# 1. Introduction and literature review

**1.1.Introduction** Obesity is a common disorder in our country. It is proven as predisposing factor of increasing morbidity and mortality in cardiovascular and neurovascular disease. In presence of nutritional abundance( excess energy intake), Sedentary life style and influence importantly by genetic endowment, endocrine and neuronal system increases adipose energy store and produces adverse health consequences (Ajay et al., 2014).

Patients with metabolic disorders, such as obesity frequently develop liver steatosis, a pathology characterized by the deposition of large fat droplets in the hepatic parenchymal cells. In obese subjects, the enhanced rate of lipolysis leads to an increased availability of free fatty acids responsible for an exaggerated synthesis and deposition of fats in the hepatocytes (Luyckx et al.,1998). Also some evidences noted that the presence of obesity is related to cirrhosis (cryptogenic cirrhosis) and hepatic carcinoma, also in patient with nonalcoholic fatty liver disease observed in liver units, obesity and weight gain are systematically associated with advanced fibrosis and fibrosis progression (Giulio et al., 2008).

**1.2.Literature Review1.2.1.Obesity:** Obesity is defined as a condition of abnormal or excessive fat accumulation in adipose tissue, to the extent that health is impaired1.

The amount of excess fat in absolute terms, and its distribution in the body - either around the waist and trunk (abdominal, central or android obesity) or peripherally around the body (Ofei, 2005).1. 2.1.1. Causes of Obesity:

causes of obesity and their risk factors are the following:

**Nutrition**: hyper-eating is now often a hard habit to break among those overweight and obese. Not only this, those who are obese tend to eat faster, there being a correlation between behavior and body weight, as the faster they eat, the more full signals can be missed, intentionally or not. The increased use of high-fructose sugar-flavored soft drinks is a prime suspect in the growth of obesity (Anderson, Matsa, 2011). Lack of physical activity: Modern living has facilitated a more sedentary lifestyle for many people. Contributing factors have included the increase in labor-saving devices at work, home, transit and play, Sustained physical activity helps protect against weight increase, overweight and obesity, as well as enhancing fitness. In addition, inadequate physical activity can itself be an independent health risk factor, so physical inactivity is both a cause and a consequence of obesity (Michaud et al., 2007). Socio-economic factors: obesity prevalence among adult men is currently similar at all income levels with a tendency to be slightly higher at higher income levels, although among adult females, obesity prevalence increases as household income decreases (Ogden, 2010b). among boys and girls, obesity prevalence generally decreases as household income increases and as the education of the head of household increases, although these relationships are not consistent across race and ethnic groups (Ogden, 2010c).

**1.2.1.2.Types of Obesity:**according to whether or not cause syndrome there are:**simple obesity:**obesity caused by ingesting too much heat energy and consuming less energy and so storing too much fat.**Secondary obesity:**it's symptoms obesity taking some disease as primary disease, occupying under 5% of total obesity. The primary diseases are cushing's syndrome, metabolic syndrome and polycystic ovary syndrome (Wing et al.,1991).according to fat distribution obesity classified into:**Central obesity:**also known as abdominal obesity, is when excessive abdominal fat around the stomach and abdomen has built up to the extent that it is likely to have a negative impact on health (yusuf et al., 2004).

Abdominal obesity is not confined only to the eldery and obese subject, its linked to Alzheimer disease and metabolic and vascular disease (razay,vreugdenhil, wilcock, 2006). **Peripheral obesity:** is accumulation of fat around the hips and thigh areas, this means that the hips are

almost rounded and the buttocks look larger compared to normal subjects (Sukru et al., 2015).according to body shape classified into: Apple shaped obesity: The apple shaped woman carries most her body fat in the abdominal region. She will generally have narrow hips, larger breasts, and a relatively large waist. Apple-shaped women have more fat surrounding their internal organs (visceral fat). This kind of fat presents many more risks than subcutaneous fat; it decreases insulin sensitivity, raises blood pressure, and decreases levels of good cholesterol (high density lipoprotein). These are all key indicators of heart disease risk and diabetes risk. The higher the waist to hip ratio, the higher the risk ( van et al.,1993). Pear shaped obesity: The pear-shaped woman carries most of her body fat around the hips, thighs, and buttocks. She will generally have a smaller upper body (smaller breasts) and a heavier lower body. The risks for the overweight pear-shaped woman are quite different to the apple shape. A pear-shaped woman will typically be more susceptible to cellulite and varicose veins. However recent research shows that the health benefits of the pear shape may not be what was first thought (Singh, 1994).

# 1.2.1.3. Pathophsyology of Obesity:

There are many possible pathophysiological mechanisms involved in the development and maintenance of obesity, many investigators postulated that leptin was a satiety factor ,mutations in the leptin gene resulted in the obese phenotype (consdine et al., 1995)Also many other hormonal mechanisms have been elucidated that participate in the regulation of appetite and food intake, storage patterns of adipose tissue and development of insulin resistance, also other mediators as the adipokines that produce by adipose tissue modify many obesity related diseases. Leptin and ghrelin are considered to be complementary in their influence on appetite, with ghrelin produce by the stomach modulating short term appetitive control. Leptin is produce by adipose tissue to signal fat storage reverses in the body, and mediate long term appetitive control (Hamann, Matthaei, 1996). **1.2.1.4.Complication of Obesity:** 

