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Pattern and Prevalence of Different Complications of Liver Cirrhosis in Medical Intensive Care Unit of Zagazig University Hospitals

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ABSTRACT

Background: Cirrhosis is a common outcome of chronic liver disease (CLD). Research on the effects of liver cirrhosis complications in intensive care units (ICU) are still poor and inadequate in Egypt.

Objective: The aim of the present study was to determine pattern, prevalence, and prognostic significance of liver cirrhosis complications in ICU patients.

Patients and methods: The study included 303 patients with CLD at medical ICU in Zagazig university hospitals. All participants in this study were subjected to full history, thorough clinical examination, laboratory investigation, upper GIT endoscopy and radiological investigations. Assessment of liver disease severity including child-Pugh score and MELD score were performed. Deaths from complications of cirrhosis, progressive liver failure and hepatocellular carcinoma were considered to be liver related.

Results: The least frequent complication (3.3%) for CLD disease among the studied population was hepatorenal syndrome (HRS). Mortality rates were higher in patients with the age group of 63-73 years, in male patients and in those who were from rural areas. Higher levels of ALT, AST, PTT, INR, serum creatinine and BUN were associated with higher incidence of mortality. Coagulopathy and hyponatremia were the most common causes of death, followed by variceal bleeding and ascites. Length of hospital stay and fresh frozen plasma (FFP) transfusion, could predict the in-hospital mortality. **Conclusion:** CLD is a universal problem and considered as one of the most challenging health problem in Egypt. End-stage liver disease leads to a rise in morbidity and mortality. Coagulopathy was the most common complication for CLD. Length of hospital stay and FFP transfusion were good predictor for in-hospital mortality.

Keywords: Liver Cirrhosis, ICU, Risks, Complications**.**

INTRODUCTION

Hepatocellular necrosis increased connective tissue, hepatic regeneration, nodular development, and fibrotic tissue all contribute to the significant degeneration of the hepatic morphological components that characterize hepatic cirrhosis, a degenerative illness. Cirrhosis of the liver is a major financial burden on the healthcare system and a frequent cause of morbidity and mortality [(1)].

Cirrhosis, which results from chronic liver disease, is most frequently brought on by hepatitis C virus (HCV), alcoholic liver disease, and non-alcoholic steatohepatitis. The most common causes of cirrhosis are hepatitis B virus (HBV) and HCV. Cirrhosis can also result from autoimmune hepatitis, primary biliary cholangitis, and hemochromatosis [(2)].

Complicating factors brought on by impaired hepatocellular function include hepatic encephalopathy, spontaneous bacterial peritonitis, and abnormal coagulation. Variceal hemorrhage, hepatorenal syndrome (HRS), and hepatopulmonary syndrome are consequences of portal hypertension. Hepatocellular carcinoma (HCC) is the last cirrhosis-related consequence [(1)]. Hepatic encephalopathy (HE), a common neurologic complication of cirrhosis, is considered to affect between 30 and 70% of cirrhotic people [(3)].

HE is a neurological or cognitive complication brought on by liver disease or portosystemic shunting. Clinical disorders range widely, from mild cognitive impairments to coma [(4)]. When the PNL in the paracentesis fluid was more than 250/mm3, it was possible to diagnose spontaneous bacterial peritonitis [(1)]. Hospitalization rates for people with cirrhosis and ascites range from 7% to 30%, according to reports [(5)].

One of the most dangerous adverse effects of liver cirrhosis with portal hypertension is esophageal variceal hemorrhage. From 8 to 35% of patients will experience bleeding over the first two years of follow-up. The size of the varices, the level of liver failure (Child-Pugh score), the rise in the hepatic venous wedge pressure gradient (HVPG), and the presence of mucosal red signals found during endoscopy all affect the risk of the initial variceal bleeding [(6)].

HRS frequently involves ascites and portal hypertension. Decompensated cirrhosis patients commonly have renal impairment, which affects 20% of hospitalized patients [(7)].

HCC is the main liver cancer with the greatest incidence rate. It is becoming more common and is closely related to chronic liver disease. Cirrhosis is the main risk factor for this malignancy. In 2012, the number of cancer cases recorded globally reached an all-time high of 14 million; during the following 20 years, that figure is anticipated to increase to 22 million [(8)]. Regrettably, there is a significant knowledge vacuum about the epidemiology of the liver cirrhosis complication in Egypt, which has to be filled. The current study aimed to evaluate pattern, frequency and risks of complications of liver cirrhosis in medical intensive care unit (ICU) of Zagazig University Hospitals.

