

Study of Hyponatremia in Cirrhosis of Liver And Its Complications – A Prospective Cross Sectional Study

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Abstract

Background: Cirrhosis of liver is the commonest complication of long term consumption of alcohol. Alcohol consumption is on a rise in our community. Hyponatremia is one of the factors which determines the prognosis. The level of serum sodium has significant role in the occurrence of decompensation in a cirrhotic patient.

Aims and Objectives: This study is to determine the prevalence of hyponatremia in cirrhotic patients and its correlation with the occurrence of complications in those patients.

Materials and methods: A prospective study was conducted in 150 inpatients at the Government Medical College, Ernakulam who were admitted with diagnosis of cirrhosis. Patients who had cirrhosis with hyponatremia were followed up for monitoring of complications and compared with eunatremic cirrhosis group.

Results and discussion: Among the 150 patients studied, 81 had hyponatremia, which is 56% of the study population. Remaining 44% had normal sodium value. Mild, moderate and severe cases were 33%, 17% and 4% respectively which was comparable to other studies. Oedema and ascites were seen more in group with hyponatremia. Complications like Portal hypertension, Hepatic encephalopathy and multiple hospital admissions were also higher in the hyponatremia group.

The complications in cirrhosis were directly proportional to the level of hyponatremia, with more complications seen in severe hyponatremias which was statistically significant.

Incidence of Hepato renal syndrome was found to be higher in hyponatremia group though not statistically significant. The correlation between secondary bacterial peritonitis and hyponatremia could not be evaluated due to less number of diagnostic paracentesis. Mortality in the study group was 46.9%, 50% and 66.7% in mild moderate and severe categories of hyponatremia respectively, which had statistically significant correlation

Conclusion: Prevalence of hyponatremia was significant in the study population. Complications of cirrhosis like portal hypertension, hepatic encephalopathy, multiple admission, hepatorenal syndrome and mortality were noted to be high in hyponatremic group than in eunatremic group of patients with cirrhosis.

Keywords: Hyponatremia, Ascites, Oedema, Portal hypertension, Hepatic - encephalopathy, Secondary bacterial peritonitis, Multiple Admissions, Mortality

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I. Introduction

The prevalence of alcoholism in Kerala is 20-38%. This alarming number shows that it is a cause of major health concern in Kerala. Considering the magnitude of the problem, there is still not many studies or researches done on cirrhosis and its complications in our state. Alcohol consumption is one of the commonest causes of cirrhosis. Hyponatremia is a proven prognostic indicator of cirrhosis.¹ The study thus becomes relevant by evaluating the complications and outcomes of cirrhosis patients in a major tertiary healthcare centre in Kerala.

Alcoholism and stages of cirrhosis¹

The three types of liver injury due to acute alcohol intake is classified as

- 1) Alcoholic fatty change (Steatosis): May be reversible after abstinence. Invariably steatosis occurs if consumption exceeds 80 g of alcohol per day.
- 2) Acute alcoholic hepatitis: Develops due to large amount of alcohol consumption for a long period of time. It has been found that 15–20 years of excessive drinking is necessary to develop alcoholic hepatitis. There is prominence of cholestasis. It is more severe in females
- 3) Cirrhosis: Cirrhosis is the severe most form of alcoholic liver injury and is usually of the micro nodular variety. The risk increases in continuous drinkers compared to binge drinkers. Collagen deposition will be pericellular, in the space of Disse, and round the central veins (central hyaline sclerosis).

Factors increasing susceptibility to ALD

1. Lifetime intake of alcohol Female sex
2. Genetic factors
3. Drinking without food
4. Binge drinking
5. High concentration alcoholic drinks—for example, spirits
6. Drinking multiple different alcoholic beverages.

Clinical features

1. Nausea
2. Abdominal discomfort
3. Diarrhoea
4. Jaundice
5. Ascites
6. Encephalopathy
7. Upper gastrointestinal bleeding.²

