Risk of Surgery in Patients with Liver Cirrhosis

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Background and aim: Chronic liver disease patients often undergo surgery for indications other than liver transplantation and may face increased perioperative risk due to surgical and anesthesia-related complications. The current study's objectives were to assess the risk of surgery in cirrhotic patients and to identify various variables that influence postoperative outcomes.

Methods: 231 participants underwent non-hepatic surgery under general anesthesia categorized into 117 cirrhotic patients and 114 non-cirrhotic (controls). All participants were subjected to complete clinical and laboratory evaluations (pre-operative, and post-operative) with an assessment of postoperative outcomes. For cirrhotic patients, the severity of liver disease was assessed by Child-Pugh and MELD scores.

Results: In cirrhotic patients, hepatic causes are considerably the cause of not having surgery, additionally, the majority of patients who underwent surgery had Child-Pugh scores of A or B (42.7 % and 44.5%,respectively), whereas only 12.8% had Child-Pugh C. Hepatic complications including HE, decompensation, and SBP were more frequent in patients with CTP grades B and C than those with grade A. Postoperative mortality significantly associated with higher white blood cells (WBCs), serum creatinine, and MELD score (p=0.001, 0.049, and 0.002,respectively), and lower serum albumin (p=0.028). AUC for WBCs, serum creatinine, MELD score, and serum albumin was 0.958, 0.759, 0.963, and 0.765 respectively at cut-off >11.5, >1.2, ≤2.3, and >15 respectively.

Conclusion: Operative complications (hepatic and non-hepatic)are more frequent in patients with CTP grades B and C than those with grade A. Postoperative mortality significantly associated with higher WBCs, serum creatinine, and MELD score, and lower serum albumin.

INTRODUCTION

The final stage of the liver's progressive fibrosis is liver cirrhosis. Liver cirrhosis can result from a variety of assaults, most notably chronic viral hepatitis (HBV and HCV), metabolic disorders, in addition to alcoholic and nonalcoholic steatohepatitis **[1]**. According to estimates, liver cirrhosis ranks as the 13th most common cause of death worldwide. In 2010, it was noticed that liver cirrhosis gave a share in 31 million or 1.2% of global disability-adjusted life years (DALYs). Worldwide, liver cirrhosis was assorted as 23rd leading cause of disease burden **[2]**.

Despite having the highest rate of HCV infection in the world for years, Egypt has made the biggest strides toward the disease's eradication **[3]**. The emergence of highly effective all-oral, interferon free, direct acting antiviral (DAA) medications for patients with cirrhosis has transformed the treatment options for HCV patients and the majority of patients can now achieve viral clearance even with the presence of cirrhosis

Patients with cirrhosis are living longer with more advanced disease thanks to better medical and surgical therapy, despite global increases in the prevalence of chronic liver disease

(CLD) caused by viral hepatitis and nonalcoholic steatohepatitis (NASH). Consequently, they are at risk for other diseases and morbidities that cirrhotic patients might not have previously experienced **[4]**.

Surgery is frequently performed on patients with chronic liver disease for purposes other than liver transplantation, and may face increased perioperative risk due to both anesthesia- and surgery-related issues. In their final two years of life, 10% of patients with severe liver disease need a surgical procedure other than a liver transplant. Surgery may also be performed on people with undiagnosed CLD, with cirrhosis only being identified intraoperatively based on a macroscopic evaluation **[5]** any surgical procedure in undetected cirrhotic patients could have disastrous consequences.

CLD patients undergoing surgery have substantially higher rates of Surgery-related complications and mortality. Additionally, ICU admission, mechanical ventilation, and renal replacement therapy have all been demonstrated to independently increase hospital mortality among patients with CLD **[6]**.

The risk of surgery in patients with liver cirrhosis vary depending on the severity of liver disease, the clinical setting as well as type of surgery. The severity and nature of the underlying CLD as well as the type of surgery have a significant impact on postoperative outcomes. The Child-Turcotte-Pugh (CTP) score has been the primary indicator of surgical risk in cirrhotic patients for over 30 years, but more recent research indicates that the Model for End-Stage Liver Disease (MELD) score may be more accurate **[7]**. The current study's objectives were to assess the risk of surgery in patients with liver cirrhosis and to identify various variables that may influence the outcome of surgery in these patients.

METHODS

This prospective case-control research was carried out in Tropical Medicine and Anesthesia Departments, Faculty of Medicine, Menoufia University in collaboration with El-Helal Orthopedic and General Surgery Hospital, Cairo between September 2019 to March 2021. This study was performed on 231 participants who underwent non hepatic surgery under general anesthesia. Their work up included preoperative evaluation for their fitness of operations, intra operative event and their follow up & outcome after surgery.

Based on the presence or absence of CLD study participants were grouped into one of two groups; **Group I:** included 117 patients with evidence of liver cirrhosis they were 71 (60.7%) males and 46 (39.3%) females with mean age (53.00±24.04) ranging from 36 to 70 and **Group II**: 114 healthy participants without any evidence (clinical, laboratory and imaging) of liver disease as controls, they were 66 (57.9%) males and 48 (42.1%) females with mean age (50.50± 24.75). Preoperative management in patients with established liver illness attempts to identify the underlying cause, optimize liver function by enhancing nutritional status, correct coagulopathy, and treat HE, as well as portal hypertension and ascites.

For all participants, preoperative assessment including history, clinical evaluation, laboratory, and imaging evaluation was performed. History of smoking and other co-morbidities (history of DM and HTN and their treatments) was assessed. Besides, history of upper GIT bleeding (hematemesis, melena or bleeding per rectum) and history of upper GIT endoscopy. Assessment of drug history including antiviral therapy (HCV, HBV), diuretics and medication to control coagulopathy. Full clinical evaluation focusing on signs of liver affection including bleeding tendency, jaundice, edema of lower limbs, and history of hepatic encephalopathy.

Preoperative laboratory evaluation: laboratory investigations comprised complete blood count (CBC), liver function tests [prothrombin time, the international normalized ratio (INR), alanine transferase (ALT), aspartate transferase (AST), serum albumin, total & direct bilirubin], kidney function tests and serum electrolytes. Viral markers including HCV Ab, HBVsAg and HIV Ab were done by ELISA.

Preoperative radiological evaluation: Abdominal ultrasonography was done for all participants for evaluating liver size, ecohopattern and portal vein (diameter and patency), evaluating spleen size, echopattern, focal lesions, and perisplenic collaterals, assessing the presence and grading of ascites, as well as evidence of echoes, adhesions or loculations. Other radiological assessments were required for patients according to type and indication of surgery.