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PATIENTS AND METHODS

A cross-sectional study was carried out on cirrhotic patients at medical ICU of Zagazig University Hospitals. The current study has been conducted in period between September 2019 and February 2020.

Inclusion criteria: Adult patients above 18 years, both genders, who diagnosed with liver cirrhosis.

Exclusion criteria: Patients with ascites due to tuberculosis or malignancy, patients with malignancies other than hepatocellular carcinoma were excluded from this study.

All participants in this study were subjected to:

1) Full history and clinical examination according to included work sheet:

All patients were asked about current symptomatology including abdominal pain, anorexia, fatigue, vomiting, fever, dizziness, altered conscious level, oliguria, abdominal distension, hematemesis, melena and bleeding tendency. Past history included diabetes mellitus, hypertension, hepatotoxic drugs and operations. General examination: for signs of CLD including: jaundice, pallor, leukonychia, lower limb edema, gynecomastia, palmar erythema, spider nevi and parotid enlargement. Abdominal examination included hepatomegaly, splenomegaly and ascites. Recorded complications included ascites, spontaneous bacterial peritonitis (SBP), variceal bleeding, HE, hyponatremia, infection, hepatic hydrothorax, HRS, hepatopulmonary syndromes, HCC and death.

2) Laboratory investigations: An automatic blood meter was used to count all the blood [(9)]. Liver function tests (ALT, AST, ALPH, and GGT) were measured calorimetrically using a Dialap auto analyzer for serum total protein and albumin, total and direct bilirubin, and liver enzymes [(10)]. Blood urea nitrogen and serum creatinine were measured calorimetrically using a Dialap auto analyzer for kidney function assays [(11)]. Virus-marker serological test: ELISA, an enzyme-linked immunosorbent test technology, is used to measure HBV and HCV antibodies [(12)].

Also, Alpha-feto protein (AFP), coagulation profile (PTT and INR), ESR, serum electrolytes (sodium, potassium, serum copper, and serum ferritin) were measured. AMA, ANA, LKMA, and ASMA, are examples of autoimmune markers used to diagnose auto immune hepatitis. For the purpose of diagnosing spontaneous bacterial peritonitis, ascetic fluid must undergo physical, biochemical, WBC (total and differential) and RBC counting analysis.

3) Upper GIT endoscopy for variceal bleeding.

4) Radiological investigations: Computed tomography (CT) or magnetic resonance imaging (MRI) in suspicion of liver cancer. Pelvi-abdominal ultrasound: with special stress on liver (size, texture, border, homogeneity, periportal thickening, hepatic veins and pattern); focal lesion (number, site, size, echogenicity, shape, and neovascularization)

- Portal vein: diameter, patency, direction of flow, respiratory variation and velocity by color Doppler assessment.
- Spleen: size, diameter of splenic vein, collaterals.

5) Other investigations that were done during stay in ICU when needed.

Operational design:

With an ultrasound, CT, or MRI, the presence of coarse echoes and a nodular liver contour were employed to determine the existence of cirrhosis. The primary doctor identified the cause of the patient's cirrhosis based on the clinical history, serology, and biochemistry. Cirrhosis was classified as being caused by either chronic hepatitis B (CHB) or chronic hepatitis C (CHC) based on the presence of anti-HCV IgG or hepatitis B surface antigen (HBsAg), respectively. Alcoholic liver cirrhosis was identified in patients who consumed more than 20 units of alcohol per week for males and 14 units per week for women. In the absence of considerable alcohol usage and other co-occurring chronic liver disease causes, hepatic steatosis on imaging was utilized to diagnose non-alcoholic fatty liver disease (NAFLD).

Anti-mitochondrial antibodies (AMA) that were positive allowed for the diagnosis of primary biliary cirrhosis (PBC). Autoimmune hepatitis (AIH) was diagnosed using anti-liver antibodies such as ANA, ASMA, LKMA, and elevated globulin percentage. Wilson's condition was identified using clinical symptoms, low serum caeruloplasmin, positive Kayser-Fleishcer rings, and elevated 24-hour urine copper, if these tests were available. The patient was identified as having cryptogenic liver cirrhosis despite the fact that all of the aforementioned tests came back negative, there was no evidence of excessive alcohol intake, and there were no radiological symptoms of hepatic steatosis. A dual etiology was considered when two etiological causes had an equal contribution.

