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Comparative Investigation of Renal, Hepatic and Coagulation Diagnostic Factors in Patients with Cirrhosis and Hepatitis

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A B S T R A C T

Introduction: Evaluating the level of kidney, liver, coagulation, and blood diagnostic markers in cirrhosis and hepatitis patients can help in early diagnosis, timely treatment, and prevention of complications of these diseases.

Materials & Methods: This study is an analytical cross-sectional study. After obtaining the necessary permits by referring to the medical records department of Abadan and Khorramshahr educational hospitals, the information of patients (148 patients) with liver cirrhosis and hepatitis admitted from March 21, 2017, to March 19, 2020, available in the HIS, was obtained. Patient data was analysed using IBM SPSS software (version 16). Data compared means among study groups using t-tests and two-way ANOVA. A p-value < 0.05 was considered statistically significant.

Results: In both diseases, the mean levels of Hb and Hct were lower than the normal range, while the mean of FBS, total and direct bilirubin, AST, ALT, ALP, PT, and INR were higher than the normal range. Comparing the markers between liver cirrhosis and hepatitis, the mean levels of BS, FBS, BUN, and creatinine were significantly higher in cirrhosis. The means of LDL, Na, direct and total bilirubin, AST, and ALT were significantly higher in hepatitis.

Conclusion: According to the research, cirrhosis tends to occur at an older age than hepatitis. Both diseases are more prevalent among men. In cirrhosis, mean blood sugar and renal markers (creatinine and BUN) were significantly higher than in hepatitis. Liver diagnostic markers (direct and total bilirubin, AST, and ALT) and LDL were significantly higher in hepatitis than in cirrhosis.

Keywords: Hepatitis, Liver Cirrhosis, Biomarkers

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Introduction

The liver is essential in metabolising protein, fat, and carbohydrates. It also has diverse functions such as detoxification, elimination, formation, and inactivation of mediators and non-specific defence mechanisms (1, 2).

Various factors, such as pathogens, metabolites, viruses, alcohol, and toxins, can impair liver function, potentially causing acute or chronic injury and leading to end-stage liver disease. While sharing similarities, liver diseases have distinct characteristics and treatment needs, creating a significant global economic and social burden (3).

Cirrhosis is caused by progressive fibrosis due to chronic liver diseases and is among the top ten causes of death in the US. However, 69% of those affected are unaware of liver disease (4, 5). One of the complications of cirrhosis is hepatorenal syndrome (HRS), which reduces kidney function, and severe manifestations of kidney failure are seen in these people (6). Anaemia occurs in 75% of cases of liver cirrhosis, making it the most common complication (7). Patients with cirrhosis often have coagulation imbalances due to decreased liver synthesis of coagulation factors, resulting in high INR and prolonged PT (8).

Viral hepatitis, whether acute or chronic, is the primary cause of hepatitis worldwide (9). Viral hepatitis due to HAV, HBV, HCV, HDV, and HEV affects hundreds of millions of people globally. Most deaths from viral hepatitis are due to hepatitis B and hepatitis C (10). Acute HBV infection and acute exacerbation of chronic HBV infection can cause acute liver injury (ALI) or fulminant hepatitis (FH) (11). Several mechanisms lead to renal impairment in viral hepatitis, including the formation of immune complexes with the virus, the production of antibodies against altered hepatocytes or other infected cells, or direct cytopathic effects of the virus (12). HCV infection is associated with various glomerular diseases. The most common is type 1 proliferative membranous glomerulonephritis, often in type 2 mixed cryoglobulinemia (13). Both acute and chronic HEV infections have been reported to cause proliferative-membranous glomerulonephritis and membranous glomerulonephritis (14). Aplastic anaemia associated with acute hepatitis is a rare type of anemia characterized by severe pancytopenia (15). Hypocholesterolemia is more common in male cirrhosis patients with viral hepatitis (16).

The aim of this study was to offer insights into diagnostic markers for the kidney, liver, and blood coagulation in patients with cirrhosis and hepatitis. This information could assist physiologists and medical researchers in investigating complex cases and promoting early diagnosis and treatment.

