Chapter One

1.1 Introduction

Metabolic syndrome defined according to the criteria proposed by " China Diabetes Society " (CDS) and unified , were three or more of the following risk factors : overweight or obesity , BMI ≥ 25.0 kg/m² , abdominal obesity was defined as elevated WC ≥ 85 cm in male , ≥ 80 cm in female , hypertension , systolic blood presser (SBP) ≥ 140 mmHg , or diastolic blood presser (DBP) ≥ 90 mmHg , or previous diagnosis of hypertension , dyslipidemia , TG ≥ 1.7 mmol/l (150 mg/ dl) or low HDL-C ≤ 0.9 mmol/l in men , ≤ 1.0 mmol/l (40 mg/ dl) in women. and hyperglycemia, FBG ≥ 6.1 mmol/l (110 mg/ dl) or 2HPP, PG ≥ 7.8 mmol/l (140 mg/dl). or previous diagnosis with hyperglycemia. (Alberti *et al*., 2006; Shuang *et al*., Krithika *et al*., 2016; Shumei *et al*., 2017).

Alkaline Phosphatase (ALP) an enzyme belongs to a group of enzymes that catalyze the hydrolysis of various phosphomonoesters at an alkaline pH, which present on cell surface in most human tissue. The highest concentrations are found in the intestine, liver, spleen, placenta and kidney, the specific location of enzyme within those tissues account for the more predominant elevations in certain disorders. (Bishop *et al*., 2008; Shauna *et al*., 2015).

γ- Glutamyltranspeptidase (GGT) is an enzyme involved in the transfer of the γ-glutamyl peptide to amino acids, H2O, and other small peptide, is found primarily in tissues of kidney, brain, prostate, pancreas and liver. Clinical applications of assay however are confined mainly to elevation of liver and biliary system disorders. (Bishop *et al*., 2008; Shauna *et al*., 2015).

1.2. Rationale:

Metabolic syndrome is a serious medical condition increase incidence of multiple cancers, social community stigma, secological increase incidence of chronic depression, and economic effect of the life quality this problem found all over the world and Sudan, its fatal unless controlled and treated properly .

Serum ALP and GGT are early biomarkers for metabolic syndrome risk for liver cancer.

Mets prevalence is about 20-25 % of the world's adult population with increased prevalence in advanced ages. (Carr *et al*., 2004; Alberti *et al*., 2006). Therefore, the present studies hypothized that individuals with MetS have 2–20-year odds for future CVD and diabetes.

Objectives:

1.3.1. General Objectives:

To assess the serum ALP and GGT levels among metabolic syndrome patients.

1.3.2. Specific objectives:

1. To measure and compare the mean concentration of ALP and GGT levels.
2. To calculate the BMI in study Groups.
3. To correlate between ALP, GGT and study group variables (BMI, duration, gender and age).

Chapter Two

2. Literature Review

2.1. Metabolic syndrome:

The term metabolic syndrome dates back to at least the late 1950s, but came into common usage in the late 1970s. The terms metabolic syndrome, insulin resistance syndrome, syndrome X, dysmetabolic syndrome X, mixed metabolic syndrome. (George *et al*., 2005)

The metabolic syndrome (visceral obesity, dyslipidemia, hyperglycemia, and hypertension), has become one of the major public-health challenges worldwide, the clustering received scant attention until 1988 when Reaven described syndrome X: insulin resistance hyperglycemia, hypertension, low HDL-cholesterol, and raised VLDL-triglycerides. (George *et al*., 2005)

2.1.1. Sign and symptoms:

Metabolic syndrome has no symptoms, although a large waist circumference (central obesity) is a visible sign.

Blood sugar is very high, might have sign and symptoms of diabetes (including increased thirst and urination, fatigue, and blurred vision).

Impaired fasting glucose, insulin resistance, or prediabetes.

High blood pressure.

Decreased fasting serum HDL cholesterol.

Elevated fasting serum triglyceride level (Knowler *et al*., 2002)

2.1.2. Diagnosis:

Several organizations have criteria for diagnosing metabolic syndrome .according to guidelines used by the National Institute of Health, have metabolic syndrome if have three or more of these traits or are taking medication to control them:

2.1.2.1 Large waist circumference:

a waistline that measure at least 35 inches (89 centimeters) for women and 40 inches (102 centimeters) for men .

2.1.2.2 High triglyceride level:

150 mg/dl or 1.7 mmol/l or higher of this type of fat found in blood. (Knowler *et al*., 2002; Chiasson *et al*., 2003; Carr *et al*., 2004; Krithika *et al*., 2016).

2.1.2.3 Reduced high- density lipoprotein (HDL) cholesterol:

Less than 40 mg/dl (1.04 mmol/l) in men or less than 50 mg/dl (1.3 mmol/l) in women of this good cholesterol.

2.1.2.4 Increased blood pressure:

130/85 mmHg or higher.

2.1.2.5 Elevated fasting blood sugar :

100 mg/dl (5.6 mmol/l) or higher. (Knowler *et al*., 2002; Chiasson *et al*., 2003; Carr *et al*., 2004; Krithika *et al*., 2016)

2.1.3. Prevention and Treatment:

Various strategies have been proposed to prevent the development of metabolic syndrome.

A healthy lifestyle as:

2.1.3.1 Eat better : Adopt a diet rich in whole grains , fruits, vegetables, lean meats and fish and low fat or fat-free dairy products and avoid processed, which often contain partially hydrogenated vegetable oils, and is high in salt and added sugar .

2.1.3.2 Get active: Incorporate at least 150 minutes of moderately vigorous physical activity into weekly routine. Walking is easiest place to start, but may want to experiment to find something else like to do that gets heart rate up. If needed, break exercise up into several short, 10 minutes sessions throughout the day to reach goal. (Knowler *et al*., 2002; Chiasson *et al*., 2003; Carr *et al.*, 2004)

2.1.3.3 Lose weight: Reduce risk by successfully losing weight and keeping it off. Learn recommended calories intake, the amount of food calories consuming and the energy calories burning off with different level of physical activity. Balance healthy level of exercise when change in lifestyle alone do not control the conditions related to metabolic syndrome, health practitioner may prescribe medications to control blood pressure, cholesterol, and other symptoms. Carefully following practitioner's instructions can help prevent many of the long term effects of metabolic syndrome. Every step counts and hard work and attention to these areas will make a difference in health. (Knowler *et al*., 2002; Chiasson *et al*., 2003; Carr *et al*., 2004)

2.1.3.4 Stopping smoking: smoking cigarettes worsens the health consequences of metabolic syndrome. Talk to doctor if you need help quitting.

