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ORIGINAL ARTICLE

Diagnostic Role of Presepsin in Patients with Liver Cirrhosis and Bacterial Infection

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ABSTRACT

Background: Presepsin is secreted in response to bacterial phagocytosis, and it has been found that people with liver cirrhosis are at a higher risk of developing bacterial infections. We aimed to evaluate the diagnostic role of presepsin in Patients with liver cirrhosis and bacterial infection.

Methods: Our case-control study included 96 cases with liver cirrhosis, divided into 2 groups according to the results of culture and sensitivity. Group I involved 48 patients with liver cirrhosis (child B or C) with a bacterial infection. Group II: involved 48 cases with liver cirrhosis (child B or C) without bacterial infection. Estimation of serum presepsin level was done for all participants.

Results: The C reactive protein (CRP), serum procalcitonin, and presepsin (Log PSP) were significantly higher among cirrhotic patients cases with bacterial infection with p-value <0.001 for each when compared to cirrhotic patients without bacterial infection, significant positive correlations were found between Log(PSP) and both CRP and serum procalcitonin (p=0.004, 0.003 respectively). At a cut-off value of <3.1 log PSP could diagnose bacterial infection with the area under the curve 0.698, with specificity of 63.3%, sensitivity of 54.2%, positive predictive value (PPV) of 66.5%, negative predictive value (NPV) of 64.5% and overall accuracy 68.8%. The combination of CRP and Log PSP had the best diagnostic value with the best sensitivity of 95.8%, specificity of 93.7%, PPV of 93.9%, and NPV of 95.7%.

Conclusions: Presepsin can play a role in diagnosing bacterial infection in patients with liver cirrhosis. Presepsin and CRP increased the diagnostic accuracy of bacterial infection in cirrhotic patients.

Keywords: Presepsin; Liver Cirrhosis; Bacterial Infection

INTRODUCTION

Many diseases and disorders, such as hepatitis and severe alcoholism, can lead to the advanced stage of liver scarring known as cirrhosis. Even with the right antibiotics and resuscitation therapy, bacterial infection is a leading cause of morbidity and mortality in cirrhosis. Patients with cirrhosis have weakened immune systems, making them more vulnerable to bacterial infections (both at home and in hospitals) and to chronic conditions caused by a wide range of uncommon pathogens [1].

Bacterial infection can be diagnosed using a wide variety of laboratory tests. Non-culture-based testing can be categorized into four groups: indirect, direct, culture-based, and nucleic acid amplification tests (NAATs). Inflammation can be confirmed using indirect

tests such as C-reactive protein (CRP) and peripheral white cell count (WCC). Still, they cannot distinguish between the bacterial and the non-bacterial causes. The procalcitonin (PCT) test is considered much more expensive than the other white cell counts or CRP, while PCT is considered the most specific [2].

Instead of reflecting an infection, C-reactive protein may reflect a chronic inflammatory state. Acute or chronic liver failure or renal dysfunction may cause a misleading increase in procalcitonin [3].

Presepsin, or soluble CD14 subtype, was first identified in 2005 as a molecule significantly higher in sepsis patients compared to healthy controls and patients presenting with non-infectious systemic inflammatory response syndrome (SIRS). Presepsin's secretion mechanism is linked to bacterial phagocytosis, and it has been shown that this causes its levels to rise, specifically in patients with bacterial infection [4].

Cases with liver cirrhosis and infections-related organ failure benefited most from the diagnostic accuracy of presepsin. Patients with liver cirrhosis benefit from a more precise diagnosis of infection when CRP and presepsin are used together as biomarkers. In the first 24 hours after hospital admission, a high presepsin level was associated with an increased risk of death [5]. For this debate about what test would be more specific or diagnostic, this research aimed to evaluate the diagnostic role of presepsin in cases with liver cirrhosis and bacterial infection.

PATIENTS AND METHODS

This case-control study was done in Tropical Medicine Department (ICU and ward) and Medical Biochemistry Department at Zagazig University Hospitals from December 2021 to February 2023.

The study included 96 patients with liver cirrhosis; their average age was 51-75 years old, and they were admitted with symptoms such as hematemesis, abdominal pain, ascites, and hepatic encephalopathy.

