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**The Effect of Hemodialysis on Alanine
Transaminase And Aspartate
transaminase(ALT&AST) levels in Patients with
Renal Failure**

تأثير الغسيل الدموي علي مستويات انزيمات (الالانين والاسبارتات الناقلين للأمين) في مرضي
الفشل الكلوي

**Desertion submitted in partial fulfillment for master degree
(M.Sc) in clinical chemistry**

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Dedication

TO:

My family.....

My friends.....

My supervisor.....

*With
love*

Ahlam.....

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Thanks first and last to (ALLAH) who enabled me to conduct this study by the grace of him and give me strength and patience, jewel immense debt and respect to my supervisor Dr: Nuha Algaili Abu Baker for her continuous supervision, patience, wisdom, critical comments, invaluable sound advice and careful guidance.

Special thanks and sincere respect to the laboratory technologists in ELnaw hospital for valuable suggestion and close supervision and guidance throughout the course of this work.

Words can never help to express my feelings towards every one stand beside me to carry work, so I would like to thanks all those who offered me as stance and help me to complete this work.

Abstract:

This study was carried out to measure serum levels of the liver enzymes; aspartate transaminase and alanine transaminase in patients with renal failure under hemodialysis. Eighty samples were collected from patients in period between January to March 2015, chosen randomly from ALnaw teaching hospital and Alrebat teaching hospitals, and forty apparently, healthy individuals as controls, to assess the effect of hemodialysis on liver transaminases enzymes level.

Measure serum aspartate transaminase and alanine transaminase were measured by using autoanalyzer mindray BS 200, and results were analyzed using statistical of package social science (SPSS), computer program.

The study showed that the serum levels of aspartate transaminase "AST", and alanine transaminase "ALT" were significantly decreased, (p-value =0.00) in the patients under hemodialysis group. Mean \pm SD controls versus cases. (34 \pm 7 versus 15 \pm 5 u/l) for AST, (24 \pm 7 versus 10 \pm 4 u/l) for ALT.

Also the serum levels of liver transaminase enzymes were measured in 20 cases with renal failure under hemodialysis, to compare the levels of them before dialysis and post dialysis, showed (AST&ALT) were significantly decreased (p-value=0.00) in cases before dialysis when compared to the levels of them after dialysis. Mean \pm SD for predialysis versus post dialysis. (13 \pm 4 versus 22 \pm 4 u/l) for AST, (8 \pm 4 versus 17 \pm 3 u/l) for ALT.

The study indicates that there was no significant difference between the levels of liver transaminase enzymes according to gender "males or females". The results as follow;

Mean \pm SD for male versus female

(10 \pm 4 versus 9 \pm 4 u/l, p-value \leq 0.42) for ALT.

(15 \pm 6 versus 15 \pm 5 u/l, p-value \leq 0.96) for AST.

Also the findings of this study showed that, there was insignificant correlation between body mass index and liver transaminase (AST&ALT) activity, (p-value \leq 0.2 for ALT and \leq 0.6 for AST). Also insignificant correlation between duration of dialysis and (AST&ALT) activity. (P-value \leq 0.8 for ALT and \leq 0.4 for AST).

It is concluded that; the levels of transaminase (AST&ALT) are significantly decreased in patients with renal failure under hemodialysis, and significantly decreased when compared levels of them before dialysis to levels after dialysis.

مستخلص الدراسة

أجريت هذه الدراسة لمقارنه مستويات اثنين من الإنزيمات الكبدية "إنزيم الاسبارتات الناقل للامين وإنزيم الألانين الناقل للامين" في مرضي الفشل الكلوي الذين يخضعون للغسيل الدموي. ثمانون عينه أخذت من هؤلاء المرضى ف الفترة مابين شهر يناير وحتى نهاية مارس . تم اختيارهم بطريقه عشوائية من مستشفى النو , ومستشفى الرباط الجامعي , مع أربعون من الأصحاء كمجموعه تحكم "مجموعه ضابطه" لنقيس مدي تأثير الغسيل الدموي علي مستويات الإنزيمات الكبدية " الاسبارتات الناقل للأمين , والالانين الناقل للامين".

تم قياس مستويات الإنزيمات الكبدية بواسطة جهاز الكيمياء السريري مينيدي , وتم تحليل البيانات بواسطة برنامج الحزمة الإحصائية للعلوم الاجتماعية.

توصلت نتائج هذه الدراسة إلي أن هناك انخفاض ملحوظ في مستويات الاسبارتات والالانين الناقلين للامين في المرضى الذين يخضعون للغسيل الدموي. وكان الاحتمال الإحصائي للمقارنة 0,00 وكانت النتائج كالآتي:-

"المتوسط+ الانحراف المعياري عند المجموعه الضابطة مقارنه بالمرضي"

5±15 مقابل 7±34 وحده/لتر بالنسبة لإنزيم الاسبارتات الناقل للامين .

4±10 مقابل 7±24 وحده/لتر بالنسبة لإنزيم الالانين الناقل للامين .

أيضا تم قياس الإنزيمات الكبدية "الاسبارتات والالانين الناقلين للامين" عند 20 مريض بالفشل الكلوي يخضع للغسيل الدموي, لنقارن مستويات الإنزيمين بعد الغسيل وقبل الغسيل. وجد ان كان هناك انخفاض ملحوظ في مستويات الاسبارتات والالانين الناقلين للامين في المرضى قبل الغسيل مقارنه بالمستويات ما بعد الغسيل. وكان الاحتمال الإحصائي للمقارنة 0,00 وكانت النتائج كالآتي:-

"المتوسط+ الانحراف المعياري عند المرضى قبل الغسيل مقارنه بما بعد الغسيل"

4±13 مقابل 4±22 وحده/لتر بالنسبة لإنزيم الاسبارتات الناقل للأمين .

4±8 مقابل 3±17 وحده/لتر بالنسبة لإنزيم الالانين الناقل للأمين .

في هذه الدراسة أيضا وجد انه لا يوجد تغيير ملحوظ في مستويات الإنزيمات الكبدية الناقلة للأمين تباعا للجنس "ذكر أو أنثي" وكانت النتائج كالآتي:

"المتوسط + الانحراف المعياري عند المرضى الذكور مقارنة بالإناث "

4±10 مقابل 4±9 وحدة/لتر, الاحتمال الإحصائي ≥ 0.42 بالنسبة لإنزيم الالانين الناقل للأمين

6±15 مقابل 5±15 وحدة/لتر, الاحتمال الإحصائي ≥ 0.96 بالنسبة لإنزيم الاسبارتات الناقل للأمين .

أيضا خلصت النتائج إلي انه ليس هناك علاقة ملحوظة بين ارتفاع مؤشر كتله الجسم وبين التغير في مستويات الالانين والاسبارتات الناقلين للأمين وكان الاحتمال الإحصائي ≥ 0.2 بالنسبة لإنزيم الالانين الناقل للأمين, و ≥ 0.6 بالنسبة لإنزيم الاسبارتات الناقل للأمين. كما وجد أيضا انه ليس هناك علاقة ملحوظة بين الفترة الزمنية للغسيل وبين مستويات الالانين الناقل للأمين (الاحتمال الإحصائي ≥ 0.8) والاسبارتات الناقل للأمين (الاحتمال الإحصائي ≥ 0.4).

خلصت هذه الدراسة إلي أن مستويات الإنزيمات الناقلة للأمين يحدث بها نقصان ملحوظ في مرضي الفشل الكلوي الذين يخضعون للغسيل الدموي. كما أن مستويات هذه الإنزيمات تنخفض قبل الغسيل الدموي مقارنة بما بعده .

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Abbreviations:

abbreviation	Meaning
ALT	Alanine Transaminase
ALP	Alkaline Phosphatase
AST	Aspartate Transaminase
BMI	Body Mass Index
CKD	Chronic Kidney Disease
ESRD	End Stage Renal Disease
GGT	Gama Glutamyle Tranferase
GFR	Glomerular Filtration Rate
HD	Hemodialysis
HCV	Hepatitis C Virus
LFTs	Liver Function Tests
NTP	Nucleotide Phosphatase
RFTs	Renal Function Tests
SGOT	Serum Glutamic-Oxaloacetic Transaminase
SGPT	Serum Glutamic-Pyruvic Transaminase

Chapter one

1.1 Introduction

Kidneys are the organs that help filter waste products from the blood. They are also involved in regulating blood pressure, electrolyte balance, and red blood cell production in the body. Kidneys are located just below the rib cage, one on each side of the spine. Renal failure is a condition in which the kidneys fail to remove metabolic end-products from the blood and regulate the fluid, electrolyte, and pH balance of the extracellular fluids. Renal failure can occur as an acute or a chronic disorder.

(Benjamin; 2011)

End stage renal failure (ESRD) is when the kidneys stop working well enough without dialysis or a transplant. This kind of kidney failure is permanent.

Hemodialysis is most commonly used to treat people with end-stage kidney disease; Blood is filtered using a dialyzer and dialysis machine. During a hemodialysis session, your blood flows a little bit at a time through a special filter inside the machine. The filter removes wastes and extra fluids from your blood, but retains the proper balance of minerals such as potassium and sodium. Once the blood is cleaned, it is returned to the body. (Melinda; 2014).

Liver enzyme tests are a group of blood tests that detect inflammation and damage to the liver. They can also check how well the liver is working. Liver enzyme testing includes ALT, AST, and alkaline phosphatase.

Aminotransferases are enzymes (proteins that help speed up chemical reactions in the body) that are found mainly in the liver, but also in other tissues, such as muscles. They are a part of the normal metabolic processes in the liver and are responsible for transferring amino acids (components that build proteins) from one molecule to another. ALT was formerly known as serum glutamic-pyruvic transaminase (SGPT) and AST as serum glutamic-oxaloacetic transaminase (SGOT).

Elevated levels of liver enzymes in general signify some form of liver (or hepatic) damage or injury.

some studies have shown that patients with chronic kidney disease (CKD) on hemodialysis may have lower serum levels of liver enzymes than those with normal renal function for reasons may be lower because of a deficiency in vitamin B6, which is a coenzyme of ALT& AST or hemodilution, which occurs because of water retention in patients with renal failure before an hemodialysis session. This profile may adversely affect the diagnosis, clinical management, and treatment of liver disease in these patients (Luiset *al*; 2014).

