A Dissertation on

"A CLINICAL STUDY OF RISK FACTORS AND CLINICAL FEATURES IN PATIENTS OF SBP WITH CIRRHOSIS AND ASCITES IN A TERTIARY CARE HOSPITAL SALEM''

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for the award of the degree of

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GOVERNMENT MOHAN KUMARAMANGALAM

MEDICAL COLLEGE HOSPITAL,

SALEM TAMIL NADU, INDIA.

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled **"A CLINICAL STUDY OF RISK FACTORS AND CLINICAL FEATURES IN PATIENTS OF SBP WITH CIRRHOSIS AND ASCITES IN GOVERNMENT MOHAN KUMARAMANGALAM MEDICAL COLLEGE HOSPITAL, SALEM."** is a bonafide and genuine research work carried out by me under the guidance **Dr. M.MANJULA, M.D.,** Professor of the Department, Department of general medicine, Government Mohan Kumaramangalam Medical College Hospital, Salem, Tamil Nadu, India.

Date :

Place : Salem

Signature of the Candidate

DR.VEERAMANI C

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Signature of the Guide,
Prof DR.M.MANULA M.D
Department of General Medicine
Govt. Mohana Kumaramangalam Medical college,salem

CERTIFICATE FROM THE HOD

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Signature of the HOD,
Dr.S.SURESH KANNA M.D
Professor and HOD,
Department of General Medicine
Govt. Mohan Kumaramangalam Medical college, Salem.

CERTIFICATE FROM THE DEAN

This is to certify that the dissertation entitled **"A CLINICAL STUDY OF RISK FACTORS AND CLINICAL FEATURES IN PATIENTS OF SBP WITH CIRRHOSIS AND ASCITES IN GOVERNMENT MOHAN KUMARAMANGALAM MEDICAL COLLEGE HOSPITAL, SALEM."** is the bonafide work done by **Dr.VEERAMANI.C** in partial fulfillment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for **M.D General Medicine Branch I** examination to be held in **April 2020.**

Signature of the Dean,
DR.K.THIRUMAL BABU M.D DM
THE DEAN,
Govt. Mohan Kumaramangalam
Medical College, Salem.

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SALEM, TAMILNADU
College: Phone No.0427-2383313 Fax No:0427-2383193
E-Mail ID: deangmkmcslm@gmail.com
Hospital: Phone No: 0427 - 2210674, 2210757 Fax : 0427 - 2210876
E-Mail ID: msgmkmchsalem@gmail.com

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Guide/Principal Investigator	DR.S.R.SUBRAMANIAN, MD., Professor and HOD of General Medicine, GMKMC, Salem-30.
Student	Dr.C. VEERAMANI, 1st Year, Post Graduate Student of MD (General Medicine), GMKMC, Salem
Name & Address of Institution	Govt. Mohan Kumaramangalam Medical College & Hospital, Salem, Tamil Nadu.
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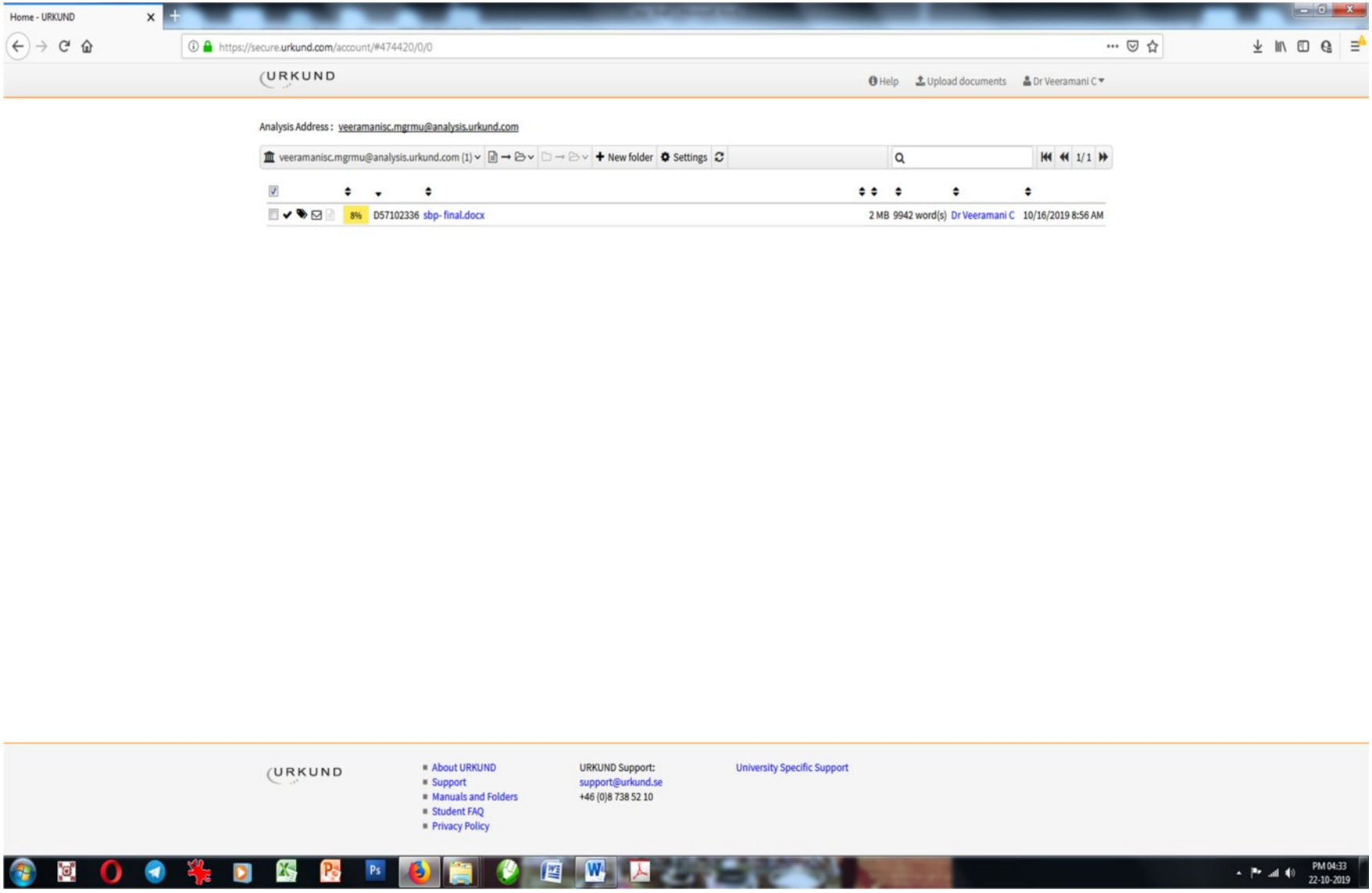
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ABBREVIATION

1. SBP – Spontaneous Bacterial Peritonitis
2. CNNA - Culture Negative Neutrocytic Ascites
3. INR – International Normalised Ratio
4. TIPS – Transjugular Intrahepatic Portal Systemic shunt
5. UKELD – United Kingdom Model End stage Liver Disease
6. MELD – Modified End stage Liver Disease
7. PT – Prothrombin Time
8. US FDA – United States Food and Drug Administration
9. RAAS – Renin Angiotensin Aldosterone System
10. ADH – Anti Diuretic Hormone
11. SAAG – Serum Ascites Albumin Gradient
12. PMN – Poly morphonuclear cells
13. EDTA – Ethylene Diamine Tetra Acetic acid
14. NSAID – Non-Steroidal Anti Inflammatory Drug
15. LVP – Le Veen Peritoneal shunt
16. HE – Hepatic Encephalopathy
17. VATS – Video Assisted Thoracoscopy
18. TNF – Tumour Necrosis Factor
19. IL – Interleukin
20. MNB – Monomicrobial Non-neutrocytic Bacterascites
21. CT – Computed Tomography
22. MRI - Magnetic Resonance Imaging

23. UGI – Upper Gastro Intestinal

24. HRS – Hepatorenal Syndrome

25. SIBO – Small Intestine Bacterial Overgrowth

26. AASLD – American Association for the Study of Liver Disease

27. MRSA – Methicillin Resistant Staphylococcal Aureus

28. USG – Ultrasonogram

ABSTRACT

BACKGROUND

Cirrhosis of Liver is the common hepatological disorder seen in clinical practice. Ascites is the Consequence of portal hypertension which is characteristic clinical feature of cirrhosis. One of the predisposing factors which is responsible for subsequent deterioration in the condition of cirrhosis patient is appearance of spontaneous bacterial peritonitis.

INTRODUCTION:

Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation of liver due to various causes. Ascites is the Consequence of portal hypertension which is characteristic clinical feature of cirrhosis. The development of ascites is a marker of prognosis in liver cirrhosis, as it indicates a reduction in 1- and 5-year survival rates by15% and 23.5%, respectively[9].

The symptoms and signs of SBP are fever, abdominal pain, abdominal tenderness, rebound tenderness, altered mental status. Although 87% of patients with SBP are symptomatic[2], at the time the infection is diagnosed the symptoms and signs of infection are often subtle such as slight change in mental status.

AIMS & OBJECTIVES OF STUDY:

1. To determine the Prevalence of spontaneous bacterial peritonitis & variants in patients of cirrhosis of liver with ascites.
2. To study clinical profile of spontaneous bacterial peritonitis & its variants.

MATERIALS AND METHODS:

Source of Data: This Study was conducted on patients admitted to Government Mohankumaramangalam medical college, Salem.

Study Subjects: Total of 100 patients who were confirmed of hepatic cirrhosis with ascites by history and clinical examination were screened for SBP and were studied thoroughly with regards to cytological, microbiological and biomedical tests.

RESULTS:

Total of 100 patients who were confirmed of hepatic cirrhosis with ascites by ultra sound were screened for SBP and were studied thoroughly with regards to history, clinical examination, cytological, microbiological and biomedical tests. In present study the prevalence of Spontaneous Bacterial Peritonitis is found to be 16%. Among this 16%, 3 patients (18.75%) were Culture Negative Neutrocytic Ascites (CNNA), 12(75%) were spontaneous bacterial peritonitis(SBP) and 1(6.25%) patients was Mono Bacterial Non Neutrocytic Bacterascitis. (MNB).

CONCLUSION:

Cirrhotic cases with constitutional symptoms must be compulsorily screened for SBP and started on Antibiotic therapy to reduce the mortality. SBP being the problem in cirrhosis with ascites, all cirrhotics should be screened for SBP with at least ascitic fluid analysis, PMN cell count and culture of ascitic fluid.

To maximize survival, it is important that paracentesis is performed in all patients with ascites at the time of hospitalization. So that infection can be detected

and treated promptly. These patients must be treated with antibiotics aggressively as they have poor prognosis and high mortality if not treated early.

KEYWORDS

Cirrhosis of liver, Spontaneous Bacterial Peritonitis(SBP), Culture Negative Neutrocytic Ascites(CNNA), Mono Bacterial Non Neutrocytic Bacter Ascites. (MNB).

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 source of infection like intra – abdominal inflammatory focus eg: abscess, acute pancreatitis, cholecystitis, intestinal perforation, it is called Spontaneous. Correia and Conn coined the term spontaneous bacterial peritonitis in 1975.

Ascitic fluid infection can be classified into 5 categories based on ascitic culture results, PMN count, and presence or absence of a surgical source of infection Of the 3 subtypes of spontaneous ascitic fluid infection, the prototype is SBP. positive ascitic fluid culture and an elevated ascitic fluid absolute PMN count (i.e., at least 250/mm3 [0.25 × 109/L]) without evidence of an intra-abdominal surgically treatable source of infection.

The prevalence of SBP in hospitals is said to be between 10 % to 30%. Prior to the development of antibiotics the inpatient mortality of SBP was as high as 90 %. Patients at risk of developing spontaneous bacterial peritonitis are those with active variceal bleed, ascites protein less than 10g/dl and with a prior history of SBP. When a cirrhotic patient, particularly with encephalopathy and jaundice deteriorates, SBP should be suspected.

Spontaneous bacterial peritonitis is the result of overgrowth of a specific organism in the intestine, translocation of that microbe from the intestine to mesenteric lymph nodes, and resulting spontaneous bacteremia and subsequent colonization of susceptible ascitic fluid. When bacteria enter the fluid in the abdomen, by whatever route, a battle ensues between the virulence factors of the organism and the Immune defenses of the host. Low-protein ascitic fluid (e.g., protein content < 1 g/dL [10 g/L]) is particularly susceptible to SBP. The endogenous antimicrobial (opsonic) activity of human ascitic fluid correlates directly with the protein concentration of the fluid. Patients with deficient ascitic fluid opsonic activity are predisposed to SBP. Patients with detectable ascitic fluid opsonic activity appear to be protected from SBP unless they are exposed to a particularly virulent organism (e.g.,Salmonella)

AIM OF THE STUDY:

Early detection of SBP in patients with cirrhosis to improve the morbidity and mortality of the patients:

OBJECTIVES OF THE STUDY:

1) To determine the prevalence, risk factors, clinical profile, Microbiological and biochemical spectrum and variants of Spontaneous Bacterial Peritonitis**.**
2) To study the natural course of disease

REVIEW OF LITERATURE

The prevalence of SBP in decompensated cirrhosis varies from 10% – 40% especifically in Asia. Among Arab patients, it was documented that about 10.4% of patients with cirrhotic ascites of NFALD origin had culture-positive ascitic fluid infection, whereas in another study about 29.0% had culture-negative neutrocytic ascites (CNNA). Another report from north India population reported that 30% of hospitalized decompensated liver diseased individual patients had SBP or its variants.

In various studies, ascitic fluid analysis has reported a prevalence of SBP is 10 - 27%. Andreu et al reported a prevalence of SBP was 28%, while Amrapurkar DN, Vishwanathan[4], desai et.al, found it to be 22.5%. Romney et.al, in a study involving 67 ascitis patients has not found a single case CNNA and only 10 of MNB. Obstein, KL et.al, in a retrospective study of patients with cirrhosis and ascites reported the prevalence of SBP was 29 (26%) of 111 patients with cirrhosis.

SBP was documented in predominantly elderly age group, with most patients were in 5th and 6th decade. Mean age at the time of diagnosis of SBP was about 50years. Mean age of diagnosis of SBP in Filik L, UnalS et. al was 49.9 years. About 39 years in N Rawat, MK Bhatnagar et.al 15 series. Dilshad Muhammad et.al, 13 cases if SBP from Faisalabad studied in 50 patients of cirrhosis with ascites. Among that 27 (54%) were males and 23 (46%) were females cases.

The main type of spontaneous ascitic fluid infection is the spontaneous bacterial peritonitis. ‘Spontaneous bacterial peritonitis’ term was coined by Conn and

in Correia 1975. The aim of the team was to differentiate bacterial peritonitis from secondary surgical peritonitis.

The prevalence of SBP in decompensated cirrhosis varies from 10% – 40% especially in Asia. Among Arab patients, it was documented that about 10.4% of patients with cirrhotic ascites of NFALD origin had culture-positive ascitic fluid infection, whereas in another study about 29.0% had culture-negative neutrocytic ascites (CNNA). Another report from north India population reported that 30% of hospitalized decompensated liver diseased individual patients had SBP or its variants.

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The mortality of SBP is very high across the world. For that to prevent, diagnosis and to treat this condition, the British Society of Gastroenterology (BSG) has given some suggestions towards the importance of early detection and prompt treatment. It has shown the reduction of hospital stay and mortality from 90% to 20% evident by various studies.

Mr Runyon[12,13] has noticed several deaths due to ascitic fluid infection before the antibiotic era. That time SBP prevalence in hospitals is ranged between 10 % to

30%. The inpatient mortality of SBP was as very high up to 90 % before the advent of antibiotics[6]. Risk factors for development of SBP are upper GI variceal bleed, ascitic fluid protein <10g/L and prior history of SBP.

The asymptomatic SBP prevalence is very less as evident in some literatures, which means patient is having microorganism in the ascitic fluid but they are free of any symptoms like fever abdominal pain and distension.

The Mayo Clinic Division of Gastroenterology and Hepatology conducted a study in 1994 reported that prevalence of asymptomatic SBP was very low. There were several other factor consider for the absence of clinical features of SBP.

In Pakistan, they conducted a study in 2008 at military hospital Rawalpindi, where the prevalence was as low as about 5%.

Cadranel JF et.al, study also showed the low prevalence of asymptomatic SBP. They suggest that exploration of ascitic fluid should be considered without causing much risk to the patient. The mortality of asymptomatic SBP was very low when compared to symptomatic SBP.

