ABENHA MEDICAL JOURNAL bmj
Print ISSN 1110-208X
Online ISSN 2357-0016

Original article

Assessment of Serum-Ascites Vitamin D Gradient (SADG) in Spontaneous Bacterial Peritonitis

Sabry A. Awad [a], Mohammed E. El Shewi [a], Sayed M. Abd-El-Aliem [a], Omar M. Sabry [b]

[a] Department of Hepatology, Gastroenterology and Infectious Diseases, Faculty of Medicine Benha University, Egypt.
[b] Department of Hepatology, Gastroenterology and Infectious Diseases, Theodor Bilharz Research Institute (TBRI), Giza, Egypt

Corresponding to: Sayed M. Abd-El-Aliem, Department of Hepatology, Gastroenterology and Infectious Diseases, Faculty of Medicine Benha University, Egypt.

Email:

doctorsayed@gmail.com

Received: 4 June 2024

Accepted:7 September 2024

Abstract

Background: Spontaneous bacterial peritonitis (SBP) is a severe infection occurring in patients with decompensated liver cirrhosis and ascites. The diagnosis of SBP is typically confirmed by an ascitic fluid polymorphonuclear (PMN) count ≥250 cells/mm³. Recent studies suggest that vitamin D, due to its immunomodulatory properties, may play a role in the pathophysiology of SBP. This study aimed to evaluate the serum-ascites vitamin D gradient (SADG) as a potential diagnostic marker for SBP. **Methods:** This cross-sectional study included 50 cirrhotic patients with portal hypertensive ascites, divided into two groups: 25 patients with SBP (Group I) and 25 patients without SBP (Group II). Serum and ascitic fluid samples were collected to measure 25-hydroxy vitamin D levels, from which the SADG was calculated. Additional biochemical and clinical data were also recorded. **Results:** The SADG was significantly lower in the SBP group compared to the non-SBP group (1.6 ± 4.4 ng/mL vs. 3.0 ± 4.3 ng/mL; p = 0.001). A SADG cutoff value of <0.55 ng/mL demonstrated 72% sensitivity and 76% specificity (AUC = 0.77, p = 0.0008) for distinguishing between the two groups. Serum vitamin D levels were also significantly lower in SBP patients (7.9 ± 5.5 ng/mL vs. 11.4 ± 6.1 ng/mL; p = 0.014). **Conclusions:** SADG appears to be a promising marker for the diagnosis of SBP in cirrhotic patients with ascites. Its utility in clinical practice could enhance early detection and management of this life-threatening condition.

Keywords: Serum-Ascites Vitamin D Gradient, Spontaneous Bacterial Peritonitis, Liver Cirrhosis

Introduction:

Spontaneous bacterial peritonitis (SBP) is an infection of the ascetic fluid that occurs in the setting of decompensated liver cirrhosis when there is no intra-abdominal inflammatory focus or any other contagious source of infection (1, 2). It is the most common infection in patients with cirrhosis (3) with prevalence of about 20 % in one epidemiological study (4)reaching up to 25.24% in another one (5), risk of recurrence of 69% and one-year mortality reaching 62% (6) . Its major complication is the development of hepatorenal syndrome which occurs in one third of the patients and has a fatal mortality reaching 50% two weeks after diagnosis, approaching 100% within months in type I (7). An ascetic fluid PMN count above 250 per cubic mm is now universally accepted as the gold standard for its diagnosis (8).

Vitamin D is better classified as a pro-hormone as it can be synthesized by the ultraviolet B rays exposed skin and its metabolite 1-25 hydroxy vit D acts as a high affinity ligand to the transcription factor Vitamin D receptor (VDR) which is expressed on different tissues for example pituitary, skin and immune cells and controls more than 1000 gene (9, 10). In addition to its classic functions in regulating calcium phosphorus homeostasis and controlling bone metabolism (11) several experimental observations have validated the importance of vitamin D immunological functions. Among these are that VDR is expressed on the majority of immune cells (12), that 1-25 hydroxy vitamin D has been shown to increase chemotaxis, autophagy, and phago-lysosomal fusion of innate immune cells (13) (14) and that vitamin D behaves as a locally-produced, locally-acting effector of hematopoietic cell differentiation and the immune response (15).

