725
UA	0.594	0.048	0.055	0.500	0.688

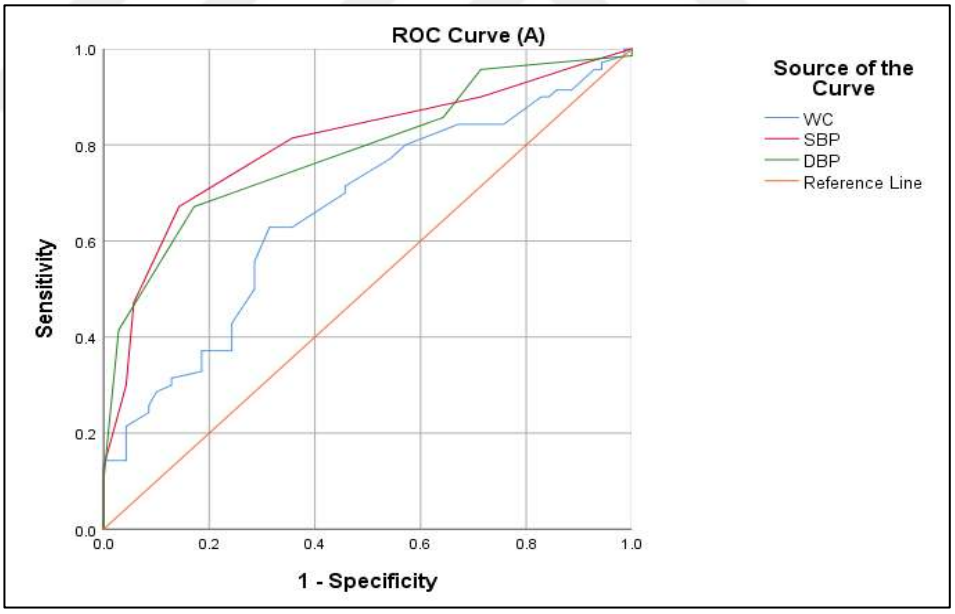

Figure 4.27 Area under the curve of WC, SBP, and DBP

[1] Standard error

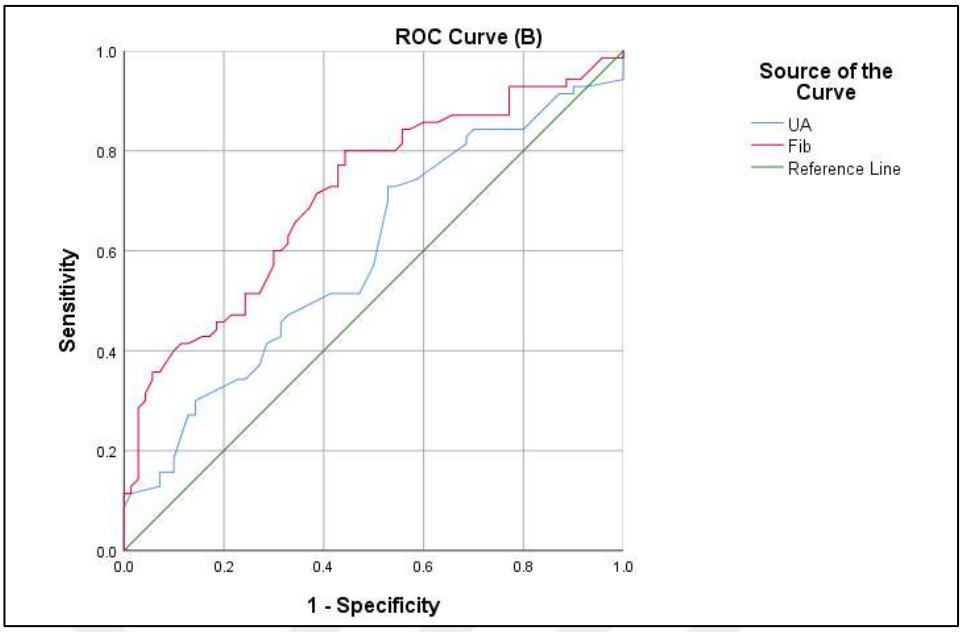

Figure 4.28 Area under the curve of UA and Fib

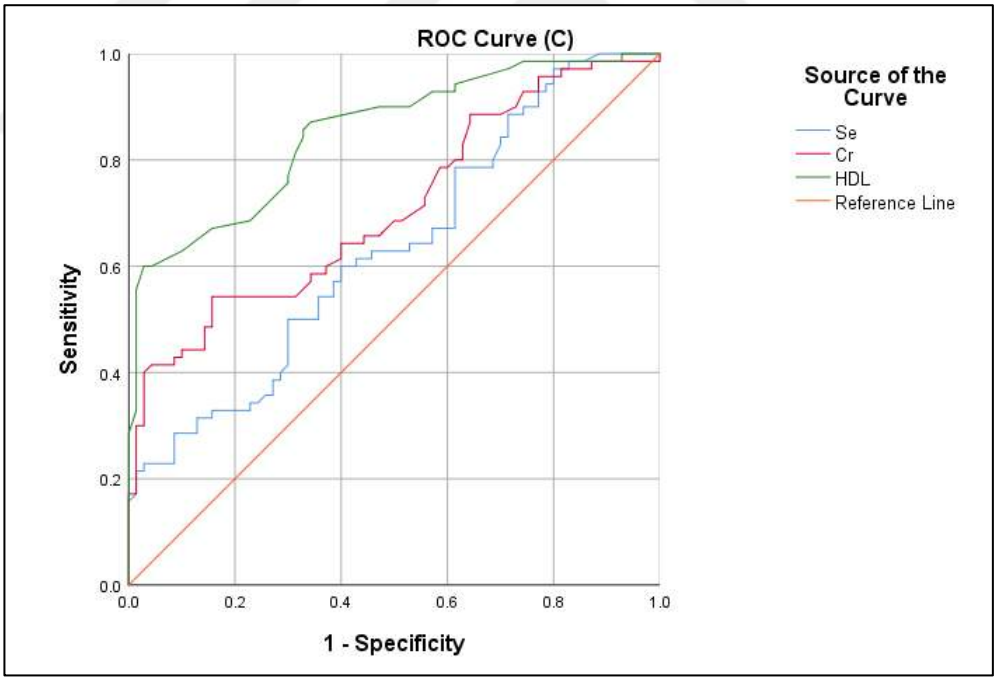

Figure 4.29 Area under the curve of Se, Cr and HDL

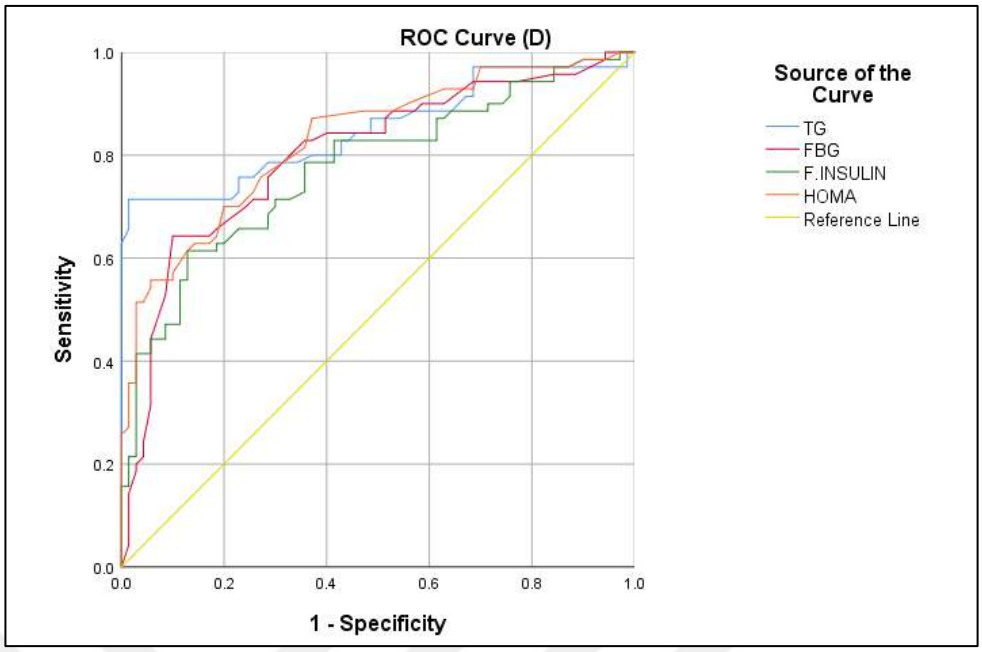

Figure 4.30 Area under the curve of TG, FBG, F. INSULIN, and HOMA-IR

5. DISCUSSION

MetS is a gradual state that includes a broad range of illnesses, each with its own set of metabolic abnormalities that manifest at different times. Plasma and serum biomarkers can be used to detect and monitor these abnormalities (Srikanthan *et al.* 2016). MetS is a heterogeneous, complex condition that has been attached to an increased risk of T2DM, atherosclerosis, and CVD. MetS is diagnosed when at least three of the following characteristics are present: elevated FBG, hypertension, visceral abdominal obesity, elevated triglyceridemia, and low HDL levels (Moebus and Stang 2007).

This study was conducted to find out the role of some trace elements (selenium and chromium) in the MetS along with some vital parameters that are related to the MetS, and then to study the effect of age, gender and BMI on all the variables. Relatively inexpensive