Preoperative assessment of liver disease severity: For cirrhotic patients we estimated liver disease severity by Child-Turcotte-Pugh score (CTP) and MELD scores, we calculated Child-Turcotte-Pugh score (CTP) that depends on assessment of patient's ascites, serum albumin, total bilirubin, prothrombin time and history of hepatic encephalopathy [8], and MELD score was calculated by using the following equation:

MELD = (9.6 × loge [creatinine mg/dl]) + (3.8 × loge [bilirubin mg/dl]) + (11.2 × loge [INR]) + 6.4. [9]

Preoperative classification of surgery: We classified cirrhotic and non-cirrhotic patients regarding time of operative intervention into: elective surgery and emergency surgery. [10]

Intra-operative assessment including: Type of anesthetic agent, Duration of operation, Intra operative complication (bleeding- anoxia, etc…), and Necessity for blood transfusion, number of units, fresh frozen plasma and platelet transfusion during operation.

Post-operative outcome assessment: The need for intensive care unit admission post operatively, clinical assessment for complications which may be either hepatic or non-hepatic complications. Hepatic complications including signs and symptoms of severe hepatic decompensation (hepatic encephalopathy (HE), jaundice, ascites, hematemesis and spontaneous bacterial peritonitis (SBP). Non hepatic complications included chest infection, surgical complications and others. Laboratory assessment post operatively and follow up included CBC, Liver profile including serum bilirubin, ALT, AST, and albumin, Prothrombin time and concentration (PT & PC) and international normalized ratio (INR), blood urea and serum creatinine, serum electrolytes.

Postoperative mortality: Postoperative mortality was reported and was classified into Hepatic causes as a result of sever liver decompensation (Hematemesis, hepatic encephalopathy, SBP and HRS) or non-hepatic causes as chest infection and surgical complications.

Statistical analysis of the data:

Data were collected, tabulated and statistically analyzed using an IBM compatible personal computer with Statistical Package for the Social Sciences (SPSS) version 23 (SPSS Inc. Released 2015. IBM SPSS statistics for windows, version 23.0, Armnok, NY: IBM Corp.). Two types of statistical analysis were performed: Descriptive statistics included, mean (x) and standard deviation (SD) and analytic statistics included chi-square test ($\chi 2$) Student's t-test, Inter-group comparison, P value<0.05 was considered statistically significant.

RESULTS

Based on the presence or absence of CLD study participants were categorized into one of two groups; Group I included 117 patients with evidence of liver cirrhosis and Group II comprised 114 healthy participants without any evidence of liver disease as controls.

Table 1 summarized the comparison between the two studied groups regarding the demographic and clinical data: cirrhotic patients ranged in age between 36- 70 years with a mean age of 53.00±24.04 years and non-cirrhotic patients ranged in age between 33-68 years with a mean age 50.50± 24.75 years. We noticed that the mean of age as well as gender distributions did not differ between the two groups. Smoking history, hypertension, and diabetes mellitus were not significantly different between the two groups in terms of the existence of comorbid disorders (p = 0.974, 0.814, and 0.874 respectively). However, only cirrhotic patients reported history of hepatic encephalopathy (14.5%), hematemesis and/or melena (10.3%) and bleeding from other sites including epistaxis, bleeding gums (8.5%)

Concerning the history of previous upper GIT endoscopy; esophageal Varices and or PHG were reported in 24.8% of cirrhotic patients, and gastritis was notified in 15.4% and 8.8 % in cirrhotic and non-cirrhotic respectively with a statistically significant difference (p <0.001). Regarding the general examination; pallor was considerably different between the two groups (p <0.001). Jaundice, flapping tremors, and lower limb edema were detected in 11.1%, 6.8%, and 29.1% respectively in cirrhotic patients **(table 1).**

Table 1 demonstrates that, ascites was mild to moderate in 12% of cases and massive in 2.6%, whereas 85.4% of cirrhotic patients did not have ascites. Hepatomegaly and splenomegaly were also seen in 53.8% and 63.2% of cases, respectively. Umbilical hernias were more

frequent in cirrhotic patients than in non-cirrhotic patients (p = 0.021).

According to the preoperative laboratory investigations, **table 2 and figures 1A & 1B** reveal that there was a statistically significant difference in Hb concentration, platelet count, ALT, AST, serum albumin, total bilirubin, INR, and blood urea between the cirrhotic and non-cirrhotic patient groups. The cirrhotic group as compared to the non-cirrhotic group, Hb concentration, platelets count, and serum albumin were significantly lower, and ALT, AST, total bilirubin, and blood urea were significantly higher. Regarding the total leucocyte count, serum creatinine, serum Na or serum K, and INR, there was no discernible difference between the patient groups.

The indications for surgery and classification of surgery regarding urgency either elective or emergent of the studied groups were presented in **supplementary table 1.** Regarding patients who underwent surgery or did not, as well as the types of surgery (elective and emergency), there were a statistically non-significant differences between the cirrhotic and non-cirrhotic groups (p>0.05). Even though there were no statistically significant differences between the cirrhotic and non-cirrhotic patients who underwent surgery (operated) or did not (non-operated) (p = 0.074), and their types (elective and emergency), there was still a tendency for cirrhotic patients to be not operated as shown in **supplementary table 2.** In cirrhotic patients, hepatic causes were considerably linked to the explanation of not having surgery **(supplementary table 3).** The Child Pugh score and grading in cirrhotic patients are shown in **figure 1C**. The majority of patients had a Child Pugh score of A or B (42.7 or 44.5, respectively), whereas only 12.8 had a Child Pugh C.

Only cirrhotic patients required preoperative plasma (40.2%) or platelet transfusion (7.84%) or urgent upper endoscopy (9.8%), in addition, preoperative blood transfusion and ICU admission were more common in cirrhotic patients (p < 0.001 and 0.025 respectively). These patients also required urgent intraoperative measures (plasma or platelet transfusion) and postoperative ICU admission (27.45%) **(table 3).** The requirement for post-operative ICU admission was greater in emergency procedures, and there was a statistically significant difference between patients with elective and emergency operations in both cirrhotic and non-cirrhotic groups (p = 0.012 and 0.003, respectively). Additionally, patients with cirrhosis who were merely undergoing emergency procedures needed platelet transfusions. Contrarily, there was no statistically significant difference in the need for intra-operative blood transfusions between patients undergoing elective or emergency procedures in the cirrhotic and non-cirrhotic groups (p>0.05) as displayed on **supplementary table 2**.

