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Original Research Article

Acute renal failure in cirrhosis of liver: a hospital based observational study

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ABSTRACT

Background: In general, there is a propensity among the physicians to label a patient with cirrhosis developing a raised creatinine level as HRS and treat it as such thereby ignoring the other causes particularly in this part of the country. This study was undertaken to find out the causes of acute renal failure and their outcome in cirrhotic patients.
Methods: One forty three cirrhotic patients with acute renal failure were enrolled and investigated for causes of renal failure and their outcomes.
Results: 92 (64.33%) patients had single factor whereas 51 (35.66%) patients had multiple factors (two or more), causing renal failure. Hypovolemia (34.27%) was the most common cause of renal failure followed by herbal medications (11.19%), HRS (11.19%) and infections (7.69%) as a single factor. Among multiple factors, 45 (31.46%) patients had hypovolemia followed by 36 (25.17%), 18 (12.58%) and 8 (5.59%) patients having infections, herbal medications and use of nephrotoxic drugs respectively. Reversibility was seen in 72 (50.35%) patients and more common in hypovolemia (85.71%) as a single factor. Total all-cause mortality was 33 (23%) and highest mortality was seen in HRS 75% (n=12) followed by infections (45.45%) and herbal medications (25%).
Conclusions: Hypovolemia was the most common cause of renal failure followed by infections, herbal medications and hepatorenal syndrome. Early detection and proper volume replacement are the key points in the management. Detailed history regarding use of herbal medications is also very important issue.

Keywords: Infections, Herbal medications, Hepatorenal syndrome, Nephrotoxic drugs

INTRODUCTION

Acute Renal failure or acute kidney injury (AKI) is a common complication in cirrhosis of liver reported as 30-40% in various studies.[1-3]

Cirrhosis is usually complicated by portal hypertension as well as resultant splanchnic vasodilatation. However extra splanchnic circulation and hence renal perfusion is maintained by sympathetic over activity but with increasing in severity of cirrhosis, this mechanism fails to maintain adequate cardiac output and renal perfusion aided and abetted by cirrhotic cardiomyopathy in 50% cirrhotic patients. All this together with activation of RAAS (renin angiotensin-aldosterone system) leads to increased susceptibility to AKI in cirrhosis particularly if associated with factors compromising renal circulation like hypovolemia, sepsis, nephrotoxins particularly NSAIDS (non-steroidal anti-inflammatory drugs) which normally suppress the vasodilator effects of renal prostaglandins.

In a study the factors listed as provoking AKI in cirrhotics (prerenal and ATN) were over use of diuretics, diarrhoea due to lactulose, vomiting and poor intake of food as well as fluid, GI bleeding, large volume paracentesis without salt free albumin infusion, use of

nephrotoxins etc. This group of patients were also prone to develop type 1 HRS and type 2 HRS.

The basic pathogenesis of HRS (hepatorenal syndrome) is splanchnic vasodilatation, renal vasoconstriction and low cardiac output which can lead to poor renal perfusion and renal failure. The prognosis is better with appropriate volume replacement or elimination of precipitating factors in patient with hypovolemic renal failure when compared to HRS and infections.[2]

In type 1 HRS, there is rapid deterioration of renal function in a period of two weeks or less with an increase in serum creatinine level more than 2.5mg/dL.[4,5] The most common triggers include severe bacterial infections, GI bleeding, surgical procedure and acute liver injury. SBP is the major bacterial infections which predisposes to develop HRS in cirrhotic patients.[6] Type 1 HRS carries a very poor prognosis with only 2 weeks of median survival period, if not treated.[7]

In type 2 HRS, there is more slowly progressive impairment of renal function than type 1, with serum creatinine levels usually ranging from 1.5 to 2.5mg/dl.[4,6] Type 2 HRS patients typically have refractory ascites and carry a median survival period of 6 months without undergo liver transplantation.

