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Effect of Chronic Kidney Disease on Liver Functions

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ABSTRACT

Liver function is effective in people with chronic kidney disease (CKD) that is one of the causes of death and disability in many countries around the world. Additionally, to their effects on serum albumin and total proteins by reducing their levels in blood. The current study was included 54 randomly ill cases, with ages ranging from (45 -75) years, who attended Private Kidney and Urology clinics in the city of Mosul, and were diagnosed by specialized Physicians for the period from September to June 2022. It included 31 males and 23 females. In addition, 30 apparently healthy 15 males and 15 females as the control group.

Results indicate a decrease in the liver's performance of its function, and this was indicated by a significant decrease at $P \leq 0.05$ in some liver enzymes, such as alanine aminotransferase (ALT), aspartate aminotransferase (AST) and significant increase at $P \leq 0.05$ of alkaline phosphatase.

Keywords: CKD, ALT, AST, ALP.

INTRODUCTION

In the late 19th century, reports by Frerichs (1861) and Flint (1863) noted an association among advanced liver disease, ascites, and oliguric renal failure in the absence of significant renal histologic changes. Almost 100 yr. later, in an article by Hecker and Sherlock (Hecker and Sherlock,1956), the pathogenesis of Hepato Renal syndrome (HRS) was unraveled. The authors demonstrated the lack of major renal histologic changes despite the severity of kidney failure (Wadei *et al*., 2006; Al-Shamaa and Al-Obaidi, 2018).

The prevalence of chronic kidney disease has increased worldwide than it used to be. Today, the disease affects about 10-15% of the adult population with different stages of the disease. And that the percentage of people over the age of 60 years was higher than the rest of the ages, as the infection rate reached about 39%, compared to ages between (40-50) years, when the infection rate reached about 13% (Cockwell and Fisher, 2020; Mahmmod and Al-Rawi, 2020).

A family history of kidney disease is a risk factor for CKD. Some studies indicate this approximately 24% of patients with CKD in its final stages have at least a first-degree relative, as well as a previous history of urinary tract problems, urinary tract obstruction, stones, decrease in kidney mass (single kidney), nephrotoxins, polyuria analgesic abuse, and low birth weight (Babić *et al*., 2021).

The liver is the largest gland in the body occupying 2.5% of total body weight and providing a host of functions necessary for maintaining normal physiological homeostasis. Despite the complexity of its functions, the liver has a homogenous appearance (Juza and Pauli, 2014).

The basic functional unit of the liver is the liver lobules, which are a cylindrical structure several millimeters in length and (0.8 to 2.0) millimeters in diameter. The human liver contains 50,000 to 100,000 individual lobules. (Guyton and Hall, 2020).

The most commonly used indicators of liver damage are (AST) and (ALT) which were formerly referred to as glutamic pyruvic transaminase GPT and glutamic oxaloacetic transaminase GOT. These are the enzymes normally found in liver cells that leak out of these cells and make their way into the blood when liver cells are infected. GPT is thought to be a more specific indicator of hepatitis as GOT is also found in other organs such as the heart and skeletal muscles (Mahmood *et al*., 2019).

AST exists as cytosolic and mitochondrial isoenzymes and is found in the liver, heart muscle, skeletal muscle, kidneys, brain, pancreas, lungs, leukocytes, and red cells. It is not as sensitive or liver specific as ALT, and the elevation in AST may be considered secondary to non-hepatic causes as well. AST activity in neonates and infants is approximately twice that in adults, but these levels drop to adult levels by about six months (Mohammed-Ali *et al.*, 2020).

ALT is a cellular enzyme found in high concentrations in the liver. The half-life of ALT is approximately 47 ± 10 hours. ALT is usually higher than AST in most types of liver disease as the activity of both enzymes is predominantly cytosolic in liver cells. Hepatocyte injury and not necessarily cell death results in the release of these enzymes into the circulation. AST and ALT values are higher in normal males than in females (Lala *et al*., 2021).