Assessment of liver disease severity:

Severity of liver disease was assessed using length of stay in hospital. In addition, Child-Pugh, MELD and MELD-sodium scores were calculated on the basis of laboratory values obtained within 24 h of admission.

Child-Pugh score:

It included two continuous variables (bilirubin and albumin) and three discrete variables (ascites, encephalopathy and international normalized ratio [INR])**.** The score was divided into three classes: 5-6 points ⇒ Class A & 7-9 points ⇒ Class B& 10-15 points ⇒ Class C.

MELD score: The formulas used for the calculations were as follows:

MELD score = 3.78 × ln (serum bilirubin [mg/dL]) + 11.2 × ln (INR) + 9.57 × ln (serum creatinine [mg/dL]) + 6.43**.** MELD-Na score = MELD score + 1.59 (135 – Na) with maximum and minimum Na values of 135 and 120 m.mol/L, respectively. MELD score ranges from 6 to 40 but extremes can become apparent. The 3-month mortality prediction is listed below [(13)]. MELD score > 40 ⇒ 71.3% mortality; MELD score 30–39 ⇒ 52.6% mortality; MELD score 20–29 ⇒ 19.6% mortality; MELD score 10–19 ⇒ 6.0% mortality; MELD score < 9 ⇒ 1.9% mortality.

In addition, all therapeutic interventions were recorded, including abdominal paracentesis, endoscopic intervention, mechanical breathing, hemodialysis, and transfusions of blood, platelets, and fresh frozen plasma (FFP). Liver-related deaths included those brought on by cirrhosis complications, progressive liver failure, and HCC.

Ethical Consideration:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University. Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical Package for Social Sciences (SPSS) version 20 for Windows was used to code, process, and analyse the obtained data (IBM SPSS Inc, Chicago, IL, USA).

Using the Shapiro Walk test, the distribution of the data was examined for normality. Frequencies and relative percentages were used to depict qualitative data. To determine differences between two or more sets of qualitative variables, use the chi square test (X^2). Quantitative information was presented as mean± SD. Two independent groups of normally distributed variables were compared using the independent samples t-test (parametric data). P value less than 0.05 was regarded as significant.

RESULTS

Table 1 summarizes the different complication according to the etiology of CLD. HBV and HCV were the most frequent etiological factors for CLD among the studied patients.

Table (1): Complications of liver cirrhosis according to etiology (n=303).

Variable	HBV (n=42)	HCV (n=195)	HBV + HCV (n=10)	AIH (n=7)	PBC (n=5)	PSC (n=2)	NASH (n=31)	Hemochromatosis (n=1)	Wilson's disease (n=1)	Cryptogenic (n=9)
Ascites	18 (42.8%)	70 (35.8)	1 (10%)	4 (57.2%)	0 (0%)	1 (50%)	11 (35.4%)	0 (0%)	0 (0%)	4 (44.4%)
HE (grade)	8 (19%)	65 (33.3%)	3 (30%)	2 (28.6%)	0 (0%)	1 (50%)	14 (45.1%)	1 (100%)	0 (0%)	1 (11.1%)
SBP	10 (23.8%)	36 (18.5%)	1 (10%)	0 (0%)	0 (0%)	0 (0%)	4 (12.9%)	0 (0%)	0 (0%)	2 (22.2%)
Infection	15 (35.7%)	67 (34.4%)	2 (20%)	0 (0%)	1 (20%)	0 (0%)	9 (29%)	1 (100%)	1 (100%)	5 (55.6%)
Hepatic hydrothorax	7 (16.7%)	62 (31.8%)	6 (60%)	0 (0%)	1 (20%)	1 (50%)	16 (51.6%)	1 (100%)	1 (100%)	3 (33.3%)
HRS	3 (7.1%)	6 (3.1%)	1 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Esophageal varix	13 (30.9%)	66 (33.8%)	4 (40%)	0 (0%)	3 (60%)	1 (50%)	5 (16.1%)	0 (0%)	0 (0%)	5 (55.5%)
Gastric varix	3 (7.1%)	22 (11.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Variceal bleeding	18 (42.8%)	100 (51.2%)	5 (50%)	0 (0%)	2 (40%)	1 (50%)	14 (45.1%)	1 (100%)	0 (0%)	6 (66.7%)
Intractable Ascites	9 (21.4%)	38 (19.5%)	1 (10%)	1 (14.3%)	0 (0%)	0 (0%)	6 (19.4%)	0 (0%)	0 (0%)	0 (0%)
Coagulopathy	27 (64.3%)	114 (58.5%)	4 (40%)	3 (42.9%)	2 (40%)	2 (100%)	16 (51.6%)	1 (100%)	0 (0%)	2 (22.2%)
Portal vein thrombosis	12 (28.6%)	66 (33.8%)	2 (20%)	1 (14.3%)	0 (0%)	0 (0%)	9 (29%)	1 (100%)	0 (0%)	3 (33.3%)
Hyponatremia	14 (33.3%)	83 (42.6%)	5 (50%)	1 (14.3%)	0 (0%)	1 (50%)	12 (38.7%)	1 (100%)	0 (0%)	3 (33.3%)
HCC	5 (11.9%)	56 (28.7%)	3 (30%)	0 (0%)	1 (20%)	0 (0%)	5 (16.1%)	1 (100%)	1 (100%)	3 (133.3%)

