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Impact of Serum levels of Bicarbonate and Electrolytes on Adverse Clinical Outcomes in Cirrhotics

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Abstract

Background: It is well known that acid-base imbalances and low serum bicarbonate are linked to increased illness severity.

Aim: To examine the prognostic significance of information obtained from arterial blood gas (ABG)-related parameters and serum electrolytes at the time of hospital admission on adverse clinical outcomes, the length of LOS, and other factors.

Methods: A total of 357 candidate individuals with liver cirrhosis were screened for enrollment in this prospective study. 329 patients agreed to participate who had evidence of liver cirrhosis or presented with signs and symptoms suggesting decompensated liver cirrhosis. Individuals with diabetes ketoacidosis, acute coronary syndrome, fulminant liver failure, preexisting end-stage renal disease, or chronic obstructive pulmonary disease (a total of 208) weren't involved in the research. Then, 121 patients who were hospitalized in the Internal Medicine department or treated in ICU with a confirmed diagnosis of decompensated cirrhosis (age ≥ 18 years) were prospectively recruited and monitored throughout the research period.

Results: This research involved 121 cases with a confirmed diagnosis of cirrhosis. Regarding the PH, normal PH were 76 (62.8%) patients, acidemia 22 (18.2%), alkalemia 23 (18.2). There were 73 (60.4%) patients were child C score at time of admission. The mean MELD score was 19.26± 9.01. The mean MELD-PaCO2-HCO3 was 23.79 ± 7.45 while the mean MELD-bicarbonate was 16.35±7.22**.** As a regimen of management, serum electrolyte acid base correction was used in 33 (27.3%) cases, while endoscopy or band ligation was performed in 40 (33.1%) cases. Medication for Na and K correction were used in 6 (5%) and 17 (14%) cases respectively. Vasopressors were used in 12 (9.9%) cases who were admitted to the ICU. None of the cases underwent renal replacement therapy.

Conclusion: The high incidence of metabolic acidosis and the frequency of organ failures are strong predictors of death in critically ill individuals with cirrhosis, leading to a poor prognosis and a high mortality rate.

Keywords: Bicarbonate, Electrolytes, Cirrhosis

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Introduction

Several metabolic processes are carried out by the liver that are included in acid- base balance, which is important for regular cellular and organ function. In early cirrhosis, while hypoalbuminemia and respiratory alkalosis cause alkalosis, dilutional hypervolemia and hyperchloremia cause acidosis.

Patients with liver dysfunction often develop multiple complex co-existing metabolic acid-base disorders as the severity of cirrhosis progresses. (1)
The most prevalent type of acidosis in intensive care unit (ICU) patients with cirrhosis is lactic acidosis. In decompensated cirrhotic patients, hypoalbuminemia alkalosis is the primary alkalinizing metabolic disorder. Also, the variable mechanisms of loss or retention of HCO3 in cirrhotic patients result in changes in serum chloride, which are then followed by hyperchloremic acidosis or hypochloremic alkalosis. (2)
Individuals with cirrhosis are more susceptible to potassium depletion even in the presence of normokalaemia due to the various potassium wasting mechanisms that are both inherent to the illness and the outcome of treatment. (3) Activation of the renin-angiotensin system and the release of the antidiuretic hormone cause salt and water retention, which in turn cause hyponatremia. This hypervolemia is exacerbated by the effects of portal hypertension, which can be treated with extensive diuretics and therapeutic paracentesis. Extrahepatic organ dysfunction may also cause aggravation of acid-base disorders (encephalopathy and renal dysfunction). (4)
It is well known that acid-base imbalances and low serum bicarbonate are linked to increased illness severity, and that they are also risk factors for mortality and poor hospital outcomes. (5)Although there has been a paucity of information on the significance of serum electrolytes, especially bicarbonate, abnormal acid-base test results in hospital length of stay (LOS) and outcomes of hospitalized cirrhotic individuals over the past decade.
Based on the aforementioned information, there is a real need for prospective studies to describe the frequency and various acid-base conditions in cirrhotic patients. In addition to studying the significance of serum electrolyte levels, especially serum bicarbonate, on adverse hospital outcomes and the duration of LOS for hospitalized cirrhotic patients, comparing the prognostic value of the MELD score to the prognostic value of the conventional equations of the original MELD and Child-Pugh and adding these characteristics to the model of end-stage liver disease (MELD) may help to improve the prognostic value of the MELD score. Therefore, this study's goal was to examine the prognostic significance of information obtained for ABG-related parameters and serum electrolytes at the time of hospital admission on adverse clinical outcomes, the length of LOS, and other factors.

