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ORIGINAL ARTICLE

Serum Liver Enzyme Level in Chronic Kidney Disease Patients: A Prospective Observational Study

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ABSTRACT
Chronic kidney disease (CKD) impacts numerous body systems and is a big worldwide health concern. CKD is a big public health concern because of the high death rate; it affects more than 10% of the global population. This research examines the differences in liver function parameters among CKD patients receiving hemodialysis treatment. This study compares the levels of liver enzymes, bilirubin, total protein, and albumin throughout different phases of chronic kidney disease. A prospective observational study was conducted on 400 out of which 373 in-patients with chronic kidney disease were recruited from tertiary care teaching hospitals. Standard lab methods were used to check liver enzymes and uric acid levels. Statistical research was used to find out how liver enzyme levels changed over time. A chronic kidney disease progressed from stage 1 to stage 5, the study found that hepatic parameters were elevated and progressively depleted. Variations in alkaline phosphatase, aminotransferases, albumin, total bilirubin, direct bilirubin, and total protein levels were noted throughout several phases of chronic kidney disease. Lower levels of liver enzymes were linked to hemodialysis treatments, which may have a beneficial effect on liver function. There is a strong correlation between uric acid and certain liver enzymes, suggesting possible connections between kidney and liver function; this, in turn, supports the idea that hemodialysis may play a therapeutic role in managing hepatic complications in CKD patients. Further research is required to understand the mechanisms and the potential therapeutic implications of these findings.
Keywords: *Chronic Kidney Disease, Liver enzymes, Hemodialysis, Uric acid*

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INTRODUCTION

Changes in kidney structure or function that remain longer than three months are referred to as chronic kidney disease (CKD) according to the Kidney Disease Improving Global Outcomes (KDIGO) recommendations [1]. Because it affects over 10% of the world's population, CKD mortality has been a major issue in public health for many years. The risk of CKD is 50% higher in people with diabetes and hypertension [2]. In 2010, CKD was the 18th most common cause of death, showing a fourfold rise from 1990 [3]. A Glomerular filtration rate (GFR) of < 60 mL/min/1.73 m^2, albuminuria of 30 mg or more per 24 hours, or signs of kidney disease (such as hematuria or structural abnormalities like polycystic or dysplastic kidneys) lasting over 3 months [4]. Urea and creatinine are specific biomarkers for deteriorated renal function. Uric acid is non-specific as it can also elevate in other physiological conditions, but is markedly elevated in CKD [5]. The assessment and monitoring of hepatic illnesses often involve the measurement of serum levels of enzymes, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) [6-8]. Elevated uric acid leads to an increase in hepatic parameters because of high oxidative stress on liver enzymes. However, the casual

relationship between hyperuricemia and elevated hepatic enzymes is controversial. Patients on hemodialysis (HD) who have CKD may have lower blood levels of liver enzymes than those who have adequate renal function [9]. Hence, this prospective observational study aimed to determine the correlation between hemodialysis and serum levels of liver enzymes in CKD patients and if hyperuricemia is associated with higher hepatic enzymes.

MATERIAL AND METHODS

Study Design

A prospective observational study was done to examine the alterations in liver function markers in patients undergoing hemodialysis for chronic kidney disease (CKD). This study design is advantageous for evaluating the relationships between hemodialysis treatment and liver functions, perhaps enhancing our comprehension of how CKD and its heightened parameters impact liver health. It could also offer an understanding of possible treatments or modifications in hemodialysis procedures to reduce any negative impacts on liver function. Discovering unexpected findings or connections between liver function and CKD could lead to new research and therapeutic management opportunities.

Study population

Out of 400 randomly enrolled participants, only 373 were analysed for the study after excluding the other 27 who didn't meet the inclusion criteria. Patients were enrolled based on inclusion and exclusion criteria, Inclusion criteria were patients ≥18 years, diagnosed with CKD in-patient of the general medicine and nephrology department, and patients willing to participate in the study. Exclusion criteria included pregnant and lactation women, psychiatric patients, Patients suffering from hepatic disease, and patients under critical conditions.

Diagnostic criteria

Hyperuricemia was characterized by SUA >7 mg/dL in both men and women. Serum ALT and AST levels >35 U/L, Alkaline phosphatase 30 to 120 IU/L, total protein 6.0-8.3 g/dl, albumin 3.5-5.3 g/dl, total bilirubin 0.2-1.2 mg/dl, and direct bilirubin 0-0.3 mg/dl for both men and women were considered to indicate an elevated level of liver enzymes according to established cutoffs. When at least one liver enzyme was found to be higher than the reference range, it was determined that the participant had either liver dysfunction or abnormal levels of liver enzymes.

