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Relation of Insulin like Growth Factor-1 to Bacterial Translocation in Cirrhotic Patients with Spontaneous Bacterial Peritonitis

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ABSTRACT

Background: Spontaneous bacterial peritonitis (SBP) is one of most common acute bacterial infections of ascitic fluid (AF) that occur in cirrhotic patients.

Objective: This study aimed to compare serum levels of IGF-1 between patients with SBP and those with aseptic ascites and assess the relationship between serum IGF-1 level and the occurrence of bacterial translocation indicated by presence of its marker LBP.

Patients and Methods: Serum insulin like growth factor 1(IGF-1) and lipopolysaccharide-binding protein (LBP) levels were measured in a group of 49 patients with spontaneous peritonitis (SBP) and group of 39 patients with aseptic ascites.

Results: Total, symptomatic (36) and asymptomatic (13) SBP patients had significantly lower IGF1 and significantly higher LBP when compared to aseptic ascites patients. Moreover, symptomatic SBP had significantly higher LBP when compared to asymptomatic SBP patients. Serum LBP was significantly higher in symptomatic patients with positive AF culture results than those with negative culture results [23.1 ng/mL (2.9-62.1) versus 15.1 ng/mL (2.5-87.8) P: 0.037], AUC of LBP was 0.955 which carry good discrimination between SBP patients and those with aseptic ascites. Blood and AF culture growth results and type of isolated organism did not differ significantly among symptomatic and asymptomatic SBP patients. The most frequently isolated organism from blood and AF culture was E. coli followed by coagulase negative staphylococci.

Conclusions: SBP occurs more frequently in cirrhotic Child C patients who displayed lower serum IGF-1 levels and higher serum LBP levels than cirrhotic patients with aseptic ascites, besides there was a significant negative correlation between serum IGF-1 and LBP levels indicating that decreased serum IGF-1 level in advanced liver disease contributes to occurrence of microbial translocation.

Keywords: Cirrhotic Patients, SBP, IGF-1, LBP, Bacterial Translocation.

INTRODUCTION

One of the most frequent acute bacterial infections in AF in people with cirrhosis is SBP. Its diagnosis is dependent on the AF having a polymorphonuclear cell count (PMN) of at least 250 cells/mm^3, even if no bacteria have been isolated from the fluid [(1,2)], and without an intra-abdominal source of infection or cancer that can be surgically treated [(3)]. Because of acute renal damage or acute-on-chronic liver failure, cirrhotic individuals with SBP had a dismal prognosis [(4)].

In patients with cirrhosis, bacterial translocation (BT), defined as the movement of viable microorganisms or bacterial endotoxins (e.g., bacterial lipopolysaccharide (LPS), peptidoglycan, lipopeptide) from the intestinal lumen to the mesenteric lymph nodes and extra-intestinal locations, coupled with immune dysfunction related to cirrhosis, is recognized as the primary mechanism contributing to the onset of SBP [(2)]. Deficiency of IGF-1 that act as anabolic hormone with trophic effects on intestinal epithelial cells could contribute to intestinal barrier dysfunction [(5)].

When hepatocytes create LBP in response to bacteremia and endotoxemia, it binds particularly to the lipid A of bacterial LPS, facilitating its transport to myeloid cell receptors like CD14 and triggering a cascade of inflammatory reactions. As a stand-in for BT, peripheral blood LBP levels have been employed[(6)].

In this study, we hypothesized that cirrhotic patients have low levels of IGF-1 and this low level may contribute to BT of gut flora and the occurrence of SBP. So, the aim of this study was to compare serum levels of IGF-1 between patients with SBP and those with aseptic ascites and assess the relationship between serum IGF-1 level and the occurrence of BT indicated by presence of its marker LBP.

SUBJECTS AND METHODS

During the period between October 2019 and October 2020, this cross sectional (comparative) study was carried out.

This study was conducted on eighty-eight adult (≥ 18 years) cirrhotic patients presented to Specialized Medical Hospital, Mansoura University with ascites on top of liver cirrhosis with respect to exclusion criteria including infection other than peritonitis, malignancies including hepatocellular carcinoma (HCC), drugs that might influence the determination of cytokines, such as pentoxifylline, steroidal or non-steroidal anti-inflammatory or immunosuppressive

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drugs; antibiotic therapy during the week preceding admission.

