# INCIDENCE OF SPONTANEOUS BACTERIAL PERITONITIS AND ITS VARIANTS WITH SPECIFIC REFERENCE TO ITS OUTCOME ON DISEASE PROGRESSSION AND MORTALITY

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# CERTIFICATE

This is to certify that this dissertation entitled **"INCIDENCE OF SPONTANEOUS BACTERIAL PERITONITIS AND ITS VARIANTS WITH SPECIFIC REFERENCE TO ITS OUTCOME ON DISEASE PROGRESSION AND MORTALITY"** submitted by **Dr.G.SATHYA** to the faculty of Medical Gastroenterology, The Tamilnadu Dr.MGR Medical University, Guindy, Chennai-600032 in partial fulfillment of the requirement for the award of DM Degree, Branch IV (Medical Gastroenterology) is a bonafide work carried out by her under my direct supervision and guidance.

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# CONTENTS

# INTRODUCTION

Spontaneous bacterial peritonitis is the most frequent and important complication of cirrhosis with ascites. SBP is most frequently seen in severely decompensated cirrhotic patients. Since the infection occurs in the absence of a contiguous source of infection like intra – abdominal inflammatory focus eg: abscess, acute pancreatitis, cholecystitis, intestinal perforation, it is called Spontaneous.

Based on culture, polymorphonuclear neutrophil counts of the ascitic fluid and the presence or absence of a surgical source of infection, ascitic fluid infection can be catagorized into five types. There are three types of spontaneous ascitic fluid infections. Spontaneous bacterial peritonitis is the prototype among them.

SBP accounts for 25% of all infections and 9% of hospitalised patients with cirrhosis[(1)]. When a cirrhotic patient, particularly with encephalopathy and or jaundice detoriates, SBP should be suspected. An ascitic fluid protein of less than 1 g/dl predisposes to SBP[(2)]. Patients with a previous episode of SBP are at a particular risk. Patients with variceal bleeding are also at high risk of developing SBP.

Systemic vascular changes in response to the infection can lead to renal complications in patients with SBP[(3)]. Prognosis is worse in patients with SBP. They have a high morbidity and mortality. 10% to 20% of patients die during that hospital admission. The median survival of a patient who develops SBP is

approximately 9 months[4]. SBP recurrence is also not uncommon. The 1 year probability of SBP recurrence is 69%.

In patients with uncomplicated SBP (i.e. no renal dysfunction, no encephalopathy), SBP resolution and immediate survival is 100 %, whether the patients receive oral or intravenous antibiotics[5]. Recurrent SBP in a cirrhotic patient with ascites is an indication for hepatic transplantation, because of reduced survival.

# REVIEW OF LITERATURE

The prototype form of spontaneous ascitic fluid infection is the spontaneous bacterial peritonitis[6]. The term spontaneous bacterial peritonitis was coined by Corriea and Conn in 1975. Their aim was to differentiate spontaneous bacterial peritonitis from surgical peritonitis[7].

Classification for ascitic fluid infections was proposed in 1998[8]. This classification is based on the ascitic fluid culture, the counts of the polymorphonuclear neutrophils and also depending on the absence or presence of a surgically treatable source of infection

**Classification of Ascitic fluid infection:**

**1.** Spontaneous ascitic fluid infection

Spontaneous bacterial peritonitis

Culture negative neutrocytic ascites

Monomicrobial nonneutrocytic ascites

**2. Secondary bacterial peritonitis**

Gut perforation

Non perforation

**3. Polymicrobial bacterascites**

**SPONTANEOUS BACTERIAL PERITONITIS:**

The diagnosis of this form is made in the presence of an elevated polymorphonuclear neutrophil count ≥ 250 cells/cumm and a ascitic fluid culture positivity and without any evidence of surgically treatable external or intra - abdominal source of infection[9]. Most of the cases show growth of a single organism[10]

**Culture negative nonneutrocytic ascites:**

The term CNNA was proposed in 1984[11]. It is a variant of SBP which is associated with a lower mortality as compared to SBP[12]. A PMN count of > 250 cells /cumm and a negative ascitic fluid culture in the absence of even a single dose of antibiotic suggest CNNA[11]. Such and Runyon[8] have proposed that other causes of neutrocytic ascites (tuberculous peritonitis, peritoneal carcinomatosis, pancreatitis) must be ruled out before a diagnosis of CNNA is made. These patients must be treated similar to SBP patients as their clinical presentation, therapeutic and prognostic characteristics resemble that of SBP.

**Monomicrobial nonneutrocytic ascites:**

This variant is diagnosed when the PMN counts are < 250 cells/cumm and the ascitic fluid shows culture positivity for a single organism with no evidence of surgically treatable cause of intraabdominal source of infection[13].

**SECONDARY BACTERIAL PERITONITIS:**

This is diagnosed when the ascitic fluid PMN counts are ≥ 250 cells/cumm, culture showing polymicrobial organisms and an identifiable

surgically treatable intraabdominal primary source of infection.The infection can occur with or without intestinal perforation[14].

**POLYMICROBIAL BACTERASCITES:**

This variant is diagnosed when the PMN counts are < 250 cells/cumm and the ascitic fluid shows cultures of multiple organisms. Earlier studies[8] have shown that this is a rare event seen in about 1 in 1000 paracentesis, occurring due to inadvertent perforation of the intestines while performing paracentesis. They have identified various risk factors for this iatrogenic form of infection which include multiple surgical scars, ileus and the inexperience of the operator in performing the procedure.

**PREVALANCE OF SPONTANEOUS BACTERIAL PERITONITIS:**

In the 1980's, approximately 10% of the ascitic fluid were found to be infected at the time of admission to hospital. A low frequency might be due to the infrequency of paracentesis and the low diagnostic efficacy of bacterial cultures. In the recent days SBP is identified earlier itself due to better techniques of ascitic fluid analysis and culture and also due to routine paracentesis performed at the time of admission and hence the complication rate is reduced to < 1%[15].

In the recent days, paracentesis is performed as a routine in patients with ascites getting admitted to the hospital for various reasons.In patients with a positive culture fluid, Monomicrobial Bacterascites constitute about 1/3 rd and the remaining 2/3 rd constitue SBP[13].

Prevalence of CNNA is largely dependent on culture techniques[15]. The frequency of Polymicrobial bacterascites is low, seen in about 1 per 1000 patients[16]. About 0 - 2% of patients with ascites at the time of admission to the hospital are found to have Secondary bacterial peritonitis[17]. About 5% of the patients initially diagnosed as to have SBP are later proved to be secondary bacterial peritonitis.

**PATHOGENESIS:**

Harold Conn in 1975 used the term spontaneous in describing bacterial peritonitis in the ascites patient to indicate that the infection appeared from nowhere[7]. Current evidence suggests that the spontaneous ascitic fluid infections are due to translocation of the bacteria from the intestine to the mesenteric lymph nodes which results in spontaneous bacteremia and subsequent colonization of ascitic fluid[18].

**INTESTINAL BACTERIAL TRANSLOCATION:**

Study conducted in 1998 has shown that about 30 to 48% of patients with cirrhosis have colonization of the upper bowel with colonic bacteria and the rate of colonization increases in patients with more advanced liver disease[8].

Bauer et al and Guarner et al have demonstrated the overgrowth of a specific organism, particularly potentially pathogenic bacteria such as enterobacteriaceae. It has been found that intestinal bacterial overgrowth is a

prerequisite for bacterial translocation in experimental animals with cirrhosis[19,20].

In the study by Such et al, it was proposed that intestinal bacterial overgrowth in patients with cirrhosis may be due to a combination of alteration in the local IgA immune response and delay in the intestinal transit[8].

Also in cirrhotics, there are changes in the Paneth cell Defensins, presence of portal hypertensive enteropathy and a decrease in pancreato – biliary secretions[21].

Wiest and Tsao[22] in their study have shown that three main factors are found to be linked in the pathological bacterial translocation.

These include:

1) Alterations in the gut microbiota

2) Increase in the intestinal permeability

3) Impairment in the host defence

**GUT MICROBIOTA:**

Spontaneous infections of the ascitic fluid are mainly gut derived bacteria[23]. Gram negative aerobic rods such as E coli and Klebsiella pneumoniae are the causative in majority of cases of SBP. The enteric nature of these organisms indicate the gut as their source[6]. Occasionally Pneumococcus

is also isolated that does not reside in the gut. These organisms cause SBP and MNB. Anaerobes account for only 1% of SBP[24].

SBP, MNB, CNNA are probably as a result of the colonization of susceptible ascitic fluid as a result of spontaneous bacteremia or the weeping of bacteria laden lymph from the liver capsule as it forms ascitic fluid. Although direct transmural migration of bacteria from the gut into ascitic fluid has been postulated, the loss of gut mucosal integrity has also been documented. Bacteria translocate from the gut lumen across the submucosal lymphatics and are detected in mesenteric lymph nodes[25]. From the mesenteric lymph nodes the bacteria spreads to spleen, liver or blood stream.

**INTESTINAL PERMEABILITY :**

Along with a reduction in intestinal motility, structural and functional alterations in the intestinal mucosa have been demonstrated in patients with cirrhosis. These changes lead to an increase in the permeability of intestine to bacterial products.

The intestinal permeability is also altered by the changes occurring in the mitochondrial functioning of the enterocytes and an increased oxidative stress of the intestinal mucosa[26, 27].

**HOST DEFENCE FACTORS:**

Alterations occur in the local and systemic immune defences in patients with cirrhosis which can lead to spontaneous infection of ascitic fluid. In healthy individuals, bacteria that colonize the lymph nodes are killed by local

immune defences. However in the setting of cirrhosis, several forms of immune deficiency is seen which favour the spread of bacteria to the blood stream. Several abnormalities occur in both the humoral and cellular bactericidal systems. A poor function and phagocytic activity of neutrophils , decreased serum complement levels, a decreased macrophage function and reticuloendothelial system dysfunction[28] is common in cirrhosis. These defects in host defences would lead to frequent and prolonged bacteremia.

## LOCAL ASCITIC – PERITONEAL HOST DEFENCE IN PERITONITIS:

Ascites per se may be considered as a risk factor for the development of peritonitis. In healthy individuals, an efficient peritoneal defence mechanism clears off the entering organisms very efficiently[29]. But due to deficiencies in local defence mechanisms against bacteria in cirrhosis, the clearance of peritoneal bacteria is limited.

The absolute number of PMN influx per cumm of ascitic fluid and the overall killing capacity determines the bacterial clearance. The resident macrophages attract PMN by releasing chemotactic factors and also by activating the complement factors. One of the most potent chemokine identified is the Monocyte Chemotactic protein 1. In patients with cirrhosis due to alcohol, a functional polymorphism in this chemotactic protein has been demonstrated which has been proposed as a risk factor for the development of SBP in these patients[30]. A chemotactic gradient is essential to achieve appropriate neutrophil recruitment into the peritoneal cavity. Unfortunately

little is known about the influx, efflux, and kinetics of neutrophils in ascitic fluid in cirrhosis.

Opsonic and bactericidal activity is reduced in patients with cirrhosis. A low opsonic activity is associated with a low C3 level and a low total protein content[31]. A C3 level of < 13 mg /dl is associated with ascitic fluid infection. The incidence rates of SBP have been consistently < 1% when the ascitic fluid protein levels are >1.5g/dl. With protein levels of < 1.5 mg/dl of ascitic fluid, the risk of SBP increases parelling the decrease in protein content and the incidence rate increases to 27 – 44% at levels < 1g /dl[32].

The levels of adipokines in ascites which modulate the inflammatory response are found elevated in the presence of SBP. These include adiponectin, visfatin and resistin[33].

**SYSTEMIC RISK FACTORS & LIVER DYSFUNCTION:**

A decreased reticuloendothelial system activity in patients with cirrhosis is associated with a higher rate of incidence of SBP. A study[34] in 1984 has demonstrated a relationship between bacteraemia, SBP and impaired reticuloendothelial activity and this impairment in function is due to either functional and/or anatomical shunts.

Various markers of advanced liver dysfunction have been identified as important risk factors for the development of SBP in a study done in 2007[35].

These include :

1) bilirubin level greater than 3.2 mg/dl

2) platelet count of less than 98,000 /cumm

3) each point of MELD increases the risk of SBP by about 11%

**GENETIC INFLUENCE:**

Studies have demonstrated the various genetic variants influencing host defence mechanisms[36,37]. Persons with genetic variants such as CARD 15/NOD 2[36] and TLR 2[37] polymorphisms have been found associated with an increased probability of acquiring SBP.

**INFLUENCE OF MEDICATIONS:**

The chances of SBP in a cirrhotic patient with ascites can be influenced by the use of adjunct medications like proton pump inhibitors. Use of PPI may lead to pathological bacterial translocation by facilitating SIBO. This has been proved by a retrospective study[38]. Cirrhotic patients are found to have frequent inadequate overuse of PPIs which increases the risk of acquiring SBP.