and clinically applicable markers were chosen and not only for research purposes. Based on the findings of our research, it appeared that it was necessary to expedite the intervention to maintain the normal glucose balance and prevent the risk of developing T2DM and the occurrence of other complications, both more and less serious.

It was noted that age and weight gain had a clear effect on some parameters, more than that of sex. Therefore, there is an urgent need for more studies to confirm the maintenance of a stable and better lifestyle and healthy food consumption due to its direct intervention with metabolic diseases that have become a major cause of most other associated diseases.

5.1 Fasting Blood Glucose

According to the AHA criteria adopted in this study Table 2.1 the FBG was considered one of the diagnostic criteria for MetS if the concentration was (FBG $\geq$ 100 mg / dL), and although our study excluded people with chronic diabetes, a significant increase in the concentration of FBG was observed compared to the control. This study agreed with (Rajput *et al.* 2019), which showed a significant increase in fasting glucose levels in the MetS compared to the control group. As expected, the results of our study showed that

one of the causes of the development of T2DM in patients with MetS is due to high levels of fasting glucose. Some studies point to this concept (Lee *et al.* 2020).

The data of the current study clearly showed the effect of age on the concentration of FBG in MetS subjects compared to the control group. In all age groups, there was a significant increase in FBG concentration compared to control. In the same table, our study showed an increase in the mean FBG concentration of G3 more than G2 and this was more than G1. This study was consistent with (Suastika *et al.* 2011), which showed that the elderly had the highest levels of FBG compared to the younger-aged.

The findings showed a considerable rise in FBG concentration in MetS participants, both males and females, as compared to controls. The mean of FBG concentration in females was higher than that of males. Hyperglycemia was found to be a substantially greater contributor to the MetS in women (Beigh and Jain 2012).

In comparison to controls, all BMI groups of MetS participants had a significant rise in FBG concentration. Many previous studies had proven that being overweight was one of the risks of developing T2DM (Meigs *et al.* 2006). Our study found that the highest concentration mean of FBG was in overweight individuals. This was similar to the results of a study conducted by (Agrawal *et al.* 2017).

