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FREQUENCY OF SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH FIRST PRESENTATION OF ASCITES: A MULTICENTER PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background: Ascites, commonly resulting from chronic liver disease, often complicates with spontaneous bacterial peritonitis (SBP), a life-threatening condition with high morbidity and mortality. Limited data exists on the frequency of SBP in first-episode ascites, particularly in developing countries.

Objective: To determine the frequency of SBP in patients presenting with first-episode ascites and to evaluate its association with liver disease severity and etiology.

Methods: This multicenter, prospective observational study was conducted from September 2022 to December 2024, at Bannu Medical College / Khalifa Gul Nawaz Teaching Hospital, Bannu; Muhammad College of Medicine / Muhammad Teaching Hospital; Jinnah Medical College & Teaching Hospital, Peshawar; Aga Khan University Hospital, Karachi. Adult patients (≥18 years) with newly diagnosed ascites were included. Diagnostic paracentesis was performed, and SBP was diagnosed based on a polymorphonuclear leukocyte (PMN) count of ≥250 cells/mm³, regardless of culture results. Data were analyzed using SPSS version.

Results: A total of 217 patients were enrolled. The mean age was 53.1 ± 11.4 years, and 65.4% were male. Chronic liver disease was the most common etiology (87.1%). SBP was diagnosed in 48 patients, yielding a frequency of 22.1%. SBP was significantly more common in patients with chronic liver disease-related ascites and was strongly associated with advanced liver disease, especially in Child-Pugh class C ($p < 0.05$).

Conclusion: SBP is common even in first-episode ascites, affecting more than one-fifth of patients. Its strong association with advanced liver disease underscores the importance of routine diagnostic paracentesis for early diagnosis and timely treatment.

Keywords: Spontaneous Bacterial Peritonitis, Ascites, First-Episode, Chronic Liver Disease, Child-Pugh, Diagnostic Paracentesis, Mortality, Prospective Study, Multicenter, Pakistan

INTRODUCTION

Ascites is the commonest complication of chronic liver disease and signifies a turning point in the natural history of cirrhosis. About 50-60% of patients with compensated cirrhosis will develop ascites within 10 years from diagnosis, and its occurrence is accompanied by a drastic decrease in their overall survival (median of less than two years) coupled with an approximately one-year mortality rate ≈20% [1]. The appearance of new ascites is indicating portal hypertension and hepatic decompensation, often result in repeated hospital admissions, low quality of life and significant economic burden on health services. Spontaneous bacterial peritonitis (SBP) is considered one of the most severe and life-threatening complication of ascites. SBP is an infection of the ascitic fluid without an evident surgically correctable intraabdominal source. It results from bacterial translocation to the mesenteric lymph nodes, hematogenous spread of bacteria and seeding of ascites. Mechanisms including changes in gut permeability, small intestinal microflora abnormalities, impairment of opsonic activity of ascitic fluid, and impaired immune function in cirrhosis are central to the development of this [2]. SBP carries a high mortality and morbidity. Although there have been improvements in diagnostic tests and the availability of antimicrobial therapy, the in-hospital mortality is between 20% to 30%, while one-year mortality is over 50%, especially among patients with underlying liver disease [3]. Early identification and initiation of antibiotic treatment were seen to greatly influence the outcome and emphasize on early diagnosis. The clinical presentation of SBP is non-specific, with low-grade fever, abdominal pain and change in mental status or frank asymptomatic ascitic fluid infection. Classic symptoms of peritonitis are commonly missing especially in cirrhotic patients with attenuated inflammatory reaction. Therefore, SBP may be easily missed if diagnostic paracentesis is not regularly undertaken [4]. This diagnostic dilemma is especially pertinent in patients with the initial episode of ascites, where the attending team may not fully appreciate the risk of infection. Current recommendations by international guidelines suggest diagnostic paracentesis should be performed in all patients with ascites on presentation to hospital, irrespective of whether there are any symptoms of infection. SBP is defined as ascites with a polymorphonuclear (PMN) leukocyte count of ≥250 cells/mm³, in the absence or presence of positive bacterial culture [5]. Nonetheless, although guidelines stipulate that routine paracentesis should be performed as part of the initial evaluation in these patients, compliance is often poor and many do not have daily access to this procedure particularly in resource-poor settings. The majority of reports on SBP are based on prospective studies that involve hospitalized cirrhotic or cirrhotic patients with recurrent ascites. Information on the rate of SBP at the initial manifestation of ascites is scarce, especially in developing countries. This is a crucial deficiency because in many cases the first episode of ascites can be already complicated by SBP and s failure to identify infection at this point may lead to a delayed treatment and worse outcomes. SBP rates between 10% and 30% in patients with ascites have also been reported in other studies, however the heterogeneity of selected study populations as well as inclusion criteria and the diagnostic procedures applied preclude generalization [6]. In addition, the microbiology of SBP has changed with time. Among the organisms, gram-negative species such as Escherichia coli and Klebsiella pneumoniae tended to be predominant historically; however, several recent reports showed an emergence of gram-positive bacteria and multidrug-resistant (MDR) organisms in previous antibiotic users or in patients who are frequently hospitalized [7]. Identification of the prevalence and features of SBP at the first presentation may provide valuable information for an initial choice of empiric antibiotic therapy and the spread of infection. In areas of the world with a high prevalence of chronic liver disease from viral hepatitis, alcoholic liver disease, and non-alcoholic fatty liver disease (NAFLD), ascites remains a common cause for hospital admissions. Restricted access to early hepatology care and late presentation adds to the burden of complications like SBP. Local epidemiological information is important to guide management decisions and emphasize the importance of adherence to diagnostic criteria. This study was conducted