When available, histology was used to confirm the diagnosis of cirrhosis; otherwise, a combination of the patient's clinical, imaging, and laboratory results was used. The severity of liver disease was estimated using the Child-Pugh scoring system [(7)] computed using laboratory test results obtained at admission.

SBP was diagnosed when a PMN count in AF exceeded 250 cells/mm^3 in the absence of clinical, radiographic, or laboratory evidence indicating secondary peritonitis, hemorrhagic ascites, pancreatitis, mycobacterial or fungal peritonitis, or carcinomatosis.

Ten ml venous blood samples were collected from each patient under sterile conditions after an 8 hour overnight fasting. Five ml venous blood were inoculated in BacT/ALERT® 3D 60 automated blood culture bottles (Biomérieux, France). The rest was used for complete blood count by automated blood cell counter (Phoenix NCC-3300, NeoMedica, Serbia), INR using (Coatron A4: System, TECO,Germany) total serum bilirubin, ALT, AST, serum albumin, and serum creatinine by (Cobas C311, Switzerland).

Estimation of serum IGF1 and LBP levels using ELISA commercial kits with the principles of quantitative sandwich ELISA was performed (Human LBP ELISA kit NBP2-68051 supplied by Novus Biologicals and Quantikine IGF1 ELISA, R and D systems Inc.614 Mckinely Place NE, Minneapolis, MN 55413, USA respectively). Serum was pre-treated to release IGF-1 from binding proteins and the assays was carried after manufacturer instructions.

A paracentesis was conducted using a standard sterile procedure to obtain AF samples from the participants participating in this study. AF samples (10 ml) were inoculated into BacT/ALERT® 3D 60 automated blood culture bottles (Biomérieux, France) and to Lowenstein Jensen medium. AF white blood cells (WBCs) and PMN counting by automatic cell analyzer (CELL-DYN Emerald, Germany) and determination of AF glucose, albumin and LDH level using Cobas C311 was also carried out.

An automated continuous-monitoring BacT/ALERT® 3D 60 automated blood culture bottles (Biomérieux, France) was used for blood and ascetic fluid (AF) culture.

Before being discarded as negative, bottles were incubated for five days. If they signaled positive before then, they were sub-cultured in accordance with laboratory operating procedure. Standards-compliant identification tests were conducted. The bacterial isolates were identified by colony morphology, hemolysis on blood agar, Gram-stained smears, the Catalase test, the Coagulase test, and biochemical reactions with the manual and automated VITEK® 2 COMPACT system (Biomérieux, France).

Ethical approval:

This study has been approved by Mansoura University's Faculty of Medicine Ethics Committee. (MS.19.07.748-2019/07/29). After receiving all of the information, all the patient signed their consent. The Helsinki Declaration was followed throughout the course of the study.

Statistical analysis

Software called SPSS Statistics for PC, Version 20.0, was used to edit, code, and tabulate the gathered data. Shapiro test was used to examine the distribution of the data. The frequency and percentage of the qualitative data were displayed. Quantitative data were presented as mean, standard deviation (SD), median, and range and were compared by independent t-test. Qualitative data were presented as frequency and percentage and were compared by Chi-Square test. Spearman's correlation, ROC Curve (receiver operating characteristic), and kappa test to assess the agreement between the methods were also used. Statistical significance was defined as P-values less than 0.05.

RESULTS

According to results of ascetic fluid PMN count, patients were classified into: **Group 1** included 49 patients with SBP (This group was further subdivided into: **Group Ia** with 36 symptomatic SBP and **group Ib** with 13 asymptomatic SBP patients) and **Group 2** included 39 patients with aseptic ascites. Groups were matched as regard age and gender (Table 1).

Table (1): Gender and age in the studied groups.