Patients aged more than 18 years old who had post hepatitis B and/ or C cirrhotic patients with proven bacterial infection, Cirrhotic patients with symptoms going with the presence of bacterial infection as fever, tachycardia, abdominal pain, cough, and dysuria were included in our study.

Cirrhotic patients were categorized into 2 groups according to the culture and sensitivity results.

Group I comprised 48 patients with liver cirrhosis (Child B or C) with a bacterial infection. Group II included 48 patients with liver cirrhosis (child B or C) without bacterial infection.

We excluded cases with cirrhotic liver associated with viral, parasitic, or fungal infection, who had malignancy, e.g., leukemia, lymphoma, and HCC, with acute liver cell failure, and cirrhotic patient with renal impairment.

This study followed the guidelines [the World Medical Association's Code of Ethics (Declaration of Helsinki) for human studies]. All participants provided informed and written consent. The Institutional Review Board has approved this research (#9046/24-10-2021).

All the included children were subjected to entire history taking, and general and local examinations were done on all participants. Laboratory investigations: Complete urine and stool analysis, Complete blood count, Coagulation profile PT, PTT, and INR, Liver and kidney function test, Viral markers including HBs antigen (Ag), HCV antibody (Ab), Diabetic profile including fasting blood glucose, and Inflammatory markers: CRP and procalcitonin, Fib-4 was calculated for each patient according to the formula: [6]. FIB-4=Age (years)×AST (U/L)/[PLT(10^9/L)×$ALT^{1/2}$ (U/L)], Culture and sensitivity of body fluids, e.g., urine, sputum, blood, and ascitic fluid, Samples were sent for culture and sensitivity testing.

Detection of serum presepsin using a double-antibody sandwich enzyme-linked immunosorbent assay (ELISA) to assay the Human presepsin（PSPN） level in serum.

STATISTICAL ANALYSIS

Microsoft Office Excel 2010 for Windows (Microsoft Cor., Redmond, WA, USA) and SPSS 22.0 for Windows were used to gather, tabulate, and analyze all data (IBM Inc., Chicago, IL, USA) For normally distributed data, we used the Shapiro-Walk test and the Student's t-test; for non-normally distributed data, we used the Mann-Whitney U-test. Chi-square and Fisher's exact tests were used to compare categorical data. LogPSP was correlated with other factors via the use of Spearman's r. To determine the most sensitive and specific cutoff values for inflammatory indicators to diagnose bacterial infection, a receiver operating characteristic (ROC) curve analysis was performed with the following cutoffs: 0.90 or more for excellent, 0.80 or more for good, 0.70 or more for fair, 0.60 or more for bad, and 0.6 or less for failing. Maximum accuracy was used to determine the best possible cutoff.

RESULTS

The MELD score and Child score were significantly increased (p=0.012 and 0.001 respectively) among cirrhotic patients with bacterial infection, and there was a statistically insignificant difference between both groups as regards age, gender, residence, marital status, smoking, hypertension, and diabetes (Table 1).

The white blood cell count significantly increased among cirrhotic cases with bacterial infections. In contrast, Hb level and platelet count were significantly decreased among cirrhotic patients with bacterial infection when compared with cirrhotic patients without bacterial infection (p<0.001 for each) (Table 2).

The CRP, serum procalcitonin, and presepsin (Log PSP) were significantly increased among cirrhotic patients with bacterial infection when compared to cirrhotic patients without bacterial infection (P<0.001 for each) (Table 3).

Spontaneous bacterial peritonitis (SBP) was the most common source of bacterial infection (25%), followed by urinary tract infection (14.6%) then bacteremia (10.4%) and pneumonia (10.4%). Among cirrhotic patients with a bacterial infection, infection mainly arises from a single site (60%) and, to a lesser extent, arises from two or three sites. Among cirrhotic patients with bacterial infection, E. coli is the most common organism causing SBP and UTI, while streptococci is the most common organism causing bacteremia and pneumonia (Table 4).

Positive significant correlations were found between Log (PSP) and both CRP and serum procalcitonin, while there was no statistically significant correlation with other studied parameters (p=0.004, 0.003 respectively) (Table 5).

