



## TO STUDY THE CLINICAL, BIOCHEMICAL, SEROLOGICAL AND RADIOLOGICAL HEPATIC PROFILE IN PATIENTS OF CHRONIC KIDNEY DISEASE ON MAINTENANCE HEMODIALYSIS.

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### Abstract

**Background:** Chronic kidney disease (CKD) is a silent epidemic of the 21<sup>st</sup> century. Although the connection between the kidney and liver is well recognized and intricate, it is still not entirely understood. Hepatic disorders in CKD may range from mild form of transaminitis to life threatening decompensated chronic liver disease. Many of these manifestations may have correctable underlying etiologies.

**Aim & Objective:** To study the spectrum of clinical, hepatic biochemical, serological and radiological profile in patients of CKD on maintenance hemodialysis (HD).

**Methodology:** The present study was a prospective observational study which was conducted in the Department of Gastroenterology, MMIMSR, Mullana from January 2023 to January 2024 with a sample size of 100 patients. All indoor and outdoor cases of CKD were enrolled for the study and screened for various hepatic complaints. Written informed consent and institutional ethical clearance was obtained in all the cases. Complete anonymity of the patient was maintained in all the cases. All the selected patients were subjected to various biochemical, serological, and radiological investigations.

**Results:** The mean age of subjects was 55.5 years. 71% were male and 29% were female. The most common etiology of CKD was systemic arterial hypertension (39%). During serological examination, 16% were positive for Anti HCV Ab while 11% were positive for HBsAg and only 2% were positive for HIV. It was observed that AST (SGOT), ALT (SGPT), GGT and Serum albumin mean values were on lower side in patients of CKD on maintenance HD. On Ultrasonography, 40% subjects had normal liver while 29% had Grade 1 fatty liver, 15% had Grade 2 fatty liver, 2% had Grade 3 fatty liver and 14% had chronic liver disease.

**Conclusion:** In summary, our study reinforces that hepatic disease is common and manifests in multiple ways in CKD subjects, likely due to the intricate interplay between liver and kidney functions. CKD potentially initiates and exacerbates early stages of hepatic disease, progressing to more severe states. A comprehensive, interdisciplinary approach is essential, necessitating collaboration between hepatologists and nephrologists for timely and effective management of these patients.

## INTRODUCTION

The nephrons' progressive and permanent degradation is the cause of chronic kidney disease (CKD). The clinical syndrome of uremia develops as a result of the kidney's excretory, metabolic, and endocrine functions being impaired due to the reduced effective functioning of kidney tissue.<sup>1</sup> CKD has now become a global public health concern, with a frequency of 8–16%.<sup>2</sup> Due to the absence of a national registry, the incidence of CKD in India is not well known.<sup>3</sup> Nonetheless, estimates suggest that as many as 785 persons per million may have CKD in India.<sup>4</sup>

Globally, there are many different causes of chronic kidney disease (CKD). However, the most common primary diseases that lead to CKD and, eventually, end-stage renal disease (ESRD) are primary glomerulonephritis, hypertension, hereditary or cystic diseases, chronic tubulointerstitial nephritis, secondary glomerulonephritis, or vasculitis.<sup>5</sup> The following five clinical risk factors for rapid CKD progression: proteinuria, hypertension, hyperglycemia, and black race. Furthermore, there is evidence linking faster CKD progression to environmental exposures like lead, smoking, metabolic syndrome, lead, and obesity, as well as maybe certain analgesic drugs.<sup>6</sup> The patient should be given a range of alternatives for renal replacement therapy once the progression of CKD is identified. These options include HD, peritoneal dialysis, and kidney transplantation.<sup>7</sup> Information about conservative and palliative care management should be given to patients who choose not to get renal replacement therapy. Patients with cirrhosis require specific care from the clinician when treating renal illness; this may involve liver transplantation as well as possibly combined kidney and liver transplants.<sup>8</sup> Curiously, recent research has indicated that patients with CKD on HD may have lower serum levels of liver enzymes than people with normal renal function. The diagnosis, clinical management, and course of treatment of liver disease in these patients may be negatively impacted by this profile.<sup>9</sup> Patients with chronic kidney disease (CKD) can experience lower morbidity and mortality rates if their existence is identified, diagnosed early, and treated appropriately.

## AIMS AND OBJECTIVES

1. To study the spectrum of clinical and hepatic biochemical profile in patients of CKD on maintenance hemodialysis.
2. To study the spectrum of serological and hepatic radiological profile in patients of CKD on maintenance hemodialysis.