	Group 1 (Patients with SBP) (n = 49)	**Group 2 (Patients with Aseptic ascites) (n= 39)**	**P**
Gender Male Female	 34 (69.4%) 15 (30.6%)	 25 (64.1%) 14 (35.9%)	0.600
Age (years) Mean ± SD. Median (Min. – Max.)	 57.92 ± 9.17 58.0(40.0 – 76.0)	 61.30 ± 7.11 62.0(42.0 – 73.0)	0.665

The most common underling etiology of cirrhosis in SBP and aseptic ascites groups was HCV infection in 41/49 (83.7%) and 32/39 (82.1%) respectively, followed by nonalcoholic steatohepatitis in 5/49 (10.2%) within SBP patients and 2^{ry} biliary cirrhosis in 3/39 (7.7%) within aseptic ascites group. Mostly patients with SBP [31/49 (63.3%)] particularly those who were symptomatic [25/36 (69.4%)] were within Child C class while aseptic ascites patients were mostly within Child B class (25/39 (64.1%), with statistically significant differences between each of total and symptomatic SBP patients versus aseptic ascites patients (P=0.011 and 0.004 respectively).

Previous history of GIT bleeding and endoscopic management were more frequent in SBP patients than those with aseptic ascites (32.7% compared to 15.4%) and (30.6% versus 15.4%) respectively but it did not reach significant level (P = 0.063 and 0.096 respectively). While symptomatic SBP subgroup patients showed significantly higher frequency of GIT bleeding when compared to aseptic ascites patients (P=0.021).

Within symptomatic SBP patients, abdominal pain was the most frequent presenting symptom (77.8%), followed by fever (30.6%), encephalopathy (27.8%), vomiting (25%), diarrhea (19.4%), oliguria (16.7%) and lastly constipation (13.9%).

Total leucocyte count (TLC) and absolute granulocyte count (AGC) were significantly higher in total (P<0.001), symptomatic (P: 0.016 and <0.001) and asymptomatic (P<0.001) SBP patients compared to those with aseptic ascites. Moreover, TLC, AGC were significantly higher in symptomatic than asymptomatic SBP patients (P=0.043 and 0.038 respectively). Hemoglobin, RBCs, platelets, INR, AST, ALT, albumin, Na, K did not differ significantly among studied groups and subgroups (P>0.05).

Serum total and direct bilirubin were significantly higher in symptomatic versus asymptomatic SBP patients (P: 0.008 and 0.003 respectively) while their levels were higher in symptomatic SBP compared to aseptic ascites patients but not reaching significant levels (P: 0.053 and 0.063 respectively). Serum creatinine level was significantly higher in total, symptomatic, asymptomatic SBP patients compared to aseptic ascites patients (P=0.003, 0.046 and 0.004 respectively). CRP level was significantly higher in total, symptomatic and asymptomatic SBP patient compared to those with aseptic ascites patients (P <0.001). AF TLC, PMN were significantly higher in symptomatic SBP versus asymptomatic patients **(**P: 0.003 and 0.005 respectively) (Table 2).

Table (2): Laboratory findings of studied patients.

	Total SBP N=49	**Asymptomatic SBP N=13**	**Symptomatic SBP N=36**	**Aseptic ascites N=39**
TLC (X 10^9/L)	7.2(2.8-20.9)	5.7(2.9-18.7)	8.4(2.8-20.9)	4(2.8-17.8)
AGC (X 10^9/L)	4.8(2-17.1)	3.7(2.4-17)	5.5(2-17.1)	2.2(1.3-6.1)
Hemoglobin (g/dL)	10.5(6.1-14.4)	11.3(7.3-14.4)	10.3(6.1-14.1)	10.8(6.3-15.5)
Platelets (X10^9/L)	117(14-354)	117(55-300)	117(14-354)	112(12-629)
INR	1.4(1-6.6)	1.4(1-3.2)	1.5(1.1-6.6)	1.4(1-3.2)
AST (U/L)	48.7(16-216)	56(27-85)	48(16-216)	46(20-229)
ALT (U/L)	25(8-85)	25(13-37)	24.9(8-85)	23(8-106)
Albumin (g/dL)	2.1(1.3-3.3)	2.3(1.7-2.5)	2.1(1.3-3.3)	2.3(1.3-4)
Total bilirubin (mg/dL)	1.9(0.3-17)	1.2(0.6-17)	2.5(0.3-14)	1.5(0.3-36.9)
Direct bilirubin (mg/dL)	0.8(0.1-11.5)	0.6(0.2-11.5)	1.2(0.1-10.5)	0.5(0.1-22.6)
Creatinine (mg/dL)	1.6(0.5-4.8)	1.7(0.7-4.4)	1.6(0.5-4.8)	1.1(0.4-2.8)
CRP level (mg/L)	48(4-96)	24(4-96)	48(12-96)	6(3-48)
AF Total WBCS	1400(400-11000)	700(400-4400)	1650(400-11000)	300(100-1100)
AF PMN	675(260-10010)	420(260-3608)	990(275-10010)	160(40-225)
AF Albumin	0.7(0.1-1.9)	0.7(0.3-1)	0.6(0.1-1.9)	0.9(0.1-2.4)
AF glucose (mg/dL)	157(78-350)	178(78-350)	153.5(79-267)	143(90-441)
AF LDH (U/L)	135(65-428)	135(78-264)	134(65-428)	76(48-180)
SAAG	1.43(1.12-2.44)	1.47(1.22-2.20)	1.43(1.12-2.44)	1.40(1.16-1.84)