Additionally, the albuminuria or proteinuria is one of the most important biomarkers to diagnose CKD. Albumin protein constitutes the highest percentage of soluble proteins in the blood, which reaches more than 60% when compared with the rest of the blood proteins. The reason for this percentage is due to the inability of this protein to pass through the blood vessel to remain dissolved in the blood plasma Albumin is an important carrier for compounds that are not soluble in water in the blood (Belinskaia *et al*., 2023).

The molecular weight of this protein is about 65 kilodaltons, and it is composed of 585 amino acids. It is an antioxidant in blood plasma by inhibiting oxidants, hydroxyl radicals (OH), peroxyl radicals (ROO) and hypochlorous acid (HOCI). When albumin is exposed to oxidative stress continuously, it will lead to morphological and functional changes that may lead to denaturation of

the protein due to the influence of thiol groups (SH) in it. Chronic kidney disease, especially dialysis patients, suffer from this effect, which reduces the role of albumin for its role as an antioxidant (Belinskaia *et al*., 2020).

MATERIAL AND METHODS

Study sample:

The current study included 54 randomly ill cases, with ages ranging from (45 -75) years, who attended Private Kidney and Urology Clinics in the city of Mosul, and were diagnosed by specialized Physicians for the period from September to June 2022. It included 31 males and 23 females. In addition, 30 apparently healthy 15 males and 15 females as a control group. The samples were divided into three age groups, the first group, whose ages ranged between 45-55, included 21 samples (8 Female and 13 Male). The second group, whose ages ranged between 56-65, included 18 samples (9 Female and 9 Male) and with regard to the last group, whose ages ranged between 66-75, it included 15 samples (6 Female and 9 Male). The samples were measured using Auto Biochemistry Smart 150 device. The study was conducted in Biology Department.

Blood sample:

5.0 ml of venous blood was drawn after fasting for a period ranging between 10-12 hours, then blood samples were placed in gel tubes and left for 15 minutes until clot formation using centrifugation at 3000 rpm for 10 minutes to separate serum. The blood serum was divided into Eppendorf tubes of 1.5 ml, then kept at a temperature at -80 °C using a deep freezer to further experiments. The blood samples used were based on questionnaire patients who smoked or had corona infections were excluded

Enzymes measurement

In the current study, were studied some biochemical variables in patients with CKD. The activities of ALT, AST, ALP, and concentration of albumin, total protein in blood serum were estimated using a ready-made analysis kit prepared by Biolabo-France (Tietz, 1999), the level of urea and creatinine in the blood was estimated using a kit prepared by the Italian company (Giesse Diagnostics) and using Chemistry Analyzer Smart-150 (Geno TEK)

Statistical analysis:

The data were analyzed according to the system of simple and universal experiments using a completely randomized design. The different information was significantly distinguished by different letters of the alphabet under the probability level of 1% and performed by Duncan's test, one-way ANOVA at value of $P \leq 0.05$ by SPSS version 26 (George and Mallery, 2020).

RESULT AND DISCUSSION

The results as shown in (Table 1 and 2) appear there is a significant reduction in AST, ALT activities, Albumin and T. Protein concentrations compared with control group at $P \leq 0.05$, the differences were at different ages and for both sexes, directly proportional to the progression of chronic kidney disease. As the patient gets older, the impact of chronic kidney disease becomes more serious and may lead to death. Conversely, the activity of ALP concentration was significantly increased compared to the control group the differences were at different ages and for both sexes.

On the other hand, albumin and Protein concentrations indicated a significant reduction at $P \leq 0.05$ in patients of all ages compared to control group, for both sexes.