## MATERIAL AND METHODS

The present study was a prospective observational study which was conducted in the Department of Gastroenterology, MMIMSR, Mullana from January 2023 to January 2024 with a sample size of 100 patients. All indoor and outdoor patients of CKD were enrolled for the study and screened for various hepatic complaints. Written informed consent and institutional ethical clearance was obtained in all the cases. Complete anonymity of the patient was maintained in all the cases.

## Inclusion Criteria

1. Adults > 18 years of age with CKD on maintenance hemodialysis having any clinical, biochemical, serological or radiological hepatic manifestation
2. Patients who give written consent for the study.

### Exclusion Criteria

1. Patients of CKD who are not on maintenance hemodialysis.
2. Patients who have undergone renal transplant.
3. Patients who refuse to give consent.

### Study Methods:

Patients of CKD undergoing maintenance hemodialysis were enrolled for the study. They underwent a thorough physical examination for the disease, and the history and cause of the illness were recorded. All the selected patients will be subjected to various biochemical, serological, and radiological investigations.

### Statistical Methods

All statistical analysis was performed using SPSS software (version 20, SPSS Inc, Chicago, IL). Continuous data was expressed as mean + standard deviation and analyzed, whereas categorical variables was expressed as quantities and analyzed. p-value < 0.05 was considered significant for the analysis.

### RESULTS

Majority of study subjects (69%) were above 50 years of age and only 13% of CKD on maintenance hemodialysis patients were below 40 years of age. The mean age of the study subjects was 55.5 ± 13.5 years with range from 22 years to 81 years. 71% were male and only 29% were female. The most common etiology of CKD was systemic arterial hypertension seen in 39% of subjects followed by diabetes mellitus in 24% and in 6% of study subjects both were present. (Table 1)

The most common symptom with which the study subjects presented were shortness of breath (37%) followed by pedal oedema (16%), decreased urine output (14%), abdominal distension (12%), cough (7%), vomiting (5%), fever (4%), altered sensorium (3%), anasarca (1%) and UGI bleed (1%). (Table 1)

**Table 1:** Demographic characteristics of Study Subjects

Characteristic	Frequency (n=100)	Percentage (%)
<b>Age Group</b>		
<40	13	13
41-50	18	18
51-60	34	34
>60	35	35
<b>Gender</b>		
Female	29	29
Male	71	71
<b>Etiology of CKD</b>		
Systemic arterial hypertension (SAH)	39	39
Diabetes Mellitus (DM)	24	24
SAH +DM	6	6
Others	9	9
Undetermined	22	22
<b>Chief Complaint</b>		
Shortness Of Breath	37	37
Pedal Oedema	16	16
Decreased Urine Output	14	14
Abdominal Distension	12	12
Cough	7	7
Vomiting	5	5
Fever	4	4
Altered Sensorium	3	3
Anasarca	1	1
UGI Bleed	1	1

Table 2 shows that pallor was seen in 93% of study subjects of CKD on maintenance hemodialysis while icterus was seen in only 7% of study subjects. 55% of study subjects had generalized oedema. 12% of study subjects had ascites.

**Table 2:** Clinical characteristics of Study Subjects

Clinical Characteristics	Frequency (n=100)	Percentage (%)
Pallor	93	93
Icterus	7	7
Edema	55	55
Ascites	12	12

During serological evaluation, 16% were positive for Anti HCV Ab while 11% were positive for HBsAg and only 2% were positive for HIV. (Table 3)

**Table 3:** Serological Evaluation of Study Subjects

Viral Markers	Frequency (n=100)	Percentage (%)
Anti HCV	16	16
HBsAg	11	11
HIV	2	2

Table 4 shows the mean values of various biochemical parameters in the study subjects. It was observed that AST (SGOT), ALT (SGPT), GGT and Serum albumin mean values were on lower side in patients of CKD on maintenance HD.