Alcoholic liver cirrhosis is one of the major global health problem. Cirrhosis is a condition of chronic progressive parenchymal necrosis, regeneration, and diffuse fibrosis, resulting in alteration of the lobular architecture throughout the whole of the liver. These islands, or nodules, are called “Pseudo lobules” because there is loss of normal lobular architecture. Depending upon the size, the defect is called “macro nodular” or “micro nodular cirrhosis.” The histological abnormality involves the whole of the liver. While fibrosis is a reversible process, cirrhosis is not. The disease being often silent, the exact prevalence of cirrhosis is not known. Nearly 30% to 40% of cases are discovered during autopsy Liver is vulnerable to wide variety of toxic, metabolic, microbial and circulatory insults.³ Cirrhosis liver is one of the prime non communicable diseases, which is expected to be a main health care concern of the 21st century. In the present world, the number of people suffering from liver disorders is on the rise. This may be due to the alteration in lifestyle with increased alcohol consumption and many stress related factors. Identification of the demography of patients with cirrhosis is of great importance in the current health care scenario for the calculation of prevalence of this frustrating disease. There is a lot of research in the field of cirrhosis and its various complications. All these studies are done to assess the role of hyponatremia as an independent risk factor for complications of cirrhosis and its possible implication in prevention. This study will enlighten the role of hyponatremia in complications of cirrhosis of liver.²

Hyponatremia is a common electrolyte abnormality in cirrhosis of liver, as a result of increased serum level of renin/aldosterone due to portal hypertension, decreased vascular response to vasoactive drugs and reduced solute free water clearance. Diuretic usage is another cause for hyponatremia. In advanced cirrhosis, hyponatremia is a common finding. Even though it is very rarely severe, it is enough to represent a life threatening condition. Hyponatremia has an adverse prognostic meaning as it indicates an advanced disease with severe cardiovascular dysfunction. Severe hyponatremia, intractable ascites and decreased arterial pressure are findings clinically seen in patients with advanced cirrhosis. . Hyponatremia in cirrhosis results from an impaired effective volume, mostly due to vasodilation of peripheral arteries. This leads to AVP secretion and reduced renal perfusion and glomerular filtration rate so as to impair free-water clearance. The clinical manifestations of hyponatremia in cirrhosis does not differ from those seen in patients without cirrhosis. However, due to the concomitant abnormalities in nitrogen metabolism, symptoms of hyponatremia are often present with and hardly distinguishable from symptoms related to hepatic encephalopathy. Treatment of hyponatremia in cirrhosis mainly relies on the correction of effective volume status. Hyponatremia can be a key prognostic factor in patients with cirrhosis of liver when it is added to MELD score. Thus, hyponatremia could be useful in predicting prognosis & development of complications in cirrhotic patients.

II. Methodology

According to OXFORD TEXT BOOK OF MEDICINE the prevalence of hyponatremia in cirrhotic patient is observed to be 38%. The sample size was calculated as 147. All patients with cirrhosis satisfying the inclusion and exclusion criteria, admitted in the wards from January 2015 to December 2016, a total of 150 patients were included in the study. Inclusion criteria was all inpatients with history, clinical features and USG evidence of cirrhosis. Patients with cardiac failure, chronic kidney disease, on drugs like S.S.R.I., T.C.A., M.A.O were excluded. Data was entered in Microsoft excel spread sheet and analysed using SPSS.

III. Results

Distribution of age in the study was 20-80years from the data obtained from 150 patients and the mean age in years was 51.83+/- 9.77years it can be seen that the mean age of the population is 40-60 years

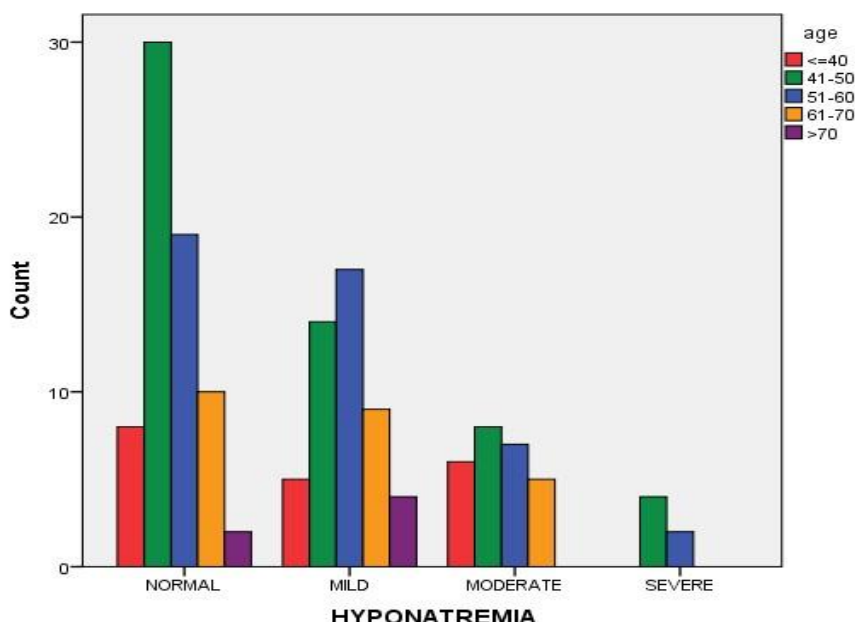


Figure 1. Shows number of patients in each age group with normal sodium level and with mild, moderate and severe hyponatremia.

