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Hyponatremia As A Predictor of Death in End Stage Liver Disease Patients

KEYWORDS: hyponatremia, END Stage liver disease, urinary sodium

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ABSTRACT *Background: Hyponatremia, defined as serum sodium concentration less than 135 mEq/L. The prevalence of hyponatremia in the ICU can be as high as 30% to 40%. Regarding end stage liver disease (ESLD) patients; hyponatremia is a common problem and is associated with increased duration of hospital stay and increased morbidity and mortality. Aim of the work is to detect the prognostic value of hyponatremia in end stage liver disease (ESLD) patients and its impact on the outcome of these patient. Patients and methods: 118 patients were grouped on the basis of serum sodium concentration at time of presentation. Results: Mortality was found to be insignificantly higher in hyponatremic patients with serum sodium level <130 mEq/L (88.89%) when compared to those with serum sodium level >130 mEq/L (83.7%). The study also showed significant decrease in serum sodium level at the end of the study compared to time of admission (p-value 0.0001). Conclusion: Hyponatremia is common among ESLD patients, and it is positively associated with long duration till death of patients, it is significantly decreased from start to end of study meaning that progressive hyponatremia is a strong predictor of death in ESLD patients*

Introduction:

Hyponatremia, defined as serum sodium concentration less than 135 mEq/L (Schrier, 2000), represents relative excess of body water relative to body sodium content, because sodium is the major extracellular solute (approximately 90 percent of these solutes), changes in total body sodium result in similar changes in extracellular volume (Vander et al., 2001).

The prevalence of hyponatremia in the ICU can be as high as 30% to 40% (Lohani et al., 2011).

As regard end stage liver disease patients; hyponatremia is a common problem and is associated with increased duration of hospital stay and increased morbidity and mortality (Friedman et al., 2012).

The pathogenesis of hyponatremia in patients with advanced cirrhosis is directly related to the hemodynamic changes and secondary neurohumoral adaptations that occur, resulting in an impaired ability to excrete ingested water. The severity of the hyponatremia is related to the severity of the cirrhosis (Ginès and Guevara, 2008).

The normal concentration range of sodium in the plasma is 135 - 145 mill equivalents per liter, making sodium the ion with the most significant osmotic effect in the extracellular fluid (Sangella et al., 1989). Under normal circumstances, renal excretion of sodium is regulated so that balance is maintained between intake and output and ECF volume is stabilized.

Hyponatremia is a common problem in patients with advanced cirrhosis. Variety of factors can contribute to the development of hyponatremia in patients with cirrhosis. The most important factor is systemic vasodilatation, which leads to activation of endogenous vasoconstrictors including antidiuretic hormone (ADH); ADH promotes the water retention that is responsible for the fall in serum sodium.

Because the increase in ADH secretion (and therefore the degree of water retention) is roughly proportional to the severity of the cirrhosis, the degree of hyponatremia parallels the severity of the hepatic disease and is of prognostic value.

A serum sodium concentration below 130 meq/L carries a relatively poor prognosis, whereas values below 125 meq/L often indicate impending hepatorenal syndrome (Arroyo et al., 1994).

In patients without liver disease, hyponatremia is associated with a broad variety of neurological manifestations related to the existence of brain edema, such as headache, disorientation, confusion, focal neurological deficits, seizures, and, in some cases, death due to cerebral herniation. The most important factor in determining the severity of neurological symptoms is the rate of fall in serum sodium levels, so patients with acute hyponatremia having a much higher incidence of neurological symptoms than patients with chronic hyponatremia (Adrogué, 2000).

Besides hepatic encephalopathy, hyponatremia has also been reported to be associated with other complications of cirrhosis. Specifically, bacterial infections resulting in spontaneous bacterial peritonitis (Follo et al., 1994).

Also, Low serum sodium levels are a very common finding in patients with hepatorenal syndrome (Ginès et al., 2006)

In the majority of patients, the existence of hyponatremia before liver transplantation carries a poor prognosis and is associated with increased risk of renal failure and neurological complications (Londoño et al., 2006 & Dawwas et al., 2007). Patients may also develop central pontine myelinolysis after transplantation, (Abbasoglu et al., 1998).