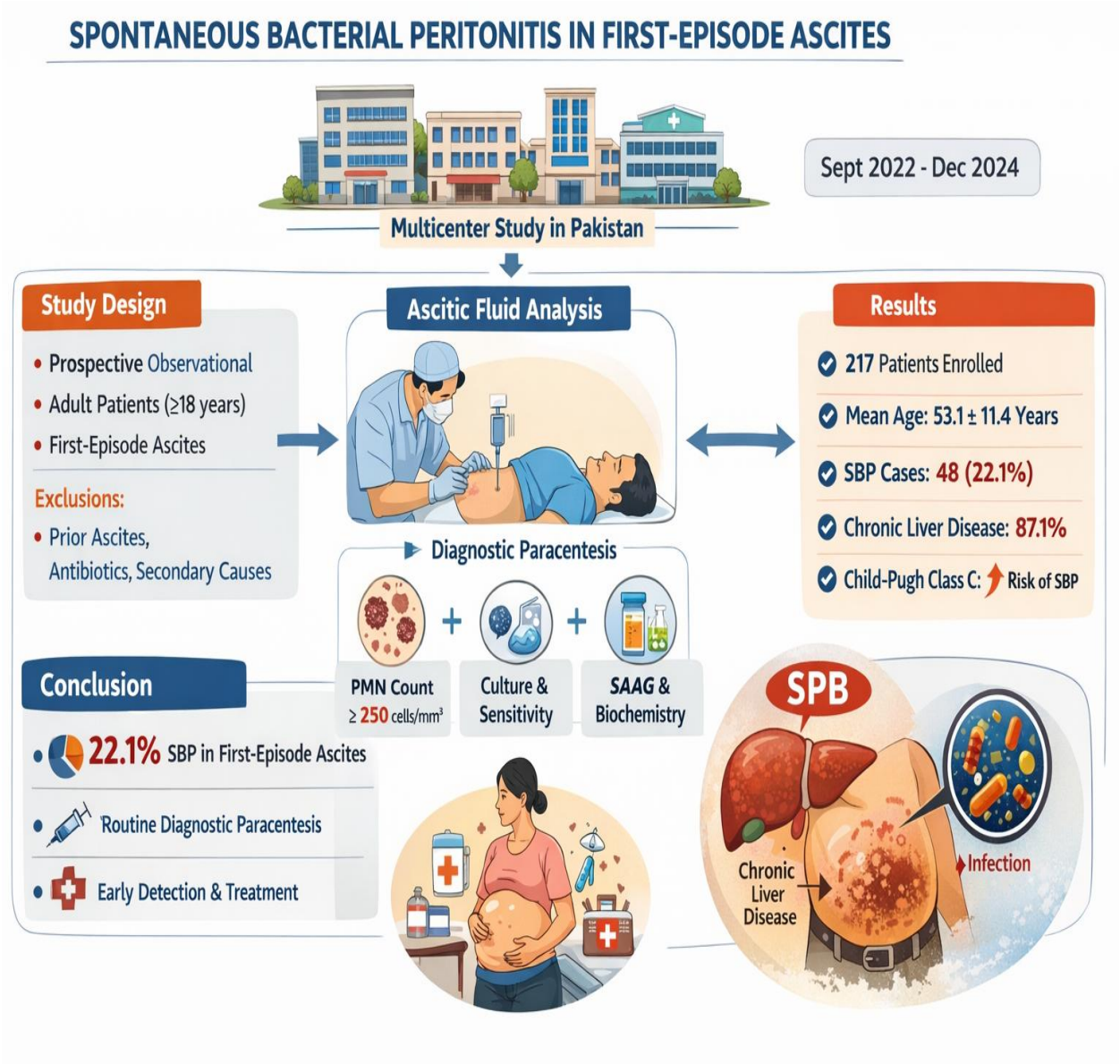
to assess the prevalence of spontaneous bacterial peritonitis in patients with a new diagnosis of ascites during two-year period from September 1st, 2022 until December 31st, 2024. By specifically studying first-episode ascites, we hope to emphasize the prevalence of SBP at initial presentation and underscore the need for a routine diagnostic paracentesis in everyone. An early detection of SBP at this stage may offer timely treatment, decrease complications and increase the patients' overall outcome.