	PRESENT		ABSENT	
	Count	Column N %	Count	Column N %
ALCOHOLIC	137	91.33%	13	8.67%
PALLOR	79	52.67%	71	47.33%
ICTERUS	93	62.00%	57	38.00%
EDEMA	102	68.00%	48	32.00%
PAROTIDOMEGALY	71	47.33%	79	52.67%
LOSS OF BODY HAIR	102	68.00%	48	32.00%
GYNAECOMASTIA	75	50.00%	75	50.00%
ASCITES	92	61.33%	58	38.67%
PALMAR ERYTHEMA	3	2.00%	147	98.00%
SPIDER NAEVI	43	28.67%	107	71.33%

Table 1-Clinical features in cirrhosis

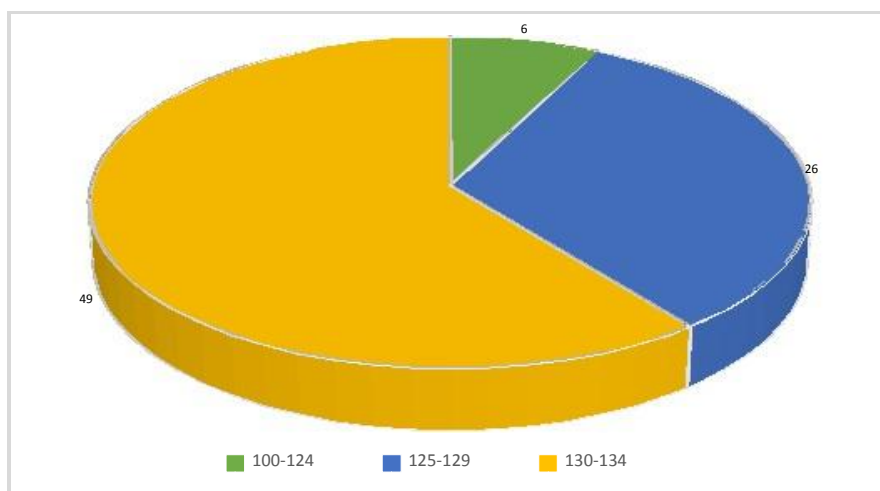


Figure 2 - Distribution of severity of hyponatremia

Figure 2 shows that most of the patients 49 (60.5%) have mild hyponatremia, 26 have (32.1%) moderate hyponatremia and 6 have (7.4%) severe hyponatremia.

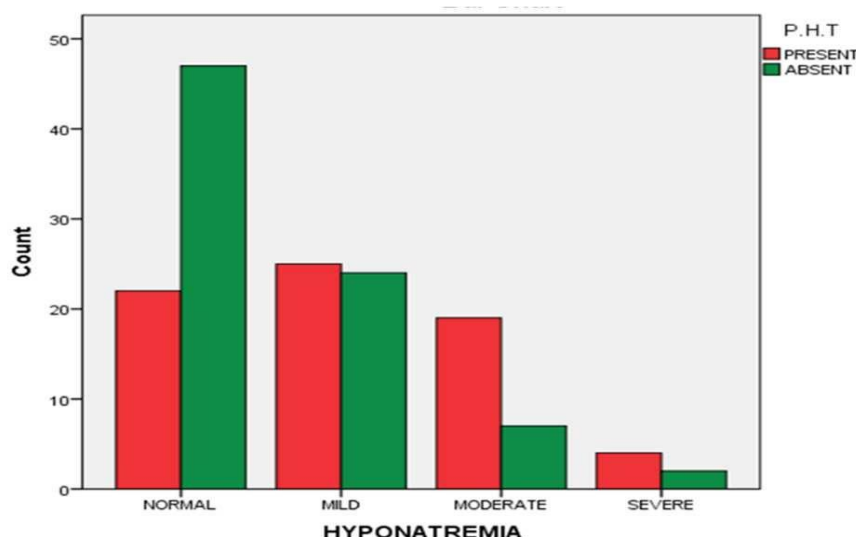


Figure 3-Relation of PHT to Hyponatremia

Patients with Portal Hypertension had more numbers with hyponatremia compared to patients with normal sodium level and as severity of hyponatremia increases, more are the cases of Portal Hypertension. In Figure 3 the bar graph shows red bars for Portal Hypertension and green bars show absence of Portal Hypertension.