The prevalence of hepatitis C virus (HCV) infection is significantly higher in hemodialysis patients than in the general population.

Studies have revealed that Patients with chronic kidney disease (CKD) who are undergoing hemodialysis and are infected with hepatitis C virus (HCV) have been shown to present with lower serum levels of alanine aminotransferase (ALT) and (AST) than HCV-infected patients with normal renal function. ALT serum levels are lower in patients with renal failure undergoing hemodialysis compared with the population that has normal renal function. (ALT&AST) levels may be lower due to hemodilution, which occurs because of water retention in patients with chronic kidney disease (CKD) before an hemodialysis HD session (Isabellaet *al*; 2012).

1.2 Rationale:

Renal failure is a devastating medical, social and economic problem in Sudan and it is fatal unless treated properly. Recent studies were done in Sudan to determine the mortality rate and causes of mortality and found that the mortality rate was 7.44% per year and the leading cause of death was infections (45%) and cardiovascular (22%) diseases. (Mohamed Elhafiz; 2008). According to the latest WHO data published in April 2011 Kidney Disease Deaths in Sudan reached 8,782 or 2.38% of total deaths, ranked the renal failure in 7th top 20 causes of death in Sudan.

Studies have revealed that alanine transaminase and aspartate transaminase (ALT&AST) serum levels are lower in patients with renal failure compared with patients with normal renal function, which raises the question of whether the lower levels are related to chronic kidney disease factors or to the hemodialysis treatment. Many studies around the world were done and showed that these enzymes are decreased in patient under hemodialysis and returned that to many causes but they were not discovered the real cause.

On the other hand the hepatitis is the most risk disease happened to patients under dialysis, and the liver enzymes (AST&ALT) are one of tests used to diagnosis hepatitis and other liver diseases.

This study was conducted to high light the effect of hemodialysis on liver transaminases in Sudanese patients with renal failure patients under hemodialysis.

1.3 Objectives

1. General objective:

To assess the effect of hemodialysis on the levels of serum liver enzymes (AST&ALT) in patient with renal failure.

2. Specific objectives:

1. To estimate levels of (AST&ALT) in patients with renal failure under dialysis comparison with control group.
2. To compare the levels of aspartate and alanine transaminase (AST&ALT) levels predialysis and postdialysis.
3. To correlate between body mass index (BMI), duration of dialysis and liver enzymes (ALT&AST) in patients with renal failure under hemodialysis.

Chapter two

Chapter two

2. Literature review

2.1The renal:

2.1.1 Renal anatomy:

The kidneys are paired, bean shaped organs located retroperitoneally on either side of the spinal column. Macroscopically, a fibrous capsule of connective tissue encloses each kidney. When dissected longitudinally, two regions can be clearly discerned an outer region called the cortex and an inner region called the medulla. The pelvis can also be seen. It is basin like cavity at the upper end of ureter into which newly formed urine passes. (Michel Bishop; 2010). The bilateral ureters are thick-walled canals, connecting the kidneys to the urinary bladder. Urine is temporarily stored in the bladder until voided from the body by way of the urethra. The nephrons are functional units of the kidney that can be only seen microscopically. Each nephron is a complex apparatus comprised of five basic parts. The glomerulus is a capillary tuft surrounded by the expanded end of a renal tubule known as Bowman's capsule. The proximal convoluted tubules located in the cortex, the long loop of henle composed of thin descending limb, which spans the medulla, and the ascending limb which located in both the medulla and the cortex. The distal convoluted tubules located in the cortex and the collecting duct formed by two or more distal convoluted tubules as they pass back down through the cortex and the medulla to collect the urine that drains from each nephrons. (Michel Bishop; 2010)

2.1.2 Renal physiology:-

There are three basic renal processes:

2.1.2.1:-Glomerular filtration: Is filtering of incoming blood. Several factors facilitate filtration like high pressure in the glomerular capillaries and semi permeable glomerular basement membrane. This means that water, electrolytes, and small dissolved solutes, such as glucose, amino acid, urea and creatinin, pass freely through the basement membrane and enter the proximal convoluted tubules. Other blood constituents such as albumin and many plasma proteins are too large to be filtered. In addition because the basement membrane is negatively charged, negatively charged molecules, such as proteins are repelled (Micael.Bishop;2010).

2.1.2.2:-Tubular reabsorption: is return the bulk of each valuable substance back to blood circulation .thus 75% of water, sodium, and chloride; 100% of the glucose; almost all of the amino acids, vitamins, and protein, and varying amounts of urea, uric acid, and ions.

2.1.2.3:-Tubular secretion: used in two way; Tubular secretion describes the movement of substances from peri tubular capillary plasma to the tubular lumen, and when tubule cells secret products of their own cellular metabolism into the filtrate in the tubular lumen. (Micael Bishop; 2010).

2.1.3 Renal function test:-

Renal function tests (RFTs) is a group of tests used to assess if the renal system is functioning well or not. Or if there is abnormal pain, symptoms, or injury to one of the two kidneys

2.1.3.1 Clearance measurements:

Clearance is defined as the volume of plasma from which a measured amounts of substance can be completely eliminated into the urine per unit of time expressed in milliliters per minute

Creatinine is a nearly ideal substance for the measurement of clearance synthesized at a constant rate for a given individual and cleared essentially only by glomerular filtration. It is not reabsorbed and is only slightly secreted by the proximal tubule. Serum creatinine levels are higher in males than females due to the direct correlation with muscle mass. Analysis of creatinine is simple and inexpensive using colorimetric assays.

Calculation of creatinine clearance has become the standard laboratory method to determine glomerular filtration rate (GFR).

Urea clearance was one of the first clearance tests performed. Urea is freely filtered at the glomerulus and approximately 40% reabsorbed by the tubules. For this reason, it does not provide a full clearance assessment. But we can estimate urea randomly by any chemical or enzymatic method available. Urea concentration gives general background on how kidney functions. (Micael.Bishop; 2010)

CystatinC:-Is a low-molecular-weight protein produced by nucleated cells. It is freely filtered by the glomerulus reabsorbed, and catabolized by the proximal tubule. A rise in cystatin C is often detectable before there is a measureable decrease in glomerular filtration rate GFR or increase in creatinine.

2.1.3.2 Urine Electrophoresis: normal urinary protein excretion only about 50–150 mg every 24 hours. Proteinuria may develop when there are defects in renal reabsorption or glomerular capillary permeability or when there is a significant increase in serum immune globulins. As a result, urine electrophoresis is used primarily to distinguish between acute glomerular nephropathy and tubular proteinuria. It is also used to screen for abnormal monoclonal or polyclonal globulins.

2.1.3.3 B2-Microglobulin (B2-M) is a small, nonglycosylated peptide found on the surface of most nucleated cells. Elevated levels in serum indicate increased cellular turnover as seen in myeloproliferative and lymphoproliferative disorders, inflammation, and renal failure. Measurement of serum B₂-M is used clinically to assess renal tubular function in renal transplant patients, with elevated levels indicating organ rejection.

2.1.3.4 microalbuminuria describes small amounts of albumin in urine. Urine micro albumin measurement is important in the management of patients with diabetes mellitus, who are at serious risk of developing nephropathy over their lifetimes

2.1.3.5 Urinalysis (UA) permits a detailed, in-depth assessment of renal status with an easily obtained specimen. UA also serves as a quick indicator of an individual's glucose status and hepatic-biliary function. Routine UA includes assessment of physical characteristics, chemical analyses,

And a microscopic examination of the sediment from a (random) urine specimen.(Micael Bishop; 2010).

2.1.4 Renal failure:

Renal failure is a condition in which the kidneys fail to remove metabolic end-products from the blood and regulate the fluid, electrolyte, and pH balance of the extracellular fluids. Renal failure can occur as an acute or a chronic disorder.

2.1.4.1 Acute renal failure:

Is a sudden, sharp decline in renal function as a result of an acute toxic or hypoxic insult to the kidneys, defined as occurring when the GFR is reduced to less than 10ml/minute.

This syndrome is subdivided into three types:

2.1.4.1.1 Pre renal failure: the defect in the blood supply before it reaches the kidney. Causes can include cardiovascular system failure and consequent hypo volemia.

2.1.4.1.2 Primary renal failure: the defect involves the kidney. Most common cause is acute tubular necrosis.

2.1.4.1.3 Post renal failure: the defect lies in the urinary tract as consequence of lower urinary tract obstruction or rupture of the urinary bladder. (Micael Bishop; 2010)

2.1.4.2 Chronic renal failure:-

Chronic renal failure describes abnormal kidney function and/or structure. There is evidence that treatment can prevent or delay the progression of chronic kidney disease, reduce or prevent the development of complications, and reduce the risk of cardiovascular disease (CVD).

The Chronic renal failure is based on the presence of kidney damage (i.e. albuminuria) or decreased kidney function (i.e. glomerular filtration rate (GFR) <60 ml/minute per 1.73 m^2) for three months or more, irrespective of clinical diagnosis. (Levey *et al*; 2012).

2.1.4.2.1 Causes:-

Poorly controlled diabetes

Poorly controlled high blood pressure

Chronic glomerulonephritis.

Polycystic kidney disease, Reflux nephropathy (damage caused by urine backflow from the bladder into the ureters and kidney), Nephrotic syndrome, Alport's disease, Kidney stones, and Prostate disease. (Benjamin; 2011).

2.1.4.2.2 Symptoms:-

Patients with chronic renal failure stages 1-3 (GFR >30 mL/min/1.73 m²) are generally asymptomatic. Typically, it is not until stages 4-5 (GFR < 30 mL/min/1.73 m²) that endocrine/metabolic derangements or disturbances in water or electrolyte balance become clinically manifest..

Lethargy

Weakness

Shortness of breath

Generalized swelling (edema)

Generalized weakness due to anemia

Loss of appetite

Lethargy

Fatigue

Congestive heart failure

Metabolic acidosis

High blood potassium (hyperkalemia)

Fatal heart rhythm disturbances (arrhythmias) including ventricular tachycardia and ventricular fibrillation.

Rising urea levels in the blood (uremia) may lead to brain encephalopathy, pericarditis (inflammation of the heart lining), or low calcium blood levels (hypocalcemia). (Benjamin; 2015).

2.1.4.2.3 Stage

Stage 1

Slightly diminished function; kidney damage with normal or relatively high GFR (≥ 90 ml/min/1.73 m²).