METHODOLOGY

This was a multicenter, prospective observational study conducted across five hospitals in Pakista, Bannu Medical College / Khalifa Gul Nawaz Teaching Hospital, Bannu; Muhammad College of Medicine / Muhammad Teaching Hospital; Jinnah Medical College & Teaching Hospital, Peshawar; Aga Khan University Hospital, Karachi and Lady Reading Hospital, Peshawar. The study took place over a two-year period, from September 2022 to December, 2024. Adult patients (≥18 years) presenting with first-episode ascites were included, provided they gave written informed consent. Patients with a history of prior ascites or spontaneous bacterial peritonitis (SBP), those already on antibiotic therapy at presentation, or those with secondary peritonitis (including tuberculous peritonitis, malignant ascites, or pancreatic ascites) were excluded from the study. The sample size was determined using the WHO formula for single population proportion:

$$n = \frac{Z^2 \times p \times (1-p)}{d^2}$$

where Z = 1.96, p = 0.17 (estimated prevalence of SBP from previous studies), and d = 0.05 (margin of error). The minimum required sample size was 217 patients; however, due to the limited study duration, 210 patients who met the inclusion criteria were enrolled. At the time of admission, demographic, clinical, and laboratory data were collected through a structured proforma. All patients underwent diagnostic paracentesis under aseptic precautions, and ascitic fluid was sent for analysis, including total leukocyte count, polymorphonuclear (PMN) cell count, gram stain, bacterial culture and sensitivity, protein concentration, and serum-ascitic albumin gradient (SAAG). SBP was defined by a PMN count ≥250 cells/mm³ in the ascitic fluid, regardless of culture results. The data were recorded and analyzed using SPSS version 26. Descriptive statistics were used to present categorical data as frequencies and percentages. The relationship between variables was assessed using the Chi-square test, with a significance level set at $p < 0.05$. The study was approved by the Institutional Review Board (IRB) / Ethical Review Committee (ERC), with approval reference number 17, dated March 2022.



"Figure Study Design, Diagnostic Approach, and Outcomes of Spontaneous Bacterial Peritonitis in First-Episode Ascites

RESULTS

A total of 217 consecutive patients with initial ascites were enrolled, and mean age was 53.1 ± 11.4 years, male was predominant (65.4%) as indicated in Table 1. Chronic liver diseases were the most frequent underlying cause of ascites (87.1%) followed by cardiac, nephrotic and other etiologies (Table 2). 48 out of the 217 developed SBP and thus an incidence rate of 22.1%. On SBP: Forty-eight (22.1%) patients were diagnosed to have it, while majority (169, 77.9%) had no evidence for it (Table-III). The general and overall incidence of SBP in patients with first-episode ascites is depicted in Fig 1. The relationship between SBP and liver disease severity was statistically significant, with increased SBP cases noted for the Child-Pugh class C patients as compare to classes A and B ($p < 0.05$) as shown in Figure 2. Moreover, SBP was significantly more common in patients who presented with ascites due to chronic liver disease than in those of non-hepatic origin ($p < 0.05$).

