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Study the Relation between Blood Ammonia Level and Esophageal Varices in Egyptian Patients with Liver Cirrhosis

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ABSTRACT

Objective: To investigate the diagnostic utility of venous ammonia level, as a non-invasive marker of the presence of esophageal varices, in patients with liver cirrhosis.
Background: Esophageal varices (EV) are dilated submucosal distal esophageal veins connecting the portal and systemic circulations. This happens due to portal hypertension (most commonly a result of cirrhosis), resistance to portal blood flow, and increased portal venous blood inflow. The most common fatal complication of cirrhosis is variceal rupture.
Patients and methods: The study was carried out on 120 adult Egyptian patients with liver cirrhosis, and 20 healthy subjects matched age and sex. The patients were randomly selected from those attending the Internal Medicine Department, Menoufia University, and Internal Medicine Department, Damanhur teaching hospitals from October 2018 to December 2019 years.
Results: Child-Pugh score MELD score, APRI score, and FIB4 had a sensitivity of 86%, 95%, 85%, 79%, and 85% respectively, and specificity of 80%, 65%, 70%, 68%, and 82% respectively in the detection of esophageal varices among the studied groups. there were no significant correlations between blood ammonia in the studied groups with Child-Pugh score, MELD score, APRI, FIB-4, platelet count, bilirubin, PT%, albumin, spleen diameter, and portal vein diameter ($P > 0.05$). platelet, albumin, blood ammonia, Child-Pugh score, MELD score, spleen diameter, and portal vein diameter are independent predictors for the presence of esophageal varices ($P < 0.5$). Hb level, MELD score, and liver diameter are predictors for esophageal variceal bleeding ($P < 0.05$).
Conclusion: Blood ammonia was significantly higher in cirrhotic patients with esophageal varices than in patients without esophageal varices, blood ammonia has 86% sensitivity and 80% specificity for the prediction of the presence of esophageal varices and blood ammonia level is a valuable, simple noninvasive marker for the prediction of the presence of esophageal varices but not the risk of bleeding.
Key words: blood ammonia, esophageal varices, liver cirrhosis, portal hypertension, splanchnic vessels

Abbreviations:
EV: esophageal varices,
BMI: body mass index,
RBCs: Red Blood Cells,
WBCs: White Blood Cells,
PLTs: platelets,
ALT: alanine aminotransferase,
AST: aspartate aminotransferase,
GGT: gamma-glutamyl transferase,
INR: international normalized ratio,
Hepatitis B virus antigen: HBsAg,
anti-HCV Ab: hepatitis C virus antibodies,
ANA: antinuclear antibodies,
ASMA: anti-smooth muscles antibodies,
LKM: liver kidney microsomal,
AFP: alpha-fetoprotein.

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INTRODUCTION

Esophageal varices (EV) are dilated submucosal distal esophageal veins

connecting the portal and systemic circulations. This happens due to portal hypertension (most commonly a result of cirrhosis), resistance to portal blood flow, and increased portal venous blood inflow. The most common fatal complication of cirrhosis is variceal rupture (1). Prevalence of varices increases with the severity of liver disease (Child-Pugh class A 42.7%, class B 70.7%, and class C 75.5%). The incidence of esophageal varices in cirrhotic patients is around 5% at the end of one year and 28% at the end of three years. Small varices progress to large varices at a rate of 10% to 12% annually (2). Approximately 50% of all patients with a new diagnosis of cirrhosis have gastrointestinal varices (3). The annual risk of variceal bleeding among small and large varices is 5% and 15% respectively. The six-week mortality rate among patients with index variceal bleeding is approximately 20%. The risk of rebreeding without endoscopic intervention is almost 60% with an increased mortality rate (33%) (4).