Materials and methods

Study Design

This study was a retrospective cross-sectional analysis comparing laboratory diagnostic factors between two groups of patients with liver cirrhosis and types of hepatitis (A, B, and C).

Setting and Participants

The study includes patients with liver cirrhosis and types of hepatitis (A, B, and C) admitted to Abadan and Khorramshahr educational hospitals in southwestern Iran from March 21, 2017, to March 19, 2020. The inclusion criteria for this study consisted of all patients with liver cirrhosis and hepatitis types A, B, and C who were admitted to Abadan and Khorramshahr educational hospitals. These admissions were based on diagnoses made by specialists in internal medicine, infectious diseases, and gastroenterology. Additionally, the clinical and laboratory diagnostic markers, including those related to kidney function, liver function, and coagulation, had to be available in the patient records and the Hospital Information System (HIS).

The exclusion criteria applied to patients who had cirrhosis and hepatitis but whose clinical and laboratory information was incomplete or unavailable at the time of their admission to the

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educational hospitals of Abadan University of Medical Sciences.

Sample Size

In this study, the sampling method was a census, and a total of 148 patients, consisting of 80 with liver cirrhosis and 68 with hepatitis whose laboratory information was complete, were studied.

Measurements & Validity and Reliability

Sample collection and culture

After obtaining the necessary permits, the research team collected data on hospitalised patients (with liver cirrhosis and hepatitis) from March 21, 2017, to March 19, 2020. This was done by visiting the medical records departments of hospitals in Abadan and Khorramshahr. The team gathered clinical and laboratory data from the patients' medical records and the HIS. The information was organised into relevant checklists and then recorded in SPSS software.

Statistical and Data Analysis

Data collected from patients were entered into IBM SPSS statistical software (version 16) for analysis. Descriptive statistics, including frequency, percentage, mean, and standard deviation, were used to summarise the socio-demographic and clinical characteristics of the study participants. The t-test and two-way analysis of variance, followed by Tukey's post hoc test, were utilized to compare means among the study groups. A p-value < 0.05 was considered statistically significant.

Results

The study examined 148 patients, with 80 (54.1%) diagnosed with liver cirrhosis and 68 (45.9%) with hepatitis. Of these, 92 (62.2%) were men, and the mean age of participants was 47.55±24.14 with a range of 3-91 years. Men accounted for the majority of both groups: 63.7% (51) of cirrhotic patients and 60.3% (41) of hepatitis patients, with the rest being women (Table 1).

Table 1. Frequency distribution and percentage/mean and standard deviation of age and gender based on the type of liver disease.

Variable		frequency (percentage) / mean (standard deviation)	
		Hepatitis	Cirrhosis
Age		34.09(22.54)	58.99(19.09)
gender	Women	27(39.7)	29(36.3)
	Men	41(60.3)	51(63.7)

In patients with cirrhosis, the following laboratory values were found to be above the normal range: fasting blood sugar (FBS) 147.34±81.71, random blood sugar (BS) 167.12±96.56, blood urea nitrogen (BUN) 25.73±22.37, creatinine 1.59±1.23, alkaline phosphatase (ALP) 463.16±372.52, aspartate aminotransferase (AST) 56.62±38.07, alanine aminotransferase (ALT) 39.65±32.54, prothrombin time (PT) 15.15±3.99, international normalised ratio (INR) 1.52±0.83, total bilirubin 3.95±5.13 and direct bilirubin 1.99±3.51. The mean of High-Density Lipoprotein (HDL) was below the normal range. However, haemoglobin 10.62±2.86 and haematocrit 33.23±8.06 were lower than the normal range (Table 2).

In patients with hepatitis, the mean of FBS 102.56±40.31, low-density lipoprotein (LDL) 135.75±46.30, triglycerides (TG) 171.71±117.11, ALP 496.98±369.92, AST 107.18±62.06, ALT 81.74±51.23, PT 14.23±5.74, INR 1.32±0.69, total bilirubin 7.06±7.89, and direct bilirubin 4.53±5.80 were found to be above the normal range. Conversely, the mean of HDL 32.50±17.60 was

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below the normal range. Additionally, the mean of haemoglobin 11.93±2.09 and haematocrit 36.13±6.47 was lower than what is typically considered normal (Table 2).

