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RESEARCH ARTICLE

Serum Interleukin 22 Levels in Predicting spontaneous bacterial peritonitis in hepatitis C virus related liver Cirrhosis in comparison with Serum Total Leukocytic count and C Reactive Protein in Egyptian Patients.

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Abstract

Ascitic fluid infections are considered serious complications in cirrhotic patients with high morbidity and mortality. Assuming that IL-22 possesses hepato protective properties in end-stage liver disease, IL-22 may be a relevant factor for progression of liver cirrhosis and development of hepatic complications as spontaneous bacterial peritonitis (SBP). To evaluate the role of serum Interleukin-22 levels in predicting SBP in hepatitis C virus related liver cirrhosis in comparison to TLC and CRP. The study included 20 patients with SBP furtherly subdivided into 2 groups according to culture result, 20 patients with sterile cirrhotic ascites and 20 cirrhotic patients without ascites. Serum IL22 levels , serum TLC and CRP levels were assessed for all patients. Our results showed that IL22,TLC and CRP levels were elevated in SBP when compared to sterile cirrhotic ascites with marked elevation of IL22 in culture positive SBP with a diagnostic level of 20 pg/ml with 100% Sensitivity and 83% Specificity . **Conclusion:** Determination of serum IL22 levels seems to play an increasingly important role in the rapid detection and identification of cirrhosis related ascitic fluid infection, culture positive SBP in particular for prompt initiation of appropriate therapy that might be helpful increasing overall survival of patients at high risk of SBP development.

INTRODUCTION

The development of ascites in cirrhosis indicates a poor prognosis with mortality of approximately 40% at 1 year and 50% at 2 years with increased risk for other complications of liver disease, including refractory ascites, spontaneous bacterial peritonitis (SBP), hyponatremia, or hepatorenal syndrome (HRS) **(1)**.

The presence of ascitic fluid infection is determined based on the number of polymorphnuclear leucocytes (PMNL)and the culture positivity in the ascitic fluid. Accordingly (SBP) classified with respect to ascitic fluid infection into: typical spontaneous bacterial peritonitis (SBP)(with (PMNL)) count >250 /mm3 and positive ascitic fluid culture without any evidence of external or intra abdominal source of infection or malignancy),culture-negative SBP(with PMNL >250 /mm3 and a negative ascitic fluid culture), bacterascites (with a positive ascitic fluid culture and an ascitic PMNL count <250 cells/mm3), sterile ascites(with PMNL <250/ mm3 and a negative ascitic fluid culture). **(2)**

Ascitic fluid infections are considered serious complications in cirrhotic patients with a reported incidence of 8–30% and high morbidity and mortality **(2)**

Nonetheless, in the emergency setting, performing ascitic fluid culture examination is time consuming and not always available indicating the need for easy to apply, rapid and reliable markers to predict diagnosis in patients with ascites **(2).**

There is increasingly evidence that several cytokines mediate hepatic inflammation, apoptosis and necrosis of liver cells, cholestasis and fibrosis. Interestingly, the same mediators also mediate the regeneration of liver tissue after injury **(3).**

Most acute and chronic liver diseases are characterized by inflammation processes with enhanced expression of various pro- and anti- inflammatory cytokines in the liver . Cytokines, in general, play an important role in host defense mechanism, and it is only under certain conditions that they may mediate deleterious results and contribute to the manifestations of tissue injury **(4).**

SBP is associated with an important production of inflammatory mediators . In these patients cytokines are released to blood and ascites, in response to hepatic injury **(5).**

Interleukin 22 (IL-22) was originally identified as an IL-10-related T cell-derived inducible factor (IL-TIF), belonging to IL-10 family. It is now known that IL-22 is mainly produced by T helper 17 (Th17), T helper22 (Th22), natural killer (NK), and NKT cells etc. IL-22 mainly targets epithelial cells including hepatocytes, playing an important role in controlling bacterial infection, homeostasis, and tissue repair. **(6).**

Enhanced IL-22 expression is associated with diseases triggered by or accompanied with immunoactivation, among others: psoriasis , inflammatory bowel diseases , rheumatoid arthritis and abdominal sepsis . **(7)**