CATEGORIZATION OF ASCITC FLUID INFECTION:

Classification of ascitic fluid infections was proposed in 1998. This classification is mainly based on the ascitic fluid culture, the absolute polymorphonuclear cells and also depending on the presence or absence a surgical cause of infection.[55,56]

Classification of Ascitic fluid infection:

1. Spontaneous infection of ascitic fluid.
    - Spontaneous bacterial peritonitis,(SBP)
    - Culture negative neutrophilic ascites,(CNNA)
    - Monomicrobial non-neutrophilic ascites.(MNB)

2. **Secondary bacterial peritonitis.**
    - Perforation of GUT
    - Non-perforation

3. **Polymicrobial bacterial ascites**

SPONTANEOUS BACTERIAL PERITONITIS(SBP)

The diagnosis of SBP is made in the presence of an elevated polymorphonuclear cell count ≥ 250 cells/cu .mm and a ascitic fluid culture positive organism and without any evidence of surgically treatable external source or intra-abdominal source of infection. Most of the patients show growth of a single organism which is diagnostic of SBP.[58]

CULTURE NEGATIVE NON-NEUTROCYTIC ASCITIS:(CNNA)

The term CNNA was coined in 1984. It is also a variant of SBP which is associated with less frequent mortality as compared to SBP. A polymorphonuclear cell count of > 250 cells /cu.mm and a negative culture of ascitic fluid in the absence of even a single dose of antibiotic injection suggest CNNA.[62] Runyon have proposed that other causative factors of neutrophilic ascites are tuberculous peritonitis, peritoneal carcinomatosis, pancreatitis and must be ruled out before the diagnosis of CNNA is made out.[11] All these patients must be treated similar to SBP patients and their clinical presentation, therapeutic management and prognostic characteristics resemble that of spontaneous bacterial peritonitis.

MONOBACTERIAL NON-NEUTROCYTIC BACTERASCITIS:(MNB)

This variant of SBP is diagnosed when the neutrophil counts are < 250 cells/cu.mm and the ascitic fluid will have culture positivity for a single organism without evidence of surgically treatable cause of intra-abdominal source of infection.[34]

SECONDARY BACTERIAL PERITONITIS:

The diagnosis of SBP is made when the ascitic fluid PMN counts are ≥ 250 cells/cu.mm, culture showing polymicrobial organisms and an identifiable cause surgically treatable primary source of intraabdominal infection. The infection can occur with or without perforation of intestine.

POLYMICROBIAL BACTERIAL ASCITES:

The variant of PMB ascites is diagnosed when the neutrophil counts is < 250 cells/cu.mm and the ascitic fluid shows cultures positive for multiple organisms. Earlier studies have shown that this variant is a rare type seen in about 1 in 1000 cases of paracentesis, occurring mainly due to inadvertent perforation of the intestines while performing therapeutic or diagnostic paracentesis. They have found various risk factors for this iatrogenic source of infection which include multiple surgical scars, paralytic ileus and the inexperience of the operator while performing this procedure.

PREVALANCE OF SPONTANEOUS BACTERIAL PERITONITIS:

In 1980's, about 10% of the ascitic fluid were found to be infected at the time of admission into hospital. A low frequency may be due to the infrequency aseptic measures of paracentesis and the low diagnostic efficacy of bacterial culture methods. In the recent days of medical practice SBP is identified earlier stages itself, due to better tapping and diagnostic techniques of ascitic fluid analysis and culture methods and also due to routine paracentesis performed at the time of admission in hospital and hence the complication rate is reduced down to < 1% of patients.

Nowadays, paracentesis is performed as a routine in patients with ascites who get admitted to the hospital for various reasons. In the patients with positive ascitic culture fluid, Mono-microbial non-neutrocytic scites constitute about 1/3rd of ascitic fluid infection and the remaining 2/3 rd was SBP.

Prevalence of CNNA is mainly dependent on ascitic culture techniques. The frequency of Polymicrobial bacterial ascites is very low, and it is seen in about 1 per 1000 patients. Approximately 0-2% of patients with ascites at the time of admission in the hospital was demonstrated to have Secondary bacterial peritonitis. Approximately, around 5% of the patients initially determined to have SBP were later found to be secondary bacterial peritonitis.

ANATOMY OF PERITONEAL CAVITY

The peritoneum is a thin serous membrane that lines the walls of the abdominal and pelvic cavities and clothes the viscera. The peritoneum secretes a small amount of serous fluid, the peritoneal fluid which lubricates the surfaces of the peritoneum and allows free movement between the viscera.[9]

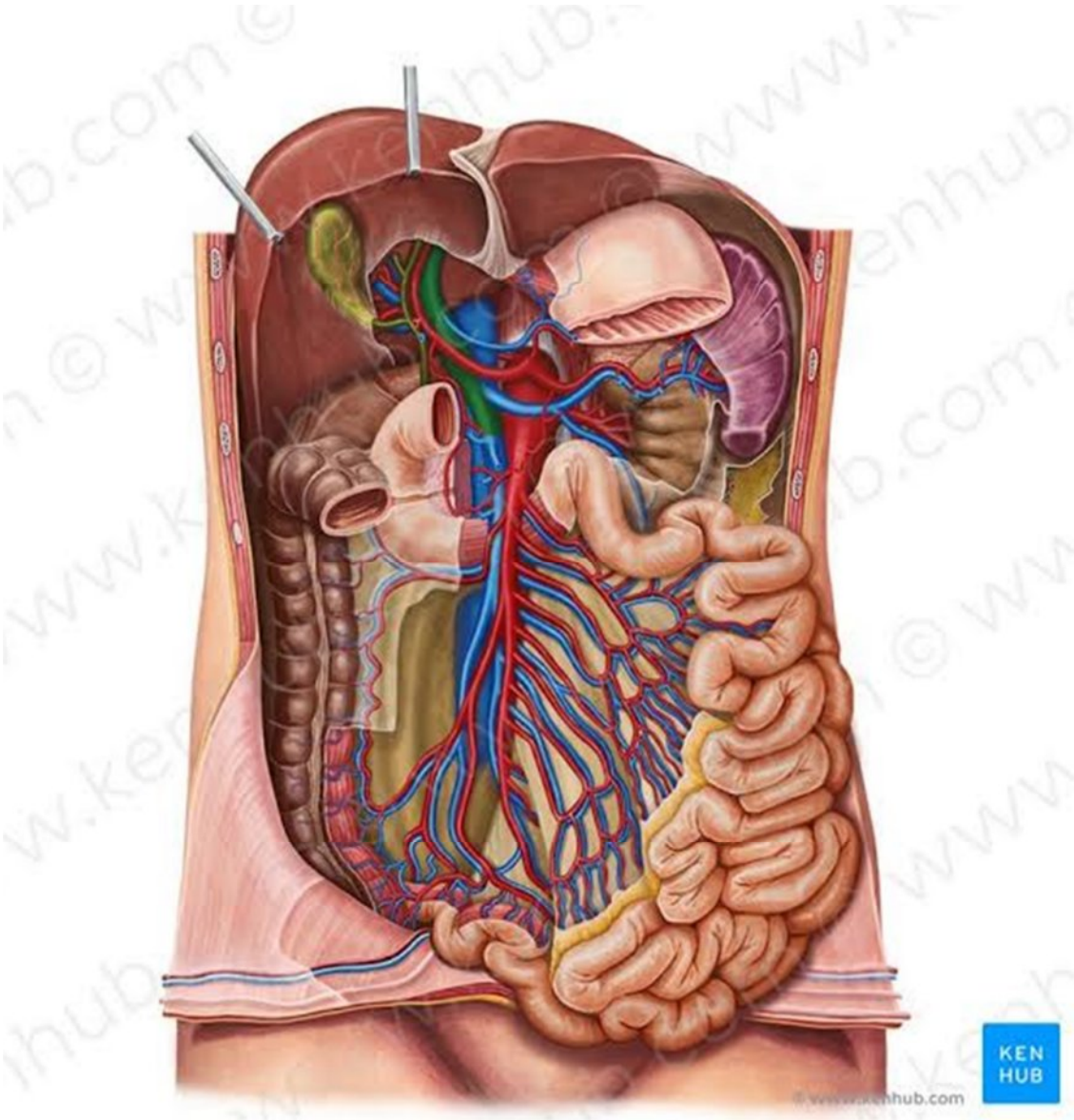


FIG:1 ANATOMY OF PERITONEAL CAVITY

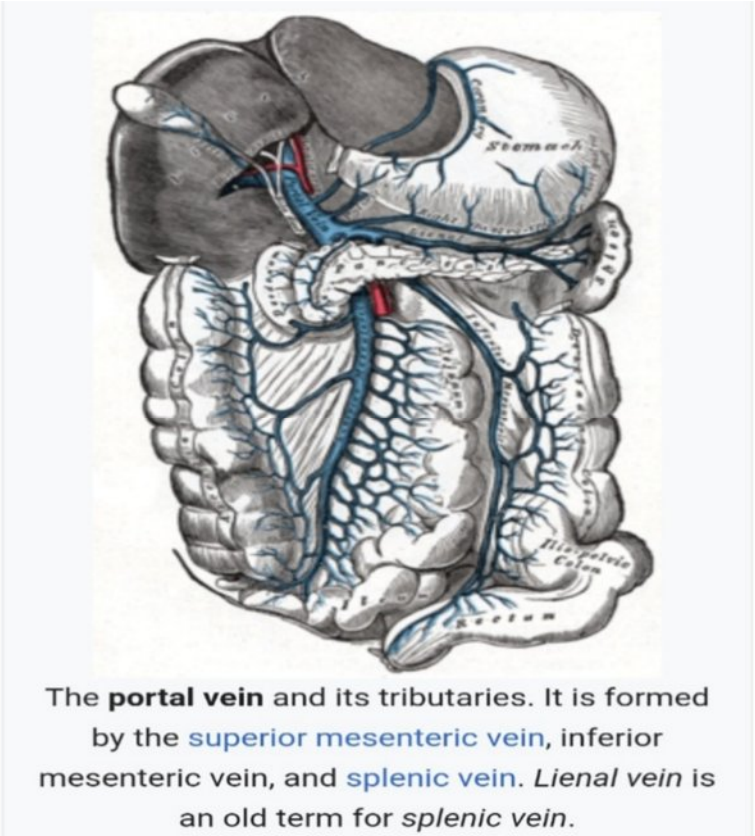
ANATOMY OF PORTAL VEIN

The portal vein is formed by the confluence of the splenic vein and the superior mesenteric vein behind the neck of the pancreas.[9] The various tributaries of portal vein are Superior mesenteric vein, Inferior mesenteric vein, Splenic vein, Left gastric vein, Right gastric vein, Cystic vein and the Paraumbilical vein. There are various sites of porto systemic and porto retroperitoneal anastomosis. They are

1. At the lower end of oesophagus
2. At rectal venous plexus
3. At periumbilical vein

The pathophysiology of oesophageal varices formation due to portal hypertension is made clear by this anatomy. As massive hematemesis per se is a sole cause for spontaneous bacterial peritonitis, prompt treatment of oesophageal varices plays a key role in prevention of SBP.

FIG 2: ANATOMY OF PORTAL VEIN AND ITS TRIBUTRIES



The **portal vein** and its tributaries. It is formed by the superior mesenteric vein, inferior mesenteric vein, and splenic vein. *Lienal vein* is an old term for *splenic vein*.

CIRRHOSIS OF LIVER

Cirrhosis is a condition that is defined histopathological and has a variety of clinical manifestations and complications, some of which can be life-threatening. The pathologic features consist of the development of fibrosis points that there is architectural distortion with the formation of regenerative nodules. This results in a decrease in hepatocellular mass, and thus function, and an alteration of blood flow. The induction of fibrosis occurs with activation of hepatic stellate cells, resulting in the formation of increased amounts of collagen and other components of the extracellular matrix.[9]

Patients who have cirrhosis have varying degrees of compensated liver function, and clinicians need to differentiate between those who have stable, compensated cirrhosis and those who have decompensated cirrhosis. Patients who have developed complications of their liver disease and have become decompensated should be considered for liver transplantation. Many of the complications of cirrhosis will require specific therapy.

Portal hypertension[14] is a significant complicating feature of decompensated cirrhosis and is responsible for the development of ascites and bleeding from esophagogastric varices, two complications that signify decompensated cirrhosis.[9] Loss of hepatocellular function results in jaundice, coagulation disorders, and hypoalbuminemia and contributes to the causes of portosystemic encephalopathy.

Some of the scoring systems used to assess the prognosis of cirrhosis of liver includes the,

1) Model End - stage Liver Disease [MELD][9] score which takes into account the serum bilirubin, creatinine and INR. If serum sodium is also taken into consideration, it is known as UKELD . It was initial taken as a guideline for a three month mortality score in post TIPS patients. Later on it was used to determine prognosis and prioritizing the patients for liver transplant It is given by the formula

   MELD = 3.78×ln[serum bilirubin (mg/dL)] + 11.2×ln[INR] + 9.57×ln[serum creatinine (mg/dL)] + 6.43×aetiology(0: cholestatic or alcoholic, 1: otherwise)

2) Child Pugh's score[8] that helps in planning the outcome of liver transplant and mortality which also takes into account bilirubin, ascites ,INR, albumin level and presence of encephalopathy . It was initially used to calculate prognosis of chronic liver disease but now it has gained interest in knowing the strength of the treatment and the need for liver transplant.

Table 1. Showing the calculation of child pugh's Turcotte scoring method

Measure	1 point	2 points	3 points
Total bilirubin, µmol/l (mg/dl)	<34 (<2)	34-50 (2-3)	>50 (>3)
Serum albumin, g/dl	>3.5	2.8-3.5	<2.8
Prothrombin time, prolongation (secs)	<4.0	4.0-6.0	> 6.0
Ascites	None	Mild	Moderate to Severe
Hepatic encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)

Classification of CPT score and interpretation given in this table.

Points	Class	One year survival	Two year survival
5-6	A	100%	85%
7-9	B	81%	57%
10-15	C	45%	35%

MADDREY'S DISCRIMANT FACTOR:

This is one of the important prognostic factor for the alcoholic liver disease. In this, score is calculated based on patient's prothrombin time(sec) and serum total bilirubin in mg/dl. The score of more than 32 indicates in-hospital mortality in 1 month is about 35 to 45 %.[16]

Here, the formula is given as

DF SCORE = 4.6 x (PT test - control) + SR.Bilirubin in mg/dl

DIAGNOSTIC MODALITY BY IMAGING:

Various Imaging techniques used in diagnosing cirrhosis of liver including an ultrasonogram, computed tomography(CT), magnetic resonance imaging(MRI) and Elastography(FIBROSCAN). Elastography is consider as the gold standard diagnostic modality for cirrhosis detection. Liver biopsy was also considered to be a test for cirrhosis before the era of USG and Elastography.[8]

HEPATIC ENCEPHALOPATHY:

The term hepatic encephalopathy (HE) encompasses a wide array of transient and subtle reversible neurologic and psychiatric manifestations usually found in patients with chronic liver disease and portal hypertension, but also seen in patients with acute liver failure.[21] HE develops in 50% to 70% of patients with cirrhosis, and its occurrence is a poor prognostic indicator, with projected 1- and 3-year survival rates of 42% and 23%, respectively, without liver transplantation. Neurotoxin involved in HE is ammonia, which is produced primarily in the colon, where bacteria

metabolize proteins and other nitrogen-based products into ammonia. Enterocytes synthesize ammonia from glutamine. Once produced, ammonia enters the portal circulation and, under normal conditions, is metabolized and cleared by hepatocytes. In cirrhosis and portal hypertension, reduced hepatocyte function and portosystemic shunting contribute to increased circulating ammonia levels.

Increased permeability of the blood-brain barrier increases the uptake and extraction of ammonia by the cerebellum and basal ganglia. Acute hyperammonemia appears to have a direct effect on brain edema, astrocyte swelling, and transport of neurally active compounds such as myoinositol, thereby contributing to HE. No specific laboratory findings indicate the presence of HE definitively.