5.2 Homeostasis Model Assessment

MetS is known as insulin resistance syndrome (Roberts *et al.* 2013). In this study, the effect of MetS was clear on non-diabetic participants, as high levels of HOMA-IR were observed compared to control. These results are consistent with the findings of a study conducted by (Belhayara *et al.* 2020). The HOMA-IR model is used to calculate insulin sensitivity and β-cell function using fasting plasma insulin and glucose concentrations.

Our study noted that the mean of HOMA-IR among males was higher than that of females. This study was matched with (Cho *et al.* 2017). Recent research had found that

men and women had different levels of insulin resistance and body composition, and that greater amounts of visceral and hepatic fat, combined with the lack of estrogen's protective effect, may be linked to higher insulin resistance in male than in female (Geer and Shen 2009). Insulin resistance and MetS were found to be highly linked, and the number of MetS components was directly connected to HOMA-IR levels. The risk of MetS increased with the increase in HOMA-IR (Esteghamati *et al.* 2010).

Our data showed a significant increase in all age groups compared to the control, but Age-G2 recorded the highest means of HOMA-IR. Moreover, levels had decreased in the Age-G3 may be because we studied non-diabetic people. These results were matched with (Gayoso *et al.* 2013). In their study, they noticed that HOMA-IR levels increased in women in the fifth decade and decreased with ageing.

Also, these results observed that HOMA-IR levels increased in obese and overweight individuals more than those with normal weight. The results were similar to (Shashaj *et al.* 2016). Because waist circumference was a valid biomarker of visceral obesity, several research (Ferrannini *et al.* 1997) suggested that patients with greater waist circumference in addition to obesity had higher levels of HOMA-IR.

5.3 Fasting Insulin

The pathogenesis of MetS is still a topic of discussion, but hyperinsulinemia is one of the main characteristics of a cluster (Sung *et al.* 2011). Measuring fasting plasma insulin to assess hyperinsulinemia may be a sensible clinical option for assessing insulin resistance (Williams *et al.* 2002). Our study observed a significant increase in fasting insulin concentration in non-diabetic MetS subjects compared to control despite the similarity of BMI between patients and control. Concentration of fasting insulin decreased with increasing age. The results were agreed with a cross-sectional study of a Chinese population that included 35,327 participants (Pang *et al.* 2018). When a deterioration in glucose balance occurs, insulin levels increased gradually, but when the FBG reached a certain level, it becomes difficult for a β cell to maintain the increased level of insulin

(DeFronzo 2004). As a result of the body's reaction to hyperinsulinemia, insulin resistance occured (Huang 2009)

In the present study, insulin mean showed an increase in males compared to females and this similar to study reported by (Gayoso *et al.* 2013). Gender played a role in the pathophysiology of a variety of diseases, including metabolic diseases like diabetes. Men were more likely than women to get diabetes, especially in middle-aged populations. In line with this, In response to nutritional problems, males were more likely than females to acquire obesity, insulin resistance, and hyperglycemia (Tramunt *et al.* 2020).

When compared to controls, the fasting insulin levels of normal, overweight, and obese non-diabetic MetS participants increased significantly. This increase was greatest in the mean of overweight and obese more than the normal weight group. This clearly indicated the effect of BMI on the parameters of MetS. These results were similar to those reported by (Ärnlöv *et al.* 2011) in their study. They found 160 people developed T2DM over the course of the 20-year study, and those who were overweight or obese, as well as those who had MetS, had a greater risk of diabetes than those who were normal weight and did not have the syndrome. A higher BMI had consistently been linked to a higher risk of T2DM (Nyamdorj *et al.* 2008).

