

Evaluation of Granulocyte Elastase Enzyme in Diagnosis of Spontaneous Bacterial Peritonitis

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Background and study aim: The most common infections in decompensated liver cirrhotic ascites patients are cases of spontaneous bacterial peritonitis (SBP), which account for 40%–70% of cases. SBP is a bacterial infection that occurs in absence of an evident intra-abdominal or surgically treatable source of infection.

Patients and methods: This study was conducted on 80 patients with liver cirrhosis and ascites; 40 patients of them without SBP (group A) and 40 patients of them with SBP (group B) who were admitted to the Hepatology, Gastroenterology and Infectious Diseases Department, Benha University Hospital in the period between April 2014 and October 2014. Full history taking, clinical examination and laboratory investigation were done. Ascitic fluid

analysis was done including detection of granulocyte elastase level.

Results: Granulocyte elastase was markedly elevated in group B; mean ascitic fluid GE ELISA (4.1 ± 2.8) comparing with group A (0.8 ± 0.7) and it revealed a high statistically significant association between SBP and GE (P value < 0.05). SBP was more common in child C. Fever, hypotension and abdominal pain were more common in SBP group.

Conclusion: Granulocyte elastase is increased in cases of SBP, cutoff value of ascitic fluid (GE) for diagnosis of SBP at 0.88 ng/mL had 100% sensitivity, 75% specificity, 80% positive predictive value, 100% negative predictive value and 87.5% accuracy.

INTRODUCTION

Liver cirrhosis is the clinical end-stage of different entities of chronic liver disease when patients suffer from substantial mortality and morbidity, both of which are positively correlated with disease severity [1]. Cirrhosis represents the final common histological pathway for a wide variety of chronic liver diseases. Cirrhosis is defined histologically as a diffuse hepatic process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules. Some patients with cirrhosis are completely asymptomatic and have a reasonably normal life expectancy. Other individuals have a multitude of the most severe symptoms of end-stage liver disease and have a limited chance for survival. Common signs and symptoms may stem from decreased

hepatic synthetic function, decreased detoxification capabilities of the liver (e.g, hepatic encephalopathy), or portal hypertension (e.g, variceal bleeding) [2].

Ascites is defined as an accumulation of excessive fluid within the peritoneal cavity and may be a complication of both hepatic and non-hepatic diseases. The 4 most common causes of ascites are cirrhosis, neoplasm, congestive heart failure, and tuberculous peritonitis [3].

Spontaneous bacterial peritonitis (SBP) is defined as the infection of ascitic fluid (AF) in the absence of a contiguous source of infection and/or an intra-abdominal inflammatory focus. An ascitic fluid polymorphonuclear (PMN) leucocyte count $\geq 250/\text{mm}^3$ irrespective of the AF culture result is universally accepted nowadays as the

best surrogate marker for diagnosing SBP. Frequently the results of the manual or automated PMN count do not reach the hands of the responsible medical personnel in a timely manner [4].

Alternative methods using automated PMN counting [5], reagent strips [6], or ascitic fluid lactoferrin [7] have been developed. Unfortunately, their diagnostic accuracies are limited. Therefore, an accurate and convenient method of rapid diagnosis of SBP remains an unmet clinical need [8].

Granulocyte elastase (GE) is a powerful proteolytic enzyme that is released by PMNs when degranulated in infectious processes [9]. However more studies are needed to evaluate the accuracy of this test in diagnosis of SBP.

PATIENTS AND METHODS

Study design:

Cross-sectional study.

Patients:

We enrolled in the study 80 patients with decompensated chronic liver disease and ascites 40 patients of them without SBP (group A) and 40 patients of them with SBP (group B) who were admitted to the Hepatology, Gastroenterology and Infectious Diseases Department, Benha University Hospital in the period between April 2014 and October 2014 after approval of ethical committee of Benha Faculty of Medicine. The study was performed after written informed consent from all patients.

Fulfilling all criteria detailed below.

Inclusion criteria:

Ascitic patients with clinical, laboratory and ultrasonographic findings of liver cirrhosis were included when:

1. Age >18 years.
2. Symptoms and signs suggest SBP as fever and abdominal pain.

Exclusion criteria:

Patients were excluded when they had any of the following criteria:

1. Patients with antibiotic therapy within one month before.
2. Recent abdominal surgery (< 3 months).
3. Abdominal malignancy as HCC and Colorectal carcinoma.