In Egypt, chronic liver diseases are common due to the higher prevalence of viral hepatitis C and Schistosomiasis (5). In cirrhosis. the main portion of blood ammonia carried by portal blood is shunted by portosystemic shunts to systemic circulation could be a good mirror of portosystemic collaterals and consequently portal hypertension (6). The possibility of identifying cirrhotic patients with EV or other collateral presence by other non-invasive means is appealing. It could decrease the necessity of endoscopic screening with reduced healthcare costs. Increased spleen volume is an independent predictor of large EV in liver cirrhosis (7). Blood ammonia levels have been found to correlate with the severity of liver disease and the existence of portosystemic shunts, especially esophageal varices. Accumulation of ammonia in splanchnic vessels in cases of liver function impairment results in vasodilatation and increased portal blood flow (8). Therefore, the aim of this study was to investigate the diagnostic utility of venous ammonia level, as a non-invasive marker of the presence of esophageal varices, in patients with liver cirrhosis.

MATERIAL AND METHODS

The study was carried out on 120 adult Egyptian patients with liver cirrhosis, and 20 healthy subjects matched age and sex. The patients were randomly selected from those attending the Internal Medicine Department, Menoufia University, and Internal Medicine Department, Damanhour teaching hospitals from October 2018 to December 2019 years.

Inclusion criteria

Patients with liver cirrhosis of different etiology which a without varies.

Exclusion criteria

Pregnant and lactating females, patients with portal vein thrombosis and patients with hepatocellular carcinoma.

For all subjects the following procedures were performed:

Careful history taking regarding: A purposely designed sheet was performed for all patients included in this study, including: Personal history: (name, age, sex, address, residence, occupation, marital status, and special habits (smoking, alcohol), Past history: (Any medical disease and its nature, duration, treatment, and any drug intake and its regimen and duration of intake), Family history: of any similar condition and History of bleeding, and encephalopathy.

Clinical examination: Complete general with special emphasis on: (Arterial blood pressure, weight, height, body mass index (BMI) and presence of ascites, hepatosplenomegaly, icterus, spider angioma).

Laboratory investigations: all patients and control were subjected to investigations as follow:

Complete blood count: Red blood Cells (RBCs), White Blood Cells (WBCs), and platelets (PLTs). Kidney functions: (Including blood urea and serum creatinine, Liver Profile: (Including serum albumin, alanine amino-transferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), bilirubin, and international normalized ratio (INR) and HBsAg and anti-HCV Ab: All patients were tested for HBsAg (Hepatitis B virus antigen) and anti-HCV Ab (Hepatitis C virus antibodies) to determine the cause of liver cirrhosis. Serum antinuclear antibodies (ANA), anti-smooth muscles antibodies (ASMA), serum IgG, and anti-liver kidney microsomal (LKM) tests were carried out for patients suspected to have autoimmune hepatitis.

Alpha-fetoprotein (AFP): Alpha-fetoprotein (AFP) measurements were taken with the AxSYM AFP immunoassay test (Abbott, USA)

Abdominal ultrasound: (liver size, splenic bi-polar diameter (longest axis) in cm, ascites, portal vein diameter, splenic vein diameter and hepatic vein: patency and dilatation) (9).

Upper GI endoscopy: An upper gastrointestinal endoscopy was performed for all the patients to evaluate the presence and grading of esophageal varices (10). Esophageal varices were detected and graded from I to IV (11)., (grade I, varices at the level of mucosa; grade II, varices smaller than 5mm and fulfilling less than 1/3 of the esophageal lumen; grade III, varices larger than 5mm and fulfilling more than 1/3 of the esophageal lumen; grade IV, varices occupying more than 2/3 of the esophageal lumen).

Statistical analysis

Data were tabulated and analyzed statistically using MICROSOFT EXCEL 2019 and SPSS v. 21 (SPSS Inc., Chicago, IL, USA. Statistical analysis was done using descriptive and analytical tests. Descriptive includes percentage (%), mean and standard deviation. Analytical includes Chi-square (χ^2), ANOVA (f) test, Kruskal-Wallis test (nonparametric test). Considering P-value < 0.05 statistically significant.