In fact, IL-22 has protective functions in models of microbe/infection-driven inflammation at host/environment interfaces , likely by up-regulating anti-microbial peptides , inducible nitric oxide (NO) synthase and mucus production **(6).**

IL-22 is a well-documented antioxidant factor for hepatocytes via the upregulation of anti-oxidative genes (e.g., metallothioneins 1 and 2) . Finally, IL-22 has a potent anti apoptotic, anti-steatotic, anti fungal , and anti microbial effects . **(8).**

In the cirrhotic liver,IL22 may be secreted to protect residual healthy liver tissue. Assuming that IL-22 possesses hepato protective properties in end-stage liver disease, IL-22 may be a relevant factor for progression of liver cirrhosis and development of hepatic complications as (SBP) **(9)**

This study is done to evaluate the role of serum Interleukin-22 levels in predicting spontaneous bacterial peritonitis in hepatitis C virus related liver cirrhosis in comparison to TLC and CRP .

Patients and Methods

Study design:

This study was conducted on 60 patients from January 2014 to February 2015 admitted at the internal medicine department Ain shams university hospitals suffering from Hepatitis C virus induced liver cirrhosis and ascitic fluid infection.

The patients were classified according to presence and/or sterility of ascitic fluid at time of admission into 3 groups:

Group 1:(combination group: typical culture positive SBP and culture negative SBP) Include twenty patients aged from 48-62 years old (mean age: 55.2±5.02) (4 females 20% and 16 males 80%) with ascitic fluid infection (spontaneous bacterial peritonitis and its sub types) diagnosed by PMNL<or>250 mm3and/or positive ascitic fluid culture at time of admission.

Then group1(combination group) was subdivided into:

Group 1A: including 14 (70%) patients with typical culture positive SBP (PMNL>250mm3 and positive ascitic fluid culture) at time of admission.

Group 1B: including 6 (30%) patients with culture negative SBP(PMNL>250mm3 and negative ascitic fluid culture) at time of admission.

Group 2: Include twenty patients aged from 48-62 years old(mean age: 55.6±4.55), (5 females25% and 15 males75%) with sterile cirrhotic ascites(PMNL <250 mm3 and a negative ascitic fluid culture) at time of admission.

Group 3: : Include twenty patients aged from48-62 years old(mean age: 54.8±5.15), (9 females 45% and11 males 55%) with liver cirrhosis without ascites at time of the study.

Patients with clinical evidence of infections other than SBP, malignancy, chronic and auto immune diseases and on drugs affecting CRP level as statins and fibrates were excluded from the study.

A written informed consent was obtained for all patients enrolled in the study .

Methods

All patients were subjected to the following:

1-Full history taking and clinical examination

2-Laboratory assessment:
A-Complete blood count (CBC) .B- liver function tests : Alanine aminotransferase(ALT), Aspartate aminotransferase (AST) ,serum albumin ,total and direct bilirubin, Prothrombin time (PT) and International normalization ratio (INR).
C- C- reactive protein (CRP) titre.
-Serum CRP levels were quantified by using the latex slide test (semi-quantitative test) according to the manufacturer's (Teco Diagnostics, Anaheim,CA 92807,U.S.A) instructions. With sensitivity: greater than 0.8 mg/dL and 92.9% precision.
D-HCV-Ab by enzyme linked immunosorbent assay (ELISA) and markers to exclude associated causes of liver disease ; HbsAG, Serum ceruloplasmin , ferritin levels, ANA(anti nuclear antibody) , ASMA(anti smooth muscle antibody) and Bilharzial hemagglutination test ,AFP.
E-Fasting blood glucose level , blood urea , serum creatinine and lipid profile .
3- Ascitic fluid analysis
Ascitic fluid sampling obtained under complete aseptic abdominal paracentesis for the following:
a- Detection of PMNL count .b- Bacteriologic culture for aerobic , anerobic and Gram stained organisms .c-Chemical analysis for albumin , glucose and LDH .d-Serum ascitis albumin gradient (SAAG).