5.4 Dyslipidemia

The abnormalities of lipid and lipoprotein metabolism were linked to the development of CVD and T2DM (Iqbal *et al.* 2017). In people with insulin resistance, abnormalities in lipoprotein metabolism played a big role in their higher cardiovascular risk (Ginsberg *et al.* 2006). Our study showed a significant increase in TG concentration for non-diabetic subjects with MetS compared to control, and this significant increase was present in all age and BMI groups for males and females. While it showed a significant decrease in HDL concentration. The presented results showed that the mean of TG concentration continue to increase and HDL concentration mean decreased with age. These results were matched with a study of (Cho *et al.* 2020). An increased in TG and a reduction in HDL

were characterized dyslipidemia (Christian and Su 2014), leads to the increase of probably atherogenic lipid and lipoproteins (Su *et al.* 2014, Soran *et al.* 2016).

Insulin resistance appeared to be the most likely relationship between obesity and obesity-related metabolic dyslipidemia (Klop *et al.* 2013, Vekic *et al.* 2019). Our study reported elevated levels of triglycerides in MetS cases in all BMI groups. These levels were higher for males than for females. The results were agreed with the comparative study that included 500 participants with 294 males and 206 females (Beigh and Jain 2012), in which a higher level of triglycerides was observed in males than in females. Low levels of high-density lipoproteins were also lower in men than in women in our data, which was consistent with (Yang *et al.* 2019).

5.5 Uric Acid

For a long time, uric acid was regarded to be a byproduct of obesity and hypertension, rather than a significant cardiovascular risk factor, because uric acid was not considered to increase CVD by causing HTN, insulin resistance, or kidney disease (Kanbay *et al.* 2016). Our results showed a significant increase in uric acid levels in MetS cases compared to control. These results matched with (Wang *et al.* 2018). The mean of UA concentrations was higher in males than in females, but no significant differences were observed between the two groups. The results agreed with (Foster *et al.* 2020). However, whether high uric acid levels were a risk factor or merely a biomarker in the progression and development of MetS was still debated (Soltani *et al.* 2013). In both animal and human models, hyperuricemia had been demonstrated to cause endothelial dysfunction (Khosla *et al.* 2005). The synthesis and bioavailability of NO had been found to be inhibited by uric acid, which was required for the action of insulin (Wu and Meininger 2009). Recent research suggested that nucleic acid metabolism played a role, with stimulation of adenosine monophosphate (AMP) deaminase promoting fat accumulation and insulin resistance and activation of AMP activated protein kinase promoting fat breakdown and decreasing gluconeogenesis (Lanaspa *et al.* 2012, Lanaspa *et al.* 2015). Uric acid, a product of the AMP deaminase enzyme, appeare to play a role in fat accumulation (Choi *et al.* 2014, Cicerchi *et al.* 2014).

Our study found higher levels of uric acid in younger adult in their twenties, thirties and forties than in older age groups. These findings were matched with (Jeong and Suh 2019). In younger adults, uric acid levels may be a major risk factor for MetS.

5.6 Fibrinogen

Plasma fibrinogen is a marker for both cardiovascular and nonvascular death (Padron *et al.* 2021). Increased fibrinogen levels may lead to a prothrombotic condition. Cross-sectional studies imply a relationship between fibrinogen and MetS or its components, while cohort study results remain controversial (Ding *et al.* 2015). In our results, an increase in fibrinogen levels was observed in people with MetS compared to control. These results were in agreement with the study of (Basoglu *et al.* 2011). Also, consistent with the report of (Khunger *et al.* 2020). Our data did not reveal significant differences in the concentration of fibrinogen when dividing the participants into age groups or when increasing body mass, and no difference was observed between males and females despite the high levels of fibrinogen in all groups when compared to the control group. A prothrombotic condition as a result of endothelial dysfunction and hypercoagulability caused by a dysbalance of coagulation factors and proteins involved in fibrinolysis control is a significant pathological change evident in the MetS (Palomo *et al.* 2010).