RESULTS

In the current study, there was no significant difference among the studied groups as regards their age, gender, and HBs Ag (P>0.05). In all studied groups, 58 patients had negative HCV Ab and HBs Ag, but all of there had schistosomiasis (27 in group A, 21 in group B, and 10 in group C). While, a significant difference between A, B, and C regarding history of encephalopathy, presence of jaundice, pallor, ascites, LL edema, splenomegaly, palmar erythema (P<0.05), (*table 1*). In the current study, there was a significant difference

Table 1 - Comparison among the studied groups regarding demographic data, etiology of liver cirrhosis, symptoms and signs

Studied variables	Studied groups				Test of sig.	P-value
	Group A (N=40)	Group B (N= 40)	Group C (N=40)	Group D (N=20)		
Age / years					F	
Mean± SD	53.7±8.72	56.9±8.64	54.3±6.93	55.40±10.4	1.10	
Range	40.0-70.0	48.0-75.0	35.0-67.0	42.0 – 70.0		0.34^{NS}
Gender	N (%)	N (%)	N (%)	N (%)	χ^2	0.14^{NS}
Male	23(57.5%)	15(37.5%)	15(37.5%)	11(55%)	5.11	
Female	17(42.5%)	25(62.5%)	25(62.5%)	9(45%)		
HCV Ab						P1:0.17
Negative	27(67.5%)	21(52.5%)	10(25%)	--	14.8	P2:0.001**
Positive	13(32.5%)	19(47.5%)	30(75%)			P3:0.011*
HBs Ag						P1:0.07
Negative	37(92.5%)	40(100%)	40(100%)	--	6.15	P2:0.07
Positive	3(7.5%)	0(0.00%)	0(0.00%)			P3: 1.0
History of encephalopathy						P1:0.13
Absent	8(20%)	14 (35%)	6(15%)	--	4.84	P2:0.56
Present	32(80%)	26(65%)	34(85%)			P3:0.04*
Jaundice						P1:0.011*
Absent	18(45%)	7(17.5%)	19(47.5%)	--	8.59	P2:0.83
Present	22(55%)	31(82.5%)	21(52.5%)			P3:0.006**
Pallor						P1:0.001**
Absent	18(45%)	32(80%)	20(50%)	--	11.8	P2:0.65
Present	22(55%)	8(20%)	20(50%)			P3:0.004**
Ascites						
Absent	7(17.5%)	8(20%)	6(15%)	--	11.2	P1:0.06
Mild	33(82.5%)	27(67.5%)	34(85%)			P2:0.76
Marked	0(0.00%)	5(12.5%)	0(0.00%)			P3:0.047*
L.L edema						P1:1.00
Absent	4(10%)	4(10%)	11(27.5%)	--	6.13	P2:0.04*
Present	36(90%)	36(90%)	29(72.5%)			P3:0.04*
Splenomegaly						P1:0.001**
Absent	0(0.00%)	10(25%)	0(0.00%)	--	21.8	P2:1.00
Present	40(100%)	30(75%)	40(100%)			P3:0.001**
Palmar erythema						P1:0.038*
Absent	26(65%)	34(85%)	36(90%)	--	8.75	P2:0.007**
Present	14(35%)	6(15%)	4(10%)			P3:0.49

F: ANOVA test significance level P-value < 0.05 χ^2 chi-squared test SD: standard deviation

between groups A, B, C, and D regarding Hb levels, platelet count, WBC, ALT, AST, total bilirubin, serum albumin, PT, INR, AFP, blood urea and serum creatinine. Blood ammonia was significantly higher in group A (189.8±89.3), and group B (168.4±81.2) than group C (94.7±20.2) and group D (52.6±15.5) (P=0.001 for all), (*table 2*).