The major diseases associated with obesity are hypertension, atherosclerosis, and diabetes, as well as certain types of cancer. Less well-known complications include hepatic steatosis, gallbladder disease, pulmonary function impairment, endocrine abnormalities, obstetric complications, trauma to the weight-bearing joints, gout, cutaneous disease, proteinuria, increased hemoglobin concentration, and possibly immunologic impairment (George, Bray ,1985).1.2.1.5.Management of Obesity: The main treatment for obesity consists of dieting and physical exercise. Diet programs may produce weight loss over the short term, but maintaining

this weight loss is frequently difficult and often requires making exercise and a lower food energy diet a permanent part of a person's lifestyle (Tate et al., 2007). In the short-term low carbohydrate diets appear better than low fat diets for weight loss. In the long term; however, all types of low-carbohydrate and low-fat diets appear equally beneficial. Decreased intake of sweet drinks is also related to weight-loss. (Johnston et al., 2014). Success rates of long-term weight loss maintenance with lifestyle changes are low, ranging from 2–20%. Dietary and lifestyle changes are effective in limiting excessive weight gain in pregnancy and improve outcomes for both the mother and the child. Intensive behavioral counseling is recommended in those who are both obese and have other risk factors for heart disease (LeFevre, Michael, 2014). Five medications have evidence for long-term use orlistat, lorcaserin, liraglutide, phenterminetopiramate, and naltrexone-bupropion. They result in weight loss after one year ranged from 3.0 to 6.7 kg over placebo (Longo et al, 2017). European regulatory authorities rejected the latter two drugs in part because of associations of heart valve problems with lorcaserin and more general heart and blood vessel problems with phentermine-topiramate (Wolfe, 2013). Orlistat use is associated with high rates of gastrointestinal side effects and concerns have been raised about negative effects on the kidneys (Chang et al., 2014). The most effective treatment for obesity is bariatric surgery. The types of procedures include laparoscopic adjustable gastric banding, Roux-en-Y gastric bypass, vertical-sleeve gastrectomy, and biliopancreatic diversion. Surgery for severe obesity is associated with long-term weight loss, improvement in obesity related conditions (Wolfe,2013).**1.2.2. Body Mass Index(BMI):** also called quetelet index is a value derived from the mass (weight) and the height of of an individual, is defined as the body mass divided by the square of the body height and expressed in units of Kg/m<sup>2</sup>.BMI is an attempt to quantify the amount of tissue mass(muscle, fat and bone) in an individual and categorize that person as underweight, normal weight, overweight or obese based on the value .(Malcolm, 2015). commonly accepted BMI ranges are underweight: under 18.5 Kg/m<sup>2</sup>, normal 18.5 to 25 Kg/m<sup>2</sup>, over weight: 25 to 30 Kg/m<sup>2</sup>, obese over 30 kg/m<sup>2</sup>(eknoyan, Garabed,2007)**1.2.2.1. Categories of BMI:** A frequent use of the BMI to assess how much an individual's body weight departs from what is normal or desirable for a person's height, the weight excess or deficiency may, in part, be accounted for by body fat (adipose tissue) or by other factors as muscularity also affect BMI. The World Health Organization regards a BMI of less than 18.5 as underweight and may indicate malnutrition, an

eating disorders, or other health problems, while a BMI equal to or greater than 25 is considered overweight and above 30 is considered obese (WHO,2006)BMI is used differently for children. It is calculated in the same way as for adults, but then compared to typical values for other children of the same age instead of comparison against fixed thresholds for under or overweight, the BMI is compared against the percentile for children of the same sex and age (wang, youfa,2012)A BMI that is less than 5th percentile is considered underweight and above 95th percentile is considered obese. The children with BMI between the 85th and 95th are considered to be overweight (shiwaku et al., 2003)1.2.2.2 Applications of BMI: BMI is generally used in public health as a means of correlation between groups related by general mass and can use as means of estimating adiposity. In clinical practice BMI categories are generally regards as satisfactory tool for measuring whether sedentary individuals are under, overweight or obese (kronmal, 1993)1.2.2.3 Alternatives Expressions for BMI:

I. BMI Prime: A modification of BMI System, is the ratio of actual BMI to upper limit optimal BMI( currently defined as 25 Kg/m²). People with BMI prime less than 0.74 are underweight; those between 0.74 and 1.00 or greater are overweight (gadzik, james, 2006) II. Waist Circumference: Is a good indicator of visceral fat, which poses more health risks than fat according to National Institute of Health, waist circumference in excess of 102 centimeters for men and 88 for non-pregnant women is considered a high risk fortype- 2diabetes, dyslipidemia, hypertension and cardiovascular diseases. So it is a better indicator for obesity related disease risk than BMI (morkedal et.al, 2011). Waist to hip circumference ratio has also been used, but has been found to be no better than waist circumference alone, but more complicated to measure (samaras, Thomas, 2007).

**based Body Shape Index:**Is fat more rigorous and is based upon four key measurements: the body surface area, vertical trunk circumference, waist circumference and height (Rahman et al., 2015).

#### 1.2.3. liver Enzymes:

#### **1.2.3.1.** Alanine Transaminase(ALT):

Is a transaminase enzyme, also called alanine aminotransferase and was formerly called glutamate-pyruvate transaminase or serum glutamic-pyruvic transaminase. ALT is found in plasma and various body tissues, but most common in the liver (karmen et al.,1955).

Functions of ALT: ALT catalyzes the transfer of amino group from L-alanine to α-

ketoglutarate, the products of this reversible transamination reaction being pyruvate and L-glutamate .ALT require the coenzyme pyridoxal phosphate which is converted into pyridoxamine in the first phase of reaction, when an amino acid converted into a keto acid (wang et al., 2012)Clinical Significance of ALT:ALT is commonly measured as a part of a diagnostic evaluation of hepatocellular injury to determine liver health. It's always measure in international units/liter (IU/L) .While sources vary specific reference range values for patients, 10\_40 IU/L is the standard reference range for experimental studies (ghouri et al., 2010).