Table 1: Demographic Characteristics of Study Population (n = 217)

Variable	Value
Total patients	217

Mean age (years)	53.1 ± 11.4
Male	142 (65.4%)
Female	75 (34.6%)

The study population consisted predominantly of middle-aged adults, with a clear male predominance. This demographic distribution is consistent with the known epidemiology of chronic liver disease in the region.

Table 2: Etiology of Ascites in Study Participants

Etiology	Frequency (%)
Chronic liver disease	189 (87.1%)
Heart failure	13 (6.0%)
Nephrotic syndrome	9 (4.1%)
Others	6 (2.8%)

Chronic liver disease was the leading cause of ascites, accounting for more than four-fifths of cases. Non-hepatic causes such as cardiac and renal diseases constituted a minority of presentations.

Table 3: Frequency of Spontaneous Bacterial Peritonitis

SBP Status	Frequency (%)
SBP present	48 (22.1%)
No SBP	169 (77.9%)

Spontaneous bacterial peritonitis was diagnosed in **22.1%** of patients at first presentation of ascites, highlighting a substantial burden of infection even in initial episodes.

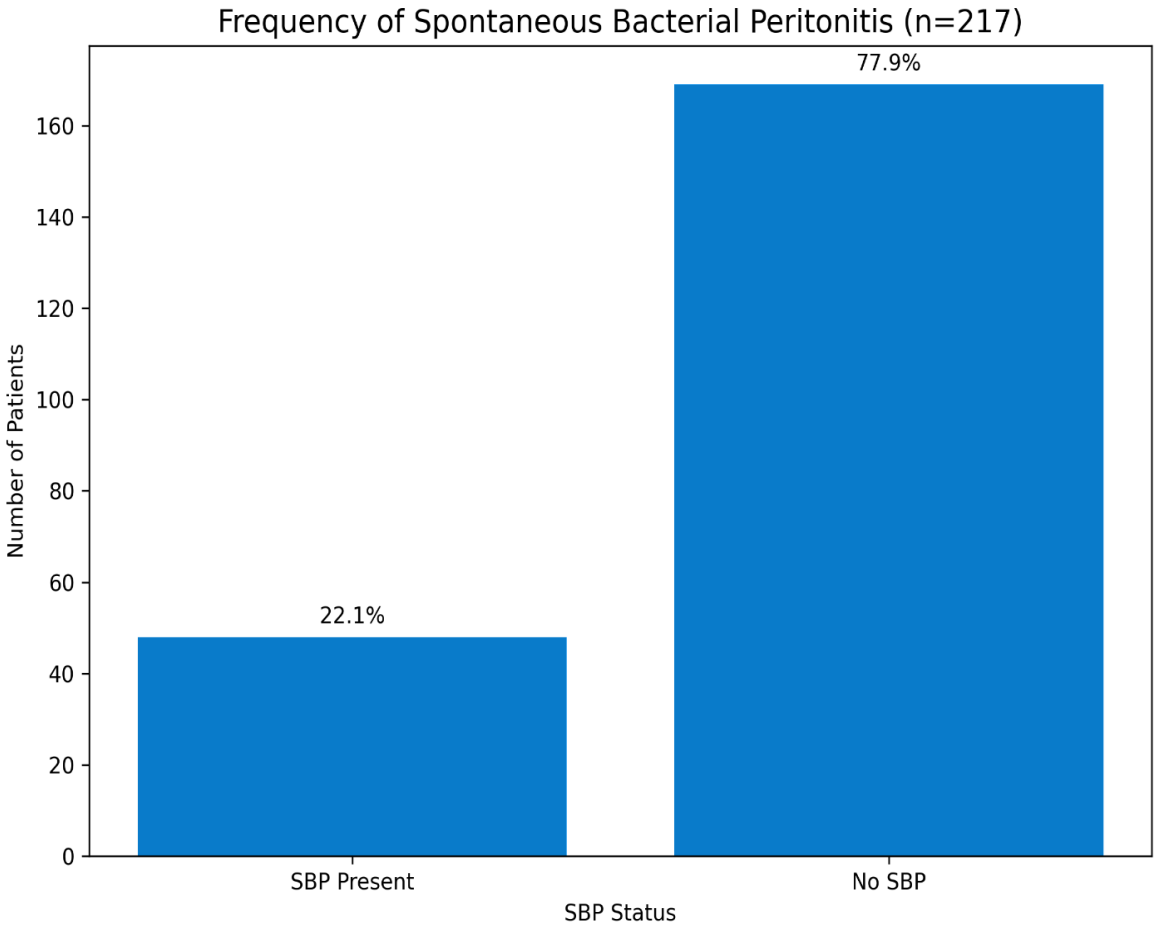


Figure 1 demonstrates the frequency of spontaneous bacterial peritonitis among patients presenting with ascites for the first time. SBP was detected in 22.1% of patients, emphasizing the need for routine diagnostic paracentesis at initial presentation.