FIG 3:SHOWING WEST HEVAN GRADING OF HEPATIC ENCEPHALOPATHY:

West Haven Criteria		
Grade	**Intellectual Function**	**Neuromuscular Function**
0	Normal	Normal
Minimal	Normal examination findings; subtle changes in work or driving	Minor abnormalities of visual perception or on psychometric or number tests
1	Personality changes, attention deficits, irritability, depressed state	Tremor and incoordination
2	Changes in sleep-wake cycle, lethargy, mood and behavioral changes, cognitive dysfunction	Asterixis, ataxic gait, speech abnormalities (slow and slurred)
3	Altered level of consciousness (somnolence), confusion, disorientation, and amnesia	Muscular rigidity, nystagmus, clonus, Babinski sign, hyporeflexia
4	Stupor and coma	Oculocephalic reflex, unresponsiveness to noxious stimuli

Nonabsorbable disaccharides have been the cornerstone the treatment of HE. Oral lactulose or lactitol are metabolized by colonic bacteria to by-products that appear to have beneficial effects. by causing catharsis and reducing intestinal pH, thereby inhibiting ammonia absorption.[68]

Antibiotics are generally used as second-line agents after lactulose or in patients who are intolerant of nonabsorbable disaccharides. Rifaximin given orally in a dose of 550 mg twice daily was approved in 2010 for the treatment of chronic HE and reduction in the risk of recurrence of overt HE in patients with advanced liver disease. Newer therapeutic modality is usage of Acarbose. It is an α- glucosidase inhibitor which inhibit the absorption of carbohydrates in the intestines and it delivers enhanced load of carbohydrate to the colon. This increases the saccharolytic to proteolytic flora which reduces the level of ammonia.

ASCITES

Ascites refers to a pathologic fluid accumulation within the peritoneal cavity. Chronic liver disease with portal hypertension is the most common cause for ascites. The Peripheral Arterial Vasodilation hypothesis is the most widely accepted explanation for ascites development and renal dysfunction in cirrhosis, as fits hemodynamic data better than the prior Underfill or Backward Theory and Overflow theory.[9]

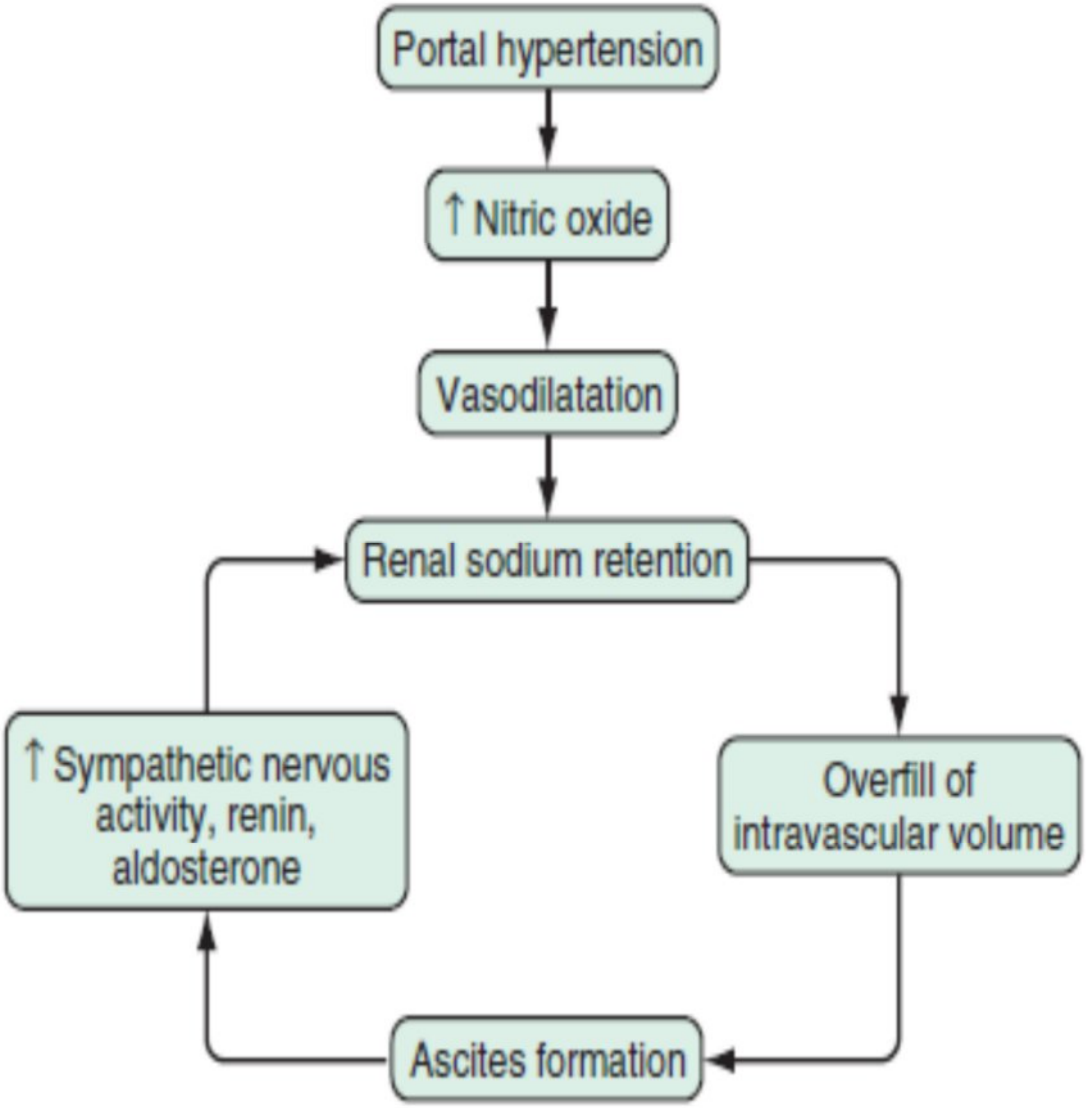


FIG 4:: pathophysiology of ascitic fluid formation.

As the portal hypertension increases, splanchnic vasodilation occurs which plays a key role in the pathogenesis of ascites formation . More over endotoxemia that causes accumulation of nitric oxide and prostaglandins also adds on to the insult This endotoxins get accumulated in the blood due to the portosystemic shunting and decreased reticuloendothelial function.

Due to the depletion of the central arterial pressure , the counter measures will be activated in the form of RAAS activity , increased sympathetic activity and ADH release is also enhanced . Ascites forms as leakage of fluid from splanchnic vessels overcomes reabsorption by lymphatics due to worsening splanchnic capillary permeability, declining oncotic pressure and increasing hydraulic pressure gradients across the splanchnic circulation

Patients typically note an increase in abdominal girth that is often accompanied by the development of peripheral edema. The development of ascites is often insidious, and it is surprising that some patients wait so long and become so distended before seeking medical attention. Patients usually have at least 1–2 L of fluid in the abdomen before they are aware that there is an increase. If ascitic fluid is massive, respiratory function can be compromised, and patients will complain of shortness of breath.

Hepatic hydrothorax may also occur in this setting, contributing to respiratory symptoms. Patients with massive ascites are often malnourished and have muscle wasting and excessive fatigue and weakness. In patients with ascites , renal secretion of prostaglandins particularly PGE2 initially helps to maintain the glomerular filtration but as the PGE2 production comes down , the glomerular filtration rate which leads to renal function deteriorates.[8] Other factors which contributes to ascites formation in cirrhosis are decreased oncotic pressure and an increased production of hepatic lymph due to post sinusoidal obstruction.[9]

The ascitic fluid total protein concentration was used to classify ascites as either exudative (at least 2.5 g/dL [25 g/L]) or transudative (<2.5 g/dL [25 g/L]). The serum-ascites albumin gradient (SAAG) has been proved to categorize ascites better than the total protein concentration or other parameters. The gradient is calculated by subtracting ascitic fluid albumin from serum albumin. If the SAAG is 1.1 g/dl (11 g/L) or greater, the patient can be considered to have portal hypertension with an accuracy of approximately 97%. Also, if the serum albumin minus ascitic fluid total protein gradient is 1.1 g/dL (11 g/L) or greater, the patient has portal hypertension because the ascitic fluid albumin concentration cannot be greater than the ascitic fluid total protein concentration. Conversely, if the SAAG is less than 1.1 g/dL (11 g/L), the patient is unlikely to have portal hypertension. The SAAG explains where the albumin came from liver or bowel.

Any inflammatory process can result in an elevated ascitic fluid WBC count. SBP is the most common cause of inflammation of ascitic fluid and the most common cause of an elevated ascitic WBC count. The total WBC count, as well as the absolute PMN count, is elevated in SBP, and PMNs usually account for more than 70% of the total WBC count. Also, in tuberculous peritonitis and peritoneal carcinomatosis, the total ascitic WBC count is frequently elevated, but usually with a predominance of lymphocytes.

Ascites can lead to various complications . Due to the accumulation of fluid patient will have gastrointestinal disturbances like early satiety, bloating and dyspeptic features . Sponatenous Bacterial peritonitis or peritonitis secondary to any other cause can be a life threatening complication as the mortality is very high. Due to volume

loss into the third space severe hypotension can occur and protein exudation can lead to hypoalbuminemia. Ascites can also cause respiratory insult as it pushes the diaphragm which on long standing period can lead to respiratory failure . Due to the hypoproteinemia and the decrease in oncotic pressure , there is also of the fluid in the other spaces like the pleural space and the pericardial space . Paralytic ileus due to electrolyte imbalance and associated pancreatitis is also seen in a few patients. Long standing untreated ascites can also cause surgical complication like umbilical hernia which can lead to obstructive hernia and spontaneously rupture and cause infection.

REFRACTORY ASCITES

Refractory ascites is defined as ascites unresponsive to a sodium-restricted diet and high-dose diuretic treatment. Refractoriness may manifest as minimal or no weight loss despite diuretics or the development of complications of diuretics.

Treatment includes

1. **Serial paracentesis** :–

   It must be done every 2 weeks.[9] In cases where the Na excretion via urine is very minimal, this modality has improved the burden of ascites. But while doing large paracentesis i.e more than 5 litres, it is always advisable to give albumin infusion (6 to 8 g) for every litre of ascites fluid taken.[69]

   As the mortality is very high at a rate of 21 % in the next 6 months, Liver transplantation must also be kept in mind.

2. **TIPS** - Five randomized controlled trials have shown improved control of ascites with TIPS compared to serial LVP's in patients with refractory ascites (62% vs. 24%). However, there was also more cases of encephalopathy with TIPS (39% vs 23%). The incidence of new or worsening HE was 20-31%.
3. **Peritoneovenous shunt**. - Peritoneovenous shunt has high complication rates and so is only used on rare occasions in patients who are not candidates for paracentesis, transplant or TIPS.

PATHOGENESIS OF SBP:

The term spontaneous is used in describing bacterial peritonitis in the ascites patient to indicate that the infection appeared from nowhere. 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.[8]

The three main factors which are found to be linked in the pathological bacterial translocation are

1) Alterations in the gut microbiota
2) Increase in the intestinal permeability
3) Impairment in the host defence

Spontaneous infections of the ascitic fluid are mainly gut derived bacteria. 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. Occasionally Pneumococcus is also isolated that does not reside in the gut. These organisms cause SBP and. Anaerobes account for only 1% of SBP. 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. 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.

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 is common in cirrhosis. These defects in host defences would lead to frequent and prolonged bacteremia.

The decreased protein level in the ascitic fluid is considered a risk factor for SBP as the opsonin level is also decreased which play a key role in the defence mechanism. In the initial phase , the bacteria accumulates in the fluid and it can lead to bacterascites.[10] Mostly it is Monomicrobial Nonneutrocytic Bacterascites (MNB) unless the intergrity of the mucosa is lost which can cause Polymicrobial invasion. Later on as the opsonins and macrophages fail as in the case of chronic liver disease,[23] the ultimate defence mechanism that is recruitment of neutrophils occur which leads to neutrocytic ascites . But as the function of the neutrophils are lost in cirrhosis liver, it culminates in SBP .

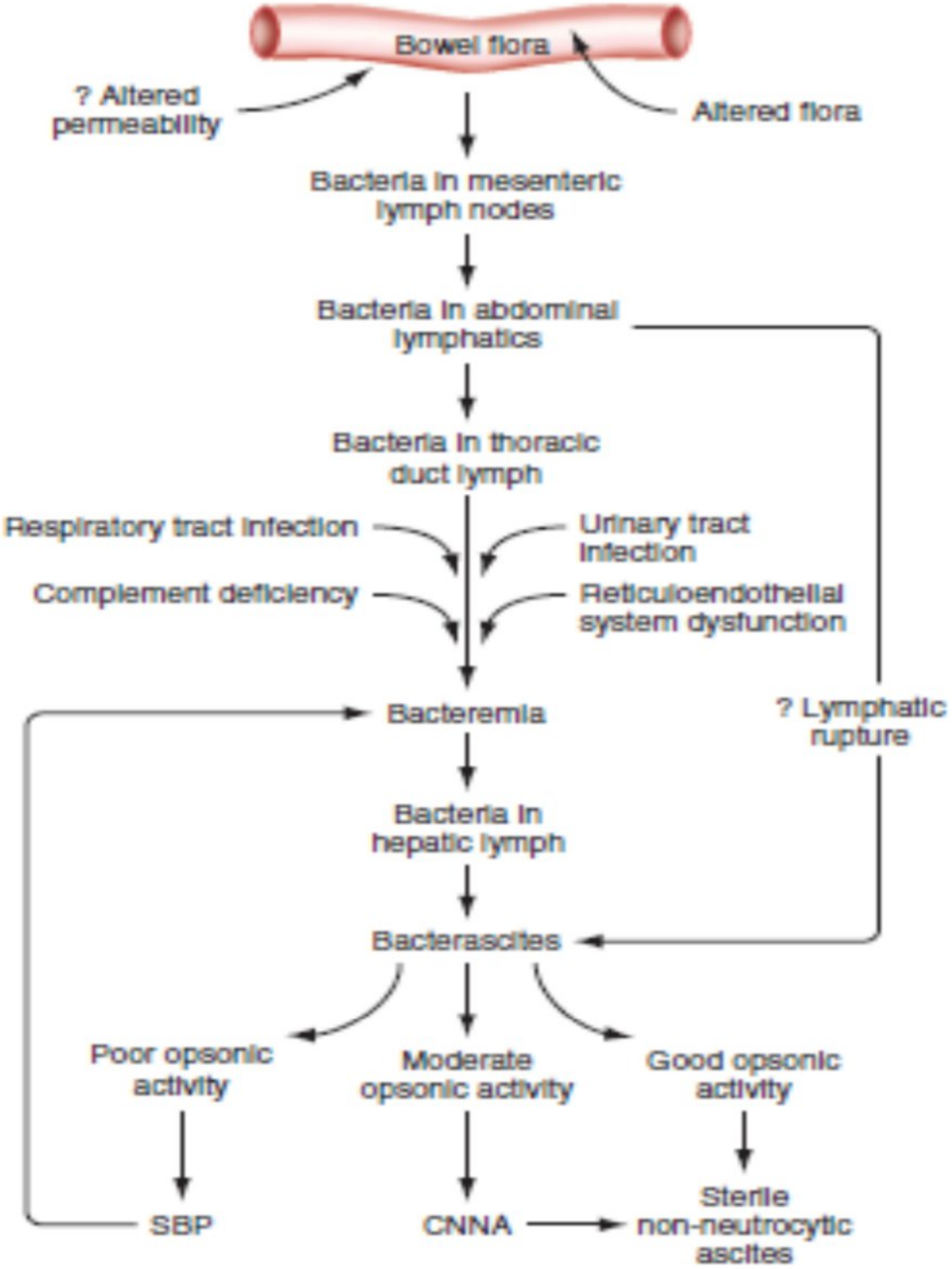


FIG 5: Pathophysiology of ascitis.

So, the differentiation of the diagnosis into bacterascites, CNNA, MNB and neutocytic ascites eventually to SBP all depends on where the disease process stops and the fluid is taken up for diagnosis.

