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Original Research Article

TO DETERMINE KIND AND PRECIPITATING RISK FACTORS OF ACUTE KIDNEY INJURY IN PATIENTS WITH LIVER CIRRHOSIS

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ABSTRACT

Background: Aims: To determine the types of acute kidney injury in patients with liver cirrhosis and identify the precipitating causal (risk) factors for Acute Kidney Injury in patients with liver cirrhosis.

Materials and Methods: It is descriptive, observational study in Department of General Medicine, in acute kidney injury among liver cirrhosis patient for a period of 15 months. Patients above 18 years of age with clinical features of decompensated liver cirrhosis are selected.

Results: In this study on the basis of ICA AKI criteria, Incidence of AKI was found to be 43.6%. Out of total AKI population maximum had Pre Renal type of AKI followed by HRS AKI, and Intrinsic Renal AKI. No case of Post Renal AKI was diagnosed. Our study had male predominance, with incidence of AKI found more in middle aged population and among overall patients Alcohol was the predominant cause of Liver cirrhosis. The risk factors for AKI are older age, oliguria, low MAP, Hepatic Encephalopathy, Sepsis and shock There are higher chances of mortality in liver cirrhosis patients those who have AKI.

Conclusion: AKI was common among patients with liver cirrhosis with high in-patient mortality. Identification of these precipitants and independent predictors of AKI may lead to prompt and targeted treatment with reduction in patient mortality.

Keywords: Acute Kidney Injury, Non- alcoholic fatty liver disease, Chronic liver disease.

INTRODUCTION

Cirrhosis is a condition that is defined histopathologically and has a variety of clinical manifestations and complications, some of which can be life-threatening The pathologic features of cirrhosis consist of the development of fibrosis to the point that there is architectural distortion with the formation of regenerative nodules.[1] Liver cirrhosis is the morphologic change and a diffuse process characterised by fibrosis and disruption of the entire normal liver architecture into abnormal regenerative nodules. It is the result of long standing inflammation and/or direct toxic insults to the liver, leading to altered liver function, portal hypertension and neoplastic transformation which may be caused by chronic alcohol abuse, chronic infection with Hepatitis B and C viruses; auto-immune hepatitis, drugs, metabolic disease such as nonalcoholic fatty liver disease (NAFLD) and hereditary abnormalities like iron deposition (haemochromatosis) and copper deposition (Wilson‘s disease).[2,3] The severity of hepatic dysfunction has been largely assessed by Child- Turcotte- Pugh (CTP) score (parameters are ascites, hepatic encephalopathy, bilirubin, International Normalized Ratio (INR) and serum

albumin levels); and the Model for End- Stage Liver Disease (MELD-which consists of bilirubin, creatinine and INR). Clinically, features of advanced or decompensated liver cirrhosis associated with portal hypertension such as ascites, splenomegaly and bleeding varices, hepatic encephalopathy, renal dysfunction.[3,5,6]

In a multicentric study in India, out of 13,014 cases of chronic liver disease (CLD), 33.9% presented with decompensated cirrhosis. Alcoholism (34.3%) was the commonest cause of cirrhosis, whereas hepatitis B (33.3%) was the main cause of CLD in general and noncirrhotic CLD (40.8%).[7]

Acute kidney injury (AKI) is characterized by the sudden impairment of kidney filtration and excretion function over days to weeks resulting in the retention of nitrogenous and other products normally cleared by the kidneys. AKI is not a single disease but, rather, heterogeneous group of conditions that share common diagnostic features: specifically, an increase in the blood urea nitrogen (BUN) concentration and/or an increase in the plasma or serum creatinine concentration often associated with a reduction in urine volume.[4]

Kidney dysfunction is a common and life-threatening event in patients with liver cirrhosis. Acute kidney injury (AKI) has an estimated prevalence of 20–50% among hospitalized patients with cirrhosis. Cirrhotic patients with renal dysfunction have higher morbidity than those without renal dysfunction. Many cases of renal dysfunction in patients with decompensated cirrhosis are functional in nature, without any basic renal structure abnormality,[10] which precipitated mainly by overdose of diuretics, large-volume paracentesis without albumin replacement, gastrointestinal bleeding, bacterial infections, diarrhea, nephrotoxic drugs.[11] Newer International Club of Ascites-AKI (ICA-AKI) criteria, introduced in 2015, are useful in the diagnosis and prognostication of patients with decompensated liver cirrhosis.[12]

Early recognition of risk factors for renal dysfunction in these patients can decrease morbidity and mortality rates and will help in the management of cirrhosis by retarding the progression of renal dysfunction, thus improving quality of life of patients. There is lack of data available in respect of renal dysfunction in CLD patients specially at industrial organization like Railways, hence our study will try to fill the gap.

MATERIALS AND METHODS

It is descriptive, Observational study in Department of General Medicine, Northern Railway Central Hospital, New Delhi in acute kidney injury among liver cirrhosis patient for a period of 15 months (March2021 - July2022).