There was no significant difference between surviving and dead as regard sex, residence, smoking and co-morbidities. However, patients with age of 63-73 years and age of 43-53 years had higher significant death rate **(Table 2).**

Table (2): Clinical outcomes of study populations according to baseline characteristics.

Patients	Surviving (n=198)	Dead (n=105)	Test	P-value
Age groups of patients				
≤23-33	0 (0%)	3 (2.9%)		
33-43	14 (7.1%)	4 (3.8%)		
43-53	46 (23.2%)	27 (25.7%)	χ^2 13.51	0.019 (S)
53-63	66 (33.3%)	21 (20%)		
63-73	52 (26.3%)	37 (35.2%)		
≥73	20 (10.1%)	13 (12.4%)		
Sex				
Male	120 (60.6%)	64 (61%)	χ^2 0.003	0.95 (NS)
Female	78 (39.4%)	41 (39%)		
Residence				
Rural	124 (62.6%)	69 (65.7%)	χ^2 0.282	0.595 (NS)
Urban	74 (37.4%)	36 (34.3%)		
Smoking				
No	116 (58.6%)	69 (65.7%)	χ^2 1.461	0.226 (NS)
Yes	82 (41.4%)	36 (34.3%)		
Co-morbidities				
DM	79 (39.9%)	34 (32.4%)	χ^2 1.65	0.198 (NS)
HTN	46 (23.2%)	33 (31.4%)	χ^2 2.38	0.122 (NS)
Renal	12 (6.1%)	7 (6.7%)	χ^2 0.043	0.836 (NS)

P ≤0.05 is significant.

No difference between surviving and dead as regard etiology of liver cirrhosis. While dead had a significant higher incidence of renal dialysis and fresh frozen plasma transfusion requirement. Otherwise surviving had a significant higher requirement of endoscopic band ligation **(Table 3)**. Dead has significant higher levels ALT, AST, PTT, serum creatinine and platelets **(Table 4)**.

Table (3): Clinical outcomes of study populations according to etiology and procedures.

Variable	Surviving (n=198)	Dead (n=105)	Test	P-value
Etiology				
HBV	27 (13.6%)	15 (14.3%)		
HCV	126 (63.6%)	69 (65.7%)		
HBV + HCV	7 (3.5%)	3 (2.9%)		
AIH	3 (1.5%)	4 (3.8%)		
1ry biliary cirrhosis	5 (2.5%)	0 (0%)	χ^2 7.69	0.565 (NS)
1ry sclerosing cholangitis	1 (0.5%)	1 (1%)		
NASH	21 (10.6%)	10 (9.5%)		
Hemochromatosis	0 (0%)	1 (1%)		
Wilson's disease	1 (0.5%)	0 (0%)		
Cryptogenic	7 (3.5%)	2 (1.9%)		
Alcoholic	0 (0%)	0 (0%)		
Procedures during admission & medication				
Abdominal paracentesis	51 (25.8%)	24 (22.9%)	χ^2 0.309	0.578 (NS)
Endoscopic bandage	69 (34.8%)	23 (21.9%)	χ^2 5.42	0.019 **(S)**
Mechanical ventilation	4 (2%)	3 (2.9%)	χ^2 0.212	0.64 (NS)
Renal dialysis	3 (1.5%)	6 (5.7%)	χ^2 4.18	0.040 **(S)**
Blood transfusion	57 (28.8%)	27 (25.7%)	χ^2 0.322	0.57 (NS)
Platelet transfusion	3 (1.5%)	0 (0%)	χ^2 1.602	0.20 (NS)
Fresh frozen plasma transfusion	108 (54.5%)	72 (68.6%)	χ^2 5.579	0.018 **(S)**
Vasopressor	39 (19.7%)	27 (25.7%)	χ^2 1.453	0.228 (NS)

Table (4): Clinical outcomes of study populations according to laboratory findings.