Herbal medication is a very common practice in this part of the country to treat jaundice or any other chronic illness although true prevalence and incidence cannot be ascertained. Use of herbal medicine is basically due to peer influence, disappointment with current therapies and belief that herbal medicine has no side effects. Unidentified herbal medicines are potentially nephrotoxic, as reported by various studies. The kidney injury with unidentified herbal medicine may cause acute tubular necrosis, acute interstitial nephritis and electrolyte imbalance. The exact lesion or pathological changes can only be diagnosed by biopsy.[8,9] Use of herbal medications in cirrhosis also carries a potential risk for renal failure.

In general, there is a propensity among the physicians to label a patient with cirrhosis developing a raised creatinine level as HRS and treat it as such thereby ignoring the more common causes of hypovolemia and nephrotoxins in this part of the country.

However, the causes of renal failure are not properly evaluated in this part of the country. Therefore, this study was undertaken to find out the causes of acute renal failure and outcome in cirrhotic patients. So, as to provide a proper guide to adequate management.

METHODS

The study was a hospital based observational study, conducted from April 2017 to November 2018, in the department of Medicine, Assam Medical College and Hospital, Dibrugarh, Assam.

Inclusion criteria

All cirrhotic patients with renal failure consecutively admitted in our hospital were included in this study.

Exclusion criteria

Cirrhotic patients with pre-existing intrinsic renal diseases were excluded from this study.

Definitions

Liver cirrhosis

Cirrhosis of liver was diagnosed by clinical examination, laboratory investigations and imaging findings as well as histopathological report whenever available. The cause cirrhosis and hospitalization were evaluated and established in all cirrhotic patients. MELD score and Child-Pugh score (CPS) were used to describe disease severity.[10]

Renal failure (RF)

Renal failure was defined as the rise of serum creatinine equal or more than 1.5mg/dl either at time of admission or during the period of hospitalization.[11] This serum creatinine value (1.5mg/dl) has been adopted by Several consensus and conferences to define as renal failure in cirrhotic patients as a cut off.[10,11] The serum creatinine values were obtained on the day of admission and subsequently every alternate day during hospital stay till discharge or death.

Different categories of renal failure included were:

- Bacterial infections induced RF
- Pre-renal or hypovolemia induced RF
- HRS
- Drugs (nephrotoxins) induced or contrast induced RF
- Herbal medications induced RF
- Multiple factors induced RF.

Infections-induced RF

Renal failure was ascribed to infection whenever the episode of infection was suspected or diagnosed by clinical, laboratory and imaging findings within 48 hours of rise of creatinine levels. The diagnosis of SBP was made when polymorphonuclear count more than 250/mm^3 in ascitic fluid in the absence of infection in the abdominal or peritoneal cavity.[12,13]

Bacterial infections were diagnosed by urine analysis, urine culture and blood culture if required. Ascitic fluid analysis was performed in every patient with ascites and fluid culture was done in every suspected bacterial peritonitis, whereas chest X-ray was done whenever indicated.[14]

Prerenal or hypovolemia-induced RF

Renal failure due to hypovolemia was assumed in presence of bleeding from gastrointestinal tract, or dehydration due to intensive diuretics therapy, gastrointestinal fluid loss like diarrhea or vomiting, excessive use of lactulose, decrease salt and fluid intake, large volume paracentesis without albumin infusion.[15]

Drug-induced RF

Drug induced renal failure or nephrotoxicity in cirrhotic patients was diagnosed when there was a history of diuretics therapy, anti hypertensive drug, NSAIDS or any drugs that can cause AIN (acute interstitial nephritis) and/ or ATN (acute tubular necrosis).

Herbal medications induced RF

History of ingestion of herbal medicine was especially investigated.