According to Table 4, the mean values of TLC, blood urea, and serum creatinine significantly increased in the cirrhotic group while the mean values of serum albumin, INR, and Na significantly decreased post-operatively compared to their pre-operative levels. In non-cirrhotic patients, there was significant increase in mean values of TLC and platelets count with significant decrease in mean values of Hb concentrations and serum Na post-operative compared to pre-operative values, however, no significant changes were noted regarding liver functions **(figures 1D and 1E).**

Regarding the prevalence of post-operative morbidity and mortality, there was a statistically significant difference between the cirrhotic and non-cirrhotic groups (p = 0.016 and 0.048), with more frequent adverse outcomes being detected in the cirrhotic group **(figure 1F).**

Concerning the post-operative health problems in the cirrhotic group, there was a significant difference between patients who underwent elective and emergency procedures, with elective procedures experiencing more frequent complications either hepatic or non-hepatic and only emergency procedures experiencing post-operative mortality. Hepatic complications including HE, decompensation, SBP, and melena were more frequent in patients with Child Pugh grade B and C than those with grade A. In non-cirrhotic patients, there was a statistically non-significant difference between elective and emergency operations regarding post-operative morbidity, but only emergency operations were associated with post-operative mortality **(figures 2A-D).**

Preoperative data from the cirrhotic group were compared between survived and dead patients. We found that the dead patients significantly had higher total leucocyte count, serum creatinine, and MELD score (p 0.001, 0.049, and 0.002, respectively), as well as lower serum albumin (p

= 0.028) as illustrated in **table 5 and figures 2A-D.** Additionally, the ROC curve was applied to identify the sensitivity of each in predicting operative outcome. AUC for total leucocyte count, serum creatinine, MELD score and serum albumin was 0.958, 0.759, 0.963, and 0.765 respectively at cut off >11.5, >1.2, ≤2.3, and >15 respectively **(table 6 and figure 3E).**

Table (1): Demographic data and clinical characteristics (history and examination) of the studied groups.

History and Examination	Cirrhoticgroup (n = 117)		Non-Cirrhotic group (n = 114)		X^2	P value
	No.	%	No.	%		
Sex						
Male	71	60.7	66	57.9	0.186	0.666
Female	46	39.3	38	42.1		
Comorbidity						
Smoking	52	44.44	50	43.86	2.021	0.974
DM	36	30.77	34	29.82	6.034	0.814
HTN	38	32.48	40	35.09	4.011	0.874
History of hepatic encephalopathy	17	14.5	0	0	NA	---
History of GIT bleeding						
Hematemesis and/or melena	12	10.3	0	0	NA	----
Bleeding from other sites	10	8.5	0	0	NA	----
Previous Upper GIT endoscopy						
Esophageal Varices and or PHG	29	24.8	0	0	NA	----
Gastritis	18	15.4	10	8.8	39.334	**<0.001***
Peptic Ulcer	1	0.9	0	0	NA	----
General examinations						
Pallor	17	14.5	5	4.4	20.14	**<0.001***
Jaundice	13	11.1	0	0	NA	---
Flapping tremors	8	6.8	0	0	NA	---
Cutaneous manifestations	40	34.2	0	0	NA	----
Lower limb edema	34	29.1	0	0	NA	----
Conscious state						
Fully conscious	110	94.0	114	100	3.253	0.933
DCL	7	6	0	0		
Local examination Ascites						
No ascites	100	85.4	0	0	NA	---
Mild to moderate	14	12.0	0	0	NA	---
Tense	3	2.6				
Liver						
Hepatomegaly	63	53.8	2	1.8	11.542	**0.035***
Average size	22	18.8	112	98.2		
Shrunken	22	18.8	0	0		
Spleen						
Average size	40	34.2	114	100	13.742	**0.023***
Splenomegaly	74	63.2	0	0		
Huge spleen	3	2.6	0	0		
Hernia						
Inguinal hernia	11	9.4	17	14.90	5.041	0.074
Umbilical hernia	7	5.9	1	0.9	14.312	**0.021***

HTN: Hypertension, DM: diabetes mellitus, DCL: Disturbed conscious level, PHG: Portal hypertensive gastropathy, GIT: gastrointestinal tract, Cutaneous manifestations: including palmar erythema, spider navai, white nails, ecchymosis patches and skin pigmentations. Bleeding from other sites: epistaxis, bleeding gums, X^2 chi-squared, test *significant

Table (2): Pre-operative laboratory investigations of the studied groups.

Pre-operative labs	Cirrhoticgroup (n = 117)	Non- Cirrhotic group (n = 114)	t test	P value
Hb (gm/dl)				
Mean ±SD	9.45±6.43	11.75±5.30	2.470	**0.014***
Range	4.90 – 14	8.0 – 15.50		
Total leucocytic count (**x** 10^9/L)				
Mean ±SD	8.85±8.70	9.75±7.42	1.504	0.134
Range	2.70 – 15.0	4.5 – 15.0		
Platelets (x 10^3 /L)				
Mean ±SD	168.50±178.90	290.0±155.56	5.819	**<0.001***
Range	42.0 – 295.0	180.0 – 400.0		
ALT (U/L)				
Mean ±SD	45.00±58.61	34.50±28.99	U=7.42	**<0.001***
Range	10.0 – 85.0	14.0 – 55.0		
AST (U/L)				
Mean ±SD	87.00±51.76	74.00±79.20	U=5.81	**<0.001***
Range	8.0 – 200.0	18.0 – 130.0		
Serum Albumin (g/dl)				
Mean ±SD	2.65±1.91	4.35±1.20	6.49	**<0.001***
Range	1.30 – 4.00	3.50 – 5.20		
Serum total Bilirubin (mg/dl)				
Mean ±SD	4.25±4.60	1.00±0.42	4.090	**<0.001***
Range	1.00 – 7.50	0.70 – 1.30		
INR				
Mean ±SD	2.45±2.19	1.05±0.21	X^2=1.82	0.078
Range	0.90 – 3.60	0.90 – 1.20		
Blood Urea (mg/dl)				
Mean ±SD	37.50±38.89	14.50±10.61	9.027	**0.002***
Range	10 - 65	7 - 22		
Serum Creatinine (mg/dl)				
Mean ± SD	0.40±0.14	0.95±0.49	0.164	0.910
Range	0.50 – 3.0	0.60 – 1.30		
Serum Na (mmol/L)				
Mean ±SD	131.00±16.97	137.00±9.90	0.064	0.982
Range	119.0 – 143.0	130.0 – 144.0		
Serum K (mmol/L)				
Mean ±SD	3.80±1.41	4.20±1.27	1.315	0.191
Range	2.8 – 4.8	3.3 – 5.1		