Patients and methods

This is an observational prospective research was performed at Sohag University hospital, Internal Medicine department, and intermediate care unit (ICU) during the period from October 2021- June 2022. The research protocol was approved by the Ethics Committee of Sohag Faculty of Medicine. Written informed consent was obtained from all participants.
A total of 357 candidate cases with liver cirrhosis were screened for enrollment in this prospective study. 329 patients agreed to participate who had evidence of liver cirrhosis or presented with signs and symptoms suggesting decompensated liver cirrhosis. People who were diagnosed with diabetic ketoacidosis, acute coronary syndrome, fulminant liver failure, pre-existing end-stage renal disease, or chronic obstructive pulmonary disease were not allowed to participate in the trial. There were 208 individuals who were not allowed to participate. Following that, 121 individuals with a confirmed diagnosis of decompensated cirrhosis (age ≥ 18 years) who were hospitalized in the Internal Medicine department or were treated in the ICU were prospectively added and tracked throughout the course of the research.
We excluded patients with compensated cirrhosis. Also, cirrhotic patients below 18 years, diabetic ketoacidosis, acute coronary syndrome, fulminant liver failure, pre-existing end-stage renal disease, chronic obstructive pulmonary disease, systolic heart failure, and prescriptions for HCO3 therapy prior to hospitalization were excluded.
All cases were subjected to a full history taking, clinical assessment, laboratory investigations (full blood count, serum albumin, total bilirubin, ALT, AST, prothrombin time, concentration , INR, serum creatinine, Blood urea nitrogen (BUN), serum sodium, potassium, calcium, urine analysis, fasting blood glucose, ABG-pH, arterial partial pressure of

carbon dioxide (PaCO2), arterial partial pressure of oxygen (PaO2), arterial oxygen saturation (SaO2), peritoneal fluid analysis in ascites and bicarbonate (HCO3) and Base excess) and imaging (Chest-X ray to exclude chronic pulmonary disease, electrocardiogram (ECG) to exclude acute coronary syndrome and abdominal ultrasonography).

We follow up the following during the admission:

- Presence of acute kidney injury, portosyste-mic encephalopathy, hepatorenal syndrome, ascites, gastrointestinal bleeding, hepatocellular carcinoma, spontaneous bacterial peritonitis.
- Child-Pugh score
- MELD score
- MELD-$PaCO_2$-HCO_3 & MELD- Bicarbonate
- Intensive care unit admission
- Admitted to ICU directly or transferred within days of hospitalization.
- Laboratory and imaging results
- Endoscopic and surgical procedures
- Medications (Na, K, bicarbonate, and other therapies)
- Vasopressors, and renal replacement therapy
- Serum electrolytes and acid base corrections

Statistical analysis:

The statistical analysis was performed using (SPSS, Inc., Chicago, IL), Version 20.0 (IBM SPSS STATISTICS.). Quantitative data is represented as mean ±SD, and the Pearson x2 test or Fisher exact test is utilized to compare differences between dichotomous variables. The normality of variables was checked using the Shapiro-Wilk test. A parametric test (t-test) is used for the assessment of differences between numerical variables with a normal distribution. Accordingly, the nonparametric test (Mann- Whitney u-test) was utilized to compare the mean between the two categorical groups and the Kruskall-Wallis test for more than two groups) when datasets were found to be not normally distributed. Kaplan-Meier plots were presented for the time from admission to each of the major composite outcomes and deaths for the patient subgroups. The figures were generated using GraphPad Prism version 5.02 (San Diego, CA). Statistical significance is assumed at the P-value of 0.5 in all analyses.

Results

For studying the frequency of acid-base disorders among hospitalized cirrhotic patients and their clinical characteristics, 121 cases with a confirmed diagnosis of cirrhosis (age ≥ 18 years) who were admitted to the internal medicine department or were treated in the ICU were prospectively followed during the study period (10 months). Also, those patients were studied to explore prognostic values of data obtained for the ABG-related parameters and serum electrolytes at this time of hospital admission in adverse clinical outcomes, mortality.

Patient demographics and descriptive data:

Baseline characteristics of the study cohort are presented in **Table 1**. More than half of the cases 70 (57.9%) were females and 51 (42.1%) were males. As regards residence, 77 (63.6%) patients were living in rural areas and 44 (36.4%) cases were living in urban areas. Manual work was most common in our study, representing 52 (43%) cases, followed by non-workers in 43 (35.5%) cases, farmers in 14 (11.6%) cases, and employees in 12 (9.9%).

The most frequent cause of liver cirrhosis was HCV, which was found in (48.8%) of cases, followed by bilharziasis in (28.9%) of cases, HBV in (9.1%) cases, unknown causes in (5.8%) cases. primary biliary cirrhosis in (3.3%) cases and autoimmune causes in (1.7%) cases. Out of 121 patients, 46 (38%) cases with HCV were on direct-acting antiviral (DAAs) therapy since 2 to 20 years. Encephalopathy was the most common cause of hospital admission 60 (49.58%) followed by hematemesis and melena in 43 (35.5%) cases, and generalized anasarca in 18 (14.9%). As regard clinical presentation, ascites and edema were the most common (63.6%), followed by encephalopathy in 56 (49.58%), and jaundice in (28.1%) cases, spider nevi in (8.3%) cases and organomegaly in 22 (18.2%).

Outcome Data and Main Results:

There were different complications that were found in the studied group. The most common complication reported was Ascites in 70 (57.9%)

followed by encephalopathy in (52.1%) cases, and GIT bleeding in 51 (42.1%) cases. AKI was found in 34 (28.1%) cases while 14 (11.6%) cased complicated by spontaneous bacterial peritonitis.