Hepatorenal syndrome

HRS was defined by using diagnostic criteria of the international ascites club consensus Workshop in 2007, include:[4,6]

- Cirrhosis with ascites,
- Serum creatinine level more than 1.5mg/dl.
- No improvement of serum creatinine level to 1.5mg/dl or below after at least 48 hours of withdrawal of diuretics and adequate volume expansion with normal saline and intravenous albumin infusion.
- Absence of shock
- No current or recent treatment with nephrotoxic drugs
- No parenchymal renal disease excluded by abnormal USG findings and no proteniuria of more than 500mg/day, microhematuria (more than 50RBC/hpf)

Due to lack of specific diagnostic markers, it was diagnosed by exclusion of other renal diseases. It is extremely important to be ruled out hypovolemic renal failure via adequate volume replacement with crystalloids and intravenous albumin.[16]

Multiple factors induced RF

When renal failure resulted from multiple factors (two or more), it was labelled as multiple factors induced renal failure in cirrhosis. In this observational study, patients were evaluated by clinical examination and laboratory investigations. The clinical evaluation of the patients included a detailed medical history with thorough general and systemic examination. The investigations included complete hemogram, liver function tests, prothrombin time (PT), INR, serum sodium, serum potassium, blood glucose, renal function tests, urine analysis, ultrasound abdomen with special comments on renal parenchyma and presence of ascites, upper gastrointestinal endoscopy, chest x-ray and ascitic fluid examination, wherever indicated. Informed consent was taken from the patients.

Once the diagnosis of ARF was confirmed, drugs that may potentially induce renal failure such as nephrotoxic drugs or diuretics were stopped immediately. patients with hypovolemia were treated with plasma volume expander by giving 1.5 liters of normal saline, and the effect on urine output and renal function test were carried out.

Cirrhotic patients with presumed bacterial infection were empirically treated with antibiotics based on local sensitivity reports followed by specific antimicrobial therapy as per culture sensitivity and radiological reports. If there was no improvement or serum creatinine level still higher than 1.5mg/dl after at least 2 days of diuretic withdrawal and adequate volume expansion or 72 hours after antibiotic therapy with observable control of infections, HRS was diagnosed and treated with inj terlipressin along with 20% salt free human albumin infusion1. HRS was confirmed after exclusion of intrinsic renal disease by ultrasound and urinary protein estimation (<500mg/24 hours).[1,16] Hemodialysis was done whenever indicated in cirrhotic renal failure patients.[15]

Outcomes of the patients were assigned as

- Reversible, if serum creatinine level was reversed to normal or its base line and
- Irreversible renal failure, if serum creatinine level did not reverse or still higher than 1.5mg/dl during hospital stay or death.

Irreversible renal failure group were also categorized, based on serum creatinine at the time of diagnosis and at hospital discharge/death as stable or progressive. Patients with serum creatinine level which was inexorably increasing during hospitalization were termed as progressive while stable patients were those in whom serum creatinine level did not come down normal despite a fall from the initial level.

Statistical analysis

Frequencies and percentage of quantitative variables were presented with Mean±SD (standard deviation). The collected data was tabulated in MS(Microsoft) Excel Worksheet and computer-based analysis was done using the Statistical product and service solutions (SPSS) 22.0 software (SPSS, Chicago, Illinois, USA).

RESULTS

A total of 143 cirrhotic patients with acute renal failure were included in this study. Among them, 138 patients were males (96.50%) with age range of 30-78 years.

Majority of the cirrhosis were due to alcohol (n=133) consumption. Severity of the liver disease was described with Child Pugh Score (CPS) and MELD score. Etiology and severity of the cirrhotic patients are described in Table 1.

Table 1: Etiology and severity of cirrhotic patients (n = 143).

Etiology of cirrhosis	Number (n)	Percentage (%)
Alcohol	133	93.01
HBV	6	4.20
Alcohol/HBV	3	2.10
NASH	1	0.70
Child-Pugh score	**Number (n)**	**Percentage (%)**
A (5-6)	2	1.40
B (7-9)	40	27.97
C (10-15)	101	70.63
	Mean±SD	**Range**
MELD score	27.43±7.11	14-49

Table 2: Clinical features of cirrhotic patients with renal failure (n = 143).