Stage 2

Mild reduction in GFR (60–89 ml/min/1.73 m²) with kidney damage: Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine test or imaging studies.

Stage 3

Moderate reduction in GFR (30–59 ml/min/1.73 m²):. British guidelines distinguish between stage 3A (GFR 45–59) and stage 3B (GFR 30–44) for purposes of screening and referral.

Stage 4

Severe reduction in GFR (15–29 ml/min/1.73 m²)[1] Preparation for renal replacement therapy

Stage 5

Established kidney failure (GFR < 15 ml/min/1.73 m², permanent renal replacement therapy. (Waknine;2012).

2.1.4.2.4 Investigation

Investigations are focused on assessment of renal function and therefore stage of chronic kidney disease, identification of the underlying cause and assessment of complications of chronic kidney disease.

Assessment of renal function:

- Serum urea is a poor marker of renal function, because it varies significantly with hydration and diet, is not produced constantly and is reabsorbed by the kidney
- Serum creatinine also has significant limitations. The level can remain within the normal range despite the loss of over 50% of renal function
- GFR

Biochemistry-

Plasma glucose: to detect undiagnosed diabetes or assess control of diabetes-

- Serum sodium: usually normal, but may be low-
- Serum potassium: raised
- Serum bicarbonate: low
- Serum albumin: hypoalbuminaemia in patients who are nephrotic and/or malnourished (low levels at the start of dialysis are associated with a poor prognosis.
- Serum calcium: may be normal, low or high
- Serum phosphate: usually high
- Serum alkaline phosphatase: raised when bone disease develops-
- Serum parathyroid hormone: rises progressively with declining renal function
- Serum cholesterol and triglycerides: dyslipidaemia is common-

Hematology:

- Normochromic normocytic anemia; hemoglobin falls with progressive chronic kidney disease.
- White cells and platelets are usually normal.

(Levey; 2012)

2.1.4.2.5 Chronic renal failure and hepatitis C

Hepatitis C is a type of infectious virus that is spread through the blood. Also referred to as HCV, this form of hepatitis is considered dangerous because its symptoms may not show up for months, or even years after the initial infection occurs and may either be acute or chronic. Furthermore, there is no vaccine available for this type of hepatitis. (Kristeen ; 2014).

Both HCV and chronic renal disease are common and potentially serious medical problems throughout the world. In recent years, it has become clear that these two conditions are linked in several important ways. Indeed, some forms of renal disease are precipitated by HCV infection. However, patients with end-stage renal disease (ESRD) are at increased risk for acquiring HCV infection,.HCV infection results in an increase in serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), a nonspecific marker of liver damage. The diagnostic value of ALT,AST measurement to assess acute or chronic HCV infection however, rather weak in chronic kidney disease (CKD) patients, particularly in those on renal replacement therapy with hemodialysis or kidney transplant, since normal aminotransferase levels have been often reported in this patient population . This inconsistency has been ascribed to vitamin B6 deficiency, presence of uremic toxins, or UV-absorbing components in the blood that could alter the transaminase detection. Moreover, serum ALT level does not correlate with the viral load or with tissue liver injury, further indicating the shortcoming of this tool to monitor HCV infection. (Giuseppe; 2009).

Hemodialysis patients are at particular high risk for blood borne infections because of prolonged vascular access and potential for exposure to contaminated equipment. It has been estimated that, among patients on hemodialysis. (Giuseppe; 2009).

Studies have revealed that Patients with chronic kidney disease (CKD) who are undergoing hemodialysis (HD) and are infected with hepatitis C virus (HCV) have been shown to present with lower serum levels of alanine aminotransferase (ALT) than HCV-infected patients with normal renal function, Even in non-infected HCV patients, ALT serum levels are lower in patients with renal failure undergoing hemodialysis compared with the population that has normal renal function. ALT levels may be lower because of a deficiency in vitamin B6, which is a coenzyme of ALT, or hemodilution, which occurs because of water retention in patients with renal failure before anhemodialysis session. (Isabella *et al*; 2012).

2.1.5 Dialysis:-

Dialysis cleanses the body of waste products in the body by use of filter systems.

2.1.5.1 Type of dialysis: -There are two types of dialysis; 1) hemodialysis, and 2) peritoneal dialysis.

2.1.5.1.1 Hemodialysis: uses a machine filter called a dialyzer or artificial kidney to remove excess water and salt, to balance the other electrolytes in the body, and to remove waste products of metabolism. Blood is removed from the body and flows through tubing into the machine, where it passes next to a filter membrane. A specialized chemical solution (dialysate) flows on the other side of the membrane. The dialysate is formulated to draw impurities from the blood through the

filter membrane. Blood and dialysate never touch in the artificial kidney machine.

For this type of dialysis, access to the blood vessels needs to be surgically created so that large amounts of blood can flow into the machine and back to the body. Surgeons can build a fistula, a connection between a large artery and vein in the body, usually in the arm, that allows a large amount of blood flow into the vein. This makes the vein swell or dilate, and its walls become thicker so that it can tolerate repeated needle sticks to attach tubing from the body to the machine. Since it takes many weeks or months for a fistula to mature enough to be used, significant planning is required if hemodialysis is to be considered as an option.

If the kidney failure happens acutely and there is no time to build a fistula, special catheters may be inserted into the larger blood vessels of the arm, leg, or chest. These catheters may be left in place for weeks. In some diseases, the need for dialysis will be temporary, but if the expectation is that dialysis will continue for a prolonged period of time, these catheters act as a bridge until a fistula can be planned, placed, and matured. (Benjamin; 2011).

Dialysis treatments normally occur three times a week and last a few hours at a time. Most commonly, patients travel to an outpatient center to have dialysis, but home dialysis therapy is becoming an option for some. Outpatient dialysis is available on some cruise ships. They are equipped with dialysis machines with trained health care professionals ready to care for those with kidney failure while traveling. (Benjamin; 2011).

2.1.5.1.2 Peritoneal dialysis: uses the lining of the abdominal cavity as the dialysis filter to rid the body of waste and to balance electrolyte levels. A catheter is placed in the abdominal cavity through the

abdominal wall by a surgeon, and it is expected to remain in place for the long-term. The dialysis solution is then dripped in through the catheter and left in the abdominal cavity for a few hours and then is drained out. In that time, waste products leech from the blood flowing through the lining of the abdomen (peritoneum), and attach themselves to the fluid that has been instilled by the catheters. Often, patients instill the dialysate fluid before bedtime, and drain it in the morning.(Benjamin; 2011)

There are benefits and complications for each type of dialysis. Not every patient can choose which type he or she would prefer. The treatment decision depends on the patient's illness and their past medical history along with other issues. Usually, the nephrologist (kidney specialist) will have a long discussion with the patient and family to decide what will be the best option available.

Dialysis is life-saving. Without it, patients whose kidneys no longer function would die relatively quickly due to electrolyte abnormalities and the buildup of toxins in the blood stream. Patients may live many years with dialysis but other underlying and associated illnesses often are the cause of death. (Benjamin; 2011)

2.1.5.2 Side effect of dialysis

The National Kidney Foundation's list of the five most common side effects:

2.1.5.2.1 Low blood pressure is the most common side effect of dialysis, affecting one out of four patients at some point over the course of dialysis treatments. The two primary causes are gaining excess fluid weight between sessions and having a weak heart.

2.1.5.2.2 Nausea and vomiting are associated with kidney disease in general but low blood pressure and excess fluid weight gain are also common causes. If experienced during a dialysis treatment, inform the nurse who can adjust the machine accordingly.

2.1.5.2.3 Dry or itchy skin is experienced by many patients undergoing dialysis, especially in the winter.

2.1.5.2.4 Restless leg syndrome is another common side effect that causes patients to keep moving their legs as a result of the leg nerves and muscles creating a crawly or prickly sensation. Restless leg syndrome can be tied to some forms of kidney disease, diabetes, hardening of the arteries, or a vitamin B deficiency..

2.1.5.2.5 Muscle cramping causes extreme discomfort to many patients. (National Kidney Foundation; 2015).

2.2 The liver

Is the largest organ that occupies the upper part of abdominal cavity, it lies almost entirely under cover the ribs and costal cartilage and extends across the epigastric region (Snell; 2008).

There are, on the surface, four lobes right, left caudate and quadrate, the falciform ligament divides the liver into two main lobes right and left with the right lobe being the largest and is sub divided into the right lobe proper, the caudate lobe and quadrate lobe. (Cars Well; 1992).

2.2.1 Liver function

2.2.1.1 Synthetic function:-

The liver synthesizes many major biological compounds as proteins (excluding immunoglobulin and complements), enzymes (AST, ALT ALP 5-NT and GGT), most coagulation factor including fibrinogen, factors 2 5 7 9 12 13. Also it synthesizes lipoproteins such as VLDL and HDL. (Crook; 2006).

2.2.1.2 Metabolic function:-

Liver has many metabolic functions include glycolysis, glucogenesis, lipolysis, lipogenesis, glycogenolysis and glycogenesis (Bishop *et al*; 2005).

2.2.1.3. Storage function:-

The liver is the storage site for all fat soluble vitamins such as (A D K E) and several water soluble vitamins such as (B12). It is also responsible for conversion of carotene into vitamin A. (Bishop; *et al* 2005).

2.2.1.4. Detoxification function:-

Liver is responsible for many detoxification mechanisms including oxidation, reduction, hydroxylation, carboxylation, demethylation and hydrolysis. These mechanisms convert many noxious insoluble compounds into less toxic or more water soluble (Bishop; *et al* 2005).

2.2.1.5. Excretory and Secretary Function:-

One of the most important processes is the bile excretion that comprise of bile acids, bile salts, bile pigments, cholesterol and other extracted from the blood. (Bishop; *et al* 2005).

2.2.3. Liver enzymes

Enzymes are specific biologic proteins that catalyze biochemical reactions without altering the equilibrium point of the reaction or being consumed or changed in composition. The catalyzed reactions are frequently specific and essential to physiologic functions, such as the hydration of carbon dioxide, nerve conduction, muscle contraction, nutrient degradation, and energy use. Found in all body tissue, enzymes frequently appear in the serum following cellular injury or, sometimes, in smaller amounts, from degraded cells. (Michel Bishop; 2006)

Liver enzymes are proteins made by the liver that are measured in the blood, with a blood draw. Liver enzymes tell us how well your liver is functioning. Elevated liver enzymes may indicate inflammation or damage to cells in the liver. Inflamed or injured liver cells leak higher than normal amounts of certain chemicals, including liver enzymes, into the bloodstream, which can result in elevated liver enzymes on blood tests. (Florkin ; 2002)

2.2.3.1 Transaminases:

Aminotransferases constitute a group of enzymes that catalyze the interconversion of amino-acids and 2-oxoacids by transfer of the amino groups.