PREDISPOSING FACTORS FOR SBP INCLUDE:

- 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[64,65]

CLINICAL PRESENTATION:

About 87% of patients are symptomatic at the time of diagnosis. The symptoms and signs are often subtle or usually misinterpreted. 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.[8]

Common features of ascitis are.[9]

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%

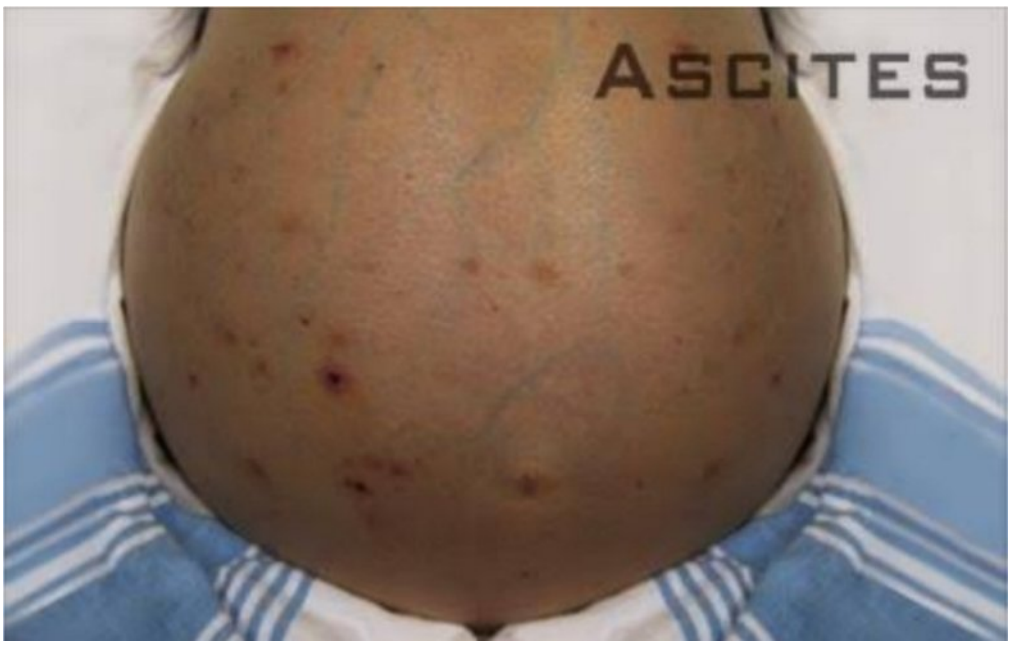


FIG 6:CLINICAL IMAGE OF ASCITIS PATIENT

1

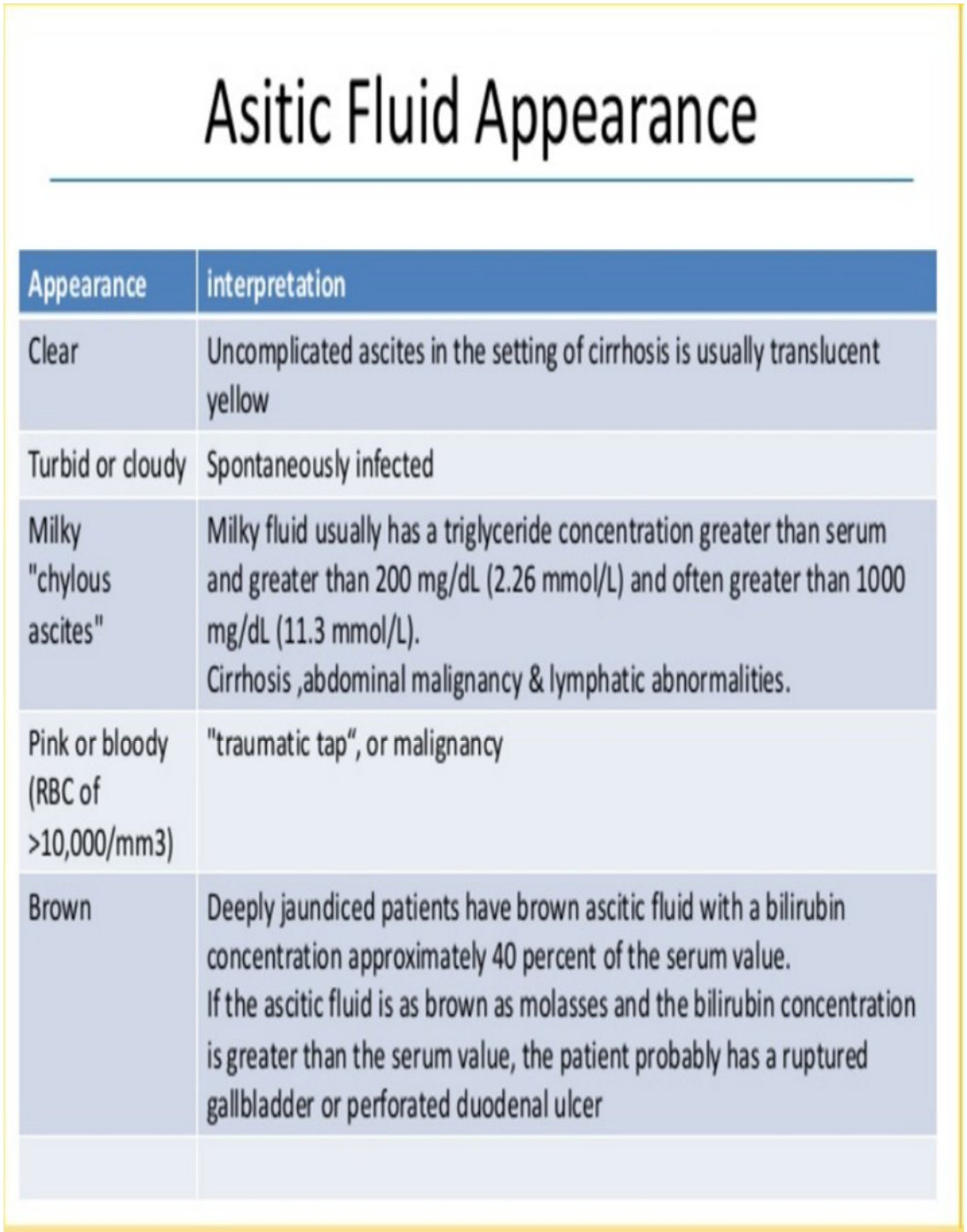
INVESTIGATIONS:

Before investigating in to the analysis of the ascitic fluid by paracentesis which denotes the diagnosis, a complete hemogram will show an increased amount polymorphonuclear cells with low platelets. The renal function test will also be deranged values in most cases and some patients can also have an unexplained metabolic acidosis at the initial presentation.

Diagnostic paracentesis with ascitic fluid analysis is the only way to confirm Spontaneous Bacterial Peritonitis.[8] It should be done in any new onset ascites including cardiac failure, renal failure in nephrotic syndrome and Budd Chiari syndrome. It also to be done in any cirrhosis with unexplained encephalopathy and renal failure cases. Moreover, in a sudden deterioration of general condition of a patient should also prompt us to diagnose SBP.

The ascitic fluid neutrophil count more than 250 cells/µl indicates the need of antibiotic therapy. Bed side inoculation of the ascitic fluid into the culture media has increased tendency to detect microbes. About 10 ml of ascitic fluid is needed for optimal results because sensitivity of the culture depends upon to the amount of sample taken for incubation and culture.

FIG 7: Types of Ascites according to appearance



Asitic Fluid Appearance

Appearance	interpretation
Clear	Uncomplicated ascites in the setting of cirrhosis is usually translucent yellow
Turbid or cloudy	Spontaneously infected
Milky "chylous ascites"	Milky fluid usually has a triglyceride concentration greater than serum and greater than 200 mg/dL (2.26 mmol/L) and often greater than 1000 mg/dL (11.3 mmol/L). Cirrhosis ,abdominal malignancy & lymphatic abnormalities.
Pink or bloody (RBC of >10,000/mm3)	"traumatic tap", or malignancy
Brown	Deeply jaundiced patients have brown ascitic fluid with a bilirubin concentration approximately 40 percent of the serum value. If the ascitic fluid is as brown as molasses and the bilirubin concentration is greater than the serum value, the patient probably has a ruptured gallbladder or perforated duodenal ulcer

Other non-valuable parameters like LDH(lactate dehydrogenase) can be measured in ascitic fluid along with other biochemical analysis. More than 400sigmaU/l is significant.

Imaging modality plays a key role in the confirming the ascites and also helpful in assessing the paracentesis procedure. Sometime It will give the etiological factor of the ascites. USG abdomen and pelvis are the most cost effective, safe and radiation free imaging technique.

High end imaging techniques like CT and MRI will identify the aetiologies like carcinoma of pelvic organs, TB abdomen and/or pancreatitis.

FIG 8: CT ABDOMEN SHOWING ASCITIS AND OTHER ORGANS.

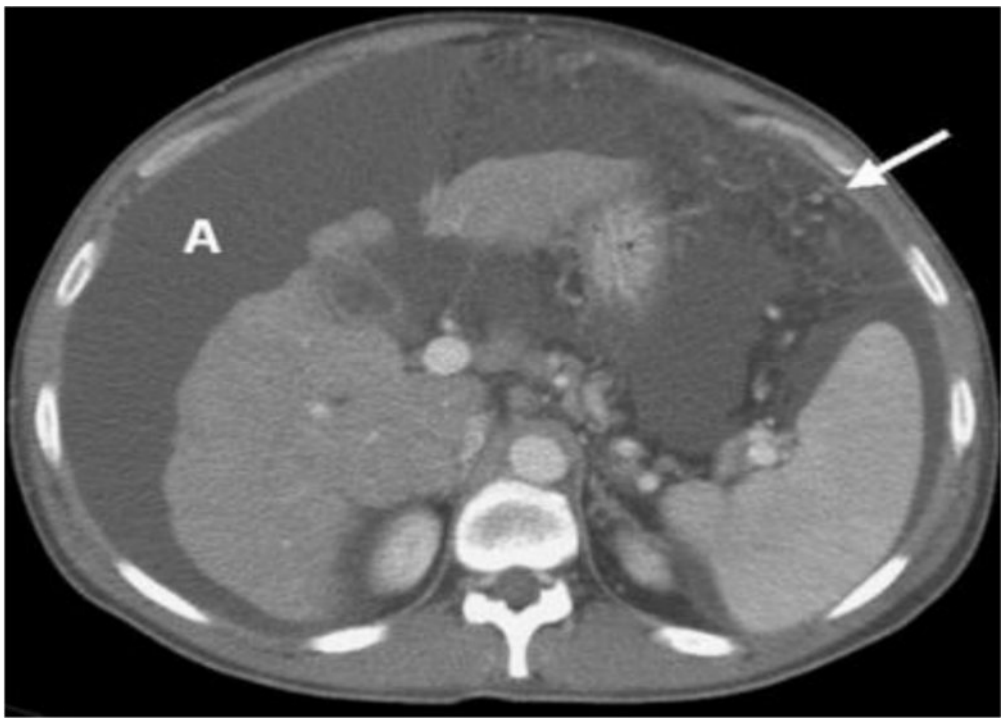


FIG 9: USG ABDOMEN SHOWING ASCITIS.

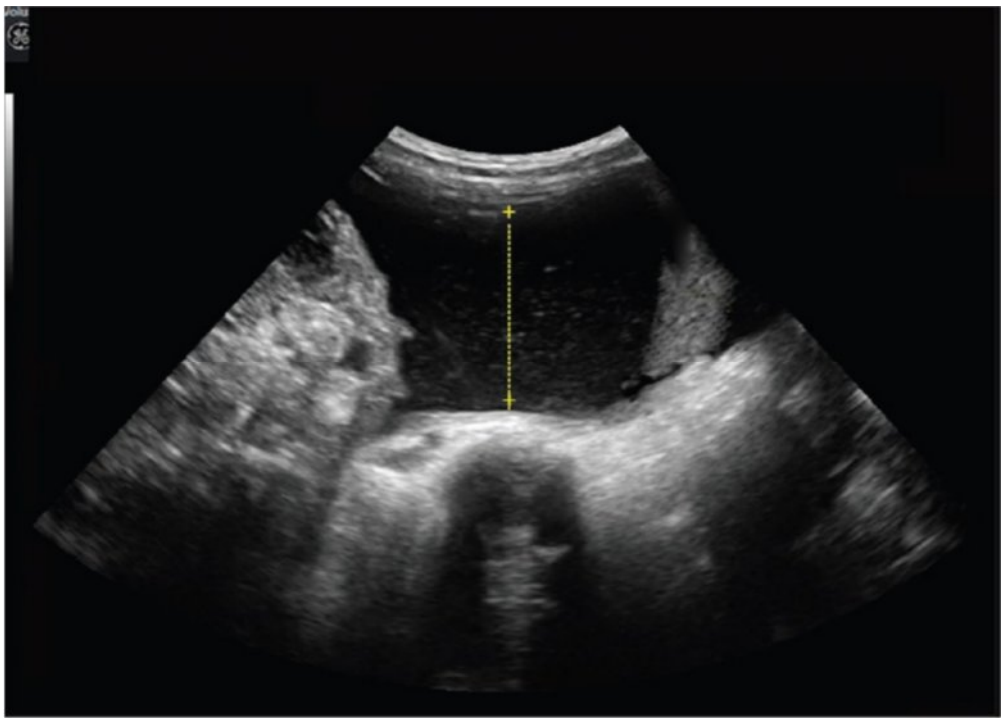
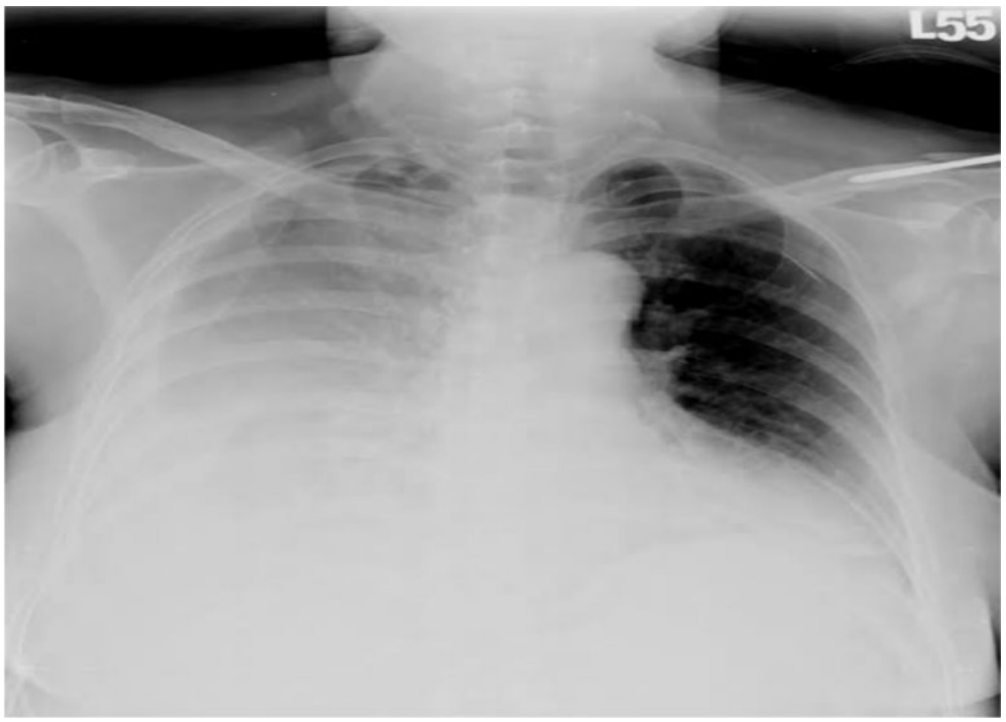


FIG 10:CHEST X RAY SHOWING HEPATIC HYDROTHORAX



DIAGNOSIS:

Diagnostic paracentesis with analysis of the ascitic fluid is the only method to confirm Spontaneous Bacterial Peritonitis.[8]

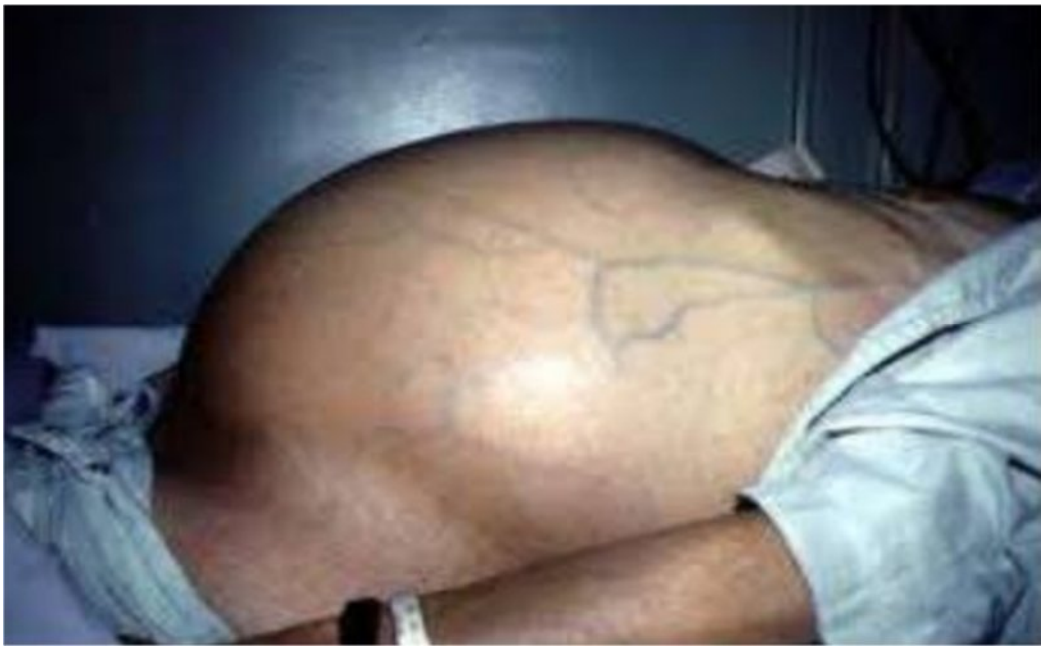
The main parameters to be taken into consideration are :

1. Cell count – neutrophil count
2. Culture sensitivity

As mentioned above a total count of neutrophil more than 250 cells/ cu.mm warrants the start of antibiotic therapy . Bed side inoculation of the ascitic fluid has increased the detection of the culprit organism. An optimal 10ml of fluid inoculation gives a good result . The sensitivity of the culture analysis has shown drastic reduction in linear proportion to the amount of sample taken .

