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Frequency of hyponatremia and its common complications among patients with hepatic encephalopathy

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Abstract

The main theme of this study was to determine the frequency of hyponatremia and its common complications among patients suffering of hepatic encephalopathy due to liver cirrhosis. Descriptive cross sectional study was designed for current research. The samples were obtained from department of medicine, Lady Reading Hospital Peshawar, Pakistan. Total of 139 patients with hepatic encephalopathy and hyponatremia were analysed in this cross sectional study. Hepatic encephalopathy was ranked on the basis of West Haven classification (4 grades). Relationship of hyponatremia was correlated with severity grade of encephalopathy using Spearman rank correlation test. Male to female samples ratio was 1.48:1. The patient's average age was 49.23 ± 10.24 years. Hyponatremia was found in 30 patients (21.60%). The most common complication was Worsening of Hepatic Encephalopathy which was observed in 15 patients (10.80%). Spontaneous Bacterial Peritonitis was also found in 9.4% patients. Higher probability of a possibly negative effect of lower serum sodium concentration and even a slight decline in the cirrhosis clinical course has been concluded.

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Introduction

Cirrhosis is basically a progressive, fibrosing, diffuse and nodular situation that disturbs the complete normal structural design of the liver (Crawford, 2005). Mainly, portal hypertension, spontaneous bacterial peritonitis, hepatorenal syndrome, variceal bleeding and hepatic encephalopathy (HE) are the main complications of cirrhosis (Heidelbaugh and Sherbondy, 2006). The clinical course of patients having chronic liver disease (CLD) is often complex due to the development of anomalies in renal function, electrolyte levels and hyponatremia and such are the record common condition seen in these patients (Poordad, 2007). More than half of the cirrhosis patientsin Pakistan (51.6%) hold the serum sodium concentration lower than standard range (< 135 meq/L) and 26.7% hold range< 130 meq/L. Hyponatremia is basicallya common problem of progressive cirrhosis associated with the damage in renal capacity to eradicate solute free water and causes water retention that is unequal to the sodium retention, thus initiating a sodium reduction in serum and hypo-osmolality (Cordoba and Blei, 2007). Current studies state that almost half of the cirrhosis and portal hypertension patients are with hyponatremia (Angeli *et al*., 2006). Hyponatremia is commonly present in the victims with decompensate cirrhosis due to an abnormal homeostasis regulation of body fluid (Ginès *et al*., 2006). In HE, hyponatremia is associated with various adverse outcomes including spontaneous bacterial peritonitis (10%), worsening of HE after admission (32%), longer hospital stays, refractory as cites, hepatorenal syndrome (13%) (Quittnat and Gross, 2006),and hospital death (26.3%) (Borroni *et al*., 2005; Heuman, 2010). The projected prevalence of hyponatremia was found to be in 26.7% patients (serum sodium < 130 meq/L) and 24.9% (serum sodium 131-135 meq/L) (Shaikh *et al*., 2010) and in another study it was found 50% (Saad *et al*., 2006). Patients with hyponatremia tend to have more severe as cites (p = 0.001). HE was higher in patients having serum sodium <130 meq/L (p= 0.001).

Complications related with cirrhosis were also amplified considerably in mild hyponatremia patients (having serum sodium 131-135 meq/L) compared with patients having normal serum sodium (>135 meq/L) (Heuman, 2010).The present study aim was to determine the incidence of hyponatremia and its common complications among patients presenting with HE due to cirrhosis liver (CL).

Materials and methods

Patients studied

During this study, sum of 139 consecutive patients with HE due to liver cirrhosis were studied in department of medicine, Lady Reading Hospital, Peshawar. Investigation of sequential patients was planned to escape any prejudice due to assortment of patients. Inclusion criteria of patients for this study was: (1) Hepatic encephalopathy patients with liver cirrhosis following West Haven criteria for the grading of HE; and (2) age group of 30 years and above. The exclusion criteria included; (1) patients with acute fulminant hepatitis; (2) patients having co-morbid conditions like diabetes (fasting blood glucose of ≥ 126mg/dl) and hypertension (Blood Pressure of ≥ 140/90mmHg); (3) patients having spontaneous bacterial peritonitis on admission; and (4) patients with concomitant chronic renal failure and those on hemodialysis.

Inform consent

Consent was taken from the ethical committee of hospital. Patients were inducted from the medical units of Lady Reading Hospital, admitted through casualty and outpatient department (OPD). The study purpose was explained to patients and informed consent was taken from the participant or next of kin. The data such as name, age, gender, and admission number of each patient were collected. Serum albumin lower than 3.5 gm/dl, extended prothrombin time of more than 14 seconds and ascetic albumin lower than 3.0 g/dl were confirmed by ultrasonography and laboratory tests. HE was diagnosed on the basis of West Haven criteria for the grading of Hepatic Encephalopathy (4 grades). Under strict aseptic measures 3cc blood was collected in 5cc syringe and sent to Lady Reading Hospital laboratory to detect hyponatremia.

