ORIGINAL ARTICLE

Relative Adrenal Insufficiency Among the Egyptian Cirrhotic Patients with Spontaneous Bacterial Peritonitis

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Abstract

Background: ***A prevalent complication in advanced Cirrhosis is spontaneous bacterial peritonitis (SBP), an infection of the ascitic fluid, where bacteria typically enter the peritoneal cavity without an apparent intra-abdominal surgically treatable source. This complication significantly escalates the risk of hospitalization and mortality, making it a critical area of study.***

Aim and objectives: ***To assess the prevalence of relative adrenal insufficiency(RAI) among Egyptian cirrhotic patients with SBP.***

Patients and methods: ***At Sayed Galal University Hospital, researchers conducted the investigation. A total of 90 patients of both genders, all of them diagnosed with cirrhosis, were referred to the Internal Medicine Department at Sayed Galal University Hospital. Patients were divided into two groups: Patients with compensated liver disease(diagnosed clinically, lab tests, and abdominal ultrasound). Patients with liver cirrhosis and SBP have polymorph nuclear leukocytes>250 cells/c.c.***

Results: ***A statistically significant(P=0.004) increased percentage of patients with RAI in the SBP group(35 patients, 77.8%) when compared with that of the cirrhosis group(22 patients, 48.9%).***

Conclusion: ***Our study demonstrates a significant association between liver disease progression and RAI among cirrhotic patients, particularly in the presence of SBP. Adrenal function, as assessed by basal and post-ACTH cortisol levels, was significantly impaired in SBP patients compared to those with stable Cirrhosis, with 77.8% of the SBP group showing RAI insufficiency versus 48.9% in the cirrhosis group. These findings underscore the critical impact of infection and systemic inflammation on adrenal responsiveness in cirrhotic patients, emphasizing the need for early detection and management of adrenal insufficiency, particularly in those with advanced disease or complications like SBP.***

Keywords: SBP; RAI; Cirrhosis

1. Introduction

Relative adrenal insufficiency (RAI) in cirrhotic patients, particularly those with spontaneous bacterial peritonitis (SBP), is a condition where the adrenal glands fail to produce adequate amounts of cortisol .[1]

Cirrhotic patients are at a higher risk of sepsis, and it is a cause of mortality .[2]

Similar pathogenic mechanisms in Cirrhosis and sepsis may lead to AI.[1]

Cirrhosis is one of the causes of death, and infections are both a consequence and the leading killer.[3] Infections as SBB significantly affect the progression of Cirrhosis.[4] Whether Cirrhosis is compensated or decompensated, RAI can happen.[5]

The purpose of the study: it is a cross-sectional study that assesses the prevalence of RAI in two groups: (cirrhotic patients without sepsis and cirrhotic patients with spontaneous bacterial peritonitis) diagnosed by history taking, laboratory tests, and abdominal ultrasonography by using the Short Synacthen Test (SST), A synthetic adrenocorticotropic hormone (ACTH) was administered intravenously. Prior to and 60 minutes after the injection of Synacthen, blood samples were taken in order to assess the serum total cortisol levels.

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2. Patients and methods

This study was conducted at Sayed Galal University Hospital and included a total of 90 patients of both genders who were diagnosed with Cirrhosis. All patients were admitted to the Internal Medicine Department at Sayed Galal University Hospital.

Study Groups:

The target population was divided into two groups: Cirrhosis Group: included 45 patients diagnosed with cirrhosis through clinical evaluation, laboratory investigations, and abdominal ultrasonography; SBP Group: Included 45 patients with liver cirrhosis and SBP. A polymorph nuclear cell count in ascitic fluid greater than 250 cells/cubic centimeter was used to diagnose SBP.

Inclusion Criteria:

Decompensated Cirrhosis with spontaneous bacterial peritonitis, hemodynamically stable patients with a mean arterial pressure (MAP) >60 mmHg, and Cirrhosis diagnosed based on clinical findings, laboratory testing, and ultrasonography in patients older than 18 years for both sexes.

Exclusion Criteria:

Hemodynamically unstable patients.