Elevated Levels of ALT: Significantly elevated levels often suggest the existence of other medical problems such as viral hepatitis, diabetes, congestive heart failure, liver damage, bile duct problems. so its commonly used as way of screening for liver problems. Elevated ALT level do not automatically mean that medical problems exist .fluctuation of ALT is normal over the course of the day, and its also increase in response to strenuous physical exercise (Watkins et al., 2006).

# **Glutmyltransferase (GGT):**

Gamma-

glutamyltransferase (also  $\gamma$ -glutamyltransferase, GGT, gamma-GT; EC 2.3.2.2) is a transferase (a type of enzyme) that catalyzes the transfer of gamma-glutamyl functional groups from molecules such as glutathione to an acceptor that may be an amino acid, a peptide or water (forming glutamate) ( Tate, Meister, 1985).GGT plays a key role in the gamma-glutamyl cycle, a pathway for the synthesis and degradation of glutathione and drug and xenobiotic detoxification ( Courtay et.al, 1992). Other evidence indicate that GGT can also exert a pro-oxidant role, with regulatory effects at various levels in cellular signal transduction and cellular pathophysiology ( Dominici, 2005). The name  $\gamma$ -glutamyltransferase is prefered by the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology. The Expert Panel on Enzymes of the International Federation of Clinical Chemistry also used this name (shaw et al.,1983). The older name is gamma-glutamyltranspeptidase (GGTP) (Whitfield,2001). **Function and Tissue Source of GGT:** 

GGT is present in the cell membranes of many tissues, including the kidneys, bile duct, pancreas, gallbladder, spleen, heart, brain, and seminal vesicles (Goldberg, 1980). It is involved in the transfer of amino acids across the cellular membrane and leukotriene metabolism (Raulf ,Stüning , König, 1985). It is also involved in glutathione metabolism by transferring the glutamyl moiety to a variety of acceptor molecules including water, certain L-amino acids, and peptides, leaving

the cysteine product to preserve intracellular homeostasis of oxidative stress (Schulman, 1975). **Medical Applications of GGT:** GGT is predominantly used as a diagnostic marker for liver disease. Latent elevations in GGT are typically seen in patients with chronic viral hepatitis infections often taking 12 months or more to present. Elevated serum GGT activity can be found in diseases of the liver, biliary system, and pancreas. In this respect, it is similar to alkaline phosphatase (ALP) in detecting disease of the biliary tract (Betro, Oon, Edwards, 1973). In general, ALP is still the first test for biliary disease. The main value of GGT over ALP is in verifying that ALP elevations are, in fact, due to biliary disease . More recently, slightly elevated serum GGT has also been found to correlate with cardiovascular diseases and is under active investigation as a cardiovascular risk marker (Emdin ,Pompella , Paolicchi, 2005).some of which appear to be related to specific pathologies such as metabolic syndrome, alcohol addiction and chronic liver disease. High body mass index is associated with type 2 diabetes only in persons with high serum GGT (Lim et al., 2007).GGT is elevated by ingestion of large quantities of alcohol. However, determination of high levels of total serum GGT activity is not specific to alcohol intoxication, Isolated elevation or disproportionate elevation compared to other liver enzymes (such as ALP or alanine transaminase) can indicate alcohol abuse or alcoholic liver disease (Kaplan, 1985). and can indicate excess alcohol consumption up to 3 or 4 weeks prior to the test. The mechanism for this elevation is unclear. Alcohol might increase GGT production by inducing hepatic microsomal production, or it might cause the leakage of GGT from hepatocytes (Barouki, 1983). Numerous drugs can raise GGT levels, including barbiturates and phenytoin, GGT elevation has also been occasionally reported following nonsteroidal antiinflammatory drugs (including aspirin), Elevated levels of GGT can also be due to congestive heart failure (Ruttmann, 2005). 1.2.3.3. Alkaline Phosphtase (ALP): Alkaline phosphatase (ALP) (EC 3.1.3.1) is a hydrolase enzyme responsible for removing phosphate groups from many types of molecules, including nucleotides, proteins, and alkaloids. The process of removing the phosphate group is called dephosphorylation. As the name suggests, alkaline phosphatases are most effective in an alkaline environment (Tamás et al., 2002). **Tissue** Sources of ALP: Alkaline phosphatases are present in many human tissues, including bone, intestine, kidney, liver, placenta and white blood cells (Kaplan, Marshall, 2005). **Functions of ALP:** ALP has a low substrate specificity and catalyzes the hydrolysis of phosphate esters in a basic environment. The major function of alkaline phosphatase is

transporting across cell membranes (Celik et al., 2009). Clinical Significance of ALP: The majority of sustained elevated ALP levels are associated with disorders of the liver or bone, or both. A variety of primary and secondary hepatic conditions maybe associated with elevated serum ALP levels. Since production is increased in response to cholestasis, serum ALP activity provides a sensitive indicator of obstructive (LiFern, Rajasoorya, 1999).

