

Management and Outcome of AKI in Patients with Cirrhosis

Gnanendra DM¹, Kiran S¹, Parvesh Kumar Jain²

¹Assistant Professor, Department of Medical Gastroenterology, BMC RI and Victoria Hospital, Bangalore, ²Professor & HOD, Department of Medical Gastroenterology, BMC RI and Victoria Hospital, Bangalore.

Abstract

Background: The increased propensity for AKI in patients with cirrhosis stems from hemodynamic abnormalities typical of patients with cirrhosis and ascites¹⁵ which is due to development of portal hypertension and portosystemic collaterals with splanchnic and systemic vasodilatation, resulting in decrease in effective arterial blood volume with increase in renin angiotensin- aldosterone system (RAAS), sympathetic nervous system, and non osmotic release of antidiuretic hormone causing sodium retention, increased intravascular volume, and a hyperdynamic circulatory state¹⁶ complemented with increased production of nitric oxide which is considered the main cause of vasodilatation in cirrhosis. **Subjects and Methods:** All participating patients of either gender admitted in department of Gastroenterology at Tertiary care hospital with age >18 years with either diagnosed or newly diagnosed case of cirrhosis of liver (including both compensated & decompensated cases) admitted with acute kidney injury diagnosed according to International Club of Ascites Classification were enrolled in this study. **Results:** Among 26 patients requiring hemodialysis, 10 (38.5%) of patients recovered from hemodialysis whereas 16 (61.5%) of patients didn't recover from hemodialysis & either died on hemodialysis or was discharged on hemodialysis which needs to be continued. **Conclusion:** Totally 25.5% of patients expired during course of treatment in hospital whereas 74.5% were survived the hospital stay.

Keywords: Outcome, AKI, Cirrhosis.

Corresponding Author: Dr Kiran S, Assistant Professor, Department of Medical Gastroenterology, BMC RI and Bowring Hospital, Bangalore.

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Introduction

AKI is a common event in cirrhotic patients with fifth leading cause of hospitalizations in these patients, although its exact prevalence is unknown and it varies widely in clinical settings.^[1] Most common cause of AKI in cirrhosis is PRERENAL AZOTEMIA (PRA), accounting for approximately 68% of the cases. HRS a special type of Pre renal AKI which is not volume-responsive, constitutes approximately 25% of the cases of Prerenal AKI; that is, it accounts for only approximately 17% of cases of AKI in hospitalized patients with cirrhosis. Acute tubular necrosis (ATN) is more common than HRS as a cause of AKI, accounting for about a third of the cases

The increased propensity for AKI in patients with cirrhosis stems from hemodynamic abnormalities typical of patients with cirrhosis and ascites which is due to development of portal hypertension and portosystemic collaterals with splanchnic and systemic vasodilatation, resulting in decrease in effective arterial blood volume with increase in renin angiotensin- aldosterone system (RAAS), sympathetic nervous system, and non osmotic release of antidiuretic hormone causing sodium retention, increased intravascular volume, and a hyperdynamic circulatory state complemented with increased production of nitric oxide which is considered

the main cause of vasodilatation in cirrhosis.^[2]

Although these compensatory mechanisms initially (in early stages of cirrhosis) (when portal hypertension is moderate, increased cardiac output compensates for a modest reduction in systemic vascular resistance, permitting the arterial pressure and effective arterial blood volume to remain within normal limits & are able to maintain a reasonable arterial pressure, however as cirrhosis progresses (in advanced stages) and vasodilatation worsens, such mechanisms are no longer adequate and patients experience a further decrease in effective blood volume with enhanced activation of vasoconstrictive systems that leads to preferential vasoconstriction in several vascular beds, most prominently in the renal and central nervous systems. This predilection toward renal vasoconstriction cannot be countered by the usual intrarenal release of vasodilatory substances such as prostaglandins owing to decreased production of these vasodilatory substances in the renal vasculature in advanced cirrhosis and vasoconstriction is exacerbated further by local release of vasoconstrictors such as endothelin and thromboxane resulting in failure of the tubuloglomerular feedback & myenteric reflexes, through which they help in autoregulation of renal hypoperfusion, resulting in essentially constant blood flow to the kidneys irrespective of fluctuations in systemic blood pressure.^[3] However, when mean arterial pressure reaches a decisive threshold around 65

mm Hg (mostly seen in advanced cirrhosis) due to cirrhotic cardiomyopathy characterized by diastolic impairment with septal ventricular hypertrophy, blunted ventricular response to stress, systolic and diastolic dysfunction, and electrophysiological abnormalities (prolongation of QT interval) & Systolic dysfunction due to impairment of both alpha -adrenergic receptor and increase in endogenous cannabinoids and cardio suppressants such as nitric oxide and inflammatory cytokines causing myocyte apoptosis.^[4]