Methods:

All participants underwent the following assessments:

Comprehensive history taking and thorough physical examination. Laboratory investigations include complete blood count, liver function tests, international normalized ratio, blood glucose levels, serum lipid profile, serum sodium and potassium levels, serum urea and creatinine levels, and ascitic fluid cytological analysis.

Short Synacthen Test (SST):

SST was conducted on the third day of hospitalization between 8:00 and 9:00 AM. A synthetic adrenocorticotropic hormone (ACTH) was administered intravenously (250 lg). Prior to and 60 minutes after the injection of Synacthen, blood samples were taken in order to assess the serum total cortisol levels.

Abdominal Ultrasonography: To assess liver characteristics and ascitic fluid.

Ethical Considerations:

All procedures adhered to the regulations of the Al-Azhar University Ethics Committee. Written informed consent was obtained from all participants prior to their inclusion in the study.

Statistical Analysis:

Data were analyzed using SPSS 25. Qualitative data were frequency and percentage. Continuous quantitative data were presented as mean ± SD. In a discrete set of numbers, the mean is the total of the values divided by the number of values. Standard deviation (SD): measures value dispersion. A low SD implies that the values are close to the established mean, while a high SD indicates a broader range. Probability: P-value < 0.05 indicated significance, < 0.001 indicated strong significance, and > 0.05 indicated insignificance.

The following tests were done:

When comparing two groups (for continuous quantitative data), use the independent sample T-test (T). Using the chi-square test, non-parametric categorical data were compared.

3. Results

Table 1. Demographic data in all studied patients.

DEMOGRAPHIC DATA		SBP GROUP (N=45)	CIRRHOSIS GROUP (N=45)	STAT. TEST	P-VALUE
SEX	Males	28 62.2%	29 64.4%	X2=0.048	0.83
	Females	17 37.8%	16 35.6%		NS
AGE	Mean ± SD	53.2±18.9	41.4±14.4	T=3.32	0.001 S
	Min-Max	20-75	22-65		

T:independent sample T-test, NS:P>0.05 is considered non-significant.

X2:chi-square test, S:P<0.05 is considered significant.

No statistically significant (P=0.83) difference between studied groups (SBP and cirrhosis) as regard sex. In SBP group, there were 28-males (62.2%) and 17-females (37.8%). While in cirrhosis group, there were 29-males (64.4%) and 16-females (35.6%).

A statistically significant (P=0.001) increased age in SBP group {mean= (53.2±18.9) with range of (20-75)} when compared with that of cirrhosis group {mean= (41.4±14.4) with range of (22-65)}, (table 1).

Table 2. Comparison of all studied groups as regard CBC in all studied patients.

CBC		SBP GROUP (N=45)	CIRRHOSIS GROUP (N=45)	T	P-VALUE
HB (G/DL)	Mean ±SD	9.8±1	11.1±1.3	-5.41	<0.001 HS
	Min-Max	8.3-11.7	8.5-13.9		
PLT (10/CC)	Mean±SD	112.3±30.7	114.7±32.9	- 0.358	0.72 NS
	Min-Max	48-150	39-151		
TLC (10/CC)	Mean±SD	12±3.9	7.8±1.9	6.51	<0.001 HS
	Min-Max	3.6-19	4.8-11.5		

T:independent sample T-test, HS:P<0.001 is considered highly significant.

High statistically significant(P<0.001) decreased Hb in SBP group {mean= (9.8±1) with range of (8.3-11.7)} when compared with that of cirrhosis group {mean= (11.1±1.3) with range of (8.5-13.9)}. No statistically significant(P=0.72) difference between studied groups (SBP and cirrhosis) as regard PLTs. in SBP group, the mean was (112.3±30.7) with range of (48-150). While in cirrhosis group, the mean was (114.7±32.9) with range of (39-151).

High statistically significant(P<0.001) increased TLC in SBP group {mean= (12±3.9) with range of (3.6-19)} when compared with that of cirrhosis group {mean= (7.8±1.9) with range of (4.8-11.5)}, (table 2; figures 1&2).