Diseases of bone associated with increased serum ALP are restricted to the presence of osteoblastic activity. Neoplasms involving bone may be associated with marked serum elevations when lesions incite osteoblastic reaction, such as metastatic adenocarcinoma of the prostate. Metabolic bone diseases usually associated with serum enrichment by the bone isoenzyme include rickets, osteomalacia, and Paget's disease (Gennari, Stefano, Merlotti, 2005). Elevated serum ALP occurring with neoplastic disease may be due to hepatic metastases, bone metastases, or direct contribution by neoplastic cells (Christensen, Stephen, 2016). In normal pregnancy increased ALP activity, averaging approximately 1.5 times ULN, can be detected between weeks 16 and 20. ALP activity increases and persists until the onset of labor. Activity then returns to normal within 3 to 6 days.24 Elevations also may be seen in complications of pregnancy such as hypertension, preeclampsia, and eclampsia, as well as in threatened abortion (LiFern, Rajasoorya, 1999). Isoenzymes of ALP: ALP exists as a number of isoenzymes, which have been studied by a variety of techniques. The major isoenzymes, which are found in the serum and have been most extensively studied, are those derived from the liver, bone, intestine, and placenta. Electrophoresis is considered the most useful single technique for ALP isoenzyme analysis. However, because there may still be some degree of overlap between the fractions, electrophoresis in combination with another separation technique may provide the most reliable information. The liver fraction migrates the fastest, followed by bone, placental, and intestinal fractions (Fleisher, Eickelberg, Elveback, 1977).

# 1.3. Rationale

Recent findings have shown that obesity can be an independent predictor of hepatic steatosis, fatty liver is a common clinical and histological condition frequently associated with alcohol consumption and excessive body weight (Stranges et al., 2014)

Obesity rate in sudan was 6.6% in 2014 (CIA, 2016). No data was found yet concering the effect of obesity on levels of ALT,GGT and ALP in Sudanese obese. This study will help health authorities to evaluate the problem more objectively and to implement appropriate measures for early prediction of liver disease among obese individuals.

**1.4. Objectives1.4.1. General objectives:**To assess the activity of ALT, GGT and ALP level among Sudaneseobese. **1.4.2. Specific objectives:** • To measure and compare the activity of ALT, GGT and ALP in study groups. • To correlate between the activity of enzymes and BMI, duration of obesity and age.

10

# 2. Materials and methods

### 2.1. Materials:

# 2.1.1 Study design:

It is a descriptive cross-sectional case control study.

# 2.1.2 Study area:

The study was done in Khartoum state, Sudan. 2.1.3 Study period:

The study was carried during the period from january to may 2017.

# 2.1.4 study population:

This study included 40 obese Sudanese individuals (19 females and 21 males) with BMI more than 30 and 40 healthy individuals (19 females and 21 males) with BMI ranged from 18-24 as control.

was matched ranged from 18-35 in both groups.

#### 2.1.5. Inclusion criteria:

Sudanese population (males and females) with BMI more than 30 were included

#### 2.1.6. Exclusion criteria:

Individuals with liver diseases, bone diseases and cardiac diseases or any disease affect the serum activity of ALT,ALP and GGT were excluded.

2.1.7 Ethical Consideration:

Permission of this study was obtained from the college of medical laboratory science sudan university of science and technology. The objectives of the study were explained to all individuals participating in the study. An informed consent was obtained from each participant in the study. **2.1.8 Sampling:** 

2.5ml Venous blood were collected in heparin container, then immediately centrifuged at 3000 rpm for 5 minutes, plasma obtained and stored at -20°C until time of analysis.

Samples were analyzed in 2 days maximumly (to avoid changes of ALP activity levels).

**2.2. Methods:** serum activity of ALT, ALP and GGTwere measured using DIRUI DR-7000D auto-analyzer. **2.2.1. Determination of ALT:** Biomed ALT reagent was used (ALT/GPT) kinetic method **2.2.1.1. Principle:** Alanine aminotransferase(ALT) catalyzes the transfer of the amino group from alanine to oxoglutarate with the formation of glutamate and pyruvate. The pyruvate is converted to lactate by LDH, the reaction is monitoring by the change in absorbance at 340 nm continuously as NADH is oxidized to NAD+ which is directly proportional to ALT activity according to the following reaction:

L-alanine + oxoglutrate----(ALT) 
$$\rightarrow$$
 Pyruvate + L-glutamate  
pyruvate+ NADH+H<sub>2</sub> ------ (LDH)  $\rightarrow$  L-lactate+NAD+ +H<sub>2</sub>O

The reduced co-enzyme consumption, observed as decrease per time, is proportional to ALT activity in the sample (appendix II).

**2.2.2. Determination of ALP:**Biomed ALP reagent was used (ALP) kinetic method .**2.2.2.1. Principle:**Alkaline phosphatase (ALP) catalyzes in alkaline medium the transfer of the phosphate group from 4-nitrophenyl phosphate to 2-amino-2methyle-1-propanol (AMP), liberating 4-nitro phenol. the catalytic concentration is determined from the rate of 4-nitrophenol formation, measured at 405 nm according to the following reaction:

p-nitrophenyl phosphate+ $H_2O$ ---(ALP)  $\rightarrow$  p-nitrophenol+ $H_3PO_4$ . (appendix III)

**2.2.3. Determination of GGT:**Biomsystems GGT reagent was used (GGT) kinetic method **2.2.3.1. Principle:**The catalytic concentration is determined from the rate of 3-carboxy-4-nitroaniline formation according to the following reaction:

3-carboxy-4-nitroaniline  $+H_2O---(GGT) \rightarrow p-nitrophenol+ H_3PO_4$ 

GGT activity in the sample determined by measuring the per time absorption increase at 405nm (appendix IV).**2.3 Quality Control :**Normal and pathologicalControl sera were used for monitoring the validity of the reaction. These controls was run at least with every working shift in which liver enzymes determinations were performed.**2.4 Data Analysis:**Statistical analysis was done by using SPSScomputer programe.Independent T-test and pearson's correlation were used.

# 3. Results

Fourty obese Sudanese individuals with BMI more than 30 were enrolled in this study to assess the activity of liver enzymes (ALT,ALP and GGT) and 40 Sudanese individuals with normal BMI were serve as control group.

