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Renal Dysfunction Amongst Cirrhosis Patients: An Exploratory Study

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Abstract

People with decompensated cirrhosis frequently experience acute renal damage, which is associated with a poor prognosis. The most common and readily recognizable cause of cirrhosis is hepatorenal syndrome type 1 (HRS-1), also known as hepatorenal syndrome-acute kidney damage. Acute kidney damage with direct links to chronic liver illness includes abdominal compartment syndrome, cardiorenal processes associated with cirrhotic cardiomyopathy and portopulmonary hypertension, and cholemic nephropathy. Some glomerular nephropathies (GNs), such as viral hepatitis and Immunoglobulin A (IgA) nephropathy, can result in acute kidney injury in cirrhosis. Understanding a medical condition's underlying etiology is essential to finding the best therapy. The best form of rehydration therapy for prerenal acute kidney damage is albumin. Both acute tubular damage and acute interstitial nephritis can be effectively treated with supportive care, removal of the underlying cause, and, in the case of the latter, corticosteroids. Acute kidney injury (AKI) is a complication of cirrhosis that calls for a comprehensive strategy to diagnose and treat it.

Key Words: Kidney, Patients, Liver Disease, Acute Kidney Injury, Cirrhosis

Introduction

Renal dysfunction is more common in cirrhotic patients than it was 20 years ago. In hospitalized patients, the incidence of acute renal injury related to cirrhosis has grown by over 200 percent since 2004, whereas the incidence of chronic kidney disease (CKD) has increased by around the same amount. Improvements in organ preservation and transplantation technology have led to a more than 200 percent increase in the number of people who are a candidate for a liver transplant due to chronic kidney disease, and an almost 500 percent increase in the number of people who have received both a liver and since acute kidney injury (AKI) and CKD are linked to poor clinical outcomes [1,2] addressing these trends is crucial [1,3] Those who suffer from AKI or AKI in addition to CKD have a mortality risk about three times higher than those who do not have renal disease [2,4].

People with cirrhosis are at a higher risk for experiencing long-term complications as a result of AKI occurrences. When AKI occurs, the prognosis for the patient is less certain, although eventually, CKD will develop [5]. Both chronic kidney illness and acute kidney injury have been linked to cirrhosis. Patients with kidney illness are at greater risk for AKI and have a lower chance of recovery from it. Patients with AKI, however, are more likely to progress to CKD [6]. Non-alcoholic fatty liver disease and its related risk factors, such as hypertension and diabetes, are thought to increase the prevalence of AKI and the incapacity to recover from it [5,6]. This research emphasizes the need of pinpointing the triggers, severity, and progression of renal impairment in cirrhotic patients.

Serum creatinine levels and/or urine output are used in the clinic to diagnose acute renal damage [7]. However, the medical history and physical examination of the patient are the best methods to detect whether or not a specific cause of AKI is present before any diagnostic tests are conducted. The only known cause of hepatorenal syndrome type 1, often known as acute kidney injury, is cirrhosis (AKI). Depending on the patient's symptoms, it may be part of the differential diagnosis (*i.e.*, inpatient *vs.* outpatient). Chemical urinalyses, full urinalyses, and microscopic investigations of urine sediment all play critical roles in diagnostic testing in the laboratory. One common approach to evaluating if obstructive uropathy is the underlying cause of acute kidney injury is to perform renal ultrasonography (AKI). Researchers have looked for biomarkers in urine to diagnose AKI in cirrhosis. “Such proteins include neutrophil gelatinase-associated lipocalin, liver fatty acid-binding protein, renal injury molecule-1, and tissue inhibitor of metalloproteinases-1” [8]. Clinical outcomes

are associated with these indicators because they disclose either the extent of the injury or the body's response to it. Prerenal azotemia and acute tubular damage are the most common precipitating factors of AKI in cirrhotic patients.