Table 2. Comparison of mean laboratory factors in two groups of liver disease.

Variable	Hepatitis	Cirrhosis	P
BS (mg/dL)	119.83(77.43)	167.12(96.56)	0.003
FBS (mg/dL)	102.56(40.31)	147.34(81.71)	0.01
BUN (mg/dL)	16.64(14.82)	25.73(22.37)	0.005
Creatinine (mg/dL)	0.91(0.66)	1.59(1.23)	0.000
Tg (mg/dL)	171.71(117.11)	89.11(32.97)	0.11
Chol (mg/dL)	160.83(83.02)	124.63(43.88)	0.34
HDL (mg/dL)	32.50(17.60)	35.47(11.95)	0.68
LDL (mg/dL)	135.75(46.30)	66.63(33.79)	0.007
Na (mEq/L)	139.02(3.82)	137.18(5.02)	0.01
K (mEq/L)	4.17(0.57)	4.23(0.76)	0.61
Ca (mg/dL)	8.81(0.78)	8.68(0.98)	0.65
ALP (U/L)	496.98(369.92)	463.16(372.52)	0.65
Total bilirubin (mg/dL)	7.06(7.89)	3.95(5.13)	0.01
Direct bilirubin (mg/dL)	4.53(5.80)	1.99(3.51)	0.006
AST (U/L)	107.18(62.06)	56.62(38.07)	0.000
ALT (U/L)	81.74(51.23)	39.65(32.54)	0.000
PT (sec)	14.23(5.74)	15.15(3.99)	0.28
PTT (sec)	36.65(13.20)	35.41(9.51)	0.53
INR	1.32(0.69)	1.52(0.83)	0.13
WBC (cells /µL)	7744.48(3886.30)	8451.64(5054.05)	0.35
RBC (millions/L)	4.31(0.76)	4.19(4.21)	0.82
Hb (g/dL)	11.93(2.09)	10.62(2.86)	0.002
Hct (%)	36.13(6.47)	33.23(8.06)	0.02
MCV (fL)	85.01(8.56)	89.17(10.41)	0.01

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MCH (pg)	29.16(4.11)	29.12(4.93)	0.96
MCHC	31.13(3.17)	31.11(3.12)	0.97
PLT (thousands/dL)	228.06(117.93)	151.88(85.85)	0.000
RDW-CV	17.92(7.74)	19.01(7.59)	0.54
RDW-SD	46.97(12.48)	53.24(7.11)	0.008

The two-way analysis of variance indicated that the mean FBS and random blood sugar in patients with liver cirrhosis were significantly higher than in patients with hepatitis, with P-values of 0.01 and 0.003, respectively (Table 2). Additionally, the interaction between gender and disease significantly affected BS (P=0.04) (Table 3).

BUN and creatinine levels were also significantly elevated in patients with liver cirrhosis compared to those with hepatitis (P=0.005 and P=0.000, respectively) (Table 2). The interaction effect of gender and disease was significant for both BUN (P=0.02) and creatinine (P=0.04) (Table 3).

Regarding lipid profiles, only LDL was significantly higher in patients with hepatitis (P=0.007) (Table 2). The lipid markers did not differ significantly based on disease type or gender (Table 3).

Among the electrolytes measured (sodium, potassium, and calcium), sodium was significantly higher in patients with hepatitis (P=0.01) (Table 2). Calcium was significantly elevated in women (P=0.005), and the interaction between disease and gender was significant for potassium (P=0.05) (Table 3).

The total and direct bilirubin means were significantly higher in patients with hepatitis (P=0.01 and P=0.006, respectively) (Table 2). However, no significant differences were observed based on gender or the interaction between disease and gender (Table 3).