Regarding the PH, normal PH were 76 (62.8%) patients, acidemia 22 (18.2%), and alkalemia 23 (18.2). There were 73(60.4%) patients were child C score at the time of admission. The mean MELD score was 19.26± 9.01. The mean MELD-PaCO2-HCO3 was 23.79 ± 7.45, while the mean MELD-bicarbonate was 16.35±7.22**.**

As a regimen of management, serum electrolyte acid base correction was used in 33 (27.3%) cases while endoscopy or band ligation was performed in 40 (33.1%) cases. Medication for Na and K correction were used in 6 (5%) and 17 (14%) cases respectively. Vasopressors were used in 12 (9.9%) cases who were admitted to the ICU. None of the cases underwent renal replacement therapy.

After applying the different roles of management as summarized before, The course of the studied group showed that (74.4%) improved, (20.7%) progressed, (5%) had a stationary course. Rather than a linear trend, a positive association was identified among hospital mortality and acid-base parameters at varying time intervals, which suggests that fluctuations in acidotic markers may play a contributing role in hospital mortality and that keeping these markers in the normal range may reduce mortality. At the end of our study, most cases (74.4%) cases survived, and 25.6% died.

Admission serum HCO3 Stratification and Clinical Characteristics:

As regard the relation between HCO3 and different numerical parameters, Age and hemoglobin was significantly lower in individuals with high HCO3 contrast with cases with normal and low HCO3 (p=0.041 &0.05 respectively). PaCo2 was significantly higher in patients with high HCO3 compared to patients with normal and low HCO3 (p=<0.0001). Also, PaO2 was significantly higher in patients with high HCO3 in contrast to patients with normal and low HCO3 (p=0.039). There was significant variation among the three groups regarding base excess (=<0.0001).

As regard the relation between HCO3 and different categorical parameters, there was significant distinction amongst the three groups regarding diabetes mellitus (p=0.005), Child -Pugh score (p=0.035), encephalopathy (p=0.022) and outcome (p=0.012), as summarized in **tables (2&3).**

***Admission serum Na Stratification and Clinical Characteristics*:**

The relation between Na and different categorical parameters is shown in table (10). This table shows that there was significant variation among the three groups concerning, ascites (p=0.016), Child -Pugh score (p=0.019), encephalopathy (p=0.023), ICU admission (p=0.045) and course (p=0.034). individuals with lower serum Na had more advanced liver disease, encephalopathy and worse outcomes **table (4)**.

As regard the relation between Na and different numerical parameters, direct bilirubin was significantly higher in cases with moderate to severe hyponatremia in contrast to patients with normal and mild hyponatremia (p=0.032). HCO3 was significantly lower in patients with moderate to severe hyponatremia compared to patients with mild hyponatremia (p=0.018). There was a significant distinction amongst the three groups regarding base excess, Ca, and PT (p=0.021, 0.002 & 0.043 correspondingly).

There was significant variance amongst the three groups concerning MELD Score, MELD-PaCo2-HCO3, and MELD-bicarbonate (p=0.000, 0.024 & 0.031 respectively), as summarized in **table (5)**

The frequency of total deaths was significantly higher in cases with low HCO3, serum Na, acidemia and alkalemia, and a high MELD score >19, as summarized in **figure (1).**

Table (1): Demographic and clinical characteristics in the examined patients

Parameters			Studied patients (N=121)
Gender	**Male / Female**		51 (42.1%) / 70 (57.9%)
Age (years)	**Mean± SD**		64.55± 10.12
	Median (Range)		65.0 (37.0- 90.0)
Residence	**Rural**		77 (63.6%)
	Urban		44 (36.4%)
Occupation	**Employee**		12 (9.9%)
	Farmer		14 (11.6%)
	Manual work		52 (43.0%)
	No work		43 (35.5%)
Special habits	**Non-smoker**		100 (82.6%)
	Smoker		21 (17.4%)
Diabetes mellitus 26 (21.5%)	**Type I DM**		3 (2.5%)
	Type II DM		23 (19.0%)
Hypertension			32 (26.4%)
Cause of liver Cirrhosis	**Post HCV**		59 (48.8%)
	Bilharziasis		35 (28.9%)
	HBV		11 (9.1%)
	Unknown		7 (5.8%)
	Primary biliary cirrhosis		4 (3.3%)
	Others		3 (2.5%)
	Autoimmune		2 (1.7%)
HCV (+) patients received DAAs			46 (38.0%)
Cause of admission	**Encephalopathy**		60 (49.58%)
	Hematemesis and melena		43 (35.5%)
	Generalized anasarca		18 (14.9%)
Clinical presentation	**Ascites and edema**		77 (63.6%)
	Encephalopathy		55 (45.5%)
	Jaundice		34 (28.1%)
	Palmar erythema		29 (24.0%)
	Fetor hepaticus		26 (21.5%)
	Organomegaly 21(14.4%)	**Hepatomegaly**	3 (2.5%)
		Splenomegaly	19 (15.7%)
	Spider nevi		10 (8.3%)