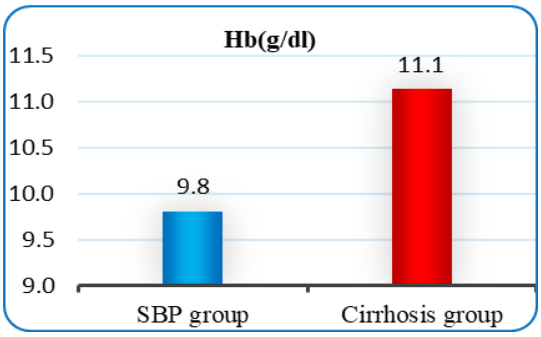

Figure 1. Comparison of all studied groups as regard Hb in all studied patients.

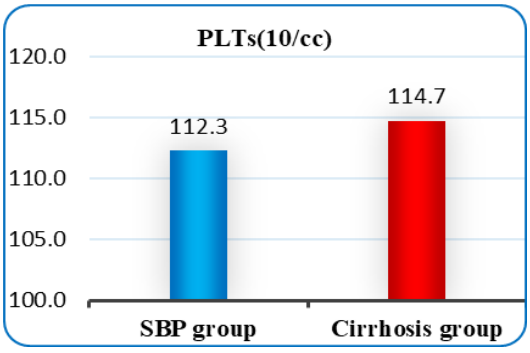

Figure 2. Comparison of all studied groups as regard PLTs in all studied patients.

Table 3. Comparison of all studied groups as regard liver functions tests in all studied patients.

LIVER FUNCTIONS TESTS		SBP GROUP (N=45)	CIRRHOSIS GROUP (N=45)	T	P-VALUE
ALT(IU/L)	Mean±SD	53±29.7	46.1±22.8	1.24	0.217
	Min-Max	7-110	15-95		NS
AST(IU/L)	Mean±SD	76.5±41.2	44.8±23.7	4.47	<0.001
	Min-Max	25-164	11-89		HS
ALBUMIN(G/DL)	Mean±SD	3.1±0.4	3.4±0.5	-	0.007
	Min-Max	2.3-3.8	2.5-4.4	2.74	S
TOTAL BILIRUBIN(MG/DL)	Mean±SD	1.98±0.79	0.97±0.64	6.65	<0.001
	Min-Max	0.5-3	0.3-2.8		HS
INR	Mean±SD	1.33±0.79	1.27±0.21	1.13	0.263
	Min-Max	1-2.1	0.8-1.7		NS

T:independent sample T-test, HS:P<0.001 is considered highly significant,

NS:P>0.05 is considered non-significant, S:P<0.05 is considered significant.

No statistically significant(P=0.217) difference between studied groups (SBP and cirrhosis) as regard ALT. in SBP group, the mean was (53±29.7) with range of (7-110). While in cirrhosis group, the mean was (46.1±22.8) with range of (15-95). High statistically significant(P<0.001) increased AST in SBP group {mean= (76.5±41.2) with range of (25-164)} when compared with that of cirrhosis group {mean= (44.8±23.7) with range of (11-89)}.

A statistically significant(P=0.007) decreased albumin in SBP group {mean= (3.1±0.4) with range of (2.3-3.8)} when compared with that of cirrhosis group {mean= (3.4±0.5) with range of (2.5-4.4)}. High statistically significant(P<0.001) increased total bilirubin in SBP group {mean= (1.98±0.79) with range of (1-2.1)} when compared with that of cirrhosis group {mean= (1.27±0.21) with range of (0.8-1.7)}.

No statistically significant(P=0.263) difference between studied groups (SBP and cirrhosis) as regard INR. in SBP group, the mean was (1.33±0.79) with range of (1-2.1). While in cirrhosis group, the mean was (1.27±0.21) with range of (0.8-1.7), (table 3; figures 3&4).

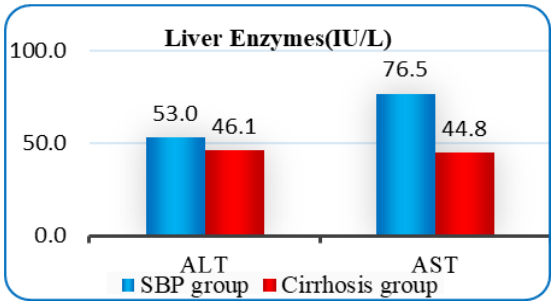

Figure 3. Comparison of all studied groups as regard liver enzymes in all studied patients.