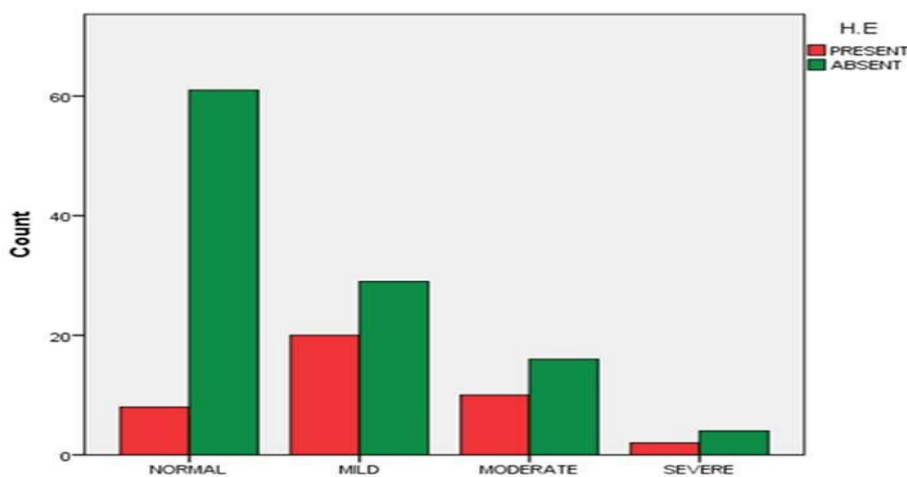


Figure 4- Relation of hyponatremia to Hepatic Encephalopathy

Figure 4 shows that the patients with hepatic encephalopathy have higher number of patients with hyponatremia as compared to patients with normal sodium level and as severity of hyponatremia increases, more are the cases of hepatic encephalopathy.

			MA		Total
			PRESENT	ABSENT	
HYPO NATREMIA	NORMAL	Count	24	45	69
		% within Normal Sodium	34.8%	65.2%	100%
	MILD	Count	27	22	49
		% within mild HYPONATREMIA	55.1%	44.9%	100%
	MODERATE	Count	19	7	26
		% within moderate HYPONATREMIA	73.1%	26.9%	100%
	SEVERE	Count	4	2	6
		% within	66.7%	33.3%	100%

		severeHYPONATREMIA			
Total		Count	74	76	150
		% within TOTAL	49.3%	50.7%	100%
Chi-Square Tests					
		Value	df	P VALUE (sig if <0.05)	
Pearson Chi-Square		13.082	3	.004	

Table 2-Relation between Hyponatremia and multiple hospital admissions in cirrhosis

Table 2 shows that the patients with hyponatremia have more percentage of multiple admissions as compared to the ones with normal sodium level and as the severity of hyponatremia increases, the percentage of multiple admissions also increases. This shows a significant correlation

				H.R.S.		Total
				PRESENT	ABSENT	
	NORMAL	Count		6	63	69
		% within Sodium		8.7%	91.3%	100%
HYPO NATREMIA	MILD	Count		7	42	49
		% within HYPONATREMIA		14.29%	85.71%	100%
	MODERATE	Count		4	22	26
		% within HYPONATREMIA		15.4%	84.6%	100%
	SEVERE	Count		1	5	6
		% within HYPONATREMIA		16.7%	83.3%	100%
Total		Count		18	132	150
		% within TOTAL		12.0%	88.0%	100%
Chi-Square Tests						
		Value	df	P VALUE (sig if <0.05)		
Pearson Chi-Square		3.361	3	.339		
N of Valid Cases		150				

Table 3- Relation between Hyponatremia and Hepatorenal syndrome in cirrhosis

Table 3-Patients with hyponatremia have increasing percentage of Hepato renal syndrome as compared to those with normal sodium level and as the severity of hyponatremia increases, the percentage of Hepato renal syndrome also increases, though not statistically significant.