Data expressed as Median (range).

Blood and ascitic fluid culture growth results and type of isolated organism did not differ significantly among symptomatic and asymptomatic SBP patients. The most frequently isolated organism from blood and AF culture was E. coli followed by coagulase negative staphylococci (Table 3).

Table (3): Ascitic fluid and blood culture results in SBP patients:

		SBP group						P values
		Total N=49		Asymptomatic N=13		symptomatic N=36		
		N	%	N	%	N	%	
Blood Culture	**No growth**	35	71.4%	9	69.2%	26	72.2%	0.838
	Growth	14	28.6%	4	30.8%	10	27.8%	
	E coli	8	16.3%	2	15.4%	6	16.7%	0.255
	Klebsiella	1	2%	1	7.7%	0	0%	
	CoNS	5	10.2%	1	7.7%	4	11.1%	
AF Culture	**No growth**	35	71.4%	9	69.2%	26	72.2%	0.838
	Growth	14	28.6%	4	30.8%	10	27.8%	
	E coli	10	20.4%	2	15.4%	8	22.2%	0.104
	Klebsiella	1	2%	1	7.7%	0	0%	
	S. aureus	2	4.1%	0	0%	2	5.6%	
	CoNS	1	2%	1	7.7%	0	0%	

p, comparison between asymptomatic and symptomatic SBP. CoNS, coagulase negative staphylococci.

Among studied 49 patients with SBP, only 10 (20.4%) patients had positive blood and AF cultures while no growth on both was obtained in 31 (63.3%) patients. Four (8.16%) patients had bacteremia with negative AF culture results and 4 (8.16%) patients had positive AF culture results without bacteremia. These results were in moderate agreement between AF and blood culture results (k= 0.600).
Total, asymptomatic, and symptomatic SBP patients had significantly lower IGF1 and significantly higher LBP when compared to aseptic ascites patients. Moreover, symptomatic SBP had significantly higher LBP when compared to asymptomatic SBP patients (Table 4).

Table (4): Serum IGF1 and LBP levels in studied patients:

Median (range)	Aseptic ascites group N=39	SBP group			P values
		Total N=49	asymptomatic N=13	symptomatic N=36	
IGF1 (ng/mL)	25.4 (1.5-155.1)	6.6 (0.1-97.3)	6.6 (0.9-46)	6.4 (0.1-97.3)	P1=0.025* P2=0.040* P3=0.041* P4=0.347
LBP (ng/mL)	2.8 (2-8.2)	15 (2.5-87.8)	12.2 (5-25.5)	18.9 (2.5-87.8)	P1<0.001* P2<0.001* P3<0.001* P4=0.015*

P1, comparison total SBP versus non SBP; P2, comparison asymptomatic SBP versus non SBP; P3, comparison symptomatic SBP versus non SBP; P4, comparison between asymptomatic and symptomatic SBP, *: Significant P value.

Patients with Child class C had significantly (P<0.001) lower IGF-1 levels [3.8 (0.1-38.19) ng/ml] and significantly (P: 0.002) higher LBP [8.5 (2.3-87.8) ng/ml] than patients with Child B [ILF1:29.3 (0.9-155.11 ng/ml)] and [LBP: 3 (2-62.1) ng/ml] respectively (Fig. 1).