4. Secondary peritonitis due to intra-abdominal infection for example: abscess, appendicitis, cholecystitis and pancreatitis.
5. Other comorbidities e.g chronic obstructive pulmonary disease, chronic renal failure and ischemic heart disease.

Clinical and Laboratory Assessment:

All patients were subjected to the following: Thorough history taking, through clinical examination, ultrasonographic evaluation and routine laboratory investigations including blood picture, liver and kidney function tests, viral markers.

Sampling:

1. Five ml blood was withdrawn by venipuncture, one ml in EDTA tube for CBC and four ml delivered into plastic tube and allowed to clot. Non-hemolyzed sera was separated by centrifugation and used for determination of creatinine, urea and liver functions (ALT, AST, total bilirubin, albumin, PT and INR).
2. Ascitic fluid sample was taken by paracentesis performed under aseptic conditions from a puncture site in the left or right lower quadrant with the patient in the supine position. All samples for diagnostic testing were immediately collected at the bedside and processed by laboratory personnel without further delay.

Methodology:

- 1- Complete blood picture using (Sysmax 5, Chuo-ku, Kobe, Japan) [10].
- 2- Renal function test: blood urea and serum creatinine were determined calorimetrically on Dialab auto analyzer [11].
- 3- Liver function tests were determined calorimetrically on Dialab auto analyzer and include the following:
 - Serum alanine transaminase (ALT).
 - Serum aspartate transaminase (AST).
 - Serum bilirubin (Total and direct).
 - Serum albumin.
 - Prothrombin time and INR were done using coagulometer [12].
- 4- Serological tests for viral markers using:
 - A. HBs Ag was determined using non – competitive sandwich assay on (ELISA) based technique [13].
 - B. HCV Antibodies were detected using a third generation enzyme linked immunosorbent assay (ELISA) technique [14].

- 5- Ascitic fluid examination for total protein content, albumin, glucose, Lactate dehydrogenase (LDH) and total and differential WBCs counting.
- 6- Ascitic fluid granulocyte elastase was measured by an enzyme-linked immunosorbent assay specific for human granulocyte elastase by a laboratory blinded to the patients' clinical information and other laboratory results. The kit was supplied from *Sunred-bio*, Shanghai, China.

Statistical analysis:

Statistical presentation and analysis of the present study was conducted SPSS V.20. Data was expressed into two phases:

I Descriptive 1- Mean value (X) and Standard Deviation [SD]: for quantitative data. 2- Frequency and percentage for qualitative data.

II Analytic by t-student test and Chi-square test. P value >0.05 was considered statistically non significant P value ≤ 0.05 was considered statistically significant. P value ≤ 0.001 was considered statistically highly significant.

RESULTS

Sixty one of them (76.3%) were males and nineteen (23.7%) were females (Table 1).

By comparison between group A and group B regarding demographic data, there was no statistical significant difference regarding gender, age or residence (P value >0.05) (Table 2).

Seventy seven patients (96.3%) of studied patients were HCV Ab positive and three patients (3.7%) were HBsAg positive and no patient has co-infection (Table 3).

By comparison between group A and group B regarding clinical presentation; abdominal pain and vomiting were founded in 55% and 25% of studied patients in group A. While in group B they had founded in 75% and 45% without

statistically significant difference (P value >0.05) (Table 4).

Jaundice, disorientation and flapping tremor were present in 60%, 52.5% and 50% respectively in group A. While they were present in 65%, 75% and 42.5% respectively in group B without statistical significant difference between both groups (P value >0.05). There was statistical significant difference between both groups regarding systolic blood pressure and temperature (Table 5).

By comparison between group A and group B regarding initial laboratory data. There was no statistical significant difference between both groups (P value >0.05) (Table 6).

By comparison between group A and group B regarding ascitic fluid protein, glucose and LDG, there was no statistical significant difference (P value > 0.05) (Table 7).

By comparison between group A and group B regarding ascitic fluid granulocyte elastase. There was high statistically significant difference between both groups regarding granulocyte elastase (P value < 0.05) (Table 8).

SBP was more common in Child Turcotte Pugh Score class C (87, 5%), while 65% of patients with sterile ascites are Child Turcotte Pugh Score class C (Table 9).

There was a highly statistical significant difference regarding TLC and PMN count in ascitic fluid of SBP group compared to non SBP group (Table 10).

There was a highly statistical significant difference regarding PMN count in ascitic fluid, ascitic fluid (GE) test of SBP group compared to non SBP group (Table 11).