Hb: hemoglobin, AST: aspartate aminotransferase, INR: international normalized ratio, PLT: platelet count, ALT: Alanine transaminase t: independent t test U: Mann-Whitney U test *significant

S. Table (1): Indications for surgery (elective or emergency) of the studiedgroups.

Indication of operation	Cirrhotic group (n = 117)		X^2	P value	Non-Cirrhotic group (n = 114)		X^2	P value
	Elective (n= 94)	Emergency (n= 23)			Elective (n=100)	Emergency (n=14)		
	No. (%)	No. (%)			No. (%)	No. (%)		
• **General surgery**								**0.028***
– Cholecystectomy	**49(41.9)**	**6 (5.1)**			**59(59.0)**	**5(35.71)**	**4.16**	----
– Thyroidectomy	12(12.77)	0(0.0)	**10.22**	**<0.001***	17(17.0)	0(0.0)	**NA**	----
– Hernial repair	8(8.51)	0(0.0)	**NA**	----	6(6.0)	0(0.0)	**NA**	----
– Piles operations	16(17.02)	2(8.70)	**NA**	----	18(18.0)	0(0.0)	**NA**	----
– Hemicolectomy	9(9.57)	0(0.0)	**NA**	----	11(11.0)	0(0.0)	**NA**	----
– Exploration:	2(2.13)	0(0.0)	**NA**	----	0(0.0)	0(0.0)	**NA**	
• Perforated PU/vescus			**NA**	----				----
• Intestinal obstruction	0(0.0)	2(8.70)	**NA**	----	0(0.0)	3(21.43)	**NA**	----
• Traumatic splenic tear	0(0.0)	1(4.35)	**NA**	----	0(0.0)	2(14.29)	**NA**	----
– Total hysterectomy	0(0.0)	1(4.35)	**NA**	----	0(0.0)	0(0.0)	**NA**	----
– Splenoctomy for hemolytic anemia	1(1.06)	0(0.0)	**NA**	----	3(3.0)	0(0.0)	**NA**	----
– Breast mass	1(1.06)	0(0.0)	**NA**	----	0(0.0)	0(0.0)	**NA**	
	0(0.0)	0(0.0)	**NA**	----	4(4.0)	0(0.0)	**NA**	----
• **Orthopedic surgery**	**29(30.85)**	**4(17.39)**			**26(26.0)**	**1(7.14)**		
Open RIF for fractures	27(28.72)	4(17.39)	**3.24**	**0.012**	26(26.0)	1(7.14)	**11.32**	**<0.001***
Closed RIF	2(2.13)	0(0.0)			0(0.0)	0(0.0)		
• **Neurosurgery**	**16(17.02)**	**3(13.4)**			**14(14.0)**	**1(7.14)**		
– Lumbar discectomy	10(10.64)	0(0.0)			9(9.0)	0(0.0)		
– Posterolateral lumbar fusion	6(6.38)	0(0.0)	**1.36**	0.564	5(5.0)	0(0.0)	**4.17**	**0.046**
– Post traumatic spine fixation	0(0.0)	3(13.4)			0(0.0)	1(7.14)		
• **Uro-surgery**	**0(0.0)**	**4(17.39)**						
Post traumatic					**0(0.0)**	**0(0.0)**		
– Urinary bladder repair	0(0.0)	2(8.70)	**NA**	----	0(0.0)	0(0.0)	**NA**	----
– Kidney repair	0(0.0)	1(4.35)			0(0.0)	0(0.0)		
Prostatectomy	0(0.0)	1(4.35)			0(0.0)	0(0.0)		
Maxillo Facial surgery	**0(0.0)**	**6(26.09)**	**NA**	----	**1 (1.0)**	**7(50.0)**	**20.31**	**<0.001***

PU: peptic Ulcer, **RIF:** Reduction and internal fixation **Maxillo Facial surgery:** includes repair of fracture maxilla, fracture mandible and fracture zygomatic arch. **Piles operations:** lateral sphinocterotomy /Hemorrhoidectomy **Urgent ORIF:** Fracture Acetabulum (1), Fracturs neck femur (1), Multiple fracture with vascular injury (2) **X^2:** chisquared test *significant

S. Table (2): Number of patients who underwent surgery (operated) or not (non-operated) in spite of the need for surgery of studied groups.

Variable	Cirrhoticgroup (n = 117)		Non-Cirrhotic group (n = 114)		X^2	P value
	No.	%	No.	%		
Operated	102	87.18	109	95.61	1.89	0.074
Non-operated	15	12.82	5	4.39		
Operated	102	87.18	109	95.61		
• Elective	83	70.94	97	85.09	2.22	0.236
• Emergency	19	16.24	12	10.53		
Non-operated	15	12.82	5	4.39		
• Elective	11	9.40	3	2.63	1.35	0.056
• Emergency	4	3.42	2	1.75		

S. Table (3): Causes of not performing operations in studied patients and the outcome.

Indication for Operation	N	Urgency	Child grade	Cause of not doing operation		Outcome
				Hepatic cause	Non-hepatic cause	
Cirrhotic group						
General surgery Inguinal Hernia	**5** 1	Elective	**B**	Hematemesis/ OV/large HFL/Mets	---	Postponed
CGB	1	Elective	**A**	---	Melena/Hb drop/Active DU	Postponed
Umbilical hernia	1	Elective	**B**	Hematemesis/OV	---	Postponed
Piles	1	Elective	**B**	SBP/Severe decompensation	---	Died pre- operative
RTA/Splenic tear	1	Urgent	**B**	Severe decompensation/ coma	Hemorrhagic shock	Died pre- operative
Orthopedics RTA/multiple fractures with vascular injury	**8** 3	Urgent	**C** **C** **B**	Deep coma	Hemorrhagic shock	Died pre- operative
Fracture Humerus	1	Elective	**A**	---	Melena/Duo mass	Postponed
Fracture Forearm	1	Elective	**B**	Hematemesis/ Severe PHG	---	Postponed
Fracture Forearm	1	Elective	**B**	Severe decompensation	---	Died pre- operative
Fracture Radius	1	Elective	**C**	HE	---	Postponed
Fracture clavicle	1	Elective	**C**	HE	---	Postponed
Neurosurgery lumbar disc	**2**	Elective	**A**	---	Melena-NSAID ulcers	Postponed
Non-cirrhotic group						
Lumbar disc	1	Elective	----	Hematemesis/GU		Postponed
Exploration ➢ Perforated viscus ➢ Gastric obstruction/DU	1 1	Urgent Urgent	------ -------	Septic shock Hematemesis		Died Preoperative Died Preoperative
CGB	1	Elective	------	Melena/NSAIDs		Postponed
Fracture clavicle	1	Elective	-----	Chest infection		Postponed

CBG: calcular gall bladder, OV: Oesophageal varices, HE: Hepatic Encephalopathy RTA: Road traffic accident PHG: Portal hypertensive gastropathy Hb: hemoglobin HFL: hepatic focal lesion SBP: Spontaneous bacterial peritonitis. NSAIDS: non-steroidal anti-inflammatory drugs.