Other parameters that are taken into consideration is the Lactate Dehydrogenase (LDH) level . A level of greater than 400 sigma units was considered as useful tools for determining the diagnosis.

FIG 11: POSITIONING OF THE PATIENT DURING PARACENTESIS



TREATMENT FOR SBP:

A prompt use of antibiotics in a case of SBP has shown improvement in the outcome of patients but still as per literature the mortality is still high as of 10 to 30%. The decision to begin empirical antibiotic treatment in patients with bacterascites must be individualized. Many episodes resolve without treatment.[56]

ANTIBIOTIC	DOSE	ROUTE	DURATION
CEFOTAXIME	2g 8-12hrs	IV	5days
ALTERNATIVES			
CEFTRIAXONE	2g 12hrs	IV	5days
AMOXICILLIN + CLAVULANATE	1.2 g	ORAL	2days
OFLOXACIN	400mg 12hrs	ORAL	7days

Table 3: Treatment of ascitic fluid infection.

HOSPITAL ACQUIRED INFECTION OF ASCITIS: CARBAPENEMS

Supplemental administration of intravenous albumin (which may have anti-inflammatory effects in addition to expanding plasma volume) prevents further renal impairment and reduces mortality, particularly in patients with a serum creatinine greater than 1 mg/dL (83.3 mcmol/L), blood urea nitrogen greater than 30 mg/dL (10.8 mmol/L), or total bilirubin greater than 4 mg/dL (68.4 mcmol/L).[27]

In survivors of bacterial peritonitis, the risk of recurrent peritonitis may be decreased by long-term ciprofloxacin[61] (eg, 500 mg orally once per day) or norfloxacin (400 mg orally daily) or trimethoprim-sulfamethoxazole (eg, one double-strength tablet once per day).[69,70]

RECURRENT PERITONITIS

The causative organism is often resistant to fluoroquinolones and may become multidrug resistant in some cases.[25] In high-risk cirrhotic patients without prior peritonitis (eg, those with an ascitic protein less than 1.5 g/dL and serum bilirubin greater than 3 mg/dL (51.3 mcmol/L), serum creatinine greater than 1.2 mg/dL (99.96 mc.mol/L), blood urea nitrogen 25 mg/dL or more (9 mmol/L or more), or sodium 130 mEq/L or less [130 mmol/L or less]), the risk of peritonitis, hepatorenal syndrome, and mortality for at least 1 year may be reduced by prophylactic trimethoprim-sulfamethoxazole, one double-strength tablet once per day, ciprofloxacin, 500 mg once per day, or norfloxacin, 400 mg orally once a day. In patients hospitalized for acute variceal bleeding, intravenous ceftriaxone (1 g per day),[71] followed by oral trimethoprim-sulfamethoxazole (one double-strength tablet once per day) or

ciprofloxacin (500 mg every 12 hours), for a total of 7 days, reduces the risk of bacterial peritonitis. Nonantibiotic prophylactic strategies, including probiotics, bile acids, and statins, are under study

MATERIALS AND METHODS

STUDY DESIGN:

CROSS SECTIONAL, HOSPITAL BASED OBSERVATIONAL STUDY

STUDY SUBJECTS:

Total of 100 patients who were admitted in medicine department, confirmed of hepatic cirrhosis with ascites by clinical and radiological methods and they were screened for SBP. They were studied thoroughly with clinical history and examination, cytological, microbiological and biomedical tests were undergone.

SOURCE OF SUBJECTS:

Cases who got admitted in the medicine department for Ascites in GMKMC hospital, Salem.

SOURCE OF DATA

Data collected for study purpose after obtaining informed consent from the patients admitted in medical ward in GMKMC Hospital, Salem.

DURATION OF STUDY

February 2018 to February 2019

INCLUSION CRITERIA:

1) Patients with Cirrhosis of liver was diagnosed on the basis of clinical and radiological features suggestive of chronic liver disease.
2) Either sex
3) All adult patients with liver cirrhosis with ascites using the following criteria,
    - One clinical sign of hepatocellular failure.
    - One clinical sign of portal hypertension.
    - Sonographic signs of cirrhosis/ PHT
    - Diagnosis of SBP as established with PMN cells > 250/mm3

EXCLUSION CRITERIA:

1. Patient refusal
2. Patient who had received antibiotics within 3 weeks prior to admission.
3. Patients with secondary peritonitis.
4. TB ascites
5. Malignant ascites

STUDY METHODOLOGY

SBP was diagnosed by following criteria,

An ascitic fluid neutrophil count (PMN) greater than 250 cells/ mm3.

Or

A positive ascitic fluid culture, and an absence of a primary source of infection in abdomen.

Ascitic fluid for analysis was taken under aseptic precautions as soon as the patients were admitted before giving antibiotics to the patients.

CLINICAL EVALUATION:

A detailed clinical history was obtained from the study population and through examination of the patient was done. Ascites was graded as per the International Ascites Club criteria. The West Haven classification was used to grade the severity of Hepatic encephalopathy. The study group was subjected to the Biochemical, microbiological, Radiological investigations and Endoscopy.

LABORATORY INVESTIGATIONS:

Blood investigations includes haemoglobin, WBC count, platelet count, serum bilirubin – total, direct, indirect, SGOT, SGPT, SAP, serum proteins total, albumin, globulin, PT, INR, renal function tests including serum urea, serum creatinine, and viral markers like HBsAg, Anti HCV were done in all the patients.

All the patients were classified based on CHILD PUGH TURCOTTE' S score

ASCITIC FLUID COLLECTION:

Under strict aseptic precautions diagnostic paracentesis was done after proper positioning of the patient. The site of abdomen for tapping was marked by clinical guidance. Povidone iodine solution as antiseptic was used for skin disinfection. Abdominal draping was done by sterile towels. 22gauge needle was used for paracentesis. Z technique was applied for tapping of ascitic the fluid. 30 ml of the ascitic fluid was drained using two syringes. The blood culture bottles were inoculated by blood for culture. For ascitic fluid culture, about 10 ml of the ascitic fluid was inoculated directly into 50 ml blood culture bottles containing culture media -aerobic and anaerobic each at the bedside under strict aseptic precautions immediately after draining the fluid by using a sterile needle.[15]

About 30 to 50ml of ascitic fluid was tapped in each patient under aseptic precautions.

1. 10ml of ascitic fluid was immediately inoculated in to blood culture bottles for cell count and gram staining analysis.
2. 10ml of ascitic fluid was sent to the laboratory in sterile culture tubes for conventional culture and sensitivity.
3. 10ml of ascitic fluid was sent for biochemical and cytological examination to the laboratory.

Ascitic fluid samples were analysed for the type of cells and cell count. Gram's stain was done in all cases. Ascitic fluid was cultured to know the presence of pathogenic organisms and antibiotic sensitivity.

Other investigations like chest X- ray, ECG, plain X- ray abdomen, UGI endoscopy were also done according to the patient need.

Diagnostic Criteria:[15]

1. An ascitic fluid neutrophil count (PMN) >250 cells/ mm3. Or
2. A positive culture in ascitic fluid, And
3. An absence of a primary source of infection in blood stream.

RESULTS AND ANALYSIS

Totally 100 patients were studied with regards to both thorough history and clinical examination, cytological, microbiological and biomedical tests based on the need for study purpose without affecting patient's health. The observations of the study were analysed.

AGE		
	Frequency	**Percent**
Upto 30 yrs	5	5.0
31 - 40 yrs	22	22.0
41 - 50 yrs	41	41.0
51 - 60 yrs	22	22.0
Above 60 yrs	10	10.0
Total	100	100.0

Table 4: Age wise distribution of study population shown in this chart

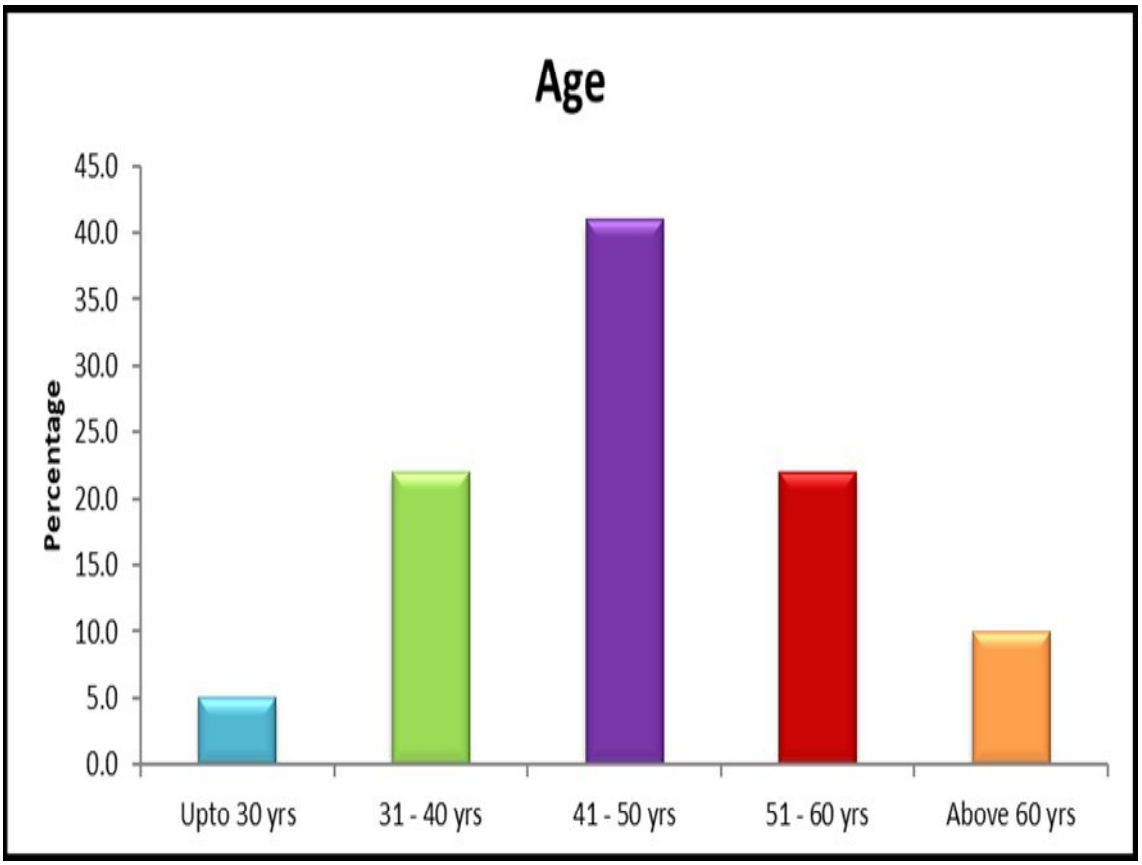


Chart 1: Percentage of study population with specific age intervals.

Age distribution of study population ranged widely with youngest patient being 20 years and oldest patient of 73 years. Mean age of the study population is 47.47 years. Maximum number of patients are found in age group of 31-60 years

GENDER

In the present study males were 92% and 8% of cirrhotic population were females. Hence in this study also there are more Male patients compared to female patients with a ratio of about 11. Alcoholism is common in Male populations. Alcoholics are more prone to develop cirrhosis with Ascites.

GENDER		
	Frequency	**Percent**
Female	8	8.0
Male	92	92.0
Total	100	100

Table 5: Gender distribution in the study.

Even though Alcoholism is less common in females, but when they consume alcohol frequently, more susceptible to develop alcoholic liver disease at lower levels due to low body mass index. Because of stigma they do not disclose alcohol intake, duration, quantity and frequency of alcohol consumption.