A cutoff value of ascitic fluid (GE) for diagnosis of SBP at 0.88ng/mL had 100% sensitivity, 75% specificity, 80% positive predictive value, 100% negative predictive value and had 87.5% accuracy (Figure 1).

Table (1): Demographic description of studied patients

Variable	Number (80)	%
Gender:		
Male	61	76.3%
Female	19	23.7%

Table (2): Comparison between group A (Non SBP) and group B (SBP) regarding demographic features

Variable	Group A Non SBP (N = 40)	Group B SBP (N = 40)	P. Value
Female	13 (32.5%)	6 (15%)	0.07
Male	27 (67.5%)	34 (85%)	
Rural	27 (67.5%)	34 (85%)	0.07
Urban	13 (32.5%)	6 (15%)	
Age	58.3±8.3	55.8±7.5	0.2

Table (3): Etiology of the chronic liver disease in studied patients. (Virological markers)

Variable	Number (80)	%
HCV Ab(+ve)	77	96.25%
HBS Ag(+ve)	3	3.75%

Table (4): Comparison between group A (Non SBP) and group B(SBP) regarding clinical presentations

Variable	Group A Non SBP (N = 40)	Group B SBP (N = 40)	P. Value
Main Complain:			
1-Abdominal pain	19 (47.5%)	23 (57.5%)	0.4
2-Marked abdominal enlargement	9 (22.5%)	4 (10%)	0.1
3-Fever	11 (27.5%)	13 (32.5%)	0.6
5-Vomiting	0	3 (7.5%)	0.08
6-Hematemesis	7 (17.5%)	4 (10%)	0.3
Symptoms			
1-Abdominal pain	22 (55%)	30 (75%)	0.06
2-Vomiting	10 (25%)	18 (45%)	0.06
3-Diarrhea	4 (10%)	8 (20%)	0.2
4-Hematemesis	6 (15%)	6 (15%)	1
5-Melena	6 (15%)	6 (15%)	0.5

Table (5): Comparison between group A (Non SBP) and group B (SBP) regarding clinical examinations

Variable	Group A Non SBP (N = 40)	Group B SBP (N = 40)	P. Value
Vital signs:			
1-systolic BP	101.9±14.8	96±9.1	0.03
2-diastolic BP	65.5±10.4	64.8±5.9	0.7
3-Temperature	37.5±0.8	37.9±0.8	0.05
4-Respiratory rate	17.6±2.3	17.3±2.9	0.6
General examination:			
1-Jaundice	24 (60%)	26 (65%)	0.6
2-lower limb edema	40 (100%)	40 (100%)	NA
3-disorientation	21(52.5)	30(75%)	0.4
4-Flabbing tremor	20(50%)	17(42.5%)	0.5
5-Hepatic encephalopathy	19(47.5%)	14(35%)	0.2

Table (6): Comparison between group A (Non SBP) and group B (SBP) regarding initial laboratory data

Parameters	Group A Non SBP (N = 40)	Group B SBP (N = 40)	P. Value
Hemoglobin (g/dl)	9.5±0.9	9.6±0.9	0.8
WBC×1000/mm ³	8.7±4.1	8.7±3.4	0.9
Platelet×1000/mm ³	83.83±29.03	93.5±23.73	0.12
Prothrombin time (second)	16.2±1.5	16.6±2	0.4
INR	1.6±0.2	1.6±0.3	0.3
ALT (IU\L)	50.7±21.2	52.1±16.3	0.7
AST (IU\L)	58±21	53.6±17.8	0.3
Albumin (g/dl)	2.1±0.4	2.1±0.3	0.7
Bilirubin Total (mg/dl)	3.5±1.6	3.8±1.7	0.5
Bilirubin Direct (mg/dl)	2.3±1.2	2.4±1.2	0.6
Urea (mg/dl)	73.3±35.5	73±20	0.9
Creatinine (mg/dl)	1.6±0.6	1.8±0.6	0.07

Table (7): Comparison between group A (Non SBP) and group B(SBP) regarding ascitic fluid analysis

Parameters	Group A Non SBP (N=40)	Group B SBP (n=40)	P value
Ascitic fluid protein (g/L) Normal(0.3-4.0g/dL)	1.5±0.5	1.3±0.4	0.09
Ascitic fluid Glucose (mg/L)	156.8±63	146.9±49.3	0.4
Ascitic fluid LDH (IU/L) Normal<400 IU/L	185.3±64.9	201.6±55.9	0.2

Table (8): Comparison between group A (Non SBP) and group B(SBP) regarding ascitic fluid granulocyte elastase