It is known that serum sodium in cirrhosis below 130 mmol/l is associated with a median transplant-free survival of less than 6 months (Heuman et al., 2004)

The model for end stage liver disease (MELD) is used to predict the outcome of patients with cirrhosis. Incorporation of serum sodium (Na) into MELD may further increase its prognostic ability (Hsua et al., 2012).

Aim of the work is to detect the prognostic value of hyponatremia in end stage liver disease (ESLD) patients and its impact on the outcome of these patient.

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Patients and methods
A single center, observational, prospective study was conducted on end stage liver disease patients, who were admitted in hepatology intensive care unit, Mansoura Specialized Medical Hospital, Mansoura University, . Patients were followed up for six month duration study included 118 patients. Patients were grouped on the basis of serum sodium concentration at the first time of presentation into:

1) Group1: Serum sodium more than 135 up to 145 mEq /l; that is the normal serum sodium level (control group), This group included 17 patients.
2) Group2: Serum sodium < 135 mEq/L (hyponatraemic group)

➢ **This group was further divided into 3 more groups according to level of decrease in serum sodium:**
a) Mild hyponatremia(131-135). It included 20 patients.
b) Moderate hyponatremia(121-130).It included 53 patients.
c) Severe hyponatremia less than or equal to 120. It included 28 patients.

Inclusion criteria:
All patient with ESLD (defined as decompensated liver cirrhosis; either vascular or cellular decompansation), who were admitted in hepatology ICU. Exclusion criteria: A) Patients with medical disorders that may affect serum sodium level as; Uncontrolled hyperglycemic states, Congestive heart failure due to cardiac cause, Nephrotic syndrome, Adrenal insufficiency, Syndrome of inappropriate ADH secretion (SIADH), Hypothyroidism, Patients with cerebral insult, Patients with gastroenteritis, burns and open wounds. B) Patients under treatment with some drugs affecting the sodium level in blood as; Diuretics and Mannitol.

All the patients were subjected to the following:
Full medical history, including Drug history, Full clinical evaluation, laboratory measurement including; liver and renal function tests, CBC, Virology markers, ABG, Serum electrolytes (sodium and potassium) ;on every day of ICU stay. RBG, Urine analysis and Urinary sodium.

Brain CT (to exclude other causes of confusional state) and Upper gastrointestinal endoscopy. Patients also are subjected to score calculation APACHE II (Acute Physiology and Chronic Health Evaluation) for assessment of ICU severity (Knaus et al., 1985), Child Turcot Pugh (C.T.P) (Pugh et al., 1973) and mainly MELD score and MELD Na score

Model of End Stage Liver Disease: (MELD) score
MELD = 3.8[Ln serum bilirubin (mg/dL)] + 11.2[Ln INR] + 9.6[Ln serum creatinine (mg/dL)] + 6.4(etiology).Ln: natural logarithm. [Etiology: 0 if cholestatic or alcoholic, 1 if other etiologies] (Freeman et al., 2002).

Model of End Stage Liver Disease with serum sodium (MELD Na) it is a new predictor of wait list mortality in end stage liver disease.

MELD Na Score = MELD Score+ 140 – Serum Na - (0.025 * MELD Score * (140 – Serum Na)) (Kim et al., 2008).Study endpoints was, end of the six month duration or Death.

Statistical analysis:
All analyses were carried out using SPSS. Continuous data was expressed in the form of means ± SD, while categorical data was expressed in the form of count and percent. The student t-test and the chi-square test were used. One way ANOVA was used to detect any significance among the four groups, Pearson correlation coefficient for parametric variables and Spearman correlation for non parametric variables. P values of less than 0.05 were considered statistically significant. Kaplan-Meier survival analysis and Cox regression were used to detect the likelihood of death and binary logistic regression to detect the predictors of the outcome.