Sample size estimation:

n = sample size

Zα at 95% CI = 1.96

p = proportion or prevalence of interest, q = 100-p

d = precision

Based on a study conducted by Arora MS, Kaushik et al,[13]

Proportion of acute kidney injury among liver cirrhosis patient was 40.6%. Considering this value as p = 40.6%, d = precision = 10%

N = 1.96*1.96*0.406*0.594/ 0.10*0.10 = 93

We took minimum sample size as100 for the study.

Patients of liver cirrhosis with clinical features of hepatic decompensation, hospitalized or attending OPD at General Medicine Department were enrolled in the study after applying inclusion and exclusion criteria.

Inclusion Criteria: Subjects above 18 years of age with clinical features of decompensated liver cirrhosis.

Exclusion Criteria: Patient suffering from CKD, structural kidney disease , Heart failure primary (hepatocellular carcinoma or cholangiocarcinoma) metastatic malignancies post liver transplant patients with renal stone disease or history of treatment for renal calculi, Admitted patients with total admission period of <48hrs.

The data for this study was collected from patients diagnosed with liver cirrhosis, admitted or attending OPD(Medicine) in Department of General Medicine, Northern Railway Central Hospital, having any of the clinical signs of Hepatic decompensation such as gross ascites, UGI bleeding, encephalopathy, and jaundice. Patient who are diagnosed with decompensated cirrhosis features were admitted.

Cirrhosis was diagnosed on the basis of: Ultrasound signs of cirrhosis, morphology changes(nodularity) and clinical evaluation, liver function tests, signs of portal hypertension, and/or clinical of previous hepatic decompensation in patients with chronic liver diseases.

Clinical evaluation of all selected patients was done for the presence of AKI in them, which will include detailed history, clinical examination, and investigations like liver function test, renal function tests, complete blood count, serum uric acid, serum calcium, serum phosphorus, serology for hepatitis B and C, prothrombin time INR, ascitic fluid analysis (whenever required), urine analysis, urine sodium and creatinine and abdominal ultrasonography. In admitted patients SCr was monitored during the period of hospitalization.

Criteria for baseline serum creatinine, diagnosis and staging of AKI along with diagnosis of HRS-AKI was made according to The Revised Consensus Recommendations of the International Club of Ascites (ICA) by applying ICA-AKI criteria.

AKI type was diagnosed and classified as: Prerenal: (all or any of the two criteria mentioned below)

- when patients had a history of fluid losses (vomiting, diarrhea, upper gastrointestinal bleed, dehydration), in the preceding days, low mean arterial pressure.

- when SCr was normalized after tapering or withdrawing diuretics, and/or saline administration or after antibiotic treatment and saline administration in infections.
- Laboratory parameters include a urine specific gravity ≥1.020 and or Fractional excretion of sodium (FENa) <1% (this lab parameter was taken when patient is on diuretic treatment).[8]

Intrinsic renal AKI:

- when history of use of nephrotoxic agents, infection and prolonged volume depletion, microhematuria, proteinuria, or cast in urine along with urine specific gravity < 1.010 and/or FENa > 2%.[9]

HRS-AKI: was diagnosed as per criteria defined by the International Club of Ascites (ICA-AKI).

Postrenal AKI: when imaging showed pelvicalyceal dilatation.

Precipitating risk factors for AKI were assessed. Factors are: -Infection (sepsis, SBP), upper GI/variceal bleed, diarrhea /vomiting, Drugs affecting renal functions (NSAIDs, ARB, ACE inhibitor, diuretics),shock, ascites, encephalopathy. Assessment was done from patient history for UGI bleed (passage of black stools, hematemesis), dehydration, diuretic use, NSAIDs, ARB ACE inhibitor use.

Infection was assessed by: clinical signs like fever, respiratory rate>20/min, tachycardia and lab parameters like leukocytosis with neutrophilia and/or pulmonary infiltration radiologically(pneumonia), and/or urine WBC count >15cells/hpf or urine culture positive for urinary tract infection.

Ascites was diagnosed by clinical examination and /or by Ultrasound.

Hepatic encephalopathy was assessed and graded as per West Haven criteria.

SBP (spontaneous bacterial peritonitis): when ascitic fluid TLC >250 cells(PMN)/mm3, without any evident intra-abdominal source of infection.

Shock:, diagnosis of shock was based on clinical findings, hypotension MAP(mean arterial pressure) <70mm of Hg , with associated tachycardia, clinical signs of tissue hypoperfusion. Lab parameters at the time of admission and discharge was analysed and compared

Based on above methodology AKI types was determined and risk factors for AKI were assessed. Data of demography, clinical findings, lab parameters along with risk factors were recorded analyzed and compared between patients with and without AKI.

Data was entered in MS excel and analysis was done using SPSS 21.0 version. Data will be presented as mean and standard deviation for continuous variables and as percentages for categorical variables. Unpaired t test was done to compare two means. Chi-square test was done to find out association between categorical variables. P value of less than 0.05 was considered significant.