Variable	Group A (mean± SD)	Group B (Mean ± SD)	P value
Ascitic fluid granulocyte elastase (ng)	0.8±1.1	4.1±2.8	≤0.001

Table (9): Comparison between group A (Non SBP) and group B(SBP) regarding Child-Turcotte-Pugh classification

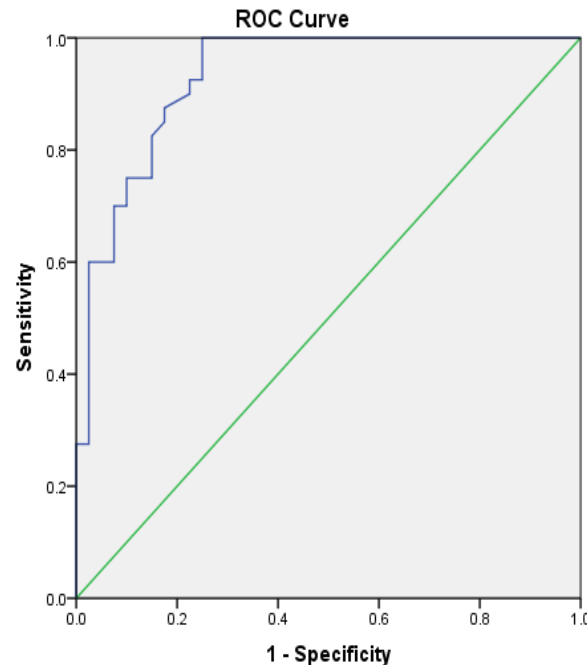
Child Turcotte Pugh Score	Group A Non-SBP patients (N=40)	Group B SBP patients (n=40)
Child(A)	0(0%)	0(0%)
Child(B)	14(35%)	5(12.5%)
Child(C)	26(65%)	35(87.5%)

Table (10): Comparison between group A (Non SBP) and group B(SBP) regarding ascitic fluid WBCS counts and differential

Variable	Group A Non-SBP patients (N=40)	Group B SBP patients (n=40)	P value
Ascitic fluid TLC	95.5±50.4	2300.3±2157.8	≤0.001
Ascitic fluid PMN	76.3±39.8	1671.2±1096.5	≤0.001

Table (11): Comparison between group A (Non SBP) and group B(SBP) regarding ascitic fluid WBCS counts and granulocyte elastase

Variable	Group A Non-SBP patients (N=40)		Group B SBP patients (n=40)		P value
Ascitic fluid PMN > 250	0	0	40	100.0	≤0.001
Ascitic fluid granulocyte elastase > 0.88	2	5	40	100.0	≤0.001



Diagonal segments are produced by ties.

Figure (1): ROC curve for diagnosis of SBP by ascetic fluid granulocyte elastase by ELISA test

DISCUSSION

Ascites is the most common complication in patients with decompensated cirrhosis. Approximately 50% of patients with compensated cirrhosis will develop ascites over a 10-year period [15].

The most common infections in decompensated cirrhotic patients are cases of spontaneous bacterial peritonitis (SBP), which accounts for 40%–70% of cases, followed by urinary tract infections, pneumonia and cellulitis [16].

In this cross sectional comparative study which conducted on 80 patients with cirrhotic ascites, there was no statistical significant difference regarding gender and this in agree with study performed by Puri et al. [17] who reported that gender had no effect on incidence of SBP. Also the studies done by Chang et al.; Amany et al. and Nouh et al. [18-20] had found no statistical significant relation between SBP and gender. This result was not in agreement with the study done by Ageely et al. [21] included 115 cirrhotic ascitic patients, 46 of them had SBP who stated that SBP was frequent in males but was not influenced by the severity of liver disease or age. In this study mean age of patients in group A (58.3 ± 8.3) and mean age of patients in group B (55.8 ± 7.5) without statistically significant difference.

Puri et al.; Chan et al.; Amany et al. and Nouh et al. [17-20] had founded that age seem to have no effect on the incidence of SBP.

In this study, seventy seven patients (96.3%) of the studied population were HCV Ab positive and three patients (3.7%) were HBsAg positive in agree with Amany et al.; Nouh et al. and Rizk et al. [19,20,22] demonstrated that HCV infection being the most frequent cause of chronic liver disease in Egypt. This was documented by Strickland [23] that Clinical studies showed 70% to 90% of patients with chronic hepatitis, cirrhosis, or hepatocellular carcinoma had HCV infections.