There are many potential predictors of HRS-1 that can be evaluated through risk assessments. Amount of creatinine in the blood at the start of treatment. The risk of HRS-1 developing and the likelihood of a full recovery from AKI are both diminished in patients with higher blood creatinine levels [6]. "People with lower mean arterial pressure at baseline are more likely to develop HRS-1, and they also have more trouble recovering from acute renal injury" [9]. Changes in blood volume, blood pressure, and coagulation are some of the hemodynamic parameters that might shift. Long-term exposure to hyperdynamic conditions increases the risk of diastolic dysfunction and reduces the heart's reactivity. Thus, patients are more likely to have HRS-1 and circulatory problems [10]. Acute-on-chronic liver failure is a condition more commonly seen in people with decompensated cirrhosis. Acute hepatic decompensation and severe multi-organ failure characterize this condition [11]. "Kidney impairment is more common in hospitalized patients with acute-on-chronic liver failure than in the general population, usually as a result of the initial injury (*e.g.*, infection and hemorrhage). Albumin is beneficial in preventing AKI and HRS-1 in patients with spontaneous bacterial peritonitis." This is a noteworthy finding because so many people in this patient population have these symptoms as a result of the underlying disease [12]. The prognosis and treatment of acute kidney injury and liver disease are affected by their underlying causes. Those who aren't candidates for a liver transplant should give serious thought to the benefits and drawbacks of receiving one.

Cirrhosis of the liver affects people all over the world. Acute kidney injury (AKI) is a potentially fatal consequence of liver cirrhosis, especially in the setting of decompensated cirrhosis [13]. Twenty percent to fifty percent of hospitalized patients with liver cirrhosis have acute renal failure, whereas only one percent develop chronic kidney disease. [14, 15] High mortality rates of up to 90% have been connected with Acute Kidney Injury (AKI) in patients with liver cirrhosis [16]. Patients with acute kidney injury typically have much more extensive and costly hospital stays [17]. "When evaluating the severity of hepatic dysfunction, the Child-Pugh score and its subscores are commonly used in conjunction with AKI, and there is good evidence that they are reliable predictors of mortality in patients with

decompensated liver cirrhosis" [13]. The attributes of the present study aims at exploring (i) the study on renal dysfunction presentation in Cirrhosis patients; (ii) the understanding on mechanisms of renal dysfunction.

Materials and Methods

A total of 200 participants were selected for the study. The participants consisted of 100 patients, who suffered from liver diseases. The control group comprises another 100 healthy individuals. The mean age of the 100 patients, was 45.7 years ± 12.7 years). The mean age of the controls was 46.27 years ± 13 years. The mean age of both, however, differed non-significantly. There were 92 males and 8 females.

EXPERIMENTAL

Proportional Stratified Sampling Method was employed to recruit study sample from the population. The study population comprised of the patients suffering from liver diseases, who visited the hospital and also those who were admitted .

Patients Stratification Criteria

Patients were stratified on the basis of following criteria as given below:

1. Serum Aminotransferase Level
2. Presence of Ascites

The study population are catogorized into the following groups:

GROUP 1, Patients, with SGPT level >300 IU, along with SGPT value > SGOT value and without the presence of Ascites, were diagnosed as viral hepatitis

GROUP 2, Patients, who had SGPT level < 300 IU, along with SGOT value > SGPT value and were without the presence of Ascites, were diagnosed as Non Ascites cirrhosis (compensated cirrhosis).

GROUP 3, Patients with SGPT level < 300 IU, along with SGOT value > SGPT value and presence of Ascites (as determined by clinical examination), were diagnosed as Ascites cirrhosis (Decompensated cirrhosis).

Results and Discussion

Clinical Signs and Symptoms

Jaundice was observed in 33/33 (100%) of patients in Group 1, 8/30 (26.6%) of the patients in Group 2, and 27/37 (72.9%) of the patients in Group 3. Abdominal discomfort was present in 30/33 (90.9%), 6/30 (20%), and 20/37 (54.5%) in viral hepatitis, non-ascites cirrhosis, and ascites cirrhosis Groups1, 2, and 3 respectively. Ascites were present in 37/37 (100%) of the patients in Group 3. Ascites were not observed in Group 1 and Group 2 patients. Delirium and flapping tremors were observed in 3/37 (8%) in Group 3 only. Haematemesiswas has seen in 23/37 (62%) of patients in Group 3 only. Fever was the symptom, observed in 27/33, (81.8%) of the patients with viral hepatitis in Group 1 and 9/37 (24%) of the patients with ascites cirrhosis in Group 3. Fever was absent in Group 2 patients. Oedema was observed in 28/37 (75.6%) of the patients in Group3 as shown in (table 2). Oedema was not observed in patients of viral hepatitis in Group1, and non-ascites cirrhosis, in Group 2.

