



Outcome of patients of acute kidney injury in chronic liver disease

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Introduction: Chronic liver disease (CLD) is also a common clinical problem afflicting mankind. Occurrence of Acute kidney injury in patients with chronic liver disease is frequent finding which makes prognosis of CLD even poorer. **Material and methods:** A prospective cohort observational study on 100 adult patients of chronic liver disease with AKI conducted over a period of 24 months from August 2016 to August 2018 at Sri Aurobindo medical college and postgraduate institute. Detailed clinical examination and biochemical tests were done. Univariate and multivariate logistic regression (odds ratio) analyses were used. **Results:** 87% were males and 13% were females. Maximum no. of patients found in AKI stage III 40% followed by stage I 36% then stage II 24%. Among these 31% patient recover after treatment, 26% partially recovered and 43% patient didn't response to treatment. Overall 75% survived while 25% died in this study. **Conclusion:** Majority of Patients with Prerenal AKI had full recovery, as compared to HRS-AKI and intrinsic AKI where full recovery was less common. Patients in stage 1 AKI had more proportion of patients with full recovery than stages 2 and 3. Regarding outcome, Patients in stage 1 and stage 2 has higher survival rates as compared to stage 3, which is statistically significant.

Keywords: Acute Kidney Injury, Chronic liver disease, HRS-AKI, Outcome

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Introduction

Patients with cirrhosis are unique in a way that they can also develop hepatorenal syndrome (HRS), a type of prerenal injury which occurs in patients with advanced liver disease [1]. With a yearly incidence of 8–12%, HRS-AKI is quite common in decompensated cirrhosis with ascites [2].

As AKI significantly impacts the outcome of patients with cirrhosis, it is important to prevent the development of AKI if possible and to identify the cause early enough so that appropriate treatment measures can be instituted [3,4,5].

Incidence of AKI varies from 3% to 7% in hospitalized patient and 25% to 30% in intensive care unit (ICU) patient, approximately 5% to 6% patients who develop AKI, had to undergo dialysis. However, despite adequate treatment mortality is still about 60% and higher [6,7].

Patients with cirrhosis should be advised to maintain adequate hydration and avoid nephrotoxic medications, specifically NSAIDS, aminoglycoside antibiotics, and angiotensin-converting enzyme (ACE) inhibitors [8]. Cirrhosis is an immunocompromised state, and these patients are at increased risk of infection [9]. Therefore, early evaluation and treatment of infection is imperative for patients with cirrhosis who develop an AKI [10].

This study is done to assess outcome of patients and its association with the staging of AKI to understand the disease severity, so that it will help in understanding of disease pattern & outcome of patients.

Material and Methods

The present study is a hospital-based observational study conducted over a period of 24 months from August 2016 to August 2018 at Sri Aurobindo medical college and postgraduate institute, Indore. Consecutively admitted 100 adult patients of chronic liver disease with AKI were chosen for the study.

Study Design: Observational Study

Inclusion Criteria

01. Age more than 18 years.
02. Diagnosed case of chronic liver disease.
03. Patient of acute kidney injury in chronic liver disease.

Exclusion Criteria

01. Known case of CKD.
02. Patients of chronic diseases such as active tuberculosis, malignancy.

Collection of data: Detailed clinical interview and physical examination were done at the time of admission. Clinical events (infection, AKI, bleeding, ascites, and encephalopathy) were carefully evaluated, then these patients were subjected to appropriate investigations.

During hospitalization complete hemogram, serum Total bilirubin, unconjugated bilirubin and conjugated bilirubin, serum total protein serum albumin, serum globulin, PT (Prothrombin time)/ INR, alkaline phosphatase, Blood urea (BU), serum creatinine (sCr) at admission and daily till patient improve or discharge & baseline report noted if available, serum electrolytes and ABG (arterial blood gas analysis) done at admission and done whenever required, viral markers (HBsAg & Anti HCV, HIV) were investigated.

Culture of ascitic fluid, blood, urine, and sputum were performed when an infection is suspected. Urine routine microscopy, urine electrolytes whenever relevant, ascitic fluid microscopy done when patients have ascites, Ultrasonography of Whole abdomen, chest x ray, and the other lab investigation which were required for evaluation and treatment of patients. The diagnosis of cirrhosis was based on clinical evaluation by a hepatologist using laboratory values, liver imaging, endoscopy, and (when available) liver biopsy [11]. Cirrhosis staged clinically by Child-Pugh classification (CPC) with scoring system of 5-15 score of 5 to 6 being CPC-A, 7 to 9 CPC-B and 10 to 15 being CPC -C [1].