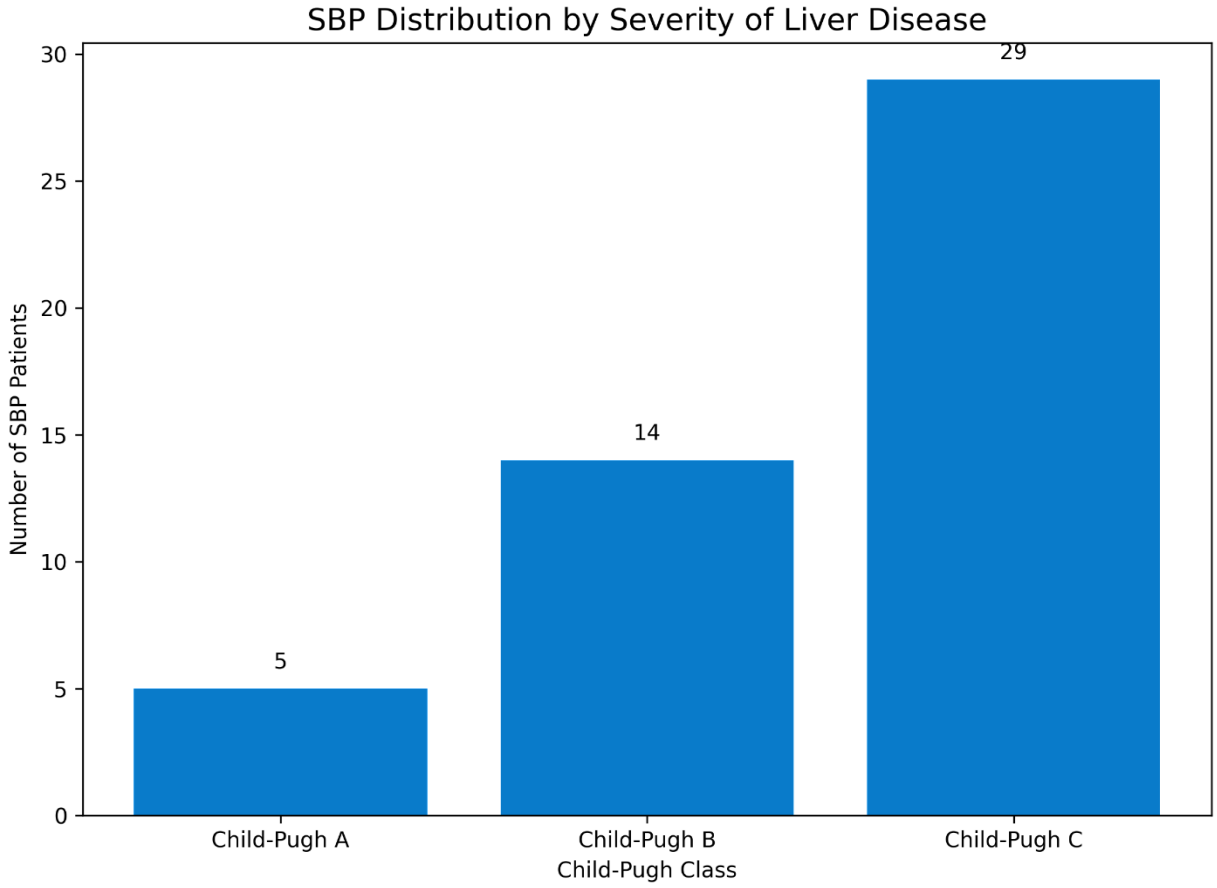


Figure 2 shows an increasing frequency of spontaneous bacterial peritonitis with advancing Child-Pugh class, with the highest number of cases observed in Child-Pugh class C, indicating a strong association between disease severity and risk of infection

DISCUSSION

In the present series too, there was a significant association of SBP with severity of liver disease; Child-Pugh C patients had more prevalence to have SBP followed by those in classes B and A who showed significantly lower incidence ($p < 0.05$). This would be consistent with previous findings that the risk of SBP is independently higher in decompensated cirrhosis, which may be secondary to defective hepatic immune monitoring and low ascites complement and opsonic activity [11,13]. The association between the Child-Pugh score and SBP development is also supported by large cohort studies, underlining the disease severity as one of the primary determinants of infection susceptibility [7,9]. In addition, patients with CLD ascites had a higher prevalence of SBP than those with non-hepatic (cardiac or nephrotic) ascites ($p < 0.05$). This is supported by the literature, reporting that portal hypertension and cirrhosis-related gut barrier damage underlie bacterial translocation, a phenomenon poorly documented in non-cirrhotic ascites [12,14]. Previous studies have shown that low ascitic protein (AP) levels, found frequently in cirrhosis and can be an independent factor of SBP risk [8,18]. Although the endpoint of this study was not positivity, (since it is a cut-off point for the PMN count ≥250 cells/mm ^{3} to diagnose it) and it represents an international standard in practice [14,16], we chose diagnostic criterion that could touch positive or negative culture risk cases of BP. Culture-negative SBP has been shown to have the same clinical and prognostic significance As culture-positive which emphasize that treatment should not rely only on microbiological documentation [15, 19]. As a whole, these statistically significant findings establish that current guideline-concordant practice decouples the decision to perform diagnostic paracentesis from indices of poor outcome [(that is, absence of symptoms), too few of which are detected reliably in clinical practice for sorting out when to sample ascites fluid at hospital presentation from when not (14,16,20).