Clinical features		
Age (in years)	**Mean±SD**	**Range**
	48.27±10.02	30-78
Sex	**Number (n)**	**Percentage**
Male	138	96.50%
Female	5	3.50%
Presenting features	**Number (n)**	**Percentage**
Ascites/ distension of abdomen	121	84.62%
Jaundice	87	60.84%
Fever	53	37.06%
Pain abdomen	51	35.66%
Hepatic encephalopathy	43	30.07%
UGI bleeding	33	23.08%
Diarrhoea	26	18.18%
Vomiting	22	15.38%
Treatment history	**Number (n)**	**Percentage**
Decreased fluid intake	60	41.96%
Decreased salt intake	34	23.78%
Herbal medication	34	23.78%
Intensive diuretic therapy	31	21.68%
Lactulose therapy	22	15.38%
Use of nephrotoxic drug	8	5.59%
Large volume paracentesis	7	4.90%

Common presenting features were ascites (n= 121, 84.62%), jaundice (n=87, 60.84%), fever (n=53, 37.06%), hepatic encephalopathy (n=43, 30.07%) and UGI bleeding (n=33, 23.08%). Regarding treatment history, large number of patients were treated with salt and fluid restriction, diuretics and lactulose therapy. History of herbal medications, use of nephrotoxic drugs and large volume paracentesis were present in 34(23.78%), 8(5.59%) and 7(4.90%) patients respectively. Clinical features of cirrhotic patients are presented in the Table 2.

Table 3: Basic laboratory features of cirrhotic patients with renal failure (n = 143).

	Mean±SD	Range
Hb gm%	7.89±2.18	3.00±15.00
WBC	10788.11 ±5153.96	2600.00 ±26000.00
Platelet count	124643.36 ±51283.58	20000.00 ±340000.00
RBC count	2.78±0.77	1.20±6.12
Blood urea (mg/dl)	71.56±40.90	14.00±231.00
Serum creatinine (mg/dl)		
At the time of admission	2.77±1.86	0.90±17.00
During hospital stay	2.55±2.04	0.90±10.00
Bun	33.44±19.11	6.54±107.94
Serum sodium (mEq/L)	132.04±7.97	115.00±157.00
Serum potassium (mEq/L)	3.95±0.95	1.90±7.30
Total bilirubin (mg/dl)	6.38±7.31	0.30±32.00
Serum albumin (g/dl)	2.20±0.81	1.10±6.00
PT (sec)	21.28±8.18	11.80±70.00
INR	2.07±0.85	0.90±7.18

Majority of the patients in this study were anemic (mean Hb %-7.89±2.18gm%). Mean WBC count was 10788.11±5153.96 and 51 (35.66%) patients had leukocytosis (>11,000) indicating infection but overall infection was found in 59 patients. Remaining patients had other evidences of infection e.g. urinary findings of UTI. Mean serum creatinine level was 2.77±1.86mg/dl at the time of admission with stage 2 acute renal failure. Eighty seven (60.84%) patients had jaundice with mean serum bilirubin level of 6.38±7.31mg%. Majority of the patients had hypoalbuminemia (mean albumin level 2.2±0.81gm/dl) and hepatic decompensation with mean PT of 21.28±8.18 secs and mean INR 2.07±0.85. Regarding other parameters, results did not show any significant findings in the context of the present study. Basic laboratory parameters are described in the Table 3.

Infection was found in 41.25% (n=59) of renal failure patients and SBP was the most common type of infection in 20.28% (n=29) of cirrhotic patients followed by UTI (9.09%) and sepsis (8.39%) as presented in Table 4.

One forty two (99.3%) patients had renal failure at the time of admission and one (<1%) patient developed renal failure during hospital stay. Out of 143 patients, hypovolemia (34.27%) was the most common cause of acute renal failure followed by HRS (11.19%), herbal medications (11.19%) and infections (7.69%) as single factor. Renal failure in remaining patients of cirrhosis were resulted from multiple factors (two or more). Among multiple factors, hypovolemia, infections and herbal medications were mostly responsible for acute kidney injury in cirrhosis. Hypovolemia was found in 45 (31.46%) patients followed by infections in 36 (25.17%), herbal medications in 18 (12.58%) and use of nephrotoxins in 8 (5.59%) patients along with other factors.