At a cut-off value of <3.1 log PSP could diagnose bacterial infection with the area under the curve 0.698, with specificity of 63.3%, sensitivity of 54.2%, positive predictive value (PPV) of 66.5%, negative predictive value (NPV) of 64.5% and overall accuracy 68.8% (Table 6, Figure 1).

Log PSP, CRP, and serum procalcitonin significantly increased among cirrhotic cases with bacterial infection. CRP was the most sensitive, specific, and accurate marker, while procalcitonin had the best negative predictive value in diagnosing bacterial infection among cirrhotic patients (Supplementary Table 1, Supplementary Figure 1).

A combination of CRP and Log PSP together had the best diagnostic value due to the best sensitivity, positive predictive value, negative predictive value, and accuracy, while the combination of Log PSP and serum procalcitonin was the most specific in the diagnosis of bacterial infection among cirrhotic cases (Supplementary Table 2 and Supplementary Figures 2 and 3).

Table (1): Demographic and baseline characteristics of the studied groups.

Demographic data and baseline characteristics	Without bacterial infection (N=48)		With bacterial infection (N=48)		Test	p-value (Sig.)
	No.	%	No.	%		
Gender						
Male	31	64.6%	35	72.9%	0.000[a]	1.000
Female	17	35.4%	13	27.1%		(NS)
Age (years)						
Mean±SD	62.85±5.66		62.27±6.37		0.591[b]	0.555
Median (Range)	63 (52 – 75)		61 (51 – 75)			(NS)
Residence						
Urban	16	33.3%	19	39.6%	0.405[a]	0.525
Rural	32	66.7%	29	60.4%		
Marital status						
Single	1	2.1%	1	2.1%	1.150[a]	0.765
Widowed	11	22.9%	15	31.2%		(NS)
Divorced	4	8.3%	5	10.4%		
Married	32	66.7%	27	56.2%		
Smoking						
Non smoker	20	41.7%	19	39.6%	0.168[a]	0.919
Ex-smoker	25	52.1%	25	52.1%		(NS)
Current smoker	3	6.2%	4	8.3%		
Hypertension						
Absent	38	79.1%	40	83.3%	0.043[a]	0.837
Present	10	20.9%	8	16.7%		(NS)
Diabetes mellitus						
Absent	28	58.3%	23	47.9%	1.046[a]	0.306
Present	20	41.7%	25	52.1%		(NS)
MELD score						
Mean±SD	14.06±2.97		15.37±2.85		-2.507[b]	0.012
Median (Range)	14 (6 – 22)		15 (9 – 22)			(S)
Child score						
Mean±SD	9.18±1.43		10.39±1.81		-3.297[b]	0.001
Median (Range)	9 (7 – 13)		10.50 (8 – 14)			(S)
Child B	29	60.4%	18	37.5%	5.044[a]	0.025
Child C	19	39.6%	30	62.5%		(S)

Table (2): CBC findings among the studied groups.

Complete blood count	Without bacterial infection (N=48)		With bacterial infection (N=48)		Test	p-value (Sig.)
	No.	%	No.	%		
Hemoglobin (g/dl)						
Mean±SD	10.00±0.73		9.19±0.73		5.351[c]	<0.001
Median (Range)	9.90 (7.90 – 11.40)		9.15 (7.90 – 10.60)			(HS)
Platelets count ($x10^3/mm^3$)						
Mean±SD	101.43±24.10		73.10±23.61		-4.947[b]	<0.001
Median (Range)	111 (48 – 136)		74 (34 – 120)			(HS)
WBCs count ($x10^3/mm^3$)						
Mean±SD	4.35±0.99		6.8±1.38		-8.539[b]	<0.001
Median (Range)	4 (3 – 7)		10 (6 – 17)			(HS)
Normal count	48	100%	22	45.8%	75.2[a]	<0.001
Leukocytosis	0	0%	26	54.2%		(HS)

WBCs: White blood cells

Table (3): CRP, serum procalcitonin and presepsin (Log PSP) levels among the studied groups.