The transamination reaction is important in intermediary metabolism because of its function in the synthesis and degradation of amino acids. The ketoacids formed by the reaction are ultimately oxidized by the tricarboxylic acid cycle to provide a source of energy. (Michel Bishop;2006).

Among the transaminases ALT and AST are of greatest clinical significance.

Distinct iso enzymes of both ALT and AST are present: a cytoplasmic iso enzymes and mitochondria one. In the conditions associated with a mild degree of tissue injury, the predominant form of either iso enzyme will also be present.

Sever tissue damage will result in the release of much mitochondrial enzymes as well. (Florkin ; 2002)

2.2.3.1.1 Aspartate transaminase (AST):

This enzyme is still widely known as glutamic oxaloacetic transaminase (GOT).AST catalyze transamination reaction. AST exist two different iso enzyme forms which are genetically distinct, the mitochondrial and cytoplasmic form. AST is found in highest concentration in heart compared with other tissues of the body such as liver, skeletal muscle and kidney (Mauro; 2006). The two major iso enzymes have been demonstrated in plasma following tissue damage, their differentiation has not been shown to be of much diagnostic value.

2.2.3.1.2 Clinical application:

Increased activities of AST in plasma are of considerable diagnostic help in recognition of myocardial infarction and other conditions associated with myocardial damage (e.g. rheumatic carditis). Peak levels of plasma AST observed after myocardial infarction are usually between 60 and 300 i.u/l (reference value 10 – 15u/l). (Wilkinson; 1976).

Measurement of plasma AST may also be of value when investigating patients with acute liver damage. In these patients, enzymic activity is usually more than 200i.u/l. if the damage is severe enough to cause jaundice. The peak may occur in the prodromal stage of disease.

In chronic liver disease much smaller, elevations are frequently observed.

These may indicate the presence of continuing hepatocellular damage. Increased activity of plasma AST occurs in patients with muscular dystrophy, but the extent of the rise is relatively much smaller than the increase in creatine kinase activity. High plasma AST activity may also be in patient's acute renal failure or pulmonary infarction, acute pancreatitis, or when liver damage occurs secondary to heart failure or pulmonary infarction.

Transaminases are widely distributed in animal tissue. Both AST and ALT are normally present in human plasma, bile, cerebrospinal fluid and saliva, but none is found in urine unless a kidney lesion is present. (Berg; 2000).

2.2.3.1.3 Alanine transaminase (ALT):

This enzyme, still frequently called glutamic pyruvic transaminase (GOT), is also widely distributed, but its concentration in most tissues is

considerable less than AST. However, in liver, the activities of the two enzymes are of the same magnitude. (Baron; 2001)

ALT is a protein which, found in the blood in elevated quantities, generally indicates liver damage. It is found mainly in liver cells and there it offers little other advantages. In most liver disease, the AST increase is less than that of ALT (AST/ALT ratio is less than 1), except in alcohol related liver injury where the ratio is usually more than 2. (Berg-Mayer; 2000).

2.2.3.1.4 Clinical application:

Plasma ALT activity is very commonly measured as a test for hepatocellular damage. In early viral hepatitis and other types of acute liver cell injury, it is usually increased to greater extent than AST.

Whereas plasma AST activity tends to be higher than ALT activity in patients with chronic hepatic disease. Small increases in plasma ALT occur in un complicated myocardial infarction: larger increase may occur when there is cardiac failure, presumably as a result of liver congestion.

Since ALT is widely distributed, increased plasma activity may be observed in many other conditions associated with tissue injury. For instance, plasma ALT activity sometimes rise in acute pancreatitis, acute renal disease and disseminated carcinoma, but these findings are not sufficiently specific to be of much assistance in diagnosis. (Bowers; 1972).

2.2.3.1.5 AST/ALT ratio

Ratio of AST to ALT has been used as a diagnostic aid

AST: ALT ratio of more than 2:1 is characteristic in patients with alcoholic liver disease

A raised AST level out of proportion to the ALT level appears to be caused by a differential reduction in hepatic ALT due to deficiency of the cofactor pyridoxine-5-phosphate

AST: ALT ratio of more than 2:0 is suggestive of alcoholic liver disease - however this result does not preclude other diagnoses

a raised ALT level to more than 500 IU/L suggests a diagnosis other than alcoholic liver disease, even if the AST:ALT ratio is greater than 2:0

Other blood tests also suggestive of the presence of alcoholic liver disease include raised of serum gamma-glutamyltranspeptidase (GGT) level and mean corpuscular volume

In viral hepatitis:

The AST: ALT ratio, which is typically less than 1:0 (particularly true in patients with hepatitis C), can rise to greater values as fibrosis and cirrhosis develop.

Exact mechanism of AST: ALT ratio alteration in progression of liver disease is unclear, and the correlation with and accuracy in predicting degree of fibrosis and presence of cirrhosis are controversial.

In many forms of acute and chronic liver injury or steatosis (fatty infiltration of the liver), the ratio is less than or equal to 1. (Gopal; 2000).

2.2.4 Liver Diseases:

Liver disease is any disturbance of liver function that causes illness. The liver is responsible for many critical functions within the body and should it become diseased or injured, the loss of those functions can cause significant damage to the body. Liver disease is also referred to as hepatic disease

Infectious hepatitis:

The term "hepatitis" means inflammation, and liver cells can become inflamed because of infection.

Hepatitis A is a viral infection that is spread primarily through the fecal-oral route when small amounts of infected fecal matter are inadvertently ingested. Hepatitis A causes an acute inflammation of the liver which generally resolves spontaneously. The hepatitis A vaccine can prevent this infection. Thorough hand washing, especially when preparing food is the best way to prevent the spread of hepatitis A.

Hepatitis B is spread by exposure to body fluids (needles from drug abusers, contaminated blood, and sexual contact) and can cause an acute infection, but can also progress to cause chronic inflammation (chronic hepatitis) that can lead to cirrhosis and liver cancer. The hepatitis B vaccine can prevent this infection.

Hepatitis C causes chronic hepatitis. An infected individual may not recall any acute illness. Hepatitis C is spread by exposure to body fluids (needles from drug abusers, contaminated blood, and some forms of sexual contact). Chronic hepatitis C may lead to cirrhosis and liver cancer. At present, there is no vaccine against this virus. There is a recommendation to test all people born between 1945 and 1965 for

Hepatitis C antibody to identify people who do not know that they have contracted the disease.

Hepatitis D is a virus that requires concomitant infection with hepatitis B to survive, and is spread via body fluid exposure (needles from drug abusers, contaminated blood, and sexual contact).

Hepatitis E is a virus that is spread via exposure to contaminated food and water. (Benjamin; 2011).

2.3 Studies review:

On study done by Federal University of Pernambuco (UFPE), Department of Internal Medicine reviewed the literature regarding the serum levels of the enzymes aspartate aminotransferase, alanine aminotransferase in patients with chronic kidney disease on hemodialysis. Showed that, Since the 1970s, studies have shown that AST and ALT serum levels were decreased in CKD patients undergoing hemodialysis. It was hypothesized that this reduction could be caused by factors such as the withdrawal of aminotransferases during the session. In assessing the possibility of this pyridoxine deficit,

In the 1980s, Jung et al. evaluated the levels of aminotransferases in CKD patients on HD and did not observe differences between the values prior to and after the addition of pyridoxal 5'-phosphate (PLP).

In the 1990s, Ono et al. performed a prospective study in which they administered pyridoxine (30 mg/day) to 52 CKD patients on hemodialysis for 5 weeks. There were positive correlations between pyridoxine and AST levels ($r=0.57$; $p<0.01$) and ALT levels ($r=0.68$; $p<0.01$). The mean serum levels of AST and ALT were significantly lower in Group 1 than in Group 2. These researchers concluded that the

low AST and ALT levels in patients on HD were partly due to a deficiency in pyridoxine, which serves as a coenzyme in the synthesis of the aminotransferases.

(Huang et al; 2002) evaluated the homocysteine serum levels in 145 patients on HD. All patients had elevated homocysteine levels, which were inversely related to the AST levels ($r=0.4$; $p<0.001$). There was no relationship between serum homocysteine and ALT levels

Subsequently, some researchers have suggested that the aminotransferase serum levels could be reduced even during conservative treatment at earlier stages of CKD. (Fabrizi et al; 2002) observed that the CKD patients on dialysis had decreased AST and ALT serum levels compared with the healthy controls

In more recently study from (Department of Chemical Pathology, Ladoke Akintola University of Technology Teaching Hospital, Nigeria). A total of 100 subjects were used to carry out the study. 50 were CKD patients who have not undergone dialysis therapy, while the remaining 50 were apparently healthy adults. The levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were estimated using colorimetric method. The results indicated that both AST and ALT were significantly low ($p<0.05$) in both sexes when compared with their counterparts in the control group. (Mujeeb; 2014)

Chapter three

3. Materials and methods

3.1 Materials

3.1.1 Study approach

A quantitative method were used to measure Aspartate transaminase and Alanine transaminase (AST&ALT) activity in Sudanese patients with renal failure in Khartoum state, during the period from January to March 2015.

3.1.2 Study design:

This is a cross- sectional, control, and hospital case based study.

3.1.3 Study area:

This study was conducted in Alnaw hospital, and Alrebat hospital, in Khartoum state.

3.1.4 Target population:

The study included patients with renal failure (males and females) under hemodialysis.

3.1.5 Sample size:

A total of 80 patients with renal failure were enrolled in this study, and (40) apparently healthy volunteers' (age and sex matched with the test group) were included to serve as control.

3.1.6 Inclusion and Exclusion criteria:

Sudanese patients with end stage renal failure and apparently healthy volunteers were included, while patients with hepatitis positive were excluded.

3.1.7 Ethical consideration:

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

3.1.8 Data collection:

The Clinical data were obtained from history, clinical examination and hospital follow up records and were recorded on a questionnaire sheet.