Paracentesis and culture techniques

Diagnostic paracentesis was carried out at the bedside using a sterile method with a 23-G needle attached to a 20-cc syringe .
Immediately after the paracentesis needle and attached syringe were withdrawn from the abdomen, the 'skin' needle was removed and replaced with a sterile needle to minimize the risk of skin flora growing in the cultures.
Then, aspirated ascitic fluid was collected into ethylene diamine tetra acetic acid tubes and was analyzed within 3 h of aspiration for total and differential leukocyte counts.
Ascitic fluid was then centrifuged in the laboratory for 3 min and analyzed for glucose ,albumin ,lactate dehydrogenase (LDH) and a smear was carried out and stained with Gram stain.
Peritoneal fluid collected from patients was cultured via two methods. Initially, 20-mL peritoneal fluid was inoculated in aerobic blood culture bottles. These bottles were then placed into an automated BacT/Alert 3D (Memmert) culture system. Bottle incubation and subsequent testing were carried out according to the manufacturer's(Egyptian Diagnostic Media, Egypt) protocol. (Incubated at 35-37°C and examined daily for up to 14 days).
The remaining sample was used in conventional culture methods (i.e. inoculating blood agar and MacConkey agar). The conventional agar were incubated at 35°C in both aerobic and anerobic conditions for up to 3 days before being discarded as negative. Bacterial identification and antimicrobial susceptibility testing were carried out using standard procedures .

4-Radiological assessment:
A-Pelvi-abdominal ultrasound; to confirm presence of ascitis and exclude hepatocelleur carcinoma (HCC).
B- ECHO-heart to exclude ischemic heart disease.
5-Evaluation of serum level of Interleukin-22 (normal value up to 18 pg/ml)

Quantification of IL-22 serum levels

Interleukin-22 level of serum samples which were taken at the same time with the ascitic samples were quantified by using the IL-22 Quantikine enzyme linked immunosorbent assay (ELISA) according to the manufacturer's (BosterImmunoleader, Fermont , CA94538 USA) instructions. With range (9 pg/ml- 1000 pg/ml).

Statistical analysis

All the data from patients were collected ,tabulated and statistically analyzed using SPSS 15 for windows.
-Descriptive statistics: mean, standard deviation (±SD), minimum, maximum and range of numerical data. Frequency and percentage of non numerical data.
- One way ANOVA test was used to compare means of different parameters between more than two groups.-Linear regression analysis was used to detect independent effect of different factors on serum level of IL22.-Student`s(t) test was used to test the difference between the mean values of some parameters(for continuous variables)
-Pearson correlation coefficient to test the correlation between two parameters.
-Receiver operating characteristic (ROC) curves were plotted to get a cut off value for IL22,TLC and CRP and test its sensitivity and specificity in diagnosis of the disease.
P value less than 0.01 = Highly significant (HS), less than 0.05 = Significant (S)
and more than 0.05 = Non significant (NS)

Results:

This study was conducted on 60 patients with matched age and sex (age: 55.38±4.97, 70% were males) suffering from Hepatitis C virus induced liver cirrhosis and ascitic fluid infection including typical(culture positive SBP) (23.3%), culture-negative SBP (10%), sterile ascites (33.3%) and cirrhotic patients without ascites(33.3).

Table(1):Comparison of different parameters of all patients included in the study:

	Group						F	P value
	group 1 (N=20)		group 2 (N=20)		group 3 (N=20)			
	Mean	SD	Mean	SD	Mean	SD		
Age	55.2	5.02	55.60	4.55	54.80	5.15	47.91	0.816 NS
Weight	76.95	9.42	75.90	8.04	71.35	6.66	2.69	0.08 NS
FBG	83.6	7.51	83.0	6.92	81.8	9.31	0.27	0.77NS
Hb	10.1	.72	9.81	.83	10.2	.67	2.818	.368 NS
TLC	12.64	2.90	6.90	1.25	7.35	1.35	51.697	<0.01 HS
Plt	80.25	11.29	75.75	10.74	99.55	12.58	23.921	<0.01 HS
ALT	42.85	7.52	40.85	5.41	61.50	11.23	36.727	<0.01 HS
AST	52.15	9.65	51.95	6.41	61.20	12.04	6.002	<0.01 HS
S albumin	2.22	.42	2.31	.38	2.77	.27	13.087	<0.01 HS
T bilirubin	2.71	.57	2.50	.48	1.98	.40	11.829	<0.01 HS
D bilirubin	1.51	.33	1.43	.36	1.28	.34	2.219	.118 NS
INR	1.98	.51	1.93	.36	1.27	.14	22.273	<0.01 HS
Urea	63.05	13.87	67.05	18.40	72.95	14.73	1.990	.146 NS
Creat	1.09	.19	1.01	.23	1.04	.21	.985	.380 NS
AFP	12.75	4.68	11.85	4.43	7.80	3.68	7.581	<0.01 HS
CRP	34.60	15.43	17.60	13.23	5.35	3.08	30.647	<0.01 HS
S ferritin	176.50	25.19	180.05	29.58	183.75	45.79	.219	.804 NS
S IL22	25.8	10.8	11.8	2.8	11.3	3.1	2.28	<0.01 HS
Ceruloplasmin	26.50	4.22	25.25	3.84	26.35	4.77	.505	.606 NS
PT	19.30	4.17	20.80	4.12	14.50	1.67	17.478	<0.01 HS

HB :Hemoglobin level TLC: Total leucocytic count PLT: Platelets Creat: Serum creatinine
ALT: Alanine aminotransferase AST:Aspartate aminotransferase
AFP: Alpha feto protein INR: International normalization ratio ANA:Anti nuclear antibody CRP:C reactive protein S albumin; Serum albumin PT: Prothrombin time
S Ferritin; Serum Ferritin IL22;Interlukin 22 FBG: Fasting blood glucose
HS: highly significant NS: non significant

On comparing mean values of IL22,CRP,TLC and AF PMNL in different groups we found that :
Serum IL22 levels were determined to be significantly higher in patients with SBP (Group1) than IL22 levels in sterile ascites(Group2) and cirrhotic patients without ascitis(Group3) (25.8±10.8 vs. 11.8±2.8 and 11.3±3.1 respectively with p<0.001 in both ,While it was significantly higher in patients with positive bacterial culture in ascitic fluid (Group1A) compared to patients without culture positivity (Group1B) 30.8±8.2 vs. 14.1±5.6 p<0.001**).(Table 2)**

A Statistically significant difference between Group (1) and Group(2) / Group (1) and Group(3)/ Group (1A)and Group (1B) as regard TLC, CRP and IL22, While between Group (2)and Group(3)the only statistically significant difference was in CRP level**.**
Concerning AF PMNL ; a Statistically highly significant difference between Group (1) and Group(2) /Group (1A)and Group(2)/Group (1A)and Group (1B) .

Table 2 : Comparison of different parameters of all patients included in the study:

	Group			F	P value
	group 1 (N=20)	group 2 (N=20)	group 3 (N=20)		

	Mean	SD	Mean	SD	Mean	SD		
TLC	12.64	2.90	6.90	1.25	7.35	1.35	51.697	<0.01 HS
CRP	34.60	15.43	17.60	13.23	5.35	3.08	30.647	<0.01 HS
S IL22	25.8	10.8	11.8	2.8	11.3	3.1	2.28	<0.01 HS
AF PMNL	3689	3817	88.85	47.66			4.22	<0.01 HS

TLC: Total leucocytic count CRP:C reactive protein IL22;Interlukin 22
HS: highly significant NS: non significant

Post hoc test results:

			P value
IL22	Group 1	Group 2	<0.01 HS
	Group 1	Group 3	<0.01 HS
TLC	Group 1	Group 2	<0.01 HS
	Group 1	Group 3	<0.01 HS
CRP	Group 1	Group 2	<0.01 HS
	Group 1	Group 3	<0.01 HS
	Group 2	Group 3	<0.01 HS

Table3:Description of AF parameters for patients with SBP (Group 1) (N=20):

	Min	Max	Mean	SD
SAAG	1.20	2.50	1.8500	.38594
AF PMNL	440.00	14000.00	3689.5000	3817.91687
AF glucose	22.00	96.00	61.1000	30.08917
AF albumin	.80	2.00	1.2050	.24810
AF LDH	220.00	420.00	314.5000	49.01396
			N	**%**
AF culture	**Negative**		6	30.0%
	E coli		12	60.0%
	Strept		2	10.0%