Whereas, Non selective Beta Blockers have been shown to prevent SBP[39]. Various experimental settings have reported that an improvement in the chemotaxis, killing capacity and release of proinflammatory cytokines is found in patients who are on beta blockers[40].

**CNNA:**

CNNA episodes are due to insensitive culture methods. Here the number of bacteria are insufficient to reach the threshold of detectability[15]. Studies have shown that a small percentage of specimens of neutrocytic ascitic fluid grow no organisms even when optimal culture methods are used for culture of bacteria[9].

In the setting of sensitive culture techniques, CNNA probably represents spontaneously resolving SBP in which the tap is performed after all bacteria have been killed by the host defences but before the PMN count has normalised. Canawati et al in their study have shown that culture by inoculation of ascitic fluid into agar plates and broth probably may require at least 100 organisms /ml[15]. Also CNNA may probably be due to antibiotic treatment, even a single dose and due to inadequate volume of fluid inoculated.

**MNB:**

Mononuclear non – neutrocytic bacterascites (positive culture, PMN <250 cells/cumm) was labelled in the older literature as Asymptomatic Bacterascites. Human and animal studies have shown that MNB is common. They usually resolve without antibiotic treatment[41]. The invading bacteria are efficiently eradicated by the hosts defence mechanisms on most of the occasions. The fluid shows no increase in ascitic PMN's and it becomes sterile. But when the organism is virulent and the defences are weak, they can progress to SBP[13]. An ascitic fluid infection in the early stage may be probably indicated by MNB. Bacterascites is much more common than SBP.

**SECONDARY BACTERIAL PERITONITIS:**

Pathogenesis of secondary bacterial peritonitis occurs in the setting of frank intestinal perforation or without frank perforation. In frank intestinal perforation, the ascitic fluid is flooded by billions of bacteria. In the absence of frank perforation, bacteria may enter the ascitic fluid by crossing the inflammed tissue planes as in the case with perinephric abscess or empyema of the gall bladder[16].

**POLYMICROBIAL BACTERASCITES:**

Polymicrobial bacterascites occurs in the setting of inadvertent bowel puncture with paracentesis needle while doing the procedure. Bowel contents with bacteria are released into the ascitic fluid and leads to infection. But with high protein ascites, it usually resolves without antibiotic therapy[16].

**BACTERIAL FLORA:**

Various studies have demonstrated Gram negative bacteria as the most frequent group of organisms isolated. They contribute to about 60% of episodes of SBP[15]. Eschcerichia Coli, followed by Klebsiella pneumonia and streptococci (mostly pneumococci) cause most episodes of SBP & MNB. Gram positive cocci account for about 25% of the episodes and they include Pneumococcus, Strep viridians, Staph aureus and the most frequently isolated species are the streptococci. Although anaerobes dominate the colonic flora they are isolated rarely from the ascitic fluid. This probably may be explained by the fact that the intestinal wall and surrounding tissues contain a high

content of oxygen which might inhibit the growth of anaerobes.And also the anaerobes have a relative inability to translocate across the intestinal mucosa and this may lead to a rarity of demonstration in ascitic fluid[8]. Older reports have shown that 6% of cases of SBP were due to anaerobes, but recent reports have shown anaerobes in approximately 1% of cases of SBP & MNB[15, 24]. The detection of anaerobes in ascitic fluid should raise the suspicion of a case of secondary bacterial peritonitis left unrecognised. An increasing incidence of SBP due to gram positive organisms has been demonstrated by studies[42].

**PREDISPOSING FACTORS FOR SBP INCLUDE[8]:**

Child Pugh Class C

Ascitic fluid protein < 1g /dl

Ascitic fluid C3 levels < 13 mg / dl

Gastrointestinal bleeding

Urinary tract infection

Iatrogenic factors : urinary bladder and intravascular catheterisation

Previous episodes of SBP

In patients with cirrhosis, cirrhosis is itself a form of acquired immunodeficiency status. A pre-existing phagocytic dysfunction and an ascitic fluid with a low protein concentration in a cirrhotic can predispose them to bacterial infection. 70 % of the patients who develop SBP are in class C and the remainder being class B.

Andreu et al have demonstrated a serum total bilirubin level of >2.5 mg /dl is an independent risk factor for development of SBP[43].

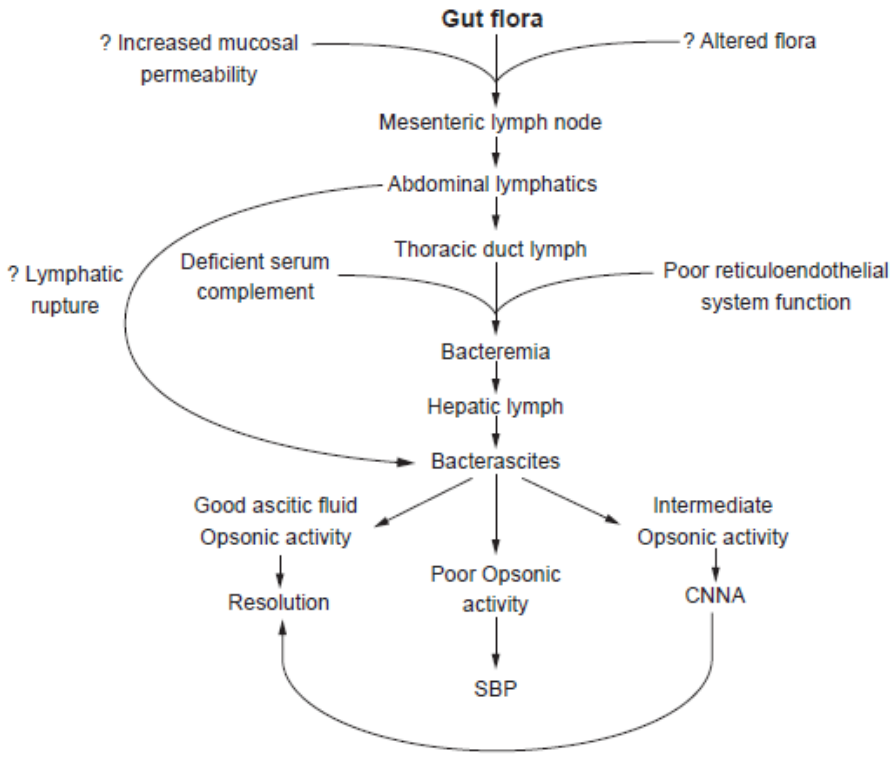
A direct correlation between total protein level, complement components and opsonic activity explains why an ascitic fluid total protein level of <1 g/dl is a risk factor for the development of ascitic fluid infection

In patients with gastrointestinal hemorrhage, the probability of nosocomial infection following hospitalization is approximately 50% and 20% have ascitic fluid infection at the time of admission to the hospital[44]. The risk peaks about 48 hrs after the onset of the bleed. Study done in 1996[45] has reported that the gastrointestinal hemorrhage leads to a status of shock. An increased bacterial translocation occurs from the intestines to extraintestinal sites and there is a decreased effectiveness of the reticuloendothelial system in the status of shock.

Such and Runyon have reported in their study that ascitic fluid infections in 4% of patients have occurred due to intravascular catheters.

Those patients who survive an episode of SBP are at a higher rate of recurrence: 43% at 6 months, 69% at 1 yr, and 74% at 2 yrs[8].

## PATHOGENESIS OF SPONTANEOUS ASCITIC FLUID INFECTION




## CLINICAL PRESENTATION:

About 87% of patients are symptomatic at the time of diagnosis [13].The symptoms and signs are often subtle or usually misinterpreted[13]. Minor changes in the mental status may be the sole evidence of infection. These mental changes would only be detected by family members or family physician.

The most frequently observed symptoms according to Such and Runyon[8] are

1) fever – 69 %

2) abdominal pain - 59%

3) hepatic encephalopathy – 54%

4) abdominal tenderness - 49%

5) diarrhea – 32%

6) ileus – 30%

7) shock – 21%

8) hypothermia – 17%

9) Asymptomatic – 10%

**DIAGNOSIS:**

Many patients with SBP are asymptomatic[46]. So whenever a patient with ascites gets admitted to the hospital regardless of the presence or absence of clinical symptoms suggestive of SBP, a diagnostic paracentesis should be performed. Clinical detoriation in a patient with ascites in the form of fever, abdominal pain or increasing abdominal distension is more suggestive of ascitic fluid infection.

Ascitic fluid analysis for TC, PMN count, biochemistry and a simultaneous bedside inoculation of the ascitic fluid into the blood culture bottles must be done. A prompt diagnosis should be made and treatment should not be delayed until the culture results become available. Guidelines suggest that diagnosis should be based on a fixed cut-off of PMN count in the ascitic fluid[6]. A cut-off value with the greatest sensitivity is 250 PMN cells /cumm and with greatest specificity is 500 PMN cells /cumm[47]. However, the most sensitive cut-off of 250 is used for diagnosis not to miss cases. SBP caused by gram positive cocci has been reported to have a PMN count of < 250 /cumm.

PMN cells should be corrected in case of hemorrhagic ascites i.e. red blood cell count >10,000 /cumm. Subtraction of one PMN per 250 RBC's should be made to adjust for the presence of blood in ascites.

**USE OF AUTOMATED CELL COUNTER:**

PMN in the ascitic fluid can be determined either by manual counting chamber under a light microscope or by automated cell counter. The specific method to be used is not stated in the current guidelines .The use of automated cell counters has been recently validated in patients with cirrhotic ascites according to Riggio et al[48 ,49]. They reveal sufficient sensitivity in the detection of SBP and hence are recommended.

**USE OF REAGENT TEST STRIPS:**

Use of reagent test strips to assess leucocyte esterase activity of activated PMNs needs to be confirmed in large multicentre trials and the test is not interpretable in bloody, chylous or bloody ascites. Mendeler et al[50] in their study recommend the usage of a reagent strip test that has been developed recently which has been calibrated to a cut – off of 250 PMN/cumm in ascitic fluid. This has been shown to have a sensitivity of 100% and a negative predictive value of 100%.However large multicentre trials are needed to validate its use.

**CULTURE METHODS:**

Runyon et al proposed culture of the ascitic fluid to be done by bedside inoculation of the ascitic fluid into blood culture bottles[15]. About 10 ml of

inoculum into the bottle has shown to optimise the results in standard 100 ml bottle. In the older method agar plates inoculation and some broth with a few drops of fluid were used for culture of the ascitic fluid. They were very insensitive methods and only 50 % of the neutrocytic samples demonstrated bacterial growth. Bedside inoculation of the ascitic fluid into blood culture bottles has shown to increase the sensitivity to nearly 80%[51, 52]. Culture is also essential for assessment of the susceptibility of the organism to antibiotic. False negative reports can occur due to error in the handling processes and a delay in the transport of the ascitic fluid[53].

**BACTERIAL DNA DETECTION:**

Detection of bacterial DNA using gene probes is now commercially available. Frances et al have demonstrated bacterial DNA in ascitic fluid in about 40% of patients with cirrhosis, which is derived mainly from gram - negative bacteria[54]. The incidence of SBP in these patients is not predicted by the detection of bacterial DNA either in ascites or in serum. The main advantage of this system of detection of bacterial DNA would be to identify the causative bacteria immediately so that a targeted antibiotic treatment can be started early and prevent mortality.

**OTHER MARKERS OF INFLAMMATION IN ASCITIC FLUID:**

The utility of other tests in ascitic fluid such as ascitic fluid pH, LDH, Cholesterol, Fibronectin, α 1 – AT, Glysosaminoglycans has not proven any benefit and these tests are not recommended[8]

**RULING SECONDARY BACTERIAL PERITONITIS:**

Since the mortality associated with secondary bacterial peritonitis is high, they should be diagnosed early and differentiated from SBP[55]. Timely surgery is essential in them to prevent death during hospitalization. The clinical symptoms and signs closely resemble that of SBP and also a classic surgical abdomen does not develop even with perforation of the colon.

Intestinal perforation should be suspected in the setting of a neutrocytic ascites with at least two of the following three criteria[56]:

1) ascitic fluid total protein >1 g /dl

2) glucose < 50 mg / dl

3) LDH > 225 mU /ml

This is proposed by Runyon et al and has a sensitivity of < 68%. Ascitic fluid culture in a perforated viscus is nearly always polymicrobial. When there is no response to antibiotic therapy in a suspected case of SBP, then secondary bacterial peritonitis should be considered and ruled out.

**TREAMENT OF SBP:**

Treatment should be started immediately after diagnosis of SBP and it is empirical since culture results are not available at that time point. The antibiotics used should have a high killing capacity against the bacteria and also should achieve high concentrations in the ascitic fluid .Most data support

the use of Cefotaxime 2 g intravenously every 8 hours as the empirical antibiotic.

Antibiotics without any data on their penetrating capacity of the ascitic fluid should be avoided. Empirical treatment is indicated in patients with an ascitic fluid PMN count of ≥ 250 cells/cumm and with clinical features suspicious of ascitic fluid infection. The difference in the type of antibiotic treatment to be used in nosocomial and community – acquired SBP is not addressed to by any guidelines. High rates of bacterial multiresistance and mortality are seen in patients with nosocomial acquired SBP[57]. Health care associated infections are also more frequent in cirrhotic patients[58].

