

## **The Impact of Renal Function on Liver Cirrhosis among Patients in Wasit Governorate, Iraq**

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### **ABSTRACT**

In Al-Kut city's AL-Zahraa general hospital, this study was carried out for individuals with liver cirrhosis to evaluate their serum levels of ALT, AST, GGT, ALP, urea, creatinine, T.Protein, Albumin, and Bilirubin. The 50 patients ranged in age from 20 to 60, with 29 male and 21 female individuals. Based on the patient's medical history and physical examination, liver cirrhosis was determined to affect both sexes of the patient. The 30 control groups were drawn from the medical personnel and family of those who did not exhibit any indications or symptoms of renal liver disease or kidney diseases. With ages ranging from 22 to 66, there were 20 men and 10 women. Eight to fourteen hours following the patients' overnight fasts, blood samples were obtained. The research reveals the following.

Serum ALT, AST and GGT concentrations in liver cirrhosis patients were found to be significantly increased compared with control group ( $P < 0.01$ ). Serum Bilirubin (Total) and direct Bilirubin concentrations in liver cirrhosis patients were found to be significantly high compared with control group ( $P < 0.5$ ), ( $P < 0.01$ ) respectively. Serum Albumin concentrations in liver cirrhosis patients were found to be no significantly lower compared with control group ( $P > 0.5$ ). Serum Total protein concentrations in liver cirrhosis patients were found to be no significantly lower compared with control group ( $P \leq 0.5$ ). Serum Alkaline phosphatase (ALP) concentrations in liver cirrhosis patients were found to be significantly increased compared with control group ( $P < 0.01$ ). Serum urea, creatinine, Uric acid and ammonia level concentrations in liver cirrhosis patients were found to be significantly high compared with control group ( $P < 0.01$ ).

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### **INTRODUCTION**

The liver, the second-largest organ, plays a crucial role in host defense against microorganisms and plays a significant role in converting ammonia to urea, destroying old red blood cells, and storing sugar. It also supplies components of the innate immune response, including acute phase and complement proteins, as well as inflammatory cytokines. The liver secretes bile, essential for digestion and absorption of fat and fat-soluble vitamins, and aids in excretory function by secreting endogenous and exogenous substances. These substances are reabsorbed through the small bowel wall and ultimately excreted through the kidneys. [1,2] Liver cirrhosis is an advanced liver disease caused by acute or chronic liver injury, such as alcohol abuse, obesity, and hepatitis virus infection. It results from permanent damage or scarring of the liver, causing blockage of blood flow and preventing normal metabolic and regulatory processes [3,4]. Cirrhosis is an

advanced stage of liver fibrosis, accompanied by distortion of the hepatic vasculature. This vascular distortion leads to shunting of portal and arterial blood supply directly into the hepatic outflow, compromising exchange between hepatic sinusoids and adjacent liver parenchyma [5]. Cirrhosis is a diffuse process characterized by tissue fibrosis and the conversion of normal liver architecture into structurally abnormal nodules [6]. Key morphological features of cirrhosis include diffuse fibrosis, regenerative nodules, altered lobular architecture, and intrahepatic vascular shunts between afferent and efferent liver vessels [7]. Liver transplantation is often required for patients with decompensated liver cirrhosis. [8] Cirrhosis prevalence worldwide is unknown, with an estimated 0.15% prevalence in the USA, 400,000 deaths, and 373,000 hospital discharges in 1998 [8]. However, this may be underestimated due to the high prevalence of undiagnosed cirrhosis in both NASH and hepatitis C. Similar