2.1.3.5 Managing stress: physical activity, medication, yoga and other programs can help handle stress and improve emotional and physical health. (Knowler *et al*., 2002; Chiasson *et al*., 2003; Carr *et al*., 2004)

2.1.4. Causes:

2.1.4.1 Stress: recent research indicates prolonged chronic stress can contribute to the hypothalamic-pituitary-adrenal axis (HPA-axis). High cortisol levels to circulate, which results in raising glucose and insulin levels dyslipidemia and hypertension

2.1.4.2 Central obesity: central obesity is a key feature of the syndrome, being both a symptom and a cause of it in that the increasing adiposity often reflected in high waist circumference both often results from and often contributes to insulin resistance. However, despite the importance of obesity, patients who are of normal weight may also be insulin- resistant and have the syndrome.

2.1.4.3 Sedentary lifestyle: many component of metabolic syndrome are associated with a sedentary lifestyle, including increased adipose tissue (predominantly central); reduced HDL cholesterol; and a trend toward increased triglycerides, blood pressure, and glucose in genetically susceptible. (Knowler *et al*., 2002; Chiasson *et al*., 2003; Carr *et al*., 2004)

2.1.4.4 Aging: metabolic syndrome affects 60% of the US population older than age 50. With respect to that demographic, the percentage of women having the syndrome is higher than that of men. The age dependency of the syndrome's prevalence is seen in most populations around the world. (Knowler *et al*., 2002; Chiasson *et al*., 2003; Carr *et al*., 2004)

2.1.4.5 Psychiatric illnesses

2.1.4.6 Alcohol abuse (Knowler *et al*., 2002; Chiasson *et al*., 2003; Carr *et al*., 2004).

2.1.5. Risk factors:

Risk increase when more components of metabolic syndrome are present.

The following factors increase chances of having metabolic syndrome:

2.1.5.1 Age: risk of metabolic syndrome increases with age.

2.1.5.2 Race: in the United States, Mexican-Americans appear to be at the greatest risk of developing metabolic syndrome.

2.1.5.3 Obesity: carrying too much weight, especially in abdomen, increases risk of metabolic syndrome.

2.1.5.4 Diabetes: more likely to metabolic syndrome if had diabetes during pregnancy (gestational diabetes) or if have a family history of type 2 diabetes.

2.1.5.5 Other diseases: risk of metabolic syndrome is higher if ever had non-alcoholic fatty liver disease, cardiovascular disease, polycystic ovary syndrome. (Knowler *et al*., 2002; Krithika *et al*., 2016)

2.1.6. Management: Food and Drug Administration:

The first line treatment is changing of lifestyle a healthy lifestyle, drug treatment is frequently required.

Diuretics and ACE inhibitors may be used to treat hypertension.

Cholesterol drugs may be used to lower LDL cholesterol and triglycerides levels, if they are elevated, and to raised HDL levels if they are low. Use of drugs that decrease insulin resistance, e.g., metformin and thiazolidinedione. (Knowler *et al*., 2002; Krithika *et al*., 2016).

2.2. Liver:

Liver is largest internal organ, site on the right hand side of the belly and is one of the vital organs of the body. Responsible of hundreds chemical actions that body needs to survive, also it is a gland because it secretes chemicals that are used by other part of the body, for these reasons the liver is both an organ and a gland. Has two sections right and left lobes. And it is an organ only found in vertebrates. (Bishop *et al*., 2008; William *et al*., 2008; Shauna *et al*., 2015; Shuang *et al*., 2016).

Has many functions such as: manufacturing triglycerides, cholesterol and proteins. Many different disease processes can occur in the liver such as cirrhosis, cancer.

Symptoms of liver disease include: jaundice, abdominal pain, swelling, confusion, bleeding, edema, fatigue and weight loss. (Bishop *et al*., 2008; William *et al*., 2008; Shauna *et al*., 2015; Shuang *et al*., 2016).

2.2.1. γ-glutamyltranspeptidase (GGT):

γ -glutamyltranspeptidase GGT catalyzes the transfer of the γ -glutamyl group from peptides and compounds that contain it to an acceptor. Substrates for GGT include; the γ -glutamyl acceptor, some amino acid or peptide, or even water, in which case simple hydrolysis takes place. The enzyme acts only on peptides or peptide like compounds containing a terminal glutamate residue joined to the remainder of the compound through the terminal. (Ray *et al*., 2008; Setor *et al*., 2014).

2.2.1.1 Biochemistry of GGT: is present in proximal renal tubule, liver, pancreas, and intestine. The enzyme is present in cytoplasm (microsomes), but the larger fraction is located in the cell membrane and may transport amino

acids and peptides into the cell across the cell membrane in the form of γ - glutamyl-peptides. (Ray *et al*., 2008; Setor *et al*., 2014).

2.2.1.2Clinical Significance:

Even though renal tissue has the highest concentration of GGT, the enzyme present in serum originates primarily from the hepatobiliary system. It is a sensitive indicator of the presence of hepatobiliary disease, being elevated in most subjects with liver disease regardless of cause. Its clinical utility, however, is limited by the lack of specificity. Like ALP, it is highest in cases of intrahepatic or post hepatic biliary obstruction, reaching activities some 5 to 30 times the upper reference limit. High elevations of GGT are also observed in patients with either primary or metastatic liver neoplasms. In these conditions, changes may occur earlier and are more pronounced than those with the other liver enzymes. Moderate elevations (two to five times the upper reference limit) occur in infectious hepatitis. Small increases of GGT activity are observed in patients with fatty livers, and similar but transient increases are noted in cases of drug intoxication. In acute and chronic pancreatitis and in some pancreatic malignancies (especially if associated with hepatobiliary obstruction), enzyme activity may be 5 to 15 times the upper reference limit. (Ray *et al*., 2008; Setor *et al*., 2014).

Elevated activities of GGT are found in the sera of patients with alcoholic hepatitis and in the majority of sera from people who are heavy drinkers. Increased concentrations of the enzyme are also found in serum of subjects receiving anticonvulsiant drugs, such as phenytoin and phenobarbital. Such an increase of GGT activity in serum may reflect induction of new enzyme activity by the action of the alcohol and drugs and or their toxic effects on

microsomal structures in liver cells. (Bishop *et al*., 2008; William *et al*., 2008; Shauna *et al*., 2015; Shuang *et al*., 2016).

2.2.2. Alkaline Phosphatase (ALP):

ALP is nonspecific enzyme capable of reacting with many different substrates. Specifically the ALP functions to liberate inorganic phosphate from an organic phosphate ester with concomitant production of an alcohol at alkaline pH 9.0 to 10.0. (Ray *et al*., 2008; Setor *et al*., 2014).