Inflammatory markers	Without bacterial infection (N=48)		With bacterial infection (N=48)		Test	p-value (Sig.)
	No.	%	No.	%		
CRP (mg/L)						
Mean±SD	10.22±8.63		47.68±16.13		-8.183[b]	<0.001
Median (Range)	7 (3 – 42)		44.50 (19 – 87)			(HS)
Serum Procalcitonin(ng/mL)						
Mean±SD	0.29±0.04		1.71±1.56		-6.199[b]	<0.001
Median (Range)	0.29 (0.10 – 0.40)		1.20 (0 – 6)			(HS)
LogPSP (ng/L)						
Mean±SD	2.8±1.1		3.3±1.3		-3.868[c]	<0.001
Median (Range)	3.10 (1.8 – 4.2)		4.15 (2.8– 4.5)			(HS)

CRP: C-reactive protein, **Log PSP**: Log presepsin

Table (4): Site and etiology of bacterial infection among cirrhotic patients with bacterial infection.

Culture findings	Cirrhotic patients With bacterial infection (N=48)	
	No.	%
Ascitic fluid culture		
Negative	23	47.9%
Positive	25	52.1%
Negative	23	47.9%
Gram -ve bacteria	20	41.7%
Gram +ve bacteria	5	10.4%
Negative	23	47.9%
E. coli	12	25%
Klebsiella	8	16.7%
Staphylococcus	5	10.4%
Urine culture		
Negative	28	58.3%
Positive	20	41.7%
Negative	28	58.3%
E. coli	10	20.8%
Klebsiella	4	8.3%
Enterococci	6	12.5%
Blood culture		
Negative	31	64.6%
Positive	17	35.4%
Negative	31	64.6%
Streptococci	7	14.6%
Pseudomonas aeruginosa	4	8.3%
E. coli	3	6.2%
Enterococci	3	6.2%
Sputum culture		
Negative	39	81.2%
Positive	9	18.8%
Negative	39	81.2%
S. pneumonia	4	8.3%
H. influenza	3	6.2%
Pseudomonas aeruginosa	2	4.2%
Culture Positivity		
Ascitic fluid alone	12	25%
Blood alone	5	10.4%
Urine alone	7	14.6%
Sputum alone	5	10.4%
Ascitic + Blood	3	6.2%
Ascitic + Urine	6	12.5%
Blood + Urine	2	4.2%
Blood + Sputum	3	6.2%
Urine + Sputum	1	2.1%

Ascitic + Blood + Urine	4	8.3%
Single site	29	60.4%
Double sites	15	31.2%
Three sites	4	8.3%

Table (5): Correlation between LogPSP (ng/L) and the studied variables in cirrhotic patients with bacterial infection.

Study variables	r	p-value	(Sig.)
Age (years)	-0.030	0.841	(NS)
MELD score	+0.186	0.206	(NS)
Child score	-0.195	0.184	(NS)
Heart Rate (b/min)	-0.025	0.864	(NS)
Temperature (°C)	0.029	0.842	(NS)
Hemoglobin (g/dl)	-0.016	0.913	(NS)
Platelets count ($\times 10^3/mm^3$)	+0.001	0.993	(NS)
WBCs count ($x10^3/mm^3$)	+0.065	0.659	(NS)
TSB (mg/dl)	+0.009	0.953	(NS)
DSB (mg/dl)	+0.023	0.879	(NS)
Protein (g/dl)	-0.169	0.251	(NS)
Albumin (g/dl)	0.230	0.116	(NS)
AST (u/l)	-0.026	0.861	(NS)
ALT (u/l)	+0.201	0.171	(NS)
INR	-0.007	0.960	(NS)
BUN (mg/dl)	-0.104	0.483	(NS)
Creatinine (mg/dl)	+0.264	0.069	(NS)
FBS (mg/dl)	+0.110	0.457	(NS)
Na (mmol/l)	+0.001	0.997	(NS)
CRP (mg/L)	+0.412	0.004	(S)
Serum Procalcitonin (ng/mL)	+0.175	0.003	(S)
Ascitic fluid TLC ($cell/mm^3$)	-0.026	0.862	(NS)
Ascitic fluid PMNL ($cell/mm^3$)	-0.057	0.702	(NS)

WBCs: white blood cells, **TSB**: total serum bilirubin, **DSB:** direct serum bilirubin, **AST**: aspartate aminotransferase, **ALT**: Alanine transaminase, **INR**: International normalized ratio, **BUN**: blood urea nitrogen, **FBS**: fasting blood sugar, **CRP:** C reactive protein

Table (6): LogPSP as a diagnostic marker for bacterial infection; ROC curve analysis.