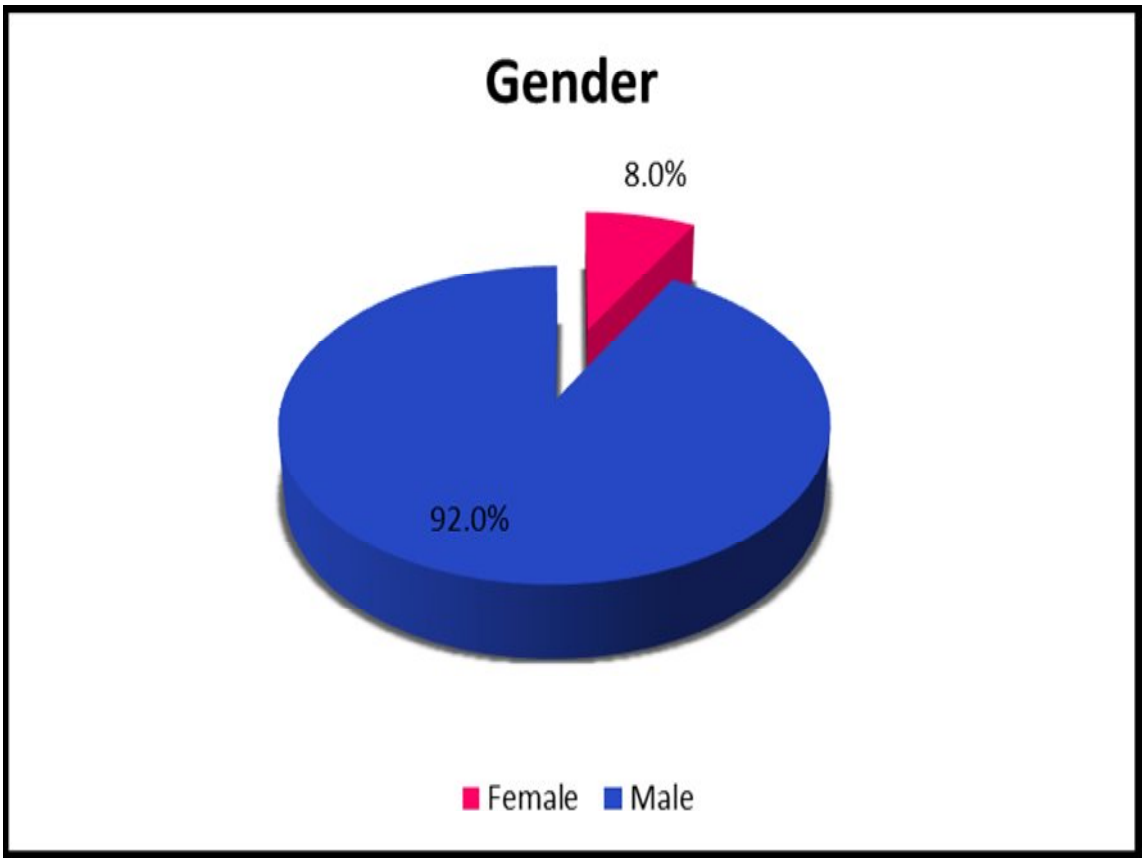


Chart 2: Gender wise distribution of study population

ALCOHOLISM

Among the 100 study population 90% were alcoholics and 10% were non-alcoholics

ALCOHOL		
	Frequency	**Percent**
No	10	10.0
Yes	90	90.0
Total	100	100.0

Table 6: Percentage of alcoholics and non-alcoholics

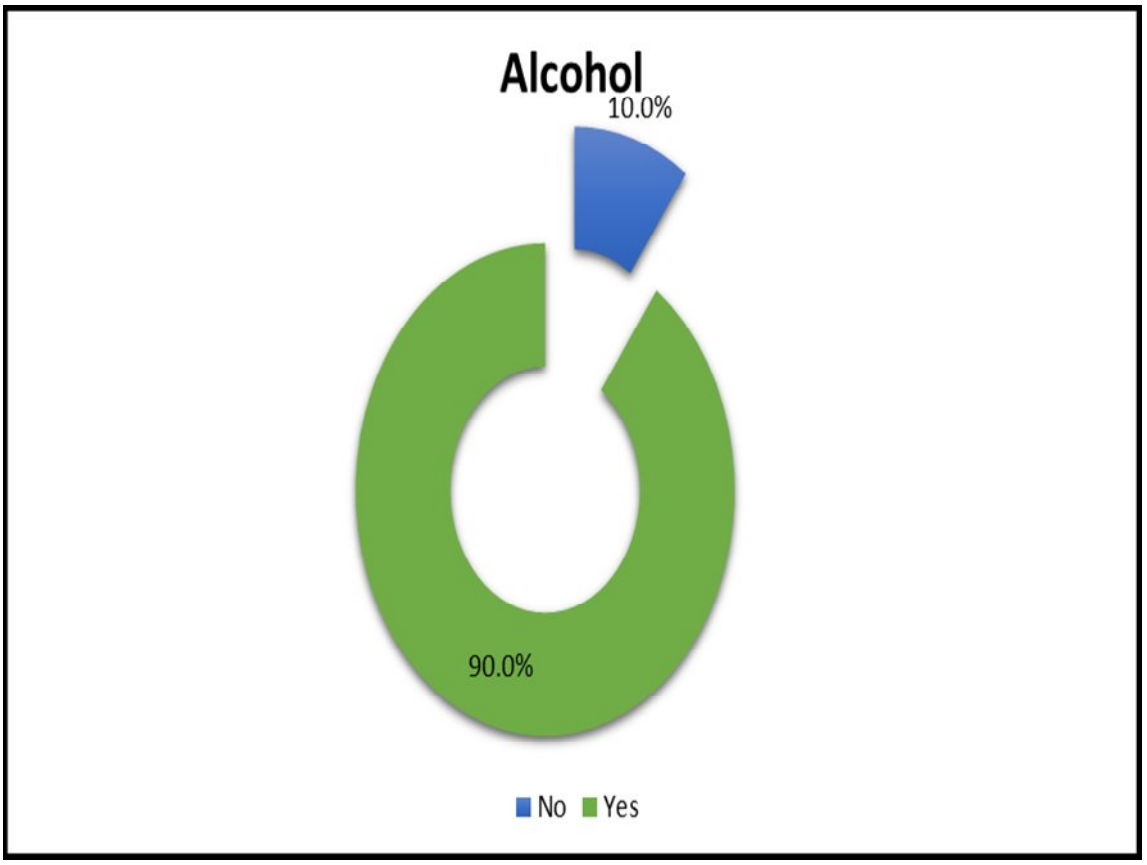


Chart 3: alcoholic and non-alcoholic population.

DURATION OF CIRRHOSIS

Among the 100study population 16% were less than 2 yrs, 31% were between 3 to 5 yrs and 23% were above 5 yrs duration of having liver cirrhosis.

DURATION OF CIRRHOSIS (YRS)		
	Frequency	**Percent**
UPTO 2 YRS	16	16.0
3 TO 5 YRS	61	61.0
ABOVE 5 YRS	23	23.0
TOTAL	100	100

Table 7: Duration of cirrhosis in study subject

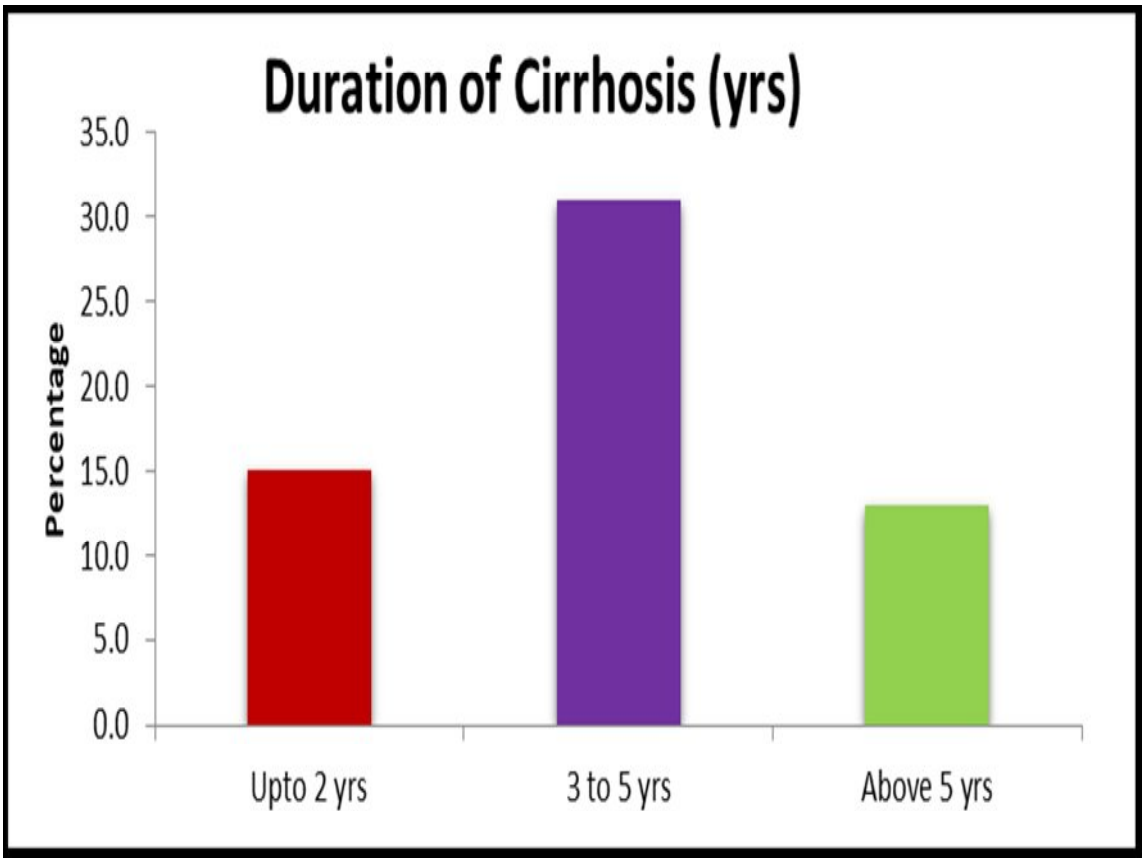


Chart 4: duration of cirrhosis among the study group

SYMPTOMATOLOGY

All study patients had free fluid in abdomen which was moderate to massive in degree. 18% of cases had fever it was continuous and intermittent. About 21% had abdominal tenderness at the time of admission, it was vague pain, distributed all over the abdomen, lasted entire day. There is no relieving factors.

About 13% patients had Jaundice as the presenting complaints along with abdominal distension, associated with yellow discoloration of urine. While 17% of cases were admitted with history of altered sensorium ranging from daytime somnolence, restlessness to drowsiness. Asterixis was the presented in 12% of patients among the study population.

Symptoms	Number of patients	Percentage
Abdominal distention	100	100%
Swelling of lower limbs	38	38%
Jaundice	13	13%
Fever	18	18%
Abdominal pain	21	21%
Vomiting	4	4%
Altered sensorium	8	8%

Table 8: Details of symptoms

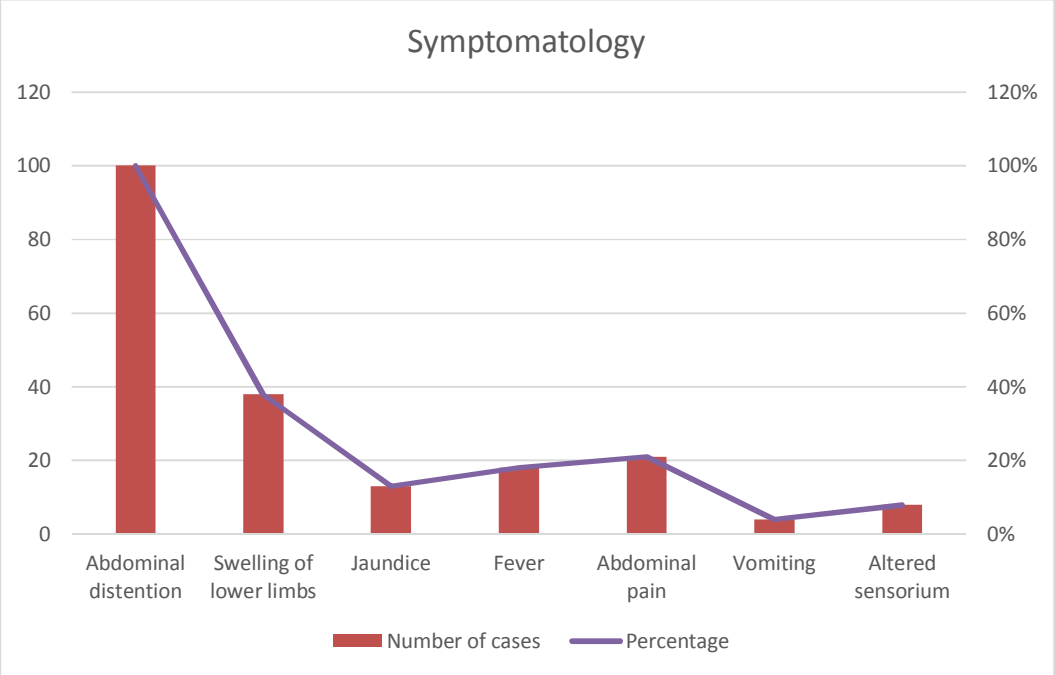


Chart 5: Symptomatology

PHYSICAL SIGNS:

All the study population in this group had moderate to severe ascites, among them 40% of cases had tense ascites. Icterus was seen in 13% of cases. Serum Bilirubin level ranged from 0.3–4.6 mg/dl (mean value of 1.70). Pedal edema was seen in 48% patients. Fever was seen in 18% of cases. Asterixis was seen in 12% of patients. Hepatomegaly was seen in 6% of patients only those who were in early phase of cirrhosis and was having moderate ascites. Abdominal tenderness was seen in 21% of patients.

All the cases were undergone ultrasound for evidence of portal hypertension and to confirm the diagnosis.

SIGNS CORRELATION WITH SBP

Signs	No. of patient s	Positive SBP	PMN >250/m m^3	Culture positive	Percentage
Jaundice	13	13	15	13	100%
Fever	18	16	15	13	88%
Abdominal tenderness	21	16	15	1	76%
Asterixis	12	12	12	9	100%
Altered sensorium	17	16	15	13	94.11%

Table 9: clinical signs in correlation with SBP

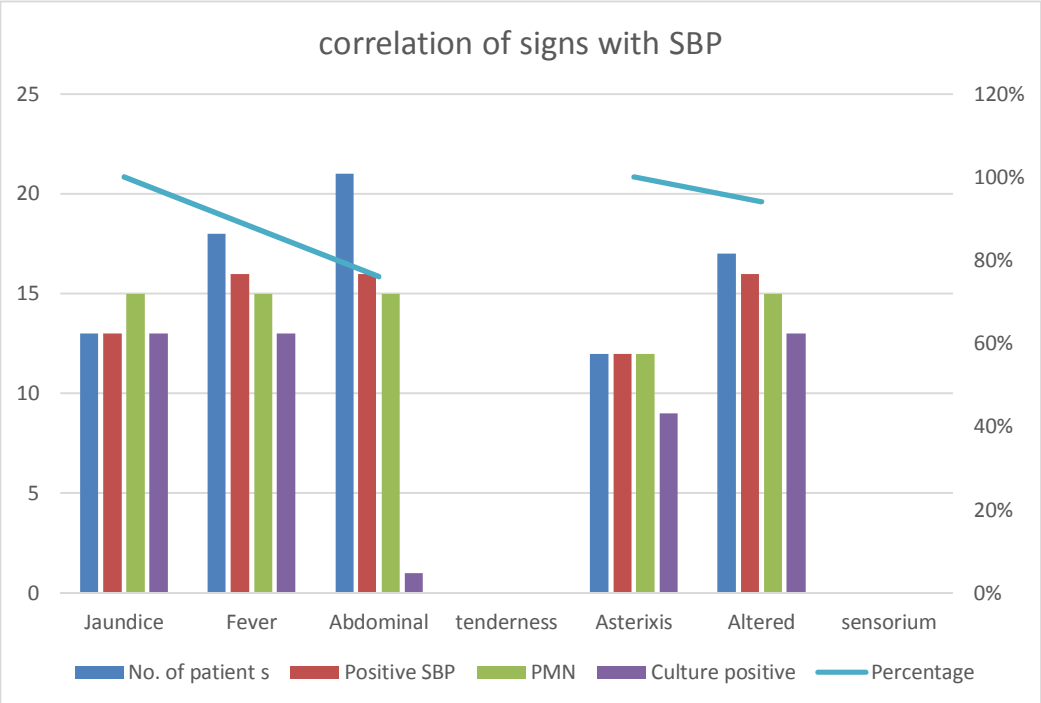


Chart 6: correlation of signs with SBP

FEVER:

Among 100 study population, only 18% of cases had fever as a presenting complaints, of which 16 out of 18 cases diagnosed as SBP about 88% of fever cases were diagnosed to have SBP.

FEVER		
	Frequency	**Percent**
No	82	82.0
Yes	18	18.0
Total	100	100.0

fever distribution among the study population

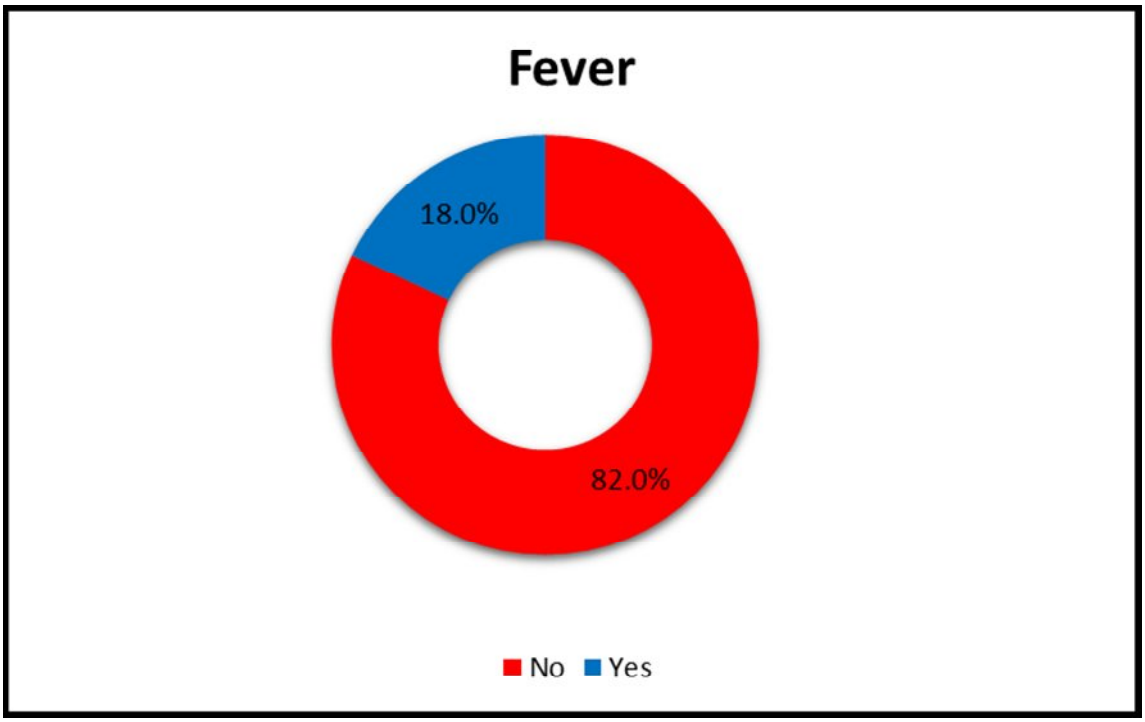


Chart 7: distribution of fever and non-fever cases as percentage

ABDOMINAL TENDERNESS

About 22% of study population had fever as a presenting complaints among 100 cases. In that 16 out of 22 cases of abdominal tenderness patients diagnosed to have SBP, about 72.72% of abdominal tenderness patients were diagnosed as SBP.