Results
The study included 118 patients, 17 as a control with normal serum Na and 101 with hyponatremia. In this work the commonest cause of liver disease was chronic hepatitis C (74%), (table-1). The prevalence of hyponatremia in ESLD patients who were admitted in the hepatology ICU was as high as 85.5%, when sreum sodium was < 135 mEq/L, and it was 68.6 % when serum sodium was < 130 mEq/L, (table-4). With the mean arterial pressure in hyponatremic group was lower than in the normonatremic group; although statistically not significant, (table-2). Hemoglobin and hematocrit were found to be significantly lower in hyponatremic group compared to normonatremic one, and it showed no significant difference in serum bilirubin, INR, and serum albumin in hyponatremic group versus normonatrmic, Serum potassium level was found to be insignificantly higher in hyponatremic group of patients when compared to normonatrmic one, Urinary sodium was found to be insignificantly different between the two groups, (table-3). MELD and APACHEII scores showed non-significant increase in the hyponatremic group compared to normonatremic one, (tables-2, 3). While MELDNa score was significantly higher in the hyponatremic group. CTP, MELD, and APACHEII scores were found to be significantly higher in patients with cirrhosis who died during their ICU stay compared to those who survived, (table-5).Serum sodium level was found to be negatively correlated with the duration of hospital stay, and positively correlated with the duration till outcome (death), (table-6). Mortality was found to be in significantly higher in hyponatremic patients with serum sodium level <130 mEq/L (88.89%) when compared to those patients with serum sodium level >130 mEq/L (83.7%), (table-7).

The study also showed significant decrease in serum sodium level at the end of the study compared to at time of admission, (table-8). Moreover in the present work progressive hyponatremia was found to be significant predictor of mortality, each one m.Eq. /L decrease in serum sodium will increase the risk of death by about 1.7 fold, (table-11). However hyponatremia, by itself, was not a significant predictor of the mortality.

Table-1: Etiology of liver pathology in end stage liver disease patients:

	Numbers of patients n=118	Percentage
HCV	88	74%
HBV	2	1.8%
Bilharzia	2	1.8%
Undiagnosed	26	22.4%

Table-2: Clinical and demographic baseline characteristics of end stage liver disease patients (ESLD) (n=118): hyponatrmic versus normonatremic patients.

	Whole group (n=118)	Na<135 mEq/L (n=93)	Na≥135 mEq/L (n=25)	P-value
Age(mean±SD)Year	57.7±9.9	57.02±9.96	60.48±9.42	0.123
Gender Males/total (percent%)	73 (61.9%)	55/93	17/25	0.49
Mean arterial blood pressure (mean±SD) (mmHg)	95.42±15.41	95.13±15.13	96.8±17.17	0.636
APACHE II score (mean±SD) (points)	16.81±4.78	17 ± 4.68	15.63±5.377	0.29
Hypertensive n. (percent %)	11 (9.3%)	8/11	3/11	0.636
Diabetes n. (percent %)	46 (39%)	35/46	11/46	0.616

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	Whole group (n=118)	Na<135 mEq/L (n=93)	Na≥135 mEq/L (n=25)	P-value
Hepatocellular carcinoma n.(percent %)	32(27%)	27/32	5/32	0.76

APACHEII: Acute Physiology and Chronic Health Evaluation. SD: standard deviation.
P value of ≤ 0.05 was considered significant.

Table-3: Biochemical characteristics of ESLD patients (n=118) compared according to serum sodium concentration.