AF: Ascitic fluid SAAG: Serum ascites albumin gradient

Table 4: Comparison between culture positive (1A) and culture negative(1B) patients among Group1 regarding laboratory findings :

Variable	(Group 1A) (N=14)	(Group 1B) (N=6)	P
TLC	13.6±2.8	10.4±1.7	**#0.022***
IL22	30.8±8.2	14.1±5.6	**#<0.001***
CRP	39.9±14.7	22.3±9.0	**#0.015***
AF PMNL	4.7±4.2	1.4±1.4	**#0.020***

AF: Ascitic fluid #Independent t-test, *Significant

TLC, IL-22, CRP and ascitic fluid PMNL were significantly higher among positive than negative culture patients.

Table (5): Correlation between different parameters and IL22 among patients with SBP (Group1) :

	Mean	SD	Pearson correlation	P value
Group 1				
S IL22	25.8	10.86		
TLC	12.6350	2.90232	.652	.002 HS
CRP	34.6000	15.42520	.724	<.001 HS

AF PMNL	3689.500	3817.91687	.777	<.001 HS
Group 1A				
S IL22	30.8	8.2		
TLC	13.5786	2.83879	.533	.050 S
CRP	39.8571	14.74844	.593	.020 S
AF PMNL	4651.4286	4150.84766	.852	.001 HS
Group1B				
S IL22	14.133	5.63549		
TLC	10.4333	1.65731	-.460	.359 NS
CRP	22.3333	8.98146	.654	.159 NS
AF PMNL	1445	1399.16	-.249	.001 HS

In Group1 : There was a statistically significant positive correlation between serum IL22 level and TLC, CRP , ascitic fluid PMNL .

In Group 1A : Statistically significant positive correlation between serum IL22 level and TLC , CRP , Ascitic fluid PMNL levels .

In Group 1B -There was no statistically significant correlation between serum IL22 level and TLC,CRP . Only Ascitic fluid PMNL showed significant correlation with IL22.

Table (6): Receiver operating characteristic (ROC) curve for serum IL22, TLC, and CRP in predicting Group1 SBP (combination group) .

Variable	**AUC**	**SE**	**P**	**95% CI**
TLC	0.988	0.012	**<0.001***	0.000–1.000
IL22	0.888	0.055	**<0.001***	0.779–0.996
CRP	0.826	0.068	**<0.001***	0.693–0.959
Comparison between AUCs#				
	TLC	**IL22**		
IL22	**0.066**	--		
CRP	**0.022***	**0.459**		

AUC: Area under curve, **SE**: Standard error, **CI**: Confidence interval, #DeLong test, *Significant

Table (7): Receiver operating characteristic (ROC) curve for serum IL22, TLC and CRP in predicting culture positive SBP patients (Group1A):

Variable	**AUC**	**SE**	**P**	**95% CI**
TLC	0.833	0.104	**<0.001***	0.601–0.960
IL22	0.964	0.040	**<0.001***	0.773–1.000
CRP	0.827	0.096	**<0.001***	0.595–0.957
Comparison between AUCs#				
	TLC	**IL22**		
IL22	0.126	--		
CRP	0.967	0.128		

AUC: Area under curve, **SE**: Standard error, **CI**: Confidence interval, #DeLong test, *Significant

Tables (6) and figure (1) show that: TLC≥9.0(x10^3/mL) is an optimum test in predicting SBP (both culture positive and negative) (Group 1).