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

- ➤ **Table (3.1)** shows the comparison between means activity of serum ALT,ALP and GGT in obese Sudanese individuals and non-obese.
- ➤ **Table (3.2)**: Comparison between means activity of serum ALT, ALP, GGT and gender.
- Figure (3.1) a scatter plot showspositive correlation between serum ALT levels (U/L) and BMI among Obese Sudanesepeople.
- Figure (3.2) a scatter plot showspositive correlation between serum ALP levels (U/L) and BMI among Obese Sudanese people.
- Figure (3.3) a scatter plot showspositive correlation between serum ALP levels (U/L) and BMI among Obese Sudanese people.
- Figure (3.7) a scatter plot shows no correlation between serum ALT levels (U/L) and the duration of obesity
- Figure (3.8) a scatter plot showsnoCorrelation between serum ALP levels (U/L) and the duration of obesity.
- Figure (3.9) a scatter plot showspositivecorrelation between serum GGT levels (U/L) and the duration of obesity.

**Table (3.1)**: Comparison between means activity of serum ALT,ALP and GGT in obese Sudanese individuals and non-obese.

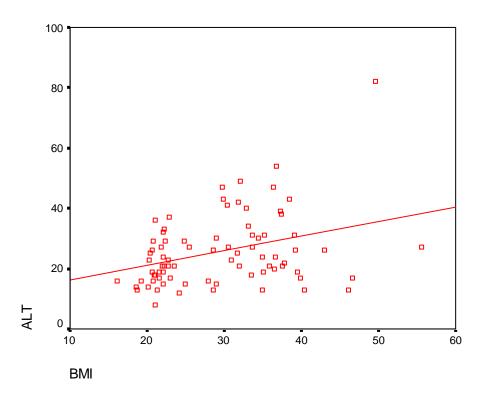
Variables	Obese(no=40)	Control (no=40)	P-value
	Mean ± SD	Mean ± SD	
ALT			0.001
	29.93±13.971	21.28±6.980	
ALP			0.000
	246.60± 42.15	176.25±45.87	
GGT			0.001
	33.70±13.92	24.60±8.22	

Independent T-test was used, significant when  $\leq 0.05$  p value considered.

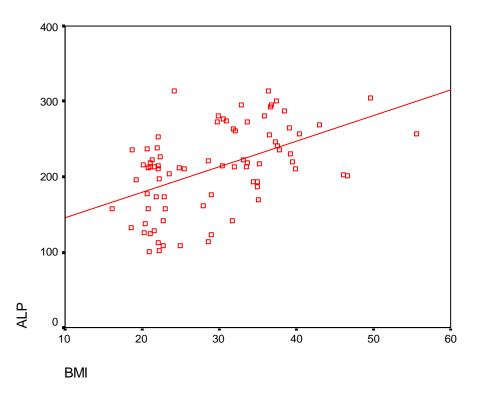
Table (3.2): Comparison between means activity of serum ALT, ALP, GGT and gender.

Variables	Male(no=42) Mean ± SD	Female (no=38) Mean ± SD	P-value
ALT	27.93±10.92	23.03±12.34	0.557
ALP	217.75± 53.99	204.63±58.69	0.301
GGT	35.12±13.18	22.55±6.52	0.000

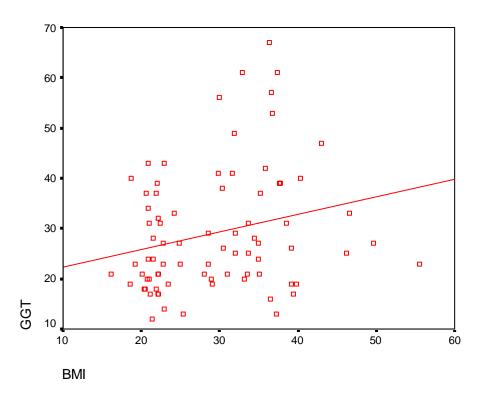
Independent T-test was used , significant when  $\leq 0.05~p$  value considered.



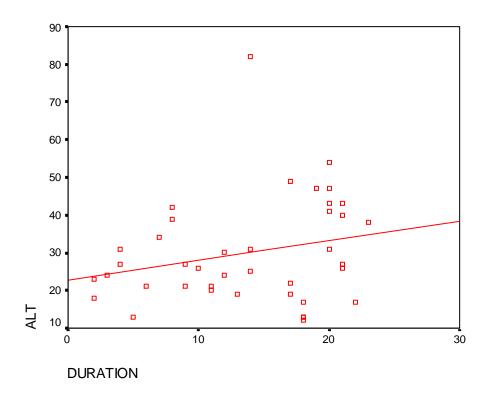
**Figure (3.1):** Correlation between serum ALT levels (U/L) and BMI among Obese Sudanese people (r=0.343, p.value=.002).



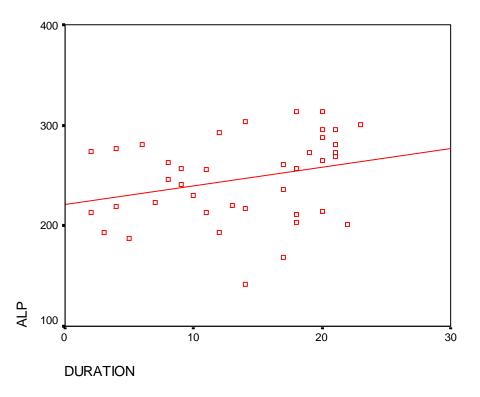
**Figure (3.2):** Correlation between serum ALP levels (U/L) and BMI among Obese Sudanese people (r=0.503, p.value=.000).