Variable (mean±SD)	Whole group (n=118)	Na <135 mEq/L (n=93)	Na≥135 mEq/L (n=25)	P- value
Serum total bilirubin (mg/dl)	8.57±7.99	8.55±7.68	9.4±10.12	0.696
Direct bilirubin (mg/dl)	6.87±6.33	6.76±5.69	7.54±5.73	0.722
Serum albumin (gm/dl)	2.14±0.45	2.11±0.44	2.31±0.52	0.095
INR	1.78±0.56	1.78±0.56	1.77±0.59	0.103
S. creatinine (mg/dl)	2.22±1.3	2.21±1.26	2.24±1.66	0.929
ALT (U/L)	77.39±142.18	80.08±154.23	62.44±53.54	0.653
Hb (gm/dl)	9.3±2.31	9.06±2.14	10.65±2.88	0.009
Hematocrite (HCT%)	28.3±6.83	27.72±6.51	31.53±8	0.035
Platelets(10^3/ml)	104.75±67	97.62±56.42	146.65±101.83	0.069
HCO3(mEq/L)	17.74±5.23	17.65±5.33	18.24±4.74	0.674
PCO2(mmHg)	28.4±6.83	28.23±6.71	29.29±7.61	0.558
PO2(mmHg)	73.98±19.69	74.23±19.9	72.59±19	0.735
S. potassium (mEq/dl)	4.51±0.97	4.56±0.98	4.15±0.77	0.168
S.sodium (mEq/dl)	125.85±10.2	123.34±8.72	140.47±4.05	0.0001
MELD	24.84±7.76	25.13±7.57	23.41±9.25	0.404
Variable median (5%-95% range)				
Random blood glucose (mg/dl)	122 (50–626)	120 (50–626)	160 (70-350)	0.486
ALT (U/L)	77.39±142.18	80.08±154.23	62.44±53.54	0.653
Urinary Na(m.Eq./24h)	19 (12 – 24)	19 (12 – 20)	19 (18 – 24)	0.447
PH	7.4 (7 – 8)	7.4 (7 – 8)	7.37 (7 – 8)	0.768
MELD Na	31 (6 – 41)	32 (16 – 41)	26 (6 – 38)	0.002

INR=international normalized ratio, MELD=model of end stage liver disease, MELDNa=model of end stage liver disease with serum sodium.

MELD = 3.8[log serum bilirubin (mg/dL)] + 11.2[log INR] + 9.6[log serum creatinine (mg/dL)] + 6.4. MELDNa=MELD+(140-Na)-{0.025*MELD*(140-Na)}.

P value was done between the hyponatremic and normonatremic groups.

The table showed significant decrease in serum sodium level (mEq/dl), hemoglobin (gm/dl), hematocrite (HCT%) and significant increase in MELDNa score. While there was no significant change in MELD score between hyponatremic versus normonatremic groups.

Table-4: Outcome of ESLD patients classified according to serum sodium level on admission in ICU into four groups:

Sodium level on admission	Number of patients/total	percent	Outcome		P value
			dead/ alive	Percent of dead	
Normonatremic (Na>135 -145 mEq/L)	17/118	14.4%	15/2	80%	0.41
Mild hyponatremia (131-135 mEq/L)	20/118	16.9%	16/4	80.3%	0.35
Moderate hyponatremia (121-130 mEq/L)	53/118	44.9%	49/4	92.45%	0.2
Severe hyponatremia (<120 mEq/L)	28/118	23.7%	23/5	88%	0.42

Table-5: Comparison of different variables between survived versus deceased patients:

Variables	Surviving (n=15)	Deceased (n=103)	P value
Age(mean±SD) (years)	53±9.66	58.3±9.76	0.06
Duration till outcome (days)	125± 48	9 ± 4	0.001
Serum sodium on admission (m.Eq./L)	128.6 ± 11.25	126 ± 10.1	0.6
Hematocrite(%)	27.79 ± 4.9	28.38 ± 7.1	0.69
WBCs(*10^3)	11.7 ± 6.9	14.4 ± 7.5	0.18
Hb (gm/dl)	9.15 ±1.7	9.3± 2.4	0.74
Potassium(m.Eq./L)	4.1 ± 1	4.5 ± 1	0.13
Urinary sodium(m. Eq./24h)	18 ± 0.1	18.6 ± 2	0.7
PCO_2(mmHg)	31 ± 9	27 ± 6.4	0.26
HCO_3(m.Eq./L)	19.4 ± 5.5	17.6 ± 4.9	0.25
Po_2(mmHg)	83.9 ± 14.3	73.54 ± 20.2	0.022
S.creatinine(mg/dl)	1.7± 1	2.2 ± 1.3	0.04
pH	7.406 ± 0.055	7.33± 0.105	0.017
S.bilirubin(mg/dl)	5.16± 6.19	9.07± 8.1	0.04
INR	1.6 ± 0.27	1.79 ± 0.59	0.52
S. albumin(gm/dl)	2.2± 0.51	2.1± 0.44	0.69
CTP (points)	11.33 ± 1.59	12.7 ± 1.2	0.005
MELD (points)	20.9± 6.9	25.4 ± 7.74	0.03
APACHE II(points)	12.3 ± 3.42	17.46 ± 4.61	0.001
MELDNa(points)	27.87 ± 7.49	30.19 ± 7.1	0.27

CTP= Child Turcot Pugh

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The table showed significant decrease in duration till the outcome, PO2 and pH and there was increase in serum creatinine level, serum bilirubin, CTP, MELD, and APACHEII scores in deceased versus survived patients

Table-6: Correlation of different variables with duration of hospital stay and duration till outcome in days.