Out 143 patients, 92 patients had renal failure due to single factor and 51 patients had multiple factors.

Table 4: Types of infection in cirrhotic patients with renal failure (n = 143).

Type of infection	Number (n)	Percentage
Sepsis	12	8.39%
GI Infection	1	0.70%
Pneunomia	4	2.80%
Spontaneous bacterial peritonitis	29	20.28%
Urinary tract infection	13	9.09%

Table 5: Causes of renal failure and in-hospital mortality among cirrhotic patients.

Cause of renal failure	Number (n)	Percentage	Death	
			n	%
Hypovolemia	49	34.27%	2	4.08%
Herbal medication	16	11.19%	4	25.00%
Infection	11	7.69%	5	45.45%
Hepatorenal syndrome type 1	16	11.19%	12	75.00%
Hypovolemia + infection	27	18.88%	5	18.52%
Hypovolemia + herbal medication	11	7.69%	1	9.09%
Herbal + infection	4	2.80%	1	25.00%
Nephrotoxic drug + infection	2	1.40%	0	0.00%
Hypovolemia + nephrotoxic drugs	2	1.40%	0	0.00%
Hypovolemia + infection + nephrotoxic drugs	2	1.40%	2	100.00%
Hypovolemia + nephrotoxic drugs + herbal	2	1.40%	1	50.00%
Hypovolemia + infection + herbal	1	0.70%	0	0.00%
Hepatorenal syndrome type 2	0	0.00%	0	0.00%

Table 6: Outcome of renal failure observed during hospitalization.

Total no. of cirrhotic patients	Reversible (<1.5mg/dl)	Irreversible (≥1.5mg/dl)	Death
143	72 (50.35%)	71 (49.65%)	33 (23.08%)

Hepatorenal disorder, which is the most lethal among the causes renal impairment in cirrhotic patients with ARF is also culmination of hypovolemia or infection. Out of 16 patients, 3 patients had de novo HRS, 1 patient had hypovolemia due to large volume paracentesis without albumin infusion, 7 patients had infections and 5 patients had both infections and hypovolemia.

Causes renal failure and mortality in cirrhosis are depicted in the Table 5 and outcome of the patients are depicted in the Table 6.

Infection induced AKI was due to SBP (n=29, 20.28%), Sepsis (n=12, 8.39%,) UTI (n=13, 9.09%), pneumonia (n=4, 2.80%) and GI infection (n=1, 0.70%).

Out of 143 patients, 99 (69.23%) patients had hypovolemia due to various causes, 59 (41.26%) patients had infections, 34 (23.78%) patients had herbal medications and 8 (5.59%) patients had history of intake of nephrotoxic drugs individually.

On assessing the outcome, out of 143 patients, 72 (50.35%) patients were reversible whereas 71 (49.65%) patients had irreversible pattern of renal failure. Outcome was affected by different etiologies of renal failure and reversibility was better with hypovolemic renal failure (85.71%) followed by infection (36.36%) and herbal medications (31.25%) as a single factor. Among irreversible renal failure, total in-hospital mortality was seen in 23.08% (n=33) cases and highest mortality was due to HRS (75%) followed by infections (45.45%) and herbal medications (25%) as a single factor.

DISCUSSION

Chronic liver disease as well as cirrhosis are very common in this part of the country due to high prevalence of alcohol consumption. Advanced stage of cirrhosis is associated with multi system involvement including renal failure.[17] In this study, we observed that renal failure in advanced stage of liver disease was more common, associated with mainly Child Pugh C (n=101, 70.63%), Child Pugh B (n=40, 27.97%) and high MELD score (27.43±7.11) this findings was similar that of Qureshi MO et al, Morsy et al, and Fasolato S et al.[3,10,18]

In this study, Renal failure was caused by single factor in 92 patients (64.33%) and renal failure in remaining 51 patients (35.66%) resulted from multiple factors (two or more).