Table1: Effect of kidney disease on male patients at different age

Parameters	45-55		56-65		66-75	
	Control N= 5	Patients N= 13	Control N= 5	Patients N= 9	Control N= 5	Patients N= 9
	Mean± SD	Mean± SD	Mean± SD	Mean± SD	Mean± SD	Mean± SD
Urea (mg/dl)	31.0±4.4^{c}	66.0±13.0^{b}	38.0±3.3^{c}	82.0±1.1^{b}	32.0±3.5^{c}	150.0±51.0^{a}
Creatinine (mg/dl)	0.9±0.4^{c}	1.9±0.4^{b}	1.1±0.05^{c}	2.0±0.5^{b}	1.0±0.07^{c}	3.3±1.5^{a}
AST(IU/ml)	27.0±4.3^{a}	16.0±1.7^{b}	16.0±1.5^{b}	13.0±1.4^{b}	25.0±3.0^{a}	14.0±3.7^{b}
ALT(IU/ml)	19.0±4.6^{ab}	17.0±2.8^{b}	21.0±2.9^{a}	14.0±2.6^{c}	18.0±3.5^{b}	11.0±3.1^{c}
ALP(IU/ml)	148.1±15.0^{c}	159.0±19.0^{bc}	156.0±24.0^{bc}	200.0±49.0^{b}	135.0±26.0^{c}	310.0±1.1^{a}
Albumin (IU/ml)	4.0±0.3^{b}	3.6±0.4^{c}	4.5±0.2^{a}	3.3±0.3^{d}	4.4±0.3^{a}	2.8±0.4^{e}
T. Protein (IU/ml)	7.2±0.6^{b}	6.6±0.7^{c}	7.5±0.6^{ab}	5.4±0.4^{d}	7.8±0.3^{a}	4.6±0.6^{e}

* The different numbers horizontally indicate the existence of significant differences at the probability level P≤0.05 according to Duncan test.

**N number of samples.

Table 2: Effect of kidney disease on female patents at different ages

Parameters	45-55		56-65		66-75	
	Control N= 5	Patients N= 8	Control N= 9	Patients N= 5	Control N= 5	Patients N= 6
	Mean± SD	Mean± SD	Mean± SD	Mean± SD	Mean± SD	Mean± SD
Urea (mg/dl)	28.0±6.9^{c}	68.0±9.8^{b}	32.0±7.0^{c}	80.0±18.0^{b}	36.0±1.2^{c}	108.0±33.0^{a}
Creatinine (mg/dl)	0.8±0.1^{c}	1.7±0.3^{b}	0.9±0.1^{c}	2.0±0.6^{b}	0.9±0.1^{c}	2.4±0.6^{a}
AST(IU/ml)	18.0±5.9^{b}	16.0±1.9^{bc}	22.0±1.0^{a}	15.0±2.0^{c}	16.0±2.3^{bc}	15.0±1.7^{c}
ALT(IU/ml)	23.6±4.0^{a}	18.76±2.1^{bc}	20.88±5.4^{ab}	16.88±2.0^{c}	17.4±3.2^{bc}	16.0±2.3^{c}
ALP(IU/ml)	125.0±15.0^{c}	183.0±2.8^{bc}	143.0±21.0^{c}	194.0±15.0^{b}	170.0±14.0^{bc}	249.0±81.0^{a}
Albumin (IU/ml)	4.2±0.4^{a}	3.6±0.5^{b}	4.0±0.3^{a}	3.0±0.3^{c}	4.2±0.2^{a}	3.0±0.5^{c}
T. Protein (IU/ml)	7.5±0.5^{a}	6.1±0.9^{b}	7.7±0.5^{a}	5.8±1.0^{bc}	7.8±0.2^{a}	5.0±1.5^{c}

* The different numbers horizontally indicate the existence of significant differences at the probability level P≤0.05 according to Duncan test.

**N number of samples.

The results of the current study indicated that there was a decrease in each of (AST) and (ALT) activities in serum of patients with chronic kidney disease compared to the control group, due to a defect in liver functions as a result of kidney damage or insufficiency in its work, which clearly led to a decrease and inefficiency of liver enzymes activity in the body, studies indicate a decrease in these two enzymes in people with different stages of CKD compared to healthy people and the last stage of the disease, which is kidney failure (Moosazadeh *et al*., 2023).

There is a relationship between the liver and the kidneys, so any damage to the liver is followed by damage to the kidneys, and vice versa. Hepatorenal syndrome (HRS) is a type of progressive kidney failure seen in people with severe liver damage. It is often caused by cirrhosis of the liver. When the kidneys stop working, toxins eventually build up in the body leading to liver failure (Orlić *et al*., 2014).

The results also show a high level of ALP enzyme activity in people with CKD, at first there is a slight increase and often increases with increasing kidney damage. (Waziri *et al*., 2019).