Sample size

Sample size was found using the formula $S = z^2 \times p \times (1-p) / m^2$. Usually, 5%, or 0.05, is thought of as the margin of error [10-11].

ETHICAL CONSIDERATION

The Institutional Ethical Committee of Maharishi Markandeshwar Institute of Medical Sciences and Research (MMIMSR), Mullana, approved the study protocol with reference number 2342. Before conducting the study, the researchers provided a clear explanation of its objectives and methodologies to the participants, and they received their informed consent.

Study Procedure

A prospective observational analysis was undertaken to evaluate the serum liver enzyme levels in individuals with chronic renal disease, both with and without dialysis. A total of 373 patients who met the predetermined inclusion and exclusion criteria were included in the study. The demographic information, clinical data, and laboratory results of the individuals were documented, and the staging of CKD was determined using eGFR. The statistical analysis encompassed the estimation of the mean and standard deviation (SD) for various parameters. Additionally, an evaluation was conducted to examine the correlation between stages of CKD and hepatic parameters. Furthermore, Pearson correlation was employed to investigate the association between uric acid levels and hepatic parameters in patients with CKD. Hepatic parameters were assessed by obtaining blood samples before and after hemodialysis. The study revealed a significant positive association between chronic kidney disease (CKD) and modified hepatic markers, which is consistent with other scholarly investigations. In general, the study offers significant contributions to our understanding of the correlation between chronic kidney disease (CKD), liver enzyme levels, and the effects of dialysis on hepatic and renal parameters.

RESULTS

The study sample consisted of all individuals who satisfied the predetermined criteria for inclusion and exclusion. The study comprised a total of 373 inpatient individuals, with 172 (51.69%) being male and 201 (48.30%) being female. The data reveals that the prevalence of CKD is higher among individuals aged 40-59, accounting for 43.16% of cases. Research has revealed that females had a higher probability of experiencing CKD advancement compared to males in both urban and rural areas. All demographic

information was incorporated and computed on a comprehensive scale, taking into account both male and female values. The average values for males were reported as 50±15.40, while for females they were 56.03±14.18. Females have a greater average age than males when it comes to having CKD. The systolic mean was 157.06±19.82 and the diastolic mean was 85.83±10.75. CKD patients exhibited elevated systolic blood pressure, while their diastolic blood pressure remained within the normal range of 140/90 mmHg as defined by the JNC VIII guidelines. The measurements of lft, rft, and bp exhibited higher values in individuals with CKD. However, liver proteins, specifically albumin and total protein, demonstrated a drop in their values compared to normal levels. As seems expected, the rft parameters exhibited an increase in all stages of CKD. The liver enzymes exhibited elevated levels out of the prescribed normal range in both male and female subjects, as depicted in Table 1.

Table 1: Demographic details of study population (n=373)

Variables	Overall	Male (n=172)	Female (n=201)	Normal	Elevated	Decreased
Age (in years)	53.32±14.99	50±15.40	56.03±14.18			
SBP (in mmHg)	157.06±19.82	156.03±19.50	158.17±20.28	156.42±19.81	158.64±18.51	
DBP (in mmHg)	85.83±10.75	87.7±9.54	83.80±11.67	85.60±10.93	86.17±10.95	
SUA (mg/dL)	8.04±6.67	8.43±8.80	7.54±3.11	8.05±6.70	8.02±6.70	
Creatinine (mg/dL)	7.18±5.07	7.08±4.65	6.64±5.47	7.33±5.23	7.18±5.07	
Urea (mg/dl)	144.84±17.35	147.87±15.50	141.59±19.96	146.55±17.86	144.84±17.35	
AST (U/L)	54.52±15.06	56.71±13.15	52.18±15.98	54.52±15.06	56.74±16.47	
ALT (U/L)	47.90±12.19	48.36±14.22	47.40±16.65	47.90±12.19	49.69±13.37	
ALP (U/L)	156.68±17.77	148.20±10.54	165.76±12.44	156.0±17.77	157.36±17.76	
Total bilirubin (mg/dL)	0.50±0.10	0.4±0.18	0.59±0.23	0.38±0.14	0.65±0.32	
Direct bilirubin (mg/dL)	0.27±0.5	0.26±0.1	0.28±0.10	0.22±0.18	0.28±0.15	
Total protein (g/dL)	5.88±1.10	5.81±1.13	5.96±1.06	5.93±1.09	5.83±1.13	5.80±1.09
Albumin (g/dL)	3.35±0.67	3.38±0.70	2.32±0.64	3.40±0.63		1.35±0.67