Serum creatinine (sCr) measured at admission and daily till patient improve or discharge which ever earlier & baseline report noted if available. During hospitalisation peak sCr value noted and compared with baseline sCr for staging of AKI.

Participants who were presented initially as a suspected case of prerenal-AKI i.e. those having hypovolemia sign of dehydration, history of volume loss like vomiting, diarrhoea, upper GI Bleed (hematemesis, per rectal bleed actively), patients on diuretics, and with hypotension are adequately resuscitated with adequate i/v fluid and blood (given to those having h/o GI Bleed and anaemia), and I/V Albumin given to those having low serum albumin.

Those patient responded to treatment (i/v fluid, i/v albumin) were classified as prerenal-AKI and those not responded to treatment were classified as having HRS-AKI with fulfilment of new criteria for HRS-AKI based on the 2015 Ascites Club Criteria given below in table no.-3 [14].

Statistical analysis plan: Continuous variables were described as means (95% confidence interval) and the difference was observed by using T test. ANOVA was carried out for >2 groups. Differences for categorical variables were assessed by the chi-square test. Univariate and multivariate logistic regression (odds ratio [OR]) analyses were used to identify those variables associated with AKI and mortality. p value< 0.05 was considered significant.

Results

Table-1: Sex wise distribution of cases.

S. No	Sex	No.of Patients
1	Female	13
2	Male	87
Total		100

Above table states that males are predominant in our study than females i.e 87% are males and 13% are females.

Table-2: Stage of AKI

S No.	Stages of AKI	No. of Patients
1	AKI-1	36
2	AKI-2	24
3	AKI-3	40
Total		100

Above table shows that maximum no. of patients found in AKI stage III 40% followed by stage I 36% then stage II 24%.

Table-3: Response to treatment.

S No.	Response to treatment	No. of Patients
1	Recover	31
2	Partial	26
3	No Response (NR)	43
Total		100

Above Table shows that 31% patient recover after treatment, 26% partially recovered and 43% patient didn't response to treatment.

Table-4: Outcome

S No.	Outcome	No. of Patients
1	Survive	75
2	Died	25
Total		100

Above table shows that 75% survived while 25% died in this study.

Table-5: Distribution of patients as per Child class with response to treatment and outcome

Child class	Response to treatment				Outcome		
	Not recovered	Partial recover	Full recover	Grand Total	DIED	SURVIVED	Grand Total
Class A	2	2	6	10	0	10	10
	20%	20%	60%	100%	0%	100%	100%
Class B	15	7	12	34	12	22	34
	44%	21%	35%	100%	35%	65%	100%
Class C	26	17	13	56	13	43	56
	46%	30%	23%	100%	23%	77%	100%
Grand Total	43	26	31	100	25	75	100

Among pts in class A 60% fully recovered, 20% partially, 20% not recovered and all of them survived. Among pts of class B 35% fully, 21% partially recovered and 44% not recovered, in which

35% died and 65% survived. Among pts of class C 23% fully, 30% partially recovered, 46% not recovered in which 23% died and 77% survived.

Table-6: Distribution of patients as per AKI staging with response to treatment and outcome

AKI staging	RESPONSE TO TREATMENT				Outcome		
	Not recovered	Partial recover	Full recover	Grand Total	DIED	SURVIVED	Grand Total
Stage 1	8	7	21	36	7	29	36
	22%	19%	58%	100%	19%	81%	100%

Stage 2	9	10	5	24	2	22	24
	38%	42%	21%	100%	8%	92%	100%
Stage 3	26	9	5	40	16	24	40
	65%	23%	13%	100%	40%	60%	100%
Grand Total	43	26	31	100	25	75	100

Above table shows Among stage 1- 22% not recovered, 19% partial recover, and 58% fully recover, regarding outcome 19% died, and 81% survived. Among stage 2- 38% not recovered, 42% partial recover, 21% full recovered, Regarding outcome 8% died and 92% survived, Among stage 3- 65% not recovered, 23% partial recover, 13% full recover, Regarding outcome 40% died, 60% survived.

Discussion

This study is an observational hospital based study. In this study we studied the outcome of AKI in cirrhosis patients and relationship between severity of cirrhosis (according to CHILD class) with the severity of AKI (according to staging of ICA-AKI in cirrhosis patients) with response to treatment and outcome.

In present study outcome of patients noted at time of discharge from hospital, in the form of patient survive or died during hospitalization whatever the patients, response to treatment. Total 75% patients survive and 25% patient died in this study.