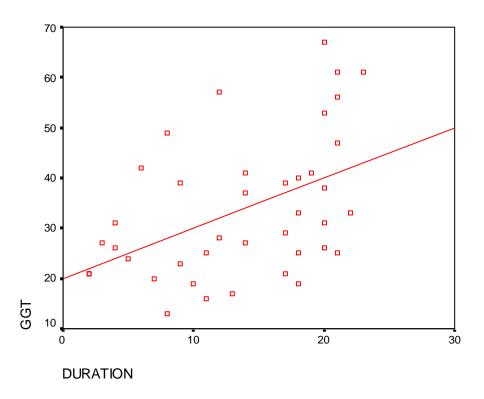
**Figure (3.3):** Correlation between serum GGT levels (U/L) and BMI among Obese Sudanese people (r=0.237, p.value=.034).



**Figure (3.7):** Correlation between serum ALT levels (U/L) and the duration of obesity (r= .241, p.value=.134).



**Figure (3.8):** Correlation between serum ALP levels (U/L) and the duration of obesity (r=.280, p.value=.081).



**Figure (3.9):** Correlation between serum GGT levels (U/L) and the duration of obesity . (r=.461, p.value=.003).

# 4. Discussion, conclusion and recommendations:

**4.1. Discussion:** This was a cross-sectional case control study aimed to measure serum activity of ALT, ALP and GGT among Sudanese obese individuals. Eighty Sudanese individuals (40 obese individuals and 40 normal weight individuals) wereenrolled in this study. After evaluation of serum activity of enzymes, the statistical analysis was done by using SPSS computer program, the results showed significant increase in the mean of ALT, ALP and GGT (in obese compared with the control (p=(0.001),(0.000) and (0.000) respectively. This results agreed with study results done by Antonmoet.al. (Antonmo et al., 1991). Who reported significant increase in the mean of liver enzyme activity of the obese subjects men (P = 0.001) for GGT, (P = 0.001)for ALT. in women, the increase was (P= 0.01) for GGT, (P =0.001) for ALT. Also the results agreed with study results done by Robinson and Whitehead (Robinsons, Whitehead, 1989). who reported marked increases in mean levels of enzymes activity with increasing body mass index (BMI) p=0.001. Also the resulst agreed with study results done by Irfan ,Shabana and Fareeha ( Irfan, Shabana, Fareeha, 2006) The study reported significant elevations of ALT and AST in obese males, ALP levels elevated significantly in obese females only. positive correlation between enzymes activity and BMI also was noted (p=0.05) The results showed positive correlation between enzymes activity of ALT, ALP, GGT and BMI (P=.002, 0.000, 0.034) respectively, and no correlation between ALT and ALP levels with gender (p=0.06,0.3) respectively. and negative correlation with GGT (p=0.000)Also the results showed no correlation between ALT and ALP with the duration of obesity (p=0.13,0.08) respectively, and positive correlation with GGT (p=0.003)

#### 4.2. Conclusion

From the results of this study is concluded that: There were an increase in means activity of serum ALT, ALP and GGT in among obese Sudanese subjects in khartoum state, which directly proportional with increasing BMI. Also the results concluded there was no correlation between serum ALT and ALP levels and Gender, but a negative correlation with serum GGT levels. And there was no correlation between serum ALT, ALP levels and the duration of obesity, but a positive correlation with GGT levels.

**4.3. Recommendations:** From this study it's recommended that:

- Fibro test can be done instead of liver biopsy.
- Further study with evaluation of  $\alpha$ -1 antitrypsin is recommended to predict the influence of liver damage on lungs.

# References

Ajay Kumar Das (2014) "Obesity and the levels of liver enzymes (ALT, AST & GGT) in East Medinipur, India. Anderson M. Land Matsa F.S (2011). "Are Restaurants Supersizing America?" American Economic Journal: Applied Economics 3 (January): 152-88. Antonmo Salvaggio, Maurizio Periti, Lino Miano, Monica Tavanelli, and Daniela Marzorati (1991), Body Mass Index and Liver Enzyme Activity in Serum, CLIN. CHEM. 37/5: 720-723 Barouki R, Chobert MN, Finidori J, Aggerbeck M, Nalpas B, Hanoune J (1983) "Ethanol effects in a rat hepatoma cell line: induction of gamma-glutamyltransferase". Hepatology. 3 (3): 323–9. Betro MG, Oon RC, Edwards JB (1973) "Gamma-glutamyltranspeptidase in diseases of the liver and bone". American Journal of Clinical Pathology. 60 (5): 672–8. PMID 4148049. Celik, Handan; Tosun, Midraci; Cetinkaya, Mehmet Bilge; Bektab, Ahmet; Malatyalýodlu, Erdal (2009) "Markedly elevated serum alkaline phosphatase level in an uncomplicated pregnancy". The Journal of Maternal-Fetal & Neonatal Medicine: The Official Journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians. 22 (8): 705–707

Chang SH, Stoll

CR, Song J, Varela JE, Eagon CJ, Colditz GA (2014) "The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003-2012". JAMA Surgery (Meta-analysis, Review). 149 (3): 275–87. Christensen, Stephen. "Elevated Alkaline Phosphatase & Cancer |". LIVESTRONG.COM. Retrieved 2016-05-10.