Low plasma levels of vitamin D have been proclaimed to occurs in 64 - 92% of patients with chronic liver disease (CLD) and it has been also reported that the incidence of vitamin D deficiency increases as the liver disease progresses (16, 17 & 18) with lower levels of circulating 25-OH vitamin D in patients complicated by infections (19).

In cirrhosis the ascitic fluid is essentially an ultrafiltrate of plasma (20) where various vitamins interchange can occur (21). Among which is vitamin D which was shown to move into the peritoneal fluid (22) especially in cases of peritonitis (23). In addition, results of two anteceding studies have shown higher levels of ascetic fluid vit D and lower levels of serum vit D in SBP patients when compared to patients with simple ascites (24, 25).

The aim of this work was to assess the serum ascetic vitamin D gradient (SADG) in SBP.

Patients and Methods:

This study was done at department of Hepatology, Gastroenterology and Infectious Disease at El-Haram Specialist Hospital

This cross-sectional study was carried out on 50 patients aged above 18 years

old, both sexes, diagnosed with portal hypertensive ascites due to liver cirrhosis. The study was done from October 2021 to March 2022 after approval from the Ethical Committee Benha University Hospitals, in Banha University Hospital (MS 5-10-2021). An informed written consent was obtained from the patients.

Exclusion criteria were clinical: patients with localized tenderness or peritoneal irritation was excluded (1), laboratory: LDH above upper limit of serum normal, glucose below 50 mg/dL, total protein above 1gm/dL in ascetic fluid analysis i.e. Runyon criteria of secondary bacterial peritonitis (26), radiological: intraperitoneal free air or any loculated inflammatory focus on abdominal ultrasound (27), vitamin D supplementation in last 2 months prior to tapping, surgery in last 6 months prior to tapping and clinical findings of Cholestatic liver cirrhosis: such as history of primary biliary cirrhosis or primary sclerosing cholangitis , predominantly conjugating hyperbilirubinemia with elevated ALP and GGT, mechanical obstruction on abdominal ultrasound.

Patients were further categorized into two equal groups: Group I: cirrhotic ascetic patients with SBP (using the ascetic fluid PMN count 250 per cubic mm or above as gold standard for diagnosis) and Group II: ascetic patients without SBP.

All patients underwent: history taking, clinical examination and laboratory investigations [complete blood count (CBC), C- reactive protein (CRP), Arterial Blood Gases (ABG), blood culture, ECG and liver and renal function tests]. Total leukocytic count (TLC), haemoglobin (Hb), platelet count (PLT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), Alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), serum albumin, total and direct bilirubin, serum creatinine, serum urea, prothrombin time (PT) and platelet count (PC)].

Blood and ascetic fluid samples were collected from each patient at the day of tapping. Both serum and ascetic sample 25-OH vitamin D levels were measured along with the ascetic fluid PMNs, LDH, glucose and total protein.

Abdominal ultrasound was performed to show presence of hepatic focal lesions, ascites, spleen size, portal vein patency etc. Child–Pugh class and MELD score was calculated for each patient to be used in the final analysis. Model for end stage liver disease (MELD) = 3.78×ln[serum bilirubin (mg/dL)] + 11.2×ln[INR] + 9.57×ln[serum creatinine (mg/dL)] + 6.43 (28).

The SADG was calculated using the formula: (25-OH vitamin D concentration in serum) – (25-OH vitamin D concentration in ascetic fluid) (25).

Sample collection and storage:

Whole blood and ascetic fluid samples were collected from each patient at the day of tapping. Five ml of whole blood were withdrawn via clean venipuncture using vacutainer tube system, one EDTA tube for CBC and one serum separator tube (SST) for blood chemistry and 25-

OH vit D3 ELISA test. Whole blood was allowed to sit for 30 minutes to allow clotting prior to the process of centrifugation at 3000 rpm for 15 minutes. Serum was removed immediately, and samples were aliquoted and stored at -80℃ until the time of assay.

Routine laboratory workup involving Complete blood picture (CBC) was performed using DXH500, Haematology analyzer, Beckman Coulter, USA. Blood chemistry including, liver function tests (ALT, AST, ALP, albumin, total & direct bilirubin & GGT), kidney function tests (creatinine & urea), microinflammatory state using CRP**,** all were performed on chemistry autoanalyzer AU480, Beckman Coulter, USA. Prothrombin time (PT), prothrombin concentration (PC) & INR were performed on automated coagulation analyzer, Stago Compact, Diagnostica Stago, Spain.