2.2.2.1 Biochemistry of ALP:

ALP activity is present in most organs of the body and is especially associated with membranes and cell surfaces located in the mucosa of the small intestine and proximal convoluted tubules of the kidney, in bone (osteoblasts), liver, and placenta. Although the exact metabolic function of the enzyme is not understood, it appears that ALP is associated with lipid transport in the intestine and with the calcification process in bone. (Bishop *et al*., 2008; William *et al*., 2008; Shauna *et al*., 2015; Shuang *et al*., 2016).

2.2.2.2 Clinical Significance:

Elevations in serum ALP activity commonly originate from the liver and bone. Consequently, serum ALP measurements are of particular interest in the investigation of hepatobiliary disease and bone disease associated with increased osteoblastic activity.

Hepatobiliary Disease The response of the liver to any form of biliary tract obstruction induces the synthesis of ALP by hepatocytes. Some of the newly formed enzyme enters the circulation to increase the enzyme activity in serum. The elevation tends to be more notable (greater than threefold) in extra hepatic

obstruction than in intrahepatic obstruction and is greater the more complete the obstruction. Serum enzyme activities may reach 10 to 12 times the upper reference limit and usually return to normal on surgical removal of the obstruction. A similar increase is seen in patients with advanced primary liver cancer or widespread secondary hepatic metastases. Liver diseases that principally affect parenchymal cells, such as infectious hepatitis, typically show only moderately (less than threefold) increased or even normal serum ALP activities. Increases may also be seen as a consequence of a reaction to drug therapy. (Ray *et al*., 2008; Setor *et al*., 2014).

Elevated ALP levels may be observed in various bone disorders. Perhaps the highest elevations of ALP activity occur in Paget's disease, other bone disorders include; osteomalacia, rickets, hyperparathyroidism and osteogenic sarcoma. In addition, increased levels are observed in healing bone fractures and during periods of physiologic bone growth. In normal pregnancy also ALP activity increased 2 to 3 times upper the reference limits. (Bishop *et al*., 2008; William *et al*., 2008; Shauna *et al*., 2015; Shuang *et al*., 2016).

2.3 Relationship between ALP, GGT and Metabolic syndrome:

GGT and ALP are Mets components. and it is increase the risk of developing a form of liver disease called Non-alcoholic fatty liver disease (hepatic component of mets) and mild elevation of ALP and GGT (biomarker of liver injury) is used to identify NAFLD, so ALP and GGT are used as early biomarker for detection NAFLD to reduce risk of cirrhosis and hepatocellular carcinoma. (Ray *et al*., 2008; Poja *et al*., 2009; Tania *et al*., 2011; Turati *et al*., 2013; Setor *et al*., 2014; Debmalya *et al*., 2015; Paul *et al*., 2016).

Chapter Three

3. Materials and methods

3.1. Materials:

3.1.1. Study approach:

A quantitative method was used to measure the level of serum alkaline phosphatase and γ-glutamyltranspeptidase enzyme in metabolic syndrome Sudanese male and female patients during the period from June to July 2018.

3.1.2. Study design:

This is case control study.

3.1.3. Study area:

The study was conducted in Aliaa Specialized Hospital.

3.1.4. Study population:

The study included patients with metabolic syndrome.

3.1.5. Sample size:

This study included 50 patients with metabolic syndrome as case and 50 healthy individual as control.

Inclusion criteria:

Sudanese patients with metabolic syndrome and healthy individual serve as control were included.

Exclusion criteria:

Patients with hepatitis A, B, C or any other liver disease, alcoholism and medication that increase ALP and GGT level were excluded.

3.1.6. Ethical consideration:

Verbal consent was taken regarding acceptance to participate in the study and reassurance of confidentiality. Before the specimen was collected, the donors knew that this specimen was collected for research purpose.

3.1.7. Data collection:

Data were collected using structural interviewing questionnaire, which was designed to collect and maintain all valuable information concerning each case examined.

3.2. Methods:

3.2.1 Sample collection and processing:

About 3ml of venous blood were collected by safe aseptic procedure. Serum may be used for the assay of ALP and GGT, the volume of sample is recommended that at least 2.5ml of whole blood is collected. In serum sample; blood should be allowed to colt at room temperature. After retraction of the clot, the sample should be centrifuged, and the serum separated. Serum sample should be stored frozen below -20C. Sample should be thawed and mixed before assay.

3.2.2. Estimation of Alkaline phosphatase level:

3.2.2.1. Principle of ALP:

Colorimetric assay.

In the presence of magnesium and zinc ions, p-nitrophenyl phosphate is cleaved by phosphatases into phosphate and p-nitrophenol.The p-nitrophenol released is directly proportional to the catalytic ALPactivity. It is determined by measuring the increase in absorbance at 409 nm.

3.2.2.2. Procedure of ALP: (Appendix II)

3.2.3. Estimation of γ-glutamyltranspeptidase:

3.2.3.1. Principle of GGT:

Enzymatic colorimetric assay

Gamma-glutamyltranspeptidase transfers the γ-glutamyl group of L γ-glutamyl–3 carboxy -4-nitroanlide to glycylglycine.The amount of 5-amino -2 nitorbenzoate liberated is proportional to the GGT activity in the sample. It is determined by measuring the increase in absorbance at 400 nm.

3.2.3.2. Procedure of GGT: (Appendix III)

3.4. Quality control:

The precision and accuracy of all methods used in this study were checked by commercially prepared control sample before it is application for the measurement of the test and control samples.

3.5. Statistical analysis:

Data obtained from this study was analyzed using statistical package for the social science (SPSS version 23). Independent t test was used for comparison and person correlation was used for correlation.

Chapter Four

4. Results:

The results of biochemical determine serum of GGT and ALP in metabolic syndrome patients (case) and control group are given in tables and figures:

Table (4.1): represents the comparison mean ±SD of GGT, ALP and BMI in case versus control group. The result showed there were significant increased (47.08 ± 35.808 versus 25.48 ± 9.132 IU/L, p- value= 0.00), (85.26 ± 30.370 versus 60.24 ± 15.533 IU/L, p- value= 0.00), (28.030 ± 3.6350 versus 22.770 ± 1.686 kg/m2, p- value= 0.00), respectively.

Figure (4.1): shows age distribution among metabolic syndrome case group, (2%) of patients between (25-39), (54%) of patients between (40-54), (38%) of patients between (55-70), (6%) of patients between (71 – 80) years.

Figure (4.2): illustrates gender distribution among metabolic syndrome case group, (62%) were females while (38%) were males.

Figure (4.3): shows correlation between GGT level and BMI in metabolic syndrome patients group. (r = 0.118 P. value = 0.415). (There was no correlation).

Figure (4.4): shows correlation between GGT level and Duration in metabolic syndrome patients group. (r=0.081, P. value=0.575). (There was no correlation).

