Homocysteine as a Diagnostic Marker in Spontaneous Bacterial Peritonitis

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Received: 17 July 2021

Accepted: 23 February 2022

Abstract

Background: Spontaneous bacterial peritonitis (SBP) is a unique and a widespread complication in cirrhotic patients. The prevalence ranges from 10 to 30% in cirrhotic ascitic patients. **Aim of work**: to evaluate role of homocysteine level in ascetic fluid in diagnosis of ascetic fluid infection. **Methods:** Patients were classified into two groups: Group I includes 45 patients with cirrhotic ascites complicated with SBP and group II includes 45 patients with cirrhotic ascites and without SBP. All patients were subjected to full history taking, complete clinical examination, as well as laboratory investigations and measurement of homocysteine level in ascetic fluid sample. **Results and conclusion**: There was no statistically significant difference found between the two studied groups regarding glucose, total protein in ascetic fluid of the studied cases. While there was statistically significant difference between them regarding albumin, TLC and neutrophils in ascetic fluid. There was highly statistically significant difference between the two studied groups regarding homocysteine in ascetic fluid of the studied cases. The predictive value for detection of SBP was 4.9, with a sensitivity of 91.11%, specificity of 93.33%, +ve predictive value of 93.2% and -ve predictive value of 91.3%, denoting that homocysteine measurement is considered as good test for prediction of spontaneous bacterial peritonitis.

Keywords: Homocysteine; liver; ascitic fluid; ascites

Introduction

Spontaneous bacterial peritonitis (SBP) is a unique and a widespread complication in cirrhotic patients. The prevalence ranges from 10 to 30% in cirrhotic ascitic patients at the time of hospital admission and about 50% develop during hospitalization, with a mortality rate about 20–30% depending on several factors. In

ascitic fluid, local and systemic immune dysfunction with bacterial translocation and reduced opsonic activity are the cornerstone mechanisms in the pathogenesis of SBP (1).

The mortality rate exceeds 80% in patients with cirrhosis who develop septic shock secondary to spontaneous bacterial peritonitis. In addition, each hour of delay in appropriate antimicrobial therapy increases the in hospital mortality rate by 1.86 time. So, it is recommended to perform a diagnostic paracentesis in all cirrhotic ascites at the time of admission and/or in the case of occurrence of signs of inflammation, hepatic encephalopathy, shock, gastrointestinal bleeding, and worsening of hepatic or renal function (2).

In SBP, the diagnosis of a classic case depends on the ascetic polymorphonuclear (PMN) cell count (>250/mm^3) and a positive ascitic fluid culture. According to the ascetic fluid analysis (culture/sensitivity and cell count) findings, two variants of SBP have been characterized, that is, bacterascites (BA) and culture-negative neutrocytic ascites (CNNA). BA has ascitic PMN cell count (< 250/mm3) and positive ascitic fluid culture. CNNA has ascitic PMN cell count (>250/mm3) and a negative culture. The diagnosis of SBP depends on the presence of ascetic PMN cell count exceeding 250/µl. Generally, this count is assessed using automated or manual counting (3).

Homocysteine (Hcy) is an amino acid that might be found in all cells in small amounts; it is a significant methionine metabolite quantitatively. In addition, Hcy can be present either in the form of disulfide proteins or freely in the body. Reduced or free form accounts for only 1–2%, in relation to a total Hcy quantity. However, about 80% is protein-bound Hcy, mostly to albumins (4).

Hcy accumulates in cells and reaches the blood if its catabolism is affected either due to enzyme defect or deficiency of required intracellular cofactors (5). Several studies of different biochemical markers in patients with ascites have been carried out for the diagnosis of SBP.

Aim of this work was to evaluate the role of homocysteine level in ascetic fluid in diagnosis of ascetic fluid infection .

Patients and methods

This cross-sectional study was conducted at Department of Hepatology, Gastroenterology and Infectious Diseases at Ahmed Maher Teaching Hospital, during the period from January 2020 to January 2021. The studied population consisted of 90 patients with ascites. Written informed consent were obtained from all participants who were fully informed about the study and advised that the study will have no extra expense for

participants according to the Committee of Ethics of Scientific Research of Benha Faculty of Medicine in Benha University.

Patients were classified into two groups: Group I includes 45 patients with cirrhotic ascites complicated with SBP and group II includes 45 patients with cirrhotic ascites and without SBP.