Ascetic fluid total leucocytic count (TLC) was manually performed using Neubauer counting chamber and PMNLs differential count was performed by microscopic examination of Giemsa-stained smear. Chemical analysis including LDH, glucose and total protein were performed on chemistry autoanalyzer AU480, Beckman Coulter, USA. Ascetic samples were aliquoted and stored at -80℃ until the time of 25-OH vit D3 ELISA assay.

Special laboratory investigations: quantitative determination of 25-hydroxy vitamin D was performed using Human 25-hydroxy vitamin D ELISA Kit, Catalog No: E1981Hu, Bioassay technology laboratory®, China. The manufacturer's instructions were strictly followed. ELISA was performed using auto washer (Tecan, Japan) and micro plate reader (Infinite F 50, Tecan, Japan) set to 450 nm. The concentration of Vitamin D in the samples was determined comparing the O.D. of the samples to the standard curve automatically generated by Magellan™ Standard software. Detection Range: 0.5-150ng/ml(25).

Serum levels of vit D3 were interpreted as follows: [Deficiency: a 25-OH vit D3 serum concentration less than 20 ng/mL, insufficiency: a 25-OH vit D3 concentrations between 21—29 ng/mL, sufficiency: a 25-OH vit D3 concentrations between 30−100 ng/mL (29)].

Ascitic Fluid Sampling:

Ascitic fluid samples were collected under sterile conditions. Prior to sampling, the patient's abdomen was cleansed with an antiseptic solution to minimize the risk of infection. Paracentesis was performed using a 22-gauge needle, typically at the left lower quadrant, under ultrasound guidance to avoid injury to abdominal organs.

Approximately 20 mL of ascitic fluid was aspirated and immediately divided into sterile containers for biochemical analysis, including total leukocyte count (TLC), polymorphonuclear (PMN) count, glucose, lactate dehydrogenase (LDH), total protein, and 25-hydroxy vitamin D measurement. Samples were promptly transported to the laboratory and processed within 30 minutes of collection. Ascitic fluid PMN count was performed manually using a Neubauer

chamber, and a differential count was done on Giemsa-stained smears.

Abdominal Ultrasound:

Patients were instructed to fast for at least 6 hours prior to the ultrasound examination to reduce bowel gas interference and ensure optimal visualization of the abdominal organs. The ultrasound was performed with the patient in a supine position, with additional scans in the left lateral decubitus position if needed. A high-resolution ultrasound machine (Philips EPIQ 7G, Philips Healthcare, USA) equipped with a 3.5 MHz convex transducer was used for the examination. The ultrasound assessed liver size, parenchymal texture, spleen size, the presence and extent of ascites, and portal vein patency. Special attention was given to the identification of any hepatic focal lesions and signs of portal hypertension. Doppler studies were also performed to evaluate portal vein flow.

Sample Size Calculation:

Depending on Buonomo et al.,(25) who found that patients with SBP were 29.6% of the suspected cases and that SADG values ranged between−4 and +12 ng/mL and that SADG was significantly lower inpatients with SBP than in those without SBP [−5.5 ng/mL (IQR: −7.4; −3.3) vs. −1.4 ng/mL (25). Assuming the standard deviation is approximately to quarter of range and means are equivalent to medians, and assuming the power = 0.80 and α=0.05, and by using PASS 11th release the minimal sample size for a cross sectional study is 41 cases (30). We recruited 50 patients.

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t-test. Qualitative variables were presented as frequency and percentage (%) and analyzed using the Chi-square or Fisher's exact test when appropriate. Pearson's correlation coefficient (r): test was used for the process of data correlation. ROC curve (Receiver Operating Characteristic Curve): was used to determine the cutoff value, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). A two-tailed P value < 0.05 was considered statistically significant.