Figure (4.5): shows correlation between GGT level and Age in metabolic syndrome patients group. (r=0.024, P. value=0.869). (There was no correlation).

Figure (4.6): shows correlation between ALP level and BMI in metabolic syndrome patients group. (r =0.301, P. value=0.034). (There was significant weak positive correlation).

Figure (4.7): shows correlation between ALP level and Duration in metabolic syndrome patients group. (r =0.103, P. value=0.478). (There was no correlation).

Figure (4.8): shows correlation between ALP level and Age in metabolic syndrome patients group. (r =0.124, P. value=0.392). (There was no correlation).

Table (4.1): Mean concentrations of GGT, ALP and BMI in case and control group.

Variable	Case Mean ± SD N = 50	Control Mean ± SD N = 50	P. value
GGT	47.08 ± 35.808	25.48 ± 9.132	0.00
ALP	85.26 ± 30.370	60.24 ± 15.533	0.00
BMI	28.030 ± 3.6350	22.770 ± 1.686	0.00

Results given in mean ± SD, P. value ≤ 0.05 is considered significant.

Independent sample T-test was used for comparison.

Table (4-2): Gender distribution among case group.

Gender	Case	Percent
Males	19	38%
Females	31	62%

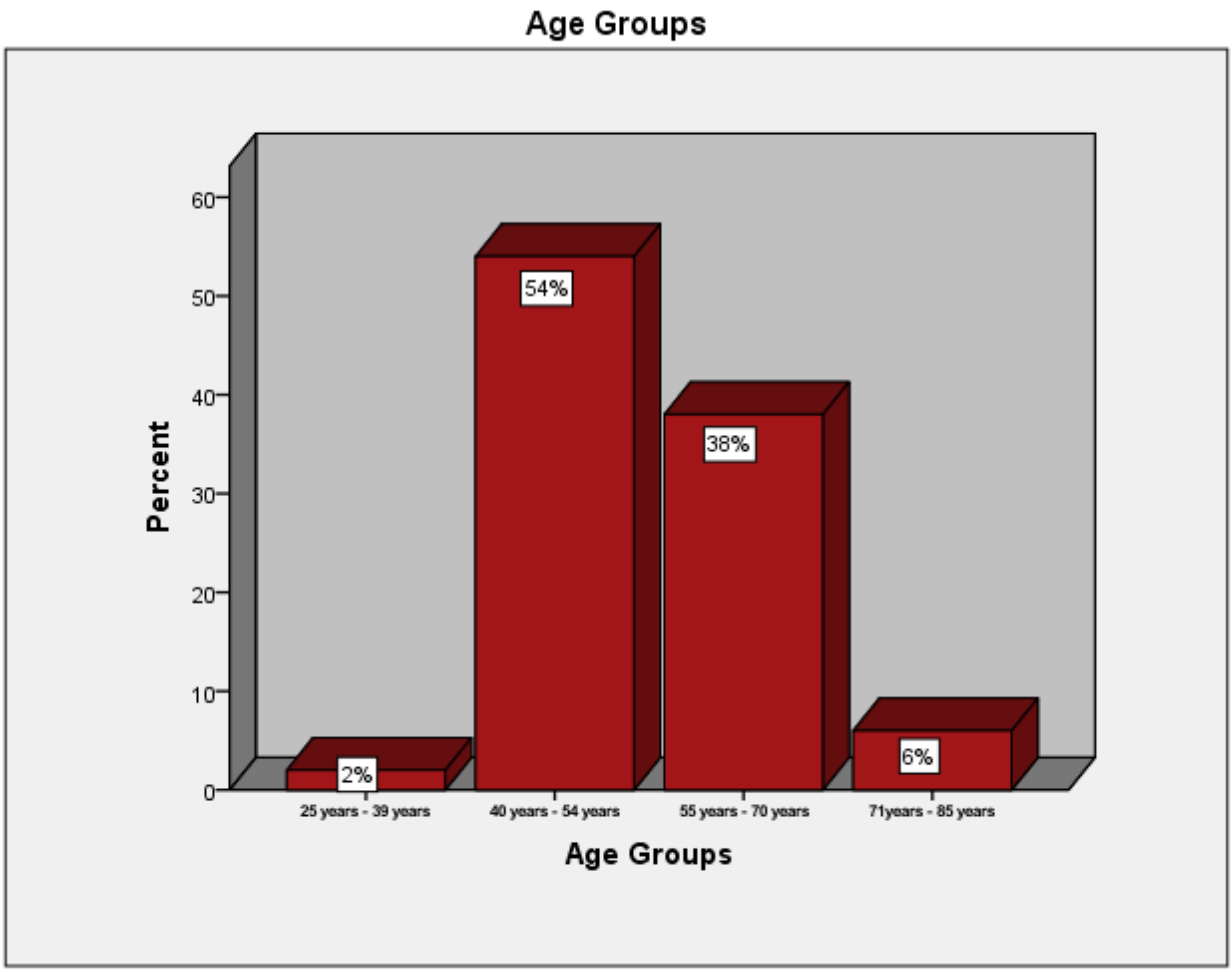

Figure (4.1): Age distribution among metabolic syndrome patients group.