Inclusion criteria

- Patients >18 years old.
- Patients suffering from liver cirrhosis and ascites, both diagnosed by clinical, laboratory and radiological investigations.
- Approval of subjects.

Exclusion criteria

- Recent abdominal surgery.
- Solid organ transplant recipients.
- Patients with documented colitis or enteritis.
- Other non-peritoneal infections (skin infections, chest infections, urinary tract infections, meningitis, dental infections gastroenteritis and biliary tract infections).
- Presence of other causes associated with homocysteinemia, such as thrombosis, neuropsychiatric illness, fractures and severe renal failure.
- Subject's refusal.
- All patients were subjected to full history taking, complete clinical examination, and laboratory investigations.

Venous blood samples (7.5 ml) were taken using sterile syringes under aseptic conditions. The collected samples were sent immediately to the laboratory of Benha University Hospital for the following laboratory investigations: complete blood count (CBC), fasting blood sugar (mg/dl), liver biochemical tests including: serum alanine aminotransferase (ALT) (IU/L) and serum aspartate aminotransferase (AST) (IU/L), serum bilirubin (total and direct) (mg/dl), serum albumin (mg/dl), serum creatinine (mg/dl).

Two milliliters of ascitic fluid were centrifuged and the supernatant was aliquoted and frozen at −20°C for the measurement of ascetic Hcy. Ascitic fluid samples were aspirated under complete aseptic conditions. Measurement of *Polymorphonuclear leukocytes (PMN)* count using hemocytometer and microscopic method, and measurement of homocysteine level in ascetic fluid sample were done by ELISA.

Statistical analysis

Data was analyzed using SPSS (statistical package for social sciences) version 22. Qualitative data were presented as number and percent, Quantitative data was tested for normality by Kolmogrov Smirnov test then described as mean and

standard deviation for normally distributed data and median and range for non-normally distributed. The appropriate statistical test was applied according to data type with the following suggested tests: Chi-Square for categorical variable. One Way ANOVA with post Hoc Tukey Test and Kruskal Wallis test with Mann-Whitney U test for pairwise comparison for comparing continuous variables. Receiver Operating characteristics curve was used to detect best cut off point for ascitic homocysteine for differentiating studied groups

Results

There was no statistically significant difference found between the two studied groups regarding gender , residence , occupation and special habit of the studied cases while there was statistically significant difference found between them regarding age of the studied cases (age in non SBP group was older than age in SBP group), (Table 1).

Fever and tachycardia were more frequent in SBP group than non SBP group while there was no statistically significant difference between the studied groups regarding blood pressure and respiratory rate.

There was no statistically significant difference found between the two studied groups regarding splenomegaly, vomiting, diarrhea, jaundice, bleeding, history of diabetes ,history of hypertension and other chronic diseases while there was statistically significant difference between them regarding tremors palmer erythema and hepatic encephalopathy (increase in SBP group in comparison to non SBP group) with highly significant difference between them regarding fever, abdominal pain, and history of SBP (increase in SBP group in comparison to non SBP group) (Table 2).

Direct bilirubin and alkaline phosphatase and total leukocyte count and low serum albumin were more frequent in SBP group in comparison to non SBP group while there was no statistically significant difference between the two groups regarding hemoglobin, platelets, AST, ALT, total bilirubin, creatinine and fasting blood sugar of the studied cases, (Table 3).

Tense ascites was more frequent in SBP group and there was no statistically significant difference found between the two studied groups regarding size of spleen and corticomedullary differentiation in ultrasound, (Table 4).

There was no statistically significant difference found between the two studied groups regarding glucose, total protein in ascetic fluid of the studied cases while there was statistically significant difference between them regarding albumin in ascetic fluid with highly significant difference between them regarding TLC and neutrophils in ascetic fluid (increase in SBP group in comparison to non SBP group), (Table 5).

There was highly statistically significant difference between the two studied groups regarding homocysteine in ascetic fluid of the studied cases, (fig. 1). ROC curve shows that the best cut off point for homocysteine level to differentiate between SBP and non SBP groups was > 4.9 with sensitivity of 91.11%, specificity of 93.33% and area under curve (AUC) of 89.1%, (fig. 2).