This process of auto regulatory mechanisms are overwhelmed and renal blood flow begins to decrease in proportion to renal perfusion pressure ultimately the amount of blood the kidney actually receives will decrease progressively predisposing patient with advanced cirrhosis to renal hypoperfusion and inability to respond to it.^[5]

Long standing hypoperfusion clearly predisposes cirrhotic patients to structural kidney injury which when coupled with a second hit such as volume loss , infection , exposure to nephrotoxic medications , leading to more pronounced decrease in volume status in cases of volume depletion whereas in case of infection , there is exaggerated inflammatory response with increased levels of pro inflammatory cytokines and long-lasting production of vasoactive mediators that can impair circulatory function and cause renal failure ultimately retarding complete renal recovery due to inability to reconstitute optimal renal perfusion even after resolution of the precipitating insult.^[6]

Subjects and Methods

Study Setting

Study was conducted at department of GASTROENTEROLOGY, Tertiary care hospital.

Type of Study

Longitudinal Prospective type of observational study.

Sample Size

Total 94 patients were enrolled during this period.

Inclusion Criteria

All participating patients of either gender admitted in department of GASTROENTEROLOGY at Tertiary care hospital with age >18 years with either diagnosed or newly diagnosed case of cirrhosis of liver(including both compensated & decompensated cases) admitted with acute kidney injury diagnosed according to International Club of Ascites Classification were enrolled in this study.

Exclusion Criteria

- Parenchymal kidney disease
- Receiving renal replacement therapy/renal or liver transplant Pregnant or nursing patient
- Refusal to participate in study .

Outcome

Patient were followed for the time during hospital stay to determine outcome in form of improvement in creatinine level , need of renal replacement therapy & condition on discharged by means of either survival or death.

Results

Table 1: Distribution based on Hemodialysis

Use of Hemodialysis	Frequency	Percent
No	68	72.3
Yes	26	27.7
Total	94	100.0

26 patients (27.7 %) required Hemodialysis in their course of treatment , whereas 72.3 % of patients didn't required Hemodialysis as mode of treatment.

Table 2: Recovered from Hemodialysis

Recovered From HD	Frequency	Percent
No	16	61.5
Yes	10	38.5
Total	26	100.0

Of 26 patients requiring hemodialysis , 10 (38.5 %) of patients recovered from hemodialysis whereas 16 (61.5 %) of patients didn't recovered from hemodialysis & either died on hemodialysis or was discharged on hemodialysis which needs to be continued.

Table 3: Progression of AKI

Progression OF AKI	Frequency	Percent
Progression	28	29.8
Regression	66	70.2
Total	94	100

29.8 % of patients shows progression in AKI inspite of treatment whereas 70.2 % of patients shows regression.

Table 4: Response to Treatment

Response To Treatment	Frequency	Percent
Complete Response	50	53.2
Partial Response	26	27.7
No Response	18	19.1
Total	94	100.0

[53.2% of patients responded completely to the treatment.

Table 5: Hospital Outcome

Hospital Outcome	Frequency	Percent
Survived	70	74.5
Expired	24	25.5
Total	94	100.0

25.5 % of patients expired during course of treatment in hospital whereas 74.5 % were survived the hospital stay.

Discussion

Acute kidney injury is one of the most common cause of mortality in patient with liver cirrhosis and seen in 20 % of hospitalized cirrhotic patient .It can be part of natural history of cirrhosis due to progressive increase in splanchnic vasodilatation causing progressive renal vasoconstriction resulting into development of Hepatorenal syndrome (HRS) or it can be part of acute event like bleeding , hypovolemia , drugs causing Pre renal AKI or due to injury to the renal tubules mostly secondary to hypoxic injury resulting into Acute tubular necrosis (ATN) . Despite the overall poor

outcomes, there is likelihood that specific treatments are available which have been shown to improve renal function and improve mortality.