3.1.9 Sample collection and processing:

Use of a local antiseptic for the skin (70%), 3 ml of venous blood was collected from the forearm of each patient and control by syringe (3ml) using venipuncturing directly into centrifuge tube which contained anticoagulant for serum preparation. Serum was separated from blood cells after centrifugation for 5 minutes at 5000 r.p.m, at room temperature and the sera were used immediately for estimation of liver enzymes.

3.2 Methods:

3.2.1 Screening test for hepatitis:

3.2.1.1 Principle:

One step test utilizes the principle of immunochromatography a unique two sites immunoassay on a membrane. As the test sample flow through the membrane assembly of the test devise the colored monoclonal anti HBs &HCs Ag colloidal gold conjugate complexes with HBs Ag in the sample. This complex move further on the membrane to the test region where it is immobilized by another monoclonal anti HBs and C Ag antiserum coated on the membrane leading to formation of a pink –

purple colored band which confirm a positive test result. Absence of this colored band in the test region indicate a negative test result. The unreacted conjugate and unbound complex if any move further on the membrane and subsequently immobilized by anti – rabbit antiserum coated on the membrane at control region forming a pink – purple band .This control band serves to validate the test result.

3.2.1.2 Requirement

Hepaview ICTs for screening of various types of hepatitis.

Serum or plasma not used haemolysis, turbid and contaminant sample.

Disposable plastic dropper.

Centrifuge.

3.2.1.3 Reagents preparation and stability

Test device contains membrane assembly predisposed with monoclonal anti HBs and C Ag antiserum-colloidal gold conjugate, rabbit IGGcolloidal gold conjugate and monoclonal anti HBs and C Ag antiserum and anti rabbit antiserum coated at respected region.

Kit may stored between 4-30°c tell the duration of shelf life.

3.2.1.4 Procedure:

Dispense 2 drops of serum/plasma specimen into sample well using the dropper provided in the kit .At the end of 15 minutes read the result.

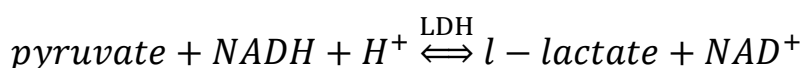
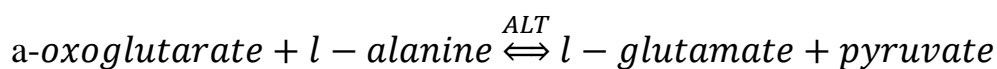
3.2.1.5 Interpretation

Positive test; a pink purple-band appear on test region.

Negative test; only one pink purple-band appear on control region.

3.2.2 Estimation of serum levels of Alanine transaminase, (appendix11):

3.2.2.1 Principle:



Alanine aminotransferase catalyzes the reversible transamination of l-alanine and α -oxoglutarate to pyruvate and l-glutamate. The pyruvate is then reduced to lactate in the presence of lactate dehydrogenase (LDH) with the concurrent oxidation of reduced B-nicotinamide adenine dinucleotide (NADH) to B-nicotinamide adenine dinucleotide (NAD). This change in absorbance is directly proportional to the activity of ALT in the sample.

3.2.2.2 Requirments

Mindray BS 200.

Automatic pipette.

Centrifuge.

Sterile needle.

70% alcohol, cotton.

Constant temperature.

Cuvette, Test tubes.

3.2.2.3 Reagents preparation and stability

The reagents and stander are provided ready to use and Stable up to the expiry date when sealed and stored at 2-8 c°.

3.2.2.4 Procedure:

	Blank	Sample
Reagent 1	1000 µl	1000 µL
Dist water 100 MI	100 µL	—
Sample	—	100 µL
Mixed, incubated for 5 min, then added:		
Reagent 2	250 µL	250 µL
Mixed thoroughly, read the absorbance after 1 min and monitor time. Read the absorbance again for additional 3 min.		
$\Delta A/\text{min} = [\Delta A/\text{min sample}] - [\Delta A/\text{min blank}]$		

3.2.2.5 Calculation:

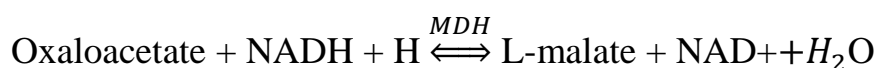
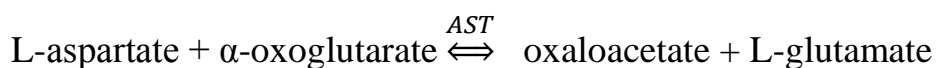
The analyzer calculates the activity of each sample automatically with a specified valid calibration factor from calibration process.

3.2.2.6 Reference Intervals

	Conventional Units	S.I.Units
Male	≤45 U/L	≤0.75 μkat/L
Female	≤34 U/L	≤0.57 μkat/L

3.2.3 Estimation of serum levels of Aspartate transaminase:

3.2.3.1 Principle:



(MDH—Malate dehydrogenase, EC1.1.1.37)

In the assay reaction, the AST catalyzes the reversible transamination of L-aspartate and α -oxoglutarate to oxaloacetate and L-glutamate. The oxaloacetate is then reduced to malate in the presence of malate dehydrogenase with NADH being oxidized to NAD⁺. The rate of the photometrically determined NADH decrease is directly proportional to the rate of formation of oxaloacetate and thus the AST activity.

3.2.3.2 Requirments

Mindray BS 200.

Automatic pipette.

Centrifuge.

Sterile needle.

70% alcohol, cotton.

Constant temperature.

Cuvette.

Test tubes

3.2.3.3 Reagents preparation and stability

The reagents and stander are provided ready to use and Stable up to the expiry date when sealed and stored at 2-8 c°.

3.2.3.4 Procedure

	Blank	Sample
Reagent 1	1000 Ml	1000 µL
Dist water 100 µL	100 µL	—
Sample	—	100 µL
Mixed, incubated for 5 min, then add:		
Reagent 2	250 µL	250 µL
Mixed thoroughly, read the absorbance after 1 min and monitor time. Read the absorbance again for additional 3 min.		
$\Delta A/\text{min} = [\Delta A/\text{min sample}] - [\Delta A/\text{min blank}]$		

3.2.3.5 Calculation:

The analyzer calculates the activity of each sample automatically with a specified valid calibration factor from calibration process.

3.2.3.6 Reference Intervals

	Conventional Units	S.I.Units
Male	≤ 35 U/L	≤ 0.58 μ kat/L
Female	≤ 31 U/L	≤ 0.52 μ kat/L

3.3 Quality control

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

3.4 Data analysis

data was analyzed using SPSS computer program, the mean and standard deviation of Alanine transaminase and Aspartate transaminase (AST&ALT) activity were obtained and the independent 't.test' used for comparison (p value of ≤ 0.05) was considered significant

Chapter Four

4. Results

The levels of the biochemical parameters of serum aspartate transaminase (AST) and alanine transaminase (ALT) activity in patients with renal failure are given in tables and figures.

Table (4-1) illustrates the ages of patients group. The result showed that the patients whose ages over fifty years were more susceptible for renal failure with a percentage of 81% compared to those with age less than fifty years (19%).

Also shows **Sex** distribution in renal failure patients group. The males' patients constitute 43(54%), while females' patients constitute 37(46%).

Table (4-2) represents the mean of body mass index (BMI) in both the study groups. BMI expressed as body weight (Kg) per height (m^2), indicated that about the most of patients under dialysis are obese ($29 \pm 4.1 \text{ kg/m}^2$), while the mean of control group is ($25 \pm 3.1 \text{ kg/m}^2$).

Table (4-3) illustrates the frequency of family history disease, patients whose have family history disease constitute 34% while those who has no family history of disease constitute 66%.

Also shows that hypertension and diabetes were significantly related to chronic renal failure. Patients with hypertension (59%), while diabetes (46%). Also a positive screening test of hepatitis was found in 20 patients (20%).

Table (4-4): shows a significant decreased in the mean of level of serum Alanine transaminase (ALT) in patients with renal failure group compared to control group. (means 10 ± 4 versus 24 ± 7 U/L; p-value=0.00).

Also showed a significant decreased in the mean of level of serum Aspartate transaminase (AST) in patients with renal failure group compared to control group. (Means 15 ± 5 versus 34 ± 7 U/L; p-value=0.00).

Table (4-5): shows a significant difference of means of Alanine transaminase in patients between the pre dialysis and post dialysis. The mean of levels of serum Alanine transaminase of patients predialysis was significantly lower than that of post dialysis. (Means 8 ± 4 versus 17 ± 3 U/L; p-value=0.00).

A significant difference of means of Aspartate transaminase in patients between the pre dialysis and post dialysis. The mean of levels of serum Aspartate transaminase of patients predialysis was significantly lower than that of post dialysis.

(Means 13 ± 4 versus 22 ± 4 U/L; p-value=0.00).

Table (4-6) shows no significant difference in the mean of level of serum Alanine transaminase (ALT) activity in male patients with renal failure and the mean of the level of (ALT) activity in female patients with renal failure. (Means 10 ± 4 versus 9 ± 4 U/L; p-value ≤ 0.428).

Table (4-7) shows no significant difference in the mean of level of serum Aspartate transaminase (AST) activity in male patients with renal failure

and the mean of the level of (AST) activity in female patients with renal failure. (Means 15 ± 6 versus 15 ± 5 U/L; $p\text{-value}\leq0.963$).

Figure (4-1), shows the distribution of patients according to age groups.

Figure (4-2), shows the comparison of frequency of both gender; (males and females) in patient group.

Figure (4-3), shows the comparison of means of alanine transaminase mean between two groups, patients and control.

Figure (4-4), shows the comparison of means of aspartate transaminase mean between two groups, patients and control.

Figure (4-5), shows the comparison of means of (ALT) level between predialysis and post dialysis.

Figure (4-6), showed the comparison of means of (AST) level between predialysis and post dialysis.

Figure (4-7): A scatter plot shows the correlation between ALT level and body mass index (BMI). Showed insignificant correlation between ALT activity and increased in body mass index, $p\text{-value}\leq0.218$).

Figure (4-8): A scatter plot shows the correlation between AST level and body mass index (BMI). Showed insignificant correlation between AST activity and increased in body mass index, $p\text{-value} \leq 0.669$).

Figure (4-9): A scatter plot shows the correlation between ALT level and duration of dialysis. Showed insignificant correlation between ALT level and increased in duration of dialysis ($r=0.024$, $p\text{-value} \leq 0.836$).