Table 1: Comparison between cases with SBP and non SBP regarding demographic data of the studied patients

		SBP **No.= 45**	**Non SBP** **No.= 45**	**Test value**	**P- value**	**Sig.**
Gender	**Male**	25 (55.6%)	20 (44.4%)	1.111*	0.292	NS
	Female	20 (44.4%)	25 (55.6%)			
Age	**Mean±SD**	59.93 ± 8.81	66.76 ± 8.98	-3.637•	0.001**	HS
	Range	30 – 87	49 – 95			
Residence	**Rural**	5 (11.1 %)	3(6.7%)	1.451	0.093	NS
	Urban	40 (88.9)	42(93.3%)			
Occupation	**Farmer**	5 (11.1 %)	3(6.7%)	1.958	0.081	NS
	Non farmer	40 (88.9)	42(93.3%)			
Special habit	**Smoker**	15(33.3%)	12 (26.7%)	1.732	0.653	NS
	No smoker	30(66.7%)	33 (73.3%)			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*:Chi-square test; •: Independent t-test

Table (2): Comparison between the two groups regarding clinical manifestation

		SBP		Non SBP		Test value*	P- value	Sig.
		No.	%	No.	%			
Fever	**Absent**	15	33.3%	39	86.7%	26.667	0.000	HS
	Present	30	66.7%	6	13.3%			
Abd Pain	**Absent**	5	11.1%	36	80.0%	43.051	0.000	HS
	Present	40	88.9%	9	20.0%			
Lower Limp Oedema	**Absent**	0	0.0%	0	0.0%	-	-	-
	Present	45	100.0%	45	100.0%			
Tremors	**Absent**	34	75.6%	42	93.3%	5.414	0.020	S
	Present	11	24.4%	3	6.7%			
Palmer Erythema	**Absent**	30	66.7%	40	88.9%	6.429	0.011	S
	Present	15	33.3%	5	11.1%			
Splenomegaly	**Absent**	7	15.6%	7	15.6%	0.000	1.000	NS
	Present	38	84.4%	38	84.4%			
Vomiting	**Absent**	42	93.3%	43	95.6%	0.212	0.645	NS
	Present	3	6.7%	2	4.4%			
Diarreha	**Absent**	43	95.6%	43	95.6%	0.000	1.000	NS
	Present	2	4.4%	2	4.4%			
Jaundice	**Absent**	7	15.6%	12	26.7%	1.668	0.197	NS
	Present	38	84.4%	33	73.3%			
Bleeding	**Absent**	43	95.6%	40	88.9%	1.394	0.238	NS
	Present	2	4.4%	5	11.1%			
Hepatic	**Absent**	34	75.6%	42	93.3%	5.414	0.020	S
Encephalopathy	**Present**	11	24.4%	3	6.7%			
History of S.B.P	**Absent**	31	68.9%	41	91.1%	6.944	0.008	HS
	Present	14	31.1%	4	8.9%			
History of diabetis	**Absent**	34	75.6%	39	86.7%	1.813	0.178	NS
	Present	11	24.4%	6	13.3%			
History of	**Absent**	43	95.6%	44	97.8%	0.345	0.557	NS
hypertension	**Present**	2	4.4%	1	2.2%			
History of other	**Absent**	38	84.4%	39	86.7%	0.090	0.764	NS
chronic diseases	**CKD**	7	15.6%	6	13.3%			
History of Bleeding	**Absent**	39	86.7%	38	84.4%	0.090	0.764	NS
	Present	6	13.3%	7	15.6%			
History Of Operation	**Absent**	43	95.6%	43	95.6%	0.000	1.000	NS
	Cholecystectomy	2	4.4%	2	4.4%			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*:Chi-square test