	Hospital stay in days		Duration till outcome in days	
	r	p	r	P
Serum sodium	-0.118	0.045	0.163	0.03
C.T.P	0.008	0.9	-0.46	0.0001
MELD	0.13	0.08	-0.304	0.001
MELDNa	0.017	0.43	-0.21	0.022
APACHE II	0.098	0.29	-0.288	0.002

R= Pearson correlation coefficient

This table shows that Serum sodium was negatively correlated to duration of hospital stay and positively correlated to duration till outcome. CTP, MELD, MELDNa and APACHEII scores were negatively correlated to the duration till the outcome in days.

Table-7: Outcome of ESLD patients classified according to serum sodium level on admission in ICU into two groups:

Sodium level on admission	Number of patients/total	Percent	Outcome	
			Dead/ alive	Percent of dead
Normo to mild hypo natremia (Na >130-145 mEq/L)	37/118	31.4%	31/6	83.7%
Moderate to severe hyponatremia (Na < or =130 mEq/L)	81/118	68.6%	72/9	88.89%

Table-8: Serum sodium level, MELD Na, APACHE II and predicted death rate at end of study versus at admission (for all patients n=118).

	Level at admission	Level at end of study	p-value
S.Na	125.84±10.81	121.28±9.62	0.0001
MELD Na	29.9±7.12	31.52±6.63	0.0001
APACHEII score	16.81±4.78	17.36±4.88	0.0001
Predicted death rates	27.62±13	29.21±13.42	0.0001

The table showed significant decrease in serum sodium level and increase in MELD Na, APACHE II score and predicted death rates at the end of the study versus at admission.

Table-9: Changes in the number of ESLD patients among the four classified groups according to serum sodium level at the end of the study versus at admission:

	Number of patients on admission	Sodium level at discharge/ death				P value
		>135 mEq/L	(131-135) mEq/L	(121-130) mEq/L	≤120 mEq/L	
>135 mEq/L	17	4	4	8	1	0.0001
(131-135) mEq/L	20	0	10	2	8	0.0001
(121-130) mEq/L	53	2	1	35	15	0.0001
≤120 mEq/L	28	0	0	1	27	0.0001
Total	118	6	15	46	51	

There was significant change in the number of patients among the four groups at the end of the study versus at admission indicating progressive hyponatremia.

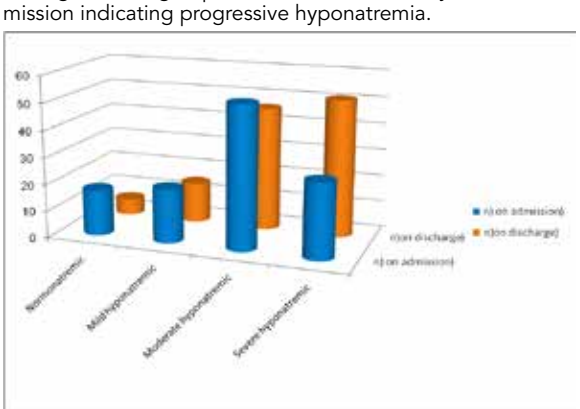

Figure-1: Changes in the number of ESLD patients among the four classified groups according to sodium level between time of admission and end of the study:

Table-10: Outcome of ESLD patients who showed progressive decrease in sodium level versus those with no decrease:

Outcome	Decrease in sodium		Total	Chi-square	P-value	Likelihood ratio
	Patients without decrease	Patients with Decrease				
Discharged alive/ total	8/15	7/15	15	8.322	0.004	7.187
Discharged dead/ total	20/103	83/103	103			