In the current study, MELD score was significantly higher in group A (25.9±4.00) than in groups B (23.0±2.96) and C (19.4±3.78) (P=0.001). The APRI

Table 2 - Comparison among the studied groups regarding laboratory investigation

Studied variables	Studied groups				Test of sig.	P-value	Post hoc p-value
	Group A (N=40)	Group B (N= 40)	Group C (N=40)	Group D (N=20)			
Hb (gm/dl)							P1:0.016*
Mean± SD	9.60±1.66	10.4±1.83	10.2±1.23	13.1±1.79	F=22.2	0.001**	P2:0.09
Range	9.06 – 10.1	9.90 – 11.0	9.81 – 10.6	12.3 – 13.9			P3:0.001**
							P4:0.43
							P5:0.001**
							P6:0.001**
Platelets $x10^3$							P1:0.71
Mean± SD	97.1±74.1	104.6±71.2	204.5±126.0	237.8±74.6	K = 44.3	0.001**	P2:0.001**
Range	28 - 272	22 – 236	41 - 472	110 - 350			P3:0.001**
							P4:0.001**
							P5:0.001**
							P6:0.18
WBCs $x10^3$							P1:0.11
Mean± SD	17.1±28.6	11.3±9.94	10.5±6.05	6.51±1.31	K = 9.99	0.019*	P2:0.07
Range	1.60 - 88	1.90 - 34	2.90 - 18	4.50 – 8.10			P3:0.02*
							P4:0.83
							P5:0.28
							P6:0.36
ALT(IU/L)							P1:0.67
Mean± SD	54.1±35.9	50.8±11.4	62.3±56.1	24.5±5.74	K = 29.6	0.001**	P2:0.31
Range	14.2 – 122	13 - 70	15 - 210	15 - 32			P3:0.003**
							P4:0.16
							P5:0.007**
							P6:0.001**
AST(IU/L)							P1:0.03*
Mean± SD	55.8±22.8	78.4±42.5	73.8±78.4	25.0±10.7	K = 47.7	0.001**	P2:0.10
Range	19.0 –89.0	50.0 – 202	11.0 – 285	11.0 – 39			P3:0.02*
							P4:0.68
							P5:0.001**
							P6:0.001**
Bilirubin (mg/dl)							P1:0.22
Mean± SD	3.80±6.49	2.46±0.70	6.41±6.53	0.85±0.09	K = 46.1	0.001**	P2:0.01*
Range	0.20 - 25	1.50 –3.96	0.50 - 18	0.70 – 1.00			P3:0.03*
							P4:0.001**
							P5:0.23
							P6:0.001**
S. Albumin (gm/dl)							P1:0.93
Mean± SD	2.96±0.52	2.97±0.57	2.76±0.48	4.16±0.19	K = 46.5	0.001**	P2:0.09
Range	2.30 –3.90	2.30 –4.10	2.10 - 3.80	3.90 - 4.50			P3:0.001**
							P4:0.1
							P5:0.001**
							P6:0.001**
PT (%)							P1:1.0
Mean± SD	55.3±17.6	55.3±11.5	67.8±15.4	86.3±3.70	K = 51.5	0.001**	P2:0.001**
Range	40 - 92	39 - 80	50 - 95	80 - 91			P3:0.001**
							P4:0.001**
							P5:0.001**
							P6:0.001**
INR							P1:0.4
Mean ±SD	1.77±0.43	1.70±0.39	1.36±0.28	1.00±0.00	K = 62.4	0.001**	P2:0.001**
Range	1.03 –2.19	1.00 –2.47	1.00 – 1.75	1.00 – 1.00			P3:0.001**
							P4:0.001**
							P5:0.001**
							P6:0.001**

Table 2 (continuation) - Comparison among the studied groups regarding laboratory investigation