All values are measured in Mean ± SD

Hepatic enzymes are categorized based on the stages of CKD and the number of patients as depicted in Table 2. These stages illustrate the development of CKD as liver markers increase and decrease. CKD patients exhibited significantly elevated levels of AST, ALT, and ALP. Elevated levels of ALP increase the probability and development of osteorenal dystrophy in people with CKD. Total bilirubin and direct bilirubin levels indicate an increase as the disease advances, increasing the risk of jaundice. Albumin and total protein levels drop as the stage of CKD increases from 1 to 5.

Table 2: Serum liver enzymes and other biochemical parameters according to CKD stages

LFT Parameters	**Stage 1**	**Stage 2**	**Stage 3**	**Stage 4**	**Stage 5**
Number of Patients	74	72	68	76	83
AST(U/L)	23±11.96	30±14.84	35.88±16.34	44.55±14.34	56.24±13.97
ALT(U/L)	37.5±9.19	42.42±8.34	47.44±8.45	49.12±9.24	57.84±9.66
ALP(U/L)	164±12.02	173.28±16.02	173.66±12.26	179±9.22	183.38±7.50
Total bilirubin(mg/dL)	1.58±0.76	0.34±0.10	0.38±0.25	0.85±0.51	0.38±0.20
Direct bilirubin(mg/dL)	1.09±0.15	0.4±0.1	0.52±0.2	0.21±0.14	0.23±0.20
Total protein(g/dL)	6.75±0.07	5.98±0.12	5.37±1.24	5.40±1.02	5.98±0.98
Albumin(g/dL)	3.75±1.48	3.57±0.24	2.92±1.12	2.10±0.55	2.44±0.61

All values are measured in Mean ± SD (CKD Stages: Stage 1= ≥90, stage 2= 60 to 89, stage 3=30 to 59, stage 4= 15 to 29, stage 5= <15)

The liver parameters in Table 3 were classified based on the stage of CKD, indicating variations in the variables according to the stage. The reduction in ALT levels can be attributed to a deficiency in vitamin

B6, a coenzyme of ALT, or hemodilution, a phenomenon observed in patients with CKD before a hemodialysis (HD) session as a result of water retention. Plasma ALP levels can arise from various sources including the liver, bone, gastrointestinal tract, and placenta. Typically, the majority of circulating enzyme levels are attributed to isoenzymes derived from the liver and bone. Renal osteodystrophy can lead to a significant increase in the bone isoenzyme of ALP, hence contributing to elevated levels of ALP in the bloodstream. Hepatitis B and C are the prevailing chronic liver illnesses observed in individuals diagnosed with CKD (Hrstic and Ostojic, 2011) [12]. Serum aminotransferase cut-off values for viral hepatitis screening in peritoneal dialysis patients may be changed. Hypoalbuminemia is common in CKD and is associated with poor outcomes. Recent studies demonstrate that low S-Alb indicates prolonged inflammation and is not a good nutritional indicator [13].

Table 3 shows that AST, ALT, and ALP levels were significantly associated with uric acid at 0.01 and 0.05 levels of significance in CKD patients. There were no substantial liver protein differences. Various causes can cause oxidative stress and inflammation, damage hepatocytes and altering serum aminotransferase levels.

Table 3: Correlation between liver enzymes and uric acid

Parameters	Uric acid r value	P value	Significance
AST(U/L)	0.51**	0.00	0.01
ALT(U/L)	0.67**	0.00	0.01
ALP(U/L)	0.22*	0.01	0.05
Total bilirubin (mg/dL)	-0.03	0.67	
Direct bilirubin(mg/dL)	0.05	0.95	
Total protein(g/dL)	0.61	0.51	
Albumin (g/dL)	0.40	0.66	