Table (3): Comparison between the two groups according to Laboratory data

		SBP No.= 45	Non SBP No.= 45	Test value	P- value	Sig.
HGB	**Mean±SD**	10.13 ± 1.55	9.62 ± 1.66	1.499•	0.138	NS
	Range	5 – 13	4.9 – 12.7			
TLC	**Median (IQR)**	13 (8.81 – 16.9)	7.2 (5.2 – 8.9)	-4.219≠	0.000	HS
	Range	2.2 – 32.8	3.49 – 25.26			
PLAT	**Median (IQR)**	94 (80 – 125)	96 (74 – 110)	-0.222•	0.824	NS
	Range	32 – 237	22 – 386			
AST	**Median (IQR)**	55 (34 – 70)	45 (34 – 69)	-0.509≠	0.611	NS
	Range	21 – 261	12 – 461			
ALT	**Median (IQR)**	27 (20 – 39)	23 (18 – 35)	-1.082≠	0.279	NS
	Range	10 – 116	6 – 320			
Serum .ALB	**Mean±SD**	2.20 ± 0.33	2.57 ± 0.43	-4.569≠	0.000	HS
	Range	1.7 – 3	1.7 – 3.4			
Bil Total	**Median (IQR)**	2.2 (1.9 – 4.2)	2 (1.2 – 2.5)	-1.960≠	0.050	NS
	Range	0.3 – 8.7	0.5 – 29			
Bil. Direct	**Median (IQR)**	1.4 (0.6 – 3)	0.8 (0.5 – 1.3)	-2.056≠	0.040	S
	Range	0.1 – 6.4	0.2 – 21			
Alk.phosp	**Mean±SD**	235.11 ± 111.52	183.22 ± 83.41	2.500•	0.014	S
	Range	61 – 620	52 – 450			
PT	**Mean±SD**	24.62 ± 9.68	21.89 ± 6.76	1.553•	0.124	NS
	Range	13 – 49.4	13 – 44.4			
INR	**Mean±SD**	1.90 ± 0.75	1.66 ± 0.59	1.656•	0.101	NS
	Range	1 – 3.8	0.15 – 3.58			
Cr	**Median (IQR)**	1 (0.8 – 2)	1.1 (0.8 – 1.8)	-0.045≠	0.965	NS
	Range	0.5 – 3.8	0.3 – 5			
F.B.S	**Mean±SD**	101.82 ± 40.10	96.89 ± 27.12	0.684•	0.496	NS
	Range	59 – 243	62 – 200			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
•: Independent t-test; ≠: Mann Whitney test

Table (4): Comparison between the two groups according to Ultrasound of the studied patients

		SBP No.	SBP %	Non SBP No.	Non SBP %	Test value*	P- value	Sig.
Cirrhotic shrunken liver	**Present**	45	100.0%	45	100.0%	-	-	-
Size Of Spleen	**Normal size**	7	15.6%	7	15.6%	0.000	1.000	NS
	Splenomegaly	38	84.4%	38	84.4%			
Ascitis	**Moderate ascities**	5	11.1%	27	60.0%	23.470	0.000	HS
	Tense	40	88.9%	18	40.0%			
Kidney	**Normal**	38	84.4%	39	86.7%			
	Abnormal corticomedullary differentiation	7	15.6%	6	13.3%	0.090	0.764	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*:Chi-square test

Table 5: Comparison between cases with SBP and non SBP according to Ascetic fluid analysis of the studied patients

		SBP No.= 45	Non SBP No.= 45	Test value	P- value	Sig.
Glucose	**Mean±SD**	156.93 ± 53.98	155.98 ± 47.93	0.089	0.929	NS
	Range	93 – 397	87 – 308			
Total Protein	**Mean±SD**	1.26 ± 0.59	1.19 ± 0.40	0.712	0.479	NS
	Range	0.5 – 3.1	0.4 – 2.8			
Alb	**Mean±SD**	0.60 ± 0.30	0.48 ± 0.15	2.527	0.013	S
	Range	0.2 – 1.7	0.2 – 0.9			
TLC	**Mean±SD**	0.70 ± 0.31	0.27 ± 0.15	8.241	0.000	HS
	Range	0.3 – 1.9	0.1 – 0.7			
Neutrophil	**Mean±SD**	68.58 ± 12.57	51.18 ± 21.30	4.720	0.000	HS
	Range	40 – 90	10 – 80			
homocys	**Mean±SD**	6.67 ± 2.53	3.83 ± 1.83	6.081	0.000	HS
	Range	1.9 – 15.5	1 – 12.5			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

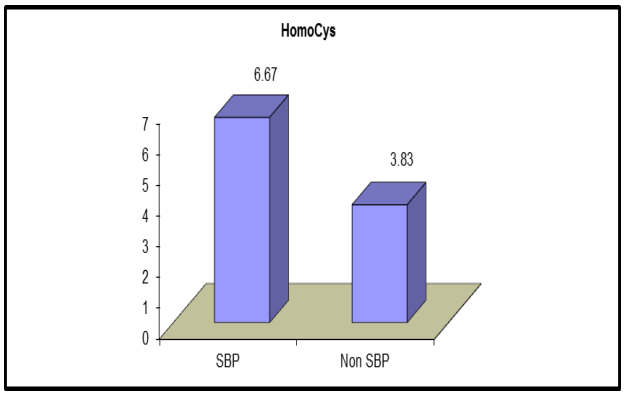

Fig 1: Comparison between cases with SBP and non SBP according to homocysteine in ascetic fluid