**COMMUNITY ACQUIRED SBP:**

In patients with no prior hospitalization and antibiotic treatment, the causative organisms for SBP are the enterobacteriaceae family, which are easily treatable. Cefotaxime or other third generation cephalosporins are the drug of choice.

Cefotaxime given in the dose of 2g IV every 8 hrs has shown to result in excellent ascitic fluid levels (20 fold killing power after a single dose). It reaches high ascitic fluid concentrations during therapy[5,59,60]. Rimola et al have achieved a resolution of infection in 77 – 98% of patients[50]. A randomised control study by Runyon and Hutchinson have shown that a duration of treatment for 5 days is as effective as10 day treatment[59]. The dosage need not be altered for hepatic or renal failure. Ceftriaxone is highly protein bound & penetrates low protein ascites poorly. Ceftriaxone has a role in

the prevention of bacterial infections in patients with cirrhosis and gastrointestinal hemorrhage.

**DOSING INTERVALS:**

Studies[61] have recommended the dosing interval of 8 – 12 hrs in ideal conditions, 8 hrs for a serum creatinine of < 3 mg /dl and 12 hrs for more severe renal failure. Dosing more frequently than every 8 hrs is not necessary because high ascitic fluid concentration of (>20 fold the MIC of >90 % of the flora) of the drug is attained after one dose and is sustained during every 8 hrs dosing[61]. Neither a loading dose nor an intraperitoneal dose appears to be necessary. When susceptibility testing results are available a more narrower spectrum antibiotic can be changed.

**OTHER IV ANTIBIOTICS:**

IV Amoxicillin / Clavulanic acid in the dose of 1g every 8 hrs has shown comparable efficacy as IV Cefotaxime in earlier trials.

Ciprofloxacin given either for 7 days IV or for 2 days IV followed by orally for 5 days results in SBP resolution rate similar to Cefotaxime.[62]

**ORAL ANTIBIOTICS:**

In patients without any complicating factors that may precipitate the therapeutic efficacy, oral treatment with Quinolones are found to be as effective as parenteral Cefotaxime in the treatment of SBP[5]. Oral Ofloxacin is administered in the dose of 400 mg bd for an average of 8 days in patients who

do not have vomiting, shock, bleeding or renal failure. Empirical use of a fluoroquinolone to prevent spontaneous bacterial peritonitis should be avoided as there is a high risk of development of resistance to these drugs in these patients[63]. But however patients with spontaneous bacterial peritonitis in whom fluoroquinolones were given as a prophylactic antibiotic are still found to be susceptible to Cefotaxime.

**NOSOCOMIAL SBP:**

The use of third generation Cephalosporins, Amoxicillin /Clavulanic acid or Quinolones in patients with Nosocomial SBP has been found to be associated with a low resolution rates[64]. The reasons for this might be due to increasing resistance to these antibiotics, the increasing incidence of extended spectrum β – lactamase (ESBL) producing bacteria as well as multiresistant gram – positive bacteria such as Enterococcus faecium or methicillin resistant Staphylococcus aureus (MRSA). 24-27% of cases of SBP are found to be due to MRSA[65]. ESBL's leads to resistance to various antibiotics including third – generation Cephalosporins and Monobactams, and also carry genes encoding resistance to antibiotics like Quinolones, Tetracyclines and antifolates. The patients with nosocomially acquired multiresistant organisms are associated with increased morbidity, mortality and health care – associated costs[57]. First – line empirical antibiotic treatment is often results in failure to response in these patients[57]. The treatment in these patients should be stratified based on the host factors as well as on the validated knowledge of the resistance profile of the bacteria in the setting in which the patient is diagnosed and treated. Previous hospitalization, within the previous three months, ICU

treatment, and prior prophylactic or therapeutic antibiotic treatment can contribute to bacterial multiresistance to antibiotics[66]. It is therefore suggested that those patients with risk factors of likelihood of developing multidrug resistance and patients with SBP acquired nosocomially, a more effective first –line empirical antibiotic treatment with a broader spectrum drug like Carbapenems should be employed. Also the rate of success of use of antibiotics like Cefotaxime and Amoxicillin – Clavulanic acid in patients with nosocomially acquired SBP is as low as 44% and so extended spectrum antibiotics are preferred These drugs can be changed later if the microbiological results reveal non – resistant antibiotic susceptible bacteria.Broad spectrum antibiotics are the choice of initial empirical therapy in patients with hospital acquired SBP, especially in those who had been on Beta – Lactams during admission, had been recently hospitalized or on Quinolone prophylaxis.

**TREATMENT OF MONOMICROBIAL BACTERASCITES:**

It is controversial whether immediate antibiotic treatment is required in a patient with Monomicrobial Bacterascites without an increase in the PMN count. They are special cases with regards to empirical treatment as many episodes resolve without treatment. But with possibility of many cirrhotic patients being asymptomatic even in the presence of infection, it is mandatory to start on antibiotic treatment. Some patients may progress to SBP, and therefore all patients should receive treatment.Empirical treatment can be discontinued after 2 -3 days later if the culture remains negative.

**TREATMENT OF CNNA :**

Empirical treatment should be started as the treating physician is not aware of that the culture would show no growth. A repeat paracentesis should be done to assess the response of polymorphonuclear count to the given treatment .The response to treatment can be confirmed by a decrease in the polymorphonuclear counts. A reduction in the PMN count below the baseline and frequently more than 80% reduction confirms the response to treatment and the treatment has to be continued for a few more days[(67)].

**ADJUVANT TREATMENT:**

SBP is associated with a worsening of renal function and Llovet et al have demonstrated renal impairment in about 33% of the patients with SBP[(68)]. This is due to the increased production of intraperitoneal nitric oxide in spontaneous bacterial peritonitis which in turn leads to an increase in the systemic vasodilatation and leads on to renal failure.

IV Albumin with Cefotaxime has prevented worsening with a concomitant improvement in the in - hospital and 3 - month mortality[(69)]. It is given in the dose of 1.5 g / kg on day 1 and 1 g / kg on day 3. Trials have shown that adjuvant administration of high – dose albumin along with antibiotics acts by decreasing the vasodilatation and increasing intravascular volume. Because of survival advantage, the use of IV albumin as a adjunct treatment has been recommended. The patients who benefit most from the administration of albumin are those with renal dysfunction at baseline, sr

creatinine > 1mg/dl and /or blood urea nitrogen >30 mg/dl and sr bilirubin > 4mg/dl.[70]

**DURATION OF TREATMENT:**

Recommended duration of treatment is for 5 days. Extension of treatment to 10 days has not been found to be superior to 5 days of treatment as shown in a comparative study[71]. Antibiotic treatment can be safely discontinued after the PMN count has decreased to < 250 cells / cumm. So a repeat paracentesis should be done after 48 hrs to determine the levels of PMN count in the ascitic fluid[14]. Current guidelines suggest that an absence of decrease in the PMN counts by at least 25% compared with the pretreatment levels after 2 days of antibiotic treatment, then the antibiotic treatment has to be changed[28].

**PREVENTION OF SBP:**

**ANTIBIOTIC PROPHYLAXIS:**

Emergence of resistant bacteria is a problem encountered in long term prophylaxis[1]. So prophylactic antibiotics are indicated only in patients with the highest risk of developing SBP. Prophylaxis is considered in patients with ascitic fluid protein concentration <1.5 mg /dl,variceal hemorrhage, child – pugh score of ≥ 9 , total bilirubin ≥ 3 mg/dl, sr creatinine of ≥ 1.2 mg /dl, sr sodium of < 130 mEq/l, or blood urea nitrogen of ≥ 25 mg/dl and those with a previous episode of SBP, Cirrhosis with gastrointestinal hemorrhage[72 ,73]. In the setting of upper GI hemorrhage, Norfloxacin 400 mg twice daily for 7 days is recommended to prevent SBP (74). Recently IV Ceftriaxone 1g daily for 7

days is found to be more effective than Norfloxacin in the setting of GI hemorrhage, and in patients with advanced cirrhosis ie: with at least two of the following : ascites, severe malnutrition, encephalopathy or bilirubin >3 mg /dl[75]. It can also be administered in patients who are vomiting blood[75]. Norfloxacin 400 mg daily is effective in reducing the risk of SBP in patients with low ascitic fluid protein and with prior episodes of SBP[72]. In patients with previous episode of SBP, Norfloxacin 400 mg orally once daily has to be given until death or liver transplantation. Some guidelines recommend the use of oral Ciprofloxacin 750 mg once weekly or Trimethoprim / Sulfamethoxazole in the dose of one double strength tablet daily as an alternative[76]. In patients with ascitic fluid total protein > 1 g /dl and without prior history of SBP, prophylaxis is not necessary as the 1 – year probability of SBP is nil[32]. Prophylactic administration of antibiotics has shown to reduce the rate of recurrence significantly. There is 66% reduction in recurrence in patients with prior SBP administered with Norfloxacin.In a cirrhotic patient with gastrointestinal hemorrhage, prophylaxis with Norfloxacin has shown to reduce the rate of infection by 73% and Ceftriaxone by 67%. In a patient with cirrhosis and ascitic fluid total protein < 1.5 g/dl, prophylaxis with Ciprofloxacin 500 mg orally daily for 1 year has shown to reduce the rate of infection by 31% and also improves the survival rate by 30%. Norfloxacin prohylaxis in the setting of predisposing conditions has shown to reduce SBP by 89%, 32% reduction in the development of hepatorenal syndrome, 52% increase in the 3-month survival and 25% increase in the 1-year survival.[74,75]

**ALTERNATIVE PROPHYLACTIC MEASURES:**

1) Since the continuous use of single antibiotic may lead on to resistance formation, antibiotic cycling should be tried to overcome this.

2) Rifaximin can be tried as it belongs to a class of antibiotics different from the antibiotics tested so far, with broad antimicrobial activity against gram positive bacteria, less bacterial resistance, acting predominantly in the small intestine[77].

3) Probiotics have been found efficacious in correcting the bacterial overgrowth, improving the neutrophil function, stabilising the mucosal barrier function, and decreasing bacterial translocation in experimental animal[79]. The development of bacterial resistance may be limited by using probiotics and trials are ongoing in this regard.

4) The bacterial infections which occur postoperatively after liver transplantation has been decreased with the addition of fibre to lactobacilli.[79]

**PROGNOSIS & OUTCOME:**

A prospective study documented a recurrence rate of 69 % at 1 year[4]. An ascitic fluid protein level of < 1 g/dl was the best predictor of recurrence. About 48 - 95% of the patients with spontaneous fluid infections died in the

past in spite of treatment during the hospitalization[80]. Recent series have reported a <10% hospital mortality[70] and the mortality can be reduced to < 5% if timely and appropriate antibiotics are started and infection is identified earlier[70].

Patients who have had already one episode of SBP are at a high risk of recurrence, with rates of 43% at 6 months, 69% at 1 year, 74% at 2 years[4]. The median survival of a patient who develops spontaneous bacterial peritonitis is 9 months.[4]

Renal impairment is a frequent complication of spontaneous bacterial peritonitis. It is reported in about 33% of episodes of SBP[68]. Administration of intravenous albumin has been found to improve survival and outcome in these patients. The main predictors of death in a patient with spontaneous bacterial peritonitis would be determined by the nosocomial acquisition of infection and associated renal dysfunction. An uncomplicated community acquired spontaneous bacterial peritonitis i.e. with no renal impairment, no hepatic encephalopathy, the resolution of SBP and immediate survival is about 100% whether they receive oral or intravenous antibiotics.[5]

An episode of SBP is an indication for liver transplantation as it is a marker for ESLD[80]. To maximise survival, paracentesis should be performed in all patients with ascites at the time of hospitalization, so that infection can be detected and treated promptly.

The probabilities of 1 year and 2 year survival rates are in the range of 30% and 20 % respectively[8].

# AIM OF THE STUDY

1) To determine the Incidence, Microbial spectrum, Clinical and Biochemical spectrum of SBP and its variants in patients with Cirrhosis and Ascites.

2) To study the natural history and outcome of patients with SBP

# MATERIALS AND METHODS

This is a prospective, observational study. The study was conducted in the Department of Digestive Diseases and Health, Anna Nagar Peripheral Hospital from August 2012 to January 2013. 180 consecutive chronic liver disease patients with ascites of varied etiology, admitted in the ward were taken for the study. 80 patients were eliminated from the study as they were associated with other causes of ascites, associated with malignancy or other comorbid illness.100 patients who fitted into the inclusion criteria were analyzed for the presence of SBP. In all patients cirrhosis was confirmed by a combination of Biochemical, Haematological parameters & Ultrasound abdomen.

Ethical committee approval was obtained before proceeding with the study. Willingness of the patients included in the study to undergo investigations was obtained, along with written informed consent.