In present study most of patients died are in Child-Pugh class C 13%, in class B 12% and in Child class A 0% patients died but no statically significance found with respect to severity of liver disease in class B v/s class C (13% v/s 12%; $p > 0.069$) it is contrary to study done by-

Jaiprakash et al [12], mortality of cirrhotic patients with respect to severity of liver disease (Child-Pugh class B and C) showed that renal disease significantly increases the mortality in patients with class C cirrhosis (78.1% vs. 53.2%; $p < 0.001$). Therefore, renal disease can be considered as an independent prognostic indicator in patients with class C cirrhosis.

This difference may be due to patients in Child class C refuses for further treatment and taken early discharge from hospital and study need to follow up of the patients for exact mortality in patients but it is beyond of our study.

In present study 7 (21.21%) patients died among

HRS-AKI and 26(78.78%) patients survive among HRS-AKI patients. The correct classification of AKI is essential since HRS-AKI, representing one of the most lethal complications of portal hypertension, requires a specific treatment approach.

However, despite adequate treatment mortality is still about 60% and higher Fagundes C et al [13]. This is contrary to present study, difference in mortality may be due to follow up is not done in present study, it's a hospital based mortality it might be high if patients were follow up for defined period of duration which beyond the our study objective. In present study 31% patients who recover

Complete from AKI and discharge from hospital, 26% patients partial recovered and in 43% no response found after treatment. In patients with complete recovery 2% patients were recovered with no specific treatment they are of prerenal type AKI, i/v albumin only given to patients in 28% patients while 70% patients receive pharmacotherapy (i/v antibiotics, albumin, inotropic support, blood transfusion and other specific treatment).

Florence wongs et al [104], observed 86 (56%) of the 153 patients had a complete renal recovery, 42 (28%) had a partial recovery, while 25 (16%) did not recover from their AKI episode. Of the patients with complete renal recovery, 3% received no specific AKI treatment, 36% received albumin only while 60% received pharmacotherapy in addition to albumin.

The respective percentages were 7%, 43% and 50% in patients with partial renal recovery. Of the 25 patients who did not have a renal recovery, pharmacotherapy was given to 14 patients (56%).

In present study partial recovery is similar but variance in complete recovery and no response to treatment found due to in Florence et al [14], study patient were of infection were taken, in our study we included the patients of all etiology.

In present study in HRS-AKI 4 cases (12.1%) full recover, 10 patients (30.3%) partial response and in 19 (57.6%) no response to treatment is noted.

HRS-AKI patients have poor prognosis most patients died within 2 weeks to 3 weeks in type 1 HRS and other patients progress to HRS type 2 mean time of dying is 6 month of onset of HRS Vicente Arroyo et al [15].

Regarding AKI Stages and Outcome of patient, Present study showing statistical significant ($p < 0.011$) correlation in relation to outcome of patient as the AKI stages increases the chance of patients dying increases. In present study ICA AKI-stage-1, 19.4% (7/36), ICA AKI-stage-2, 8.3% (2/24), ICA AKI-stage-3, 40% (16/40) within stages of AKI found died.

In other words our present study 25% patient died of which were in ICA AKI-stage-1, 28.0% (7/25), ICA AKI-stage-2, 8.0% (2/25), ICA AKI-stage-3, 64% (16/25) found died which is similar to study done by-

Belcher JM et al [133], Patients achieved a peak severity of AKIN stage 1, 26%, stage 2, 24%, and stage 3, 49%. Progression was significantly more common and peak AKI stage higher in non survivors than survivors ($P < 0.0001$). But the present study considering staging of AKI according to newer ICA-AKI criteria (2015) and Belcher JM et al [16], used AKIN criteria, which well correlated with each other our study, also prove the same.

On further elaboration of present study as stage of AKI increases the outcome of patients dependent on the stage's (i.e. as the stage of AKI increases there is more chance of dying of patients) of AKI in class C but not in the class B & class A. Outcome of Treatment in CHILD Class is not significantly associated in Acute Kidney Injury Stage's in CHILD Class A and B, but significant in CHILD Class C and overall in total cases.

Outcome of patient is not dependent on AKI stage in CHILD Class A&B, but is dependent on AKI stage in CHILD Class, means patients in CHILD class have more chance of dying as severity of AKI stages increases. In CHILD class A & B Equal chance of dying (Probability of bad outcome is more with advanced AKI in CHILD C and in over all patients but not affected in CHILD A&B).

Conclusion

Patients in stage 1 AKI had more proportion of patients with full recovery than stages 2 and 3. Regarding outcome, Patients in stage 1 and stage 2 has higher survival rates as compared to stage 3,

Which is statistically significant, As the severity of cirrhosis increases chance of AKI also increases with increasing severity of AKI stages and chance of patient's response to treatment & survival decreases. Thus prevention, early diagnosis, intervention is important to improve outcome in this patients, further study with large scale subjects is needed in future.

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