5.7 Selenium

Se is an important mineral that is required for overall well health (Duntas and Benvenga 2015). Its effects on the human body had been researched, particularly in relation to thyroid function, hypertension, cancer, T2DM, obesity, the reproductive system, inflammation, and cardiovascular disease. However, the relationship between selenium and MetS had not yet been clearly studied (Retondario *et al.* 2019). There was disagreement about the findings of investigations on the relationship between MetS and Se. Some previous studies found a positive relationship between an increase in Se concentration and the risk of MetS, and some did not notice a relationship between them, while others recorded a negative relationship (Tajaddini *et al.* 2015). The results of association between Se with MetS or its components varied, positively or negatively,

depending on the nutritional status of selenium in different countries (Mutakin *et al.* 2013). The amount of selenium in the body could be affected by both environmental and internal influences (Park *et al.* 2011).

Our study found a significant decrease in Se concentration in non-diabetic MetS cases compared to the control. In a study evaluating the possible associations between serum asymmetric dimethylarginine ADMA and several other parameters, including selenium, a negative relationship was found between Se and ADMA, which was a manifestation of MetS (Puchau *et al.* 2009). This study confirmed the role of trace element intake in ADMA modulation. In a cross-sectional study from South India that aimed to study the relationship between selenium and insulin resistance indicators in pre-diabetes patients, a decrease in selenium concentration was observed compared to healthy controls (Yadav *et al.* 2017). According to Karita *et al.*, the amount of Se in erythrocytes may be an indicator of lower total cholesterol and LDL-C following menopause in Japanese women (Karita *et al.* 2008). Moreover, Kalkan *et al.* found dyslipidemic patients with glycogen storage disorder type I and type III who did not develop early atherosclerosis had lower plasma Se concentrations than healthy controls (Kalkan *et al.* 2010). One of the leading causes of CVD was MetS (Weiss *et al.* 2004). Se had been shown to protect against CVD (Rayman 2000). Low serum Se levels had been linked to an increased risk of CVD in various studies (Ghayour *et al.* 2008).

Our results did not record significant differences in Se concentration between the age groups, and were similar for males and females. This was similar to findings of (Yang *et al.* 2010). When determining the effect of BMI, a lower level of selenium was observed in overweight and obese people than in normal weight. These findings accordance to (Mutakin *et al.* 2013).

In the current study the correlation between selenium with other parameters was found a positive with Cr, HDL, UA, and WC. While it showed a negative association with FBG, TG, Fib, and Age. No important correlation demonstrated with HOMA-IR, Fasting Insulin, SBP, DBP, and BMI. The current findings were consistent with those of the

previous reports (Mutakin *et al.* 2013, Kim and Song 2014, Chen *et al.* 2015, Yadav *et al.* 2017)

5.8 Chromium

Chromium is thought to have a crucial role in glucose and lipid metabolism in the human body (González *et al.* 2016). Increased consumption of simple sugars leads to more chromium loss (Yang *et al.* 2016). Cr binds to chromodulin in the tissue, which aids insulin activity (Chen *et al.* 2011). Humans with higher blood glucose, triglycerides, insulin, and cholesterol, as well as decreased high density lipoproteins, was shown signs of chromium insufficiency (Hummel *et al.* 2007).

Our study found a significant decrease in chromium concentration in non-diabetic MetS cases when compared with the control group. These results were similar to the results of (Chen *et al.* 2020). Bai *et al.* conducted a study on American adults to study the relationship between Cr and the incidence of MetS, and found an inverse association between low Cr concentration and the incidence of the syndrome (Bai *et al.* 2015). Nutrition rich in chromium enhances blood lipid profiles and insulin activity (Chen and Ma 2015).

Our results observed in our data that age-G3 have lower levels of chromium than other age groups. Some studies indicated a decrease in Cr concentration with age (Cynober *et al.* 2000). This may be due to poor absorption of dietary chromium. Our study recorded a decrease in chromium levels in males than in females. This may be attributed to the prevalence of obesity and triglycerides in males in our study more than in females. The inverse relationship between low chromium and obesity had been reported (Onakpoya *et al.* 2013).