Table (2): Relation between admission HCO3 with different categorical parameters

Parameters		HCO3 classification			P value
		Patients with normal HCO3 (N=17)	Patients with low HCO3 (N=94)	Patients with high HCO3 (N=10)	
Gender	**Male**	(7)41.2%	(42)44.7%	(2)20.0%	0.322
	Female	(10)58.8%	(52)55.3%	(8)80.0%	
Age (years)		68.7±7.9	64.5±10.0	57.7±11.7	**0.041**
Diabetes mellitus	**Type I DM**	(1)5.9%	(1)1.1%	(1)10.0%	**0.005**
	Type II DM	(8)47.1%	(13)13.8%	(2)20.0%	
	No	(8)47.1%	(80)85.1%	(7)70.0%	
Hypertension		(6)35.3%	(24)25.5%	(2)20.0%	0.626
Cause of liver cirrhosis	**PBC**	(1)5.9%	(3)3.2%	(0)0.0%	0.625
	Autoimmune	(0)0.0%	(2)2.1%	(0)0.0%	
	Bilharziasis	(4)23.5%	(29)30.8%	(2)20.0%	
	HBV	(2)11.8%	(8)8.5%	(1)10.0%	
	Others	(0)0.0%	(2)2.1%	(1)10.0%	
	Post HCV	(10)58.8%	(45)47.9%	(4)40.0%	
	Unknown	(0)0.0%	(5)5.3%	(2)20.0%	
Child -pugh score	**Class A**	(0)0.0%	(3)3.2%	(2)20.0%	**0.035**
	Class B	(9)52.9%	(30)31.9%	(4)40.0%	
	Class C	(8)47.1%	(61)64.9%	(4)40.0%	
Liver cirrhosis complications	**AKI or H.R .S**	(2)11.8%	(30)31.9%	(2)20.0%	0.197
	Encephalopathy	(6)35.3%	(55)58.5%	(2)20.0%	**0.022**
	GIT bleeding	(7)41.2%	(37)39.4%	(7)70.0%	0.175
	Ascites	(11)64.7%	(54)57.4%	(5)50.0%	0.746
	SBP	(1)5.9%	(12)12.8%	(1)10.0%	0.707
ICU admission		(3)17.6%	(39)41.5%	(5)50.0%	0.134
Hospital course	**Improvement**	(16)94.1%	(64)68.1%	(10)100.0%	0.063
	Progression	(1)5.9%	(24)25.5%	(0)0.0%	
	Stationary	(0)0.0%	(6)6.4%	(0)0.0%	
Outcomes	**Death**	(1)5.9%	(30)31.9%	(0)0.0%	**0.012**
	Discharge	(16)94.1%	(64)68.1%	(10)100.0%	

p≤0.05 is considered statistically significant, p≤0.01 is considered high statistically significant, X2: Pearson Chi-Square **'***test,*

Primary biliary cholangitis (PBC) , SBP: spontaneous bacterial peritonitis, Others: hemochromatosis, Wilson's Cystic disease, fibrosis and biliary atresia

Table (3): Relation between admission HCO3 with different numerical parameters.

Parameters	HCO3 classification						P-value
	Patients with normal HCO3 (N=17)		Patients with low HCO3 (N=94)		Patients with high HCO3 (N=10)		
	Mean ±SD	Median	Mean ±SD	Median	Mean ±SD	Median	
Vital signs							
Pulse	84.8±11.2	84.0	86.5±9.5	89.0	88.6±8.3	87.0	.502
Systolic BP	113.5±12.7	110.0	110.4±12.3	110.0	109.0±5.7	110.0	.378
Diastolic BP	69.4±8.3	70.0	69.8±7.5	70.0	69.0±3.2	70.0	.699
Temperature	37.1±.3	37.0	37.0±.3	37.0	39.5±8.4	36.8	.279
Respiratory rate	18.7±1.6	18.0	19.5±2.5	18.0	19.8±2.0	20.0	.281
Laboratory parameters							
WBCs	9.3±4.7	9.2	10.0±4.7	9.6	7.8±3.0	8.9	.334
Neutrophils	74.7±10.4	76.8	76.5±10.5	79.0	80.9±7.0	78.5	.461
Lymphocytes	16.5±7.0	16.0	13.3±6.7	12.3	13.6±5.1	15.0	.067
HB	10.3±2.1	10.0	9.9±1.6	9.9	9.3±1.9	9.8	**.050**
MCV	82.5±8.6	83.0	85.1±8.3	85.1	85.3±4.9	84.0	.647
PLT	165.8±89.8	142.0	176.7±104.3	159.5	150.2±96.9	135.0	.327
ALT	42.1±48.1	25.0	35.2±27.3	28.5	33.5±41.6	15.5	.246
AST	62.6±42.6	46.0	59.5±56.1	39.0	109.7±164.1	38.0	.801
TP	6.9±.6	7.0	6.7±.9	6.7	6.8±.6	7.1	.271
ALB	2.6±.5	2.6	2.7±.5	2.8	2.6±.8	2.6	.692
Total bilirubin	2.7±2.5	1.5	3.2±4.8	1.5	3.2±3.4	1.7	.881
Direct bilirubin	2.0±2.1	1.0	2.3±3.8	1.0	2.2±2.4	1.1	.898
ABG-PH	7.4±.1	7.4	7.4±.1	7.4	7.4±.1	7.4	.131
PaCO2	31.4±8.7	33.1	27.0±6.4	26.1	36.9±3.2	36.2	**.000**
PaO2	76.6±21.4	78.0	73.2±21.8	71.5	70.5±18.0	67.5	.568
SaO2	89.2±23.8	97.0	90.1±19.4	94.5	83.2±29.2	94.0	**.039**
HCO3	23.7±1.1	24.0	18.0±3.0	18.6	27.3±1.0	27.8	**.000**
Base Excess	-.3-±1.6	-.1-	-6.2-±3.5	-5.5-	-.4-±4.6	1.8	**.000**
Na+	130.6±5.4	131.0	132.1±8.5	135.0	133.2±8.9	132.5	.350
K+	3.6±.7	3.8	4.0±.9	4.0	3.9±.8	4.0	.086
Ca++	1.1±.9	1.0	1.0±.2	1.0	1.0±.2	1.0	.439
PT	15.8±4.7	15.4	16.6±5.0	15.3	17.9±8.5	15.0	.765
PC	71.2±22.3	69.5	67.1±27.7	60.0	65.2±33.6	66.3	.663
INR	1.4±.4	1.4	1.5±.4	1.4	1.7±.8	1.4	.898
S. Creatinine	1.1±.4	1.2	1.4±.6	1.2	1.0±.4	1.1	.174
BUN	36.9±14.8	35.0	39.3±16.4	37.0	37.9±12.4	32.5	.776
Blood glucose	122.1±27.1	120.0	119.4±40.1	103.0	132.8±44.0	131.0	.297
MELD Score	18.2±8.7	19.0	19.7±9.0	20.0	17.3±10.5	11.0	.722
MELD-Paco2-HCO3	21.7±9.3	25.0	24.1±6.9	23.0	24.5±9.4	23.0	.812
MELD-Bicarbonate	14.4±9.7	17.5	16.7±6.4	16.0	16.3±9.6	15.0	.823