**INCLUSION CRITERIA:**

1) Cirrhotic patients between 20 and 70 years.

2) Both sexes

3) Patients with cirrhosis and ascites

4) Patients presenting with fever, chills, abdominal pain, recent increase in the abdominal distension, confusion or coma, rebound tenderness, or signs of hepatic encephalopathy

5) Patients with ascitic fluid polymorphonuclear neutrophil count ≥ 250 cells /cumm

**EXCLUSION CRITERIA:**

1) Patients with ascites of other causes

2) Patients who had received antibiotics 2 -3 weeks prior

3) Patients with previous SBP

4) Patients with secondary bacterial peritonitis

5) Patients with infections involving other systems

**CLINICAL EVALUATION:**

A detailed history was obtained from the study group. Meticulous examination of the patient was done. Ascites was graded according to International Ascites Club criteria. West Haven criteria was used to grade the severity of Hepatic encephalopathy. The study group was subjected to Biochemical, Radiological investigations and Endoscopy.

**LABORATORY INVESTIGATIONS:**

Blood investigations - hemoglobin, WBC count, platelet count, serum bilirubin – total, direct, indirect, SGOT, SGPT, SAP, serum proteins – total, albumin, globulin, PT, INR, serum urea, serum creatinine, HBsAg, Anti HCV were done for all the patients.

CTP class and MELD score was calculated for all the patients.

**ASCITIC FLUID COLLECTION:**

Under strict aseptic precautions diagnostic paracentesis of the ascitic fluid was done. Proper positioning of the patient was done. The site of tapping on the abdomen was marked by clinical or with ultrasound guidance. Povidone iodine solution was used for skin disinfection. Abdominal draping was done with sterile towel. Sterile gloves were worn before performing the procedure. 22 gauge needle was used for tapping . Z technique was applied for tapping of the fluid. 30 ml of the ascitic fluid was obtained using two syringes. The blood culture bottles were inoculated first. For ascitic fluid culture, about 10 ml of the ascitic fluid was inoculated directly into 50 ml blood culture bottles -aerobic and anerobic media each at the bedside itself under strict aseptic precautions and using a sterile needle.

Ascitic fluid was also sent for analysis of total leucocyte count, polymorphonuclear neutrophil counts, total proteins, albumin, globulin, sugar, cytology, culture and sensitivity.

Other relevant investigations like chest X- ray, ECG, plain X- ray abdomen, UGI endoscopy were also done .

**DISTRIBUTION OF PATIENTS WITH CIRRHOSIS AND ASCITES AND THE STUDY GROUP:**

TOTAL OF 180 PATIENTS ADMITTED WITH ASCITES

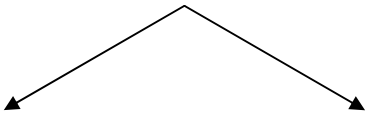
↓

80 patients were excluded

23 patients had previous episodes of SBP, 22 patients had other causes of ascites like TB, Malignancy, 20 patients had co existent other system infections like UTI, Respiratory infections, cellulitis of foot etc, 15 patients had prior antibiotic treatment.

↓

100 patients included in the study



29 pateints - SBP  71patients –Non - SBP

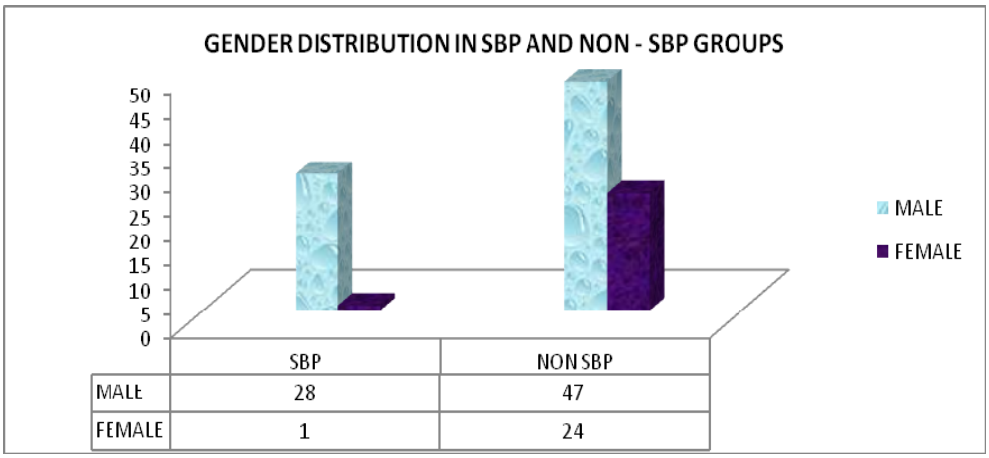
# RESULTS

The total study group included 100 patients with cirrhosis and ascites. Of these 100 patients, 75(75%) patients were males and 25 (25%) were females with a male to female ratio of 3:1.Male preponderance was seen in this study group as the main etiology of the cirrhosis is ethanol related. SBP was found in 28 male and 1 female patient and No SBP in 47 male and 24 female patients.

**TABLE – 1 : GENDER DISTRIBUTION OF THE STUDY GROUP (N=100 )**

Among the study group of 100 cases, 75(75%) were male and 25(25%) were female with a male- female ratio of 3:1.

| GENDER | SBP n=29(%) | NONSBP n=71(%) | TOTAL |
|---|---|---|---|
| MALE | 28(96.6) | 47(66.2) | 75(75) |
| FEMALE | 1(3.4) | 24(33.8) | 25(25) |
| TOTAL | 29(100) | 71(100) | 100(100) |



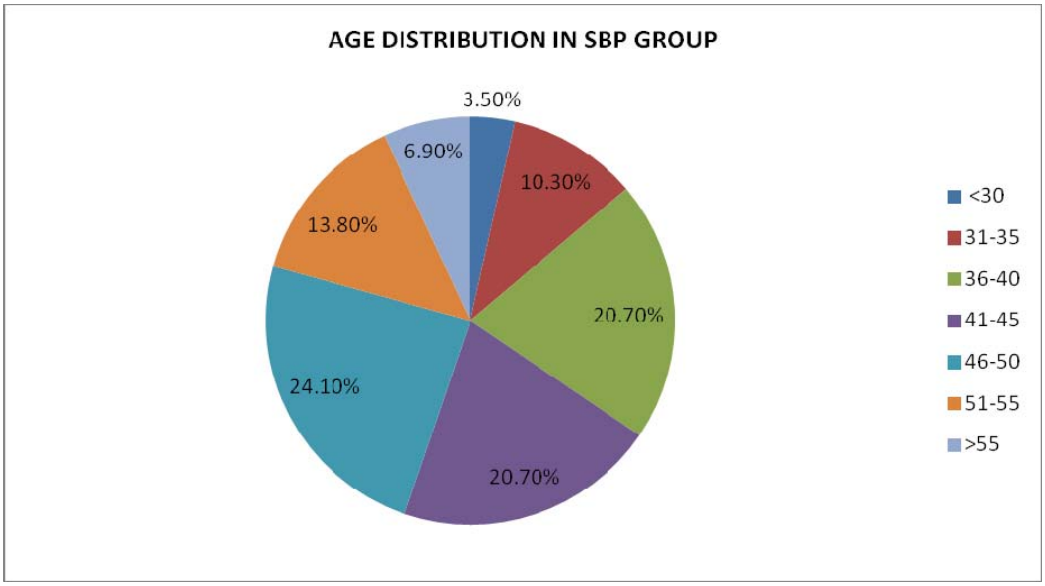
**AGE DISTRIBUTION:**

The mean age of the patients in SBP group is 44.24 ± 8.0 years and the mean age of the patients in Non– SBP group is 43.35 ± 6.0.There was only little difference in the mean age between the two groups and the P value was 0.54 which was not statistically significant.

**TABLE 2: MEAN AGE OF THE SBP AND NON – SBP GROUPS:**

| Variable | SBP | NON SBP | P Value |
|---|---|---|---|
| Age | 44.24+8.00 | 43.35+6.00 | 0.54 |

**Mean+ SD has been calculated for the variable



**ETIOLOGY:**

The etiology of the study group is varied. In the SBP group the etiology was ethanol in 23(79.3%) patients, Hepatitis B in 6(20.7%) patients. In the Non – SBP group, the etiology was ethanol in 36(50.7%) patients, Hepatitis B in 20(28.2%), Hepatitis C in 4(5.6%), NAFLD in 7(9.9%), Idiopathic in 4(5.6%) patients. Ethanol related cirrhosis was the commonest in both the groups but patients with ethanol related cirrhosis were found to be more prone to SBP ($P< 0.05$)

**TABLE 3: ETIOLOGY IN SBP AND NON SBP GROUP**

| ETIOLOGY GRADE | SBP (n=29) | | NON SBP(n=71) | | Total | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| 1(Ethanol) | 23 | 79.3 | 36 | 50.7 | 59 | 59 |
| 2(HBV) | 6 | 20.7 | 20 | 28.2 | 26 | 26 |
| 3(HCV) | 0 | 0 | 4 | 5.6 | 4 | 4 |
| 4(NAFLD) | 0 | 0 | 7 | 9.9 | 7 | 7 |
| 5(IDIOPATHIC) | 0 | 0 | 4 | 5.6 | 4 | 4 |
| TOTAL | 29 | 100 | 71 | 100 | 100 | 100 |

| Variable | SBP | NON SBP | P Value |
|---|---|---|---|
| ++Etiology | 1(1-2) | 1(1-5) | 0.003* |

++Median (range) has been calculated for the variable.

The Median of SBP and Non SBP groups is 1(Ethanol) group with range between 1-2 for SBP and 1-5 for NON SBP and there is highly significant difference in 2 groups ($p< 0.01$).

*$p< 0.05$ is considered statistically significant.

**CLINICAL SYMPTOMS:**

The patients presented with various clinical manifestations like ascites, pedal edema, fever, abdominal pain, jaundice, and UGI bleed. The patients also presented with various degrees of hepatic encepahalopathy at the time of hospitalization. Ascites was seen in all the patients of the study group. From the results it was seen that patients with SBP were found to be more commonly associated with fever, abdominal pain, jaundice, UGI bleed and with severe grades of Hepatic encephalopathy when compared to patients without SBP.

**COMPARISON OF CLINICAL SYMPTOMS BETWEEN SBP AND NON SBP GROUPS**

Chi-square test and Fisher's exact test have been used to compare the categorical variables wherever appropriate and $p<0.05$ is considered to be statistically significant.

**TABLE 4: DISTRIBUTION OF VARIOUS CLINICAL SYMPTOMS IN SBP AND NON SBP GROUPS**

| Symptoms | SBP n=29(%) | NON SBP n=71(%) | Total n=100(%) |
|---|---|---|---|
| Abdominal Pain | 24(82.8) | 18(25.3) | 42(42) |
| Fever | 17(58.6) | 10(14.1) | 27(27) |
| Jaundice | 16(55.2) | 17(23.9) | 33(33) |
| UGI Bleeding | 16(55.2) | 11(15.5) | 27(27) |
| Pedal Edema | 9(31) | 21(29.6) | 30(30) |
| Abdominal distension | 29(100) | 71(100) | 100(100) |
| He | 23(79.3) | 17(23.9) | 40(40) |

**TABLE 5 : FEVER in SBP and NON SBP group**

| FEVER | GROUP | | | | Total | | P-Value |
|---|---|---|---|---|---|---|---|
| | SBP | | NON SBP | | | | |
| | N | % | N | % | N | % | |
| PRESENT | 17 | 58.6 | 10 | 14.1 | 27 | 27 | |
| ABSENT | 12 | 41.4 | 61 | 85.9 | 73 | 73 | <0.001* |
| Total | 29 | 100 | 71 | 100 | 100 | 100 | |

OR - 8.64 ; (95% C.I- 3.19-23.41)

*p< 0.05 is considered statistically significant

**TABLE 6 : ABDOMINAL PAIN IN SBP AND NON SBP GROUP**

| ABDOMINAL PAIN | Group | | | | TOTAL | | P-Value |
|---|---|---|---|---|---|---|---|
| | SBP | | NON SBP | | | | |
| | N | % | N | % | N | % | |
| PRESENT | 24 | 82.8 | 18 | 25.3 | 42 | 42 | |
| ABSENT | 5 | 17.2 | 53 | 74.7 | 58 | 58 | <0.001* |
| Total | 29 | 100 | 71 | 100 | 100 | 100 | |

OR - 14.13 ; (95% C.I- 4.70-42.54)

*p< 0.05 is considered statistically significant

**TABLE 7 : UGI BLEEDING IN SBP AND NON SBP GROUP**

| UGI BLEEDING | GROUP | | | | Total | | P-Value |
|---|---|---|---|---|---|---|---|
| | SBP | | NON SBP | | | | |
| | N | % | N | % | N | % | |
| PRESENT | 16 | 55.2 | 11 | 15.5 | 27 | 27 | <0.001* |
| ABSENT | 13 | 44.8 | 60 | 84.5 | 73 | 73 | |
| TOTAL | 29 | 100 | 71 | 100 | 100 | 100 | |