In our data, Cr showed a positive correlation with Se, HDL, WC, and BMI. No clear correlation observed between Cr with HOMA-IR, F. Insulin, Fib, SBP, and DBP. While

negative correlation with FBG, TG, UA, and Age. This results agree with (Chen *et al.* 2017, Ngala *et al.* 2018, Farrokhian *et al.* 2020).

5.9 Waist Circumference

The primary condition that leaded to MetS is abdominal obesity. Our data was expected to notice an increase in waist circumference in cases of MetS compared to the control group. The results agreed with (Masquio *et al.* 2015). The present study showed higher means of waist circumference in males than females, and this was consistent with many previous studies (Gierach *et al.* 2014). In Age-G1, our results observed higher levels of the other age groups compared to the control group. This may be attributed to the poor lifestyle and lack of physical activity for this age group. In addition, an increase in mean waist circumference was observed for cases of MetS compared to control when grouping participants by BMI. The obesity group was the highest.

5.10 Systolic and Diastolic Blood Pressure

Metabolic abnormalities and MetS were closely correlated with hypertension (Litwin and Kułaga 2021). Our results noted an increase in systolic and diastolic blood pressure rates in cases with MetS when compared with the control group. The results accordance with (Jung *et al.* 2019). Through our current results, an increase in SBP and DBP means was observed in all age groups of subjects with MetS compared to the control, and the increase appears in the highest levels in Age-G3. Our results are in agreement with the findings of (Safar *et al.* 2011). The levels of SBP and DBP were higher in the obese group than in the other groups. The mechanisms of obesity and blood pressure were not fully understood. Physical stress on the kidneys and activation of the sympathetic nervous system and renin-angiotensin-aldosterone are thought to increase sodium reabsorption and ultimately raise blood pressure (Hall *et al.* 2018). High blood pressure was significant in both sexes. Females recorded slightly higher levels of systolic and diastolic blood pressure than males. These results were associated with (Regitz *et al.* 2007), where they found Hypertension is a significant risk factor for both men and women, however the prevalence of hypertension rises faster in women as they age than in males.

6. CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

1. The present study showed that the concentrations of Se and Cr were inversely associated with the occurrence of MetS. The results showed the important significance of these biomarkers in Mets.

2. Se and Cr showed a negative correlation with FBG, TG, while they showed a positive correlation with HDL.

3. Both Se and Cr were part of the pathogenesis of MetS. They may be in future used as predictor of the occurrence of the syndrome or have a therapeutic benefit as a supplement.

4. The study showed a clear effect of age, BMI and sex on MetS or some of its components. Cr concentrations showed an effect on age, sex and BMI, while Se concentrations had no effect on age and Sex. However, BMI was influential in Se concentration.

5. Waist circumference was useful in identifying MetS people. HDL, among other parameters, is the most useful discriminant in MetS.

6. The high levels of fibrinogen in this study compared to the control, as well as the high concentration of fasting insulin and HOMA-IR levels of non-diabetic MetS subjects, in addition to low levels of Cr and Se predicts possible complications of CVD and T2DM.

7. Uric acid played a role in the abnormalities of some components of MetS.

6.2 Recommendations

1. Expanding the sample size in a future study that includes different regions of most governorates. And an attempt to conduct an extensive review to study the MetS percentage throughout the country.
2. Study the role of other trace elements in MetS.
3. Studying the therapeutic effect of Se and Cr on improving health status, weight loss, blood sugar balance, lowering insulin resistance and blood pressure for MetS subjects.
4. Follow up the same study in childhood to avoid early complications in children.

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CURRICULUM VITAE

Personal Information

Name and Surname : Azhar Kadhim Abbood ALHAMEED

Education

MSc	Çankırı Karatekin University Graduate School of Natural and Applied Sciences Department of Chemistry	2019-Present
Undergraduate	Almuthanna University Faculty of sciences Department of Chemistry	2007-2011