pt: prothrombin time, pc:prothrombin concentration, INR:international normalized ratio, ALB: albumin, TP:totalprotein, WBCS:white blood cells, HB:hemoglobin, MCV: mean corpuscular volume

Table (4): Relation between admission serum sodium (Na) level with different categorical parameters.

Parameters		Admission serum sodium (Na) level classification			P value
		Patients with normal serum sodium (N=57)	Patients with mild hyponatremia (N=55)	Patients with moderated to severe hyponatremia (N=9)	
Gender	Male	(22) 38.6%	(25) 45.5%	(4) 44.4%	0.755
	Female	(35) 61.4%	(30) 54.5%	(5)55.6%	
Age (years)		64.9±10.4	64.2±10.2	64.4±9.0	.909
Diabetes mellitus	Type I DM	(3) 3.5%	(0) 1.8%	(1) 0.0%	0.235
	Type II DM	(6) 10.5%	(15) 27.3%	(1) 22.2%	
	No	(49) 86.0%	(39) 70.9%	(7) 77.8%	
Hypertension		(14) 24.6%	(17) 30.9%	11.1%	0.416
Cause of liver cirrhosis	PBC	(2) 3.5%	(2) 3.6%	(0)0.0%	0.974
	Autoimmune	(0) 0.0%	(2) 3.6%	(0) 0.0%	
	Bilharziasis	(15) 26.3%	(17) 30.9%	(3) 33.3%	
	HBV	(5)8.8%	(5)9.1%	(1)11.1%	
	Others	(2)3.5%	(1)1.8%	(0)0.0%	
	Post HCV	(30)52.6%	(24)43.6%	(5)55.6%	
	Unknown	(3)5.3%	(4)7.3%	(0)0.0%	
Child -pugh score	Class A	(4)7.0%	(1)1.8%	(0)0.0%	**0.019**
	Class B	(26)45.6%	(17)30.9%	(0)0.0%	
	Class C	(27)47.4%	(36)67.3%	(9)100.0%	
Liver cirrhosis complications	AKI or H.R .S	(13)22.8%	(17)30.9%	(4)44.4%	0.334
	Encephalopathy	(24)42.1%	(31)56.4%	(8)88.9%	**0.023**
	GIT bleeding	(52)52.6%	(19)34.5%	(2)22.2%	0.069
	Ascites	(27)47.4%	(38)69.1%	(5)55.6%	0.066
	SBP	(5)8.8%	(9)16.4%	(0)0.0%	0.241
ICU admission		(12) 21.1%	(16)29.1%	(5)55.6%	**0.045**
Hospital course	Improvement	(44)77.2%	(41)74.5%	(5)55.6%	**0.034**
	Progression	(9)15.8%	(14)25.5%	(2)22.2%	
	Stationary	(4)7.0%	(1) (0)0.0%	(0) (2)22.2%	
Outcomes	Death	(13)22.8%	(14)25.5%	(4)44.4%	**0.038**
	Discharge	(44)77.2%	(41)74.5%	(5)55.6%	

X2: Pearson Chi-Square test Primary biliary cholangitis (PBC)

Table (5): Relation between admission serum sodium level (Na) with different numerical parameters.