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numbers have been reported in Europe and Asian and African countries [9,10]. Up to 1% of populations may have histological cirrhosis [11]. The etiology of cirrhosis can be identified through patient history, serologic, and histologic evaluation. [12] Alcoholic liver disease and hepatitis C are the most common causes in the Western world, while hepatitis B prevails in Asia and sub-Saharan Africa. The diagnosis of cirrhosis without an apparent cause (cryptogenic cirrhosis) is rarely made. [13] Understanding the etiology of cirrhosis is crucial for predicting complications, direct treatment decisions, and discussing preventive measures [14]. Multiple etiological factors contribute to the development of cirrhosis, such as alcohol consumption, age above 50, and male gender in chronic hepatitis C, and older age obesity, insulin resistance/type 2 diabetes, hypertension, and hyperlipidemia in NASH. [15] In clinical practice, blood levels of GGT (gamma-glutamyl Transferase), ALT (alanine aminotransferase) and AST (aspartate aminotransferase) are used to index liver injury. GGT is found in liver and biliary epithelial cells, and is a sensitive marker of hepatobiliary disease, although non-specific to its cause. AST and ALT blood levels increase when the liver cell membrane is damaged and thus mark hepatocellular injury [16]. To explain their role in other diseases, GGT and ALT have been proposed as surrogate markers of fatty liver, while GGT is also seen as a marker of oxidative stress. Variation in liver enzyme levels within the normal reference range predicts disease and it is therefore important [17]. To investigate the underlying sources of variation that explain individual differences in liver enzyme levels. Genetic factors influence variation in liver enzyme levels. For adults, heritability estimates for GGT, ALT and AST range between 32–69 %, 22–44 % and 21–40 % respectively [18]. Renal failure is a severe complication in patients with liver cirrhosis. It is associated with increased mortality and morbidity. Diagnosis is a challenge because it is mainly based on serum creatinine, which does not seem to be an ideal measure of renal function in cirrhosis. The diagnosis of acute kidney injury (AKI) is based on an absolute increase of serum creatinine of  $>0.3$  mg/dl from baseline within 48 h or an increase of  $>50\%$  from baseline. This means smaller changes in serum creatinine in a shorter time frame which may lead to an early identification of renal failure in cirrhotic patients. Renal failure in cirrhosis may be due to various causes. In patients with cirrhosis, renal failure can have various causes such as parenchymal nephropathy, hypovolemia, infection and hepatorenal syndrome. Among those, hepatorenal syndrome has the worst and parenchymal nephropathy – the relatively best prognosis [19]. Prerenal failure and hepatorenal syndrome are among the most common causes of renal insufficiency in liver disease. In these patients, portal hypertension and splanchnic vasodilatation causes a shift in blood volume away from the central circulation. This reduction of centrally effective blood volume induces a stimulation of counter-regulatory mechanisms such as activation of renin-aldosterone and of the

sympathetic nervous system. This results in renal sodium retention, functional renal failure and ascites formation. Therefore, marked, fast decreases of plasma volume must be avoided in the treatment of ascites [21, 22]. The objective of this study is to find out the biochemical changes (ALT, AST, GGT, Total protein, Total and direct bilirubin, Albumin, ALP, urea, creatinine, Uric acid and ammonia level) in patients with liver cirrhosis and compare the obtained results with the results of healthy individuals as control groups.

### MATERIALS & METHODS

#### Control Groups:

A Total number of 100 patients of liver cirrhosis and 50 controls were selected for the present study from AL KRAMMA hospital & Al Zahraa hospital

#### Patients:

A total of 100 diagnosed liver cirrhosis patients admitted to Al Zahraa and Al kramma hospital and The patient was diagnosed as liver for both sexes based on the history, clinical examination and taking liver function and kidney function test. Subject was fasting 12-14 hr. at the time of blood withdrawal. Their age range between 18-60 years where included in this study throughout the period between January –march 2022.

Full history and general physical examination were obtained from the patients file.

#### Sample Collection:

Five milliliters of venous blood were drawn from each fasting patient. Slow aspiration of the venous blood sample via the needle of syringe to prevent hemolysis with tourniquet applies 15cm above the cubital fossa. All the samples that were grossly hemolysed were neglected and other samples were taken.

The samples were dropped into clean disposable tubes, left at room temperature for 30 minutes for clot formation and then centrifuged for 20 minutes at 5000 run per minute.

The serum was separated and divided into two parts; the first part 1.0 ml of serum was kept in the Eppendorf tube which is used for measuring liver function, and stored at 2-8 C. The second part of serum 1ml was kept in the Eppendorf tube and stored at 2-8 C. which is used to measure serum creatinine and urea. Similarly the blood samples were taken from the control group.

### RESULTS AND DISCUSSION

The sample of this study consisted of 100 patients diagnosed as liver Cirrhosis and 50 normal volunteers used as control group. The levels of urea, creatinine, Uric acid, Total protein, total Albumin, Direct Bilirubin, Aspartate transaminase (AST), Alanine transaminase (ALT), Gamma Glutamyl Transpeptidase (GGT), Alkaline phosphatase and (ALP) Ammonia level were estimated using enzymatic methods.

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The personal information took it also from patinas (age, gender live style)

The results in table (3.1) showed the personal information where the gender and age and smoking have effecting on result The results in table (3.2) showed patinas and control ID liver function test Total protein, total Albumin , Direct

Bilirubin Aspartate transaminase ( AST ) , Alanine transaminase ( ALT ) , Gamma Glutamyl Transpeptidase (GGT), Alkaline phosphatase and (ALP ) The results in table (3.2) showed kidney function test urea, creatinine, and Uric acid.