OR- 6.71 ; (95% C.I- 2.54-17.78)

*p< 0.05 is considered statistically significant

**TABLE 8 : HE SEVERITY IN SBP and NON- SBP**

| SEVERITY GRADE | SBP (n=29) | | NON SBP (n=71) | | Total | |
|---|---|---|---|---|---|---|
| | n | % | n | % | N | % |
| 1 | 6 | 20.7 | 54 | 76.1 | 60 | 60 |
| 2 | 10 | 34.5 | 12 | 16.9 | 22 | 22 |
| 3 | 13 | 44.8 | 5 | 7.0 | 18 | 18 |
| Total | 29 | 100 | 71 | 100 | 100 | 100 |

| Variable | SBP | NON SBP | P Value |
|---|---|---|---|
| ++ HE SEVERITY | 2(1-3) | 1(1-3) | <0.001* |

++Median (range) has been calculated(*p<0.05 is considered statistically significant).1 – west haven grade 0 &mhe,2 – west haven grade 1&2, 3- west haven grade 3 for statistical analysis

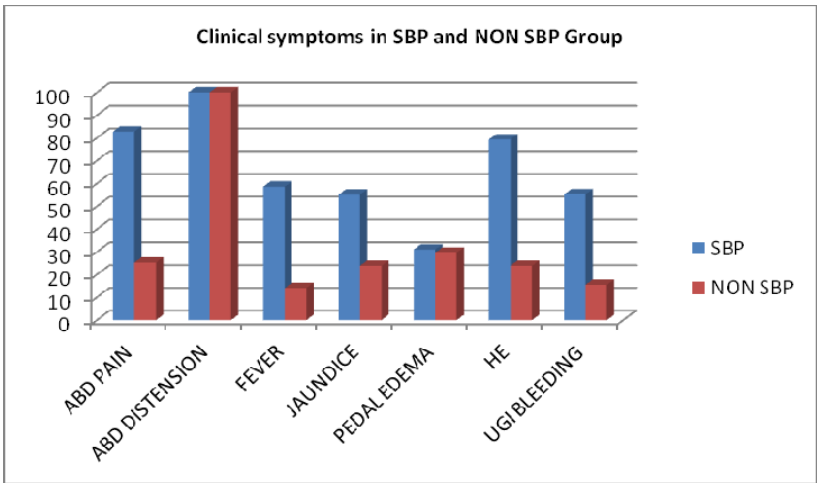
**TABLE 9 : JAUNDICE IN SBP AND NON SBP GROUP**

| JAUNDICE | GROUP | | | | Total | | P-Value |
|---|---|---|---|---|---|---|---|
| | SBP | | NON SBP | | | | |
| | N | % | N | % | N | % | |
| PRESENT | 16 | 55.2 | 17 | 23.9 | 33 | 33 | 0.0026* |
| ABSENT | 13 | 44.8 | 54 | 76.1 | 67 | 67 | |
| Total | 29 | 100 | 71 | 100 | 100 | 100 | |

Odds Ratio-3.9(95% C.I-1.57-9.74).The odds of jaundice are 3.9 times greater among SBP group compared to non SBP group and it is found to be statistically significant.* $p<0.05$ is considered statistically significant.

**TABLE 10 : PEDAL EDEMA IN SBP AND NON SBP GROUP**

| PEDAL EDEMA | GROUP | | | | Total | | P-Value |
|---|---|---|---|---|---|---|---|
| | SBP | | NON SBP | | | | |
| | N | % | N | % | N | % | |
| PRESENT | 9 | 31 | 21 | 29.6 | 30 | 30 | 0.86 |
| ABSENT | 20 | 69 | 50 | 70.4 | 70 | 30 | |
| Total | 29 | 100 | 71 | 100 | 100 | 100 | |



**CHILD PUGH SCORE:**

Child Pugh Turcott score was calculated for all the patients. In the SBP group, majority of the patients were in Child Pugh class C(62.1%) and in Non – SBP group majority were in Child Pugh class B(59.2%).The occurrence of SBP was found to be statistically highly significant in patients with Child Pugh C ($P < 0.01$).

**TABLE 11 : CTP IN SBP AND NON SBP GROUP**

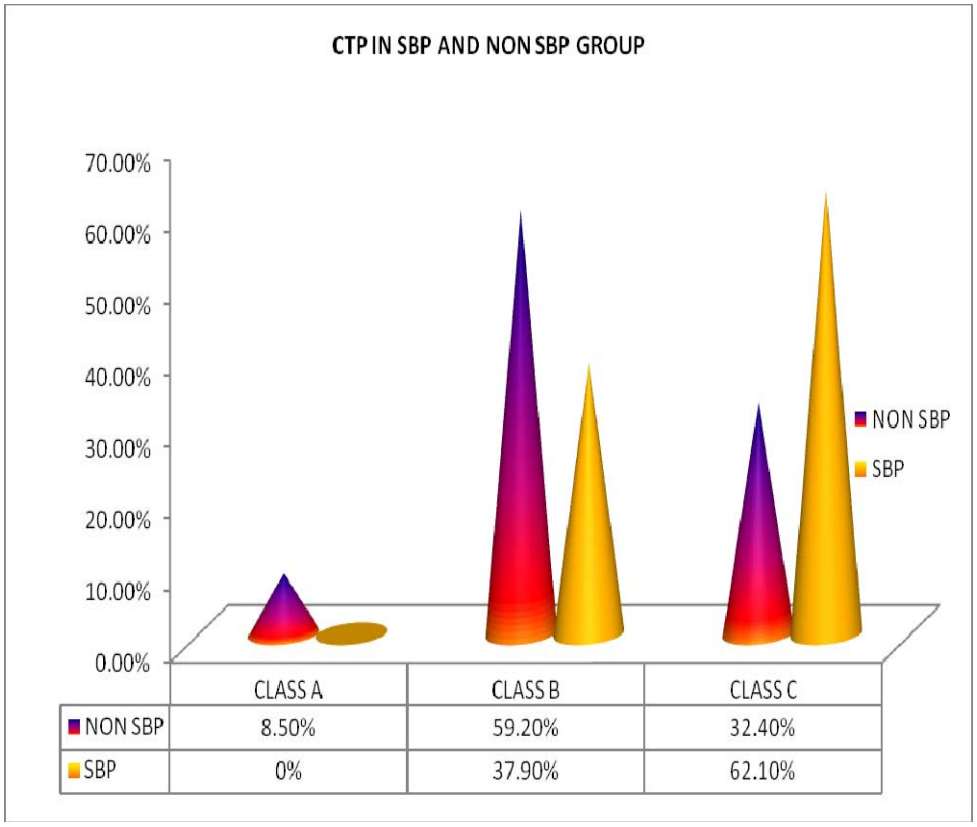
| CTP Class | SBP (n=29) | | NON SBP(n=71) | | Total | |
|---|---|---|---|---|---|---|
| | N | % | n | % | N | % |
| A | 0 | 0 | 6 | 8.5 | 6 | 6 |
| B | 11 | 37.9 | 42 | 59.2 | 53 | 53 |
| C | 18 | 62.1 | 23 | 32.3 | 41 | 41 |
| Total | 29 | 100 | 71 | 100 | 100 | 100 |

| Variable | SBP | NON SBP | P Value |
|---|---|---|---|
| ++CTP | C(B-C) | B(A-B) | 0.0036* |

++Median (range) has been calculated for the variable .

The median of SBP group is Class C compared to Class B for Non SBP group and there is a significant difference in 2 groups and it is found to be statistically highly significant ($p<0.01$)

*$p<0.05$ is considered statistically significant.




| | CLASS A | CLASS B | CLASS C |
|---|---|---|---|
| NON SBP | 8.50% | 59.20% | 32.40% |
| SBP | 0% | 37.90% | 62.10% |

**MELD SCORE:**

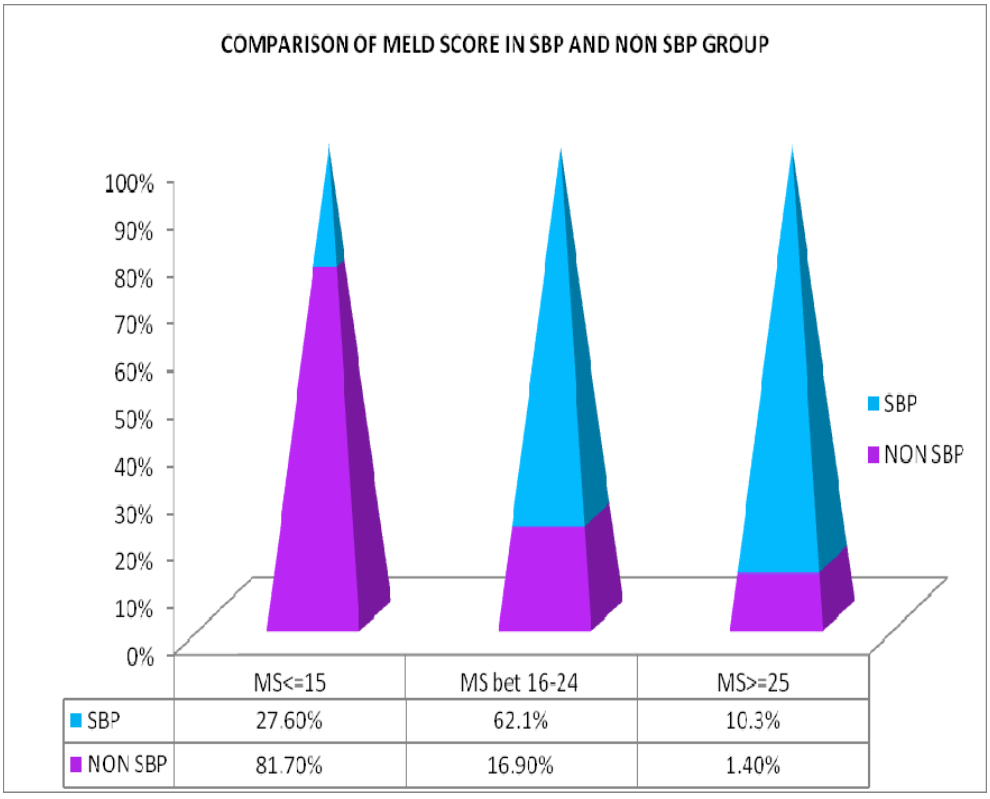
MELD score was calculated for the study group. About 62.1% of patients with SBP had a MELD score ranging from 15 – 21 with a mean of 19. This score was found to be statistically significant (P < 0.001) in SBP patients. The MELD score was found to be in the range of 10 – 14 with a mean of 13 in the Non – SBP patients.

**TABLE 12 : MELD SCORE IN SBP AND NON SBP GROUPS**

| MELD SCORE | SBP n=29(%) | NON SBP n=71(%) | TOTAL n=100(%) |
|---|---|---|---|
| 1 (<=15) | 8(27.6) | 58(81.7) | 66(66) |
| 2(16-24) | 18(62.1) | 12(16.9) | 30(30) |
| 3(>=25) | 3(10.3) | 1(1.4) | 4(4) |
| Total | 29(100) | 71(100) | 100(100) |

| ++MELD SCORE | SBP | NON SBP | P VALUE |
|---|---|---|---|
| | 2(1-3) | 1(1-3) | <*0.001 |

++Median (range) has been calculated for the variable. * p< 0.05 is considered statistically significant. The Median for SBP group lies in the 16-24 score group compared to the score of Non SBP group lying in <=15 group and there is a highly significant difference in the 2 groups with p<0.001.




| | MS<=15 | MS bet 16-24 | MS>=25 |
|---|---|---|---|
| SBP | 27.60% | 62.1% | 10.3% |
| NON SBP | 81.70% | 16.90% | 1.40% |

**ASSESSMENT OF BIOCHEMICAL PARAMETERS:**

Biochemical parameters were assessed among the two groups. Both serum and ascitic fluid were analyzed for various biochemical parameters including Hb, serum bilirubin, serum protein, serum albumin, serum creatinine, SGOT, SGPT, Platelet count, INR, Ascitic fluid total leucocyte count and polymorphonuclear neutrophil count, protein, albumin, cytology in the SBP and Non – SBP groups. Among these parameters ,the patients with SBP had statistically significant association than Non – SBP patients with regards to high ascitic fluid TLC (median of 620 vs. 170, $P<0.001$)high ascitic fluid PMN count (median of 420 vs. 82, $P<0.001$), low ascitic fluid albumin(mean of 0.63±0.34 vs. 0.94±0.30, $P<0.001$), a low ascitic fluid protein(mean of 1.15±0.34 vs. 2.27±0.64, $P<0.001$) a high serum bilirubin (mean of 6.81±6.12 vs. 3.12±2.89, $P<0.0001$), a high SGOT (median of 58 vs. 40, $P<0.05$), a low Hb value (mean of 8.74±1.92 vs. 10.07±2.26, $P<0.05$) and a high INR value (mean of 1.67±0.52 vs.1.36±0.38, $P<0.05$). Others parameters were not statistically significant. This may indicate that patients with SBP are mostly anaemic with severe liver involvement and associated coagulopathy and mostly diseased due to ethanol with a low local and systemic immunity predisposing them to infections.