All values are measured in SPSS using Pearson correlation

Table 4 shows the link between uric acid and hepatic parameters. Since the kidneys remove uric acid, decreasing GFR increases serum uric acid [14]. Hyperuricaemia may cause hypertension, renal illness, metabolic syndrome, and cardiovascular disease [15]. Increased blood uric acid indicates CKD in people with normal renal function, especially end-stage renal disease. Serum uric acid predicts CKD in IgA nephropathy [16]. Before and after dialysis, blood samples were taken to compare LFT parameters in dialysis patients. Table 4 shows that before dialysis, all liver function parameters were increased than normal with no hepatic disorders, but after dialysis, they decreased. The reduction in haemodialyzed aminotransferases may be attributable to many mechanisms, including HD elimination. Elevated blood lactate levels rapidly consume nicotinamide adenine dinucleotide phosphate (NADPH) and decrease aminotransferase concentration; uremic factors inhibit enzyme activity; and pyridoxine deficiency, a cofactor needed for transaminase biosynthesis.

Table 4: Serum level of liver enzymes among subjects undergoing hemodialysis

LFT parameters	Before dialysis	After dialysis
AST(U/L)	52.89±8.54	50.80±7.64
ALT(U/L)	46.30±6.41	44.64±6.02
ALP(U/L)	157.42±8.44	130.79±8.21
Total bilirubin(mg/dL)	0.85±0.32	0.44±0.24
Direct bilirubin(mg/dL)	0.25±0.06	0.24±0.01
Total protein(g/dL)	5.99±1.02	4.17±0.82
Albumin(g/dL)	3.35±0.67	2.74±0.70

All values are measured in Mean ± SD

DISCUSSION

Monitoring and assessing CKD is vital because it affects normal physiological activities and other organs, making it a global health concern. As demonstrated in Table 3, CKD patients had reduced albumin and total protein but greater AST, ALT, and ALP. Total and direct bilirubin affect less than other factors. Eustace *et al*. (2004) found that CKD patients have low plasma albumin levels, which prevents water from entering the vascular system and producing renal failure-related oedema [17]. The study found high ALP levels (156.68±77.77) in CKD patients, similar to Beddhu *et al.* (2009), which may contribute to the higher cardiovascular burden in this population. Table 4 shows that serum ALT (0.510**), AST (0.671**), and ALP (0.228*) were favourably linked with serum uric acid in CKD patients. The study showed that

uric acid modestly increases liver enzymes. Uric acid levels were greater in males (8.43±8.80) compared to females (7.54±3.11). AST and ALT were greater in males (24.70±46.15 and 28.36±44.22) compared to females (23.18±45.98 and 27.44±46.65), while ALP was higher in females (165.76±92.44) compared to males (148.20±60.54), indicating a higher risk of bone degeneration and CKD. Several studies have investigated uric acid and liver enzymes. Deb *et al.* (2021) found that high liver function markers (AST≥33, ALT≥30, total bilirubin≥17) were linked to high uric acid levels (≥6.8 mg/dL). Studies on liver parameters in dialysis patients show that hemodialysis reduces or eliminates blood circulation substances. We found that CKD patients on dialysis had somewhat lower mean serum liver parameters and serum aminotransferases than those on dialysis (Table 4). The study showed differences in AST and ALT values before and after dialysis: 52.89±8.54 (50.80±7.64), and 46.30±6.41 (44.64±6.02), respectively. High uric acid levels are associated with higher AST, ALT, and ALP levels, indicating hepatocyte injury and inflammation. Uric acid did not correlate with liver proteins or bilirubin. Dialysis lowers hepatic parameters, suggesting it affects liver function. CKD patients need liver function monitoring, dialysis, and personalised treatment programs to maximise patient care. Clinicians and researchers treating CKD patients may benefit from this study.

CONCLUSION

The current investigation demonstrated a robust and favourable correlation between SUA and serum AST, ALT, and ALP levels in individuals aged 18 years and above who had chronic kidney disease (CKD), regardless of any potential confounding variables. The current investigation demonstrated that hepatic parameters had elevated levels in individuals with CKD before dialysis, but subsequently decreased following the dialysis session. It is imperative to do liver function monitoring in patients with CKD who are undergoing dialysis and tailored treatment programs to enhance the quality of patient care. The present study holds potential value for doctors and researchers engaged in the management of patients with CKD. Additional investigation is required to validate whether dialysis is the underlying cause of these disparities or if other variables are implicated in the modification of the hepatic parameters. Nevertheless, additional research is required to comprehend the fundamental mechanisms implicated in the correlation between SUA and liver enzymes.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest, financial or otherwise.

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