The most common cause of single factor renal failure was pre-renal or hypovolemia (n=49, 34.27%) which compares well with findings of Morsy et al, (29.7%) and Carvalho et al, (32%) as a single factor AKI however present study findings differ from those of Choi YJ et al, (67.4%).[1,10,19] In addition, large number of patients had hypovolemia in HRS and multi factorial group. Altogether, 99 (69.23%) patients had hypovolemia including both HRS, single and multiple factors group which is almost similar finding to Yun Jung Choi et al (67.4%).[19]

Upper gastrointestinal bleeding was a very important cause of hypovolemia and found in 33 (23.08%) of patients. Other causes of hypovolemia were decrease intake of fluid (41.96%) and salt (23.78%), intensive diuretic therapy (21.68%), lactulose therapy (15.38%), diarrhoea (18.18%), vomiting (15.38%) and large volume paracentesis without albumin infusion (4.90%). Renal failure developed in majority of the patients with hypovolemia without hyovolemic shock.

Upper gastrointestinal bleeding also predisposes the bacterial infections which can cause systemic arterial vasodilatation and hemodynamic changes, may lead to renal impairment.[15] Hypovolemic renal failure is treatable and preventable condition, need early detection and proper volume replacement. Second common causes of single factor renal failure were HRS and herbal medications in 16 (11.19%) patients in each group and responsible for significant mortality and morbidity.Out of 143 patients, 16 (11.19%) cirrhotic patients had renal failure due to herbal medications as a single factor whereas 18 (12.58%) patients in multiple factors group and total of 34 (23.78%) patients had renal failure due to herbal medications. To the best of our knowledge no other study has taken up this parameter.

In this study, HRS was found in 11.19 % (n=16) cases. However, Morsy et al, (11.3%) and Carvalho et al, (12%) found similar incidence while Choi YJ et al, (6.02%) reported lower incidence.[1,10,19] HRS occurred either spontaneously or following an acute insult like hypovolemia (e.g., variceal bleeding followed by infections), SBP and also culminated from infection and hypovolemia in combination. All HRS were type 1 HRS. Authors did not find any type 2 HRS case among our patients. It may be because of difficulty in diagnosis and lack of follow up after hospital discharge.

Renal failure due infection was found in 11 (7.69%) patients as a single factor of renal failure whereas 36 and 12 patients had infection in multiple factors group and HRS group respectively. As a single factor, infection induced renal failure was less, but infection had significant contribution in HRS and multiple factor group in genesis of renal failure. Several studies have shown that infection was the most common cause of renal failure (Carvalho et al, Morsy et al) whereas in present study, total number of patients with infection was 59 (41.25%) and was in the second place below hypovolemia.[1,10] Present study results show that almost any type of bacterial infection can cause renal failure in cirrhotic patients. SBP (20.28%) was the most common infection in our study followed by sepsis and UTI and that finding was similar to Morsy et al.[10]

Among patients with multiple factors, 45 (31.46%) patients had hypovolemia, 36 (25.17%) patients had infections, 18 (12.58%) patients had herbal medications and 8 (5.59%) patients had use of nephrotoxic drugs. A combination of various factors can play their hands in the genesis of renal failure in cirrhotic patients at the same time (Table 5).

Hypovolemia was the most common cause of renal impairment in both the group. Herbal medications and HRS were in the second place behind hypovolemia in single factor group whereas infections were the second common cause in multiple factors group followed by herbal medications.