Table (3): Type of preoperative preparation and urgent intraoperative measures and postoperative ICUadmission in patients who undergo surgery groups.

Preoperative Preparation	Cirrhotic patients (n=102)		Non cirrhotic (n=109)		X^2	P value
	N	%	N	%		
Plasma	41	40.20	0	0.00	NA	---
Blood	30	29.41	10	9.17	14.04	<0.001*
Platelet	8	7.84	0	0.00	NA	---
ICU	15	14.71	6	5.50	4.98	0.025*
UGI	10	9.80	0	0.00	NA	---
Intraoperativesupport and post-operative care						
Blood	10	9.80	4	3.66	3.12	0.041*
Plasma	6	5.90	0	0.00	NA	----
Platelets	2	1.96	0	0.00	NA	----
Post-operative ICU	28	27.45	9	8.25	6.83	0.004*

ICU: Intensive Care Units UGI: upper gastrointestinal series

Table (4): Post-operative laboratory changes in comparison to pre-operative basic findings of studies groups.

Variables	Cirrhotic Patients group (n=102)				Non- Cirrhotic group (n=109)			
	Pre	Post	t test	P value	Pre	Post	t test	P value
	Mean ±SD	Mean ±SD			Mean ±SD	Mean ±SD		
Hb	10.68±1.97	10.54±1.41	0.911	0.365	11.54±1.61	10.98±1.14	5.860	**<0.001***
TLC	7.98±3.05	8.66±2.63	3.015	**0.003***	6.94±1.75	8.17±2.12	6.646	**<0.001***
PLT	163.82±69.34	165.98±70.15	0.674	0.502	230.39±44.27	250 ±30.5	5.572	**<0.001***
Serum albumin	3.10±0.69	2.41±0.38	10.453	**<0.001***	4.35±0.54	4.25±0.41	0.841	0.091
Total Bilirubin	1.56±0.68	1.59±1.04	0.317	0.752	0.97±0.13	1.12±0.55	1.018	0.070
INR	1.28±0.249	1.22±0.16	3.159	**0.002***	1.05±0.09	1.05±0.11	0.220	0.827
Blood Urea	25.65±11.51	31.77±18.62	3.325	**0.001***	14.83±3.35	14.67±4.58	0.306	0.760
Serum Creatinine	1.04±0.29	1.09±0.25	3.502	**0.001***	0.93±0.16	1.08±1.25	1.231	0.221
ALT	54.81±50.33	50.85±34.64	0.637	0.525	31±49.37	34.5±54.63	0.413	0.066
AST	73.29±68.01	65.76±47.63	0.928	0.356	45±61.24	54±64.25	0.891	0.052
Serum Na	135.66±4.37	134.69±3.92	3.552	**0.001***	138.34±2.49	134.84±12.78	2.920	**0.004***
Serum K	3.84±0.48	3.74±0.61	1.377	0.172	4.29±0.55	5.33±12.54	0.858	0.393

Hb: hemoglobin, TLC: total leucocyte count, AST: aspartate aminotransferase, INR: international normalized ratio, PLT: platelets, ALT: Alanine transaminase, Paired t test used to compare laboratory investigations pre and post operation among patients and control group t: independent t test *significant

S. Table (4): Intraoperative measures and postoperative ICUadmission in patients undergoing surgery regarding operation urgency type.

Intraoperative support	Cirrhotic group(n=102)		X^2	P value	Non-Cirrhotic group (n=109)		X^2	P value
	Elective (n=82)	Emergency (n=20)			Elective (n=97)	Emergency (n=12)		
	No. (%)	No. (%)			No. (%)	No. (%)		
Blood	6 (7.32)	4 (20.0)	1.621	0.514	3 (3.09)	1 (8.33)	0.331	0.063
Plasma	3 (3.66)	3 (15.0)	1.234	0.632	0 (0.0)	0 (0.0)	**NA**	----
Platelets	0 (0.0)	2 (10.0)	**NA**	----	0 (0.0)	0 (0.0)	**NA**	----
Post-operative ICU	14(17.0)	14(70.0)	4.67	**0.012***	4 (4.12)	5 (41.67)	7.83	**0.003***

ICU: Intensive Care Unit X^2 chi -squared test *significant

Table (5): Comparison between survived and died patients regarding preoperative data in cirrhotic group.

		Mortality		Test value	P-value
		Negative	Positive		
		No. = 98	No. = 4		
Age	Mean ± SD	53.01 ± 8.92	60.75 ± 9.36	-1.699	0.092
	Range	36 – 70	50 – 70		
Hb	Mean ± SD	10.74 ± 1.98	8.98 ± 0.41	1.779	0.078
	Range	4.9 – 14	8.5 – 9.5		
TLC	Mean ± SD	7.74 ± 2.86	13.75 ± 1.50	-4.162	< **0.001***
	Range	2.7 – 15	12 – 15		
PLT	Mean ± SD	164.27 ± 70.61	153.00 ± 22.54	0.317	0.752
	Range	42 – 295	124 – 178		
Blood urea	Mean ± SD	25.48 ± 11.58	29.75 ± 9.74	-0.726	0.470
	Range	10 – 65	18 – 40		
Serum creatinine	Mean ± SD	1.03 ± 0.29	1.33 ± 0.29	-1.994	**0.049***
	Range	0.5 – 1.7	1 – 1.7		
Alb	Mean ± SD	3.15 ± 0.68	2.08 ± 0.22	3.145	**0.002***
	Range	2 – 4	1.8 – 2.3		
INR	Mean ± SD	1.27 ± 0.24	1.50 ± 0.37	-1.818	0.072
	Range	0.9 – 2	1 – 1.9		
ALT	Median (IQR)	37 (22 - 70)	31 (21 - 40)	-0.837	0.403
	Range	10 – 305	20 – 40		
AST	Median (IQR)	61 (28 - 98)	34.5 (19 - 45)	-1.492	0.136
	Range	8 – 398	14 – 45		
Child grade	Child A	47 (48.0%)	0 (0.0%)	3.678	0.159
	Child B	41 (41.8%)	3 (75.0%)		
	Child C	10 (10.2%)	1 (25.0%)		
MELD score	Mean ± SD	11.30 ± 3.64	15.50 ± 5.20	-2.232	**0.028***
	Range	6 – 20	8 – 19		

*: Chi-square test; •: Independent t-test; ‡: Mann Whitney test

Table (6): Validity (AUC, sensitivity, specificity) of some parameters (TLC, serum creatinine, serum albumin and MELD score) to discriminate between different groups.