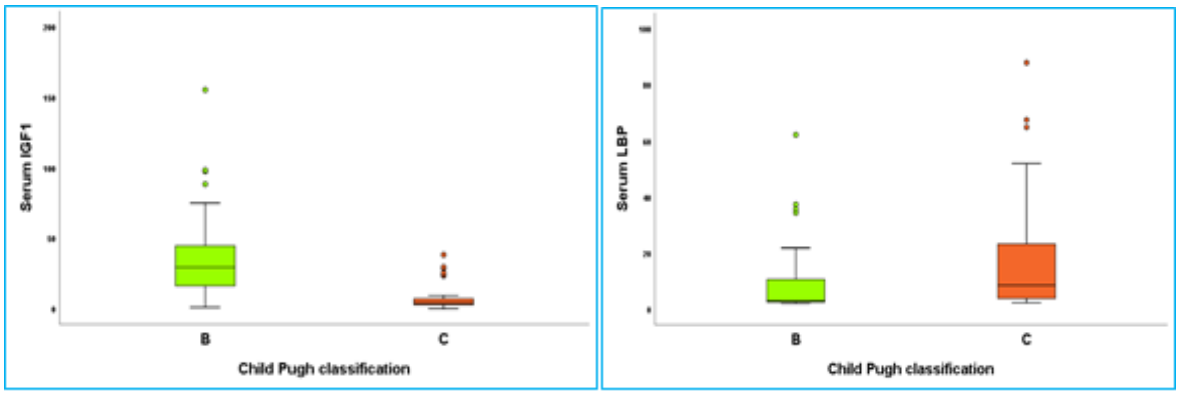

Figure (1): (A) IGF1 and (B) LBP levels according to Child classes in all studied cases.

Serum IGF1 showed significant negative correlation with blood TLC, AGC, INR, ALT, serum total and direct bilirubin, AF LDH and AF TLC and significant positive correlation with serum albumin and AF glucose and borderline negative correlation with AF PMN (P=0.057).
Serum LBP showed significant positive correlation with TLC, AGC, serum total and direct bilirubin, CRP, AF TLC, AF PMN, AF LDH and significant negative correlation with AF glucose. The relation between serum IGF1 and LBP was significant negative correlation.

Table (5): Correlations of serum IGF1 and LBP levels with other parameters in all studied patients.

	Serum IGF1		**Serum LBP**	
	R	**P**	**R**	**P**
Age (Years)	-0.061	0.570	-0.071	0.508
TLC (X 10^9/L)	-0.266	**0.012***	0.233	**0.029***
AGC (X 10^9/L)	-0.269	**0.011***	0.386	**<0.001***
Hemoglobin (g/dL)	-0.013	0.902	-0.181	0.092
RBCs (mcL)	-0.040	0.713	-0.065	0.545
Platelets (X10^9/L)	0.094	0.382	0.039	0.718
INR	-0.502	**<0.001***	0.181	0.092
AST (U/L)	-0.183	0.088	0.005	0.962
ALT (U/L)	-0.369	**<0.001**	0.067	0.533
Albumin (g/dL)	0.248	**0.020***	-0.142	0.187
Total Bilirubin (mg/dL)	-0.425	**<0.001***	0.284	**0.007***
Direct Bilirubin (mg/dL)	-0.357	**0.001***	0.286	**0.007***
Creatinine (mg/dL)	-0.035	0.744	0.208	0.052
Na (mmol/L)	0.111	0.304	-0.210	0.052
K (mmol/L)	-0.093	0.386	0.040	0.712
CRP (mg/L)	-0.086	0.428	0.448	**<0.001***
AF TLC	-0.211	**0.049***	0.632	**<0.001***
AF PMN	-0.204	0.057	0.645	**<0.001**
AF Albumin	-0.055	0.610	0.036	0.741
AF glucose (mg/dL)	0.298	**0.005**	-0.276	**0.009***
AF LDH (U/L)	-0.288	**0.006***	0.559	**<0.001***
SAAG	-0.027	0.806	0.145	0.176
IGF1 or LBP	-0.317	**0.003***	-0.317	**0.003***

R: Spearman's correlation coefficient, *: Significant P value.