Results:

Age showed a statistically significant tendency to be higher in group I when compared with group II (p=0.021). Sex, comorbidities, pulse and temperature showed no statistically significant difference between studied groups. **Table 1**

Hb level, CRP concentration and ascetic fluid PNM count was statistically significantly higher in group I when compared with group II (p=0.014, 0.017 and < 0.001 respectively). Other studied laboratory data (TLC, serum AST, serum ALT, serum urea, serum creatinine, serum total bilirubin, serum Alb and INR), CHILD classification, ascetic fluid TP and ascetic vitamin D showed no significant difference between both groups. Ascetic fluid glucose and LDH

was statistically significantly higher in group II when compared with group I (p<0.001 and 0.004). **Table 2**

Serum vit D and SADG were statically significantly lower group I when compared with group II (p<0.014 and 0.001). (**Table 3)**

Using ROC curve, it was shown that; SADG can be used to discriminate between group I and group II at a cutoff level of < 0.55, with 72% sensitivity, 76% specificity, 75% PPV and 73.1% NPV (AUC = 0.77 and p = 0.0008). **Table 4** and **Figure 1**

In group I, the higher SADG the higher the ascetic PNM and serum vitamin D i.e. There was a significant positive correlation between SADG and ascetic PNM count and serum vitamin D (p-value = 0.029, r = 0.44, p-value = 0.011, r = 0.50). There was no significant correlation between SADG and other studied data. In group II, there were a significant positive correlation between SADG and ascetic and serum vitamin D (p = 0.034, r = 0.43, p < 0.001, r = 0.78). There was no statistically significant correlation between SADG and other studied data. **Table 5**

There was no statistically significant correlation between SADG and other studied non-parametric data (sex, DM, GIT bleeding, HRS, HCC and CHILD class) in group I and II (p-value > 0.05). **Table 6**

Table 1: Comparison between studied groups as regard age, sex, comorbidities

		Group I (N = 25)	**Group II (N = 25)**	**P**
Age (years)		62.4±7.4	56.6±10.5	**0.021***
Sex	**Male**	8(32%)	14(56%)	0.087
	Female	17(68%)	11(44%)	
Comorbidities	**DM**	16(64%)	13(52%)	0.390
	GIT bleeding	9(36%)	13(52%)	0.254
	HRS	11(44%)	6(24%)	0.136
	HCC	4(16%)	2(8%)	0.384

Data are presented as mean ± SD or frequency (%). DM: diabetes mellitus, GIT: gastrointestinal tract, HRS: Hepatorenal syndrome, HCC: Hepatocellular carcinoma.

Table 2: Comparison between studied groups as regard studied laboratory data, CHILD classification, ascetic laboratory data.

		Group I (N = 25)	Group II (N = 25)	P
Hb (g/dl)		9.4±1.7	8.4±1.5	**0.014***
TLC (X10³/□l)		9.0±5.0	7.4±5.1	0.256
AST (U/L)		92.7±163.4	48.8±20.0	0.698
ALT (U/L)		72.6±144.2	30.8±11.4	0.091
Urea (mg/dl)		88.8±53.9	71.7±47.4	0.240
Creatinine (mg/dl)		1.6±0.8	1.9±2.3	0.231
CRP (mg/L)		21.2±23.2	12.9±9.8	**0.017 ***
Total bilirubin (mg/dl)		3.7±4.8	3.1±3.7	0.676
ALB (g/dl)		2.7±0.4	2.7±0.5	0.915
INR		1.4±0.4	1.6±0.5	0.358
CHILD class	**CHILD B**	7(28%)	5(20%)	0.508
	CHILD C	18(72%)	20(80%)	
Ascetic fluid	**PNM count**	789.8±665.3	44.1±41.4	**< 0.001***
	Glucose	109.9±23.3	127.2±29.3	**0.025***
	LDH	99.8±30.8	131.2±41.0	**0.004***
	TP	0.4±0.3	0.6±0.3	0.069

Data are presented as mean ± SD or frequency (%). * Significant p value <0.05. Hb: hemoglobin, TLC: total leukocytic count, AST: aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein, ALB: Albumin, INR: international normalized ratio, PNM: Perinatal mortality, LDH: Lactate dehydrogenase (U/L), TP: total protein (g/mL).

Table 3: comparison between studied groups as regard the studied markers

		Group I (N = 25)	Group II (N = 25)	*p*- value
Studied Markers	**Serum Vitamin D**	7.9±5.5	11.4±6.1	0.014*
	Ascetic vitamin D	9.1±4.7	8.4±3.8	0.550
	SADG	1.6±4.4	3.0±4.3	**0.001***

Data are presented as mean ± SD or frequency (%). * Significant p value <0.05, SADG: serum-ascites vitamin D gradient.