Figure (4-10): A scatter plot shows the correlation between AST level and duration of dialysis. Showed insignificant correlation between AST level and increased in duration of dialysis, $p\text{-value} \leq 0.466$).

Table (4-1)

Ages and gender of patients with renal failure disease:

Variables	Number	%
Age group:		
25-50 years	12	19%
51-80 years	65	81%
Gender:		
Male	43	54%
Female	37	54%

Table (4-2)

Mean of body mass index (BMI), of patients with renal failure group and control group

Variable	Patients N=80	Control N=40	p-value
BMI (kg/m ²)	29±4.1kg/m ² (19-30)	25±3kg/m ² (19-30)	≤ 0.02

Results given in mean±SD

Range between brackets.

p-value ≤0.05 consider significant.

Table (4-3)

Distribution of patients according to family history and other associated diseases:

Disease	Frequency	Percentage
Family history	27	34%
Hypertension	47	59 %
Diabetes	37	46%
Hepatitis	20	20%

Table(4-4)

Means of Alanine transaminase (ALT) and Aspartate transaminase (AST), (u/l) activity in patients with renal failure and control group:

Variables	Patients N=80	Control N=40	P-Value
ALT (u/l)	10±4 (4-22)	24±7 (14-37)	0.000*
AST (u/l)	15±5 (5-27)	34±7 (20-50)	0.000*

Results given in mean ±SD.

Range between brackets.

* P-value ≤0.05 consider significant.

Table (4-5)

Means of Alanine transaminase (ALT) and Aspartate transaminase (AST), (u/l) activity in patients with renal failure,(pre and post dialysis):

Variables	Predialysis N=20	postdialysis N=20	P-Value
ALT (u/l)	8±4	17±3	0.000*
AST (u/l)	13±4	22±4	0.000*

Results given in mean± SD.

* P-value ≤ 0.05 consider significant.

Table (4-6)

Mean of alanine transaminase(ALT) activity according to gender

Subject group	Number	Mean±SD	p-value
Males (ALT).(u/l)	43	10±4	0.428*
Females (ALT)(u/l)	37	9±4	

Results given in mean ±SD.

* P-value ≤0.05 consider significant.

Table (4-7)

Mean of aspartatetransaminase(AST) activity according to gender

Subject group	Number	Mean±SD	p-value
Males (AST).(u/l)	43	15±6	0.963*
Females (AST)(u/l)	37	15±5	

Results given in mean ±SD

* P-value ≤0.05 consider significant.

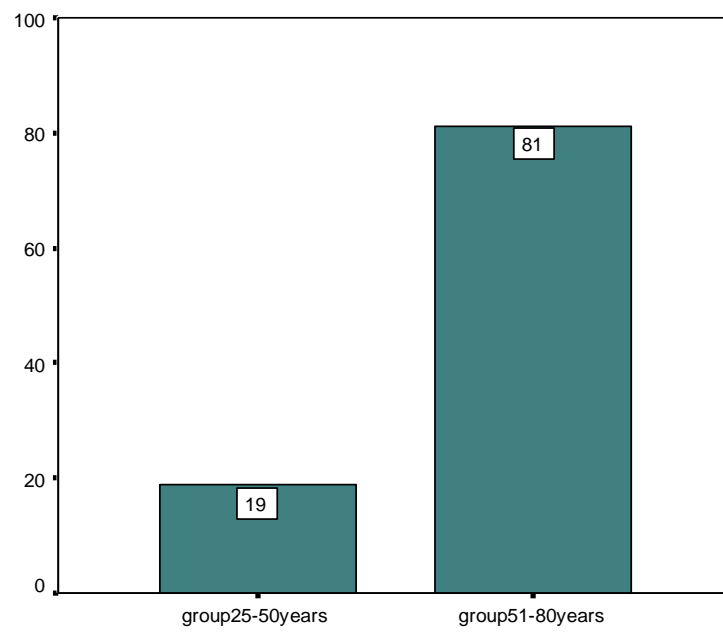


Figure (4-1): distribution of patients according to age groups.

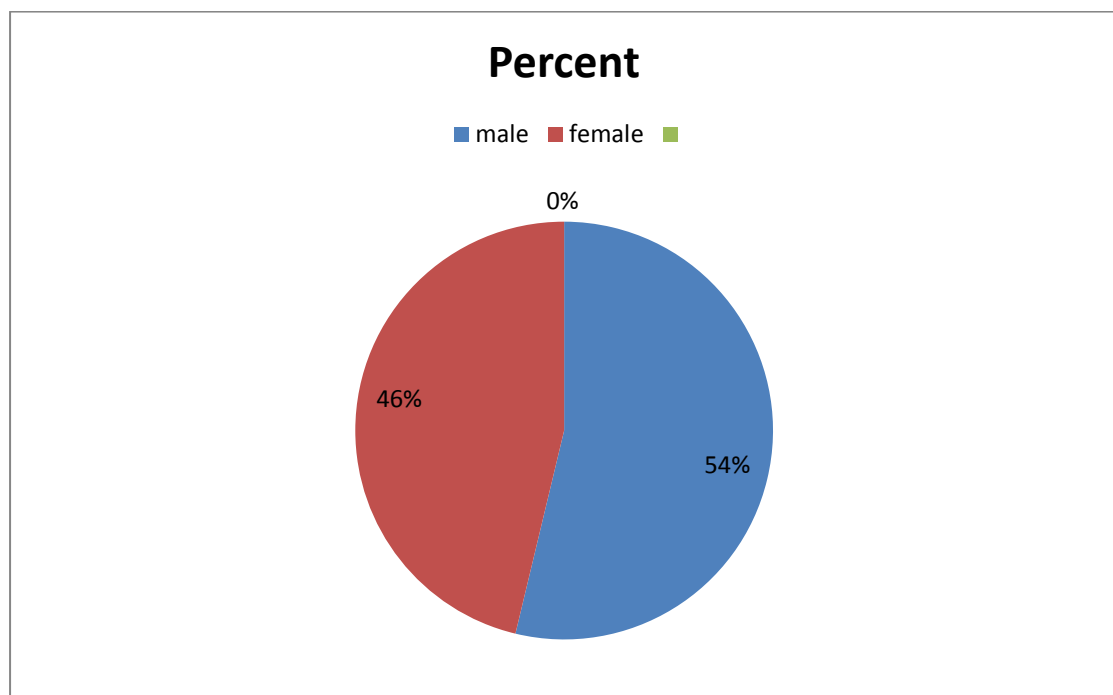


Figure (4-2), Comparison of frequency of males and females in the patients group.

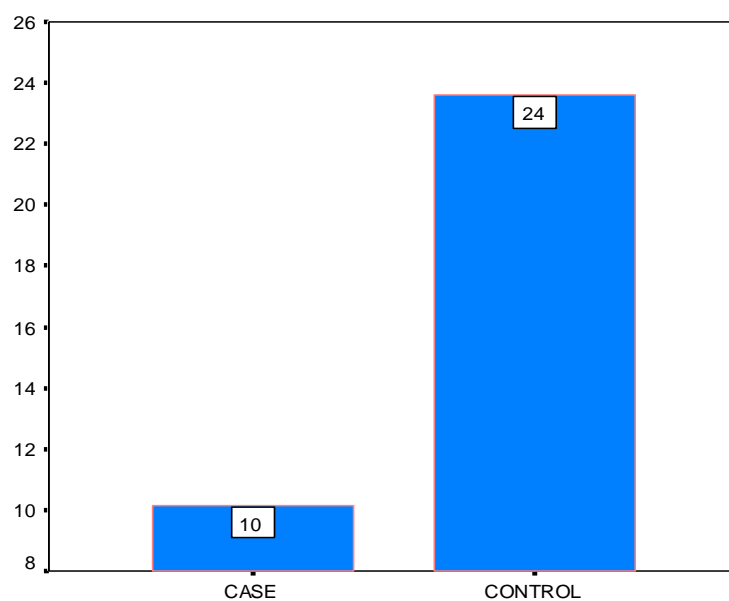
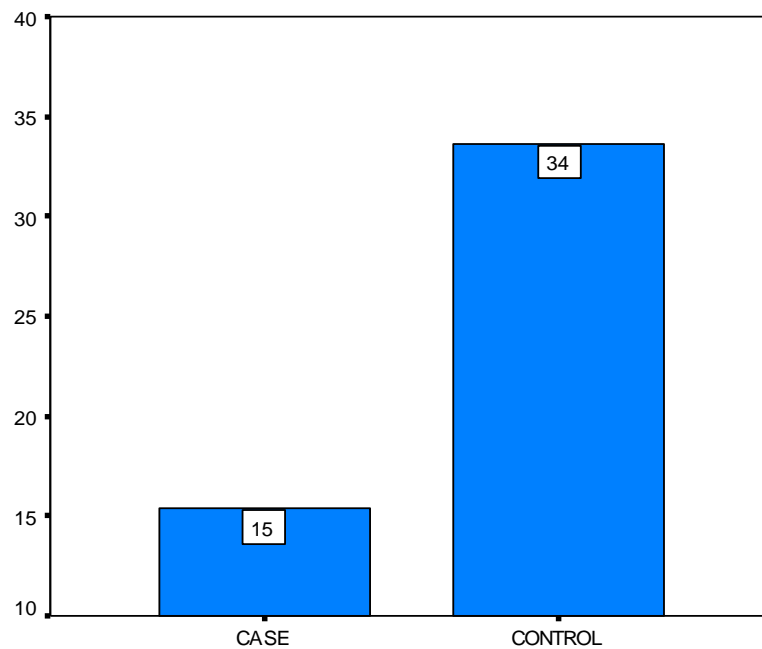
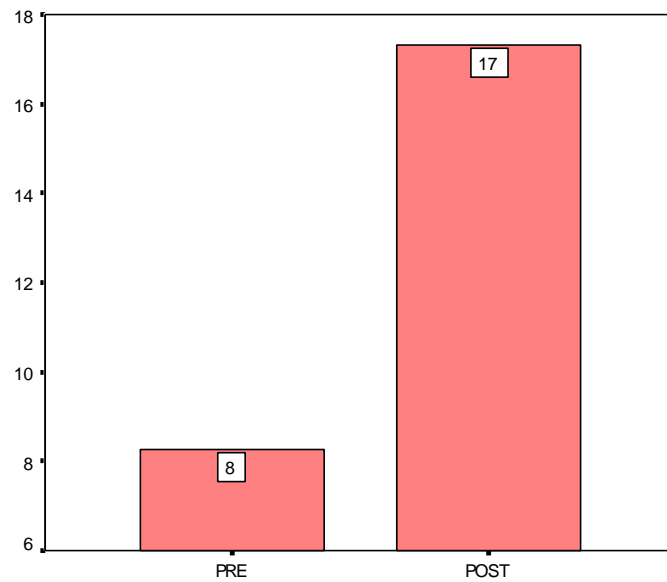