**TABLE 13 : BIO CHEMICAL DATA IN SBP AND NON SBP GROUP**

| Variable | SBP | NON SBP | P Value |
|---|---|---|---|
| **Serum Bilirubin | 6.81+6.12 | 3.12+2.89 | <0.001* |
| **Serum Protein | 6.34+0.98 | 6.65+0.81 | 0.10 |
| **Serum Creatinine | 0.88+0.21 | 0.81+0.17 | 0.09 |
| **A.Albumin | 0.63+0.34 | 0.94+0.30 | <0.001* |
| ++Plt ct | 165000(32000-251000) | 160000(72000-298000) | 0.39 |
| ++SGOT | 58(19-199) | 40(12-199) | 0.027* |
| ++SGPT | 34(12-110) | 32(12-138) | 0.87 |
| **Hb | 8.74+1.92 | 10.07+2.26 | 0.0063* |
| ++A.TLC | 620(400-48000) | 170(100-300) | <0.001* |
| **S.Albumin | 3.12+0.78 | 3.12+0.56 | 0.98 |
| **INR | 1.67+0.52 | 1.36+0.38 | 0.0013* |
| ++MELD | 19(9-27) | 13(6-31) | <0.001* |
| ++A PMN | 420(252-33120) | 82(15-189) | <0.001* |
| A.PROTEIN | 1.15+0.34 | 2.27+0.64 | <0.001 |

**Mean+ SD has been calculated for the variables.

++Median (range) has been calculated for the variables.

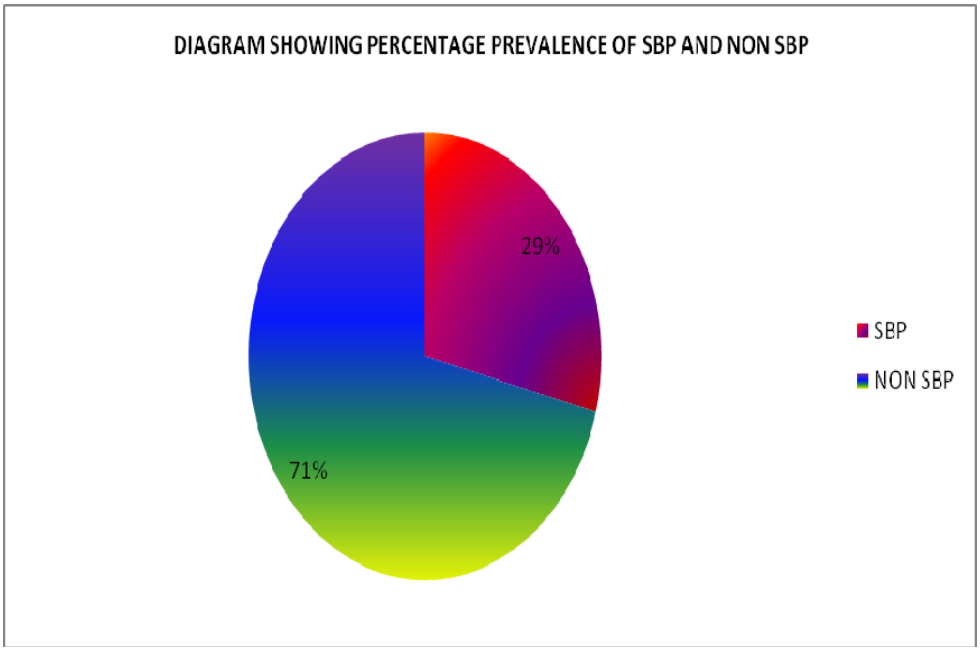
T test and Mann Whitney U test have been used to compare the variables between 2 groups accordingly and * $p< 0.05$ is considered statistically significant.

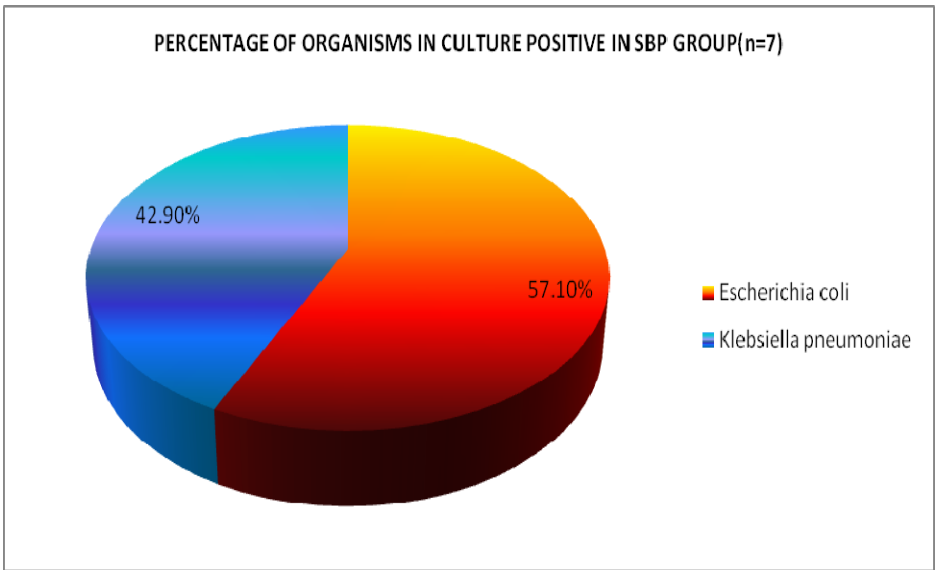
**PREVALENCE OF SBP AND MICROBIAL CULTURE:**

The reports revealed the following. 29 patients were found to have SBP, among which 7 were classic SBP and the remaining 22 were culture negative (i.e. CNNA) and 71 were Non – SBP patients. There was no case of bacterascites. The results of the bacterial culture in the 7 patients revealed Escherichia coli in 4 patients and Klebsiella pneumonia in 3 patients.

**TABLE 14: PREVALENCE OF SBP:**

| TOTAL | CLASSIC SBP (culture positive, PMN≥250) | CNNA (culture negative, PMN≥250) | NON –SBP (culture negative, PMN≥250) |
|---|---|---|---|
| 100 | 7 | 22 | 71 |






**OUTCOME :**

The outcome of the patients with SBP and Non – SBP patients were analyzed. They were followed up for a period of 3 weeks. 5 patients in the SBP group, 4 patients with Classic SBP and 1 patient with CNNA died due to various reasons. In the Non – SBP group 3 patients died .The remaining patients in both the groups improved with appropriate antibiotic and other standard of care treatment. The patients with SBP as compared to Non – SBP patients have a higher mortality and the patients with Classic SBP (culture positive) have more mortality than CNNA (culture negative) patients (80% vs. 20%).

**TABLE 15 : MORTALITY in SBP and NON SBP group**

| GROUP | MORTALITY | | | | Total | | P-Value |
|---|---|---|---|---|---|---|---|
| | YES | | NO | | | | |
| | N | % | N | % | N | % | |
| SBP | 5 | 62.5 | 24 | 26.1 | 29 | 29 | 0.043* |
| NON SBP | 3 | 37.5 | 68 | 73.9 | 71 | 71 | |
| Total | 8 | 100 | 92 | 100 | 100 | 100 | |

(Odds Ratio - 4.72 ; 95% C.I-1.05 - 21.27) The odds of mortality are 4.72 times greater among SBP group compared to non SBP group and it is found to be statistically significant. ($p<0.05$)

* $p< 0.05$ is considered statistically significant

**TABLE 16: PERCENTAGE OF MORTALITY IN CLASSIC SBP AND CNNA PATIENTS**

| CLASSIC SBP(culture positive) | CNNA (culture negative) | TOTAL |
|---|---|---|
| 4(80%) | 1(20%) | 5(100%) |

# DISCUSSION

The prevalence of SBP in patients admitted with cirrhosis, ascites and with symptoms & signs suspicious of SBP is found to be 29% in our study. It is almost similar to the study done by Amarapurkar DN et al[81] from India with a prevalence of 22%. Similar study by Andreu et al[43] reported a prevalence of SBP of 28%. Various studies have reported a prevalence of 10-30%,which is well comparable with this study. The diagnosis of SBP in this study was based on the criteria proposed by Hoefs and Runyon[9]: patients with clinical signs & symptoms of peritonitis, a positive ascitic fluid culture and ascitic fluid PMN count > 250 cells/cumm. The prevalence of SBP in this study is found to be similar to other studies.

The mean age of diagnosis of SBP in many of the Indian studies have been reported to be ranging from 39-44 yrs[82]. In this study the mean age was around 44 yrs which is comparable with other studies.

The predominant etiology in patients with SBP in this study was found to be due to ethanol related cirrhosis (79.3% in SBP and 50.7% in Non – SBP group), as during this period of study the majority of patients were due to ethanol related cirrhosis and the majority were males who frequently consume significant amounts of alcohol and present more frequently with advanced liver disease. This was in concordance with other studies. Lata et al[83] in their study have reported that the prevalence of SBP is higher in the patients with cirrhosis caused by alcohol consumption rather than by viral hepatitis .

This study showed similarity in the clinical presentations of the patients with SBP with other studies. Ascites was seen in all patients, Abdominal pain in 82%, Hepatic encephalopathy in 79 %, Fever in 58.6%, Jaundice and UGI bleed in 55%, and Pedal edema in 31%. Mihas et al[84] reported fever in 54%,abdominal pain in 57% and Hepatic encephalopathy in 67%.In the study by Amarapurkar DN et al[81], abdominal pain was the predominant symptom followed by fever and encephalopathy. The predominance of jaundice in this study may be due to the more number of patients in advanced stage of the disease. SBP may also have a non- specific clinical picture and is usually manifested by deepening of symptoms that accompany the liver cirrhosis and does not always have the classical signs and symptoms of SBP. Occurrence of SBP in asymptomatic patients also have been described in various clinical studies.

Jain et al[85] in their study reported a prevalence of SBP in 34.92%, out of 63 patients and all patients were in Child Pugh class C . Puri AS et al [86] also have reported a prevalence of SBP and its variants in 30% (21 out of 70) of the patients and 77% of the patients were in class C. In this study of 100 patients, 29(29%) were found have SBP, 7(24.2%) were found to be culture positive and 22(75.8%) patients were found to be culture negative (CNNA) and 62.1% of the patients with SBP were in Child class C ,which is consistent with other studies. The study by Amarapurkar DN et al[81] also revealed that the majority of the patients with SBP and its variants belonged to Child class C. The severity of the liver disease is the most important predisposing factor for the development of SBP.

One important finding from this study was a statistically significant association of a higher MELD score with SBP. The risk of SBP increases in patients with moderate to high MELD scores. This may indicate that MELD score can be used as a tool in predicting the development of SBP and its association with mortality. This study showed that a MELD score of 19 (median 15 -21) was associated with an increased risk of SBP. Similar result was seen in a study by Gayatri et al[87] which revealed an increased risk of SBP with a MELD score of ≥18. Obstein et al[35] showed that the mean MELD score of patients with SBP was 24.A high MELD score may be seen in patients with advanced liver disease which is associated with an impaired immunological clearance and also an increase in the intestinal permeability and bacterial translocation and hence increased risk of ascitic fluid infections.

The biochemical analysis of serum and ascitic fluid between the two groups of patients revealed that patients with SBP were found have a statistically significant association with a high ascitic fluid total leucocyte count with a mean of 620 cells. A low ascitic fluid albumin level was seen with a mean of 0.63 ± 0.34 gm/dl compared to 0.94 ± 0.30 in Non – SBP group, a low ascitic fluid protein level was seen with a mean of 1.15 ± 0.34 compared to 2.27 ± 0.64 in Non –SBP group and a high ascitic fluid PMN with a mean of 420 cells. Majority of the patients in the SBP group with culture positivity had ascitic fluid protein levels < 1 g/dl. In the Runyon BA series[88] those patients with a ascitic fluid protein <1 g/dl were found to be more predisposed to SBP. In the study by Amarapurkar DN et al[81] the mean ascitic fluid protein was 0.78±0.24 gm/dl in patients with SBP. In this study the mean ascitic fluid protein is 1.1±0.34 which is almost similar to other studies.

The patients with SBP were found to have statistical significant association with a high levels of sr bilirubin, a high SGOT levels and a low Hb levels. This might may be due to its relation with the advanced stage of the liver disease. Guarner C et al[44] in their study have found that cirrhotic patients with low ascitic fluid protein, with high bilirubin levels and/or low platelet count are at higher risk of acquiring first episode of community – acquired SBP. In this study there was no significant difference in the platelet count between the two groups. There was also no difference between the two groups in sr protein, sr creatinine, SGPT, sr albumin levels as the patients in both the group were equally deficient in their liver functioning.