Table 4: ROC Curve Analysis for SADG in Diagnosing Spontaneous Bacterial Peritonitis

Parameter	SADG
Area Under the Curve (AUC)	0.77
Sensitivity (%)	72%
Specificity (%)	76%
Positive Predictive Value (PPV) (%)	75%
Negative Predictive Value (NPV) (%)	73.1%
Cutoff Value (ng/mL)	< 0.55
P-value	**0.0008***

* Significant p value <0.05.

Table 5: Correlation study between SADG and other studied data in all studied groups

	Group I (n=75)		**Group II(n=75)**	
	r	**p-value**	**r**	**p-value**
Age	-0.16	0.442 NS	0.21	0.325 NS
Pulse	-0.18	0.4 NS	-0.26	0.203 NS
Temperature	-0.35	0.089 NS	-0.38	0.062 NS
Ascites PNM Count	**0.44**	**0.029 S**	0.13	0.544 NS
Ascetic Glucose	0.00	0.992 NS	0.12	0.56 NS
Ascetic LDH	-0.03	0.893 NS	-0.18	0.399 NS
Ascetic TP	-0.02	0.928 NS	**0.43**	**0.034 S**
Hb	-0.16	0.445 NS	-0.05	0.822 NS
TLC	0.07	0.734 NS	-0.39	0.054 NS
AST	-0.01	0.96 NS	0.07	0.726 NS
ALT	0.03	0.901 NS	-0.11	0.614 NS
Urea	0.09	0.661 NS	0.15	0.479 NS
Creat	0.06	0.769 NS	0.28	0.179 NS
CRP	-0.23	0.277 NS	-0.29	0.162 NS
T. bilirubin	-0.07	0.738 NS	-0.13	0.548 NS
Albumin	0.12	0.575 NS	-0.23	0.271 NS
INR	0.29	0.156 NS	0.00	0.999 NS
Serum Vitamin D	**0.50**	**0.011 S**	**0.78**	**< 0.001 HS**
Ascites Vitamin D	-0.14	0.508 NS	0.10	0.646 NS

r: Pearson correlation coefficient.* Significant p value <0.05. Hb: haemoglobin, TLC: total leukocytic count, AST: aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein, ALB: Albumin, INR: international normalized ratio, PNM: Perinatal mortality, LDH: Lactate dehydrogenase, TP: total protein, SADG: serum-ascites vitamin D gradient.

Table 6: Comparison between SADG and other studied non-parametric data in group I and II

Group I		**Group I**			**Group II**		
		N	**SADG**	**P**	**N**	**SADG**	**P**
Sex	**Male**	8(32%)	0.11 ± 3.2	0.191	14(56%)	4.0 ± 3.9	0.134
	Female	27(68%)	- 2.3 ± 4.6		11(44%)	1.6 ± 4.4	
DM	**No**	9(36%)	- 2.7 ± 1.9	0.309	12(48%)	1.69 ± 2.3	0.158
	Yes	16(64%)	- 0.8 ± 5.2		13(52%)	4.1 ± 5.3	
GIT bleeding	**No**	16(64%)	- 1.4 ± 3.7	0.857	12(48%)	1.8 ± 3.9	0.06
	Yes	9(36%)	- 1.7 ± 5.5		13(52%)	4.0 ± 4.4	
HRS	**No**	14(56%)	- 2.0 ± 4.9	0.584	19(76%)	2.4 ± 4.4	0.275
	Yes	11(44%)	- 1.01 ± 3.6		6(24%)	4.6 ± 3.2	
HCC	**No**	21(84%)	- 1.75 ± 4.6	0.645	23(92%)	2.8 ± 4.4	0.480
	Yes	4(16%)	- 0.62 ± 1.8		29(8%)	4.4 ± 2.4	
CHILD class	**B**	7(28%)	- 0.2 ± 4.6	0.352	5(20%)	2.06 ± 5.9	0.192
	C	18(72%)	- 2.1 ± 4.3		20(80%)	3.2 ± 3.9	

Data are presented as mean ± SD or frequency (%). * Significant p value <0.05. (%). DM: diabetes mellitus, GIT: gastrointestinal tract, HRS: Hepatorenal syndrome, HCC: Hepatocellular carcinoma.