Parameters	Admission serum sodium (Na) level classification						P-value
	Patients with normal serum sodium (N=57)		Patients with mild hyponatremia (N=55)		Patients with moderated to severe hyponatremia (N=9)		
	Mean ±SD	Median	Mean ±SD	Median	Mean ±SD	Median	
Vital signs							
Pulse	87.3±9.2	88.0	84.8±9.2	84.0	91.0±13.5	90.0	.307
Systolic BP	111.4±14.2	110.0	110.2±10.1	110.0	110.0±5.0	110.0	.738
Diastolic BP	69.6±9.1	70.0	69.0±5.4	70.0	70.0±5.0	70.0	.842
Temperature	36.9±.2	37.0	37.5±3.6	37.0	37.2±.4	37.0	.130
Respiratory rate	19.4±2.5	18.0	19.5±2.3	18.0	19.1±2.3	18.0	.827
Laboratory parameters							
WBCs	9.3±4.3	8.4	9.9±5.0	9.1	10.8±4.3	10.5	.590
Neutrophils	75.5±10.6	78.0	76.8±10.1	79.0	83.0±6.9	83.0	.161
Lymphocytes	14.2±7.0	13.9	13.8±6.7	13.0	11.3±3.6	10.0	.427
HB	9.9±1.9	9.8	10.0±2.0	10.0	10.9±2.1	10.7	.480
MCV	84.7±9.1	85.1	84.3±7.6	84.0	87.6±4.7	87.8	.328
PLT	158.5±64.1	152.0	186.8±131.1	159.0	180.2±80.8	178.0	.552
ALT	36.1±31.9	26.0	35.1±32.5	28.0	42.2±32.3	31.0	.583
AST	69.0±77.2	38.0	62.0±66.8	41.0	45.8±31.3	36.0	.874
TP	6.7±.8	7.0	6.7±.9	6.6	6.7±.5	6.8	.464
ALB	2.8±.6	2.9	2.6±.5	2.6	2.6±.6	2.6	.058
Total bilirubin	2.9±4.0	1.4	2.6±3.3	1.5	7.9±9.0	4.2	.052
Direct bilirubin	2.1±3.2	1.0	1.8±2.5	.9	6.0±7.2	3.2	**.032**
ABG-PH	7.4±.1	7.4	7.4±.1	7.4	7.3±.1	7.4	.174
Paco2	27.6±7.2	26.0	29.5±7.2	30.0	27.3±6.6	27.2	.292
PaO2	71.1±21.5	70.0	75.6±20.5	78.0	75.2±26.3	80.0	.428
SaO2	89.1±21.3	94.0	88.9±22.0	95.0	93.6±5.6	96.0	.806
HCO3	19.2±3.8	19.8	20.4±3.6	20.0	16.2±6.0	16.6	**.018**
Base Excess	-5.4-±3.8	-5.1-	-3.8-±3.7	-3.9-	-8.4-±7.0	-7.3-	**.021**
Na+	138.6±3.3	137.0	128.3±3.9	129.0	113.2±4.3	115.0	**.000**
K+	4.0±.7	3.9	3.9±.9	3.9	4.2±1.1	3.9	.812
Ca++	1.0±.2	1.0	1.0±.5	1.0	.9±.1	.9	**.002**
PT	15.6±4.5	14.8	17.5±6.2	15.4	17.5±2.3	18.0	**.043**
PC	72.1±26.7	66.3	64.7±28.6	60.0	56.2±19.7	54.8	.087
INR	1.4±.4	1.3	1.5±.5	1.4	1.7±.3	1.8	.043
S. Creatinine	1.2±.6	1.0	1.3±.6	1.2	1.5±.6	1.3	.095
BUN	35.9±13.7	35.0	41.0±16.5	40.0	44.9±21.6	42.0	.181
Blood glucose	113.7±33.3	102.0	129.2±43.3	120.0	115.6±35.5	103.0	.131
MELD Score	15.3±8.1	13.0	21.8±8.0	23.0	28.8±8.5	30.0	**.000**
MELD-paco2-hco3	22.2±7.1	23.0	24.9±7.6	26.0	27.4±6.7	24.0	**.024**
MELD-bicarbonate	14.9±6.9	15.0	17.2±7.5	18.0	19.9±5.3	17.0	**.031**