Parameter	AUC	Cut of Point	Sensitivity	Specificity	PPV	NPV
TLC	0.958	>11.5	100.0	89.8	28.6	100.0
Serum Creatinine	0.759	>1.2	75.0	74.49	10.7	98.6
Serum albumin	0.963	≤2.3	100.0	86.73	23.5	100.0
MELD score	0.765	>15	75.0	85.71	17.6	98.8

TLC: total leucocyte count

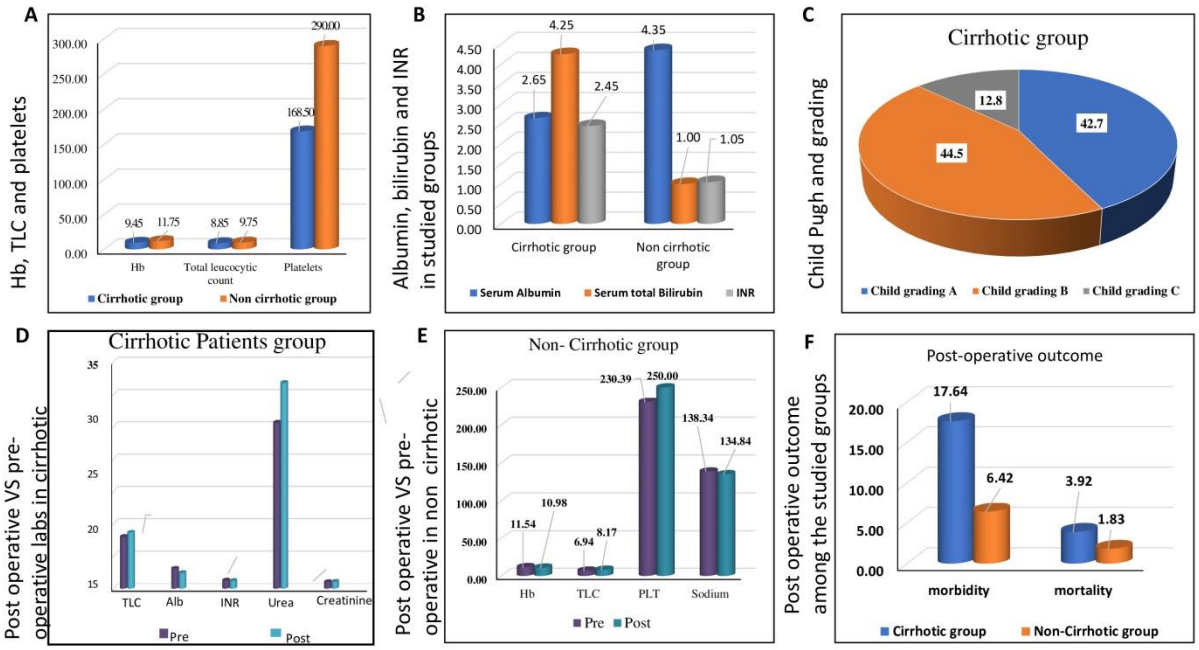

Figure (1A): Total leucocyte count, hemoglobin and Platelets among the studied groups.
Figure (1B): Serum albumin, total bilirubin and international normalized ratio among the studied groups.
Figure (1C): Child-Pugh score and grading of the studied cirrhotic group.
Figure (1D): Post-operative laboratory changes in comparison to pre-operative basic findings of cirrhotic patients group.
Figure (1E): Post-operative laboratory changes in comparison to pre-operative basic findings of non-cirrhotic group
Figure (1F): Post-operative outcome (morbidity and mortality) among the studied groups.

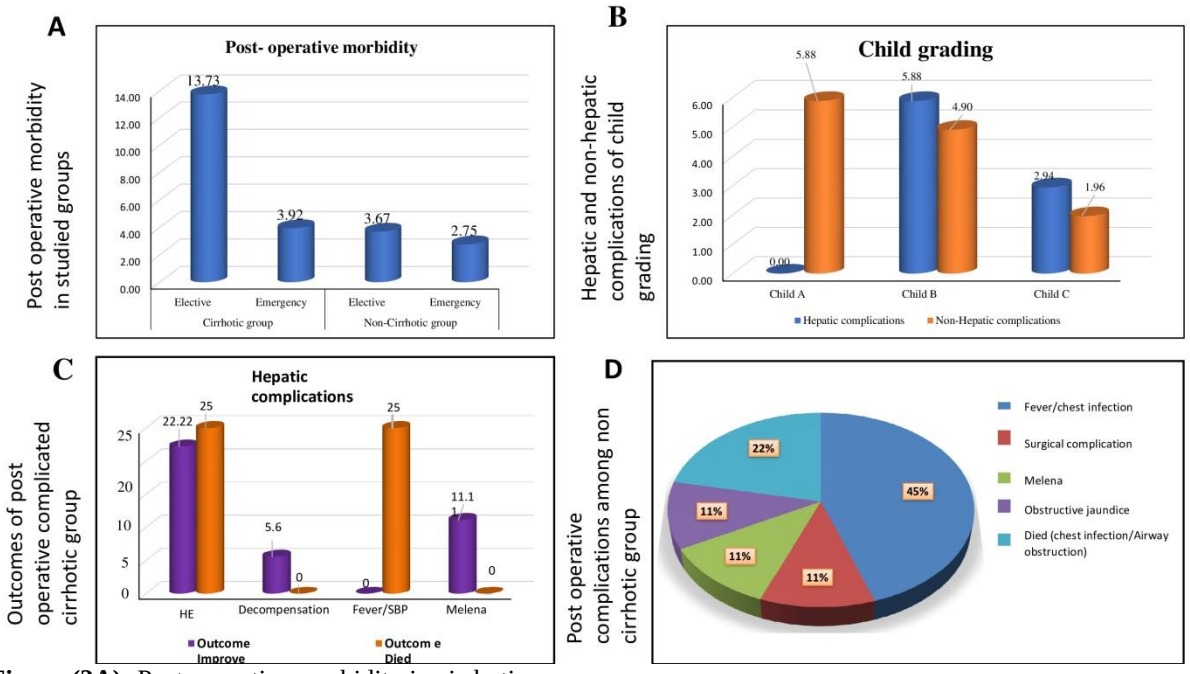

Figure (2A): Post-operative morbidity in cirrhotic group
Figure (2B): Hepatic complications and non-hepatic complications of Child grading.
Figure (2C): Outcomes of post-operative about hepatic complications in group I.
Figure (2D): Post-operative complications among non-cirrhotic group.