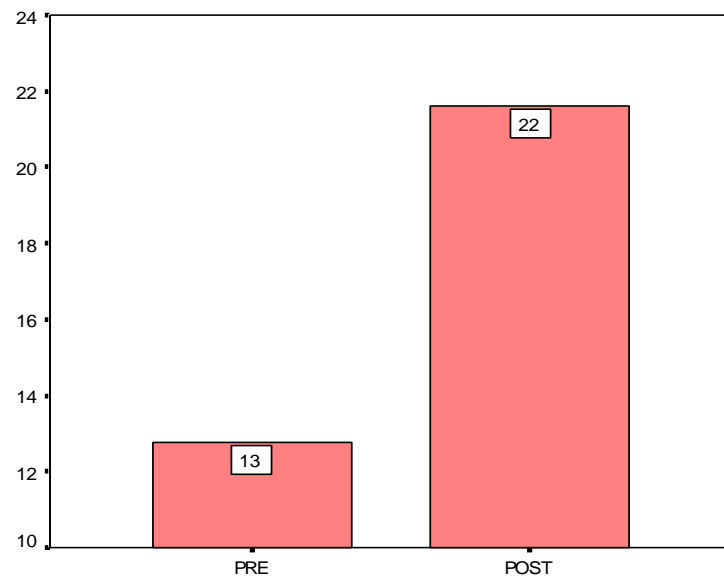
Fig (4-3), Comparison of the means of ALT (u/l), in patients with renal failure and the control group.



Fig,(4-4), Comparison of the means of AST (u/l), in patients with renal failure and the control group.



Fig,(4-5), Comparison of the means of ALT (u/l), in patients with renal failure predialysis and post dialysis.



Fig,(4-6), Comparison of the means of AST (u/l), in patients with renal failure pre dialysis and post dialysis.

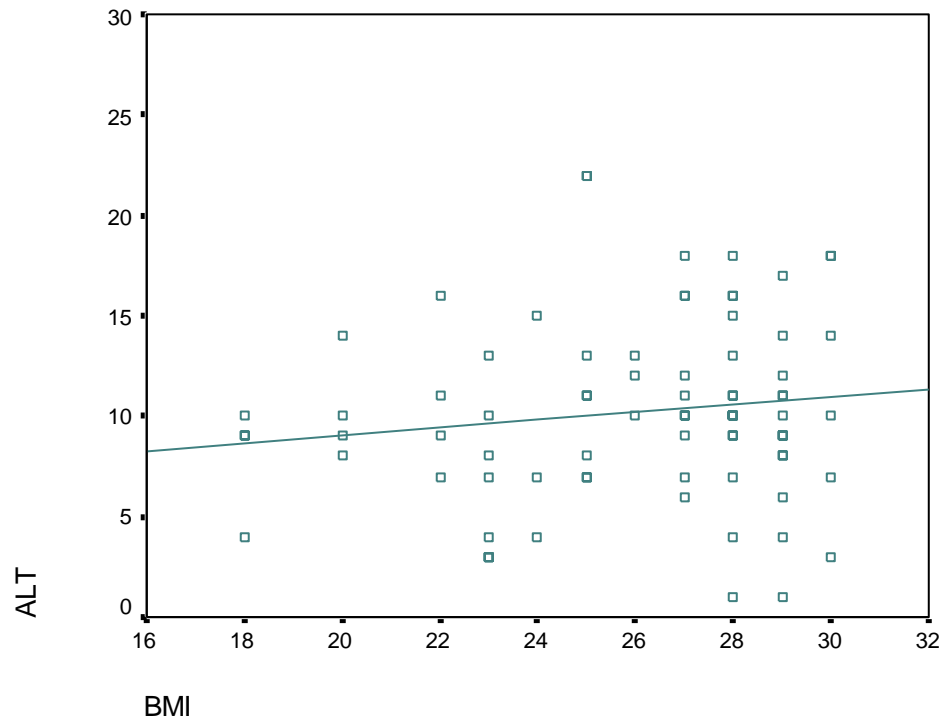


Figure (4-7): A scatter plot shows the correlation between ALT (u/l) level and body mass index(BMI)($r=0.139$, $p\text{-value}=0.218$).

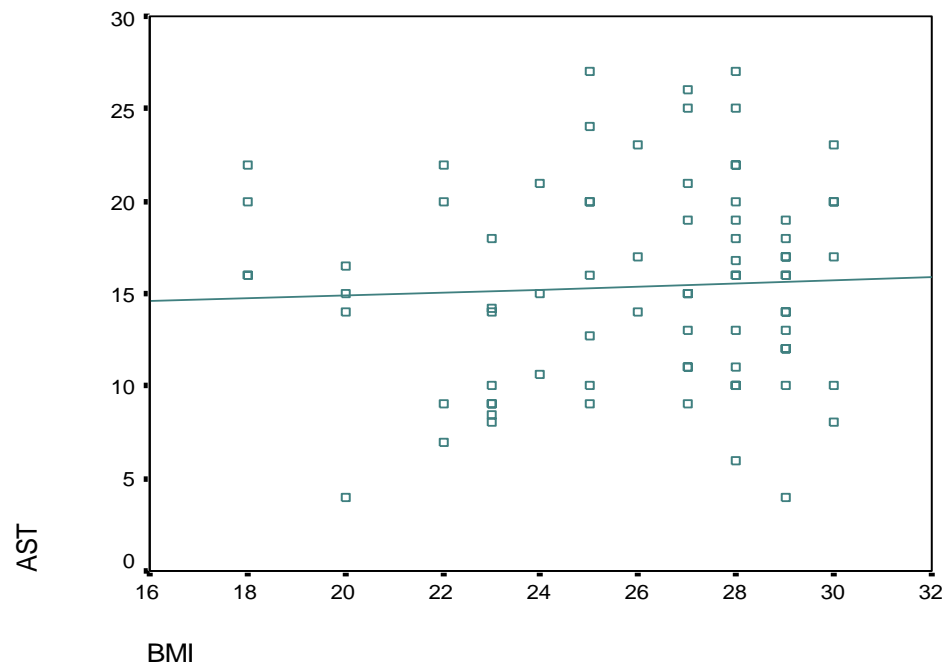


Figure (4-8):A scatter plot shows the correlation between AST level and body mass index (BMI);($r=0.048$, $p\text{-value}=0.669$) .

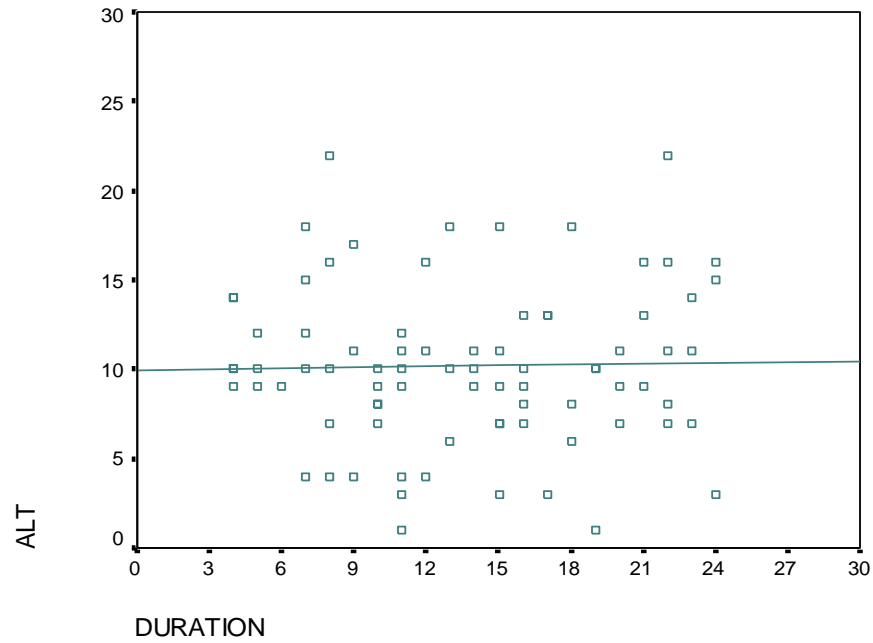


Figure (4-9):A scatter plot shows the correlation between ALT level and duration of dialysis ($r=0.024$, $p\text{-value}=0.836$) .

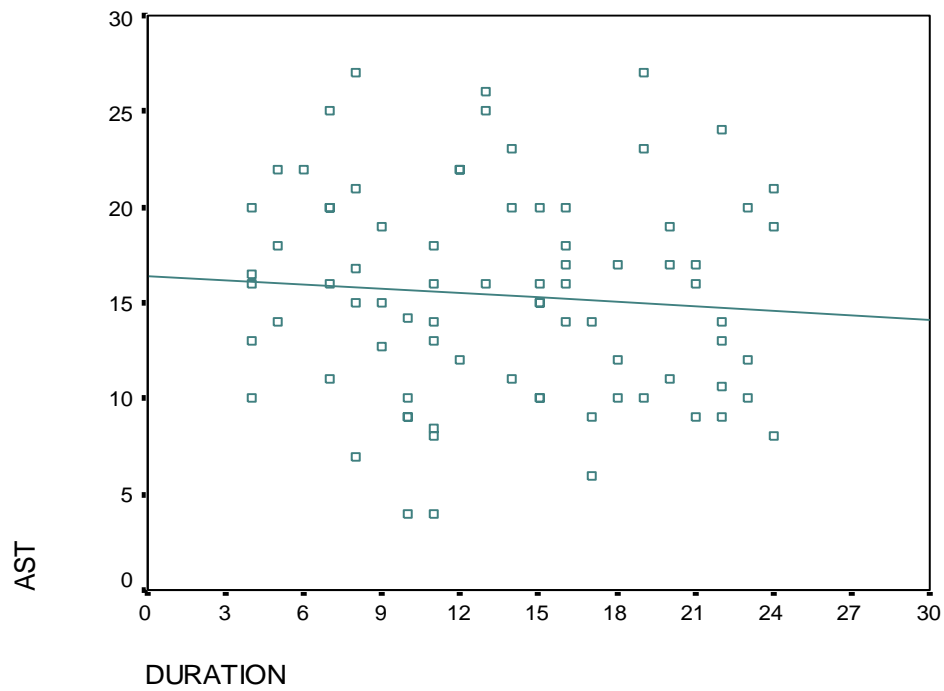


Figure (4-10):A scatter plot shows the correlation between AST level and duration of dialysis:($r = -0.083$, $p\text{-value} = 0.466$).