				DEATH		Total
				ALIVE	DEAD	
	NORMAL	Count		54	15	69
		% within Normal Sodium		78.3%	21.7%	100.0%
HYPO NATREMIA	MILD	Count		26	23	49
		% within HYPONATREMIA	mild	53.1%	46.9%	100.0%
	MODERATE	Count		13	13	26
		% within HYPONATREMIA	mod.	50.0%	50.0%	100.0%
	SEVERE	Count		2	4	6
		% within HYPONATREMIA	severe	33.3%	66.7%	100.0%
Total		Count		95	55	150
		% within TOTAL		63.3%	36.6%	100.0%
Chi-Square Tests						
		Value	df	P VALUE (sig if <0.05)		
Pearson Chi-Square		11.358	3	.010		
N of Valid Cases		150				

Table 4

Table 4 shows that patients with cirrhosis and hyponatremia has more percentage of death as compared to those with normal sodium level and as the severity of hyponatremia increases the percentage of death also increases which is statistically significant

DISCUSSION

The study shows that out of the total 150 patients, majority of patients with normal sodium levels are in the age group of 40 – 50years 43.5 % (n=30) In this age group the incidence of hyponatraemia are, mild 28.6 % (n=14), moderate 30.8 % (n=8) and severe hyponatremia 37.3 % (n=4) respectively. The age group 50 – 60 years was the major age group 67.7% with 27.5 % (n=19), 34.7 % (n=17), 26.9 % (n=7) and 33.3 % (n=2) respectively. The range was 20 – 80 years and the mean age was 51.83years with standard deviation 9.7.years This was comparable to study by Paolo Angeli et al⁵ (59.3), Samanulla et al.⁶(51.3) and Ashraf Abd et al¹(46.2) The mean age of the patient was 46.02+11.80(mean+SD) years study by Rajesh Khyalappa et al⁷. (Table 6)

Name of the Study	Mean Age
Paolo Angeli et al	59.3 yrs.
Samanulla et al	51.3 yrs.
Ashraf AbdKhalik et al	46.2 yrs.
Rajesh Khyalappa et al	46.02 yrs.
Current Study	51.8 yrs.

Table 6. Mean age

Prevalence of Hyponatremia

Study of prevalence of hyponatremia shows that 54% (n=81) of patients with cirrhosis had hyponatremia and 46% (n=69) normal sodium levels. The hyponatremias were further divided into mild (130 – 134), moderate (125 – 129) and severe (<124) and their incidence was 32.7% (n=49), 17.3% (n=26) and 4% (n=6) respectively. This data is comparable with study by Jong Hoom Kim et al⁴, study by Rajesh Khyalappa.⁷, Paolo Angeli et al⁵, Ashraf AbdKhalik et al⁸ as shown in Table 7)

Name of Study	Normal	130-134	125-129	<124
Jong Hoom Kim et al		52.7%	20%	27%
Ashraf AbdKhalik et al	40.5%	32.4%	27.02%	
Paolo Angeli et al	50.5%	27.9%	21.4%	
Samiullah Shaik et al	48.4%	24.9%	26.7%	
Rajesh Khyalappa et al	73%	17%	10%	
Current Study	46%	32.7%	17.3%	4%

Table 7- Prevalence of hyponatremia in patients admitted with cirrhosis

IV. Relation to Portal Hypertension

Relation of hyponatremia to Portal hyper tension (PHT) shows out of the 150 cases 45.33 % (n=68) have PHT. Out of the total 68 patients who had PHT, 22 patients had normal sodium (31.9%) and remaining 46 patients had hyponatremia (51%). In this 46 patients of hyponatremia, mild hyponatremia was present in 51 %, (n=25), moderate hyponatremia present in 65.38 %.(n=17) and 66.7% had severe hyponatremia .This shows severity of hyponatremia is directly related to PHT. Above relation is significant statistically This data was comparable with the study by Udaganiet al⁹, Samiullah et al¹⁰ and Ashraf et al⁸.The result obtained in our study was above this value. Summarised in Table 8

Name of Study	Normal	Mild	Moderate	Severe
PriyankUdaganani et al	33.3%	81%	95.7%	
Ashraf et al		10%	33%	
Saminulla et al		24.5%		
Current Study	31.9%	51%	65.38%	66.7%