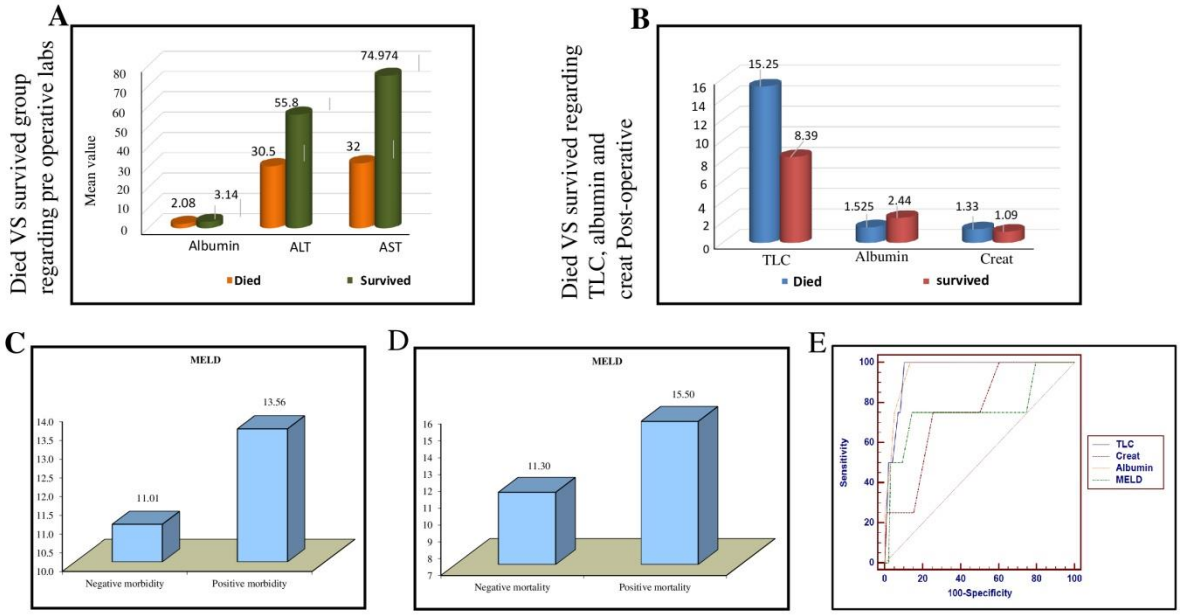

Figure (3A): Comparison between died and survived regarding Albumin, AST and ALT pre-operative.
Figure (3B): Comparison between died and survived regarding TLC, Albumin and serum creatinine post-operative.
Figure (3C): Morbidity in relation to MELD score.
Figure (3D): Mortality in relation to MELD score.
Figure (3E): ROC curve for serum creatinine and MELD score for predicting postoperative morbidity in cirrhotic patients.

DISCUSSION

Cirrhosis is caused by various liver injury mechanisms that result in necro-inflammation and fibrogenesis. Histologically, it is identified by diffuse nodular regeneration surrounded by dense fibrotic septa which significantly distorts the hepatic vascular architecture. This results in portal hypertension and in hepatic synthetic dysfunction. Clinically, cirrhosis has been considered an end-stage disease that results in death, unless liver transplantation is done, the only prophylactic measures have been esophageal varices screenings and hepatocellular carcinoma screenings **[11]**.

As the incidence of CLD and cirrhosis increases, more cirrhosis patients are undergoing surgery of various kinds. It is generally known that after surgery, individuals with underlying CLD experience higher rates of morbidity and mortality than those without. Surgery-related and anesthesia-related problems are more likely to occur in patients with liver disease than in those with a healthy liver **[12]**. There are a number of factors that contribute to poor outcomes in patients with advanced liver disease after surgery, including the fact that cirrhosis is linked to an increased output and hyperdynamic circulation, as well as a decreased hepatic perfusion that may be vulnerable to hypoxemia and hypotension related to the anesthesia **[13]**.

Cirrhosis has 2 distinct phases: compensated and decompensated. The decompensated state of cirrhosis is characterized by the presence of its consequences, including variceal bleeding, HE, ascites, SBP, HCC, hepatopulmonary syndrome (HPS), and hepatorenal syndrome (HRS), characterizes the decompensated state of the cirrhosis **[11]**. Patients with impaired liver function are known to experience decompensatory effects from anesthesia and surgery.

In spite of being known that general anesthesia reduces the arterial blood flow to liver and increases the risk of ischemic injury, spinal or epidural anesthesia may also lower mean arterial pressure, which is problematic in cirrhotic patients who already have hyperdynamic circulation as a result of peripheral vasodilatation. As coagulopathy or thrombocytopenia is present, these approaches are not preferred because of the increased risk of bleeding. Consequently, for these patients,

general anesthesia may represent the preferred option **[14]**.

In our study, we aimed to assess the surgical risk for patients with liver cirrhosis and to identify numerous variables that would influence how successfully these patients would respond to surgery. 231 participants underwent non hepatic surgery under general anesthesia. 231 individuals in this study underwent non-hepatic surgery while under general anesthesia. Their preoperative assessment of their readiness for surgery, as well as the intra operative outcome after surgery were all part of their workup.

In this work we noticed that only 12.8% of the cirrhotic patients who had surgery had a Child Pugh score of C, making the majority of them either Child Pugh score A or B, representing 42.7% and 44.5% respectively. These results were in line with those of **del Olmo and his colleagues**, in their study on non-hepatic surgery on 135 cirrhotic patients, reported that the degree of liver dysfunction before operation was evaluated as Child-Pugh grade A in 83 patients, B in 41 patients, and C in 11 patients **[15]**.

Although there were statistically non-significant differences between the cirrhotic and non-cirrhotic groups in the current study for patients who had or had not undergone surgery ($p>0.05$), there was nevertheless a trend for cirrhotic patients to be non-operated. We found that hepatic causes predominate in Child B and C, whereas non-hepatic causes predominate in patients with Child A cirrhosis.