In addition, to mortality & morbidity associated with AKI there has been absence of standardized definitions resulting into low sensitivity, specificity & causing inability to predict prognosis. There had been consistent transition over the last several years about consensus guidelines for AKI like RIFLE (2004), AKIN (2007), KDIGO (2012) to recently ICA-AKI (international club of ascites classification of AKI) criteria in 2015. ICA – AKI is more appropriate than earlier consensus as it does not uses urine output and creatinine estimation is more dynamic in nature than earlier consensus which uses static creatinine level.

According to ICA –AKI, AKI is defined by increase in creatinine level ≥ 0.3 mg/dl within 48 hrs or a percentage increase of >50 % from baseline level which is known or presumed to have occurred in 7 days. Baseline creatinine is value of creatinine in previous 3 months or value closest to hospital admission in case of multiple creatinine level in last 3 months or value at point of admission if no earlier creatinine level report available.

26 patients (27.7%) required Hemodialysis in their course of treatment , whereas 72.3 % of patients didn't required Hemodialysis as mode of treatment and of 26 patients requiring hemodialysis , 10 (38.5 %) of patients recovered from hemodialysis whereas 16 (61.5 %) of patients didn't recovered from hemodialysis & either died on hemodialysis or was discharged on hemodialysis which needs to be continued .This is comparable with Allegretti et al^[7] where 32% patients required hemodialysis from whom 9 patients (23.68 %) out of 38 patients requiring HD recovered whereas 76% patients didn't recovered from HD.

25.5 % of patients expired during course of treatment in hospital whereas 74.5 % were survived the hospital stay whereas study conducted by Scott et al ⁸ mortality was seen in 31.8% of AKI group .In study by Belcher et al shows mortality rate of 26%. Whereas in study by Allegretti et al^[7], 46.6 % died in follow up. One of the reasons for higher death percentage in their study may due to longer followup upto 90 days in their study which was only upto hospital stay in my study with no follow up of patients after discharge.

Of total 94 patients, 49 (52.13 %)(14 female & 35 male) , 27 patients (28.72 %) (5 female & 22 male) & 18 patients (19.15 %) (4 female & 14 male) are present in Prerenal , HRS & ATN respectively . When comparing Type of AKI with multiple baseline variables MAP , CTP ,MELD baseline creatinine, creatinine at AKI , CRP , Lactate , AKI CLIF SOFA score , all of these shows statistically significant correlation ($p < 0.05$) showing that all this variables are correlated with type of AKI , i.e. severe the AKI type , poorer the value which as per the expectations as is shown by study of Allegretti et al.^[7] AKI CLIF SOFA score are statistically higher in ATN group than other two groups predicting greater mortality in this patient as in my study 50 % of ATN group patients died which is lower in HRS & lowest in Pre renal group. In my study, AKI CLIF SOFA SCORE^[9] has AUROC of 0.790 & is 70% sensitive & 73 % specific in predicting mortality with cut off value of 2.5.

Similar results have been shown by Sun et al^[10] where AUROC is 0.74 with Cut off value of 2.0 & having sensitivity & specificity 53 % & 80 % respectively.

Of total 70 survival patients, 42 (60 %) have Prerenal AKI & of total 24 patients who expired during treatment, 9 (37.5 %) of these have ATN & this correlation is statistically significant ($p < 0.013$) which was also shown in study by Allegretti et al^[7] where ATN group has maximum mortality of 58 %. In my study 26 patients (27.65 %) required HD in their treatment modality of whom, 18 belong to ATN group & 4 each in PRA & HRS group, henceforth ATN constituting 69.23 % of hemodialysis group & remaining constituted by HRS & PRA group constituting 15.38% each. This correlation is statistically correlated ($p < 0.001$). This is similar to study by Allegretti et al^[7] where 31.66 % required HD which is constituted by 20 % in PRA , 34 % in HRS & 44 % in ATN group . Higher requirement of HD in ATN group in our study may be due to the fact patients are admitted late in course of disease & have higher urinary NGAL level predicting more mortality & severity of ATN.

Conclusion

Hemodialysis is required in 27.7 % as modality of treatment & among these 69.23% patients of ATN group needed HD & 65.38 % of Stage 3 AKI needs HD as modality of treatment of total 27.7 % patients needing HD, 38.5 % of these patients didn't recovered from HD.

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