**Table 4:** Biochemical Parameters of Study Subjects

Characteristic	Mean	SD
Hb	8.2	1.9
TLC	9733.9	746.8
Platelet count	200.2	101.5
Creatinine	10.0	4.8
Urea	165.1	75.6
Sodium	136.1	4.5
Potassium	4.6	0.8
Uric Acid	7.2	2.2
Calcium	8.0	1.3
Phosphorus	6.3	2.8
Total Bilirubin	0.9	1.9
Direct Bilirubin	0.6	1.5
AST (SGOT)	11.6	1.8
ALT (SGPT)	8.9	1.2
Alkaline Phosphate	128.2	16.2
Total protein	6.5	0.8
Albumin	2.9	0.4
GGT	31.2	4.0
PT/INR	1.2	0.2
RBS	167.9	59.6

On Ultrasonography, out of 100 CKD subjects on maintenance hemodialysis, 40% subjects had normal liver while 29% had Grade 1 fatty liver, 15% had Grade 2 fatty liver, 2% had Grade 3 fatty liver and 14% had chronic liver disease. (Table 5)

**Table 5:** Distribution of Study Subjects According to Hepatic USG Findings

USG Findings	Frequency (n=100)	Percentage (%)
Normal	40	40
Fatty Liver Grade 1	29	29
Fatty Liver Grade 2	15	15
Fatty Liver Grade 3	2	2
Chronic Liver Disease	14	14

## DISCUSSION

Numerous investigations have delved into the phenomenon of diminished serum levels of AST and ALT in Chronic Kidney Disease (CKD) patients undergoing hemodialysis (HD). Various hypotheses have emerged to account for this decline, including the removal of aminotransferases during HD sessions, rapid depletion of Nicotinamide Adenine Dinucleotide Phosphate (NADPH) due to elevated lactate serum levels during biochemical assays, inhibition of enzyme activity by uremic factors, and a possible deficiency of pyridoxine, a cofactor for aminotransferase synthesis.<sup>10,11</sup>

In exploring the potential pyridoxine deficit, Jung et al.<sup>12</sup> assessed aminotransferase levels in CKD patients on HD and found no disparities in values before and after the addition of pyridoxal 5'-phosphate (PLP), an active form of pyridoxine, to enzyme assays. Similarly, Gressner et al.<sup>13</sup> observed no correlation between plasma PLP levels and ALT or AST serum levels in 26 HD patients. This led to the conclusion that reduced AST and ALT levels in HD patients were partially attributed to pyridoxine deficiency, which plays a role as a coenzyme in aminotransferase synthesis.<sup>11</sup>

In a study by Sombolos et al.<sup>14</sup> involving 53 CKD patients on HD, participants were categorized into HD, isolated ultrafiltration, and euvolemic HD groups to evaluate the effects of hemodilution on serum aminotransferase levels. Euvolemic HD showed no significant differences in ALT and AST levels before and after the procedure. However, both isolated ultrafiltration and standard HD resulted in increased aminotransferase levels post-procedure, indicating that the rise in aminotransferase levels after HD primarily stems from hemoconcentration induced by ultrafiltration rather than the removal of enzymatic inhibitors.

Subsequently, researchers suggested that aminotransferase serum levels could be reduced even during conservative treatment in earlier stages of CKD. Fabrizi et al.<sup>15</sup> analyzed 407 pre-dialysis CKD patients, 171 dialysis patients, and 431 healthy controls, revealing decreased AST and ALT levels in dialysis patients compared to healthy controls. Similarly, dialysis patients exhibited lower aminotransferase serum levels compared to CKD patients undergoing conservative treatment, indicating that CKD patients experience reduced aminotransferase serum levels, with this reduction occurring prior to dialysis initiation.

In the present study, during serological examination, it was observed that 16% were positive for Anti HCV Ab, 11% were positive for HBsAg, and only 2% were positive for HIV. As expected, CKD patients on HD infected with HCV exhibited higher aminotransferase serum levels compared to non-infected counterparts on HD. For instance, CKD patients on HD co-infected with HCV demonstrated lower aminotransferase levels than infected patients without CKD.<sup>16,17</sup> Cotler et al. found lower ALT serum levels in CKD patients on HD compared to controls, posing challenges for the accurate assessment and clinical management of HD patients with viral hepatitis.<sup>18</sup>

Similarly, Baedalamnti et al. observed a decrease in HCV-RNA levels in all CKD patients with HCV infection undergoing HD, suggesting that HD might complement antiviral therapy by regulating or removing HCV-RNA and anti-HCV titers. Additionally, increases in hepatocyte growth factor (HGF) induced by HD and production of alpha interferon (IFN- $\alpha$ ) during HD potentially contribute to reduced HCV viremia and subsequent aminotransferase levels in serum.<sup>19</sup>

Although biochemical tests are less cost-effective than virological tests for detecting new cases of acute hepatitis C, aminotransferases serve as predictors of the acute form of hepatitis due to significant increases in their serum levels. However, ALT serum levels lack accuracy in diagnosing chronic HCV infection in CKD patients on HD. Efforts have been made to establish new cut-off values to improve sensitivity and specificity in diagnosing hepatocyte injury and chronic hepatitis in this population.