Serum sodium was measured using SELECTRA Auto. Among all patients, those in whom hyponatremia was detected were followed daily over next 7 days to detect its common complication in terms of worsening of HE grades, spontaneous bacterial peritonitis, hepatorenal syndrome and death. For hepatorenal syndrome investigation, urine were collected for 24 hours in graduated jar and blood urea and serum creatinine were tested.

The entire laboratory investigations were conducted by single expert pathologist fellow of College of Physicians and Surgeons Pakistan (CPSP) and all the clinical assessments were conducted under the regulation of a consultant physician.

Statistical analysis

Data were stored and evaluated in SPSS version 10. Mean ± SD were calculated for numerical values like age and serum sodium levels. Frequencies and percentage were calculated for categorical variables like gender, hyponatremia and its common clinical outcomes (worsening of HE grades, spontaneous bacterial peritonitis, hepatorenal syndrome and death). Hyponatremia and its common clinical outcomes were stratified among gender, age and baseline grade of HE to investigate the modification effect.

Results

Total of 139 patients with HE due to liver cirrhosis were studied. Males and females were 83 (59.713%) and 56 (40.29%) respectively. Male to female ratio was 1.48:1.Average age of the patients was 49.23 ± 10.24 years with range 35-71 years. Based on age, patients were classified into four categories, out of which the most common age group with HE due to liver cirrhosis was 41-50 years included 48 patients (34.5%) followed by 35(25.2%) patients of the age less than or equal to 40 years, 45 (32.4%) patients were of the age range 51-60 years and 11(7.9%) patients of age more than 60 years (Table 1).

Table 1. Age based classification of patients and hyponatremia.

Age based distribution of the patients			
Age (years)	Cumulative percent	Percent	Frequency
<40	25.2	25.2	35
41 – 50	59.7	34.5	48
51 – 60	92.1	32.4	45
>61	100.0	7.9	11
Total		100.0	139
Age based distribution of hyponatremia			
Age (years)	Hyponatremia		Frequency
	Yes	No	
<40	4 (13.3%)	31 (28.4%)	35 (25.2%)
41 – 50	9 (30.0%)	39 (35.8%)	48 (34.5%)
51 – 60	14 (46.7%)	31 (28.4%)	45 (32.4%)
>61	3 (10.0%)	8 (7.3%)	11 (7.9%)
Total	30 (100%)	109 (100%)	139 (100%)

Age based distribution of hyponatremia showed that hyponatremia was observed in high proportion in age group of 51-60 years (46.7%). Patients group having age ≤40 years have 13.3%, age group of 41-50 years contain 30% and age group having more than 60 years of age have 10%hyponatremia patients (Table 1).

Among the studied patients, hyponatremia was the most common complication found in 30 (21.6%) patients followed by Worsening of HE that observed in 15 (10.8%) patients. Spontaneous Bacterial Peritonitis was found in 13 (9.4%) patients. Hepatorenal Syndrome was observed in 9 (6.5%) patients while the hospital death was observed in 3 (2.2%) patients (Table 2).

Table 2. Spontaneous bacterial peritonitis and common complications.

Complications	Status	Frequency	Percentage (%)
Hyponatremia	Yes	30	21.6
	No	109	78.4
Spontaneous Bacterial Peritonitis	Yes	13	9.4
	No	126	90.6
Worsening of Hepatic encephalopathy	Yes	15	10.8
	No	124	89.2
Hepatorenal Syndrome	Yes	9	6.5%
	No	130	93.5%
Hospital Death	Yes	3	2.2
	No	136	97.8

Gender wise distribution of hyponatremia and its common complications in patients with HE due to liver cirrhosis are shown in Table 3. According to this distribution, maximum proportion of hyponatremia of 66.7% was observed in male patients. Among the complication, higher proportion of 61.5% Spontaneous Bacterial Peritonitis was found in male patients.

Moreover, Worsening of Hepatic encephalopathy was also observed in higher proportion in male patients of 66.7%.Proportion of hospital death was maximum in male patients (66.7%) as compared to female patients (33.3%). Unlike other complications, female patients were observed in higher risk of Hepatorenal Syndrome (54.2%) as shown in Table 3.

Table 3. Gender wise distribution of hyponatremia and its complications.