The means of AST and ALT were both significantly higher in patients with hepatitis (P=0.000 for both) (Table 2). The interaction between gender and disease for AST was also significant (P=0.02) (Table 3). Among these indicators, only calcium demonstrated a significant difference between the sexes (P=0.005), being higher in women than men. Other markers did not reveal significant differences between genders (Table 3).

Neither the type of liver disease nor gender had a significant independent effect on average coagulation factors; however, these two factors exhibited a significant interaction effect on partial thromboplastin time (PTT) (P=0.01) (Tables 2 and 4).

Table 3. Comparison of mean biochemical factors in two groups of liver disease based on gender of patients.

Variable	Hepatitis		Cirrhosis		*P***	*P****
	Women	Men	Women	Men		
BS (mg/dL)	104.75(69.42)	128.97(81.56)	193.74(121.9)	152.15(76.32)	0.56	0.04
*P**	0.001					
FBS (mg/dL)	108.50(52.26)	96.63(25.88)	165.72(101.92)	130.80(55.67)	0.28	0.59
P	0.04					

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BUN (mg/dL)	9.46(3.88)	21.31(17.32)	27.70(28.06)	24.61(18.59)	0.18	0.02
P	0.001					
Creatinine (mg/dL)	0.57(0.23)	1.12(0.75)	1.69(1.46)	1.53(1.08)	0.26	0.04
P	0.000					
Tg (mg/dL)	117(15.55)	193.60(135.71)	96.10(33.20)	81.33(32.82)	0.33	0.15
P	0.04					
Chol (mg/dL)	169(55.15)	156.75(102.01)	141.80(38.91)	105.56(43.02)	0.37	0.66
P	0.16					
HDL (mg/dL)	35(22.62)	30(19.79)	35.90(8.11)	34.86(16.83)	0.69	0.79
P	0.71					
LDL (mg/dL)	110.5(28.99)	161(55.15)	79.60(28.51)	55.83(36.40)	0.53	0.10
P	0.007					
Na (mEq/L)	139.04(3.13)	139(4.25)	137.72(5.20)	136.86(4.95)	0.56	0.60
P	0.03					
K (mEq/L)	4.02(0.47)	4.27(0.62)	4.36(0.88)	4.16(0.68)	0.83	0.05
P	0.34					
Ca (mg/dL)	9.34(0.98)	8.58(0.59)	9.14(0.77)	8.29(0.99)	0.005	0.87
P	0.37					
ALP (U/L)	607.72(337.43)	430.53(377.95)	461.67(500.93)	463.78(312.84)	0.27	0.26
P	0.47					
Total bilirubin (mg/dL)	7.43(6.14)	6.79(9.05)	3.05(4.07)	4.44(5.63)	0.77	0.44
P	0.01					
Direct bilirubin (mg/dL)	4.74(4.42)	4.38(6.69)	1.63(2.44)	2.19(3.99)	0.91	0.62
P	0.006					
AST (U/L)	129.35(62.15)	92.41(58.18)	54(36.22)	58.04(39.35)	0.06	0.02
P	0.000					
ALT (U/L)	89.85(41.80)	76.33(56.53)	40.80(31.72)	39.02(33.31)	0.31	0.44

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P	0.000		

P*: P-value of disease group, P**: P-value of gender, P***: P-value of disease group & gender interaction

Table 4. Comparison of mean coagulation factors in two groups of liver patients based on gender of the patients.

Variable	Hepatitis		Cirrhosis		*P***	*P****
	Women	Men	Women	Men		
PT (sec)	14.84(8.71)	13.81(2.22)	14.11(2.69)	15.78(4.51)	0.13	0.12
*P**	0.48					
PTT (sec)	40.61(18.91)	33.97(6.25)	33.26(6.69)	36.67(10.69)	0.42	0.01
P	0.25					
INR	1.39(1.04)	1.26(0.29)	1.29(0.48)	1.66(0.95)	0.38	0.07
P	0.28					

P*: P-value of disease group, P**: P-value of gender, P***: P-value of disease group & gender interaction

Patients with cirrhosis exhibited lower mean haemoglobin and haematocrit than those with hepatitis, which was statistically significant (P=0.002 and P=0.02, respectively) (Table 2). Meanwhile, mean corpuscular volume (MCV) and red cell distribution width-standard deviation (RDW-SD) were significantly higher in patients with cirrhosis (P=0.01 and P=0.008, respectively) (Table 2). Gender did not significantly affect the means of the examined factors. Additionally, the mean platelet count was significantly lower in patients with cirrhosis compared to those with hepatitis (P=0.000). There was a significant interaction effect of disease type and gender on platelet (P=0.04) (Table 5).