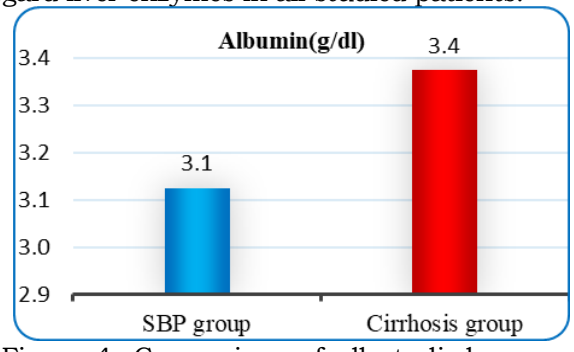

Figure 4. Comparison of all studied groups as regard albumin in all studied patients.

Table 4. Comparison of all studied groups as regard lipids profile in all studied patients.

LIPIDS PROFILE		SBP GROUP (N=45)	CIRRHOSIS GROUP (N=45)	T	P-VALUE
CHOLESTEROL (MG/DL)	Mean±SD	162.2±39.3	170.5±44	-	0.345
	Min-Max	106-229	103-230	0.95	NS
TGS (MG/DL)	Mean±SD	104.4± 3.8	101.4±33	0.49	0.625
	Min-Max	53-150	51-149		NS
LDL (MG/DL)	Mean±SD	88±35.3	105.7±39.2	-	0.027
	Min-Max	34.4-155.2	27.6-158.8	2.25	S
HDL (MG/DL)	Mean±SD	53.6±12.4	46.4±12.7	2.75	0.007
	Min-Max	30-70	30-70		S

T:independent sample T-test, NS:P>0.05 is considered non-significant,

S:P<0.05 is considered significant.

No statistically significant(P=0.345) difference between studied groups (SBP and cirrhosis) as regard cholesterol. in SBP group, the mean was (162.2±39.3) with range of (106-229). While in cirrhosis group, the mean was (170.5±44) with range of (103-230). No statistically significant(P=0.625) difference between studied groups (SBP and cirrhosis) as regard TGs. in SBP group, the mean was (104.4±23.8) with range of (53-150). While in cirrhosis group, the mean was (101.4±33) with range of (51-149).

A statistically significant(P=0.027) decreased LDL in SBP group {mean= (88±35.3) with range of (34.4-155.2)} when compared with that of cirrhosis

group {mean= (105.7±39.2) with range of (27.6-158.8)}. A statistically significant (P=0.007) increased HDL in SBP group {mean= (53.6±12.4) with range of (30-70)} when compared with that of cirrhosis group {mean= (46.4±12.7) with range of (30-70)}, (table 4; figures 5&6).

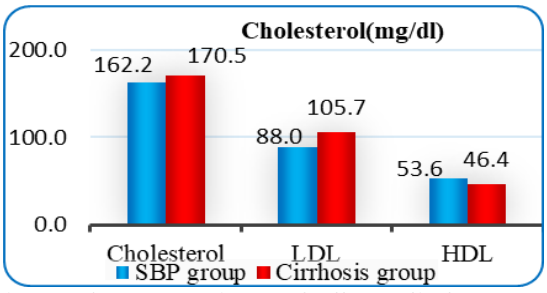

Figure 5. Comparison of all studied groups as regard cholesterol in all studied patients.

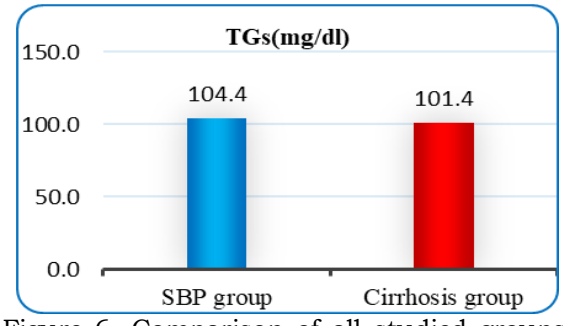

Figure 6. Comparison of all studied groups as regard TGs in all studied patients.