The INR was found to be significantly higher in the SBP patients as compared to the Non-SBP (1.67 ± 0.52 vs.1.36 ± 0.38, $P<0.05$) indicating advanced stage of the liver disease.

In this study the most frequent organism isolated was E coli (4 cases, 57.10%) followed by Klebsiella (3cases, 42.90%). The results were similar to other studies by Runyon et al and Wilcox et al[23] which showed that 27.3% and 45% of cases of SBP were due to E coli respectively. This study result was also comparable to a similar study conducted in a tertiary care hospital at Karnataka which showed E coli in 62.5% and Klebsiella in 25% of cases[89].

The mortality in this study was seen in 62.5% of SBP (4 cases in classic SBP - 80% and 1 case in CNNA – 20%) and 37.5% of Non- SBP patients. SBP patients are found to be significantly associated with mortality (P-0.043). Runyon and Hoefs[11] in their study reported a mortality of 70% and 50% respectively in culture positive and negative patients. An another study by

Pelletier et al[90] also revealed a higher mortality with culture positive SBP patients as compared to patients with CNNA. Lower mortality rate with CNNA may indicate that it is a less severe variant of SBP and patients might have a better liver function as compared to patients with Classic SBP. The patients were started on empirical antibiotic treatment of Inj Cefotaxim 2 g IV tds, with also other standard treatment of care to prevent HRS and worsening of the disease. These patients were kept under close monitoring and follow up. The SBP patients were followed up until their discharge until 3 weeks. Out of the 5 patients who died, 2 patients developed HRS inspite of antibiotic treatment and albumin infusion, out of which one patient died on the 5th day and one patient died on the 7th day not responding to treatment. One patient had a massive bout of UGI bleed on the third day and succumbed to death. Two patients died due to hepatic encephalopathy.

The mortality in SBP patients in spite of antibiotic treatment might be probably due to their poor response to antibiotics, development of HRS and progression the underlying liver disease.

The mortality in 2 of the Non- SBP patients were related to UGI bleed and 1patient died due to hepatic encephalopathy .The poor survival in SBP patients can be well explained by their advanced nature of liver disease, immunological impairment, development of drug resistance, poor response to drug therapy and renal impairment.

# CONCLUSION

1) SBP is seen in 29% of patients with cirrhosis and ascites

2) Classic SBP is seen in one – third and CNNA in two – thirds of the patients with SBP.

3) E coli is the commonest organism grown. Next is Klebsiella.

4) SBP is common in alcoholic cirrhotics.

5) Low ascitic fluid protein levels, high sr bilirubin, high INR, high MELD score and Child class C are risk factors for SBP.

6) Abdominal pain, Fever are common in patients with SBP.

7) SBP can be fatal in patients with cirrhosis and ascites.

8) The mortality in patients with culture positive SBP (Classic SBP) is more frequent than with culture negative SBP (CNNA).

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# PROFORMA

Name: Age: Sex: Address: MGE No:

Clinical history:

Abdominal pain Fever

Abdominal tenderness Jaundice

Recent increase in abdominal distension UGI bleed

Past history:

Diabetes mellitus Hyperlipidemia

Hypertension Renal problems

Previous episodes of SBP

Drug history:

Personal history:

General examination:

Pallor, icterus, pedal edema, cyanosis, clubbing,

lymphadenopathy,

signs of liver cell failure.

Vitals: PR: HR: Temp: BP:

JVP:

System examination:

ABD: CVS: RS: CNS:

Investigations:

CBC : Platelet Ct : RFT :

LFT : PT : INR :

HBsAg : Anti HCV : HIV :

Blood Sugar:

Ascitic fluid analysis :

Total count Differential Ct Total proteins

Albumin Globulin Sugar

Cytology Culture &Sensitivity

USG Abd:

Chest X- ray:

Plain X- ray Abdomen:

UGI Endoscopy :

ECG:

CTP score : MELD score:

| NAME | age | MGE NO | S bilirubin | Salbumin | Sprotein | Screatinine | SGOT | SGPT | INR | CTP class | MELD | Plt ct | A albumin | A protein |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| lakshmi | 45/F | 4214 | 0.6 | 3.3 | 6 | 0.5 | 31 | 20 | 0.91 | B | 6 | 115,000 | 0.4 | 1.4 |
| poondian | 39 /M | 1348 | 0.9 | 3.5 | 6.8 | 0.8 | 12 | 15 | 1.15 | B | 8 | 122,000 | 1 | 1.6 |
| kathiresan | 42/M | 4323 | 3.5 | 2.9 | 6.3 | 0.6 | 57 | 50 | 1.33 | C | 14 | 200,000 | 0.8 | 1.2 |
| murugan | 33/M | 999 | 3.7 | 4.8 | 7.6 | 0.9 | 35 | 22 | 1.18 | B | 13 | 210,000 | 0.9 | 1.3 |
| venkatesh | 31/M | 1283 | 1 | 3.6 | 6.6 | 0.6 | 45 | 32 | 1.28 | B | 9 | 168,000 | 0.7 | 1 |
| varadhan | 40/M | 3842 | 0.7 | 3.7 | 7 | 0.9 | 34 | 28 | 1.09 | B | 7 | 130,000 | 0.4 | 1.1 |
| parameswaran | 35/M | 1994 | 4.5 | 3 | 7.3 | 0.8 | 169 | 129 | 1.2 | C | 14 | 72,000 | 0.6 | 1.3 |
| edward | 41/M | 6845 | 1.6 | 3.2 | 7 | 1 | 72 | 68 | 1.24 | B | 11 | 232,000 | 0.4 | 1.6 |
| gnanaprakasam | 39/M | 2309 | 1.5 | 2.9 | 6.4 | 0.9 | 118 | 28 | 1.1 | C | 9 | 193,000 | 0.7 | 1.7 |
| kanagammal | 45/F | 1562 | 2 | 2.5 | 6 | 0.5 | 26 | 22 | 1.63 | C | 15 | 220,000 | 0.8 | 1.9 |
| barathi | 39/F | 2321 | 9.2 | 3.1 | 6.4 | 1.2 | 54 | 26 | 1.8 | C | 23 | 120,000 | 1.2 | 1.9 |
| sekar | 49/M | 7511 | 1.3 | 2.9 | 5.8 | 0.8 | 40 | 32 | 1.26 | B | 10 | 246,000 | 1.8 | 2.4 |
| nehru | 50/M | 7826 | 10.5 | 2.4 | 6.8 | 0.9 | 67 | 60 | 1.01 | C | 15 | 85,000 | 1.3 | 2 |
| govindaraj | 36/M | 7142 | 8.8 | 3.7 | 8.8 | 0.6 | 67 | 79 | 1.21 | B | 17 | 128,000 | 2 | 3.5 |
| karunagaran | 38/M | 1468 | 1 | 2.7 | 6.8 | 0.6 | 30 | 20 | 1.18 | B | 8 | 228,000 | 1.2 | 2.2 |
| chinnasamy | 43/M | 916 | 3.9 | 2.7 | 6.9 | 0.6 | 20 | 24 | 1.21 | C | 14 | 171,000 | 0.7 | 1.8 |
| dasaradhann | 37/M | 7463 | 7.8 | 2.8 | 6 | 0.7 | 70 | 65 | 1.12 | C | 15 | 212,000 | 0.9 | 2.2 |
| kadar | 38/M | 8120 | 4.5 | 3 | 5.8 | 0.9 | 26 | 34 | 1.14 | B | 14 | 150,000 | 1.5 | 3 |
| kasthuri | 44/F | 6526 | 3 | 2.9 | 6.5 | 0.8 | 91 | 79 | 1.2 | B | 13 | 138,000 | 1.2 | 1.9 |
| deivanai | 39/F | 4544 | 2.2 | 3 | 6 | 1 | 150 | 96 | 1.5 | B | 14 | 112,000 | 0.8 | 2.5 |
| parimala | 32/F | 1150 | 4.3 | 2.5 | 5.8 | 0.5 | 130 | 59 | 1.4 | C | 16 | 96,000 | 1.1 | 2.4 |
| kavitha | 49/F | 3554 | 5.2 | 2.5 | 6 | 0.6 | 27 | 21 | 1.06 | C | 13 | 160,000 | 1.2 | 1.8 |
| kumaravel | 37/M | 2654 | 7.5 | 3 | 6.2 | 0.9 | 31 | 14 | 1.01 | B | 14 | 210,000 | 0.8 | 1.9 |
| natchimuthu | 49/M | 4111 | 2 | 2.8 | 6 | 1.1 | 44 | 65 | 1.46 | B | 14 | 290,000 | 0.9 | 2 |
| dasaradhann | 51/M | 3467 | 3.4 | 2.4 | 5.9 | 0.8 | 26 | 40 | 1.26 | C | 14 | 185,000 | 1 | 1.9 |
| indirani | 47/M | 1213 | 2.5 | 2.5 | 5.5 | 0.9 | 16 | 14 | 1.09 | B | 11 | 242,000 | 1.3 | 2.5 |
| maniammal | 37/F | 2661 | 10.8 | 2.5 | 5 | 1.2 | 38 | 34 | 1.43 | C | 21 | 98,000 | 1.1 | 1.9 |
| loganayagi | 40/F | 4943 | 8.5 | 2.9 | 6 | 0.8 | 53 | 69 | 1.53 | C | 19 | 210,000 | 1.2 | 2 |
| amaravathy | 50/F | 3095 | 6 | 3.1 | 6.2 | 0.9 | 40 | 64 | 1.72 | C | 19 | 125,000 | 0.8 | 1.8 |
| meerjama hussain | 51/M | 851 | 1.3 | 2.4 | 6 | 1.1 | 40 | 18 | 1.26 | B | 14 | 110,000 | 1.2 | 3 |
| ambiga | 35/F | 6474 | 1.5 | 2.8 | 6.2 | 0.8 | 91 | 79 | 1.72 | B | 14 | 112,000 | 0.6 | 1.5 |
| mahalaxmi | 39/F | 1177 | 3.6 | 2.7 | 5.8 | 0.9 | 42 | 18 | 1.12 | C | 13 | 213,000 | 0.9 | 2.4 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| hemavathy | 43/F | 3283 | 2.6 | 3.4 | 7.8 | 0.6 | 48 | 62 | 1.47 | C | 14 | 190,000 | 1 | 3.2 |
| sivakumar | 45/M | 688 | 7.7 | 2.9 | 6.5 | 0.8 | 40 | 28 | 0.98 | B | 14 | 200,000 | 1.1 | 1.9 |
| sundar | 47/M | 730 | 2 | 2.5 | 5 | 0.9 | 24 | 19 | 1.15 | B | 11 | 168,000 | 0.9 | 2.6 |
| mohan | 42/M | 605 | 5.5 | 3 | 6 | 0.7 | 28 | 38 | 1.9 | C | 20 | 150,000 | 0.8 | 1.8 |
| sridar | 38/M | 591 | 3.5 | 2.9 | 5.8 | 0.9 | 47 | 57 | 1.7 | C | 17 | 100,000 | 0.9 | 1.5 |
| kabaleeswaran | 37/M | 557 | 1.3 | 2.5 | 5.5 | 0.8 | 32 | 38 | 1.26 | B | 10 | 96,000 | 0.6 | 1.8 |
| nagaraj | 46/M | 517 | 3.8 | 2.7 | 6.5 | 1 | 14 | 20 | 1.14 | C | 13 | 152,000 | 0.7 | 2.5 |
| raja | 36/M | 515 | 2.5 | 3.2 | 7 | 0.9 | 20 | 30 | 1.19 | B | 12 | 182,000 | 0.9 | 2.8 |
| chandran | 45/M | 560 | 3.5 | 2.6 | 6.2 | 1.1 | 92 | 49 | 1.81 | C | 19 | 175,000 | 1 | 3.2 |
| suseela | 47/F | 12245 | 1.1 | 2.3 | 6.4 | 0.6 | 53 | 17 | 1.72 | B | 13 | 211,000 | 0.8 | 2.5 |
| mohana | 49/F | 1654 | 0.7 | 3.6 | 6 | 0.8 | 27 | 14 | 1.2 | B | 8 | 180,000 | 0.6 | 2.8 |
| radha | 45/F | 165 | 1.5 | 3.4 | 7.9 | 0.6 | 40 | 21 | 1.48 | B | 12 | 240,000 | 0.9 | 1.8 |
| santhanam | 53/M | 2935 | 3.5 | 3.1 | 6.8 | 0.9 | 23 | 21 | 1.23 | C | 13 | 120,000 | 0.7 | 2.2 |
| karunakaran | 51/M | 2632 | 1 | 3.7 | 6.5 | 1.1 | 38 | 34 | 1.36 | A | 11 | 210,000 | 0.8 | 3.2 |
| parveen | 46/F | 267 | 0.6 | 3.2 | 7 | 0.8 | 16 | 19 | 1.2 | B | 8 | 250,000 | 1 | 3 |
| chandrasekar | 44/M | 3271 | 1.8 | 3.3 | 7.5 | 0.9 | 12 | 15 | 1.9 | B | 16 | 180,000 | 0.9 | 1.9 |
| paneerselvam | 38/M | 3579 | 1.2 | 2.5 | 6.4 | 0.8 | 54 | 30 | 1.7 | B | 13 | 160,000 | 0.8 | 2.5 |
| padma | 55/F | 1547 | 0.8 | 3.3 | 6.8 | 0.6 | 60 | 37 | 1.06 | B | 7 | 110,000 | 0.5 | 2.8 |
| purushothaman | 45/M | 2104 | 2.9 | 3.4 | 7.7 | 0.6 | 32 | 44 | 1.2 | B | 12 | 175,000 | 0.9 | 1.9 |
| stella | 33/F | 2094 | 1.5 | 4.9 | 7.5 | 0.6 | 17 | 14 | 1.39 | A | 12 | 128,000 | 1.2 | 2.4 |
| neelakandan | 49/M | 1990 | 14.9 | 2.5 | 7.6 | 0.8 | 23 | 18 | 3.67 | C | 31 | 115,000 | 1.3 | 2.8 |
| krishnamoorthy | 43/M | 2135 | 1.3 | 3 | 8.1 | 0.8 | 64 | 42 | 1.47 | B | 12 | 100,000 | 0.6 | 2 |
| rajalingam | 48/M | 7079 | 1.2 | 3.4 | 5.3 | 0.7 | 24 | 34 | 1.2 | B | 9 | 128,000 | 1.2 | 3.6 |
| dass | 46/M | 432 | 1 | 2.9 | 7.2 | 0.8 | 14 | 12 | 1.39 | B | 10 | 250,000 | 1.6 | 2.8 |
| ilangovan | 39/M | 920 | 3.8 | 3 | 7 | 0.9 | 19 | 24 | 1.9 | C | 19 | 275,000 | 0.8 | 2 |
| vijayakumar | 53/M | 6286 | 1.9 | 4.2 | 7.1 | 0.8 | 35 | 46 | 2.01 | B | 17 | 100,000 | 1.2 | 3.6 |
| simson | 54/M | 34479 | 1.7 | 3.5 | 7 | 0.9 | 70 | 109 | 1.27 | B | 11 | 190,000 | 1.1 | 3 |
| kumar | 45/M | 7997 | 3.3 | 3.9 | 7.2 | 0.6 | 199 | 104 | 1.06 | B | 12 | 145,000 | 0.7 | 1.5 |
| ayyanar | 43/M | 6556 | 1.6 | 3 | 6.8 | 0.9 | 20 | 28 | 1.16 | B | 10 | 298,000 | 1.2 | 2.8 |
| mariappan | 42/M | 6549 | 0.9 | 3.5 | 7.5 | 0.8 | 30 | 25 | 1.27 | B | 9 | 192,000 | 0.8 | 2 |
| ramanathan | 45/M | 4038 | 0.7 | 2.9 | 6.4 | 1.2 | 106 | 79 | 1.2 | B | 10 | 80,000 | 0.8 | 1.9 |
| tamilselvan | 37/M | 4167 | 0.5 | 3 | 7.8 | 0.9 | 131 | 44 | 1.2 | B | 8 | 115,000 | 0.6 | 2.2 |
| sampath | 49/M | 5498 | 1.5 | 3.3 | 7.4 | 0.9 | 49 | 57 | 1.19 | B | 10 | 96,000 | 0.5 | 2.6 |
| sengalvarayan | 55/M | 6137 | 1.6 | 3.6 | 7.6 | 0.7 | 128 | 138 | 1.39 | A | 12 | 210,000 | 0.9 | 3 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| paneerselvam | 43/M | 2878 | 0.6 | 4.6 | 9 | 1 | 54 | 30 | 1.06 | A | 7 | 160,000 | 0.8 | 1.9 |
| saraswathy | 47/F | 4421 | 0.5 | 4.4 | 6.7 | 0.7 | 20 | 24 | 1.19 | A | 8 | 138,000 | 1.1 | 3 |
| usharani | 35/F | 3271 | 1.6 | 3.2 | 6 | 0.9 | 37 | 40 | 1.38 | B | 12 | 168,000 | 0.8 | 2.9 |
| partheeban | 47/M | 4532 | 1.5 | 3.8 | 6.7 | 0.8 | 42 | 70 | 1.46 | A | 12 | 150,000 | 1.1 | 3.5 |
| sundar | 53/M | 4631 | 4 | 3 | 7.6 | 0.6 | 84 | 32 | 1.26 | B | 14 | 112,000 | 1.2 | 3.2 |