Cut-off value	SN (95%CI)	SP (95%CI)	PPV (95%CI)	NPV (95%CI)	Accuracy (95%CI)	AUROC (95%CI)	p-value (Sig.)
>3.1 ng/L	54.2% (39.2-68.6)	63.3% (57-68)	66.5% (62.1-76.6)	64.5% (56.5-71.7)	68.8% (54.5-80.6)	0.698 (0.63-0.73)	<0.001 (HS)

Table (7): Log PSP, WBCs, CRP and serum procalcitonin as diagnostic markers for bacterial infection; ROC curve analysis.

Marker	Cut-off value	SN (95%CI)	SP (95%CI)	PPV (95%CI)	NPV (95%CI)	Accuracy (95%CI)	AUROC (95%CI)	p-value (Sig.)
LogPSP	>3.1 ng/L	54.2% (39.2-68.6)	63.3% (57-68)	66.5% (62.1-76.6)	64.5% (56.5-71.7)	68.8% (54.5-80.6)	0.698 (0.63-0.73)	<0.001 (HS)
WBCs	>7x10^3 /mm^3	73.8% (70-82)	75.9% (71-83)	72.7% (63-75)	70.1 (65-73.2)	66% (62.2-70.1)	0.59 (0.53-0.65)	<0.001 (HS)
CRP	>10 mg/L	75.8% (65.7-79.5)	83.8% (72.8-88.7)	73.9% (63.7-77.9)	85.7% (75.3-88.9)	92.8% (84.3-99.1)	0.77 (0.72-0.82)	<0.001 (HS)
Serum procalcitonin	>0.4 ng/mL	55% (51-68.5)	76% (72-83)	86.3 (79.4-92)	85.9% (76.1-91.9)	91.7% (81.2-96.3)	0.65 (0.58-0.75)	<0.001 (HS)

WBCs: white blood cells, CRP: C reactive protein

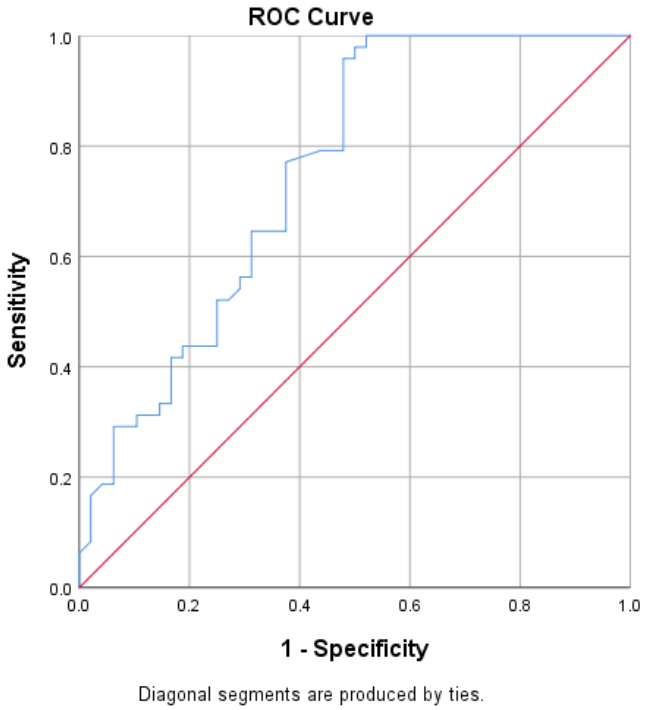

Figure (1): ROC curve analysis of LogPSP as a diagnostic marker for bacterial infection.

DISCUSSION

Bacterial infections are influenced by hepatic encephalopathy, decompensation of liver cirrhosis, and acute-on-chronic liver failure [7], so increased patient survival is linked to prompt identification and treatment of infections in cirrhotic patients [8].