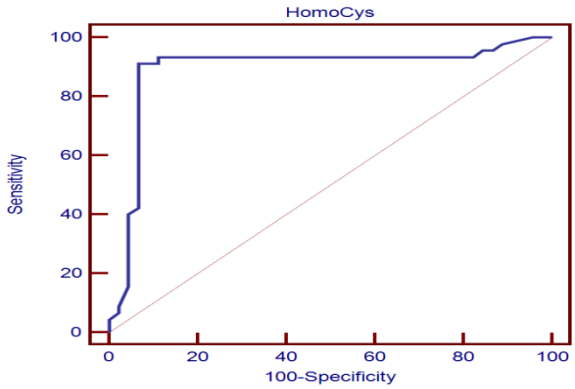

Fig 2: ROC curve of Homo Cys as a predictor between SBP and Non-SBP

Discussion

This study involved 90 patients; 45 of them (25 males and 20 females) aged between 30 - 87 with a mean age of 59.93 ± 8.81 years with liver cirrhotic ascites and spontaneous bacterial peritonitis (patient's group) and 45 (20 males and 25 females) aged between 49 – 95 years with a mean age of 66.76 ± 8.98 years with liver cirrhotic ascites without spontaneous bacterial peritonitis (control group).

In the present study, there were no statistically significant differences in the gender, residence, occupation and special habit among cases with and without spontaneous bacterial peritonitis, while there was statistically significant difference between them regarding age of the studied cases.

There was no statistically significant difference between the two studied groups regarding splenomegaly, vomiting, diarrhea, jaundice, bleeding, history of diabetes, hypertension, other chronic diseases and operations of the studied cases, while there was statistically significant difference between them regarding tremors, palmer erythema and hepatic encephalopathy with highly significant difference between then regarding fever, abdominal pain and history of SBP.

It was estimated that almost all patients with SBP had symptoms or signs that clearly suggested the presence of peritoneal infection, especially abdominal pain, fever and chills. Other patients expressed minor symptoms with deteriorating liver or renal function (6).

The clinical features among the patients of SBP were not specific and asymptomatic patients constitute a relatively high percentage (16%). Presence of ascites usually prevents the development of a rigid abdomen by separating the visceral from the parietal peritoneal surfaces (7).

It was found that fever is the most common manifestation of SBP and signs of hepatic encephalopathy, abdominal tenderness, diarrhea, ileus, shock and hypothermia. Approximately 10% of the patients with SBP are asymptomatic. Presence of ascitis usually prevents the development of a rigid abdomen by separating the visceral from the parietal peritoneal surfaces (8). In a study done in 2007 it reported 8% of their 133 cirrhotic ascitic patients as being asymptomatic and abdominal pain and tenderness were more common in their patients with SBP (9).

The present study showed that there was statistically significant difference between the two studied groups regarding tremors,

palmer erythema, hepatic encephalopathy, direct bilirubin, alkaline phosphatase and albumin in ascetic fluid with highly significant difference between them regarding fever, abdominal pain, and history of SBP, TLC, serum albumin and neutrophils in ascetic fluid.

It was found that glucose concentration in the serum and ascites were similar even during early SBP (7). It was concluded in another study that low protein concentration in the ascitic fluid has been identified as a risk factor for SBP and these patients are candidates to receive long-term prophylaxis to reduce the risk of infections and improve survival (10).

To the best for our knowledge, no previous studies evaluated the role of homocysteine in diagnosis of spontaneous bacterial peritonitis except **Abdel-Razik** (11) who studied the role of homocysteine in serum and ascetic fluid in diagnosis of spontaneous bacterial peritonitis

In our study, there was highly statistically significant difference between the two studied groups regarding homocysteine in ascetic fluid of the studied cases. In a study done in 2018 (11, serum homocysteine was assessed as a precise indicative marker for the diagnosis of all variants of SBP. Participants were classified into a non-SBP group, including 262 participants and 61 patients with SBP. Serum and ascitic homocysteine were considerably elevated in the SBP group compared to the non-SBP group.

The present study showed that SBP group had statistically significant positive correlation between homocysteine level and platelet, AST and glucose level in ascetic fluid while there was no statistically significant correlation with the other studied parameters.