Chapter five

5.1 Discussion

Kidney failure is a condition in which the kidneys fail to remove metabolic end product from the blood, so when kidney failure is reached the end stage it needs dialysis. (Benjamin; 2011).

Hemodialysis affects many substances in the blood by increasing, decreasing or removing them. This study conducted to study the effect of hemodialysis on liver enzymes activity. Two liver enzymes, alanine transaminase and aspartate transaminase (ALT&AST) were chosen for the assessment the effect of dialysis on levels of liver enzymes.

Preliminary investigation and findings obtained from specially designed questionnaire revealed that the majority of patients under dialysis participated in this study were in the average ages of about 55 years. This agreed with previous published results of many authors. (Coresh *et al*; 2003), whose finding confirmed that, after the age of 30 years, glomerular filtration rate (GFR) progressively declines at an average rate of 8 mL/min/173 m² per decade , and the risk of renal failure increased with age. This result also was agreed with result of study carried by; (Christian; 2014) showed that the average age of a British person with the renal failure is 77 years. .

Sex distribution in patients under hemodialysis of this study revealed that 54% were males. This agree with the previous study which documented in the field of nephrology, showed that women seem to be somewhat protected from developing end stage renal failure; the cumulative incidence of the disease remains low during the reproductive ages and begins to rise 10 years later. (Iseki; 1996).

Social clinical history index of patients under the study indicated that a positive family history of renal failure of first degree relatives found to be in 34% of cases. These findings may indicate that hereditary play a role in the pathogenesis of renal failure patients. This result agreed with previous study showed that, there is a high prevalence of family history –end stage renal disease among US population, about 23%. (William *et al*; 2007)

Other study showed the same result also; family history of renal disease is one of the most important risk factors associated with development of nephropathy. (Scott *et al*; 2005)

The findings of this study showed that, there was a significant difference in the body mass index (BMI; determined by dividing the weight in kilograms by the height in meter square.) between patients and control, the patients with renal failure susceptible to be more obese than control group. This made the BMI is independent factor of renal failure. This agreed with previous study which found positive correlation between increased (BMI) and risk of renal failure disease. (Elisabeth *et al*; 2005). Another study examined the relationship between increased weight (BMI) and renal function evaluated by the estimated glomerular filtration rate, Increased BMI was consistently associated with reduced glomerular filtration rate. (Ryuichi; 2008)

In this study some of diseases presented in patients with renal failure as appeared in **table (4-3)**, more than half (59%) of patients in these study were present with hypertension. It is well documented that the persistence of hypertension is one of leading cause of chronic renal failure.

Also (46%) of patients under dialysis participated in this study were present with diabetes.

This agreed with previous study showed that high risk groups that should be screened for chronic kidney disease include patients who have a family history of the disease and patients who have diabetes, hypertension.(National Kidney Foundation; 2002)

Also this result was in agreement with findings done by (Oyetunde; 2014), revealed that both hypertension and diabetes were significantly related to chronic renal failure with incidence of (43%).The results showed that diabetes, hypertension and chronic renal failure were significantly correlated ($p\text{-value} < 0.05$).

Also the result agreed with study done by(Janice;2002) which showed that, The key risk factors for kidney disease are hypertension and diabetes, which are both becoming more prevalent in the United state, 40% among patients with renal failure.

In this study the comparison of levels of liver enzyme, alanine transaminase (ALT) activity between cases and control participated in this study showed that decreasing of levels of Alanine transaminase in patients with renal failure under hemodialysis when compared with control. (10 ± 4 versus 24 ± 7 , $p\text{-value} = 0.00$).

As well as aspartate transaminase (AST) which showed that decreasing of levels of Aspartate transaminase in patients with renal failure under hemodialysis when compared with control.

(15 ± 5 versus 34 ± 7 , $p\text{-value} = 0.00$).

This result agreed with result carried by (Luis *et al*;2014) which found that serum levels of the enzymes aspartate transaminase and alanine transaminase in patients with renal failure on hemodialysis; were decreased. It was hypothesized that this reduction could be caused by factors such as the withdrawal of aminotransferases during the

hemodialysis session; the high lactate serum levels, which, during biochemical dosages, would rapidly consume Nicotinamide Adenine Dinucleotide Phosphate (NADPH) and result in low levels of aminotransferases; the presence of uremic factors that would inhibit the activity of these enzymes; and, finally, the deficiency of pyridoxine, a cofactor for the synthesis of the aminotransferases.

This agreed with study done by (Ono *et al*; 1990), showed that there were positive correlation between(ALT&AST) and pyridoxine , but disagreed with(Jung *et al*;1980) and (Yasuda *et al*;1995) whose showed there was no correlation between them.

Also this results are in agreement with the findings in (Mujeeb *et al*; 2014), showed that both AST&ALT were significantly low (p-value <0.05) in both sexes when compared with their counterparts in the control group the decrease in levels of aminotransferases in patients with renal failure who have not undergone dialysis therapy has observed in this study suggests that renal impairment has an impact on the liver enzymes.

As appear in **table (4-5)** compare the (AST&ALT) in 20 cases of renal failure, predialysis and post dialysis showed that the levels of (AST&ALT) concentration were significant decreased in pre dialysis when compared to post dialysis, ALT (8 ± 4 versus 17 ± 3 ; p-value =0.00) AST (13 ± 4 versus 22 ± 4 ; p-value =0.00)

This agreed with previous study which collected serum aminotransferases prior to and after hemodialysis sessions and observed a 15-35% increase after dialysis, which supports the hypothesis of hemoconcentration for the rise in aminotransferases observed after the dialysis procedure. (Yasuda *et al*; 1995)

Also this result agreed with other study carried by (Somboloset *al*;2012) evaluated 53 patients on hemodialysis and divided them into three groups: hemodialysis, isolated ultrafiltration, and euvolemic hemodialysis (without the removal of fluids) and verified the effects of hemodilution in the serum levels of the aminotransferases. In the patients who underwent euvolemic hemodialysis, there were no differences between the ALT and AST levels prior to and after the procedure. However, when an isolated ultrafiltration or hemodialysis was performed, there was an increase in the aminotransferase levels when compared with the values prior to and after the procedure the authors concluded that the rise in the aminotransferase serum levels after hemodialysis should primarily occur due to the hemoconcentration induced by the ultrafiltration.

Also the result agreed with (Isabella *et al*;2012) which showed the aminotransferase levels were lower in the samples collected before hemodialysis compared with the samples collected after the hemodialysis.

In this study results showed there is no significant difference between (AST & ALT) according to gender (males and females) in cases and control.

This result agreed with previous study done by (Mujeebet *al* ;2014) showed that there was no significant difference of transaminases (AST&ALT) according to gender.

In this study results showed that, there was insignificant correlation between body mass index (BMI) and ALT, ($p\text{-value} \leq 0.218$), and AST ($p\text{-value} \leq 0.669$). This result agreed with study done by (Ajay Kumar; 2014), whose showed that no significant relation was found between liver transaminase (ALT $p\text{-value} \leq 0.21$ & AST $p\text{-value} \leq 0.28$) in normal, overweight and obese individuals.

The findings of this study are disagreed with the previous study done by (Salvaggio; 1991), which showed that the percentage increase in the geometric mean of liver enzymes(AST&ALT) activity of the obese subjects (BMI greater than 30 kg/m²) compared with that of the normal subjects (BMI less than or equal to 25 kg/m²), p-value ≤ 0.01 .

Also In this study as appeared in **figures (4-9 &4-10)**, which showed no correlation between duration of dialysis and liver enzymes (AST&ALT) activity. It was suggested that; the liver transaminases start to decrease from first time of hemodialysis and Continue to decrease. After many sessions of hemodialysis. In chronic renal failure, the liver enzymes reach the steady state and are not influenced with hemodialysis sessions. This result agreed with previous study done by (Luis et al;2014), whose recorded the levels of transaminases in patients under hemodialysis and found that in first times of dialysis(AST&ALT) started to decrease and after many sessions of dialysis reached steady state.

5.2 Conclusion

From the results and findings of this study, is concluded that:

- 1- (AST&ALT) activities is significantly decreased in the blood of patients with renal failure.
- 2- (AST&ALT) activities vary in concentration before and after dialysis, make the last one is higher than the other.
- 3- Hypertension and diabetes is the most common causes of chronic renal failure in Sudan.
- 4- The gender has no effect on (AST&ALT) activities.

5.3 Recommendation

It is recommended that:

- 1- A screening test of hepatitis should be done as routine investigation for patients with renal failure under dialysis monthly.
- 2- Patients under dialysis must give a vaccine from hepatitis.
- 3- Liver enzymes test should be done as routine investigation for patients with renal failure.
- 4- More studies should be carried out on the effect of hemodialysis on liver enzymes, not just transaminase but all the liver enzymes.
- 5-Further studies should be conducted to determine the real cause of this effect.

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Appendices

Sudan University of Science and Technology

College of Graduated Studies

Questionnaire

Master Degree

TOPIC: the effect of hemodialysis on liver enzymes (AST&ALT) in renal failure patients under hemodialysis.

A: general information:

1-name..... 3- Hospital.....
3-age..... 4-sex.....

B: type of renal failure:

1-acute renal failure 2-chronic renal failure

C: hemodialysis:

1-yes 2-NO

IF yes duration of dialysis.....

D: present history of disease:

Liver disease heart disease

Bone disease others

E: past history of disease:

1-hypertention 2-liver disease

3-renal disease 4-diabetes

F: family history of renal failure yes.....no.....

G: investigation

1-serum screening for hepatitis C&B

2-serum AST.....U/L

3-serum ALT.....U/L

H: BMI=.....