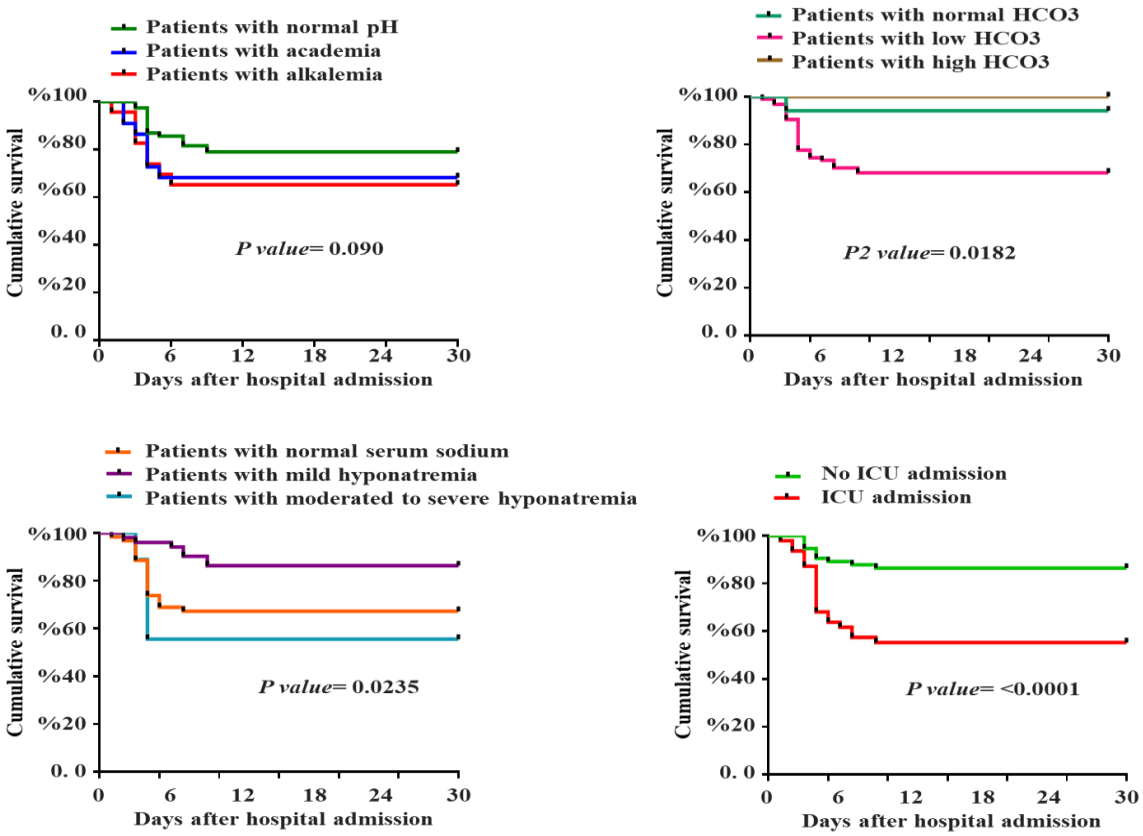

Figure (1) Kaplan- Meier curve showing overall survival in cirrhotic patients according to admission serum pH, HCO3, Na levels, and ICU admission

Discussion

In individuals with cirrhosis, acid-base disturbances are frequent. Patients frequently develop net metabolic acidosis as the severity of cirrhosis worsens, particularly those who have acute and chronic liver failure with sepsis, where elevated levels of lactic acid and unmeasured anions build up. Frequently, acidosis is accompanied by a decreased serum bicarbonate (SB) level. (6)

The importance of serum bicarbonate in cirrhosis has only received limited attention. Most of these studies are retrospective and have evaluated the influence of elevated serum lactate levels and unmeasured anion acidosis on ICU mortality. (7)

This research aimed to contrast the prognostic value of the new equations (MELD-PaCO2-HCO3 and MELD- Bicarbonate) with the original MELD score, as well as identify the prognostic value of ABG-related parameters, serum bicarbonate, and serum electrolytes at time of admission and their correlation with the development of complications, length of hospital admission prognosis, and mortality in hospitalized cirrhotic individuals.

This observational prospective research was carried out on 121 cases with a confirmed diagnosis of decompensated cirrhosis (age ≥ 18 years). Liver cirrhosis was triggered by HCV, bilharziasis, and HBV the most in the present investigation. The most prevalent reason for hospitalization was encephalopathy, whereas hematemesis and melena were the next most frequent. Most of these individuals were hospitalized due to complications of liver cirrhosis, involving ascites, encephalopathy,

acute kidney injury, and spontaneous bacterial peritonitis (SBP).

This prospective study estimated the clinical value of ABG parameters in cases with cirrhosis. Abnormal acid-base results were detected in 37% of the study group. In the present study, we found that both pH and HCO3 were independent predictors of ICU admission and death. There was significant variation among the three groups (normal pH, acidemia, and alkalemia) regarding the Child -Pugh score (p=0.016) and serum electrolyte acid base correction (p=0.003). Also, we found that patients with a lower pH had a higher incidence of AKI, HRS, GIT bleeding, and mortality in comparison to patients with a normal pH.

In the same context, **Drolz et al.** [8], a study of 178 critically sick patients with liver cirrhosis, indicated that metabolic acidosis and acidemia were related to a higher likelihood of death within 28 days. Consequently, 28-day mortality rate was 91% in cirrhosis cases with arterial pH values < 7.2 and 86% in those with arterial HCO_3- values < 15 mmol/l. We also found that the mortality rate was 100% in cirrhosis patients with arterial pH values < 7.2 and in those with arterial HCO3 values < 10 mEq/l and serum Na <110 mmol/l.

Moreover**, Gao et al.** [9] conducted a study on 975 patients with cirrhosis. Patients with metabolic acidosis had a significantly higher proportion of bacterial infection (76.7% vs. 64.8%, p<0.001), hepatorenal syndrome (24.5% vs. 15.4%, p<0.001), acute-on-chronic liver failure (ACLF; 61.5% vs. 48.0%, p<0.001), ascites (29.4% vs. 23%, p=0.023), and hepatic encephalopathy (29.4% vs. 22%, p=0.008).