Laboratory	Surviving (n=198)	Dead (n=105)	Test	P-value
Albumin (g/dL)	2.6 ± 0.5	2.49 ± 0.5	t -1.7	0.36 (NS)
Total Bilirubinl (mg/dL)	2.99 ± 0.7	2.88 ± 0.3	t 0.503	0.64 (NS)
Direct Bilirubinl (mg/dL)	2.51 ± 0.42	2.68 ± 0.51	t 0.348	0.32 (NS)
ALT(IU/L)	63.3 ± 14.1	103.6 ± 22.36	t 1.95	<0.001 (S)
AST(IU/L)	104 ± 23.22	264 ± 63.21	t 1.74	<0.001 (S)
AFP (ng/ml)	7500 ± 155	7220 ± 125	t -0.042	0.56 (NS)
PTT(sec)	40 ± 9.0	40.5 ± 8.31	t 0.404	0.045 (S)
INR	1.63 ± 0.37	1.56 ± 0.36	t -0.93	<0.001 (S)
Creatinine (mg/dL)	1.53 ± 0.32	1.52 ± 0.33	t -0.053	0.012 (S)
BUN (mg/dL)	41.53 ± 10.01	41.17 ± 9.91	t -0.092	0.005 (S)
GGT(u/Dl)	42 ± 10.01	41.1 ± 10.0	t -0.57	0.93 (NS)
ALPh (Iu/l)	110 ± 25.3	109.2 ± 24.32	t -0.163	0.18 (NS)
RBCS(10^3)	4.7 ± 1.02	4.63 ± 1.07	t - 0.454	0.23 (NS)
Hemoglobin(g/dL)	9.26 ± 1.9	9.41 ± 1.86	t 0.634	0.74 (NS)
WBCS(10^3)	10.44 ± 1.8	10 ± 2.21	t - 0.637	0.08 (NS)
Platelets(10^3)	117.1 ± 25.1	117.6 ± 26.2	t 0.05	0.016 (S)

There was no significant difference between surviving and dead as regard imaging findings **(Table 5)**.

Table (5): Clinical outcomes of study populations according to imaging findings.

Variable	Surviving (n=198)	Dead (n=105)	Test	P-value
Liver				
Enlarged	113 (57.1%)	70 (66.7%)	χ^2	0.074
Coarse	74 (37.4%)	34 (32.4%)	5.2	(NS)
Cirrhotic	11 (5.6%)	1 (1%)		
Spleen (size)				
Normal	115 (58.1%)	57 (54.3%)		
Mild	40 (20.2%)	23 (21.9%)	χ^2	0.227
Moderate	31 (15.7%)	23 (21.9%)	4.33	(NS)
Huge	12 (6.1%)	2 (1.9%)		
Ascites				
No	133 (67.2%)	67 (63.8%)	χ^2	0.49
Mild	18 (9.1%)	6 (5.7%)	2.4	(NS)
Moderate	31 (15.7%)	20 (19%)		
Marked	16 (8.1%)	12 (11.4%)		
Focal lesion (U/S)				
No	169 (85.4%)	85 (81%)	χ^2	0.323
Yes	29 (14.6%)	20 (19%)	0.977	(NS)
Focal lesion (CT/MRI)				
No	174 (87.9%)	94 (89.5%)	χ^2	0.67
Yes	24 (12.1%	11 (10.5%)	0.181	(NS)

Regarding severity assessment parameters, deaths were highly significant among hospitalized patients who stayed for 2-5 days **(Table 6)**. In univariate logistic regression, length of hospital stay, Child Turcot Pugh, FFP transfusion, endoscopic bandage, ascites and hepatic encephalopathy could predict hospital mortality among CLD patients however after adjustment in multivariate model, only LOS, and FFP transfusion seem to be better predictors for in-hospital mortality **(Table 7)**.

Table (6): Clinical outcomes of study populations according to severity assessment parameters.

	Variable	Surviving (n=198)	Dead (n=105)	Test	P-value
Length of stay (LOS)	1 day 2-5 days 5-13 days ≥ 13 days	33 (16.7%) 72 (36.4%) 63 (31.8%) 30 (15.2%)	15 (14.3%) 78 (74.3%) 9 (8.6%) 3 (2.9%)	χ^2 45.3	<0.0001 **(S)**
CTP	A B C	19 (9.6%) 116 (58.6%) 63 (31.8%)	7 (6.7%) 52 (49.5%) 46 (43.8%)	χ^2 4.44	0.108 (NS)
	MELD	15 (5-42)	15 (7-36)	MW 10266.5	0.85 (NS)

Table (7): Predictors of in hospital mortality among patients with liver cirrhosis.