RESULTS

Study was carried out in total of 117 patients with liver cirrhosis were evaluated in this study. Five participants were excluded due to incomplete investigations and Structural renal disease, while 112 participants were available for analysis.

Age and sex distribution: Total sample population was divided in 4 age groups which constitutes ≤40, 41-50, 51-60, and >60. There were 28 female which comprises 25% of the population and 84 male patients representing 75% of the population. The commonest presenting complaint was abdominal distension in 75 (67%) patients, followed by altered sensorium in 41(36.6%). The least presenting symptom was cough which accounted for 4 (3.6%). Other significant clinical presentations were gastrointestinal bleeding in 35 (31.3%), fever 33(29.5%), oliguria 22 (19.6%) and leg swelling 28(25%). No asymptomatic patients were accounted in the .

On history part we found that major population has history alcohol intake (67%) and in which recent alcohol intake history was present in 33.9%. Other relevant history was of NSAIDS use in15.2%, diuretics use in 29.5%, ACE/ARB (0%), LVP (large volume paracentesis) in14.3%. [Table 1]

During evaluation of patients we found that etiology of cirrhosis in maximum patients were alcohol intake (67.8%) and other etiologies with there respective percent.

In total 112 patients 47 patients had comorbidities, out of which hypertension and Diabetes were majorly present. Mentioned in table below. [Table]

In our population mean pulse rate was 91.7, MAP was 78 mm of Hg, MAP< 70 mm of Hg was present in 18 patients, icterus was present in majority of patients i.e.78(69.6%), splenomegaly was present in 33 patients, ascites was present in 75(67%) of patients and encephalopathy present in 41(36.6%) patients. [Table 3]

In USG all patients had coarse nodular liver, 93(83%) patients had splenomegaly, ascites was present in 96 patients (85.7%). [Table 4]

In our population mean Hb was 8.8±1.4 g/dl, mean baseline serum creatinine was 0.9±0.2mg/dl, mean peak baseline creatinine was 2.0±1.8 mg/dl with maximum value 9.4 mg/dl and minimum was 0.7 mg/dl. [Table 5]

Patients were assessed by CTP score, most of patients had CTP class B (22.3%) and C (74.1%) as shown in table.

Incidence of AKI in patients: On the basis of lab investigation and ICA AKI criteria we found that out of 112 patients of liver cirrhosis 49(43.8%) patients had AKI. [Table 6]

On the basis ICA AKI criteria AKI patient were staged as shown in table. Maximum number of patients were in Stage 2. On the basis of history, Urine analysis, FeNa, BUN/SCr ratio, USG findings and following ICA-AKI criteria we found that out of

total AKI patient, 28 (57.1%) were Pre renal type,17(34.7%) were HRS type,4(8.2%) were Renal type of AKI and no post Renal AKI found. [Table 7]
When results were compared in groups there was significant difference in age, various clinical features like oliguria, Encephalopathy.
When results were compared in different sex groups there was no significant difference in sex distribution. In other variables (significant alcohol use, clinical jaundice, ascites, splenomegaly, UGI bleed, CTP class), statistically no significant difference was found as shown in table. [Table 8]
When we compared various variables in respect of AKI versus without AKI, we found that few variables (Hb, platelet count, SGOT, SGPT, ALP, Protein, S. albumin, S.Na+, CTP score) were statistically not significant but in most of the other variables statistically significant difference was present.
It was found that mean age of patients were 54.6±9.6Yr with AKI and 50.8±7.5Yr without AKI and when we compared results were statistically significant (p= 0.022). Patients with AKI were significantly older than those without AKI.
Mean MAP was significantly lower in those with AKI compare to without AKI 73.81±6.4 versus 81.7±5.0 mm of Hg. TLC count was found significantly more in those patients with AKI compare to those without i.e. mean of 13760.5/mm3 ±6284.7 versus 9316.2/mm3 (p- <0.001). Likewise the mean total bilirubin was higher in subjects with AKI than those without, with values of 7.8 mg/dl ± 7.6 and 4.0 ± 2.7 respectively (p= <0.001)). The serum urea, BUN, baseline serum creatinine, peak serum creatinine, serum potassium, PT, INR, Urine sodium and creatinine, was higher in the subjects with renal failure than in those without renal failure. [Table 9]
In our study various known precipitating risk factors of AKI were analysed. Out of total 112 patients Sepsis was present in 42(37.5%) patients, SBP was present in 9(8%) patients, UGI bleed in 37(33%) patients, Diarrhoea/vomiting(dehydration) was present in 19(17%), LVP was present in 16 (14.3) patients. In drug history we found that 30(26.8%) patients had diuretics intake and 17(15.2) patients had NSAIDS use was found. Shock was present in 18(16.1%) of patients. [Table 10]
Out of total 49 patients with AKI 8 patients required RRT of which 6 patient expired.
Out of total 49 patients with AKI ,35(71.4%) patients were improved while 14 patients not improved, and comparing those without AKI 60 (95.2%) patients out of 63 were improved, on comparing results statistical significant result present, p=<0.001. Hence, we found that patients who did not have AKI had more chance of improvement than those with AKI.
Out of total 49 AKI patients,14 (28.6%), expired during treatment, while those without AKI patients 3(4.8%), expired during hospital course (p=<0.001). Hence we found that those patients who had AKI had higher mortality than those without. [Table 11]