ABDOMINAL TENDERNESS		
	Frequency	**Percent**
No	78	78.0
Yes	22	22.0
Total	100	100.0

Abdominal tenderness in study population

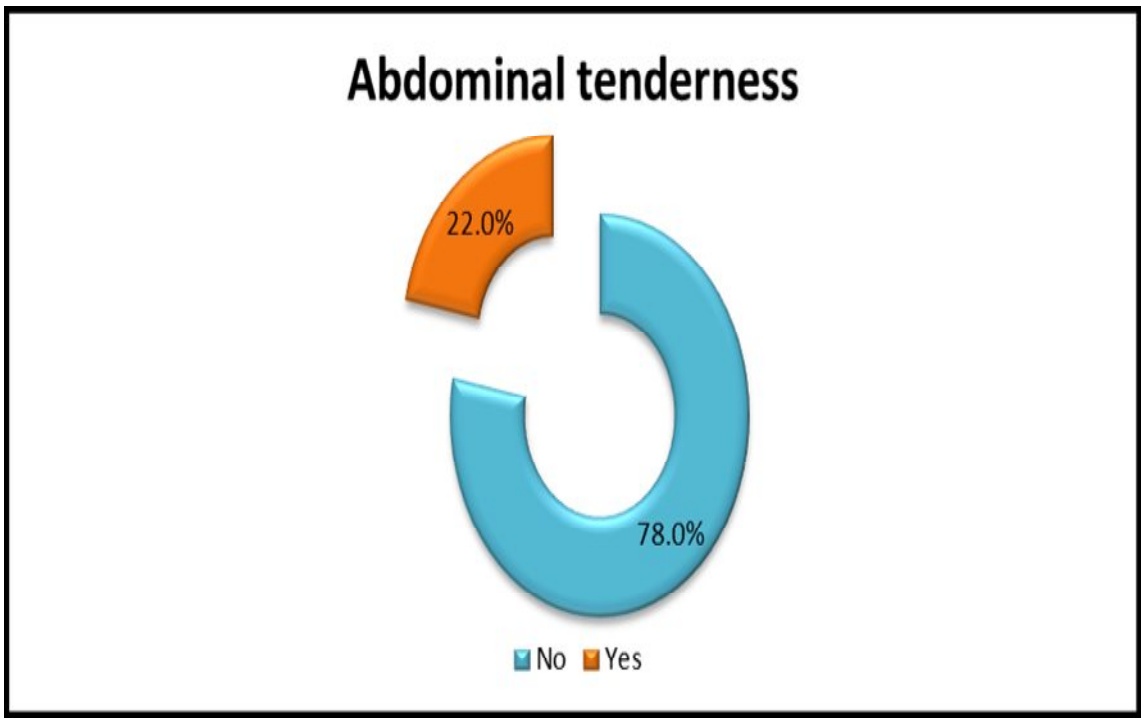


Chart 8: distribution of abdominal tenderness among study population

ASTERIXIS

About 18% of cases in the study group had asterixis as one of the presenting sign. In that 18 cases, 16 patients were diagnosed to have SBP, about 88.88% of patients with asterixis patients had SPB in our study

ASTERIXIS		
	Frequency	**Percent**
No	86	86.0
Yes	14	14.0
Total	100	100.0

Number of cases having asterixis in study

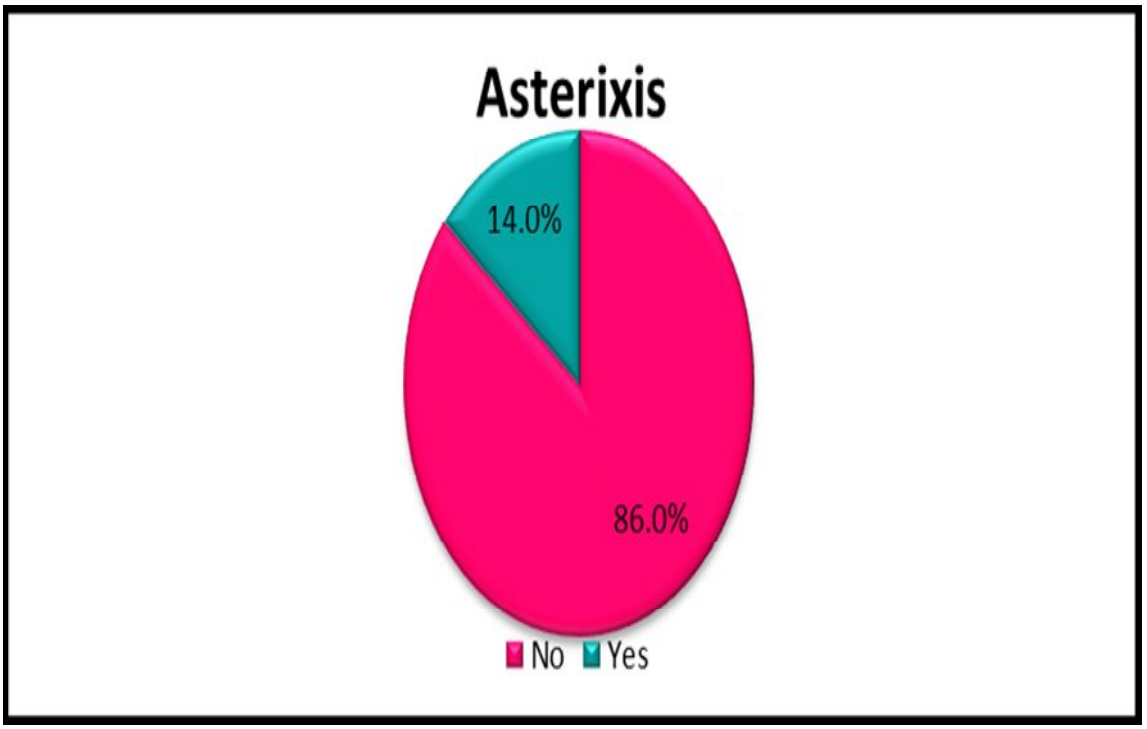


Chart 9: distribution of cases with asterixis in our study

ALTERED SENSORIUM

In our study approximately 17% of patients have mild sub-clinical form to full blown excessive daytime sleepiness levels of altered sensorium. Among patients 16 out of 17 cases were diagnosed to have SBP, about 94.11% of altered sensorium patients having SBP in our study.

ALTERED SENSORIUM		
	Frequency	**Percent**
No	83	83.0
Yes	17	17.0
Total	100	100.0

Distribution of cases with asterixis in study group

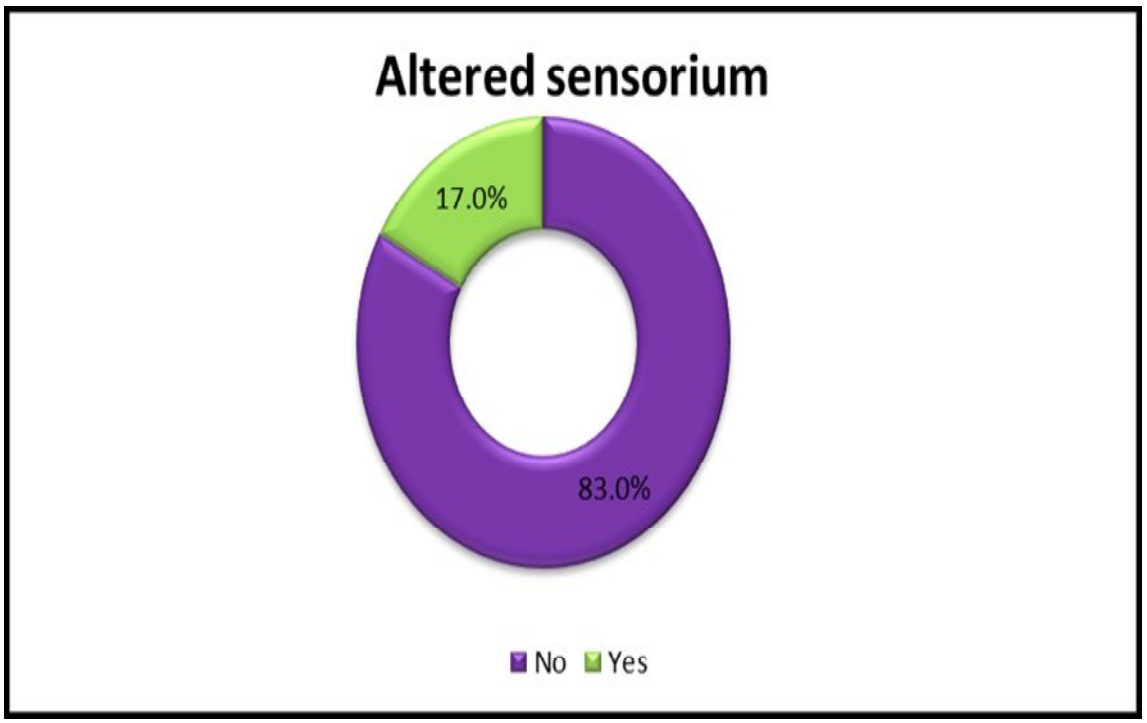


Chart 10: Distribution of individuals with altered sensorium in our study

group

PREVALENCE OF SBP:

Among the 100 patients of cirrhosis with ascites which was confirmed by clinical examination, radiological, microbiological and biochemical examination were done.in which 13 patients were found positive for SBP, in this study only 3 patients had PMN count >250/cu.mm, but culture negative for any other microorganism. About 10 subjects were culture positive and isolated Escherichia coli, 2 were klebsiella pneumonia and 1 was positive for streptococcus pneumonia organisms by 72hrs, by culture. All the positive cases were male patients. The mean age of the positive patients -48 years

Total no. of patients	Patients positive for SBP	Positive by PMN count >250/mm^3	Positive by culture	Males	Females
100	16	3	13	16	0

Table 10: prevalence of SBP in study population

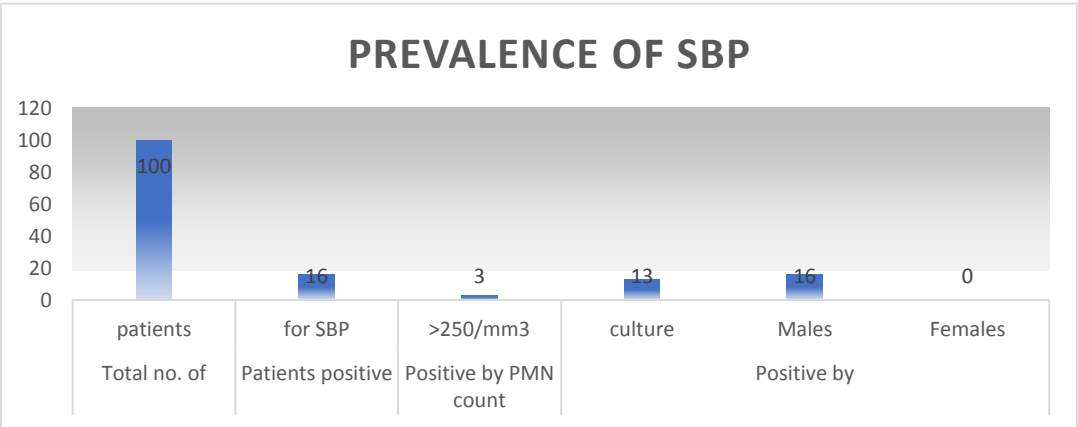


Chart 11: prevalence of SBP in study population

CULTURE POSITIVITY

Among the 16 cases of SBP, 13 cases were culture positive for various organisms which includes Spontaneous bacterial peritonitis with culture positive SBP and Mono-bacterial non-neutrocytic peritonotis. In that E. coli positive in 10 cases, Klebsiella pneumonia grown in 2 cases and streptococcus pneumonia grown in 1 cases of ascitic fluid.

CULTURE POSITIVITY		
	Frequency	**Percent**
NEG	87	87.0
POSI	13	13.0
TOTAL	100	100.0

Culture positivity and negativity among study group

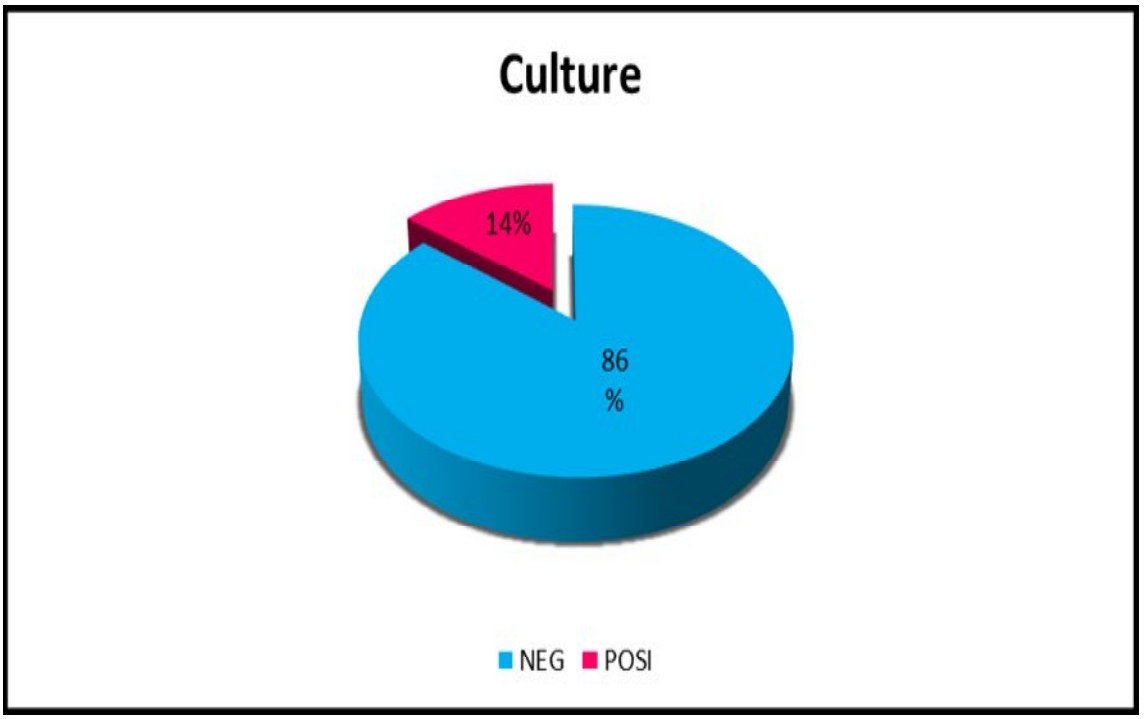


Chart 12: distribution of culture positivity among study population.

The culture positivity in our study was around 13%. In which about 10 cases were positive for E. Coli. Its around 76.92% of culture positive cases were shown E.coli in their culture. 2 cases were positive for klebsiella i.e. about 14.28% of patient's culture shown. Only one case positive for streptococcus pneumonia in ascitic fluid i.e. 7.17% of total culture positive SBP.

	Frequency	Percent
NIL	87	87.0
E.COIL	10	10.0
KLEBSIELA	2	2.0
STREPTO	1	1.0
TOTAL	100	100.0

Table 11: Total number of culture positive ascites cases

MICROBIOLOGICAL SPECTRUM

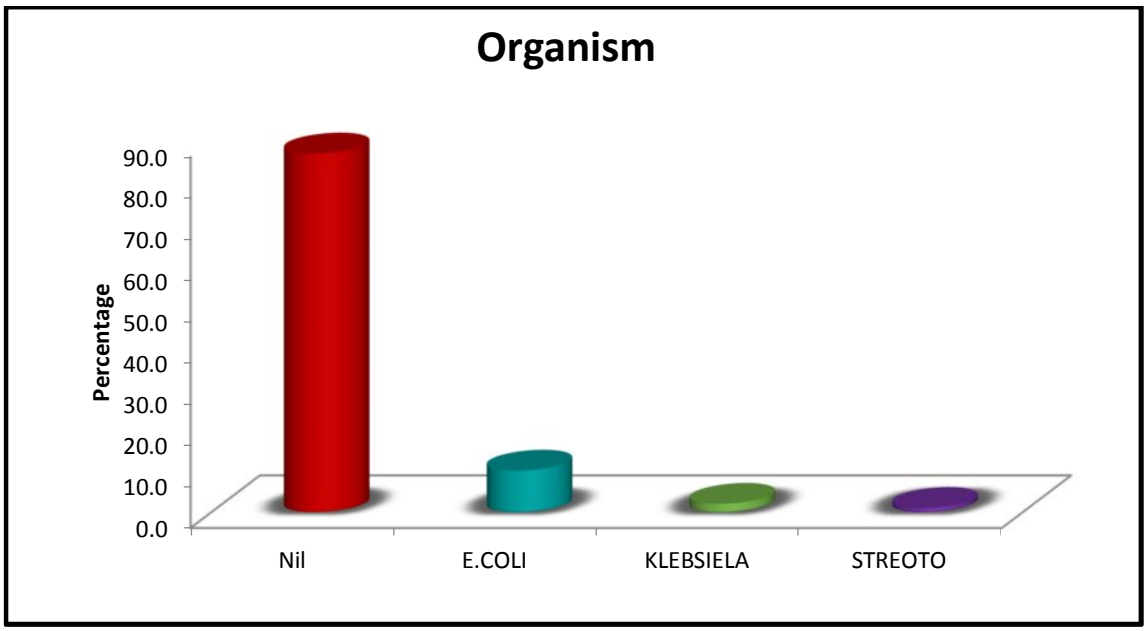


Chart 13: Microorganism distribution among the SBP in study group.