Complications	Status	Male		Female	
		Frequency	%	Frequency	%
Hyponatremia	Yes	20	66.7	10	33.3
	No	63	57.8	46	42.2
Spontaneous Bacterial Peritonitis	Yes	8	61.5	5	38.5
	No	75	59.5	51	40.5
Worsening of Hepatic encephalopathy	Yes	10	66.7	5	33.3
	No	73	58.9	51	41.1
Hepatorenal Syndrome	Yes	11	45.8	13	54.2
	No	72	62.6	43	37.4
Hospital Death	Yes	2	66.7	1	33.3
	No	81	59.6	55	40.4

Discussion

This study was aimed to define the hyponatremia frequency and its common complications among the HE patients due to liver cirrhosis. Potential results obtained from a huge multicenter study of patients suffered of hyponatremia show that there is an inverse relation between HE frequency and serum sodium levels, Hepatorenal syndrome and Spontaneous bacterial peritonitis. Patients having serum sodium concentration of 130 mEq/L, have higher proportion of such complications as compared to subjects with normal concentration (Angeli *et al*., 2006). In this study, males (64%) were exceeded in numbers than female patients (36%) and maximum of the patients (64%) were in 30 or 40years of their life. While in the western countries, alcohol is the leading reason of CL with definite male dominance to the 77:33 ratio with females and causing it the 4thmajorcommon death reason in males of USA (Menon, 2001).

This is fact that, females are more susceptible to alcohol for the development of liver disease (Marshall *et al*., 1983). In our society, gender bias is on the top where preference are given to males over females for hospitalization and treatment (Shiekh, 1998). In comparison with HCV, our results are in favor with other findings which favor the fact that HCV is a fast emerging problem and has now passed the HBV in the CL etiogenesis within Pakistan (Malik *et al*., 1996).

Severity of the liver disease could also be correlate with electrolyte imbalance (Shahid *et al*., 1983), it was observed in 28 (56%) patients and could be count as an appearance of advance cirrhosis in patients. Among these patients, 19 (38%) were with hyponatremia and 9 (18%) were with hypokalemia. The entire patients were on diuretics, while 20 among them were also suffered with diarrhea and/or vomiting and two among them had also undergone therapeutic paracentesis. All such reasons are the causative agents of electrolyte imbalance in CL patients. Therefore, care must be taken while putting them on diuretics and manage them with gastroenteritis byexamining their serum electrolytes regularly. Same findings were made in a study carried out in the same department (Ahmed *et al*., 2001). Also, the *gastrointestinal bleeding* (GIB) and infections were the common factors in another study conducted in Punjab province (Sheikh *et al*., 2001).

Our findings also show the presence of alink between spontaneous bacterial peritonitis and lower serum sodium level in agreement with another investigation carried by Angeli *et al*. (2006). This relationship possibly reveals the damage in actual blood volume circulating in cirrhosis patients in the spontaneous bacterial peritonitis situation and may cause hepatorenal syndrome in several patients, while some can suffered only of hyponatremia (Ruiz del *et al*., 2003).

The HE frequency was linked with serum sodium level in such a manner that individual with serum sodium <130 meq/L had considerably higher HE frequency 15/58 (25.8%) than patients having normal concentration 9/92 (9.7%).

Individuals having serum sodium between 131-135 meq/L had a fewer HE frequency 06/52 (11.2%) than individuals having serum sodium concentration <130 meq/L, however greater than that of patients having normal concentration. Angeli *et al*. (2006)found that 38% of the patients with serum sodium <130 meq/L had HE as compared with 24% of patients with serum sodium between 131-135 meq/L and 15% of patients had serum sodium levels >135 meq/L. Association between HE and serum sodium levels may be described based on more severe liver damage with serum sodium concentration <130 meq/L, and possibly the two actions may be pathophysiologically connected (Angeli *et al*., 2006).The fact is that the low serum sodium concentration in individuals suffered with cirrhosis are linked with a notable decline in the concentration of cerebral organic osmolytes that possibly reveal compensatory osmo-regulatory tools against swellings of cell activated by a combine effect of greater accumulation of glutamine intracellularly as a result of hyper-ammonemia and little sodium extracellularly (Haussinger *et al*., 1994; Restuccia *et al*., 2004; Haussinger, 2006). In an experiment of acute liver impairment, the presence of hyponatremia was linked with higher swelling in brain than with normal serum sodium levels (Cordoba *et al*., 1998).

Conclusion

Although, the findings do notclearly prove the link between low serum sodium concentration and these three maincirrhosis complications, yet it propose the probability of a possibly negative effect of lower serum sodium concentration and even a slightdecline in the cirrhosis clinical course. Additionally, the findings recommend that serum sodium concentration should be thorough lychecked in patients having these complications.

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