Variables	Univariate				Multivariate			
	Coefficients β	Std. Error	OR	P-value	Coefficients β	Std. Error	OR	P-value
Age	0.004	0.01	1.004	0.697 (NS)	--	--	--	--
Sex	-0.014	0.155	0.986	0.953 (NS)	--	--	--	--
HBV	0.154	0.355	1.01	0.968 (NS)	--	--	--	--
HCV	0.139	0.355	0.986	0.291 (NS)	--	--	--	--
HBV + HCV	-0.245	0.706	0.783	0.729 (NS)	--	--	--	--
Autoimmune hepatitis	0.89	0.78	2.43	0.253 (NS)	--	--	--	--
1ry biliary cirrhosis	-20.04	8255.16	0.0001	0.998 (NS)	--	--	--	--
1ry sclerosing cholangitis	0.60	1.422	1.83	0.672 (NS)	--	--	--	--
NASH	-0.14	0.412	0.87	0.735 (NS)	--	--	--	--
Hemochromatosis	20.724	14201	0.0001	0.999 (NS)	--	--	--	--
Wilson's disease	-20.04	18459	0.0001	0.991 (NS)	--	--	--	--
Cryptogenic	-0.651	0.816	0.522	0.425 (NS)	--	--	--	--
HE	-0.536	0.256	1.71	**0.03 (S)**	0.371	0.307	1.45	0.227
SBP	-0.14	0.323	0.869	0.664 (NS)	--	--	--	--
HCC	0.182	0.266	1.20	0.494 (NS)	--	--	--	--
Hydrothorax	0.069	0.257	1.07	0.789 (NS)	--	--	--	--
Infection	-0.474	0.265	0.623	0.07 (NS)	--	--	--	--
HRS	0.658	0.644	1.93	0.308 (NS)	--	--	--	--
Ascites I	-0.517	0.454	0.596	0.255 (NS)	-0.639	0.470	0.528	0.175
II	0.715	0.325	2.04	**0.028 (S)**	0.6	0.358	1.82	0.09
III	0.468	0.412	1.6	0.255 (NS)	0.33	0.449	1.39	0.46
OV I	0.163	0.605	1.18	0.788 (NS)	--	--	--	--
II	-0.504	0.385	0.604	0.189 (NS)				
III	-0.774	0.454	0.461	0.088 (NS)				
IV	-1.21	0.784	0.299	0.124 (NS)				
GV	0.419	0.429	1.52	0.329 (NS)				
Intractable ascites	0.375	0.305	1.46	0.219 (NS)	--	--	--	--
Coaguloapthy	-0.015	0.243	0.985	0.95 (NS)	--	--	--	--
PVT	0.231	0.258	1.259	0.371 (NS)	--	--	--	--
Hyponatremia	0.388	0.245	1.474	0.114 (NS)	--	--	--	--
Paracentesis	-0.158	0.284	0.854	0.58 (NS)	--	--	--	--
Endoscopic bandage	-0.645	0.28	0.52	**0.020 (S)**	-0.34	0.32	0.71	0.293
Mechanical ventilation	0.355	0.773	1.42	0.646 (NS)	--	--	--	--
Renal dialysis	1.37	0.717	3.93	0.0561 (NS)	--	--	--	--
Blood trans	-0.155	0.273	0.856	0.57 (NS)	--	--	--	--
Platelet transfusion	-19.0	6464	0.001	0.997 (NS)	--	--	--	--
FFP Transfusion	0.59	0.254	1.81	**0.0186 (S)**	0.527	0.262	1.69	**0.045 (S)**
Vasopressor	0.344	0.285	1.41	0.228 (NS)	--	--	--	--
Length of stay (LOS)								
2-5 days	-0.86	0.351	2.38	**0.0135 (S)**	0.981	0.375	2.67	**0.009 (S)**
5-13 days	1.157	0.473	0.3143	**0.0145 (S)**	-1.12	0.491	0.33	**0.023 (S)**
≥ 13 days	-1.57	0.68	0.220	**0.026 (S)**	-1.52	0.7	0.218	**0.029 (S)**
CTP	0.410	0.203	1.5	**0.043 (S)**	0.04	0.266	1.04	0.88
MELD	0.0001	0.017	1	0.99 (NS)	--	--	--	--

DISCUSSION

CLD is a global issue, and local epidemiology data revealed regional variations. The health officials in Egypt view CLD as one of the most difficult health issues. During the course of a decade, the number of CLD patients has doubled [14]. Morbidity and mortality associated with end-stage liver disease increase, and the majority of avoidable cases are ascribed to viral hepatitis, NAFLD, or alcohol use [15].