In our study, reversible pattern (n=72, 50.35%) of renal failure was more than half, regardless of the etiology and it was better than Carvalho et al, and Morsy et al, who reported 29% and 38.2% respectively.[1,10] Authors found that hypovolemia (85.71%) was the most common cause of reversible renal injury followed by infections (36.36%) and herbal medications (31.25%) in single factor group whereas no reversibility was seen with HRS. In the irreversible group (n=71, 49.65%), stabilization was seen in 28 (19.58%) patients, progression in 10 (6.99%) and death in 33 (23.08%) patients.

Mortality has been seen to differ according to the cause of renal failure. Total all-cause mortality was 23.08% and almost similar to Choi YJ et al, (22.1%) but less than Carvalho et al, (26%) and Morsy et al, (27.4%).[1,10,19] In this respect, most common cause of single factor mortality was HRS (75%), followed by infection (45.45%) and herbal medications (25%) respectively.

In the multiple factor group, 5 (18.52%) patients died due to hypovolemia + infection, 2 (100%) patients died in hypovolemia+infection+nephrotoxic group, 1patients (50%) died in hypovolemia+nephrotoxic+herbal group, hypovolemia+infection and herbal +infection group each. Mortality pattern in the multiple factor group has been shown in Table 4.

Mortality was highest with HRS (75%) that was higher than Morsy et al, (66%) but lower than Carvalho et al, (83%).[1,10] HRS was shown to have very poor prognosis. The second common cause of mortality was infection induced renal failure in which, 5 out of 11 (45.45%) patients died as single factor and 8 patients out of 36 (22.22%), died as a part of multiple factor and carries a high risk of mortality in both groups.

The 3rd common cause of mortality was herbal medication in 25% (4 out 16 patients) patients as single factor and 16.66% (3 out of 18 patients) as multiple factors and also carries a significant mortality.

In present study, use of nephrotoxic drugs didn't appear as a single factor renal failure but played a role in the genesis of renal failure along with other factors in 8 patients. Out of 8 patients, 3 patients (37.5%) died and does denoting a high mortality rate.

In this present study, we tried to highlight the causes of acute kidney injury or renal failure and outcome in cirrhotic patients, admitted in medicine wards with various presentations. There is a tendency among physicians to term this case as HRS and treat accordingly. However, causes of renal failure and outcome has not been evaluated earlier in this part of the country. Authors observed that renal failure in cirrhotic patients was due to hypovolemia followed by infections, herbal medications and HRS in that order. It was also observed that large number of renal failures culminated from combination of multiple factors (two or more factors) like hypovolemia and infections or use of nephrotoxic drugs or herbal medications. So, apart from obvious single cause of renal impairment, possibility of multiple factors should be always kept in mind while evaluating the renal failure in cirrhotic patients.

Herbal medication induced renal failure was a very important finding in our study, associated with high mortality and morbidity. So, detailed clinical history and examination are very important to detect early and manage the renal failure accordingly in cirrhotic patients. The most effective prevention of kidney injury due to herbal medications is creation of awareness among consumers and providers that they have the capacity to cause kidney injury.

The main limitations in present study were single centered study, lack of incorporating bio-markers for better recognition of the various causes of renal failure and patients not being followed up after hospital discharge. Therefore, biomarkers development to predict renal failure at an early stage and to differentiate the various etiologies of renal failure in cirrhotic patients, should be pursued.

CONCLUSION

In contrast to the general belief among physicians, hypovolemia and not hepatorenal syndrome/disorder is the most common cause of acute kidney injury or failure complicating cirrhosis of liver. Infections, nephrotoxic drugs, herbal medications being the other major etiologies of this entity. In a substantial number of patients, a combination of these factors may play their hands in the genesis of this serious complications. Furthermore, hepatorenal disorder which is the most lethal among the causes of renal failure in patients with cirrhosis with ARF is also the culmination of hypovolemia or infection. Hence, a proper etiological diagnosis in these patients specially the role of multiple factors is mandatory from treatment perspectives. A more elaborate study with a larger number of patients to define these various points will be welcome. In this context, development of biomarker/biomarkers to detect the relevant cause/ causes of renal failure in cirrhotic patients is an important issue.

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