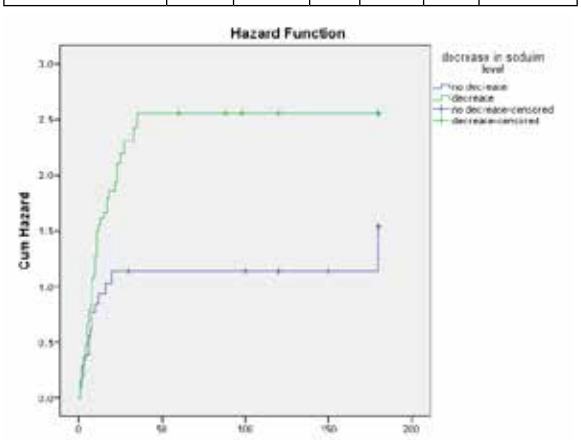

Figure-2: Hazard of death due to hyponatremia in the group with progressive decrease in serum sodium level versus that with no decrease.

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This figure showed significant increase in hazard of death in the group with progressive hyponatremia versus that with no decrease in serum sodium (p= 0.034).

Table-11: Predictors of death in ESLD patients (n=118):

VARIABLE	B	P value	OR
CTP (points)	0.22	0.005	1.24
MELD(points)	0.033	0.012	1.034
MELDNa(points)	0.23	0.119	
APACHE II (points)	0.095	0.0001	1.1
Urinary soduim (m.Eq./24h)	0.08	0.4	
Albumin (gm/dl)	-0.05	0.821	
INR	0.2	0.27	
Creatinine (mg/dl)	0.13	0.045	1.14
Bilirubin (mg/dl)	0.018	0.122	
Hb(gm/dl)	0.05	0.3	
PH	-3.54	0.0001	0.029
PO2(mmHg)	-0.011	0.038	0.989
HCT(%)	0.018	0.25	
HCO3 (m.Eq./L)	-0.03	0.12	
PCO2(mmHg)	-0.029	0.06	
Na (m.Eq./L)	0.003	0.78	
Platelets(*10^3)	0.001	0.4	
WBCS(*10^3)	0.02	0.11	
Progressive decrease in soduim	0.5	0.045	1.66

B= regression coefficient, OR= Odd's Ratio (by multi-variate cox regression).

The table showed that serum sodium level was not a significant predictor of death in ESLD patients. While progressive decrease in sodium (each one m.Eq. /L drop in serum sodium), each one point higher in CTP score, in MELD score and in APACHEII score will increase the risk of death by (1.66,1.24,1.034,1.1) folds respectively.

DISCUSSION

Hyponatremia is a common problem among patients in hospital. The prevalence of hyponatremia in patients admitted in the ICU can be as high as 30% to 40% of the total number of patients (Lohani et al., 2011). As regard end stage liver disease patients; hyponatremia is a clear problem and is associated with increased duration of hospital stay and increased morbidity and mortality (Biggins et al., 2006 & Friedman et al., 2012).

In the present study, we tried to detect prognostic value of hyponatremia in end stage liver disease patients (ESLD) in which chronic hepatitis C was the commenest cause representing (74%), and this is anticipated because the highest Hepatitis C Virus prevalence in the world occurs in Egypt (14.7%) (Mahmoud et al., 2013).

The level of hyponatremia in ESLD patients was as high as 85.5%, when serum sodium was < 135 mEq/L, and it was 68.6 % when serum sodium was < 130 mEq/L, (table-4) and this can be attributed to the severity of liver disease as all patients were ESLD.

We found that mean arterial pressure in hyponatremic group was lower than in the normonatremic group; although statistically not significant, (95.13 ± 15.13 and 96.8 ± 17.17 respectively, P-Value 0.636).This was the same as stated by Caregaro L et al., (1994) and could be attributed to the peripheral arterial vasodilation as low blood pressure is common in decompensated cirrhosis.

Also, Hemoglobin and hematocrit were found to be significantly lower in hyponatremic group compared to normonatremic one, (9.06±2.14 and 10.65 ± 2.88, P-Value 0.009) (27.72 ± 6.51 and 31.53 ± 8, P-Value 0.035) respectively. This may be attributed to upper GIT bleeding and this was also supported by Kim et al., (2009) & Eric et al., (2012) who mentioned that hyponatremia is a common problem that correlates with the severity of portal hypertension.