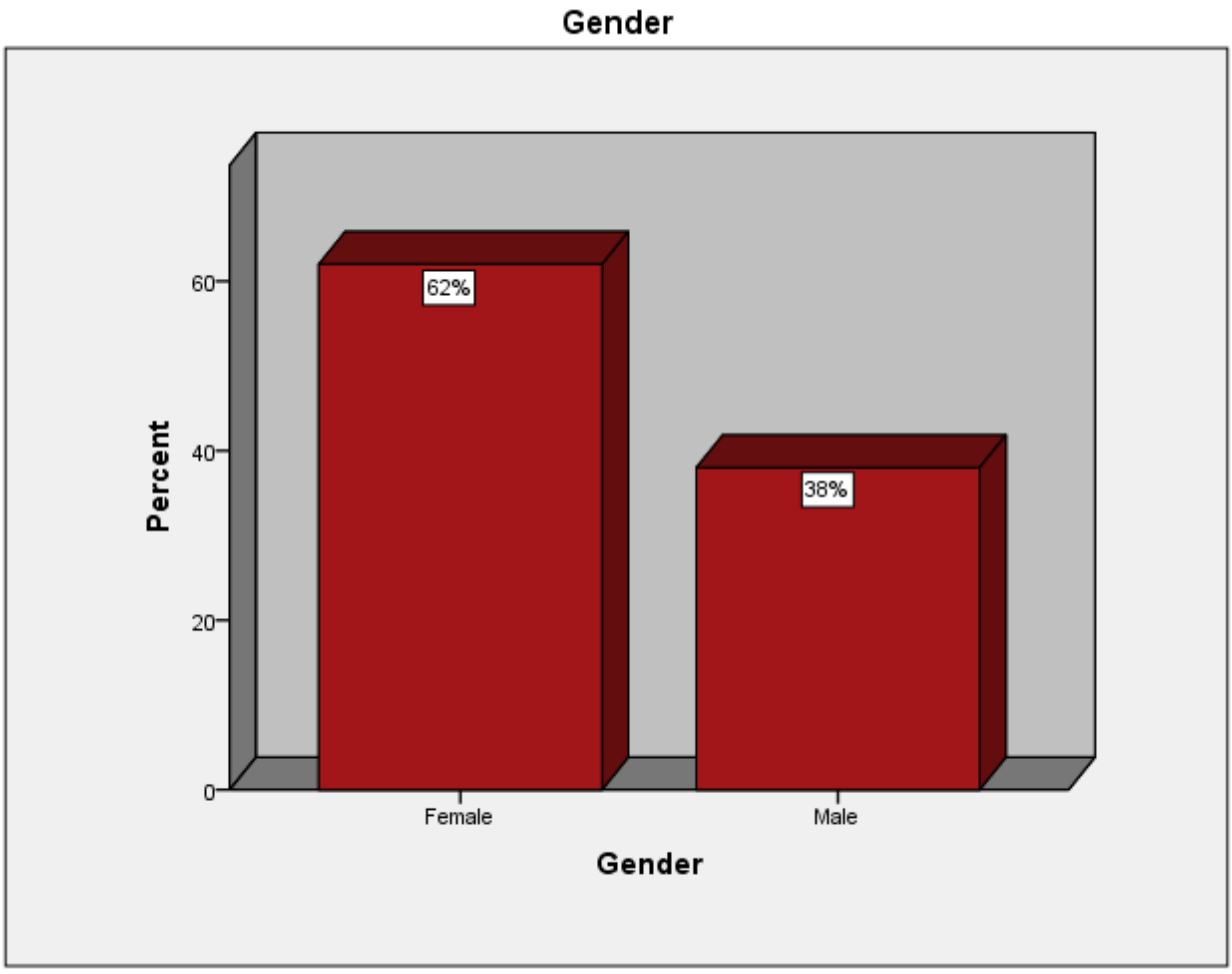

Figure (4.2): Gender distribution among metabolic syndrome patients group.

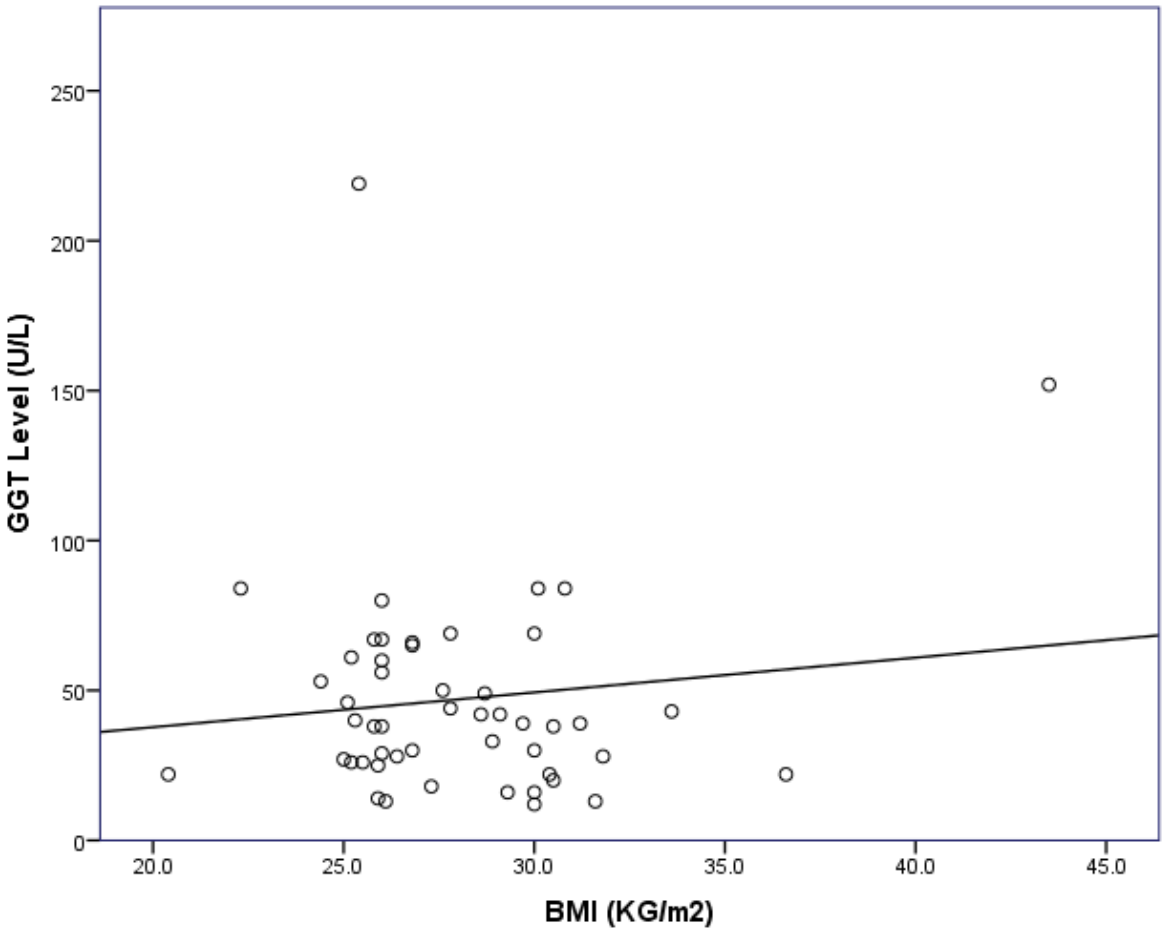

Figure (4.3): Correlation between GGT level and BMI in metabolic syndrome patients group(r = 0.118, P. value = 0.415).