The study involving 202 CKD patients on hemodialysis (HD) revealed that a lower cutoff value for alanine aminotransferase (ALT) could improve the accuracy of diagnosing chronic hepatitis C virus (HCV) infection in this population. For instance, a cutoff value of 60% of the upper limit of normal (ULN) showed a sensitivity of 67% and specificity of 75% in identifying anti-HCV-positive patients.<sup>20</sup> Similar results were found in another study with 217 HD patients, where a cutoff value of 50% of the ULN for ALT distinguished anti-HCV-positive from negative patients with a sensitivity of 67% and specificity of 83%. Additionally, for patients who were HCV-RNA-positive, the cutoff value for ALT was 45% of ULN, with a sensitivity of 71% and specificity of 80%.<sup>21</sup> These findings suggest the potential utility of lowering the ULN of ALT for diagnosing chronic HCV infection in CKD patients on HD.

Fabrizi et al. demonstrated that CKD patients infected with hepatitis B virus (HBV) and positive for HBV-DNA had higher serum levels of aminotransferases compared to those with negative HBV-DNA.<sup>22</sup> Conversely, Li et al. found no significant difference in ALT serum levels between CKD patients positive and negative for HCV-RNA, suggesting that viremia status may not affect ALT levels in these patients. However, the small sample size in Li et al.'s study may have limited the ability to detect differences.<sup>23</sup>

Although aminotransferases alone did not correlate significantly with liver histology in HCV-infected patients on HD, the AST-to-Platelet Ratio Index (APRI) was found to be a useful tool for estimating the degree of hepatic fibrosis. Studies by Schiavon et al. and Liu et al. demonstrated the efficacy of APRI in predicting liver fibrosis in CKD patients on HD infected with HCV.<sup>24,25</sup>

Gamma glutamyl transferase (GGT) serum levels in CKD patients on HD may not exhibit significant reductions compared to individuals with normal renal function. GGT levels could be influenced by hemodilution due to fluid retention in CKD patients, making them potentially useful markers, akin to aminotransferases, in diagnosing chronic HCV infection. Fabrizi et al. identified associations between GGT serum levels and hepatitis caused by HBV or HCV through multivariate analysis, suggesting their potential utility in diagnosing viral hepatitis.<sup>26</sup>

In terms of liver conditions detected via ultrasonography in CKD patients on maintenance hemodialysis, various findings were observed, including normal liver, fatty liver grades 1 to 3, and chronic liver disease. Another study documented a high prevalence of non-alcoholic fatty liver disease (NAFLD) in CKD patients, with severity positively correlated with serum creatinine and C-reactive protein levels. The severity of liver steatosis was also found to be negatively correlated with kidney function, highlighting the value of ultrasonography as a non-invasive screening method for diagnosing NAFLD in CKD patients.<sup>27</sup>

In the present study it was observed on Ultrasonography, out of 100 CKD subjects on maintenance hemodialysis, 40% subjects had normal liver while 29% had Grade 1 fatty liver, 15% had Grade 2 fatty liver, 2% had Grade 3 fatty liver and 14% had chronic liver disease. In a study by Mikolasevic et al.<sup>28</sup>, it was observed that out of 62 CKD patients 53 (85.5%) had NAFLD and of these 14/53 patients (26.4%) had also liver stiffness >7 kPa. The severity of liver steatosis was positively correlated with serum creatinine and CRP. The results suggested a high prevalence of NAFLD in CKD patients. The severity of liver steatosis is negatively correlated with kidney function. The study documents the value of ultrasonography as an effective non-invasive screening method for the diagnosis of NAFLD.

## CONCLUSION

CKD has become a prevalent noncommunicable ailment globally, ranking among the leading causes of mortality. In summary, our study reinforces that hepatic disease is common and manifests in multiple ways in CKD subjects, likely due to the intricate interplay between liver and kidney functions. CKD potentially initiates and exacerbates early stages of hepatic disease, progressing to more severe states. A comprehensive, interdisciplinary approach is essential, necessitating collaboration between hepatologists and nephrologists for timely and effective management of these patients.

**Conflicting interest-** Nothing to disclose.

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