The purpose of the current study is to illustrate the status of CLD in ICU at Zagazig University Hospital. Deep understanding of these issues can help in customization of the efforts exerted to face CLD and its complications in different countries especially large country like Egypt.

The study included 303 patients with chronic liver disease. The mean age of our patients was 57.67 (SD 11) years old, with maximum cases in age group was that between 63 to 73 years (29.4%) followed by those aged from 53 to 63 years (28.7%). In a research by **Shrestha *et al.*** [16], 130 patients with liver disease were evaluated; the majority of the patients were between the ages of 41 and 50. In a different research, the average age of people with CLD in India was 49 years old, and the ratio of men to women was 5:1 [17].

Our findings are in agreement with the findings of these studies, since most of the patients were above 40 years of age. This shows that liver diseases are more common after the fourth decade of life in our region. This is most likely due to the fact that liver damage is a chronic condition that takes time to proceed to frank hepatic cirrhosis [17]. In contrast, individuals with cirrhosis in an Italian research had a mean age of 60.3 years and a male to female ratio of 1:7. HCV infection, either by itself or in conjunction with other etiologic agents, was the most frequent cause of cirrhosis (58.6%), followed by HBV (7.6%) and alcohol consumption (16.0%) [18].

The most common complication of cirrhosis in our study was coagulopathy (56.4%), followed by upper GI bleeding (49.1%), hyponatremia (39.6%), ascites (36%), infection (33.3%), esophageal varix (32.4%), hepatic hydrothorax (32%), hepatic encephalopathy (31.3%), portal vein thrombosis (31%), HCC (28.1%), intractable ascites (18.2%), SBP (17.5%), gastric varices (8.3%). The least frequent complication for chronic liver disease among the studied population was HRS (3.3%). Regarding hepatic encephalopathy, 31.3% had HE; most of them had grade II (11.2%). In addition, 32.4% had esophageal varices, most of them had grade II (13.5%). In contrast to **Topdagi *et al.*** [1], who observed that spontaneous bacterial peritonitis (42%) and hepatic encephalopathy (26%), ascites was the most frequent consequence (83%) and was followed by esophageal hemorrhage (56%) and ascites.

The research **Acharya *et al.*** [17] found that jaundice (69.00%), ascites (63.15%), upper gastrointestinal hemorrhage (39.18%), hepatic encephalopathy (32.74%), anemia (28.07%), and splenomegaly (25.14%) were the most frequent presentations in CLD patients.

Our findings differ from those of a study carried out in the central region of India, where ascites (76.1%), splenomegaly (52.2%), jaundice (50%) upper gastrointestinal bleeding (32.2%), hepatic encephalopathy (22.2%), thrombocytopenia (16.6%), and hepatorenal syndrome (15%) were the most frequent complications [19].

The most common complication of chronic liver disease in male was coagulopathy (55.4%) followed by upper GI bleeding (54.4%), ascites (38%), hyponatremia (37%) and esophageal varices (35.3%). While, in females, was coagulopathy (58%) followed by hyponatremia (43.7%), variceal bleeding (41.2%), infection (37%), hepatic encephalopathy and ascites (32.8%). There was no statistically significant difference between male and female as regarding complications of liver cirrhosis. **Fabbian *et al.*** [20] found that upper GIT bleeding was more common in males (68%). But **Mohamed *et al.*** [21] reported that spontaneous bacterial peritonitis was more common in females. **Ahmed *et al.*** [22] found that hyponatremia was more common in males (40%).