Table 8

Relation to Hepatic Encephalopathy

Total of 43 patients (28.67%). in the study population had Hepatic .Encephalopathy. Of which 8patients with H.E had normal sodium (11.6%), 20 patients with H.E. had mild hyponatremia (40.8%). 12 patients with H.E. have moderate hyponatremia (46.15%) and 3 patients have severe hyponatremia of 50% There was strong correlation between patients with H.E. and severity of hyponatremia. This was confirmed by significant p value

Name of Study	Total	Mild	Moderate	Severe
Scott W Biggins et al	55%			
Rajesh Khyalappa et al	34%			
Milind V Patil et al	23.7%			
PriyankUdagani et al		9.5%	39.1%	
Paolo Angeli et al		14%	23%	40%
Ashraf et a		10%	25%	38%
Current Study	28.6%	40.8%	46.15%	50%

Table 9

The comparison of results of study by Paolo Angeli et al⁵, study by Ashraf et al⁸,study by Scott w. Biggins et al¹¹ study by Rajesh Khyalappa et al⁷, study by PriyankUdagani et al⁹. Hepatic encephalopathy (23.7%) in study by Milind V Patilet al³, with the present study is summarised in Table 9

Relation to Multiple admissions

Multiple admissions in patients who had normal sodium and hyponatremia shows that out of total of 73 patients (49.3%) in the study population who had multiple admission , 24 patients 34.8%.had normal sodium ,27 patients.14.2%with multiple admissions had mild hyponatremia, 19patients15.4%with multiple admissions had moderate hyponatremia and 4 patients16.7%have severe hyponatremia - Thereis a strong correlation between patients with multiple admission and severity of hyponatremia. This was confirmed by statistically significant p value. This was supported from findings from Ashraf Abd El-KhalikBarakat etal⁸ ‘hyponatremia was found to be a risk factor for increased morbidity’.

Relation to Subacute Bacterial Peritonitis

Study of distribution of Secondary bacterial peritonitis patients who are having normal sodium and hyponatremia shows that 2 patients in the study population had SBP.This was the limitation of the study as only 8 patients underwent diagnostic paracentesis of which only 2 were diagnosed to have SBP. Distribution of Hepato renal syndrome shows hyponatremia group had higher incidence compared to normal sodiumgroup. Total of 18 patients in the study population had HRS (12%).of which 6 patients with HRS had normal sodium 7 patients with HRS had mild hyponatremia 4 patients with HRS have moderate hyponatremia and 1 patient had severe hyponatremia .This was not found to be statistically significant This was similar to study by Paolo Angeli etal⁵ AshrafAbdKhaliket alRajesh Khyalappaetal.

Relation to Mortality

Distribution of mortality in patients who are having normal sodium and hyponatremia when observed, showed that total of 55 patients in the study population died which is 36.6%. Among this 15 patients had normal sodium (21.7%), 23 patients who succumbed had mild hyponatremia (46.9%), 13 patients who died had moderate hyponatremia (50%) and 4 patients had severe hyponatremia (66.7%). There is a strong correlation between patients’ death and severity of hyponatremia. This was statistically significant, p value (0.010) Table 10 The comparison of finding of AshrafAbd El-KhalikBarakatetal⁷study of Carlo Alessandria et al¹²,study by Scott w. Biggins et al¹³and study by Maria-Carlota Londono et al¹⁴with the present study is summarised in Table10

Name of the Study	Mild	Moderate	Severe	Total
Ashraf AbdKhalik et al		12%		
Carlo Alessandria et al		74%		
Scott W Biggins et al		8.9%		
Maria Carlota et al		21%		
Current Study	46.9%	50%	66.7%	26.6%

Table 10

V. Conclusion

Prevalence of Hyponatremia in patients admitted with cirrhosis was high -54%. Results received in this study were comparable with other studies done on this topic. Complications of cirrhosis like Portal HTN, Hepatic encephalopathy, Hepato renal syndrome and multiple admissions were higher in the hyponatremic group compared to normal sodium group, showing statistical significance. S.B.P. couldn't be compared due to inadequate clinical data, Fatal outcome in admitted cases of cirrhosis showed statistically significant association with serum sodium levels. Incidence of alcohol intake was high among the study population 91% Commonest comorbidities associated with study population was diabetes and hypertension, others were CAD and PTB.

Limitation of study

1. Diagnostic paracentesis was done only in limited cases with clinical suspicion of S.B.P
2. Cause of hyponatremia was not taken into account in the study, as this was not included in study objective
3. Relation of hyponatremia with increased death may be due to complications but needs further study to interpret exact mechanism of death
4. Few patients lost in follow up

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