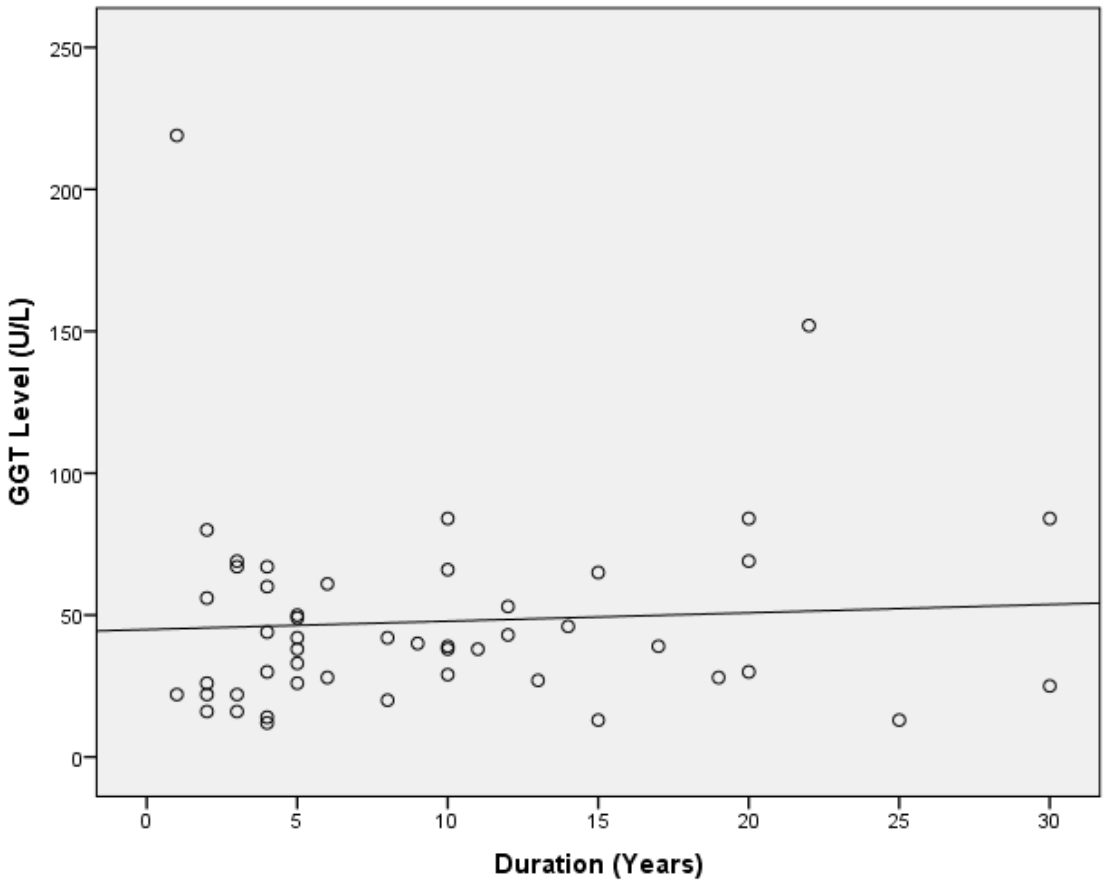

Figure (4.4): Correlation between GGT level and Duration in metabolic syndrome patients group(r=0.081, P. value=0.575).

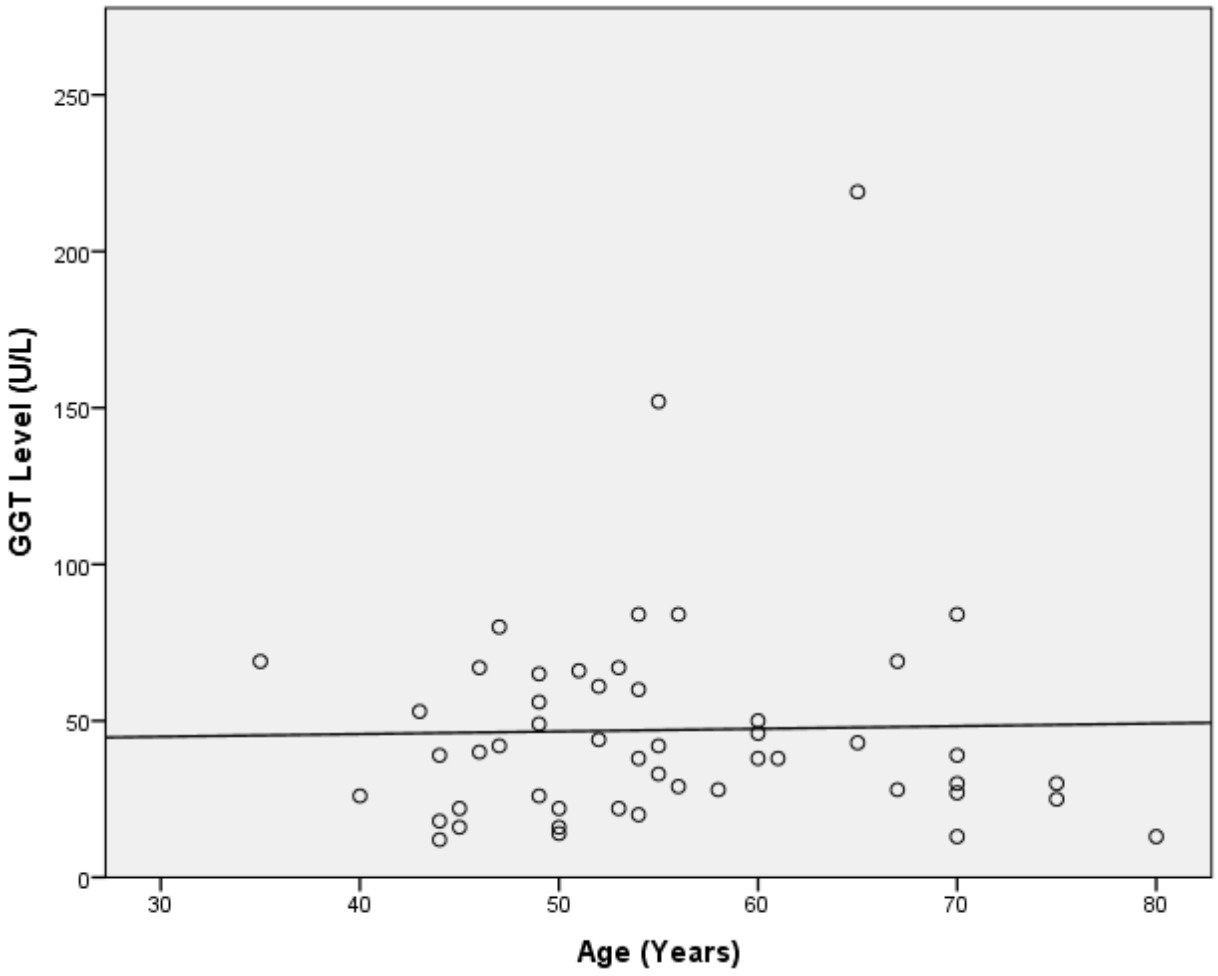

Figure (4.5): Correlation between GGT level and Age in metabolic syndrome patients group(r=0.024, P. value=0.869).