In this study, abdominal pain and vomiting were the main clinical presentations in group B compared to group A. These results were found to be close to that reported by Chang et al. and Kaymakoglu et al. [18,24] they stated that abdominal pain and fever are the most characteristic symptoms in patients with spontaneous ascitic fluid infection.

Abdominal pain was detected in 75% of SBP patients. This result was close to the study done by Wallersted et al. and Bibi et al. [25,26] demonstrated that abdominal pain was detected in 70%, 68.5% of SBP cases respectively and also was close to the study done by Badawy et al. [27] who elicited abdominal pain in 80.2% and 84.2% of two groups of SBP cases. On the other

hand study performed by Rizk et al. and Ibrahim et al. [22,28] elicited abdominal pain in 43% and 55.7% of SBP cases respectively.

In this study, hypotension and elevated temperature had statistically significant association with SBP group. These results were close to that reported by Zalam et al. [29] who stated that fever was detected in 75% of SBP cases with statistically significant association with SBP. On the other hand study performed by Bibi et al. [26] elicited fever in 52.6% of SBP cases without statistical significant difference.

In this study, hepatic encephalopathy was detected in 35% of SBP and 47.5% of non SBP cases with statistically insignificant difference. These results were close to that reported by Wallersted et al. and Bibi et al. and Nobre et al. [25,26,30] who stated that hepatic encephalopathy was detected in 20%, 24.5% and 28.9% of SBP cases respectively. These results conflict the fact that the presence of hepatic encephalopathy in the course of liver cirrhosis is a marker of severe hepatic dysfunction that correlates with high prevalence of bacterial infections most commonly SBP [31]. This can be explained by selection bias of the two groups.

On the contrary, these results were against to that reported by Zalam et al.; Llovet et al. and Elsaad et al. [29,32,33] who stated that hepatic encephalopathy was detected in 40%, 40.4% and 50% of SBP cases respectively with high statistical significance. This can be explained by development of portosystemic encephalopathy indicates decompensated liver disease and therefore, other features of decompensation, such as varices, ascites, and portal hypertension.

In this study we had found that mean hemoglobin was (9.5 ± 0.9) , mean total leucocytic count was $(8.7 \pm 4.1) \times 1000/\text{cm}^3$, mean platelet count was $(83.8 \pm 29.03) \times 1000/\text{cm}^3$ and mean prothrombin time was (16.2 ± 1.5) second in group A while mean hemoglobin was (9.6 ± 0.9) , mean total leucocytic count was $(8.7 \pm 3.4) \times 1000/\text{cm}^3$, mean Platelet count was $(93.5 \pm 23.7) \times 1000/\text{cm}^3$ and mean prothrombin time (16.6 ± 2) second in group B without statistical significant difference.

This go on line with study done by Nouh et al.; Zalam et al. and Elsaad et al. [20,29,33] demonstrated that no statistical significant differences were detected as regard TLC among both patient groups.

On the contrary, these results were against to the study done by Amany et al.; Rizk et al.;

Rodriguez-Ramos et al.; Syed et al. and Lutz et al. [19,22,34-36] reported that there was statistically significant high serum total leucocytic count in SBP group. This could be explained by that bacterial translocation to mesenteric lymph node had important immunological function associated with local/systemic inflammatory response leading to peripheral leukocytosis [37].

The present study had showed that decrease Hb %, platelet count and prolonged prothrombin time in comparison to non infected cases, this was in agreement with Gschwantler et al. and Kawasaki et al. [38,39] who stated that in patients with CLD, a sort of pancytopenia would be expected due to increased blood sequestration in the spleen and to low thrombopoietin levels.

In this study, there was no statistical significant difference between both groups regarding serum alanine transaminase, serum aspartate transaminase, serum albumin and bilirubin (total & direct). This in accordance with Nouh et al.; Rizk et al. and Zalam et al. [20,22,29] who reported no statistical significant differences were detected as regard liver function test among both groups.

On the contrary, Amany et al. and Elsaad et al. [19,33] reported statistically significant lower serum albumin level in SBP group. And also El-Gendy et al. [40] stated statistically significant elevated serum bilirubin and prolonged prothrombin time in SBP group.

In this study regarding the kidney function test, there was no statistical significant difference and this agree with Amany et al.; Nouh et al. and Zalam et al. [19,20,29] who reported no statistical significant difference comparing both groups as regards kidney function tests.