CIA world factbook( 2016) Sudan obesity adult prevalence rate. ConsidineRV, Considine EL, Williams CJ, Nyce MR, Magosin SA, Bauer TL, Rosato EL, Caro JF (1995) "Evidence against either a premature stop codon or the absence of obese gene mRNA in human obesity.journal of clinical investigation. Courtay C, Oster T, Michelet F, Visvikis A, Diederich M, Wellman M, Siest G (1992) "Gamma-glutamyltransferase: nucleotide sequence of the human pancreatic cDNA. Evidence for a ubiquitous gamma-glutamyltransferase polypeptide in human tissues".Biochemical Pharmacology. 43 (12): 2527–33

**Dominici S**, Paolicchi A, Corti A, Maellaro E, Pompella A (2005) "Prooxidant reactions promoted by soluble and cell-bound gamma-glutamyltransferase activity". Methods in Enzymology. 401: 484–501.

**Eknoyan**, Garabed (2007) "Adolphe Quetelet (1796-1874)\_ the average man and indices of obesity". Nephrology Dialysis Transplantation. 23(1):47-51

Emdin M, Pompella A, Paolicchi A (2005) "Gamma-glutamyltransferase, atherosclerosis, and

cardiovascular disease: triggering oxidative stress within the plaque". Circulation. 112 (14): 2078–80.**Gadzik**, James(2006) "How much should I weigh? Quetelet's equation, upper weight limit and BMI prime". Connecticut Medicine,70(2):81-88.

**Gennari L**, Di Stefano M, Merlotti D, (2005) "Prevalence of Paget's disease of bone in Italy". J. Bone Miner. Res. 20 (10): 1845–50

**George A**. Bray M.D (1985) Complications of Obesity: Medical And Psychological Problems;103(6\_Part\_2):1052-1062.

**Ghouri N**, Preiss D, Satter N (2010). Liver enzymes, nonalcoholic fatty liver disease and incident cardiovascular disease: a narrative review and clinical perspective of prospective data. Hepatology.52(3).**GiulioMarchesini**, SimonaMoscatiello, Silvia Di Dommizio, Gabriele Forlani (2008) "Obesity-Associated Liver Disease" J Clin Endocrinal Metab: s74-s80.

Global Database on Body Mass Index. World Health Organization" BMI Classification". Retrieved july 27, 2012.

**Goldberg DM** (1980). "Structural, functional, and clinical aspects of gamma-glutamyltransferase". CRC Critical Reviews in Clinical Laboratory Sciences. 12 (1): 1–58.

**Hamann A**, Matthaei S(1996) "Regulation of energy balance by leptin", Endocrinal diabetes. Irfan Zia Qureshi, A. Shabana and A. Fareeha (2006), Effect of Overweight and Obesity on Liver Function in a Sample From Pakistani Population, Physiology Laboratory, Department of Biological Sciences, Quaid-i-Azam University, Pakistan J. Zool., vol. 38(1), pp. 49-54.

**Johnston**, Bradley C, Kanters, Steve, Bandayrel, Kristofer; Wu, Ping, Naji, Faysal;, Siemieniuk, Reed A, Ball, Geoff D. C, Busse, Jason W, Thorlund, Kristian, Guyatt, Gordon, Jansen, Jeroen P, Mills, Edward J. (2014). "Comparison of Weight Loss Among Named Diet Programs in Overweight and Obese Adults". JAMA. 312 (9): 923–33.

**Kaplan MM**(1985). "Biochemical basis for serum enzyme abnormalities in alcoholic liver disease". In Chang NC, Chan NM. Early identification of alcohol abuse. Research Monograph No. 17. NIAAA.p. 186. Kaplan, Marshall M (2005) "Alkaline Phosphatase". New England Journal of Medicine. 286 (4): 200–202.

**Karmen A**, Wroblewski F, Ladue JS(1955) "Transaminase activity in human blood" hTe journal of clinical investigation.34(1):31-126.

**Kronmal R A** (1993)."Spurious correlation and the fallacy of the ratio standard revisited". Journal of the royal statistical society,156(3):379-92.

**LeFevre**, Michael L. (2014). "Behavioral Counseling to Promote a Healthful Diet and Physical Activity for Cardiovascular Disease Prevention in Adults With Cardiovascular Risk Factors: U.S. Preventive Services Task Force Recommendation Statement". Annals of Internal Medicine. 161: 587–93

**Li-Fern H**, Rajasoorya C (1999). "The elevated serum alkaline phosphatase--the chase that led to two endocrinopathies and one possible unifying diagnosis". Eur. J. Endocrinol. 140 (2): 143–7 **Lim JS**, Lee DH, Park JY, Jin SH, Jacobs DR (2007). "A strong interaction between serum gamma-glutamyltransferase and obesity on the risk of prevalent type 2 diabetes: results from the Third National Health and Nutrition Examination Survey". Clinical Chemistry. 53 (6): 1092–8. **Longo,** Dan L.; Heymsfield, Steven B.; Wadden, Thomas A. (2017). "Mechanisms, Pathophysiology, and Management of Obesity". New England Journal of Medicine. 376 (3): 254–266

Luyckx FH (1998)"Liver abnormalities in severely obese subjects: Effect of drastic weight loss after gastroplasty" Departments of Clinical Chemistry, Department of Medicine, CHU SartTilman, University of Lie Áge, Lie Áge, Belgium. Malcolm Kendrick (2015)." Why being overweight means you live longer: the way scintists twist the facts . Michaud, P-C, A. van Soest, T. Andreyeva (2007). "Cross-Country Variation in Obesity Patternsamong Older Americans and Europeans."SEDAP Research Paper No. 185. May 2007. Morkedal, Bjorn, Romundstad, pal R, Vatten, Lars J (2011)," informativeness of indices of blood pressure, obesity and serum lipids in relation to ischaemic heart disease mortality. European journal of Epidemiology. 26(6):457-61.**Ofie** F (2005)"Obesity – A preventable Disease, Endocrine and Metabolic Clinic, Department of Medicine and Therapeutics". University of Ghana Medical School, College of Health Sciences. Ogden C.L, LambM.M., CarrollM.D., and. FlegalK.M(2010) "Obesity and Socioeconomic Status in Adults: United States, 2005-2008." NCHS Data Brief no. 50 Ogden C.L, LambM.M, CarrollM.D, and FlegalK.M (2010). "Obesity and Socioeconomic Status in Children and Adolescents: United States, 2005-2008." NCHS Data Brief no. 51 Rahman, Syed Ashiigur, Adjeroh, Donald(2015)." plos one: surface-based body shape index and its relationship with all cause of mortility. 10(12).

