Prospective Cohort Study to Evaluate Hyponatremia as a Sequela of Acute Renal Dysfunction in Cirrhosis of Liver

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Hyponateremia *is a medical condition commonly seen in patient with progressive cirrhosis. The study was conducted on total 30 cirrhotic patients. Group 1 showed mean eGFR (93.9 ± 12 ml/min/1.73m^2) by simplified MDRD equation, significantly (p<0.001) above reference value (75 ml/min/1.73m^2) as agreed upon, lower normal value as per RIFLE classification. Group 2 showed mean eGFR (48.8 ± 14.7 ml/min/1.73m^2) significantly (p<0.001) below the normal reference value.*

Keywords: Hyponatremia, Cirrhosis.

1. INTRODUCTION

Hyponatermia is a frequent complication of advanced cirrhosis of liver. These patients mostly suffer from oedema and ascites [1]. Cirrhosis of liver is manifested by necrosis of hepatocytes, proliferation of fibrous tissues and formation of regenarative nodules. The lobular architecture is altered alongwith changed hepatic circulation [2]. Scarring of liver results into intrahepatic vascular resistance, hence, portal hypertension and formation of portosystemic collaterals [3,4]. It causes venous engorgement in splanchnic bed. This circulation is regulated by both intrinsic and extrinsic factors [5].Nitric oxide, endotoxins, glucagon and prostaglandins are the vasodilating substances, reported in cirrhosis. Nitric oxide and endothelin together, implicated in haemodynamic changes of the body [6,7].

Schrier and co-workers in 1988, proposed peripheral arterial vasodilation hypothesis. Calcitonin gene related peptide (CGRP), 37 amino acids neuropeptide is the most potent vosodilater Known [8]. It is correlated directly to cardiac output and inversely with systemic vascular resistance. It is seen highly elevated in cirrhosis [9,10]. Low effective circulatory volume stimulates high pressor baroreceptors of carotid sinus and aortic arch, subsequently the neurohumoral homeostasis system including sympathetic nervous system, renin-angiotensingen- aldosterene (RAAS), hypothalamus - neurohypophysis non osmotic released vassopresin, gets activated in the body [11,12]. Vassopresin is released by neurohypophysis mediated by the hypothalamic centre. Renin is released by juxtaglomerular apparatus of nephrons. It cleavages the angiotensinogen into angiotensin-1 and subsequently, angiotensin-2. Aldosterone is released by adrenal cortex. Now vassopresin and aldosterene both impair renal capacity to excrete sodium and solute free water causing water and sodium retention. There changes result into haemodilution, decreased plasma osmolality causing hyponatremia, and increased ECV, causing oedema and ascites.

2. AIM AND OBJECTIVES

The study aimed at to assess hyponatremia as a sequela of acute renal dysfunction in cirrhosis of liver.

The objectives of serum sodium, eGFR, serum albumin and serum bilirubin in patients suffering from cirrhosis, were satisfied.

3. METERIAL AND METHOD

3.1. Sample Design

The study was conducted on total 30 patients of cirrhosis of liver. Study population was divided into two groups, consisting of 17, males, cirrhotics with mean age (48.2 ± 10 y), in Group 1 and another 13, males, cirrhotics with mean age (50 ± 11.8 y), in Group 2, on the basis of eGFR by simplified MDRD equation as shown in Table 1.

Diagnosis was made by case history, clinical examination, confirmed by lab investigations. Patients were given information sheets and were told about objectives and details of study. Oral informed consent was taken from each patient. Data were collected at single time point from patients who visited the department as out-patients and from those already admitted in the hospital.

3.2. Data Collection

Venous blood sample collected from patients and blood sample centrifugated and sera collected for the assay of clinical parameters by following methods [13,14]:

- Estimation of serum sodium - by flame photometry method.
- Estimation of serum albumin - by bromocresol green dye method.
- Estimation of serum total bilirubin - by diazotised sulphanilic acid method.
- Estimation of serum aminotransferase (SGOT, SGPT) - by colorimetry method.
- Estimation of serum creatinine - by alkaline picrate method.

3.3. Criteria for Patients Selection

A. Inclusion criteria

- Patients of both gender.
- Patients diagnosed with liver cirrhosis.

B. Exclusion criteria

- Patients with history of any other systemic and or metabolic disorder.
- Patients suffering from acute hepatitis and obstructive disorder of liver.

3.4. Cut Off Values

- eGFR was calculated by using MDRD equation by four variables as age, gender, race and serum creatinine. A cut off value of 75 ml/min/1.73m^2 (as agreed upon lower most normal value) used to find out deviation in eGFR of patients. This criteria also used to divide the study sample in to two groups as Group 1 patients with eGFR>75 ml/min/1.73m^2 and Group 2 patients with eGFR<75 ml/min/1.73m^2
- Serum sodium normal reference value is 135-145 meq/L.
- Serum albumin normal reference value is 3.5-5 mg/dl.
- Serum total bilirubin normal reference value is 0.2-1.2 mg/dl [13-14].
- Serum amino transferases (SGOT,SGPT), normal reference value is 5-40 iu/L

4. STATISTICAL ANALYSIS

Standard statistical methods including Mean, S.D., were used for descriptive univariate analysis of data. Pearson's coefficient of correlation used to assess covariation between variable. Probable error of correlation calculated to evaluate practical certainity and reliability of correlation. Scatter plot utilized to verify the numerical values of correlation. One sample t-test, two sample independent t-test and p value of (≥0.05) utilized for inferential analysis.