Tables (7) ,figures (2) and (3) show that: IL-22≥20.0 (pg/mL) is an optimum test in predicting culture positive SBP patients (Group1A)

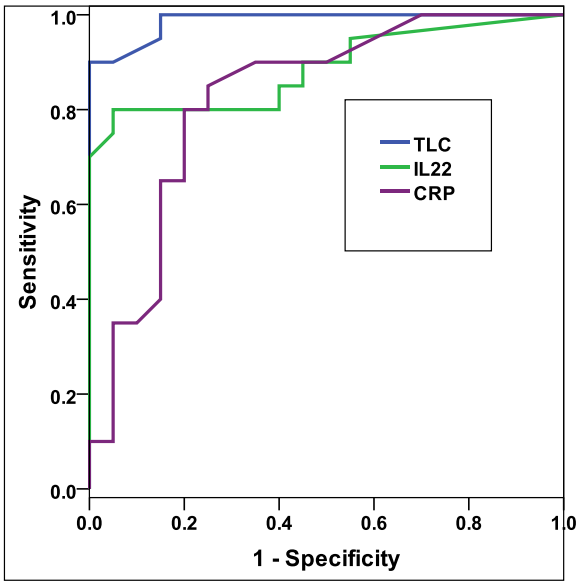


Figure (1): ROC curve for predicting Group1 (combination group)

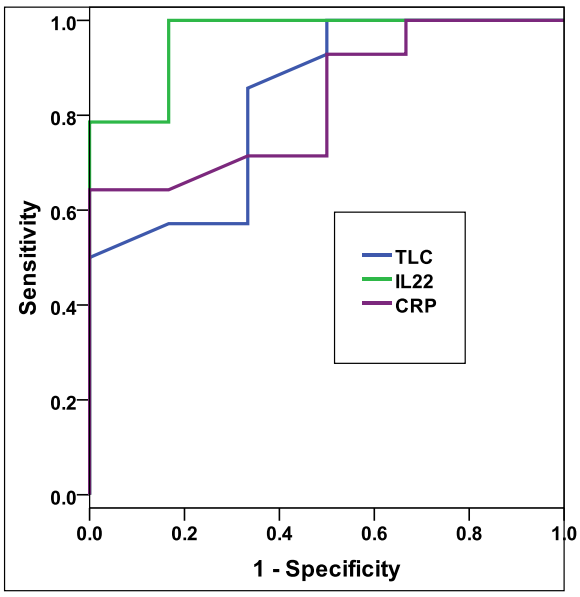


Figure (2): ROC curve in predicting culture positive patients (Group1A)