Table 1: Demographic distribution

Age group (Years)	Number of patients	Percentages
≤40	10	8.9
41-50	37	33.0
51-60	43	38.4
>60	22	19.6
Total	112	100.0
Mean+/-SD (Range)	52.5+/-8.7 (30-68)	
Gender		
Male	84	75.0
Female	28	25.0
Total	112	100.0
Clinical presentation		
Abdominal distention	75	67.0
Leg swelling	28	25.0
Black stool or Hematemesis	35	31.3
Jaundice	71	63.4
Altered sensorium	41	36.6
Fever	33	29.5
Cough	4	3.6
Oliguria	22	19.6
Diarrhea /vomiting	20	17.9

Table 2: Clinical history and Etiology of Liver Cirrhosis

Clinical history	Number of patients	Percentages
Alcoholic	76	67.9
Recent alcohol intake	38	33.9
NSAIDS	17	15.2
Diuretics	33	29.5
ACE/ARB	0	0.0
LVP	16	14.3
Etiology of Liver Cirrhosis		
Alcohol	76	67.8
HBV	3	2.7

HCV	8	7.1
NASH	19	17.0
Alcohol +HCV	2	1.8
Alcohol +HBV	3	2.7
Others	2	1.8

Table 3: Comorbidities in present study

Comorbidity	Number of patients	Percentages
Yes	47	42.0
No	65	58.0
Hypertension	20	17.9
Diabetes	24	21.4
CAD	3	2.7
Hypothyroid	5	4.5
COPD	3	2.7
CVA	4	3.6
Obesity	2	1.8
Old TB	2	1.8

Table 4: Clinical features and examination findings

Clinical features and examination findings	Number of patients	Percentages
MAP<70 mm of Hg	18	16.1
Pedal edema	30	26.8
Clinical jaundice/ icterus	78	69.6
Flaps/asterixis	33	29.5
Abdominal tenderness	13	11.6
Hepatomegaly	7	6.3
Splenomegaly	33	29.5
Ascites	75	67
Upper GI bleed	37	33
Hepatic Encephalopathy	41	36.6
Viral markers reactive		
HBsAg	6	5.3
Anti-HCV	8	7.1
USG findings		
Coarse nodular liver	112	100.0
Splenomegaly	93	83.0
Ascites	96	85.7
Dilated pelvicalyceal or ureter	0	0

Table 5: Blood investigations

Blood investigations	Mean	SD	Minimum	Maximum
Hb(g/dl)	8.8	1.4	4.0	13.4
TLC/mm^3	11260.6	5972.6	2000.0	31500.0
Platelet count($x10^3$)/ mm^3	115.6	35.6	55.0	202.0
Total bilirubin(mg/dl)	5.6	5.7	0.2	29.0
SGPT(IU/L)	41.1	24.1	12.0	147.0
SGOT(IU/L)	104.2	65.2	21.0	411.0
ALP(IU/L)	136.5	59.5	31.0	394.0
Serum protein(g/dl)	6.6	0.5	5.7	7.7
Albumin(g/dl)	2.6	0.5	1.7	4.2
Serum Na+(mmol/L)	131.1	5.5	122.0	145.0
Serum K+(mmol/L)	4.2	0.9	2.7	6.5
Serum Urea(mg/dl)	60.3	46.7	12.7	178.0
BUN(mg/dl)	28.3	21.8	6.0	83.0
PSCr(peak)(mg/dl)	2.0	1.8	0.7	9.4
BSCr(baseline)(mg/dl)	0.9	0.2	0.6	1.3
PT (sec)	28.9	10.0	15.8	58.0
INR	2.2	0.8	1.2	4.5
Urine SG	1.021	0.006	1.010	1.030
Urine sodium(mmol/L)	47.2	26.8	12.0	125.0
Urine creatinine (mg/dl)	69.1	33.8	12.2	168.6

Table 6: Classification of subjects based on severity of liver Cirrhosis

CTP class	Number of patients	Percentages
Class A (score 5-6)	4	3.6
Class B (score7-9)	25	22.3
Class C(score 10-15)	83	74.1
Total	112	100.0

Table 7: Acute kidney injury and staging

AKI	Number of patients	Percentages
Present	49	43.8
Absent	63	56.3
Total	112	100.0
Stage of AKI		
Stage 1	14	28.6
Stage 2	19	38.8
Stage 3	16	32.7
Total	49	100.0
Type of AKI		
Pre-renal	28	57.1
HRS	17	34.7
Renal	4	8.2
Post renal	0	0
Total	49	100.0