| A TLC | APMN | Hb | etiology | culture | outcome | SYMPTOMS | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 200 | 30 | 5.6 | HBV | negative | improved | abd distn | A | A | no jaundice | A | pedal edema | no he |
| 300 | 90 | 13.8 | ethanol | negative | death | abd distn | A | A | no jaundice | ugi bleed | A | no he |
| 100 | 20 | 9.8 | ETHANOL | negative | improved | abd distn | A | fever | no jaundice | A | A | he 2 |
| 150 | 15 | 10.6 | ETHANOL | negative | improved | abd distn | abd pain | A | jaundice | A | | no he |
| 200 | 40 | 9.9 | ETHANOL | negative | improved | abd distn | A | A | no jaundice | A | pedal edema | he 2 |
| 100 | 22 | 11.2 | HBV | negative | improved | abd distn | Absent | A | no jaundice | A | A | no he |
| 170 | 17 | 10.2 | ETHANOL | negative | improved | abd distn | abd pain | A | jaundice | A | A | no he |
| 110 | 15 | 6.2 | ETHANOL | negative | improved | abd distn | abd pain | A | no jaundice | A | A | he 3 |
| 100 | 25 | 7.3 | ETHANOL | negative | improved | abd distn | A | fever | no jaundice | A | A | no he |
| 100 | 45 | 11.2 | HBV | negative | improved | abd distn | A | A | no jaundice | A | pedal edema | he 2 |
| 100 | 56 | 6.8 | hcv | negative | improved | abd distn | A | A | jaundice | A | pedal edema | no he |
| 300 | 60 | 8.8 | ethanol | negative | improved | abd distn | A | A | no jaundice | ugi bleed | A | no he |
| 200 | 64 | 9 | ethanol | negative | improved | abd distn | abd pain | A | jaundice | A | pedal edema | he 2 |
| 100 | 52 | 8.3 | ethanol | negative | death | abd distn | A | A | jaundice | A | pedal edema | he 3 |
| 200 | 80 | 14.6 | hcv | negative | improved | abd distn | A | A | no jaundice | A | pedal edema | he 2 |
| 100 | 48 | 11.6 | hbv | negative | improved | abd distn | abd pain | A | no jaundice | A | pedal edema | no he |
| 100 | 66 | 9.2 | ethanol | negative | improved | abd distn | A | fever | jaundice | A | A | he 2 |
| 200 | 50 | 10 | ethanol | negative | improved | abd distn | abd pain | A | jaundice | A | pedal edema | no he |
| 150 | 45 | 10.2 | nafld | negative | improved | abd distn | A | A | no jaundice | ugi bleed | A | no he |
| 270 | 189 | 9.8 | hbv | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 200 | 88 | 7.6 | idiopathic | negative | improved | abd distn | abd pain | A | jaundice | A | A | no he |
| 300 | 171 | 6.4 | nafld | negative | improved | abd distn | A | A | jaundice | A | A | no he |
| 170 | 68 | 9.8 | ethanol | negative | improved | abd distn | A | A | jaundice | ugi bleed | A | no he |
| 200 | 162 | 11.2 | ethanol | negative | improved | abd distn | abd pain | A | no jaundice | A | A | he 2 |
| 300 | 132 | 12.8 | ETHANOL | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 200 | 108 | 11.5 | nafld | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 200 | 180 | 9.44 | hbv | negative | improved | abd distn | A | A | jaundice | ugi bleed | A | he 2 |
| 100 | 59 | 12.6 | HBV | negative | improved | abd distn | A | A | jaundice | A | A | no he |
| 300 | 159 | 6.8 | nafld | negative | improved | abd distn | abd pain | A | jaundice | A | A | no he |
| 100 | 78 | 7.8 | NAFLD | negative | improved | abd distn | A | fever | no jaundice | A | A | no he |
| 100 | 84 | 8.5 | hbv | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 200 | 138 | 11.4 | HBV | negative | improved | abd distn | abd pain | A | no jaundice | A | A | no he |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 200 | 144 | 7.1 | ethanol | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 300 | 162 | 13 | ETHANOL | negative | improved | abd distn | A | fever | jaundice | A | A | no he |
| 100 | 75 | 12.6 | ETHANOL | negative | improved | abd distn | abd pain | A | no jaundice | A | A | no he |
| 200 | 96 | 11 | ETHANOL | negative | improved | abd distn | A | A | jaundice | ugi bleed | A | he 2 |
| 300 | 171 | 11 | HBV | negative | improved | abd distn | A | A | no jaundice | A | pedal edema | he2 |
| 200 | 134 | 6.3 | ETHANOL | negative | improved | abd distn | abd pain | A | no jaundice | A | A | no he |
| 100 | 88 | 6.4 | ETHANOL | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 100 | 92 | 7.6 | ETHANOL | negative | improved | abd distn | abd pain | A | no jaundice | A | A | no he |
| 200 | 116 | 13 | HBV | negative | improved | abd distn | A | A | no jaundice | A | pedal edema | he 2 |
| 100 | 63 | 11 | hbv | negative | improved | abd distn | A | fever | no jaundice | A | A | no he |
| 100 | 48 | 6.6 | HBV | negative | improved | abd distn | abd pain | A | no jaundice | A | A | no he |
| 100 | 58 | 12.2 | idiopathic | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 100 | 81 | 10.8 | HBV | negative | improved | abd distn | A | A | no jaundice | ugi bleed | pedal edema | no he |
| 200 | 126 | 7.6 | ETHANOL | negative | death | abd distn | A | A | no jaundice | A | pedal edema | no he |
| 100 | 94 | 13 | idiopathic | negative | improved | abd distn | abd pain | A | no jaundice | A | A | no he |
| 100 | 82 | 7.5 | ETHANOL | negative | improved | abd distn | A | A | no jaundice | ugi bleed | pedal edema | no he |
| 100 | 73 | 10.8 | ETHANOL | negative | improved | abd distn | A | fever | no jaundice | A | A | no he |
| 100 | 69 | 8 | nafld | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 200 | 142 | 7.5 | ethanol | negative | improved | abd distn | abd pain | A | no jaundice | A | pedal edema | no he |
| 200 | 112 | 9.8 | HBV | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 200 | 98 | 13 | ETHANOL | negative | improved | abd distn | A | A | jaundice | A | pedal edema | he 3 |
| 100 | 64 | 12.6 | ETHANOL | negative | improved | abd distn | A | fever | no jaundice | A | A | no he |
| 100 | 58 | 10.6 | ETHANOL | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 200 | 136 | 11.7 | ETHANOL | negative | improved | abd distn | A | A | no jaundice | ugi bleed | A | no he |
| 200 | 110 | 11 | ETHANOL | negative | improved | abd distn | A | A | no jaundice | A | A | he 3 |
| 200 | 114 | 10 | HBV | negative | improved | abd distn | A | A | no jaundice | A | pedal edema | no he |
| 200 | 96 | 7.4 | ETHANOL | negative | improved | abd distn | A | A | no jaundice | ugi bleed | A | no he |
| 200 | 124 | 10 | ETHANOL | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 100 | 65 | 13 | HBV | negative | improved | abd distn | abd pain | A | no jaundice | A | A | no he |
| 200 | 102 | 11.8 | ETHANOL | negative | improved | abd distn | A | fever | no jaundice | A | A | no he |
| 100 | 78 | 14 | HCV | negative | improved | abd distn | A | A | no jaundice | A | pedal edema | he 3 |
| 200 | 94 | 7 | ETHANOL | negative | improved | abd distn | A | A | no jaundice | ugi bleed | A | he 2 |
| 100 | 85 | 11 | HBV | negative | improved | abd distn | A | A | no jaundice | A | pedal edema | no he |
| 100 | 56 | 13 | NAFLD | negative | improved | abd distn | abd pain | A | no jaundice | A | A | no he |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 200 | 184 | 10.8 | hcv | negative | improved | abd distn | A | A | no jaundice | A | A | no he |
| 100 | 38 | 10.9 | hbv | negative | improved | abd distn | A | A | no jaundice | A | pedal edema | no he |
| 100 | 44 | 10.6 | IDIOPATHIC | negative | improved | abd distn | abd pain | A | no jaundice | A | A | no he |
| 100 | 86 | 13 | HBV | negative | improved | abd distn | A | fever | no jaundice | A | A | no he |
| 200 | 106 | 11.4 | ethanol | negative | improved | abd distn | A | A | jaundice | A | pedal edema | no he |