Table 1: Demographic Characteristics of Participants

Characteristics		**Group-I Viral hepatitis**	**Group-II Non-Ascites cirrhosis**	**Group-III Ascites cirrhosis**	**Group-IV Controls**
Number		33	30	37	100
Age		37.2 ±12.6y	48 ± 8.6y	51.3 ± 11.8y	46.27± 13y
Gender	Male	28	27	37	92
	Female	5	3	0	8
Prevalence of modes of liver diseases		66.6%HAV	76.6% Alcoholic cirrhosis (23/30)	67.57%Alcoholic cirrhosis (25/37)	Nil
		21%HCV			
		9%HBV	23.4%HCV cirrhosis ((7/30)	32.43%HCV cirrhosis (12/37)	
		3%HEV			
Duration of alcohol intake (>8 years)n%		Nil	100%	100%	Nil

•*no. of individuals (n%) expressed in percentage.*

Table 2: Clinical Signs and Symptoms of Patients

Clinical Features	Group 1 33	Group 2 30	Group 3 37
Fever	27/33 (81.8%)	Nil	9/37 (24%)
Jaundice	33/33 (100%)	8/30 (26.6%)	27/37 (72.9%)
Abdominal discomfort	30/33 (90.9%)	6/30 (20%)	20/37 (54%)
Ascites	Nil	Nil	37/37 (100%)
Oedema	Nil	Nil	28/37 (75.6%)
Delirium	Nil	Nil	3/37 (8%)
Flapping tremor	Nil	Nil	3/37 (8%)
Haematemesis	Nil	Nil	23/37 (62%)

•*C/F expressed as (n) % when positive.*

Table3: Pearson's Coefficient Of Correlation BetweenVariables in Ascites Cirrhosis Patients In Group 3

Groups	rvalue	r2 value	P value	Significance
eGFR-Albumin	+0.696	0.48	<0.001	H S
Albumin-Sodium	+0.53	0.28	<0.001	H S
eGFR-Sodium	+0.498	0.249	<0.001	H S
Albumin-Creatinine	-0.67	0.45	<0.001	H.S
Albumin– BUN	-0.64	0.41	<0.001	H.S.
Bilirubin Creatinine	+0.19	0.036	0.25	N.S.

Source: Compiled by the Researcher.

H.S.→ "highly significant"
r→ "Pearson's coefficient of correlations"
N.S.→ "not significant"
r2 → "coefficient of determination"

Table 4: Pearson's Coefficient of Correlation between Variables In Ascites Cirrhosis Patients In Group 3

GROUPS	r value	r2 value	P value	Significance
Potassium-Albumin	-0.39	0.15	0.02	S.
SGPT-eGFR	+0.18	0.032	0.29	N.S.
SGPT-BUN/C	-0.04	0.0016	0.8	N.S.
INR-Creatinine	+0.002	0.000004	0.9	N.S.
INR-eGFR	-0.15	0.022	0.38	N. S.

Source: Compiled by the Researcher.

S.→ significant
N.S.→ not significant
r→ Pearson's coefficient of correlations
r2 → coefficient of determination

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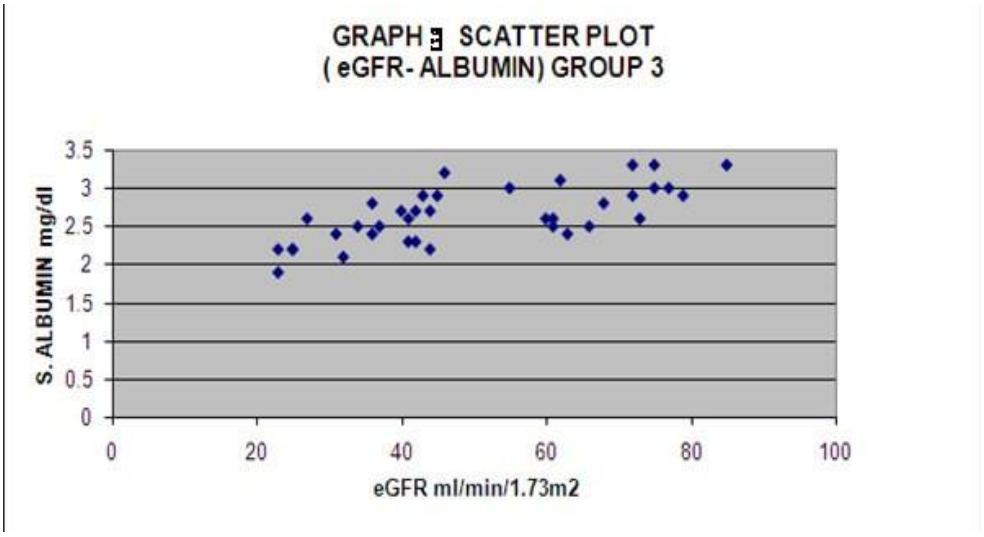

Figure 1: Scatter Plot Between eGFR and Albumin in Group 3.