Several potential biological biomarkers for diagnosing infections in cirrhotic patients were investigated. Cirrhosis patients have increased levels of C-reactive protein and procalcitonin regardless of infection, limiting the diagnostic use of these markers; nonetheless, chronically raised C-reactive protein levels identify individuals at increased risk for death shortly [9]. Because of this, novel biomarkers for the detection of bacterial infection in cirrhotic patients are urgently required. This research aimed to evaluate the usefulness of the term "presepsin" in diagnosing bacterial infection in cases with liver cirrhosis.

This study revealed no statistically significant difference regarding age, sex, residence, and marital status between the studied groups. This result agreed with that of Igna et al. [10]. Also, Child and MELD scores were significantly increased among cirrhotic patients with bacterial infection compared to those without bacterial infection in this study. (10.39±1.81versus 9.18±1.43 and15.37±2.85 versus 14.06±2.97 respectively). This result is nearly similar to the results of Sharafeddin et al. [11], who reported a significantly higher Child-pugh score and MELD score than those reported in this study (mean child score for infected patients was 13.768 ± 1.067 versus 11.553 ± 1.205 in non-infected patients). MELD for infected patients was 29.354 ± 6.667 versus 26.412 ± 6.513 in non-infected patients. This difference can be explained by the fact that the study of Sharafeddin et al. [11] was carried out on decompensated patients, most of whom were child score C.

Cirrhotic patients with bacterial infection had significantly increased WBCs and significantly decreased hemoglobin levels and platelet count compared to those without bacterial infection in this study. These results parallel Ferrarese et al. [13] and disagree with those of Papp et al. [13], who reported that the CBC findings did not differ significantly between patients with and without bacterial infection. This difference may be due to the difference in inclusion criteria and the study design.

This study revealed that SBP was the most common bacterial infection encountered in cirrhotic patients (25%), followed by UTI (14.6%), Bacteremia (10.4%), and pneumonia (10.4%). These results are parallel with that of Sharafeddin et al. [11], who reported that SBP was the most common infection among cirrhotic patients, Also this study revealed that bacterial infection in cirrhotic patients mainly arises from a single site (60%) and to lesser extent it arises from two or three sites, these findings is in agreement with that of Papp et al. [13]**.** Among cirrhotic patients with bacterial infection, E. coli was the most common organism causing SBP and UTI, while streptococci was the most common organism causing bacteremia and pneumonia. This investigation validated the prevalence of Gram-positive strains among cirrhotic patients with bacterial infection. In line with the findings of Ferrarese et al. [14].

This study revealed the presence of a significantly positive correlation between serum presepsin levels with CRP and procalcitonin levels. This agrees with the results of Papp et al. [13], While serum presepsin level showed no significant correlations with Child and MELD scores in this work. This result disagrees with that of Papp et al. [13], who reported that serum presepsin level had a significant positive correlation with Child and MELD scores; this can be explained by the fact that we carried this study on a relatively small number of patients and the difference in inclusion criteria

Also, this result disagrees with that of Ferrarese et al. [13], who reported no significant interaction between Child-Pugh classes and bacterial infection; however, log PSP increased

with increasing severity of underlying liver disease.

Also, in contrast to the result of this study, Igna et al. [10] revealed there was a positive link between the presepsin level and the MELD score and that the amount of presepsin rose with the severity of liver cirrhosis as measured by the Child-Pugh class. This difference can be explained by the fact that Igna et al. [10] conducted a large sample size study.

This study revealed that CRP was significantly increased among cirrhotic patients with bacterial infection with sensitivity (75.8%), specificity (83.8%), and the best diagnostic accuracy (92.8%). This result agreed with that of Igna et al. [10].

This study revealed that procalcitonin was significantly increased among cirrhotic patients with bacterial infection with sensitivity (55%) and specificity (76%) This is in contrast to the results of Ferrarese et al. [13], who reported that serum procalcitonin level was not significantly changed among cirrhotic patients with and without bacterial infection, this controversy is due to the presence of patients with acute kidney injury (AKI) included in his study.