It was found that homocysteine was positively correlated with the polymorphonuclear count, C-reactive protein, Child-Pugh score, and Model For End-Stage Liver Disease score as well as negatively correlated with the protein content in the ascitic fluid and estimated glomerular filtration rate. After SBP therapy, there was a marked reduction in serum and ascitic homocysteine levels (11).

In our study, there was statistically significant increase in the level of homocysteine in cases with splenomegaly while no statistically significant relation with the other studied parameters in SBP group. Also, there was statistically significant increase in the level of homocysteine in cases with splenomegaly in ultrasound while no statistically significant relation with ascitis in SBP group. But, non-SBP group showed no statistically significant relation between

homocysteine level and the clinical examination parameters.

It was demonstrated that serum and ascitic homocysteine are considerably higher in SBP participants versus non-SBP patients. Serum homocysteine may provide a reliable and noninvasive diagnostic marker for all variants of SBP (11).

Regarding the ROC curve for the prediction of SBP according to homocysteine, a cutoff value of 4.9, with a sensitivity of 91.11% and specificity of 93.33%, has a positive predictive value of 93.2% and a negative predictive value of 91.3%.

It was also found that at a cutoff value of 17.79 μmol/l, serum homocysteine had 89.3% specificity and 95.1% sensitivity for distinguishing SBP (area under the curve: 0.932) and, at a cutoff value of 16.1μmol/l, ascitic homocysteine had 84.4% specificity and 92.7% sensitivity for distinguishing SBP (area under the curve: 0.901) (11).

Several studies have evaluated several biomarkers for diagnosis of ascetic fluid infection; however, studies evaluating the role of Hcy in SBP are still limited, e.g. the study done 2018 (11), which denoted that homocysteine measurement is considered as good test for prediction of spontaneous bacterial peritonitis.

Conclusion

Ascetic fluid homocysteine level can represent a potential marker for diagnosis of spontaneous bacterial peritonitis.

References

1. Wiest R, Lawson M, Geuking M. Pathological bacterial translocation in liver cirrhosis. J Hepatol. 2014;60(1):197–209.
2. Runyon BA. Introduction to the revised American Association for the Study of Liver Diseases Practice Guideline management of adult patients with ascites due to cirrhosis 2012. Hepatology. 2013;57(4):1651–3.
3. Yachha SK, Khanna V. Ascites in childhood liver disease. Indian J Pediatr. 2006;73(9):819–24.
4. Fiskerstrand T, Refsum H, Kvalheim G, Ueland PM. Homocysteine and other thiols in plasma and urine: automated determination and sample stability. Clin Chem. 1993;39(2):263–71.
5. Škovierová H, Vidomanová E, Mahmood S, Sopková J, Drgová A, Červeňová T, et al. The molecular and cellular effect of homocysteine metabolism imbalance on human health. Int J Mol Sci. 2016;17(10):1733.
6. Yang Y-Y, Lin H-C. Bacterial infections in patients with cirrhosis. J Chinese Med Assoc. 2005;68(10):447–51.
7. Akriviadis EA, Runyon BA. Utility of an algorithm in differentiating spontaneous from secondary bacterial peritonitis. Gastroenterology. 1990;98(1):127–33.
8. Căruntu FA, Benea L. Spontaneous bacterial peritonitis: pathogenesis, diagnosis, treatment. J Gastrointestin Liver Dis. 2006;15(1):51–6.
9. Wallerstedt S, Olsson R, Simrén M, Broomé U, Wahlin S, Lööf L, et al. Abdominal tenderness

in ascites patients indicates spontaneous bacterial peritonitis. Eur J Intern Med. 2007;18(1):44–7.

10. Terg R, Fassio E, Guevara M, Cartier M, Longo C, Lucero R, et al. Ciprofloxacin in primary prophylaxis of spontaneous bacterial peritonitis: a randomized, placebo-controlled study. J Hepatol. 2008;48(5):774–9.
11. Abdel-Razik A, Eldars W, Elhelaly R, Eldeeb AA, Abdelsalam M, El-Wakeel N, et al. Homocysteine: a new diagnostic marker in spontaneous bacterial peritonitis. Eur J Gastroenterol Hepatol. 2018;30(7):779–85.

To cite this article: Samir M. Kabeel, Hany Ragheb, Sara M. Atef, Andrew R. Ragheb. Homocysteine as a Diagnostic Marker in Spontaneous Bacterial Peritonitis. BMFJ 2022;39(1):164-175. DOI: 10.21608/bmfj.2021.86746.1443