In SBP patients with positive blood culture and those with negative blood culture, the median level (range) of IGF1 [2.9 (0.1-74.89) ng/ml versus 7.9 (0.6-97.34) ng/ml] and LBP [24.0 (2.9-64.8) ng/ml versus12.1 (2.5-87.8) ng/ml] didn't differ statistically (P**:**0.690 and 0.988 respectively). Also, their levels in patients with positive and negative AF cultures [IGF1: 3.1 (0.5-74.9) ng/ml versus 7.9 (0.1-97.3) ng/ml: LBP:22.2(2.9-62.1) ng/ml versus 12.2 (2.5-87.8) ng/ml] didn't differ significantly (P: 0.681 and 0.185). Serum LBP was significantly higher in symptomatic patients with positive AF culture results than those with negative culture results [23.1 (2.9-62.1) ng/ml versus 15.1 (2.5-87.8) ng/ml P: 0.037].

Taking ascitic fluid PMNL count as a gold standard for diagnosis of SBP, ROC curve of serum LBP was conducted. The AUC for LBP was 0.955 with high accuracy (90.9%) at cut off value of 4.8 ng/ml. The calculated sensitivity, specificity, PPV and NPV were 87.8, 94.9, 87.8 and 94.9 respectively (Fig 2A). While for discrimination between negative and positive AF culture results of SBP patients, the AUC for LBP was 0.593 with accuracy of 67.3**%** at cut off value of 18 ng/ml. The calculated sensitivity, specificity, PPV and NPV were 71.4, 65.7, 71.4 and 65.7 respectively (Fig 2B).

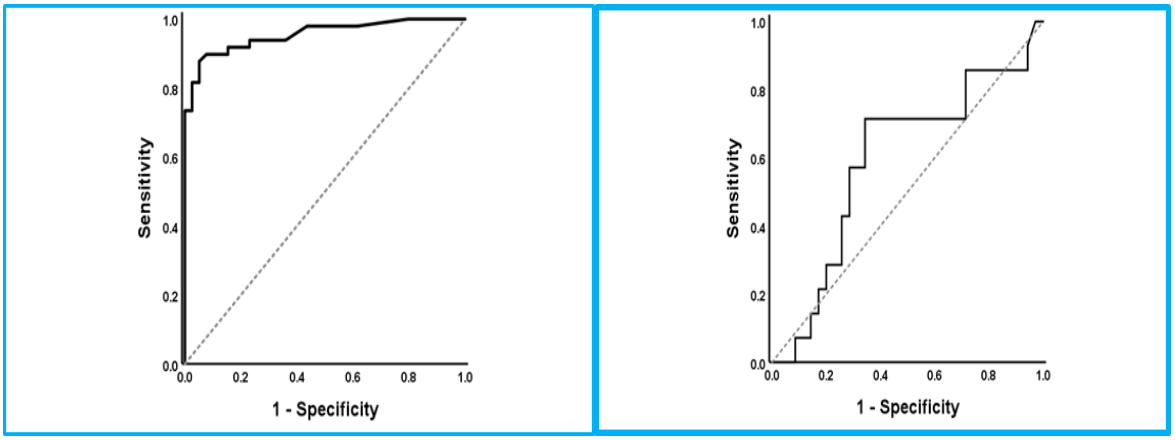

Figure (2): ROC curve of serum LBP for (A): discrimination between patients with SBP and those without SBP. (B): for discrimination between negative and positive AF culture results of SBP patients.

DISCUSSION

Among studied 49 patients with SBP included in our study, bacterial growth was detected in 28.6% of AF culture and in 27.8 of symptomatic patients, only 10 patients (20.4%) had positive blood and AF cultures while no growth on each culture was obtained in 31 patients (63.3%). Patients with negative AF culture (71.4%) met the diagnosis of culture negative neutrocytic ascites. Four patients (8.16%) had bacteremia with negative AF culture result and four patients had positive AF culture result without bacteremia with moderate agreement between AF and blood culture results. Low sensitivity of the AF culture in the diagnosis of SBP was reported previously as ascitic fluid cultures were positive in 33.3% up to 65% of SBP episodes [1,8-10].

It was also previously reported that 30-58% of SBP cases were associated with bacteremia [11]. The most frequently bacterium recovered from AF in our investigation was E. coli, which is consistent with the findings of **Oladimeji *et al.*** [12]. The main findings in the present study were significantly lower serum IGF-1 and higher serum LBP in SBP patients than in aseptic ascites patients. Also, compared to Child B patients, Child C patients had considerably greater blood LBP and lower serum IGF-1 levels. IGF-1 concentration dropped with the degree of cirrhosis (Child Pugh score), reaching noticeably low values in class C because circulatory IGF-1 is mostly generated in the liver [5].