Table 5. Comparison of the mean hematology factors of each of the two groups of liver patients based on the gender of the patients.

Variable	Hepatitis		Cirrhosis		*P***	*P****
	Women	Men	Women	Men		
WBC (cells /µL)	6801.54(2550.40)	8342.44(4462.14)	8332.14(6521.82)	8526(3960.20)	0.27	0.39
*P**	0.28					
RBC (millions/L)	4.14(0.76)	4.42(0.76)	3.64(0.93)	4.45(5.31)	0.27	0.56
P	0.72					
Hb (g/dL)	11.43(2.14)	12.25(2.03)	10.22(3.14)	10.85(2.70)	0.10	0.83
P	0.004					
Hct (%)	32.28(6.54)	36.66(6.45)	32.30(8.69)	33.79(7.69)	0.26	0.96
P	0.02					
MCV (fL)	84.27(8.69)	85.47(8.55)	89.45(7.99)	89.01(11.75)	0.82	0.62
P	0.03					

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MCH (pg)	28.71(4.42)	29.45(3.94)	28.41(3.70)	29.56(5.56)	0.23	0.79
P	0.91					
MCHC	30.38(3.01)	31.61(3.22)	31.31(2.08)	30.99(3.64)	0.40	0.16
P	0.77					
PLT (thousands/dL)	267.31(102.43)	203.17(121.47)	146.71(95.89)	155.09(79.94)	0.11	0.04
P	0.000					
RDW-CV	21.25(11.36)	15.80(2.69)	19.98(13.20)	18.66(4.55)	0.07	0.28
P	0.67					
RDW-SD	43.38(16.51)	49.27(8.68)	51.51(5.38)	53.89(7.67)	0.12	0.50
P	0.02					

P*: P-value of disease group, P**: P-value of gender, P***: P-value of disease group & gender interaction

Discussion

This study showed that of the 148 liver patients studied, there were more patients with cirrhosis than those with hepatitis, and these two diseases were observed more in men than in women. The mean age of patients with cirrhosis was higher than those with hepatitis. This study compared laboratory diagnostic factors between patients with cirrhosis and hepatitis based on age and gender.

Bokl et al. (2014) found that patients with cirrhosis had elevated PT, PTT, and INR levels, as well as decreased blood platelet levels (17). In our study, patients with cirrhosis had higher mean PT and INR levels compared to patients with hepatitis. Women with cirrhosis also had significantly lower mean platelet counts. However, the mean PTT was within the normal range.

In 2016, Rajeshwari et al. found that patients with cirrhosis had elevated AST, ALT, and ALP levels, suggesting the potential for enzyme changes to aid disease diagnosis and classification by aetiology (18). Our study showed that while both enzymes were elevated above the normal range in cirrhosis and hepatitis patients, their levels were significantly higher in the hepatitis group. Additionally, the mean ALP was elevated in both the cirrhosis and hepatitis groups.

In 2013, Youngwon et al. conducted a study on the effects of coagulation and anticoagulant factors on coagulation tests, including PT and aPTT, in patients with cirrhosis. The study included 63.5% men and 36.5% women with a mean age of 57.5 years. The laboratory markers of AST, ALT, bilirubin, and PT were higher than the normal range, while ALP, WBC, platelet, aPTT, and creatinine were reported within the normal range (19). The results of our study showed that, on average, patients with cirrhosis were over 60 years old, and a higher percentage of patients were male. Also, in patients with cirrhosis, the mean PT, AST, ALT, creatinine, ALP, and total bilirubin were higher than normal, and the mean platelets were lower than normal.