Table 8: Comparison of variables in groups between AKI and without AKI patients

Variables		AKI		without AKI		Chisquare test P value
		N	%	N	%	
Age group (Yr)	</=40	5	50.0%	5	50.0%	0.021
	41-50	10	27.0%	27	73.0%	
	51-60	19	44.2%	24	55.8%	
	>60	15	68.2%	7	31.8%	
Gender	Male	36	42.9%	48	57.1%	0.741
	Female	13	46.4%	15	53.6%	
Significant Alcohol use	Yes	30	39.5%	46	60.5%	0.185
	No	19	52.8%	17	47.2%	
Oliguria	Yes	19	86.4%	3	13.6%	<0.001
	No	30	33.3%	60	66.7%	
Clinical jaundice/ Icterus	Yes	37	47.4%	41	52.6%	0.234
	No	12	35.3%	22	64.7%	
Ascites	Yes	37	49.3%	38	50.7%	0.090
	No	12	32.4%	25	67.6%	
splenomegaly	Yes	12	36.4%	21	63.6%	0.308
	No	37	46.8%	42	53.2%	
	No	26	57.8%	19	42.2%	
UGI bleed	Yes	17	34.7%	20	31.7%	0.742
	No	32	65.3%	43	68.3%	
Encephalopathy	Yes	25	61.0%	16	39.0%	0.005
	No	24	33.8%	47	66.2%	
CTP class	Class A	2	50.0%	2	50.0%	0.197

Table 9: Precipitating risk factors for AKI and without AKI patients

Variables	AKI		without AKI	
	Mean	SD	Mean	SD
Age(Yr)	54.6	9.6	50.8	7.5
MAP(mm of Hg)	73.1	6.4	81.7	5.0
Hb(g/dl)	8.8	1.3	8.8	1.5
TLC/mm^3	13760.5	6284.7	9316.2	4950.2
Platelet count($x10^3/mm^3$)	114.9	38.7	116.1	33.3
Total bilirubin (mg/dl)	7.8	7.6	4.0	2.7
SGPT(IU/L)	44.0	29.8	38.9	18.5
SGOT(IU/L)	106.8	83.8	102.2	46.7
ALP(IU/L)	127.1	67.0	143.9	52.2
Serum protein (g/dl)	6.6	.5	6.6	.4
Serum Albumin (g/dl)	2.5	.4	2.6	.5
Serum Na+(mmol/L)	130.0	5.0	132.0	5.7
Serum K+(mmol/L)	4.5	.8	3.9	.8
Serum Urea (mg/dl)	103.9	38.8	26.3	8.2
BUN (mg/dl)	48.7	17.9	12.4	3.8
Peak SCr (mg/dl)	3.2	2.1	1.0	.1
Baseline SCr (mg/dl)	1.0	.2	.8	.2
PT(sec)	31.79	11.94	26.61	7.63
INR	2.5	.9	2.1	.5
Specific gravity	1.023	.007	1.020	.005
Urine Na+ (mmol/L)	41.0	26.7	52.0	26.1
Urine creatinine (mg/dl)	78.0	30.7	62.3	34.7
CTP score	11.5	2.3	10.8	2.0

Table 10: Precipitating risk factors of AKI and without AKI patients

Precipitating risk factors of AKI		AKI		Without AKI		Chi square test P value
		N	%	N	%	
SBP	Yes	6	12.2%	3	4.8%	0.176*
	No	43	87.8%	60	95.2%	
Sepsis	Yes	31	63.3%	11	17.5%	<0.001
	No	18	36.7%	52	82.5%	
GI bleed	Yes	17	34.7%	20	31.7%	0.742
	No	32	65.3%	43	68.3%	
Large volume paracentesis	Yes	5	10.2%	11	17.5%	0.276
	No	44	89.8%	52	82.5%	
NSAIDS use	YES	4	23.5%	13	76.5%	0.068
	NO	45	47.4%	50	52.6%	
Diuretic use	Yes	11	22.4%	19	30.2%	0.361
	No	38	77.6%	44	69.8%	
Shock	Yes	14	28.6%	4	6.3%	0.001
	No	35	71.4%	59	93.7%	

Table 11: Outcome in AKI and without AKI patients

Variables		AKI		Without AKI		Chisquare test P value
		N	%	N	%	
Improved	Yes	35	71.4%	60	95.2%	<0.001
	No	14	28.6%	3	4.8%	
Expired	Yes	14	28.6%	3	4.8%	<0.001
	No	35	71.4%	60	95.2%	

DISCUSSION

In our study we tried to determine the kind and precipitating risk factors of AKI in liver cirrhosis patients. This study showed that out of total 112 decompensated liver cirrhosis patients, considering ICA AKI criteria and lab parameters with radiological findings we found that incidence of AKI was 43.8%. In support, a study done by Arora MS, Kaushik, et al,[13] on 176 patients found that prevalence of AKI was 40.6 % ,however a study done by CR Khatua, Sahu et al,[14] done on 576 subjects, found prevalence of 54.69%. This difference may be due to low sample size of our study. AKI has an estimated prevalence of approximately 20–50% among hospitalized patients with LC in various other studies2,7,8 and is associated with poor prognosis.[10,15]