Studied variables	Studied groups				Test of sig.	P-value	Post hoc p-value
	Group A (N=40)	Group B (N= 40)	Group C (N=40)	Group D (N=20)			
AFP (ng/mL)							P1:0.13
Mean± SD	6.46±1.32	6.90±0.79	6.17±1.83	4.79±0.65	F = 11.8	0.001**	P2:0.32
Range	4.30 – 8.90	5.30 – 8.10	3.80 – 9.00	4.00 – 6.00			P3:0.003**
							P4:0.01*
							P5:0.001**
							P6:0.001**
Urea (mg/dl)							P1:0.75
Mean± SD	61.7±38.5	58.9±39.0	79.5±48.8	29.0±4.31	K = 26.9	0.001**	P2:0.046*
Range	18.7 - 147	24 - 141	22 - 182	22 - 35			P3:0.003**
							P4:0.02*
							P5:0.006**
							P6:0.001**
Creatinine (mg/dl)							P1:0.3
Mean± SD	1.00±0.29	1.13±0.44	2.96±0.52	0.77±0.18	K = 9.47	0.02*	P2:0.004**
Range	0.50 – 1.51	0.40 – 2.00	0.23 – 2.70	0.53 – 1.10			P3:0.14
							P4:0.3
							P5:0.05
							P6:0.02*
Blood ammonia (μg/dl)							P1:0.12
Mean ±SD	189.8±89.3	168.4±81.2	94.7±20.2	52.6±15.5	K=74.9	0.001*	P2:0.001**
Range	80 –352	66 – 322	43 - 128	34 - 78			P3:0.001**
							P4:0.001**
							P5:0.001**
							P6:0.001**

Significance level p-value < 0.05 F: ANOVA test K: Kruskal Wallis test **: highly significant *Significant, Hb: Hemoglobin, WBC: White blood count, CBC: Complete blood count, N: Number
P1: Comparison between group A and group B P2: Comparison between group A and group C P3: Comparison between group A and group D
P4: Comparison between group B and group C P5: Comparison between group B and group D, P6: Comparison between group C and group D

score was significantly higher in group A (2.30±1.89) and group B (2.56±1.80) than group C (1.36±1.03), (P=0.006 and 0.001 respectively). FIB-4 was significantly higher in group A (7.70±5.85) and group B (7.35±5.30) than in group C (2.96±2.28) (P = 0.001 for both), (*Table 3*).

Table 3 - Comparison among the studied groups regarding trans-abdominal ultra-sonographic findings, Child-Pugh score, MELD score, APRI score and FIB-4

Studied variables	Studied groups			F	P-value	Post hoc P-value
	Group A (N=40)	Group B (N=40)	Group C (N=40)			
Liver diameter (cm)						P1:0.001**
Mean ±SD	12.4±2.48	9.91±0.90	10.5±1.29	23.6	0.001**	P2:0.001**
Range	10 – 18.7	8.80 –12.3	9.30 - 17			P3:0.09
Spleen diameter (cm)						P1:0.16
Mean ±SD	14.9±1.14	15.8±4.67	16.5±1.25	3.17	0.046*	P2:0.008**
Range	14 – 17	9 – 26	14 - 18			P3: 0.19
Portal vein diameter(mm)						P1:0.2
Mean ±SD	13.8±0.53	13.5±1.65	11.9±1.08	29.3	0.001**	P2:0.001**
Range	13 – 14.7	10 – 16	10 - 13			P3:0.001**
Ascites	No (%)	No (%)	No (%)			
Absent	7(17.5%)	8(20%)	6(15%)	χ^2	0.006*	P1:0.16
Mild	5(12.5%)	6(15%)	0(0.00%)	86.1		P2:0.01*
Moderate	17(42.5%)	8(20%)	29(72.5%)			P3:0.001**
Marked	11(27.5%)	18(45%)	5(12.5%)			
Child-Pugh score						
Class A	0(0.00%)	0(0.00%)	4(10%)	--	--	--
Class B	20(50%)	11(27.5%)	6(15%)			
Class C	20(50%)	29(72.5%)	30(75%)			

Table 3 (continuation) - Comparison among the studied groups regarding trans-abdominal ultra-sonographic findings, Child-Pugh score, MELD score, APRI score and FIB-4