There is a consistent association between non-compliance with this rule, delayed onset of antibiotics and worsened outcome (higher mortality) as reported by both observational studies and guidelines [10,11].

CONCLUSION

SBP is not an uncommon finding, even at initial presentation. SBP was especially prevalent in patients with advanced cirrhosis (Child-Pugh class C) and was significantly associated with ascites secondary to chronic liver disease. Therefore, the early diagnosis would be cool if routine diagnostic paracentesis is done for all first-episode ascites at admission and then we confirm on treatment.

AUTHOR CONTRIBUTIONS:

The authors, from diverse institutions across multiple provinces in Pakistan, contributed significantly to this multicenter study on SBP in first-episode ascites. Each author brought unique expertise from their respective hospitals: Dr. Rahid Gul (Bannu Medical College) led data collection and analysis in Bannu, offering insights from a less-studied region. Dr. Muhammad Siddique (Muhammad College of Medicine) ensured high-quality patient care and diagnostic accuracy at his hospital. Dr. Younas Ahmad (Jinnah Medical College, Peshawar) managed patient recruitment and data collection, emphasizing the study's protocol adherence. Dr. Intikhab Alam (Jinnah Medical College, Peshawar) played a key role in data analysis and interpreting findings related to SBP and liver disease severity. Dr. Sabir Khan Afridi (Lady Reading Hospital, Peshawar), as the corresponding author, coordinated the study across centers, maintaining ethical standards and ensuring the research's smooth execution. This collaborative approach, representing different regions, allowed for a diverse patient sample and enhanced the generalizability of the study's findings across Pakistan

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