Table 5. Comparison of all studied groups as regard renal functions tests in all studied patients.

RENAL FUNCTIONS TESTS		SBP GROUP (N=45)	CIRRHOSIS GROUP (N=45)	T	P-VALUE
NA (MEQ/L)	Mean ± SD	131.6±4.5	131.2±4.3	0.48	0.633 NS
	Min-Max	125-140	125-141		
K (MEQ/L)	Mean ± SD	4.1±0.5	4.3±0.6	-2.12	0.037 S
	Min-Max	3.2-5.1	3-5.3		
UREA (MG/DL)	Mean ± SD	46.3±16.2	16.4±5.8	11.64	<0.001 HS
	Min-Max	13-75	7-24		
CREATININE (MG/DL)	Mean ± SD	1.2±0.3	1.1±0.3	1.61	0.112 NS
	Min-Max	0.6-1.5	0.6-1.5		

T:independent sample T-test, HS:P<0.001 is considered highly significant, NS:P>0.05 is considered non-significant, S:P<0.05 is considered significant.

No statistically significant(P=0.633) difference between studied groups (SBP and cirrhosis) as regard Na. in SBP group, the mean was (131.6±4.5) with range of (125-140). While in cirrhosis group, the mean was (131.2±4.3) with range of (125-141). A statistically significant(P=0.037) decreased K in SBP group {mean= (4.1±0.5) with range of (3.2-5.1)} when compared with that of cirrhosis group {mean= (4.3±0.6) with range of (3-5.3)}.

High statistically significant (P<0.001) increased Urea in SBP group {mean= (46.3±16.2) with range of (13-75)} when compared with that of cirrhosis group mean= (16.4±5.8) with range of (7-24)}. No statistically significant (P=0.112) difference between studied groups (SBP and cirrhosis) as regard creatinine. in SBP group, the mean was (1.2±0.3) with range of (0.6-1.5). While in cirrhosis group, the mean was (1.1±0.3) with range of (0.6-1.5), (table 5; figures 7&8).

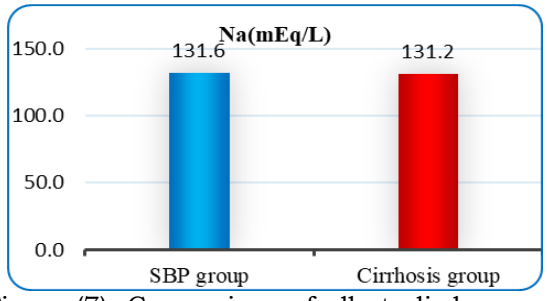

Figure (7): Comparison of all studied groups as regard Na in all studied patients.

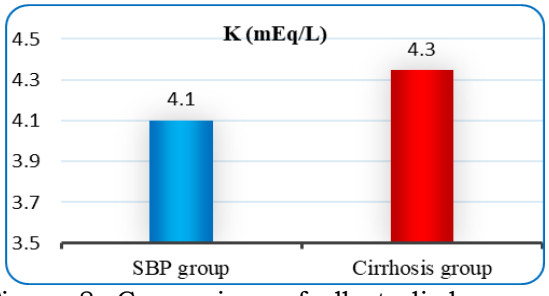

Figure 8. Comparison of all studied groups as regard K in all studied patients.

Table 6. Comparison of all studied groups as regard RAI in all studied patients.

		SBP GROUP (N= 45)		CIRRHOSIS GROUP (N= 45)		X2	P-VALUE
RELATIVE ADRENAL INSUFFICIENCY	No	10	22.2%	23	51.1%	8.09	0.004 S
	Yes	35	77.8%	22	48.9%		

X2:chi-square test, S:P<0.05 is considered significant.

A statistically significant(P=0.004) increased percentage of patients with Relative adrenal insufficiency in SBP group (35-patients 77.8%) when compared with that of cirrhosis group (22-patients 48.9%), (table 6; figure 9).