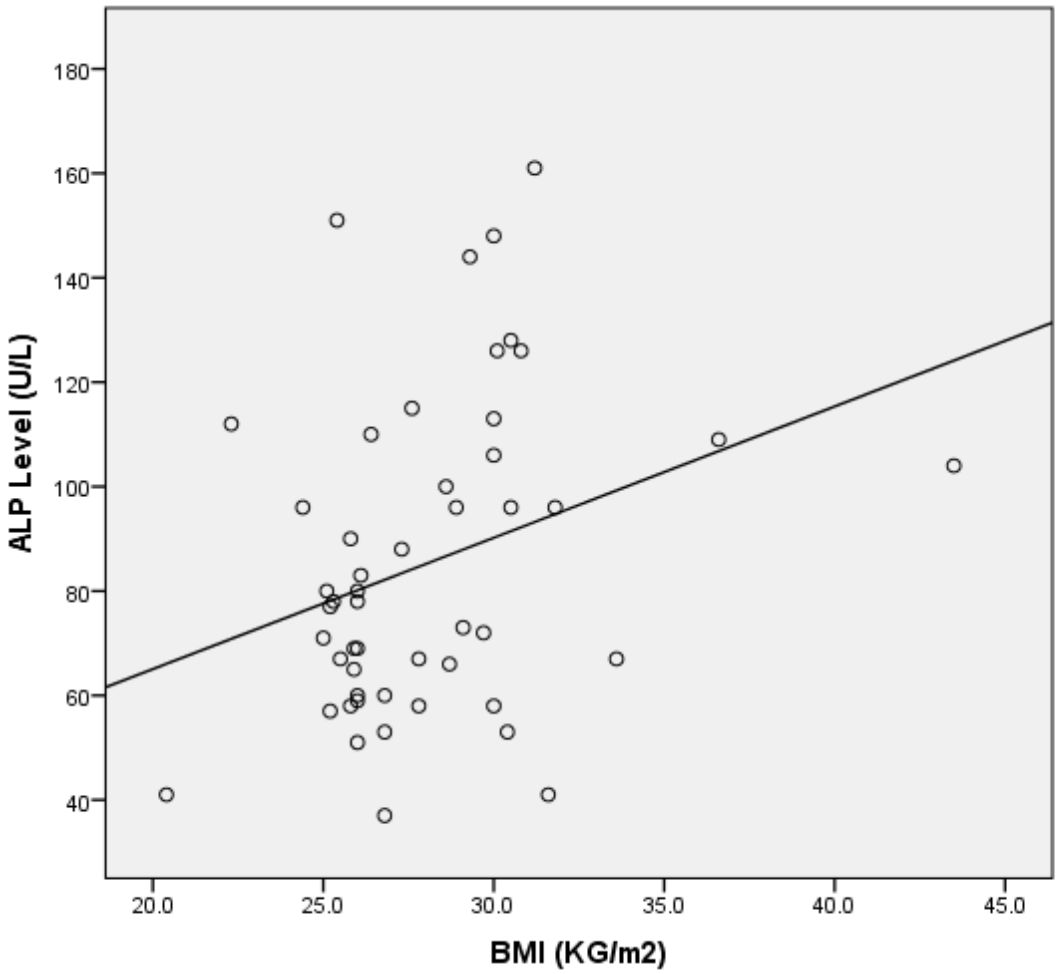

Figure (4.6): Correlation between ALP level and BMI in metabolic syndrome patients group(r =0.301, P. value=0.034).

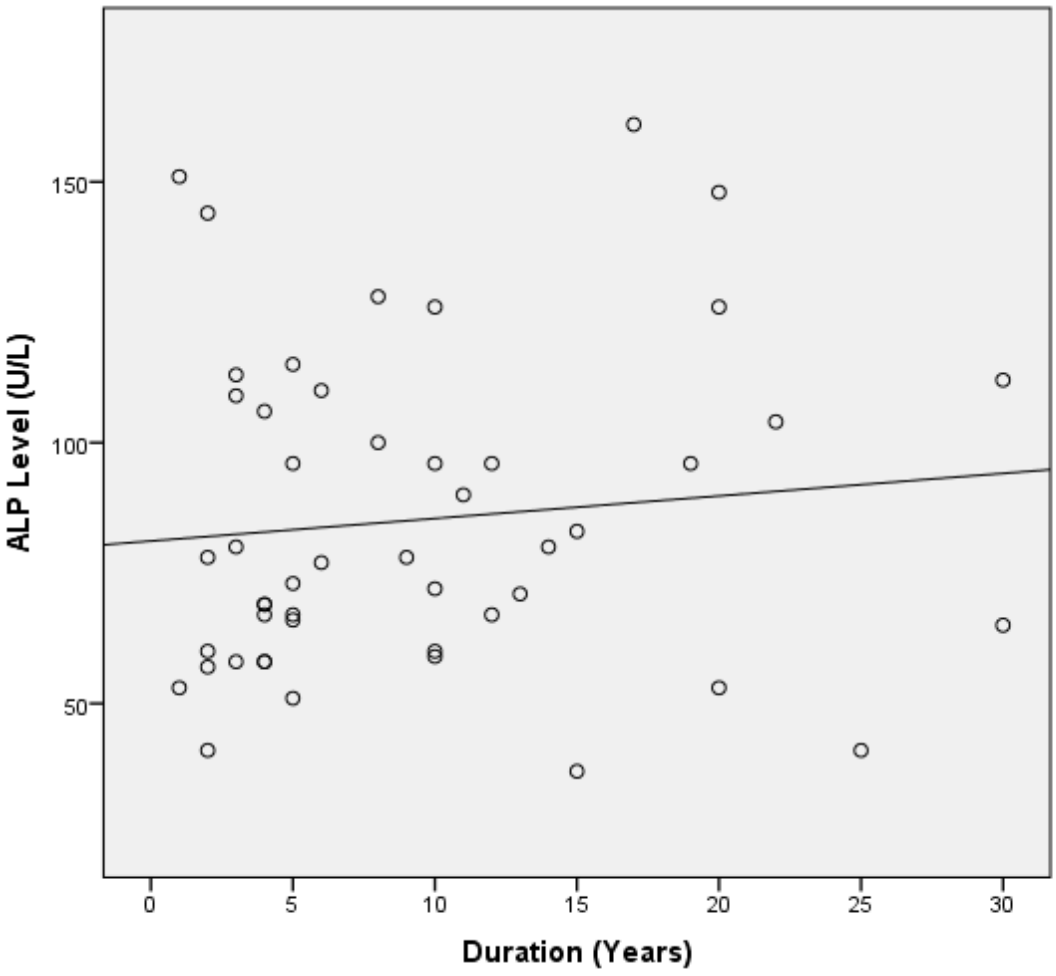

Figure (4.7): Correlation between ALP level and Duration in metabolic syndrome patients group(r =0.103, P. value=0.478).