**Table (3. 1): Age, gender for Control and Patient sample**

Sample document	Control	Patient	Unit
Age	15-30	30-60	Year
Mail	60	40	Percentage
Female	40	60	Percentage

**Table (3. 2): biochemical change liver function.**

L.F.T	Unit	control	Patient	P value
Total protein	(gm/d)	6.2±8.2	5±5.5	≥ 0.5
Albumin	(mg/dl)	3.6±5.2	2.0±2.8	> 0.5
T.Bilirubin	(mg/dl)	0.3±0.1	8.5±10.5	< 0.5
Direct Bilirubin	(mg/dl)	0.0±0.4	4.2±5.5	< 0.01
Aspartate transaminase ( AST )	(IU/L)	10±40	150±485	< 0.01
Alanine transaminase ( ALT)	(IU/L)	15±45	140±324	< 0.01
Gamma Glutamyl Transpeptidase (GGT)	(IU/L)	10±45	50±223	< 0.01
Alkaline phosphatase (ALP)	(IU/L)	30±85	85±324	< 0.01

**Table (3. 3): Renal function tests level in healthy Control and Liver cirrhosis Patients.**

R.F.T	control	Patient	Unit	P value
Urea(mg/dL)	20-40	45±86	(mg/dL)	< 0.01
Creatinine	0.5-1.5	1.6±3.5	(mg/dL)	< 0.01
Uric acid	3-7	6.5±8.6	(mg/dL)	< 0.01
Ammonia level	10±20	35±280	(µmol/L)	< 0.01

### 3.1 Measurement of Age and gender patients and control group:

Gonadal hormones have a role in the development of gender specific traits and affect primarily structure and function of gender specific organs. Studies have indicated their role in regulating structure and function of nearly every tissue and organ in the mammalian body, causing gender differences in a variety of characteristics. Sex hormones are associated with various aspects of reproduction, differentiation, development, growth and homeostasis, influence the development of female and male specific traits. A number of studies indicate its role in regulating structure and function of nearly all tissues and organs including brain, bones, liver, kidneys causing differences in males and females [23]. Protective role of estrogen has been well established in health and disease and it is responsible for the gender differences in various biochemical markers. There are a few studies available comparing liver parameters in both the genders [24, 25]. We observed a significantly low total and direct bilirubin, AST and albumin levels in women compared to men. A significant

correlation between bilirubin and AST was found. The causative factor for gender difference is inconclusive and association of liver profile and female gonadal hormones needs further research [26].

### 3.2 Measurement of serum Direct Bilirubin (AST), (ALT), (GGT), (ALP) Total protein and Albumin concentration in liver Cirrhosis patients and control group:

Cirrhosis is seen with a variety of chronic liver diseases and may take years or even decades to develop. With cirrhosis, the structure of the liver changes, forming nodules of cells surrounded by fibrous tissue [27]. This tissue does not function like healthy liver tissue and can interfere with the flow of blood and bile through the liver. As cirrhosis progresses, it can begin to affect other organs and tissues throughout the body. It is important to detect cirrhosis as soon as possible since significant liver damage may occur with few or no symptoms. Liver function tests are blood tests used to help diagnose and monitor liver disease or damage. The tests measure the levels of certain enzymes and proteins in your blood [28]. The results show significant (P< (0.01) increase

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in , Direct Bilirubin Aspartate transaminase ( AST ), Alanine transaminase ( ALT ), Gamma Glutamyl Transpeptidase (GGT), Alkaline phosphatase and (ALP ) compared with those of the control group , While Non-significant change observed in Total protein, Albumin p value > 0.05 [29].

### 3.3 Measurement of serum urea, creatinine uric acid and ammonia level concentration in chronic renal failure patients and control group:

Chronic liver disease and cirrhosis are frequently complicated with renal dysfunction and this combination leads to significant morbidity and mortality. There is considerable evidence that renal failure in patient with cirrhosis primarily related to disturbances in circulatory function-mainly, a reduction in system vascular resistance due to primary arterial vasodilatation in the splanchnic circulation, triggered by portal hypertension [30,31]. In present study, Urea, Creatinine and levels were increased in liver cirrhosis patients compared to healthy controls but not significantly non-significant change appeared in uric acid test as show in table (3.3), where The results were showing that significant levels of blood ammonia elevated in liver cirrhosis patients (35±280) compared to the healthy controls (10±20) µmol/L whit <0.001 as p value.

### CONCLUSIONS

● Serum urea, creatinine, Uric acid and Ammonia level are frequently elevated in patients with liver cirrhosis compared with control group. This combination leads to significant morbidity and mortality and that's mean liver cirrhosis effect on kidney functions

●Serum Direct Bilirubin, AST, ALT, GGT and ALP increased compared with those of the control group, while Non-significant change observed in Total protein and Albumin.

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