Our results revealed that according to HCO_3, patients were separated into 3 groups: participants with normal HCO_3, (n=17), participants with low HCO_3 (n=94), and patients with high HCO_3 (n=10). Age and hemoglobin were significantly lower in patients with high HCO_3 contrasted with participants with normal and low HCO_3 (p=0.041 &0.05 respectively). $PaCO_2$ was significantly higher in patients with high HCO_3 in contrast to cases with normal and low HCO_3 (p=<0.0001). Also, PaO_2 was significantly higher in patients with high HCO_3 compared to patients with normal and low HCO_3 (p=0.039). Serum creatinine and MELD-score were higher among patients with low serum HCO3. There was significant variance amongst the three groups concerning the Child -Pugh score (p=0.035), encephalopathy (p=0.022) and outcome (p=0.012). Abnormal SB was related to ICU admission. Death was significantly higher in low HCO3 in contrast to normal and high HCO3.

In the same context, **Schopis et al. (1)** performed A retrospective analysis was carried out on 2,693 participants, and those involved were categorized into 7 groups based on their admission SB (mEq/L) levels. These groups were split into slightly reduced (18–21), moderately decreased (14–17), and severely reduced (<14) groups, and increasing groups were separated into mildly elevated (26–29), moderately increased (30–33), and severely increased (>30) groups. They discovered that the distributions of age and gender were comparable across all of the SB groups. Patients whose SB was lower had more advanced stages of the liver disease. The lower SB groups had greater levels of serum creatinine, alanine aminotransferase, alkaline phosphatase, international normalized ratio, total bilirubin and MELD-Na, although the lower SB groups had lower levels of S. albumin (p< 0.05).

In our present study, a significant distinction in overall survival was observed according to the bicarbonate classification and a higher mortality rate was observed among cases with low SB.

Additionally, **Chen et al**.[10] performed 177 cirrhotic individuals were enrolled in a retrospective cohort analysis. The total death rate in intensive care units was 36.2%. ICU mortality was shown to be substantially associated with bicarbonate (HCO3) levels (odds ratio, 2.3; 95% confidence interval [CI], 1.0–4.8; p = 0.038).

Patients with more severe cases of cirrhosis have gradually worsened acid-base regulation. Compensated hypocapnia and respiratory alkalosis are common in stable early cirrhosis. A low effective circulatory volume caused by portal hypertension-induced vasodilation in advanced cirrhosis causes an upregulation of compensatory mechanisms, which in turn causes an increase in the resorption of free water and the subsequent dilutional acidemia Activation of the renin-angiotensin-aldosterone

system, diarrhea, and the use of diuretics are additional factors that influence acid-base status. [11]
In the present study, direct bilirubin was significantly higher in patients with moderate to severe hyponatremia compared to patients with normal and mild hyponatremia (p=0.032). HCO_3 was significantly lower in patients with moderate to severe hyponatremia compared to patients with mild hyponatremia (p=0.018). There was significant variation amongst the three groups regarding base excess, Ca, and PT (p=0.021, 0.002 & 0.043 respectively). There was a significant difference between the three groups regarding MELD Score, MELD-PaCO2-HCO3, and MELD-Bicarbonate (p=0.000, 0.024 & 0.031 respectively). Also, there was significant difference between the three groups concerning Fetor hepaticus (p=0.034), jaundice (p=0.018), ascites (p=0.016), Child -Pugh score (p=0.019), encephalopathy (p=0.023), ICU admission (p=0.045), endoscopy or surgery (p=0.007), medication Na (p=0.000), and course (p=0.034).
Our results came in context with **Biggins et al**.[12] performed ascites and hepatic encephalopathy at the time of listing were independent predictors of mortality (HR=1.86 [95% CI, 1.01-3.43], P =.048; and HR= 1.78 [95% CI, 1.01-3.15], P =.049) in a retrospective cohort investigation of 341 adult individuals with cirrhosis listed for transplantation from a single center. Nevertheless, hepatocellular carcinoma (HCC), gastrointestinal bleeding, & bacterial infection were not predictive of mortality.
Salt and water retention in cirrhosis is the main cause of hyponatremia. Splanchnic arterial vasodilatation, which lowers systemic vascular resistance and causes the release of antidiuretic hormone, also known as arginine vasopressin, is the proposed mechanism.[13]
Na+, Cl-, albumin, lactate, and unmeasured anions were considered subcomponents of BE. Increased lactic acidosis not only plays the most important role in the occurrence of metabolic acidosis but also plays the most crucial role in death. [9]
The present study shows that the MELD score >19 had good discrimination in predicting in-hospital death in critically ill patients with cirrhosis. In the context of ICU admission, the MELD score is proposed to serve as an organ failure-specific measure rather than a liver disease-specific score. The renal, hepatic, and coagulation systems are indeed taken into account when evaluating organ failure using the MELD approach. Renal impairment is strongly related to worse outcomes for cirrhosis individuals, in accordance with a large body of research. [14]

Conclusion

Metabolic acidosis is common among critically sick cirrhotic patients, and the frequency with which organ failures occur is a strong predictor of death. The MELD<19 score is useful in predicting the short-term mortality of critically sick patients with cirrhosis. HCO3 level and serum Na evaluation (objective and reproducible laboratory tests) were found to have a significant predictive value in critically ill cirrhotic cases. In this context, the prognostic value of the total bilirubin level is less evident. A significant distinction in overall survival was observed according to admission serum HCO3, serum Na levels, and ICU admission.

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