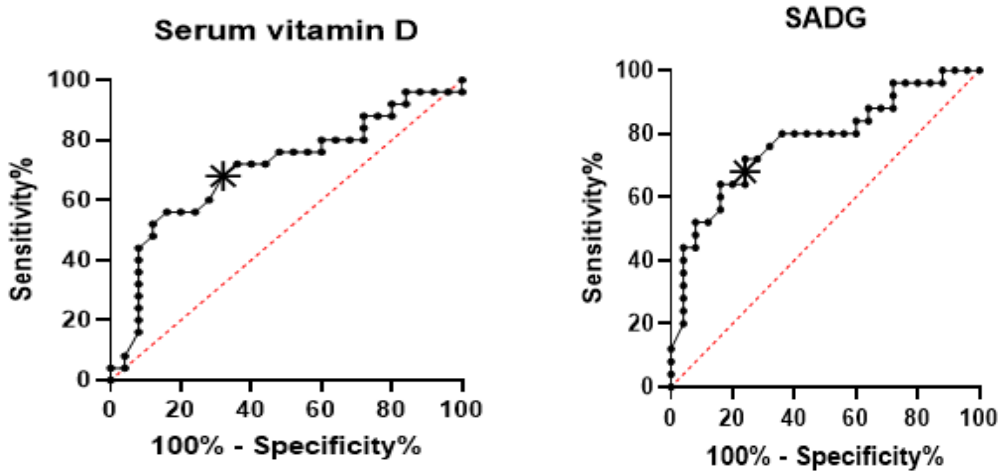

Figure 1: ROC curve between group II and group III as regard serum vitamin D and serum-ascites vitamin D gradient (SADG)

Discussion

SBP is considered the prototypical form of infection in patients with liver cirrhosis and is peculiar among those with decompensated disease being associated with significant morbidity and mortality The diagnosis of SBP is on the basis of neutrophil count in ascitic fluid of >250/mm^3 (31).

Child–Pugh score and the Model for End-Stage Liver Disease, or MELD, are both frequently used scoring systems for assessing the severity and expected mortality of chronic liver disease patients. MELD was shown to predict outcomes in cirrhotic patients with infection (31). Both scores perform better at classifying patients when performed on patients with similar etiologies and when excluding acute illnesses which specifically affect bilirubin (31).

In this study, we found a statistically significant (p = 0.001) decreased SADG in group I (- 1.6 ± 4.4) when compared with group II (3 ± 4.3). No statistically significant difference (p = 0.550) between studied groups (group I and II) as regard ascetic vitamin D level. In group I, it was (9.1 ± 4.7) while in group II, it was (8.4 ± 3.8). This is in agreement with others (25) who stated that although the vitamin D levels of both serum and ascites did not differ between patients with and without SBP; the SADG was significantly lower in patients with SBP than in those without SBP (vitamin D levels were slightly higher in the ascites of patients with SBP). This also agrees with the researches (32) who also observed a high prevalence of vitamin D deficiency in their patients (n = 79/88, 89.8%), and patients with SBP had lower serum 25-OH D concentrations than patients without SBP. The SADG was found to be significantly lower in patients with SBP than in those without SBP.

A low level of vitamin D in patients with CLD may be attributed to several mechanisms such as insufficient exposure to sunlight or an inadequate dietary intake of vitamin D (24). In addition, patients affected by CLD may have impeded intestinal luminal absorption of the dietary sources of vitamin D because of intestinal edema, which complicates portal hypertension, or to cholestasis-induced bile salt disruption (33).

The vitamin DVDR interaction and the consecutive increased expression of LL-37 may have a role in the immune response against SBP and higher levels of vitamin D in the ascites of patients with SBP can be considered indirect evidence of the activation and up regulation of this antimicrobial pathway (34)

In this study, no statistically significant difference (p-value = 0.508) between studied groups (group I and II) as regard CHILD classification. In group I, there were 7 patients (28%) CHILD B and 18 patients (72%) CHILD C while in group II, there were 5 patients (20%) CHILD B and 20 patients (80%) CHILD C. Similarly, (32) found that 92% of patients with CTP class C suffered from vitamin D deficiency, indicating that vitamin D status may be determined in part by CLD severity.

Using ROC curve, it was shown that; SADG can be used to discriminate between group I and group II at a cutoff level of < 0.55, with 72% sensitivity, 76% specificity, 75% PPV and 73.1% NPV (AUC = 0.77 and p = 0.0008). It was reported that, based on the ROC curve, the SADG with a cutoff value of ≥5.57 ng/mL had a sensitivity of 70.5%, a specificity of 68.2%, and an area under the curve of 0.67 in exclusion of SBP (32).