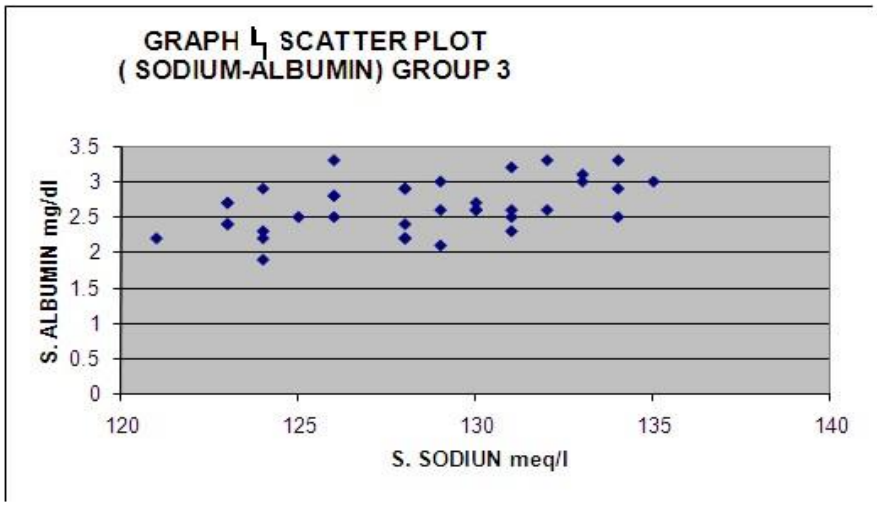

Figure 2: Scatter Plot between Sodium and Albumin in Group 3.

Urine and Ascites Fluid Investigation

Random urine analysis was done. The ascites fluid was analyzed for the estimation of polymorphonuclear cell count. Urine Protein and Urine RBCs were observed to be Negative in 100% of the patients in Groups1, 2, and 3. Urine Protein was Negative in 30% (11/37) of the ascites cirrhosis patients in Group 3. Urine Protein of value, Trace, was detected in 70% (26/37) of the ascites cirrhosis patients in Group 3. Urine Protein of more than Trace was not observed in the ascites cirrhosis patients in Group 3. RBCs in the Urine of ascites cirrhosis patients in Group 3, were Negative in 57% (21/37) of patients. Urine RBCs were observed up to (2) under a high power field, in 43% (16/37) of the ascites cirrhosis patients in Group 3. Urine RBCs of more than (2) under a high power field were not seen in patients of ascites

cirrhosis in Group 3. Renal tubule epithelial (RTE) Casts were seen in (16/37) 43% of the ascites cirrhosis patients in Group 3. No casts were seen in the urine sediment of the patients in Group 1 and Group 2. Ascites fluid analysis, revealed the presence of PMN cell count of more than 250/mm3, in (9/37), 24% of the patients of ascites cirrhosis in Group 3. The culture was positive in 16% (6/37) and negative in 8% (3/37) of patients in Group 3 as shown in (Table 3).

Table 5: Results of Ascites Fluid and Urine Investigation

Parameters	**Group 1**	**Group 2**	**Group3**	**Group 4**
UrineProtein				
Negative	100% 33/33	100% 30/30	30% (11/37)	100% 100/100
Trace	Nil	Nil	70% (26/37)	Nil
>Trace	Nil	Nil	Nil	Nil
Urine RBC				
Negative	100%	100%	57% (21/37)	100%
Up to 2 hpf	Nil	Nil	43% (16/37)	Nil
>2 hpf	Nil	Nil	Nil	Nil
Casts	Nil	Nil	(43%)16/37	Nil
PMN count	Nil	Nil	(24%) 9/37	Nil
Culture				
Positive	Nil	Nil	16% (6/37)	Nil
negative	Nil	Nil	8% (3/37)	Nil