In our study maximum population of AKI was in stage 2(38.8%), followed by stage 3(32.7%) and stage 1(28.6%). Similarly a study done on total 302 patients of liver cirrhosis by Thapa P.,KcS. et al.(2020),[16] found 42% of AKI population in stage 1, 28% in stage2,15% in stage 3, in Arora MS, Kaushik, et al,[30] found maximum patients in stage1. On the basis of history, Urine analysis, FeNa, BUN/SCr ratio, USG findings, other lab findings and following ICA-AKI criteria we found that out of total 49 patients of AKI, 28 (57.1%) were Pre renal type,17(34.7%) were HRS type,4(8.2%) were Renal type of AKI and no post Renal AKI found. Similar study was done by Thapa P.,KcS. et al,[16] found that 46% were pre-renal AKI, (30%) with HRS AKI and 12 (24%) with intrinsic renal disease. However in another study done by Arora MS, Kaushik, et al,[13] on 175 consecutive patients with decompensated cirrhosis patients found that prerenal AKI 67.6%, hepatorenal syndrome (HRS) 23.8%, intrinsic renal AKI 7%, and postrenal AKI 1.4%.In contrary to our study, a study at China by Zang F et al,[17] applied ICA AKI criteria found that HRS AKI ,was most common type of AKI in patients with acute on chronic liver failure. This may be due variation in sample size.

The subjects were mostly middle aged, with a mean age of 52.7 years in which 67.8% had alcohol etiology of cirrhosis and a male predominance was present. This finding was similar with the study done by Mohan J et al in Chennai where he found out that mean age was 48 and 85% of them had alcohol as the etiology of LC. Similarly in other studies male predominance with alcohol as major etiology was found.[16] This may be due to alcohol consumption in various ethnic groups. When we compare age and sex groups between patients with AKI with those without it was found that AKI occurrence increases at higher age groups and no significant difference was found in sex group as AKI prevalence 42.9% in male and 46.4% in female, in contrary study done by Mohan J et al there was male predominance in AKI prevalence.

When we assessed our patients on basis of clinical presentation we found that the commonest presenting complaint was abdominal distension in 75 (67%) patients, followed by altered sensorium in 41(36.6%). The least presenting symptom was cough which accounted for 4 (3.6%). Other significant clinical presentations were a gastrointestinal bleeding (UGIB) in 35 (31.3%) fever 33(29.5%), oliguria (19.6%) and leg swelling 28(25%). Therefore, most of these patients present with features of hepatic decompensation, thus already having poor prognostic indices. In the study by Lesi et al, ascites was present in 66% of the patients with liver cirrhosis while Attia gave a prevalence of 82%. In contrast, investigators from Pakistan, Brazil and Germany report a prevalence of 32%, 31% and 49%

respectively.[18,19,20] It may be due patient attending hospitals in Delhi NCR region at earlier stage of decompensation. On history part we found that major population have history significant alcohol intake (67%). Other relevant history was of NSAIDS use in15.2%, diuretics use in 29.5%.

When we evaluated etiology of cirrhosis in patients, we found that alcohol followed by NASH, HCV. HBV and others respectively. It may be due to our population belongs to good socioeconomic group. Similar studies were done by Sivanathan et al,[19] from Germany, and Choi and colleagues from South Korea, where alcohol was the predominant cause of liver cirrhosis with a prevalence of 52% and 50% respectively. In Taiwan, HBV was also found to be the commonest cause, followed by alcohol, and then HCV (54). Sivanathan recorded HCV as second at a prevalence of 28% and HBV at 14%. NASH had a prevalence of 6%. (38,57). This difference in frequencies may be due to the variation in endemicity of HBV and HCV across the different study populations.

On further evaluation of clinical features and examination findings we found that, in our population mean MAP was 78, MAP< 70 was present in 18 patients, icterus was present in majority of patients i.e.78(69.6%), splenomegaly was present in 33 patients, ascites was present in 75(67%) of patients and encephalopathy present in 41(36.6%) patients. In the same way study done by H.K. Agrawal et al,[21] on 100 Indian population ,found that icterus was present in 59 patients; 60 patients had clinically evident ascites , whereas, UGI bleed was present in 41 patients and 26 patients had features of hepatic encephalopathy.

Clinical features were compared between AKI and without AKI groups, on comparing various clinical features of Liver cirrhosis patients with AKI with those without AKI, we found that hepatic encephalopathy was present in 25 patients (61.0%) with AKI, and 16 patients (39.0%) in those without AKI, hence found statistically significant (p=0.005). Encephalopathy was seen more in those patients who had AKI and it may be a contributary factor to develop AKI in Liver cirrhosis patients. Out of 49 patients with AKI,19(86.4%) had oliguria while found in 3 (13.6%) patients those without AKI(p=<0.001). Hence we found that in patients with AKI Oliguria was significant clinical feature that those without. In other variables (significant alcohol use, clinical jaundice, ascites, splenomegaly, UGI bleed, CTP class), no significant difference found as shown in table below. Similar to our study significant correlation for hepatic encephalopathy and oliguria found in patient with AKI in the study by Watt and colleagues in their retrospective study and by H.K. Aggrawal et al,[21] in contrary to our study significant correlation was present for CTP score in LC patients with AKI , which suggested that AKI prevalence was more in higher CTP class.