Qamar et al. 2009 concluded that thrombocytopenia occurs in patients with cirrhosis, followed by leukopenia and anaemia. A combination of leukopenia and thrombocytopenia at baseline predicted increased morbidity and mortality (20). The results of the present study showed that the mean haemoglobin, haematocrit and platelet were low in patients with cirrhosis and were significantly lower than in those with hepatitis. These findings suggest

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the occurrence of anaemia and thrombocytopenia in patients with cirrhosis, which was consistent with the findings of Qamar et al. (2009) (20).

Desai et al. 2020 observed that in acute viral hepatitis in young adults, total serum bilirubin and serum AST were increased in all cases (21). Consistent with the findings of Desai et al., our results showed that the mean of AST was elevated in both hepatitis and cirrhosis patients, with significantly higher levels observed in patients with hepatitis compared to those with cirrhosis. Total serum bilirubin increased on average in the present study, which is significantly higher compared to patients with cirrhosis.

In 2020, Jalil et al. found an increase in WBC levels and a decrease in PLT and Hb levels in patients with hepatitis. These results also showed that most hepatitis patients are men between the ages of 18 and 29 (22). The results of the present study showed that, on average, patients with hepatitis are in their fourth decade of life and their mean age is lower than that of patients with cirrhosis. In the present study, most of the patients with hepatitis were men, which is consistent with the study under review. In patients with hepatitis, the mean platelet count was within the normal range; however, they had significantly more platelets than patients with cirrhosis. Additionally, the haemoglobin levels in these patients were lower than normal but higher than those of patients with cirrhosis.

In 2017, Arain et al. found that patients with cirrhosis and HBV had significantly lower levels of lipid profiles, including total cholesterol, triglycerides, VLDL-C, LDL-C, HDL-C, and total fat, compared to the control group, which indicates a decrease in blood lipids in patients (23). In the present study, among lipid markers, LDL was more than normal in hepatitis, and HDL was lower than normal in both diseases; other lipid markers were in the normal range.

Limitations and Strengths

This study had several limitations. It was conducted in educational hospitals located in Abadan and Khorramshahr, two cities in southwestern Iran, and involved a small sample size within a limited geographic area. As a result, the findings cannot be confidently generalised to other communities. Additionally, the data were not categorised by the type of hepatitis (A, B, or C) or by the severity of the disease due to the small number of subjects. Therefore, it is recommended that future studies utilise a larger sample size, include diverse communities, and examine the severity of liver disease.

Conclusion

According to this study's findings, cirrhosis typically occurs at an older age compared to various types of viral hepatitis. Both cirrhosis and hepatitis are more prevalent in men. The research identified several laboratory factors, including hepatic, coagulation, renal, and haematological parameters, that were abnormal in patients with cirrhosis and hepatitis. For instance, anaemia was observed in patients with both conditions, but those with cirrhosis experienced more severe anaemia. Liver function impairment, indicated by increased levels of AST, ALT, total bilirubin, and direct bilirubin, was more pronounced in patients with hepatitis. Notably, renal markers, including BUN and creatinine, as well as blood sugar levels, were significantly higher in patients with cirrhosis. Additionally, calcium levels were found to be significantly elevated in women, while other markers did not show significant differences between men and women.

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Ethical Considerations

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This study was approved by the Ethics Committee of Abadan University of Medical Sciences (IR.ABADANUMS.REC.1399.061).

Financial Disclosure

This study was conducted without any external financial assistance.

Competing Interests' Disclosure

The author declares that there is no conflict of interest.

Authors' contributions

Conceptualization, Methodology, Validation, Formal Analysis, Investigation, Resources, Software, Data Curation, Writing–Original Draft Preparation, Writing–Review & Editing, Visualization, Supervision, Project Administration: MKMJ, AZ, HMF, KK, SM, ER.

Writing Disclosure

No AI writing assistance was utilized in the production of this manuscript.

Data Availability Statement

The data supporting this study's findings are not publicly available because of concerns about sensitivity, but can be obtained from the corresponding author upon reasonable request.

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