Studied variables	Studied groups			F	P-value	Post hoc P-value
	Group A (N=40)	Group B (N=40)	Group C (N=40)			
Child-Pugh score						P1:0.49
Mean ±SD	9.18±1.06	9.6±1.65	8.32±2.52	K= 4.8	0.09	P2:0.30
Range	8 – 11	7 – 12	5 – 11			P3:0.08
MELD score						P1:0.001**
Mean ±SD	25.9±4.00	23.0±2.96	19.4±3.78	K=43.3	0.001**	P2:0.001**
Range	15 – 30	17 – 30	15 - 29			P3:0.001**
APRI score						P1:0.43
Mean ±SD	2.30±1.89	2.56±1.80	1.36±1.03	K=12.2	0.002**	P2:0.006**
Range	0.33 –5.80	0.53-6.36	0.42 –3.41			P3:0.001**
FIB-4						P1:0.72
Mean ±SD	7.70±5.85	7.35±5.30	2.96±2.28	K=29.0	0.001**	P2:0.001**
Range	1.43 –19.8	2.66 –19.4	1.02 - 8			P3:0.001**

Significance level p-value <0.05 F: ANOVA test **: highly significant *Significant
N: Number
P1: Comparison between group A and group B
P2: Comparison between group A and group C
P3: Comparison between group B and group C

ROC curve analysis showed that blood ammonia, Child-Pugh score MELD score, APRI score, and FIB4 had a sensitivity of 86%, 95%, 85%, 79%, and 85% respectively, and specificity of 80%, 65%, 70%, 68%, and 82% respectively in the detection of esophageal varices among the studied groups (*table 4, figure 1*).

In the current study, there were no significant correlations between blood ammonia in the studied groups with Child-Pugh score, MELD score, APRI, FIB-4, platelet count, bilirubin, PT%, albumin, spleen diameter, and portal vein diameter (P >0.05), (*table 5*). In the present study, platelet, albumin, blood ammonia, Child-Pugh score, MELD score, spleen diameter, and portal vein diameter are independent predictors for the presence of esophageal varices, (*table 6*). Hb level, MELD score, and liver diameter are predictors for esophageal variceal bleeding (*table 7*).

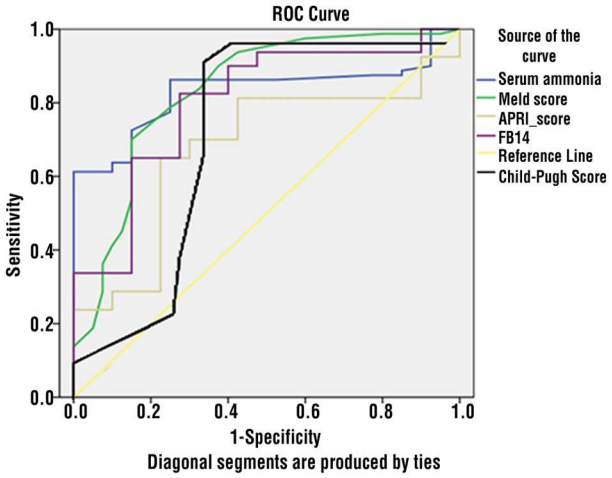

Figure 1 - Roc curve for sensitivity and specificity of blood ammonia level, APRI score and FBI4 for detection of esophageal varices

Table 4 - Sensitivity and specificity of blood ammonia level, Child-Pugh score, MELD score, APRI score, and FIB4 for detection of esophageal varices

Studied variables	AUC	Cutoff point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Blood ammonia(□g/dl)	0.832	104	86%	80%	85%	81%	84%
Child-Pugh score	0.735	8	95%	65%	78%	91%	60%
MELD score	0.833	20.5	85%	70%	85%	70%	80%
APRI score	0.773	0.88	79%	68%	77%	71%	74%
FIB4	0.867	2.80	85%	82%	68%	80%	84%

Table 5 - Spearman correlation between blood ammonia and Platelet count, bilirubin, PT, albumin, MELD score, APRI, FIB-4, liver diameter, spleen diameter, and portal vein diameter