In an Egyptian population, IGF-1's plasma level has been proven to be a reliable indicator of functional liver reserve, and its inclusion in the CTP scoring system in lieu of encephalopathy and ascites has been shown to be beneficial [13]. Also, **Yao *et al.*** [14] concluded that when it comes to identifying patients with advanced cirrhosis and forecasting a bad prognosis, the IGF-CTP score may be more accurate than the CTP and MELD scores.

This study demonstrated a substantial negative association between blood IGF-1 levels and serum LBP levels, with SBP patients having much greater serum LBP levels than those with aseptic ascites. Similarly, higher serum LBP were reported in cirrhotic patients with any overt infection [15]. In the present study, LBP could discriminate between SBP and aseptic ascites patients. AUC of LBP was 0.955 which carry good discrimination between the two groups, while there wasn't significant difference in serum LBP levels between patients with positive and negative AF culture results in total SBP patients. **Tang and Chen** [16] reported that serum LBP measurement may have diagnostic value for SBP. Also, **Agiasotelli *et al.*** [15] showed that serum lnLBP (LBP readings transformed to natural logarithms) demonstrated high diagnostic accuracy in distinguishing individuals with and without infection. In the present study, serum LBP showed significant positive correlation with CRP, blood total leucocyte and absolute neutrophil count, AF TLC, AF PMNL and AF LDH. Also, there was significant negative correlation between IGF-1 and total WBC count. Also, serum CRP was significantly higher in SBP patients than aseptic ascites patients. Similar findings were reported previously [17- 20]. The increase in the total WBC count occurs as a body defense mechanism to the translocated bacteria and its products, which in turn has occurred as a result of intestinal barrier dysfunction explained by reduced IGF-1 level.

As LBP is a bacterial translocation biomarker, bacterial translocation is possible pathogenic factor in studied patients. To our knowledge, this is the first study to assess the relationship between serum IGF-1 levels and serum LBP levels as a marker of bacterial translocation in cirrhotic patients with ascites. However, there was previous experimental studies that assess the relation between IGF-1 levels and bacterial translocation in animal model [21-23].

In carbon tetrachloride-induced cirrhotic rats, **Lorenzo-Zúñiga *et al.*** [21] examined the effects of IGF-I treatment on portal pressure, intestinal histology, permeability to endotoxins and bacteria, and intestinal expression of cyclooxygenase 2 (COX-2). They discovered that IGF-I improves intestinal barrier function and decreases endotoxemia and bacterial translocation in cirrhotic rats, and that IGF-1 reverses the decrease in TER of (IEC-6) caused by LPS. Additionally, as intestinal barrier function improves

when IGF-I therapy is administered concurrently with intestinal COX-2 expression recovery, they proposed that decreased COX-2 expression could be a contributing factor to the disruption of intestinal barrier function in cirrhotic animals. They explained the favorable effect of IGF-1 on the intestine by reduction of portal pressure and by direct protection of the mucosal barrier integrity.

Hunninghake *et al.* [22] used a mouse model of Pseudomonas bacteremia and sepsis to investigate the link between sepsis-induced reductions in IGF-1 levels and the development of bacterial translocation. They discovered that serum IGF-1 levels correlate negatively with enteric bacterial burden, which was assessed in serum using quantitative real-time polymerase chain reaction with enteric bacteria-specific primers. They also revealed that IGF-1 therapy inhibits gastrointestinal epithelial cell death and bacterial translocation.

Similarly, **Zhao *et al.*** [23] investigated the impact of IGF-1 on portal vein endotoxin levels and enterocyte apoptosis in rats with liver cirrhosis caused by carbon tetrachloride (CCL4). It was found that external IGF-1 administration decreased endotoxemia in liver cirrhosis rats by increasing intestinal expression of tight junction proteins, occludin and claudin-1, and lowering enterocyte apoptosis, which ensures a large number of tight junctions attaching points.

CONCLUSIONS

SBP occurs more frequently in cirrhotic Child C patients who displayed lower serum IGF-1 levels and higher serum LBP levels than cirrhotic patients with aseptic ascites, besides there is a significant negative correlation between serum IGF-1 and LBP levels indicating that decreased serum IGF-1 level in advanced liver disease contributes to occurrence of microbial translocation.

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