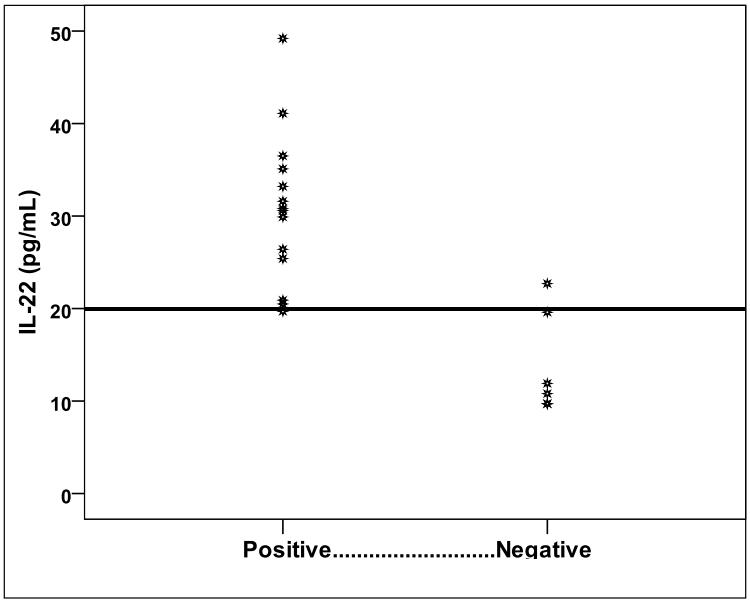
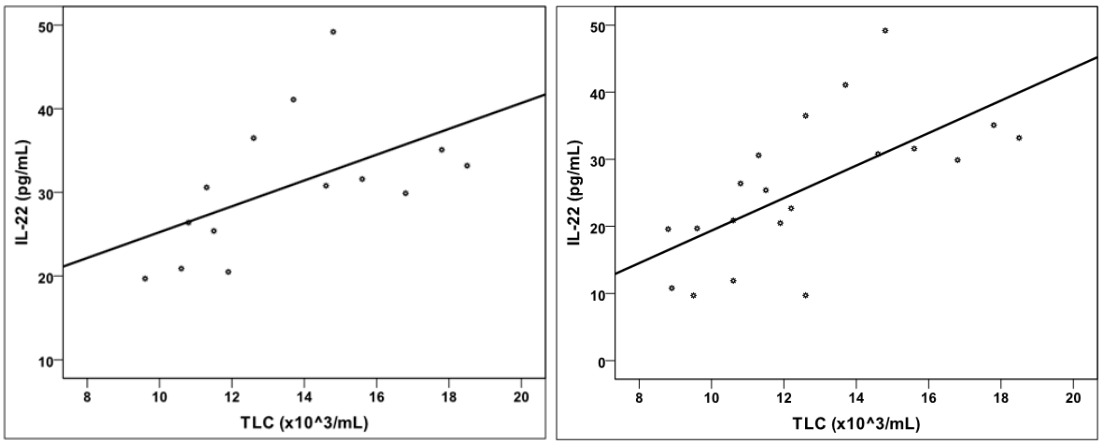
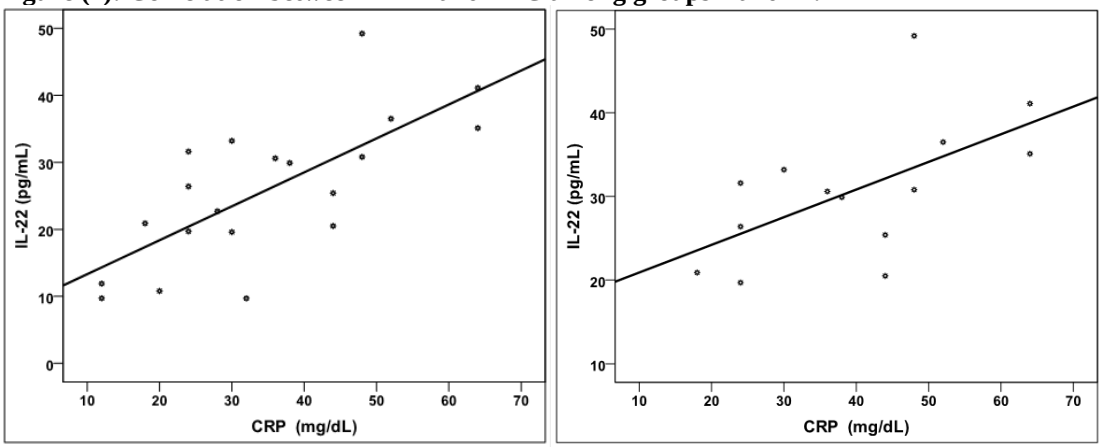


Figure (3): Value of IL-22≥20.0 (pg/mL) in predicting culture positive SBP patients.



Group 1 **Group 1A**

Figure (4): Correlation between IL-22 and TLC among groups 1 and1A.



Group 1 **Group 1A**

Figure (5): Correlation between IL-22 and CRP among groups 1 and1A.

Discussion:

Upon efforts done to search for a rapid reliable test to diagnose SBP ,studies reported enhanced cytokine production in SBP one of it is IL22 which might represent a useful diagnostic tool for SBP .So we aimed in our study to assess the role of IL22 and its relation to other inflammatory markers , including TLC and CRP to reach a more precise and rapid means to diagnose SBP.

Compatible with their ability to translocate into mesenteric lymph nodes; Escherichia coli, Klebsiella pneumoniae and other Enterobacteriaceae have been reported as the species most frequently cause SBP via bacterial translocation **(2)**. Accordingly, in our culture positive patients (n=14), E. Coli was the most commonly cultured microorganism (n=12 85%) .