Limitations of this study included that the sample size was relatively small which may have affected the statistical power of our analyses. The study was in a single center. The study participants were recruited from only two hospitals, limiting the generalizability of our findings to other patient populations. We did not evaluate the effect of treatment on serum vitamin D and SADG levels. This study was only conducted in a cross-sectional design, and a longitudinal design is needed to confirm our findings and evaluate changes in these biomarkers over time in SBP patients with cirrhotic ascites.

Conclusions:

SADG could be a potentially useful marker in SBP in patients with cirrhotic ascites. The discriminatory ability of serum vitamin D and SADG levels may have potential clinical implications in the diagnosis and management of SBP in cirrhotic ascites and in validating the importance of vitamin D as a local inflammatory substance.

References:

1. Koulaouzidis A, Leontiadis GI, Said E, Saeed AA. Bedside leucocyte esterase reagent strips in spontaneous bacterial peritonitis. Eur J Gastroenterol Hepatol. 2007;19:91-3.
2. Abdel-Samiee M, Awad SM, Mohamed AA, Abdelsameea E, Taha HA-L. Prognosis of

spontaneous bacterial peritonitis in patients with hepatocellular carcinoma. AJMS. 2023;17:179-83.
3. Fernández J, Navasa M, Gómez J, Colmenero J, Vila J, Arroyo V, et al. Bacterial infections in cirrhosis: epidemiological changes with invasive procedures and norfloxacin prophylaxis. Hepatol. 2002;35:140-8.
4. Jain M, Sanglodkar U, Venkataraman J. Risk factors predicting nosocomial, healthcare-associated and community-acquired infection in spontaneous bacterial peritonitis and survival outcome. Clin Exp Hepatol. 2019;5:133-9.
5. Duah A, Nkrumah KN. Prevalence and predictors for spontaneous bacterial peritonitis in cirrhotic patients with ascites admitted at medical block in Korle-Bu Teaching Hospital, Ghana. Pan Afr Med J. 2019;33:35-8.
6. Glaess SS, Attridge RL, Brady RL, Attridge RT. Evaluation of prophylactic antibiotic regimens on recurrence and mortality in spontaneous bacterial peritonitis. Ann Hepatol. 2019;18:841-8.
7. Ruiz-del-Arbol L, Monescillo A, Arocena C, Valer P, Ginès P, Moreira V, et al. Circulatory function and hepatorenal syndrome in cirrhosis. Hepatol. 2005;42:439-47.
8. Wong CL, Holroyd-Leduc J, Thorpe KE, Straus SE. Does this patient have bacterial peritonitis or portal hypertension? How do I perform a paracentesis and analyze the results? JAMA. 2008;299:1166-78.
9. Demer LL, Hsu JJ, Tintut Y. Steroid hormone vitamin D: Implications for cardiovascular disease. Circ Res. 2018;122:1576-85.
10. Carlberg C. Endocrine functions of vitamin D. Mol Cell Endocrinol. 2017;453:1-2.
11. Gil Á, Plaza-Diaz J, Mesa MD. Vitamin D: Classic and Novel Actions. Ann Nutr Metab. 2018;72:87-95.
12. Sassi F, Tamone C, D'Amelio P. Vitamin D: Nutrient, Hormone, and Immunomodulator. Nutrients. 2018;10:4-9.
13. Liu PT, Stenger S, Tang DH, Modlin RL. Cutting edge: vitamin D-mediated human antimicrobial activity against Mycobacterium tuberculosis is dependent on the induction of cathelicidin. J Immunol. 2007;179:2060-3.
14. White JH. Vitamin D as an inducer of cathelicidin antimicrobial peptide expression: past, present and future. J Steroid Biochem Mol Biol. 2010;121:234-8.
15. Hewison M, Gacad MA, Lemire J, Adams JS. Vitamin D as a cytokine and hematopoetic factor. Rev Endocr Metab Disord. 2001;2:217-27.
16. Arteh J, Narra S, Nair S. Prevalence of vitamin D deficiency in chronic liver disease. Dig Dis Sci. 2010;55:2624-8.
17. Heuman DM, Mihas AA, Habib A, Gilles HS, Stravitz RT, Sanyal AJ, et al. MELD-XI: a rational approach to "sickest first" liver transplantation in cirrhotic patients requiring anticoagulant therapy. Liver Transpl. 2007;13:30-7.
18. Konstantakis C, Tselekouni P, Kalafateli M, Triantos C. Vitamin D deficiency in patients with liver cirrhosis. Ann Gastroenterol. 2016;29:297-312.
19. Anty R, Tonohouan M, Ferrari-Panaia P, Piche T, Pariente A, Anstee Q, et al. Low levels of 25-hydroxy vitamin D are independently associated with the risk of bacterial infection in cirrhotic patients. Clin Transl Gastroenterol 2014;5:56-78.
20. Salvioli G, Tata C, Panini R, Pellati M, Lugli R, Gaetti E. Composition of ascitic fluid in liver cirrhosis: bile acid and lipid content. Eur J Clin Invest. 1993;23:534-9.
21. Sorrell MF, Frank O, Aquino H, Thomson AD, Howard MM, Baker H. Vitamin interchange between ascitic fluid and blood in man. Am J Clin Nutr. 1972;25:125-30.
22. Sahin G, Kirli I, Sirmagul B, Colak E, Yalcin AU. Loss via peritoneal fluid as a factor for low 25(OH)D3 level in peritoneal dialysis patients. Int Urol Nephrol. 2009;41:989-96.
23. Lin CY, Huang TP. Enhancement of ionized calcium and 1,25-dihydroxycholecalciferol loss from peritoneal fluid during peritonitis in patients treated with continuous ambulatory peritoneal dialysis. Nephron. 1991;59:90-5.
24. Zhang C, Zhao L, Ma L, Lv C, Ding Y, Xia T, et al. Vitamin D status and expression of vitamin D receptor and LL-