**Raulf**M, Stüning M, König W (1985). "Metabolism of leukotrienes by L-gamma-glutamyl-transpeptidase and dipeptidase from human polymorphonuclear granulocytes". Immunology. 55 (1): 135–47.

Razay G, Vreugdenhil A, Wilcock G (2005). "Obesity, abdominal obesity and Alzheimer disease, dementia and geriatric congestive disorders". RobinsonD and WhiteheadT P (1989). Effect of body mass and other factors on serum liver enzyme levels in men attending for well population screening, BUPA Medical Research, 300 Gray's Inn Road, London WCIX8DU, UK, Ann ClinBiochem 1989; 26: 393—400. Samaras, thomas T (2007). Human Body size and the laws of scaling: physiological, performance growth, longevity and ecological ramifications. New york: nova science . Schulman JD, Goodman SI, Mace JW, Patrick AD, Tietze F, Butler EJ (1975). "Glutathionuria: inborn error of metabolism due to tissue deficiency of gammaglutamyltranspeptidase". Biochemical and Biophysical Research Communications. 65 (1): 68–74.

Shaw LM, Strømme JH, London JL, Theodorsen L (1983)."International Federation of Clinical Chemistry. Scientific Committee, Analytical Section. Expert Panel on Enzymes. IFCC methods for measurement of enzymes; International Journal of Clinical Chemistry. 135 (3): 315F-338F. Shiwaku K, Anuurad E, Enkhmaa B, Nogi A, Kitajima K, Shimono K (2003)."Overweight Japanese with body mass indexes of 23.0\_24.9 have higher risks for obesity-associated disorders: A comparison of Japanese and Mongolians". International journal of obesity.28(1):152-58. Singh D (1994). "Is thin really beautiful and good? Relationship between waist-to-hip ratio (WHR) and female attractiveness. Personality and Individual Differences". 16(1), 123-132 Sukru Aras, SeyfettinUstunsoy and FerahArmuctu (2015). Indices of central and peripheral obesity; anthropometric measurements and laboratory parameters of metabolic syndrome and thyroiodfunction . **Tamás** L, Huttová J, Mistrk I, Kogan G (2002). "Effect of Carboxymethyl Chitin-Glucan on the Activity of Some Hydrolytic Enzymes in Maize Plants" (PDF). Chem. Pap. Tate DF, Jeffery RW, Sherwood NE, Wing RR (2007). "Long-term 56 (5): 326–329 weight losses associated with prescription of higher physical activity goals. Are higher levels of physical activity protective against weight regain?". Am. J. Clin. Nutr.(Randomized Controlled Trial). 85 (4): 954–9. Tate SS, Meister A (1985). "gamma-Glutamyltranspeptidase from kidney". Methods in Enzymology. 113: 400–19. Van der Kooy, K, Leenen, R., Seidell, J. C, Deurenberg, P, Droop, A, & Bakker, C. J (1993). Waist-hip ratio is a poor predictor of changes in visceral fat. The American journal of clinical nutrition, 57(3), 327-333. Ray KimW, Steven L. Flamm, Adrian M. Di Bisceglie, Henery C. BodenheimerJr (2008). "Serum activity of alanine aminotransferase (ALT) as an indicator of health and disease". Hepatology, 47:1363-1370.

Wang CS, Chang TT, Yao WJ, Wang ST, Chou P (2012). Impact of inceasing alanine aminotransaminase levels within normal range on incident diabetes.journal of the Formosan medical association, Taiwan Yi Zhi. 111(4) 8-201. Wang, Youfa(2012), capter 2. Use of percentiles and Z-scores in Anthropometry. In handbook Anthropometry. New york: springer.p.29

Watkins PB,

Kaplowitz N, Slattery JT, Colonese CR, Colucci SV, Stewart PW, Harris SC(2006). Aminotransferase elevations in healthy adults receiving 4 grams of acetaminophen daily: a randomized controlled trial. JAMA. 296(1):87-93

**Whitfield** JB (2001). "Gamma glutamyltransferase". Critical Reviews in Clinical Laboratory Sciences. 38 (4): 263–355.

Wing, R. R., Matthews, K. A., Kuller, L. H., Meilahn, E. N., &Plantinga, P. (1991). Waist to hip ratio in middle-aged women. Associations with behavioral and psychosocial factors and with changes in cardiovascular risk factors. Arteriosclerosis, Thrombosis, and Vascular Biology, 11(5), 1250-1257. Wolfe SM (2013). "When EMA and FDA decisions conflict: differences in patients or in regulation?". BMJ (Clinical research ed.). 347: f5140. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, Pais P,2004, effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries: case control study.

# Appendix I Quesionaire

# **Sudan University of Science and Technology**

# ALT, ALP and GGT Activity Levels among Sudanese obese

1-No:	
2-Age :	
3-Gender:	•••
4- weight :	•••
5- Height:	

A-General information:

BMI:
History of obesity:
B-laboratory investigation:
1.ALT (U/L):
2.ALP (U/L):
3.GGT (U/L):