Studied variables	Blood ammonia							
	Group A		Group B		Group C		Total cases	
	r	P value	r	P value	r	P value	r	P value
Platelet count (103)	0.195	0.23	-0.104	0.52	0.201	0.21	0.07	0.44
Bilirubin (mg/dl)	-0.087	0.77	0.093	0.13	-0.102	0.67	0.07	0.44
PT%	-0.200	0.06	0.170	0.41	-0.203	0.05	-0.04	0.78
Albumin (gm/dl)	-0.08	0.5	0.160	0.32	- 0.055	0.62	-0.009	0.93
Child-Pugh score	-0.08	0.61	-0.21	0.19	0.26	0.1	0.12	0.18
MELD score	-0.146	0.37	0.056	0.73	-0.068	0.67	0.09	0.32
APRI score	-0.110	0.49	-0.126	0.44	0.242	0.13	0.03	0.73
FIB-4	0.024	0.88	-0.260	0.1	-0.050	0.75	-0.02	0.85
Spleen diameter (cm)	-0.155	0.33	-0.091	0.57	-0.132	0.41	-0.08	0.39
Portal vein diameter (mm)	-0.058	0.72	-0.195	0.22	0.028	0.86	0.1	0.28

PT: Prothrombin time, AFP: Alpha-fetoprotein, MELD: Model for End-Stage Liver Disease, FIB-4: Fibrosis-4, APRI score: ALT to platelet ratio score

DISCUSSION

In the present study, a significant difference between the studied groups regarding Hb levels, platelet count, WBC, ALT, AST, total bilirubin, serum albumin, PT, INR, AFP, blood urea and serum creatinine. This is in contrast with studies conducted by Duah and his colleagues (12) they demonstrated that AST, ALP was found to be associated with the presence of EV among cirrhotic patients. None of these were statistically significant on multivariate analysis. As well, they found that none of the clinical features and laboratory parameters were significantly associated with the occurrence of varices in this study. In the study by Nouh and his colleagues (13) who found that Child-Pugh score class A was significantly higher in patients with EV grade I (63.33%) than patients with EV grade II (40%) and patients with EV grade III. While Child-Pugh score class B was higher in group IC (45%) than group IB (40%) and group IA (28.33%). Meanwhile, Child-Pugh score class C was higher in group IC (22.5%) than group IB (20%) and group IA (8.33%). Theses results come agree with our results. In the contrary, Gomaa and his coworkers (14) found a significant difference among

Table 6 - Multivariate logistic regression analysis for detection of independent predictors for the presence of esophageal varices

Studied variables	Odds ratio	P-value	95% C.I	
			Lower	Upper
Hb (gm/dl)	0.189	0.37	0.94	1.83
Platelet (103)	1.10	0.018*	1.00	1.01
Bilirubin (mg/dl)	0.056	0.28	0.955	1.17
Albumin (gm/dl)	2.14	0.03*	0.93	5.27
AFP (ng/mL)	0.044	0.82	0.651	1.40
blood ammonia (µ/dL)	0.950	0.003**	0.918	0.983
Child-Pugh score	1.35	0.03*	1.10	1.69
MELD score	0.802	0.005**	0.687	0.937
FIB 4	0.015	0.388	0.432	1.56
Liver diameter (cm)	0.272	0.13	0.921	1.87
Spleen diameter (cm)	1.79	0.019*	1.10	2.93
Portal vein diameter (mm)	2.06	0.001**	1.10	4.35
APRI score	0.210	0.63	0.310	1.02

Significance level at p-value <0.05 **: High significant test *Significant
Hb: hemoglobin, AFP: Alpha-fetoprotein, MELD: Model for End-Stage Liver Disease, FIB-4: Fibrosis-4, APRI score: ALT to platelet ratio score

Table 7 - Multivariate logistic regression analysis for detection of independent predictors for esophageal varices bleeding