Regarding log PSP, at cut-off value (3.1) with the area under the curve 0.698, sensitivity was 54.2%, specificity was 63.3%, positive predictive value was 66.5%, negative predictive value was 64.5% with overall accuracy of 68.8% for predicting the presence of infection.

In agreement with this study, Ferrarese et al. [13] reported that Patients with bacterial infection showed significantly higher median (range) log10PSP values than patients without. A log10PSP cutoff value of 2.87 ng/L retrieved the best diagnostic accuracy for bacterial infection in the whole cohort, displaying an AUC-ROC equal to 0.69 with a sensitivity and specificity equal to 0.66 and 0.63, respectively.

CRP and presepsin combined increase the diagnostic accuracy with a sensitivity of 95.8% and specificity of 93.7% with AUC-ROC of 0.986 more than using either Log PSP or CRP alone with AUC-ROC of 0.698 and 0.77, respectively. This result agreed with that of Papp et al. [13], who concluded that Patients with liver cirrhosis benefit from a higher diagnostic accuracy when utilizing CRP and presepsin to determine the presence of infection.

A combination of procalcitonin and presepsin revealed the most specific indicator regarding bacterial infection in cirrhotic patients (specificity 95.8%) with ROC-AUC 0.832; this value is more than using each biomarker alone as the specificity of procalcitonin, and presepsin are 76% and 63.3% respectively with ROC-AUC 0.65 and 0.698. This result is nearly similar to Ferrarese et al.'s [13].

LIMITATIONS

There are certain limitations in our study. Firstly, the sample size may be small, with 48 subjects in each group. The results may not apply to a broader population because of this understanding of the relationship between presepsin and the correlation of different bacterial infections among cirrhotic patients, so it is required to do a more prominent and representative sample. Secondly, since the study was conducted in a single hospital, there is a potential for selection bias. The patient population might not fully represent the diversity and characteristics of all individuals with bacterial infections among liver cirrhotic patients. This could affect the external validity of the study.

CONCLUSIONS

Presepsin can play a role in diagnosing bacterial infection in patients with liver cirrhosis. Presepsin and CRP increased the diagnostic accuracy of bacterial infection in cirrhotic patients.

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Figure legend:

Supplementary Figure (S1): ROC curves comparison between LogPSP, WBCs, CRP, and serum procalcitonin as diagnostic markers for bacterial infection.

Supplementary Figure (S2): ROC curves comparison between LogPSP+Procalcitonin and LogPSP+CRP as diagnostic markers for bacterial infection.

Supplementary Figure (S3): Receiver operating characteristics (ROC) curve analysis of hepcidin level as a predictor of severe CHF cases (according to ROSS grade).