•*Parameters expressed as (n) %, when positive.*

Estimated Glomerular Filtration Rate

Mean GFR (107.7± 19.7), (96.4± 16.1), (44.1± 14.9), and (108.78±18.39) ml/min/1.73mm2 were seen in patients of viral hepatitis, patients of non-ascites cirrhosis, patients of ascites cirrhosis and healthy controls in Group 1, 2, 3 and 4 respectively, as shown in Table 5. One way ANOVA test was conducted. It revealed a difference in mean GFR in four groups as depicted by $F(3,196)=127.9$, and a significance level of ($p<0.001$), highly remarkable as shown in Table 4A. Tukey's HSD, Post hoc test was performed between the mean of two groups and six types of groups were formed as (Group 1,2), (Group 1,3), (Group 1,4), (Group 2,3), (Group 2,4). It revealed a difference between all groups highly significant except (G1, G4), hepatitis and control groups. The HSD calculated value, ($q=0.38$), was below the critical value ($q0.05= 3.6$), non-significant as shown in table 4B. The mean GFR of the Groups 1, 2, and 4 were within the normal reference range (90-120 *ml/min*/1.73m2).

Group 3, (ascites cirrhosis), showed mean GFR (44.1± 14.9 ml/min/1.73m2), significantly, (t=4.44,p<0.001), lower than the hypothetical cut-off (56ml/min/1.73m2), as prescribed by (RIFLE criteria by ADQI Group, to calculate the decline in GFR).

Observations and Inferences

Renal failure was seen in 56% (37 patients of ascites cirrhosis out of a total of 67 cirrhosis patients). Further, the analysis showed that 9 out of 37 (24%) patients of ascites cirrhosis in Group 3, had a neutrophil count of more than 250/mm3, whereas, another (16 /37), 43% of the ascites cirrhosis patients in Group 3, showed renal tubules epithelial casts, as revealed in the analysis of urinary sediment, whereas, remaining 12 patients (33%) of ascites cirrhosis in Group 3, were found to be suffering from hepatorenal syndrome as shown in the Figure 3.

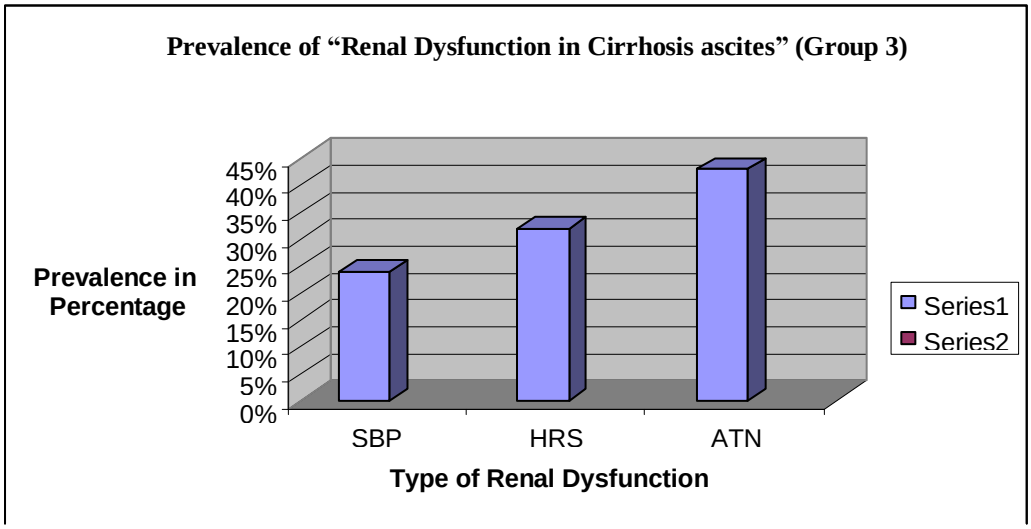

Figure 3. Prevalence of Renal Dysfunction In Group 3.