5. RESULTS

- The difference in mean age of Group 1 (48.2 ± 10 y) and mean age of Group 2 (50 ± 11.8 y) was not statistically significant (p=0.64) as shown in Table 1.

Table 1: Characteristics of studied patients.

Characteristics	Group 1	Group 2
No. of Patients	17	13
Age (Mean ± S.D.)	48.2 ± 10 y	50 ± 11.8 y
Gender	All Male	All Male
Type of Liver Disease	Cirrhosis	Progressive Cirrhosis

- Group 1 showed mean eGFR (93.9 ± 12 ml/min/1.73m^2) significantly (p<0.001) above the cut off value. Group 2 showed mean eGFR (48.8 ± 14.7 ml/min/1.73m^2) significantly (p<0.001) below the cut off value as tabulated in Table 2. A significant difference (p<0.001) was observed between mean eGFR of Group 1 and Group 2 as shown in Table 3.
- Mean serum sodium (134 ± 2.59 meq/L) of Group 1 was very slightly below the cut off value and statistically not significant (p=0.13). Group 2 exhibited mean serum sodium (125.69 ± 3.7 meq/L) significantly differed (p<0.004) from Group 1 as shown in Table 2 and 3.

- Pearson's coefficient (r=0.17) of positive correlation was obtained non significant (p=0.50) between serum sodium and eGFR in Group 1 as shown in Table 2, whereas, positive correlation (r=0.78), more than 6 times the probable error of correlation (P.E.r=0.07) with a coefficient of determination value (r^2 = 0.60), was observed highly significant (p=0.001) between serum sodium and eGFR in Group 2.
- Mean serum albumin (2.86 ± 0.46 mgd/L) of Group 1 was significantly (p=0.045) higher as compared with mean serum albumin (2.53 ± 0.38 mgd/L) of Group 2. The Group 1 and Group 2 differed significantly (p=0.045) as shown in Table 2 and 3**.**
- The difference in mean serum total bilirubin (4.4 ± 2 mgd/L) of Group 1 and mean serum total bilirubin (5 ± 2.38 mgd/L) of Group 2 has statistical significance as shown in Table 2 and 3.
- Mean serum SGOT (112.8 ± 53 iu) of Group 1 differed with Mean serum SGOT of Group 2 (108.6 ± 46.7 iu) non significantly (p=0.82) as shown in Table 2 and 3.
- SGPT (76.6 ± 30 iu) of Group 1 also has no significant (p=0.58) difference with SGPT (70 ± 31.7 iu) of Group 2 as shown in Table 2 and 3.

Table 2: Descriptive analysis of Group 1 and Group 2.

Parameters and normal value	**Group 1 N=17**		**Group 2 N=13**	
	Mean	**S.D.**	**Mean**	**S.D.**
eGFR (MDRD) (75 ml/min/1.75m^2)	93.9	12	48.8	14.7
S. Sodium (135-145 meq/L)	134	2.59	125.69	3.7
S. Albumin (3.5-5 mg/dL)	2.86	0.46	2.53	0.38
S. Total Bilirubin (0.2-1.2 mg/dL)	4.4	2	5	2.38
SGOT (0-40 iu/L)	112.8	53	108.6	46.7
SGPT (0-40 iu/L)	76.6	30	70	31.7

Table 3: Inferential analysis of Group 1 and Group 2.

Clinical Parameters	**Two Sample independent t-test**	
	p value	**Significance**
e-GFR	0.001	E.S.
S. Sodium	0.004	E.S.
S. Albumin	0.045	S
S. Total Bilirubin	0.001	E.S.
SGOT	0.82	N.S.
SGPT	0.58	N.S.

6. DISCUSSION

Minor difference in the age groups of Group 1 and Group 2 observed but statistically found to be not significant.

Renal function of Group 1, was observed to be in normal range, whereas, Group 2, showed acute renal dysfunction. Reports of abnormality in renal function in cirrhosis by earlier research workers [1,11,12,15,16], are in favour of results of present study.

Mean serum sodium of Group 1 was within normal range whereas that of Group 2 had significant low value. A positive, strong and highly significant covariation observed between hyponatrimea and acute renal dysfunction of Group 2 patients.

Both hyponatremia and renal dysfunction in cirrhosis are the manifestations of reduced effective circulatory volume causing renal hypoperfusion and activation of R.A.S.S. and non osmotic hypersecretion of vasopressin from neurohypophysis. These events progress in to hypervolumic hyponatremia and functional renal failure [17,18]. A correlation between low serum sodium and hepatorenal syndrome has been reported [16,19].

A significant reduction in mean serum albumin of Group 2 as compared to Group 1 indicated that serum albumin level decreases with the rising severity of cirrhosis. The findings of presents study are in agreement with previous research work [20].

Although mean serum total bilirubin of Group 2 was slightly higher than Group 1, indicated the declining excretory function of liver. However the mild raised value of Group 2 carried no statistical significance (p=0.48).

Both the serum amino transference (SGOT and SGPT) of Group 1 and Group 2 differed but without any statistical significance (p=0.82, p=0.58 respectively). A possible further study needed to evaluate the change in liver excretion and enzyme activity with respect to progressive cirrhosis.

7. CONCLUSION

Stated that hyponatremia is an important consequence of acute renal dysfunction in advanced cirrhosis of liver. Also approximately, two thirds of variations in hyponatremia are explained by acute renal dysfunction as indicated by (r^2=0.60).

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