37 in patients with spontaneous bacterial peritonitis. Dig Dis Sci. 2012;57:182-8.
25. Buonomo AR, Arcopinto M, Scotto R, Zappulo E, Pinchera B, Sanguedolce S, et al. The serum-ascites vitamin D gradient (SADG): A novel index in spontaneous bacterial peritonitis. Clin Res Hepatol Gastroenterol. 2019;43:57-60.
26. Akriviadis EA, Runyon BA. Utility of an algorithm in differentiating spontaneous from secondary bacterial peritonitis. Gastroenterol. 1990;98:127-33.
27. Hoffmann B, Nürnberg D, Westergaard MC. Focus on abnormal air: diagnostic ultrasonography for the acute abdomen. Eur J Emerg Med. 2012;19:284-91.
28. Kamath PS, Kim RW. The model for end-stage liver disease (MELD). Hepatol. 2007;45:797-805.
29. Holick MF. Vitamin D: important for prevention of osteoporosis, cardiovascular heart disease, type 1 diabetes, autoimmune diseases, and some cancers. South Med J. 2005;98:1024-7.
30. Hintze J. PASS 11. Kaysville, Utah, USA: NCSS, LLC. 2011;70:120-63.
31. Angeli P, Bernardi M, Villanueva C, Francoz C, Mookerjee RP, Trebicka J, et al. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol. 2018;69:406-60.
32. Abdel Hafez H, Madani H, Abdel Alem S, Farrag A, Fathy W, Abdo M. Is Serum-Ascites Vitamin D Gradient a Valid Marker for Diagnosing Spontaneous Bacterial Peritonitis in Patients with Cirrhotic Ascites? Lab Med. 2021;52:567-73.
33. Trépo E, Ouziel R, Pradat P, Momozawa Y, Quertinmont E, Gervy C, et al. Marked 25-hydroxyvitamin D deficiency is associated with poor prognosis in patients with alcoholic liver disease. J Hepatol. 2013;59:344-50.
34. Zhang C, Zhao L, Ding Y, Sheng Q, Bai H, An Z, et al. Enhanced LL-37 expression following vitamin D supplementation in patients with cirrhosis and spontaneous bacterial peritonitis. Liver Int. 2016;36:68-75.

To cite this article: Sabry A. Awad , Mohammed E. El Shewi, Sayed M. Abd-El-Aliem, Omar M. Sabry. Assessment of Serum-Ascites Vitamin D Gradient (SADG) in Spontaneous Bacterial Peritonitis. BMFJ 2025;42(1):56-67.