These results were coinciding with the study done by Rizk et al.; Lutz et al.; Ruiz Del Arbol et al. and Gill et al. [22,36,41,42] found that patients with SBP frequently develop a rapidly progressive impairment in systemic hemodynamics, leading to severe renal and hepatic failure, aggravation of portal hypertension, encephalopathy, and death. This occurs despite rapid resolution of infection and is associated with an extremely poor prognosis. Also the study performed by Follo et al. [43] stated that one third of patients with SBP develop renal impairment and it is common in patients with severely impaired liver functions. It is not worthy that hepatorenal syndrome is the extreme expression of this circulatory dysfunction [44].

In this study, SBP was more common in advanced Child-Pugh class C (87.5%) of patient in group B (SBP) compared with (65%) of patients in group A (Non SBP) meaning that the severity of the liver disease is probably an important risk factor for the development of SBP [45]. This was close to Quenzer [46] who reported that about 70% of the patients who develops SBP are in Child C class, with the remainder being class B.

By ascitic fluid analysis in studied groups, the mean ascitic fluid protein was (1.5±0.5 g/dl), mean ascitic fluid glucose was (156.8±63 mg/l) and mean ascitic fluid lactate dehydrogenase [LDH] was (185.3±64.9 IU/L) in group A. While in group B mean ascitic fluid protein was (1.3±0.4 g/dl), mean ascitic fluid glucose was (146.9±49.3 mg/l) and mean ascitic fluid LDH was (201.6±55.9 IU/L).

By comparison between studied groups, there was no statistical significant difference regarding ascitic fluid analysis ($P>0.05$), and this in accordance with Zalam et al. and Elsaad et al. [29,33] who reported that there was no statistical significant difference regarding ascitic fluid total protein, glucose and LDH levels between both groups. And also Bibi et al. [26] reported that there was no statistical significant difference regarding ascitic fluid total protein, glucose.

This result on disagreement with study performed by Amany et al. [19] stated statistical significant low ascitic fluid total protein, glucose and elevated LDH in SBP group. And also with study done by Abbass et al. [47] reported statistical significant low ascitic fluid albumin in SBP group while other parameters are statistically insignificant.

This result could be explained as both groups showed advanced liver disease so both have low proteins. Thus a follow up paracentesis is recommended as it may detect development of SBP being a high risk group. It is to be noted that, in contrast to other infected body fluids, ascitic fluid during SBP exhibited neither a rise in protein concentration nor a drop in absolute glucose concentration [48]. These results were contradictory to Sheer and Runyon [49] who reported that ascitic fluid total proteins were lower in patients with SBP than patients with sterile cirrhotic ascites and to Runyon [50] who stated that patients with low ascitic fluid total proteins (<1 g/dl) have to receive an antibiotic chemoprophylaxis as they are more prone to

recurrence of SBP than those with high ascitic fluid total protein content (>1 g/dl). Moreover, low ascitic fluid protein level <1 g/dl considered to be the most important predisposing factor for developing the first episode of SBP [51] this was confirmed by Guarner et al. [52] who observed that about one fourth of patients with ascitic fluid protein levels less than 1g/dl developed SBP during a 3-year follow-up compared to only 4% of patients with higher levels.

By comparison between group A and group B regarding ascitic fluid granulocyte elastase. There was high statistically significant association between SBP and granulocyte elastase (P value < 0.05).

This result was in agreement with the study performed by [9] reported GE level was statistically significant higher in both ascitic fluid and plasma of SBP group than in non-SBP group at the time of diagnosis.

Also this result go on line with study done by Yamazaki et al. [53] stated that ascitic fluid GE levels were significantly higher in SBP group as detected by three different methods (latex immunoassy , ELISA and reagent strip).

As regards this study, we found that cutoff of ascitic fluid (GE) for diagnosis of SBP at 0.88 ng/ml had sensitivity 100%, specificity 75% and these coincides with Yamazaki et al.s [53] who reported that cut-off diagnostic value for SBP for ascitic fluid GE latex immunoassy at 49.5 ng/ml had 85.7% sensitivity and 97.7% specificity. This difference may be due to small number of SBP patients in this study which include 58 cirrhotic ascitic patients, 12one of them only having SBP.

In conclusion, Diagnosis of SBP on clinical basis is difficult as there is extremely variable clinical presentations. fever; hypotension and abdominal pain were more common in SBP group. Granulocyte elastase (GE) is increased in cases of spontaneous bacterial peritonitis (SBP) with cutoff value of ascitic fluid (GE) for diagnosis of SBP was at >0.88ng/mL had 100% sensitivity, 75% specificity, 80% positive predictive value, 100% negative predictive value with 87.5% accuracy.

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