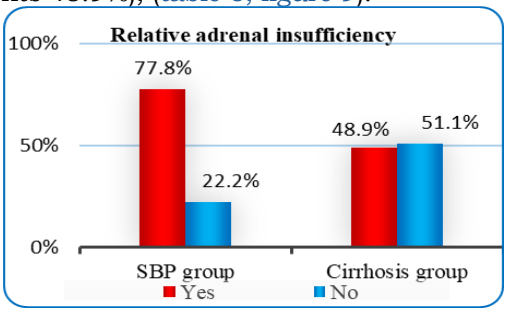

Figure 9. Comparison of all studied groups as

regard RAI in all studied patients.

Table 4. Comparison of all studied groups as regard serum cortisol levels in all studied patients.

SERUM CORTISOL(MG/DL)		SBP GROUP (N=45)	CIRRHOSIS GROUP (N=45)	T	P-VALUE
BASAL	Mean±SD	11.6±3.5	14.1±4.5	-	0.004
	Min-Max	5.9-22	5.3-22	2.98	S
30-MIN POST-ACTH	Mean±SD	16.1±4.3	21.4±7.4	-	<0.001
	Min-Max	9-26.4	9-34.2	4.22	HS
60-MIN POST-ACTH	Mean±SD	18.7±5.1	25.9±8.7	-	<0.001
	Min-Max	11.5-31.5	13-39.5	4.78	HS

T: independent sample T test, HS: P<0.001 is considered highly significant, S: P<0.05 is considered significant.

A statistically significant(P=0.004) decreased basal cortisol level in SBP group {mean= (11.6±3.5) with range of (5.9-22)} when compared with that of cirrhosis group {mean= (14.1±4.5) with range of (5.3-22)}.

High statistically significant (P<0.001) decreased cortisol level (30-min after ACTH) in SBP group {mean= (16.1±4.3) with range of (9-26.4)} when compared with that of cirrhosis group {mean= (21.4±7.4) with range of (9-34.2)}.

High statistically significant (P<0.001) decreased cortisol level (60-min after ACTH) in SBP group {mean= (18.7±5.1) with range of (11.5-31.5)} when compared with that of cirrhosis group {mean= (25.9±8.7) with range of (13-39.5)}, (table 7; figure 10).

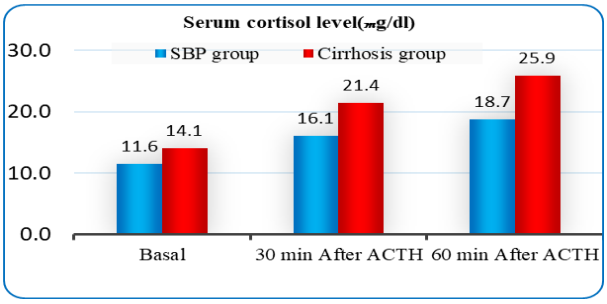

Figure 10. Comparison of all studied groups as regard serum cortisol level in all studied patients.

4. Discussion

In our study, there was no statistically significant difference in gender distribution between the SBP and cirrhosis groups(p=0.83). However, there was a significant increase in age in the SBP group (mean 53.2±18.9 years) compared to the cirrhosis group (41.4±14.4 years, p=0.001). Seventeen women (or 37.8% of the total) and twenty-two men made up the SBP group. There were 29 males (64.4% of the total) and 16 females (35.6% of the total) in the cirrhosis group.

This finding aligns with Gustot et al.,[6] who reported that advanced age is a risk factor for developing SBP in cirrhotic patients. The higher age in SBP patients might be attributed to the progressive nature of liver disease and the cumulative risk of bacterial infections with advancing age.

Our results demonstrated a highly significant decrease in hemoglobin levels in the SBP group(9.8±1g/dL) compared to the cirrhosis group (11.1±1.3g/dL, p<0.001).

This finding corresponds with Abu-Freha et al.,[7] who reported that anemia is more prevalent in cirrhotic patients with SBP due to various factors, including chronic inflammation and potential gastrointestinal bleeding.

This disagrees with Popoiag et al.,[8] who showed that there were no significant differences between the mean value of Hb was registered.

Our results demonstrated a highly significant increase in TLC in the SBP group (12±3.9) compared to the cirrhosis group (7.8±1.9, p<0.001).