At age group of 43-53 years, hematemesis was more frequent, while hematemesis and melena were common in age group >73 years. Hepatic hydrothorax was frequent in 53-63 years. However, at age group of 23-33 years intractable ascites was commonest. SBP was frequent in age group of 33-43 years, while hyponatremia was common in 63-73 years. Coagulopathy was frequent among age group of 43-53 years. In a study by **Fabbian *et al.*** [20] found upper GIT bleeding was more common in age group <55 years. With **Mohamed *et al.*** [21] reported spontaneous bacterial peritonitis was frequent in age group 55-65. Also, **Ahmed *et al.*** [22] found that hyponatremia was more common in 18-36. **Hou *et al.*** [23] reported that hepatic hydrothorax was more common in age group >55 years. In a study by **Ennaifer *et al.*** [24] intractable ascites was common in age group 53-63 years**.**

The current study had 105 (34.7%) patients inpatient mortality. Mortality rates were higher in patients with the age group of 63-73 years, in male patients and those from rural areas. In a study conducted by **Acharya *et al.*** [17] mortality rates were higher in the age group >40 years, in male patients and those from urban areas. End-stage liver disease leads to a rise in morbidity and mortality. The development of liver fibrosis and subsequent cirrhosis is driven by ongoing liver injury for long time to be decompensated. In addition, the non-survived group was found to have higher levels of ALT, AST, PTT, INR, serum creatinine, BUN, and platelets than the survived group.

In a research by **Acharya *et al.*** [17], it was discovered that the non-survived group had higher WBC, total serum bilirubin, ALT, AST, creatinine, and INR

values, had lower salt levels, platelet levels, and serum albumin levels than the group that lived.

Liver decompensation occurred in the non-survivor group, which resulted in increased blood bilirubin from inability to excrete bilirubin, liver enzymes, high bleeding susceptibility from reduced synthesis of coagulation components, and thrombocytopenia [17].

According to our study, patients who were hospitalized for 2 to 5 days had greater fatality rates; children who scored B had the greatest rates. Child scores C had the greatest mortality levels, according to a research by **Peng *et al.* [25],** which revealed that patients with longer hospital stays had a higher mortality rate. This discrepancy could be caused by the high proportion of instances scoring B as opposed to C.

Regarding the pathogenesis of liver cirrhosis, HCV (65,7%), HBV (14,3%), and NASH (9.5%) were the 3 leading causes of death. Alcohol was shown to be the leading cause of death in a research by **Acharya *et al.* [17],** followed by hepatitis B and auto immune hepatitis (12.5%). This discrepancy resulted from the fact that HCV is more common in our nation whereas alcohol use is more common in Europe and the United States.

In our study, coagulopathy (56.2%) and hyponatremia (45.7%) were the most common cause of death, followed by variceal bleeding (41.9%) and ascites (41%). HRS and gastric varix were less common cause and seen in a total of (13.9%) mortalities.

Independent of the MELD score, hyponatremia has been found to be a factor linked to liver-related mortality [26]. Earlier attempts to add serum sodium to the MELD score led to predictions of death that were more accurate than those that used the MELD score alone [27].

Septicemia (44%) was the leading cause of mortality in a research by **Juneja *et al.* [28]** followed by hepatic encephalopathy (22%), and upper GIT hemorrhage (15.2%). The greater sample size in our study and the rise in hematemesis and melena cases from bilharziasis, HCV, and HBV in Egypt may be to blame for this discrepancy.

We found that, most common procedures used in survived patients were fresh frozen plasma (54.5%), endoscopic bandage (34.8%) and blood transfusion (28.8%), while in dead people were fresh frozen plasma (68.6%), vasopressors and blood transfusion (25.7%). In contrast, a research by **Levesque *et al.* [29]** found that mechanical breathing (52%) and Molecular Adsorbant Recirculation System (25%) were the most often utilized treatments in patients who lived, followed by vasopressors (14.5%) and hemodialysis (4%). This might be as a result of the high incidence of hematemesis and melena among our patients, which are brought on by splenomegaly and portal hypertension.

In univariate logistic regression, length of hospital stay, Child-Turcotte Pugh (CTP), FFP transfusion, endoscopic bandage, ascites and hepatic encephalopathy could predict in-hospital mortality among CLD patients. With further multivariate logistic regression, length of stay, FFP transfusion could predict. Age > 60 years, ischemic heart disease, diabetes mellitus, chronic obstructive pulmonary disease, chronic kidney disease, HBV, HCV, acetaminophen, malignant infiltration, renal failure, septicemia, pneumonia, and UTI were revealed to be mortality predictors in a research by **Thanapirom *et al.* [30].** Moreover, there were several occurrences of pulmonary, heart, chest, and urinary tract infections.

CONCLUSION

CLD is a universal problem and considered as one of the most challenging health problem in Egypt. End-stage liver disease leads to a rise in morbidity and mortality. HCV was the most common etiology for CLD. Coagulopathy was the most common complication for CLD. Length of hospital stay and FFP transfusion were good predictor for in-hospital mortality.

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