Studied variables	Odds ratio	P-value	95% C.I	
			Lower	Upper
Hb (gm/dl)	0.240	0.002**	0.676	0.914
Platelet (103)	0.011	0.12	0.997	1.02
Bilirubin (mg/dl)	0.075	0.49	0.748	1.15
Albumin (gm/dl)	0.66	0.99	0.16	2.33
AFP (ng/mL)	0.472	0.06	0.981	2.61
Blood ammonia (µ/dL)	0.005	0.09	0.989	1.00
Child-Pugh score	0.89	0.35	0.53	1.44
FIB 4	1	0.45	0.88	1.12
MELD score	1.84	0.026*	1.07	3.16
Liver diameter (cm)	2.48	0.001**	0.019	0.370
Spleen diameter (cm)	0.029	0.82	0.752	1.25
Portal vein diameter (mm)	0.108	0.79	0.395	2.03
APRI score	0.137	0.37	0.849	1.54

Significance level at p-value <0.05 **: High significant test *Significant inf: infinity. Hb: hemoglobin, AFP: Alpha-fetoprotein, MELD: Model for End-Stage Liver Disease, FIB-4: Fibrosis-4, APRI score: ALT to platelet ratio score

groups as regards Child-Pugh score. They reported that the mean of Child-Pugh score was 6.1 in the cirrhotic group with mild EV, in group with moderate EV was 7.8, and in group with severe EV was 10.6.

In the current study, portal vein diameter in groups A and B was significantly higher than group C. In a cross-sectional study by El-Kalla and his colleagues (8) on 381 cirrhotic patients. They found that portal vein diameter was significantly higher in patients with EV. On the contrary of our results, they found that splenic longitudinal diameters were significantly higher in patients with EV. Also, Esmat and his colleagues (15) found a high statistically significant correlation between the presence and grade of oesophageal varices with the splenic diameter.

In the current study, blood ammonia was significantly higher in group A and B than group C and D. Ali and his colleagues (16). found that the mean values of blood ammonia in cirrhotic groups were (111.9± 39.1) umol/L while it was 45.5±4.4 umol/L in the control group. Another study by Deng and his coworkers (17). concluded that APRI and FIB-4 scores had a modest diagnostic accuracy of EVs in liver cirrhosis. Where the sensitivity of APRI and FIB-4 was 68%, 67%, respectively, and the specificity was 46% for both. This agrees with our results, that indicates Child-Pugh score showed a sensitivity of 95%. While MELD score showed a sensitivity of 85%. In addition, the APRI score showed a sensitivity of 79%. While the FIB-4 score showed a sensitivity of 85%. Also, Tarzamni and his colleagues (18) found that there are 2 independent factors to predict the presence of esophageal varices in patients with compensated liver cirrhosis: portal hypertensive index >2.08 and spleen longitudinal diameter >15.05 cm. This was near to the findings of Sarangapani and his colleagues (19) who found that splenic vein diameter equal to or above 11.5 mm can predict the presence of esophageal varices in patients with chronic liver disease. These agree with the current study revealed that platelet, albumin, blood ammonia, Child-Pugh score, MELD score, spleen diameter, and portal vein diameter are significant predictors for the presence of esophageal varices. In addition to, Rani and his colleagues (20). reported that increased splenic size and portal vein diameter were significantly associated with the presence of EVs and their values correlated with the increasing size of varices. It was a predictor for esophageal varices bleeding. This in the line with our study, that found hemoglobin level, MELD score, and liver diameter are predictors for esophageal varices bleeding.

CONCLUSION

Blood ammonia was significantly higher in cirrhotic patients with esophageal varices than in patients without esophageal varices, blood ammonia has 86% sensitivity and 80% specificity for the prediction of the presence of esophageal varices and blood ammonia level is a valuable, simple noninvasive marker for the prediction of the presence of esophageal varices but not the risk of bleeding.

Ethical consideration

All participants were volunteers. All of them signed written informed consent with explaining the aim of the study before the study initiation. Approval of the study protocol was obtained by the Ethical Scientific Committee of Menoufia University.

Conflict of interest

The authors declare no conflicts of interests.

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