High levels of ALP occur due to diabetes, renal disease, or kidney transplantation. Treatment of metabolic acidosis may reduce muscle protein degradation and improve renal function in CKD patients. Also, there is a rise in the activity of this enzyme from the normal level when suffering from renal insufficiency, its activity decreases in the presence of inorganic calcium and phosphate ions (Alvarenga *et al*., 2020).

It is worth to mention that the results demonstrate a significant decrease in the levels of albumin concentration in the blood of patients with chronic kidney disease compared with the control group. This decrease can be attributed to changes in the structure of the glomeruli membrane, which results in the leakage of albumin and some proteins of low molecular weight, as the decrease in albumin concentration is considered as a sign of the development of renal disease, and the reason may be a restriction in taking protein and protein malnutrition that causes a decrease in albumin concentration in the blood also counts as albumin albuminuria is one of the determinants of kidney function, as its levels rise when a malfunction occurs in the kidneys (Kakitapalli *et al*., 2020).

This decrease is one is one of the clinical signs of hepatic cell diseases resulting from impaired albumin synthesis. This decrease is attributed to increased albumin loss with albuminuria as a result of protein losing nephropathy (Jain and Ducatman, 2019). Also, the reduction in albumin in the blood is attributed to the damaged tissue of the kidneys or as a result of fluid retention and a decrease in the blood calcium concentration, as approximately 50% of the plasma calcium is bound to albumin. The measurement of albuminuria is the preferred method for determining chronic kidney disease (Sumida *et al*.,2020).

Preserving blood proteins is one of the important functions that the kidneys perform, and when there is a defect in the kidney function, it loses the ability to return these proteins, which causes them to be excreted with urine, and as a result, the concentration of proteins in the blood, including albumin, will decrease. Edema is also common in patients with CKD and is caused by the accumulation of body fluids within the tissues instead of returning to the blood vessels due to a low level of blood albumin (Saher *et al*., 2023).

There was no significant association between the consumption of total protein, animal protein and the incidence of chronic kidney disease. Various studies showed that dietary factors play an essential role in preventing the development and progression of chronic kidney disease (Di *et al*., 2019).

CONCLUSION

The liver and kidney share a number of pathophysiological pathways that are closely related to each other. In summary, chronic kidney disease CKD affects liver function and reduces the activity of serum aminotransferase (AST) and ALT enzymes. Furthermore, a decrease in albumin and total protein concentrations is one of the most common liver dysfunctions. In addition, elevated alkaline phosphatase (ALP) activity due to kidney damage, muscle protein degradation, albuminuria and edema. Finally, age had an effect on most of the variables under study in both sexes, while there were no significant differences in the effect between male and female patients.

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تأثير مرض الكلى المزمن على وظائف الكبد

طيبة محمد جدعان **هيثم لقمان الحيالي**

قسم علوم الحياة / كلية العلوم / جامعة الموصل

الملخص

يتأثر نشاط الكبد لدى الأشخاص المصابين بمرض الكلى المزمن الذي يعد أحد أسباب العجز والوفاة في العديد من البلدان حول العالم. فضلا عن تأثيرها على الألبومين والبروتينات الكلية عن طريق خفض مستوياتها في الدم. اشتملت الدراسة الحالية على 54 حالة ممرضة عشوائية تتراوح أعمارهم بين (45–75) عام، حضروا إلى عيادات الكلى والمسالك البولية الخاصة في مدينة الموصل وتم تشخيصهم من قبل أطباء متخصصين للفترة من سبتمبر إلى يونيو 2022. وقد تضمنت 31 ذكرًا و23 أنثى، فضلا عن 30 شخص من الأصحاء 15 ذكور و15 اناث كمجموعة ضابطة.

تشير النتائج إلى انخفاض في أداء الكبد لوظائفه، وقد دل على ذلك الانخفاض المعنوي عند $P \geq 0.05$ في فعالية بعض إنزيمات الكبد مثل الألنين امينو ترانسفيريز (ALT)، الأسبارتيت امينو ترانسفيريز (AST) وزيادة ملحوظة عند $P \geq 0.05$ في فعالية الفوسفاتيز القاعدي (ALP).

الكلمات الدالة: CKD, ALT, AST, ALP.