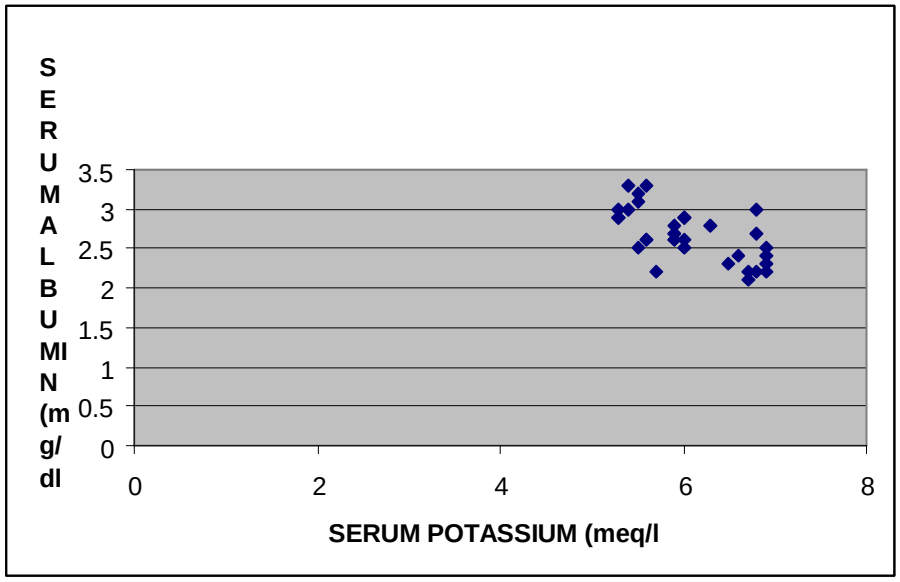

Figure 4. Scatter Plot Between S. Potassium and S. Albumin.

Patients with Ascites cirrhosis suffer from Renal failure

The ANOVA F score and Tukey's post-host test for mean eGFR (Estimated Glomerular Filtration Rate) and mean serum creatinine across four groups (Group - I, Group - II, Group - III, and Group - IV) provided the evidence. It is possible to rule out severe renal impairment by measuring the glomerular filtration rate. Estimation of creatinine clearance and, by extension, glomerular filtration rate, is made easy with the eGFR. Timed urine collections are no longer necessary thanks to this technique [18].

Discussion

An abnormally high mean serum creatinine value in Group 3 indicates renal failure in patients with ascites cirrhosis as compared to a hypothetical cut-off value of serum creatinine (p=0.001). Patients with end-stage liver disease or cirrhosis often experience a functional type of renal impairment referred to as a hepatorenal syndrome, which can lead to kidney failure. Out of a total of 67 cirrhotic patients (without ascites, n=30 and ascites cirrhosis, n=37), renal failure was found in 37 ascites cirrhotic patients in Group 3.

The hyponatremia in cirrhosis, further, worsens in patients with habitual consumption of alcohol due to intake of a large amount of fluid with little [19]. This fact is further supplemented by the prevalence of 67% of the cirrhotic ascites patients in Group 3, in the present study, who had the habit of alcoholic consumption**.**

A prevalence of hyponatremia with 46 %, 27 %, and 27 % with sodium cut-offs (130-134), (125-129), and (<129) *meq/L*, were observed in ascites cirrhosis patients in Group-3. In cirrhosis, hyponatremia is a severe complication and it can be an independent predictor of mortality in patients awaiting liver transplant [7]. The serum sodium level in cirrhosis can have important prognostic value and can be used along with other parameters in Model for end stage liver disease score (MELD) to predict the survival of patients.

The correlation between eGFR and Albumin was shown to be direct and positive in Group 3. Scientists [20] corroborated this finding by analyzing 16 patients with advanced cirrhosis and finding that 12 of them had abnormally low albumin levels. Many factors, including malnutrition, vitamin deficiencies, and impaired protein synthesis, contribute to the decline in albumin levels seen in cirrhosis.

Conclusion

The increased risk of kidney failure in cirrhotic patients is a substantial financial strain on healthcare systems worldwide [1]. Patients with cirrhosis and HRS-1 are not the only ones at risk for renal failure. “There are several potential causes, including prerenal gastrointestinal losses, cirrhotic cardiomyopathy, portopulmonary-related venous congestion, and other non-cirrhotic causes (*e.g.*, medication effect, acute tubular injury, obstructive uropathy, *etc.*).” It is critical to determine the cause of AKI before beginning treatment. Treatment with vasoconstrictor drugs may alleviate HRS-1 symptoms. Patients who have not responded to medical treatment but are good candidates for a liver transplant or who have a high possibility of improving should be offered the operation.

Our findings show that patients with decompensated cirrhosis (ascites cirrhosis) have impaired renal function, while those with viral hepatitis and non-ascites cirrhosis have normal renal function eGFR, serum creatinine, serum sodium, serum potassium, and bun/creatinine all showed significant outliers compared to normal ranges. This approach to identifying renal impairment in people with liver illness may find use in routine clinical practice. The serum albumin as the kidney function indices of cirrhosis patients with ascites fluctuate. These indices are to be clearly documented by the physician to study the connection between liver disease and renal failure.

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