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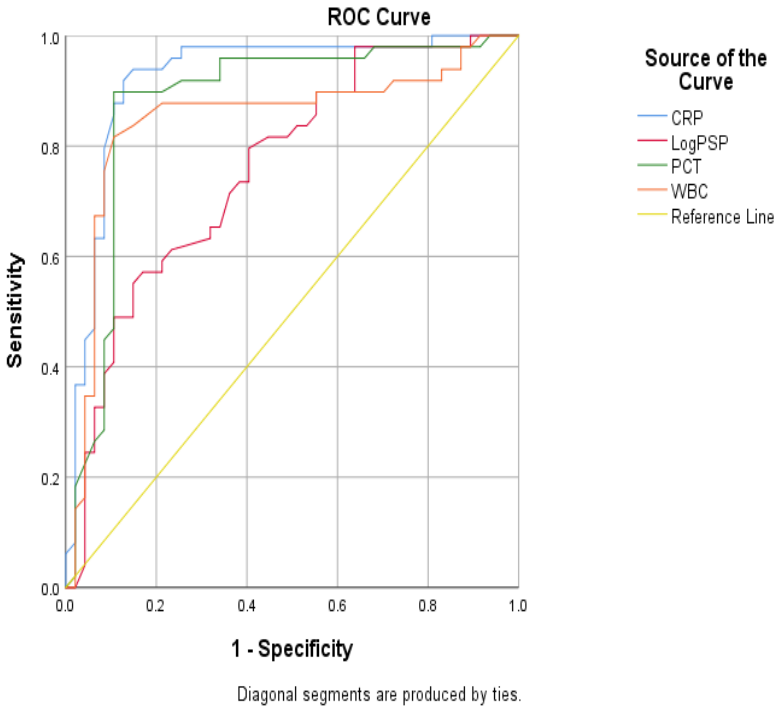
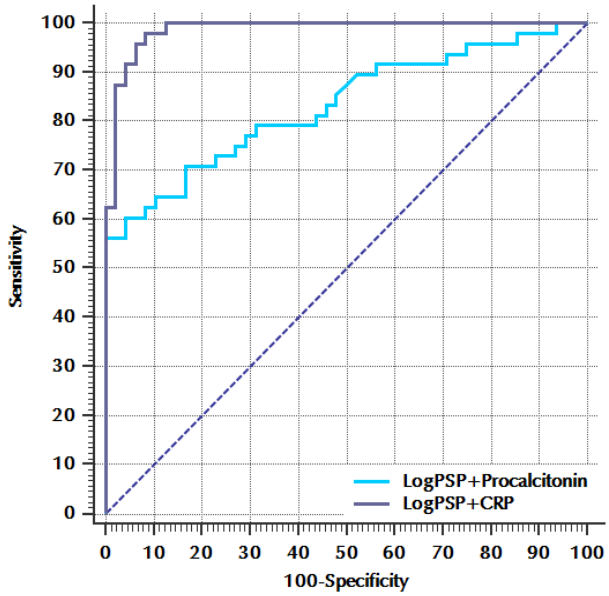
Supplementary Table (1): LogPSP+serum procalcitonin and LogPSP+CRP as diagnostic markers for bacterial infection; ROC curve analysis.

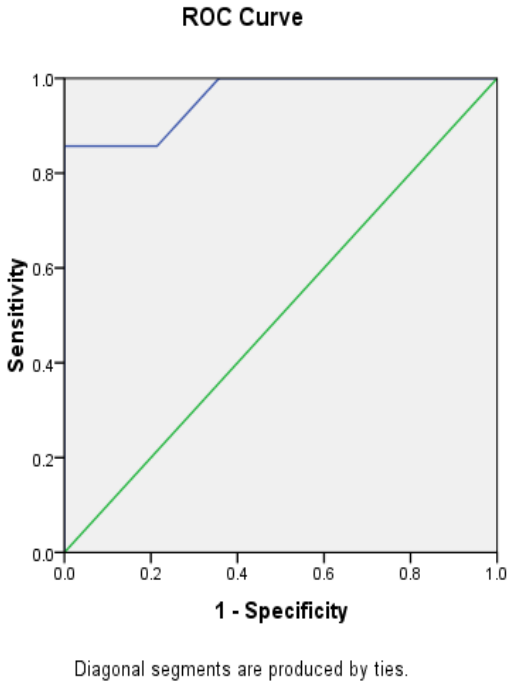
Marker	Cut-off value	SN (95%CI)	SP (95%CI)	PPV (95%CI)	NPV (95%CI)	Accuracy (95%CI)	AUROC (95%CI)	p-value (Sig.)
LogPSP+ procalcitonin	>4.96	60.4% (45.3-74.2)	95.8% (85.7-99.5)	93.5% (78.6-98.3)	70.8% (62.9-77.5)	78.1% (65.5-86.9)	0.832 (0.742-0.901)	<0.001 (HS)
LogPSP+ CRP	>34.07	95.8% (85.7-99.5)	93.7% (82.8-98.7)	93.9% (83.7-97.9)	95.7% (85.3-98.9)	94.7% (84.3-99.1)	0.986 (0.938-0.999)	<0.001 (HS)



Supplementary Figure (S1): ROC curves comparison between LogPSP, WBCs, CRP, and serum procalcitonin as diagnostic markers for bacterial infection.



Supplementary Figure (S2): ROC curves comparison between LogPSP+Procalcitonin and LogPSP+CRP as diagnostic markers for bacterial infection



Supplementary Figure (S3): Receiver operating characteristics (ROC) curve analysis of hepcidin level as a predictor of severe CHF cases (according to ROSS grade).