We found that serum IL22 levels were determined to be significantly higher in patients with SBP than IL22 levels in patients with sterile ascites. We also found that IL22 levels were significantly higher in patients with positive bacterial culture in ascetic fluid compared to patients with culture negative SBP. Our results confirm the previous results reported by Kronenberger et al 2012 who reported increased serum level of IL22 in patients with SBP than its level in patient with sterile ascites**.(9)**

These results also agree with many studies had evaluated the role of serum levels of the cytokines (IL-10, IL-6, IL-1ra and TNF- α) in diagnosis of SBP**.(8)(10)**

-As regard ascitic fluid parameters, we found that ascitic fluid PMNL count was significantly higher in patients with culture positive SBP (Group 1A) than patients with culture negative SBP (Group 1B). We also found that there was a statistically significant positive correlation between serum IL22 level and ascitic fluid PMNL count in patients with culture positive SBP (Group 1A) ($r=0.782$, $p<0.001$), which indicate that serum IL22 level directly proportionate with the severity of ascitic fluid infection.

In our study we found that CRP levels were higher in patients with SBP (Group1) than CRP levels in patients with sterile cirrhotic ascitis(Group2) and in patients with culture positive SBP (Group1A) compared to culture negative SBP (Group 1B) . These results agree with many authors who found CRP levels to be higher in cirrhotic patients with SBP **(11)(12).**

In the present study we concluded that among patients with SBP there was a statistically significant positive correlation between serum IL22 level and TLC($r=0.652$, p 0.002) and CRP($r=0.724$, $p<0.01$).This agree with the results reported by Kronenberger et al.2012 who reported that there was a significant correlation between serum IL-22 levels and CRP which is surrogate marker of ongoing inflammation**.(9)**

By constructing Receiver operating characteristic (ROC) curves for prediction of Group-1(patients with SBP) it was found that ; AUCs of IL22 ,TLC and CRP levels in combination group (Group1) were (0.888 vs 0.988 and 0.826 p=0.001)respectively and by comparing AUCs of TLC with CRP (0.988 vs 0.826 p=0.022 S),TLC with IL22 (0.988 vs 0.888 p=0.066 NS) and IL22 with CRP (0.888 vs 0.826 p=0.459 NS) This explained that TLC was significant in predicting group-1(patients with SBP). From the results of ROC analysis, Cut off value for TLC was 9($x10^3$/mL) with 90% Sensitivity and 95% Specificity(AUC: 0.988, CI 95%: 0.000-1.000, $p<0.001$)**.**

By constructing Receiver operating characteristic (ROC) curves for prediction of group-1A(patients with culture positive SBP) it was found that ; AUCs of IL22,TLC and CRP Levels in culture positive SBP(Group 1A) were (0.964 vs 0.833 and 0.827 p=0.001) respectively. On comparing AUCs of TLC with CRP (0.833 vs 0.827 p=0.967 NS),TLC with IL22 (0.833 vs 0.964 p=0.126 NS) and IL22 with CRP (0.964 vs 0.827 p=0.128 NS) This explained that IL22 was significantly perfect in predicting group-1A (patients with culture positive SBP).

From the results of ROC analysis, Cut off value for serum IL22 was 20 (pg/mL) with 100% Sensitivity and 83% Specificity (AUC: 0.964, CI 95%: 0.773-1.000, $p<0.001$), denoting that IL22 assay seem to provide satisfactory diagnostic accuracy in predicting culture positive SBP .Similarly, in a past study by Kronenberger et al. serum levels of IL22 was reported to be one of the best markers for the diagnosis of SBP, with a cut-off value of 18 pg/ml. **(9)**

This could be explained by that the functions of IL-22 are (1) sustaining the integrity and barrier functions of the tissues and (2) preventing damage caused by either invading pathogens or the inflammatory response itself **(6).**

Given that clinical judgment does not rule out SBP and thus a diagnostic paracentesis should be performed in all patients with cirrhosis and ascites at hospital admission and/or in case of gastrointestinal bleeding, shock signs of inflammation, worsening of liver/renal function or hepatic encephalopathy **(2),** rapid detection and identification of bacteria in the ascitic fluid is the key to improve the survival of cirrhotic patients with ascitic fluid infection **(13).**

In this regard, based on easy to apply, rapid and cost-effective features, determination of serum IL22 levels seems to play an increasingly important role in the rapid detection and identification of cirrhosis related ascitic fluid infection,

culture positive SBP in particular that can be predicted by serum IL22 > 20(pg/mL) for prompt initiation of appropriate therapy that might be helpful increasing overall survival of patients at high risk of SBP development.

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