Further when we compared our various variable of AKI with those without AKI group we found that, few variables (Hb, SGPT, SGOT, ALP, s.protein, s.albumin, s.sodium, CTP score)were statistically non-significant but in most of variables (age, MAP, TLC, total bilirubin, SK+,BUN, SCr, BScr, Pt INR, sp gravity, urine Na + Urine Creatinine,) stastistical difference was present suggested that mean was significantly lower in those with AKI compare to without AKI 73.81±6.4 versus 81.7±5.0mm of Hg. TLC count was found significantly more in those patients with AKI compare to those without i.e. mean of 13760.5/mm3 ±6284.7 versus 9316.2/mm3 ±4950.2 (p-<0.001). Likewise, the mean total bilirubin was higher in subjects with AKI than those without, with values of 7.8 mg/dl ± 7.6 and 4.0 ± 2.7 respectively (p= <0.001)). The serum urea, BUN, baseline serum creatinine, peak serum creatinine, serum potassium, PT, INR, Urine sodium and creatinine, was higher in the subjects with renal failure than in those without renal failure. Some of the Similar findings were found in other studies also.[18,19]

Various known risk factors precipitating AKI were analysed in our LC population, dividing patients in two groups with and those without AKI. We found that out of total 112 patients Sepsis was present in 42(37.5%)patients, SBP was present in 9(8%) patients, UGI bleed in 37(33%) patients, Diarrhoea/vomiting(dehydration) was present in 19(17%), LVP was present in 16 (14.3) patients. In drug history we found that 30(26.8%) patients had diuretics intake and 17(15.2) patients had NSAIDS use was found. Shock was present in 18(16.1%) of patients.

When we compared various precipitating factors between AKI and without AKI patients we found that in Sepsis and shock, results were statistically significant (p value<0.001 and 0.001 respectively). Out of total 42 patients of sepsis 31 had AKI, which comprises of 63.3% of total AKI population. Total 18 patients were in shock out of which 14 had AKI which comprises of 28.6% of total AKI population (49 patients).

Out of total 9 SBP patients 6 had AKI, which was consists of 12.2% of total AKI patients, but in other precipitating factors (SBP, UGI bleed, LVP, NSAIDS, Diuretics), there was no significant difference was observed.

Hence those patients of Liver cirrhosis who had sepsis and shock were more likely to develop AKI compare to those who do not had this risk factors. Similar to our study a study done on175 patients of LC by Arora MS, Kaushik, etal.(2019) in Uttarakhand population found that a significant association existed between SBP and presence of AKI, severity and type of AKI, Sepsis and shock also had significant associations with presence of AKI and its type. Sepsis was a significant precipitating factor and findings were consistent with the pathophysiology involved in the development of prerenal AKI.[13] Similarly study by Montoliu et al, H.K. Aggrawal et al on LC patients infections and SBP were the major precipitating factor related to

AKI. Studies have demonstrated that bacterial translocation from the intestinal lumen to the mesenteric lymph nodes—may play an important role in impairing circulatory function in advanced liver disease, eliciting an inflammatory response and splanchnic vasodilation resulting in further pooling of blood in splanchnic compartment and reduced renal blood flow indirectly, thus leading to renal dysfunction.[21] Contrary to our study a study done by CR Khatua, Sahu et al. on 576 LC patients use of AKI- precipitating medications was the most common cause of AKI, followed by bacterial infection. Study done by Arora MS, Kaushik, et al. in LC patients AKI had a significant association with CTP score, alcohol, spontaneous bacterial peritonitis (SBP), sepsis, and shock.

Out of total 49 patients with AKI 8 patients required RRT of which 6 patient expired. Out of total 49 patients with AKI ,35(71.4%) patients were improved while 14 patients not improved, and comparing those without AKI 60 (95.2%) patients out of 63 were improved with p=<0.001. Hence we found that patients who do not had AKI were more improved than those with AKI.

Out of total 49 AKI patients,14 (28.6%), were expired during treatment, while those without AKI patients 3(4.8%), patients were expired during hospital course(p=<0.001). Hence we found that those patients who had AKI had higher mortality than those without. Similar studies were done in support of our finding.[17,18,19]

CONCLUSION

AKI is a common occurrence in patients with decompensated Liver Cirrhosis. In this study on the basis of ICA AKI criteria, Incidence of AKI was found to be 43.6% . Out of total AKI population maximum had Pre Renal type of AKI followed by HRS AKI, and Intrinsic Renal AKI. No case of Post Renal AKI was diagnosed. Out study had male predominance, with incidence of AKI found more in middle aged population and among overall patients Alcohol was the predominant cause of Liver cirrhosis. The risk factors for AKI are older age, oliguria, low MAP, Hepatic Encephalopathy, Sepsis and shock. Higher chances of mortality in liver cirrhosis patients those who have AKI.