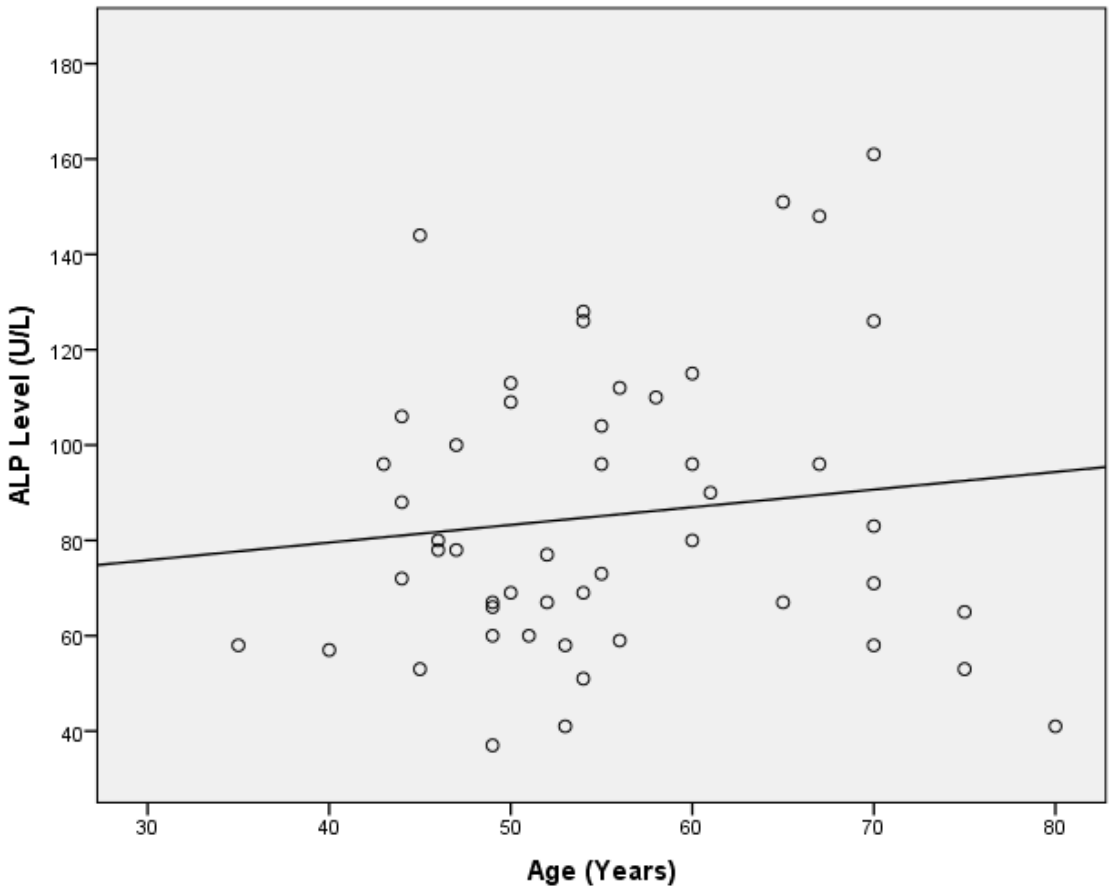

Figure (4.8): Correlation between ALP level and Age in metabolic syndrome patients group(r =0.124, P. value=0.392).

Chapter Five

5.1 Discussion:

Metabolic syndrome is a serious medical condition and increase incidence of multiple cancers risk and has effects on the life quality.

This study conducted to asses plasma levels of ALP and GGT among Sudanese metabolic syndrome patients in Khartoum state.

The findings of this study showed that Mets was most common among age groub (40-54) years. This finding agreed with another studies carried by (Ford *et al*., 2002; Shung *et al*., 2016). The findings obtained from especially designed questionnaire revealed that, it was more frequent in females than males. This finding agreed with another study carried by (Shung *et al*., 2016). Which showed that Mets patients most abundant in females than males.

The findings of this study showed, there were significant increase in mean of ALP, GGT and BMI in metabolic syndrome patients compared to control group (p-value= 0.00).GGT and ALP are Mets components and it is increase the risk of developing a form of liver disease and mild elevation of ALP and GGT indicated of liver injury. This finding agreed with another study carried by, which finding confirmed that, there were significant increase in GGT and ALP levels in metabolic syndrome patients (Perera *et al*., 2008).

Also the finding of this study showed, there were no correlation between GGT level and study variable (BMI, duration and age of metabolic syndrome patients); (r= 0.118 P- value = 0.415), (r=0.081, P- value=0.575), (r=0.024, P-value=0.869). respectively this finding disagreed with study carried by (Monica *et al*.,2005; Perera *et al*., 2008), which showed that there were

positive correlations between GGT and study variable (BMI, duration and age of metabolic syndrome patients). The study also showed there was significant weak positive correlation between ALP level and BMI of metabolic syndrome patients; (r =0.301, P- value=0.034). This finding agreed with another study carried by (Perera *et al.*, 2008).

The study also showed, there were no correlation between ALP level and study variable (duration and age) of metabolic syndrome patients; (r =0.103, P- value=0.478) and (r =0.124, P- value=0.392) respectively, this finding disagreed with another study which finding confirmed that, there were positive correlation between ALP level and study variable (duration and age) of metabolic syndrome patients. (Perera *et al.*, 2008).

5.2. Conclusions:

According to results of this study it is concluded that:

ALP and GGT are increased in metabolic syndrome patients. There was positive correlation between ALP and BMI.

5.3 Recommendations:

From the findings of this study it is recommended that:

1- ALP and GGT should be done as screening tests to prevent the complications of metabolic syndrome (Non Alcoholic Fatty Liver Disease and Liver cancer).

2- Further studies should be conducted to investigate the other liver enzymes (ALT and AST) and lipid profile levels to assess the impact of these parameters upon metabolic syndrome (Non Alcoholic Fatty Liver Disease and Liver cancer).

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Sudan University of Science and Technology

Master Degree

Estimation of ALP and GGT in Mets Patients

Name: ……

Gender: ☐ **Male** ☐ **Female**

Age: …….....years

Height: ……..... cm - Weight: ……. kg

BMI: …… kg/m2

TEL: ……

Family history diseases: …….

☐ **HT** ☐ **D.M** ☐ **obesity**

Duration of Diseases: ……..years

Medications Use: ……

Other Chronic diseases: …….

Life style: ……

☐ **Smoker** ☐ **Alcoholism** ☐ **Tobacco**

Sample: serum / heparinized plasma

Parameters:

ALP……U/L - GGT: ……U/L

Number ( )