In this work there was no significant difference in serum bilirubin, INR, and serum albumin in hyponatremic group versus normonatrmic. This may be attributed to high CTP score (late B or C) of most of these ESLD patients which depends on these items.

Serum potassium level was found to be insignificantly higher in hyponatremic group of patients (4.56 ± 0.98) when compared to normonatrmic one (4.15 ± 0.77), (P-value 0.168). This goes hand in hand with what Borroni et al., (2000) stated. This is because in ESLD patients there is accelerated protein catabolism, inactivation of aldosterone and release of vasopressin (V2) so the net result will be dilution hyponatremia and hyperkalemia (Chengshan et al., 2012)

Urinary sodium was found to be insignificantly different between the two groups, (P-Value 0.447), While Almudena et al., (2002) found that urinary sodium was significantly lower in hyponatrmic group than in normonatrmic group. This could be related to the smaller number of patients in the present study.

MELD (23.41 ± 9.25) (P-Value 0.404) and APACHEII (15.63 ± 5.377) (P-value 0.29) scores are higher in the hyponatremic group compared to normonatremic one, while MELDNa score was significantly higher in the hyponatremic group; 32 (16 – 41) ;26 (6 – 38) (P-Value0.002). As these scores are used to assess severity of illness in critically ill patients, the higher the score the more severe the disease and hyponatremia commonly occurs in ESLD. This explains why these scores especially MELDNa are higher in hyponatremic patients.

CTP, MELD, and APACHEII scores were found to be significantly higher in patients with cirrhosis who died during their ICU stay p-value were 0.005, 0.03 and 0.001 respectively, and this was the same as what was found by Eric et al., (2012) & Zhang et al., (2012).

Serum sodium level was found to be negatively correlated with the duration of hospital stay (r=-0.118), and positively correlated with the duration till outcome (death); (r=0.163.) So, hyponatremia could be associated with longer ICU stay and earlier death. This is consistent with the result of another study declaring that hyponatremia was associated with increased duration of hospital stay and increased morbidity and mortality (Friedman et al., 2012).

Mortality was found to be insignificantly higher in hyponatremia patients with serum sodium level <130 mEq/L (88.89%) when compared to those patients with serum sodium level >130 mEq/L (83.7%). This may be attributed to both larger number of patients and more advanced disease in the hyponatremia group. In another study mortality rates in cirrhotic patients admitted to ICU ranged from 36% to 86% (Aggarwal et al., 2001&Chen et al., 2004). And in the study of Chang et al., (2010), the mortality rate of hyponatremia versus normonatremic was (73.1% vs. 55.9%). But, in medical ICU of Zagazig university the mortality rate of the studied hyponatremia patients was 36.9 % (Arafa et al., 2012).

The study also showed significant decrease in serum sodium level at the end of the study compared to time of admission, (p-value 0.0001). The cumulative survival was found to be significantly decreased and the hazard of death increased in patients with progressive hyponatremia than those with stable serum sodium level during hospital stay, (figures-2). Also

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Borroni et al., (2000) stated that the death rate of patients who developed severe hyponatremia during the course of hospital stay was particularly elevated.

Moreover in the present work, progressive hyponatremia was found to be significant predictor of mortality, each one mEq/L decrease in serum sodium will increase the risk of death by about 1.7 fold. However hyponatremia, by itself, was not a significant predictor of the mortality. This goes in line with what was found by Ewout et al., (2013), who reported that hyponatremia reflects the severity of the underlying disease rather than contributing directly to mortality. This can be explained by the late stage of the hepatic patients in our study who were admitted in ICU and they suffered from other co morbidities as sepsis and renal impairment that may play important role in mortality prediction.

Conclusions

Hyponatremia is common among ESLD patients, and it is positively associated with long duration till death of patients, it is significantly decreased from start to end of study meaning that progressive hyponatremia is a strong predictor of death in ESLD patients.

Recommendations

It is advisable to frequently monitor serum sodium levels in ESLD patients admitted to hospital. Treatment of hyponatremia is mandatory as it could improve survival and outcome of patients.

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