Limitations: This study is single center study and only Delhi-NCR patients were enrolled in study. Sample size was less because of time limitation. Many patients lacks previous health records.

REFERENCES

1. Bacon BR.Cirrhosis and its complications. In Harrison‘s principle of internal medicine, Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. 2018; 20th edition, volume- I, 2405. McGraw-Hill Education.
2. Pradhan S. Redefining Cirrhosis – a brief review. J Pathol Nepal. 2013; 3(6).
3. Kumar, Vinay; Fausto, Nelson; Abbas, Abul K.; Cotran, Ramzi S. ; Robbins, Stanley L. (2005): In Robbins and Cotran Pathologic Basis of Disease (10th ed.). Philadelphia, Pa.: Saunders. P640. ISBN 0-7216-0187-1.
4. Waikar SS. Acute kidney Injury. In Harrison‘s principle of internal medicine, Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. 2018; 20th edition, volume-I,2099,2101. McGraw-Hill Education
5. Rockey DC, Friedman SL. In Zakim and Boyer's hepatology: a textbook of liver disease. Hepatic fibrosis and cirrhosis. Elsevier; 2012. 6th Edition, Philadelphia
6. Sola E, Gines P. Renal and circulatory dysfunction in cirrhosis: current management and future perspectives. J Hepatol. 2010; 53(6):1135-45.
7. Mukherjee PS, Vishnubhatla S, Amarapurkar DN, Das K, Sood A, Chawla YK, et al. Etiology and mode of presentation of chronic liver diseases in India: A multi centric study. PLoS One. 2017 Oct;12(10):e0187033.
8. Kasper, Fauci, Hauser, Longo, Jameson, Loscaolzo; Harrisons ‘ Principles of Internal Medicine (20th edition) 304,pp2101.
9. Kasper, Fauci, Hauser, Longo, Jameson, Loscaolzo; Harrisons ‘ Principles of Internal Medicine (20th edition) 304,pp2105.
10. Garcia-Tsao G, Parikh CR, Viola A. Acute kidney injury in cirrhosis. Hepatology 2008; 48:2064–77.
11. Gerbes AL. Liver cirrhosis and kidney. Dig Dis. 2016; 34:387–90.
12. Angeli P, Ginès P, Wong F, Bernardi M, Boyer TD, Gerbes A, et al. Diagnosis and management of acute kidney injury in patients with cirrhosis: revised consensus recommendations of the International Club of Ascites. J Hepatol. 2015 Apr;62(4):968– 74
13. Arora MS, Kaushik R, Ahmad S, Kaushik RM. Profile of Acute Kidney Injury in Patients with Decompensated Cirrhosis at a Tertiary-Care Center in Uttarakhand, India. Dig Dis. 2020;38(4):335-343.
14. Khatua CR, Sahu SK, Meher D, Nath G, Singh SP. Acute kidney injury in hospitalized cirrhotic patients: Risk factors, type of kidney injury, and survival. JGH Open. 2020 Dec 14;5(2):199-206.
15. Piano S, Rosi S, Maresio G. Evaluation of the Acute Kidney Injury Network criteria in hospitalized patients with liver cirrhosis and ascites. J Hepatol 2013; 59:482–9.
16. Thapa P, Kc S, Hamal AB, Sharma D, Khadka S, Karki N, Jaishi B, Tiwari PS, Vaidya A, Karki A. Prevalence of Acute Kidney Injury in Patients with Liver Cirrhosis. JNMA J Nepal Med Assoc. 2020 Aug 31;58(228):554-559.
17. Zang H, Liu F, Liu H, You S, Zhu B, Wan Z, Xin S. Incidence, risk factors and outcomes of acute kidney injury (AKI) in patients with acute-on-chronic liver failure (ACLF) of underlying cirrhosis. Hepatol Int. 2016 Sep;10(5):807-18.
18. Angeli P, Rodrıguez E, Piano S et al. Acute kidney injury and acute-on-chronic liver failure classifications in prognosis assessment of patients with acute decompensation of cirrhosis. Gut 2015;64: 1616–22
19. Sivanathan V, Kittner JM, Sprinzl MF, Weinmann A, Koch S, Wiltink J, et al. [Etiology and complications of liver cirrhosis: data from a German centre]. Deutsche medizinische Wochenschrift. 2014 Sep;139(36):1758-62.
20. Carvalho GC RCA, Kalil JR, et al. Causes of renal failure in patients with decompensated cirrhosis and its impact in hospital mortality. Annals of hepatology. 2012;11(1):90- 5
21. Aggarwal HK, Jain D, Singla S, Jain P. Assessment of renal functions in patients of chronic liver disease. Ren Fail. 2015;37(9):1457-63.