This elevation is consistent with Rimola et al.,[9] who identified leucocytosis as a characteristic feature of SBP, reflecting the inflammatory response to bacterial infection.

Our results demonstrated no significant difference between groups (p=0.72) regarding platelet count.

This disagrees with Popoiag et al.,[8] sought to identify the clinical and biological variables linked to SBP and its prognosis, with a particular emphasis on the neutrophil-to-lymphocyte ratio (NLR). Their results demonstrated a statistically significant difference in PLT mean values between the SBP and non-SBP groups. Differences in illness severity among research participants may account for this disparity.

Our study showed significantly higher AST levels in the SBP group (76.5±41.2) compared to the cirrhosis group (44.8±23.7, p<0.001). No statistically significant (P=0.217) difference between the studied groups regarding ALT.

This aligns with Fernández et al.,[10] who reported elevated liver enzymes during bacterial infections in cirrhotic patients.

We found significantly lower albumin levels in the SBP group (3.1±0.4) compared to the cirrhosis group (3.4±0.5, p=0.007).

This finding is consistent with Tsai et al.,[11] who identified hypoalbuminemia as a risk factor for SBP development and poor prognosis.

This is in contrary with Metwally et al.,[12] those who stated that the groups' serum albumin values were not significantly different from one another.

Our results demonstrated a highly significant increase was observed in total bilirubin in the SBP group (1.98±0.79) compared to the cirrhosis group (0.97±0.64, p<0.001).

Our investigation found that renal function was significantly different in the SBP group compared to the cirrhosis group. In particular, the SBP

group had noticeably greater serum urea levels (46.3±16.2 vs. 16.4±5.8, p<0.001), indicating that sepsis is associated with decreased renal function.

This contrasts with Elfaramawy[13] who reported that no significant difference in renal function was found between patients with and without sepsis. This discrepancy may be attributed to differences in study populations, sample sizes, or the severity of sepsis among participants.

Our study revealed significant impairments in adrenal function among patients with SBP compared to those with Cirrhosis alone. Basal cortisol levels were significantly lower in the SBP group (11.6±3.5) than in the cirrhosis group (14.1±4.5, p=0.004). Additionally, the post-ACTH cortisol response was markedly diminished in the SBP group, with cortisol levels at 30 minutes (16.1±4.3 vs. 21.4±7.4, p<0.001) and 60 minutes (18.7±5.1 vs. 25.9±8.7, p<0.001) significantly lower compared to the cirrhosis group, indicating a reduced adrenal reserve in SBP patients.

These findings strongly support the work of Fede et al.,[5] who reported impaired adrenal response in cirrhotic patients with infection.

A key finding of our study was the significantly higher prevalence of RAI in the SBP group (77.8%) compared to the cirrhosis group (48.9%, p=0.004).

4. Conclusion

This study includes two groups: Cirrhosis Group: included 45-patients diagnosed with Cirrhosis through clinical evaluation, laboratory investigations, and abdominal ultrasonography; SBP Group: Included 45-patients with liver cirrhosis and SBP. A polymorph nuclear cell counts in ascitic fluid greater than 250 cells/cubic centimeter was used to diagnose SBP.

Our study demonstrates a significant association between liver disease progression and adrenal insufficiency among cirrhotic patients, particularly in the presence of SBP. Adrenal function, as assessed by basal and post-ACTH cortisol levels, was significantly impaired in SBP patients compared to those with stable Cirrhosis, with 77.8% of the SBP group showing RAI versus 48.9% in the cirrhosis group. A statistically significant decrease in basal cortisol level in the SBP group when compared with that of the cirrhosis group. Highly statistically significant decreased cortisol level (30 minutes after ACTH) in the SBP group when compared with that of the cirrhosis group. No statistically significant difference between studied groups (SBP and Cirrhosis) as regard PLTs. High statistically significant increased TLC in SBP group when compared with that of cirrhosis group. These findings underscore the critical impact of infection and systemic inflammation on adrenal responsiveness in cirrhotic patients, emphasizing the need for early detection and management of adrenal insufficiency, particularly in those with advanced disease or complications like SBP.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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