Comparing the preoperative preparation of cirrhotic and non-cirrhotic patients, the current study found that 40.20% of the cirrhotic group required plasma transfusion and 7.84% required platelet transfusion, while, none of the non-cirrhotic group did. According to **Keegan and Plevak**, coagulopathy and thrombocytopenia should be treated with vitamin K replenishment, fresh-frozen plasma (FFP) administration, and possibly cryoprecipitate transfusions in order to reduce prothrombin times to within 3 seconds of normal values platelet counts should be greater than 50,000/mm^3 **[16]**.

Additionally, this study also revealed that only cirrhotic patients required intra-operative plasma and platelet transfusion, and that there was a statistically significant difference between the cirrhotic and non-cirrhotic groups in terms of the need for post-operative ICU admission and intra-operative blood transfusions.

Cirrhotic patients' hemostasis changes are complex. Cirrhosis impacts procoagulant and anticoagulant levels **[17]**. Further complicating the matter is the lack of routine diagnostics to determine how cirrhosis affects anticoagulant levels. Because of this, assessing the impact on procoagulants only and showing a higher INR in a patient with cirrhosis do not indicate an increased risk of bleeding in these patients. However, use of INR is still a frequent practice in the absence of a suitable test to assess changes in hemostasis in patients with cirrhosis **[14]**.

A cutting- novel technique called thromboelastography evaluates all the stages of clot lysis and formation. When accessible, it should be used since it assesses the blood clotting process' viscoelastic characteristics. It can accurately determine which blood product should be used based on the lack of various components involved in the formation of blood clots **[18]**. It has been demonstrated to lower the procedure's need for unnecessary transfusions and the complications that go along with it without raising bleeding complications. Fresh frozen plasma (FFP) is frequently utilized to reduce increased INR when thromboelastography is not available **[19]**.

Furthermore, thrombocytopenia is typical in cirrhotic patients. The suggested mechanisms include enhanced destruction by hypersplenism and decreased thrombopoietin synthesis, which stimulates the production of platelets in the bone marrow. If the platelet count is less than 50000/mm^3, a prophylactic platelet transfusion is recommended before surgery **[20]**.

Additionally, cirrhotic patients received pre-operative care that included nutritional supplementation, hepatic encephalopathy management, and ascites correction. We noticed that optimal management of ascites reduced certain postoperative complications such as recurrence of an umbilical hernia. Similarly, **Abbas et al.** have cautioned that surgical procedures that were previously prohibited due to ascites may become achievable in some cirrhotic patients and that pharmacological management of ascites may improve the CTP class **[14]**.

We paid close attention to any preexisting infections during the preoperative assessment

and appropriately treated them. According to a previous study, **Douard et al.** found that cirrhotic patients with undetected and untreated infections had higher rates of morbidity and mortality following the same surgery than non-cirrhotic patients **[21]**.

In this study, post-operative mean values of TLC, blood urea, and serum creatinine were significantly higher than pre-operative mean values, whereas post-operative mean values of serum albumin and serum Na were significantly lower, however, no significant changes were noted regarding liver functions in non-cirrhotic group. In accordance with the findings of **Ziser et al.** According to their findings, 20% of cirrhotic patients had worsening hepatic functions, and some of them experienced decompensation of liver cirrhosis that was not evident prior to surgery **[22]**.

In the current study, we noticed a substantial difference between patients who received elective and emergency surgeries in the cirrhotic group, with elective surgeries showing more frequent complications and only emergency surgeries revealing post-operative death. Only emergency procedures were linked to post-operative mortality in non-cirrhotic patients, however, where there was a statistically non-significant difference between elective and emergency operations regarding post-operative morbidity. Prior research has shown that patients with cirrhosis who require emergency surgery have a higher risk of morbidity and mortality unless they receive the appropriate preoperative management and care **[23]**.

Regarding the Child-Turcotte-Pugh grading, we observed a non-significant difference between survived dead and dead patients, However, dead patients only belonged to Child Pugh Grades B or C. Earlier analyses have shown less of an association between the Child-Pugh class and surgical outcomes **[24]**. Perhaps this is attributed to the small number of patients with Child-Pugh class C cirrhosis who were included in trials to avoid surgery in patients with decompensated cirrhosis and prefer conservative therapy whenever possible.

In the current study, patients who survived and those who died were compared based on preoperative data from the cirrhotic group. We noticed that the dead patient had a significantly higher serum creatinine, total leucocyte count, and MELD score together with a considerable lower serum albumin. This is closely similar to previous studies that have reported that the MELD score has largely replaced the use of the CTP score for surgical risk stratification due to the somewhat subjective nature of estimating the severity of ascites and encephalopathy. The MELD score incorporates the objective liver function-dependent components of the CTP score which have been found to be predictive of outcomes **[25, 26]**.

CONCLUSION

Hepatic and non-hepatic complications are common in cirrhotic patients including decompensation. Cirrhotic patients had considerable higher morbidity and mortality rates than controls, in both groups emergent operations are associated with undesirable outcomes. Cirrhotic patients need distinctive perioperative care. Optimal perioperative care could decease such complications. Correction of coagulopathy, care for preexisting encephalopathy, management of ascites, avoidance of sepsis, and optimizing kidney function should all be part of preoperative preparation.

Abbreviations

ALT: Alanine transaminase, AST: Aspartate aminotransferase, CTP; Child-Turcotte-Pugh, HBV: Hepatitis B virus, HCV: Hepatitis C virus, INR: International normalized ratio, MELD: Model for End-Stage Liver Disease, SBP: Spontaneous bacterial peritonitis,

Disclosure

Ethics approval and consent to participate

Before being enrolled in this study, all participants were given a description of the study and given the opportunity to give their informed consent. The study was carried out after approval from the ethical committee, Faculty of Medicine, Menoufia University and per the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and material

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors contributed significantly to the work reported, whether it be in the ideation, study design, implementation, data collection, analysis, and interpretation, or in all of these areas. They also participated in writing, revising, or critically evaluating the article, gave their final approval for the version to be published, decided on the journal to which the article has been submitted, and agreed to be responsible for all aspects of the work.

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Not applicable.

HIGHLIGHTS

- Chronic liver disease patients often undergo surgery for indications other than liver transplantation and may face increased perioperative risk due to both surgical and anesthesia-related complications.
- In cirrhotic patients, hepatic causes are considerably the cause of not having surgery, additionally, the majority of patients underwent surgery had a Child Pugh score of A or B, whereas only few had Child Pugh C.
- Hepatic and non-hepatic complications are common in cirrhotic patients including decompensation.
- Postoperative mortality significantly associated with higher WBCs, serum creatinine, and MELD score in addition to lower serum albumin.
- Cirrhotic patients need distinctive perioperative care. Optimal perioperative care could decease such complications.

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