CPT SCORE COMPARISION WITH SBP.

Among 100 cases, only 16 patients found to have SBP. It was determined either by raised PMN cell count and/or culture positivity. So the prevalence of study is about 16%. The CPT score was calculated as per the formula mentioned in previous section. In our study most of cases under Class B followed by Class A and B

CPT CLASSIFICATION		
	Frequency	**Percent**
A	22	22.0
B	65	65.0
C	13	13.0
Total	100	100.0

Distribution of child pugh's classification.

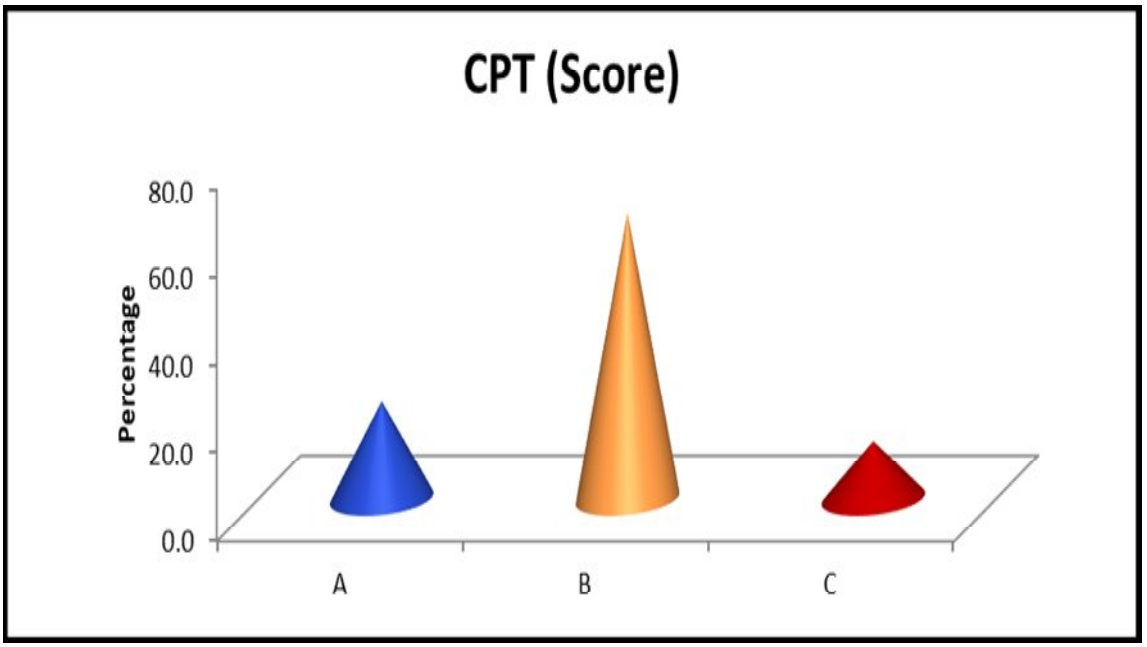


Chart 14: Distribution of cases as per CPT score

After calculating the correlation between CPT score and SBP prevalence in our study was highly significant at P <0.05.

CPT CLASS	No. of cases	Positive for SBP	PMN >250 CELLS/ CUMM	Culture positive	Percentage
CLASS A	22	0	NIL	NIL	**0%**
CLASS B	65	8	8	5	12.30%
CLASS C	13	8	8	8	62%

Table 12: Variants of SBP in CPT of liver disease

Most of the cases fit in the Class B with 65 cases. Class A was occupied by 22 cases and Class C by 13 cases. In our study the cases with Child Pugh's score as Class C were 13. Among the 13, 8cases (61.5%) had SBP, 65 cases were in CPT class B

among which 8(12.3%) had SBP. Among the culture positive, 8 out of 13 were in Class C. In the cell count criteria 8 out of 13 were in class C, but when combined 8 out of the 13 were in Class C. Among the culture positive, 8 out of 65 were in Class B. In the cell count criteria 8 out of 65 were in class B, but when combined 6 out of the 65 were in Class B.

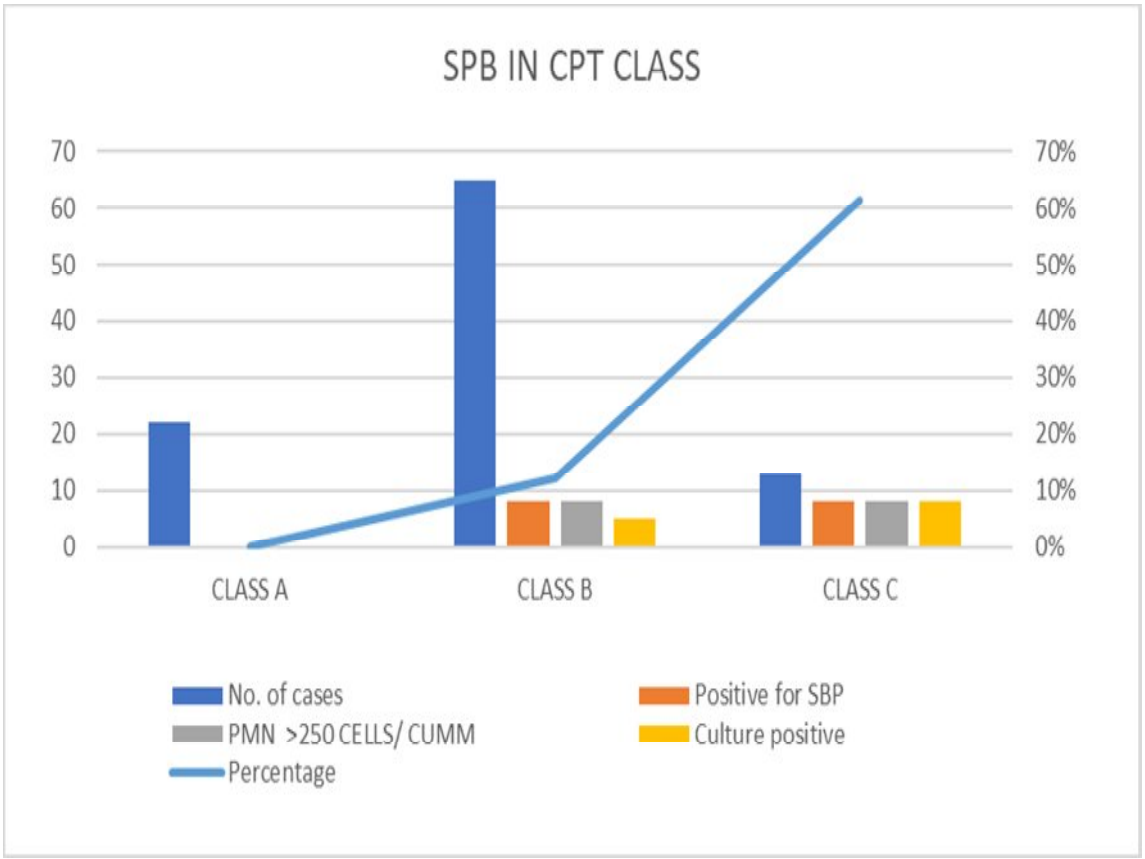


Chart 15: Variants of SBP distribution in CPT class.

CORRELATION WITH SERUM BILIRUBIN AND SBP

The raise of serum bilirubin was studied with correlation to occurrence of spontaneous bacterial peritonitis also evaluated.

Total bilirubin (mg/dl)	no. of cases	positive	percentage
0-2	92	0	0
>2	8	8	100%

Table 13: correlation with serum bilirubin and SBP

In our study, serum bilirubin study revealed that all the 8 out of 13 culture positive patients were having serum bilirubin more than 2, high cell count 8 out of 16 high count patients were showing high bilirubin and when both are positive 8 out of 14 were having hyperbilirubinemia.

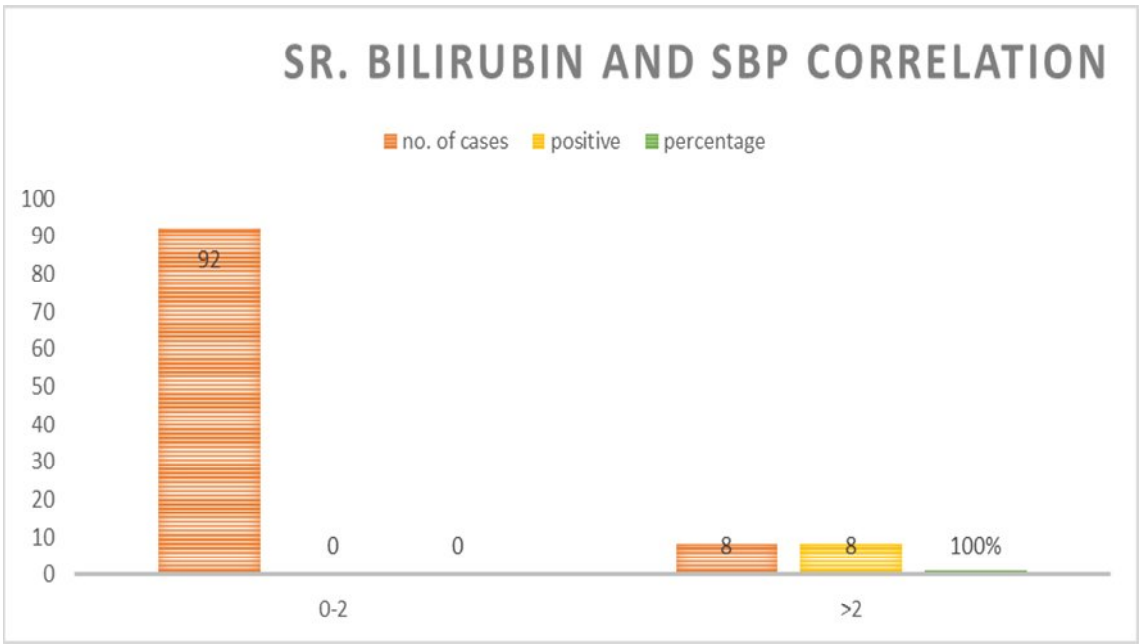


Chart 16: Sr. bilirubin and SBP correlation

VARIENTS OF SBP IN OUR STUDY

TYPES OF SBP	PMN COUNT	CULTURE	NO. OF CASES
SBP	>250	Positive	12
CNNA	>250	Negative	3
MNB	<250	Positive	1
Secondary Bacterial peritonitis	250	Positive	0
Poly microbial peritonitis	<250	Positive	0

There were 12%SBP (culture positive), 3%CNNA (only high cell count), Mono-bacterial ascites was 1% (only organism grown in culture) observed in our study conducted in tertiary care hospitals Salem.

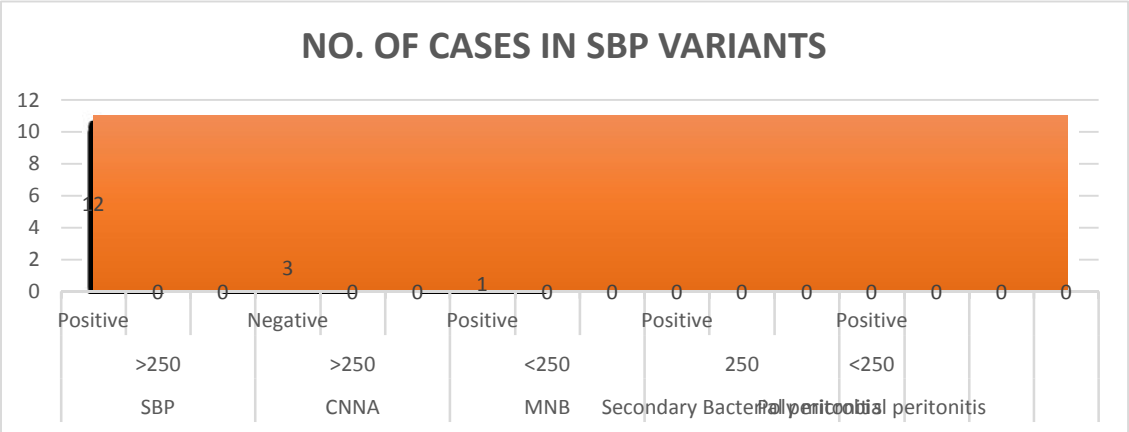


Chart 1: Prevalence of variants in our study

COMPARISON OF SBP WITH ASCITIC FLUID PROTEIN LEVEL

Ascitic fluid protein	No. of cases	PMN >250 cells	Culture positive	Both	Percentage of positive cases
<1g/dl	25	9	8	8	36%
>1g/dl	75	6	5	5	8%

Table 14: Comparison of sbp with ascitic fluid protein level

Next ascitic fluid protein levels were correlated. As mentioned in the Some literatures, the ascitic fluid protein level has a strong predilection for development of ascetic fluid infection due to the reduced action of the reticuloendothelial system due to reduced opsonin level in the ascitic fluid.

In our study, it was found that among the 13 positives for SBP 8 had protein level in the ascitic fluid less than 1 g/dl. So, comparing with the protein level of non SBP cases, the values were significant, when compared to other studies.

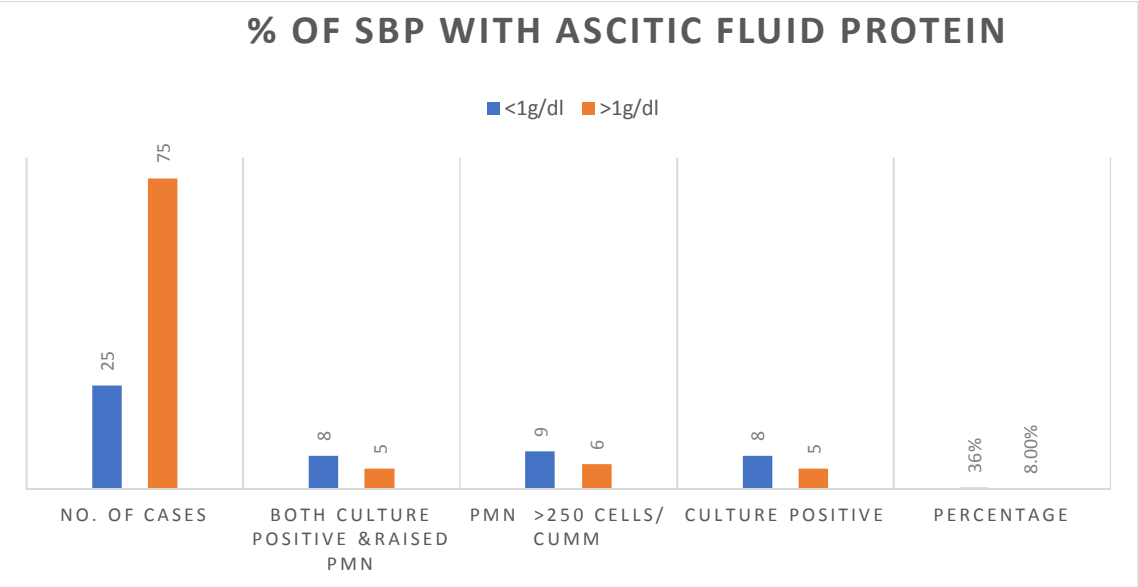


Chart 18: comparison of SBP with ascitic fluid.

DESCRIPTIVE ANALYSIS

	N	Minimum	Maximum	Mean	S.D
Age	100	20.0	73.0	47.47	10.18
Duration of Cirrhosis (yrs)	100	0.0	10.0	4.24	1.96
Cell Count	100	8.0	600.0	111.93	135.56
Sugar	100	30.0	136.0	72.81	19.28
Protein Alb	100	.1	1.8	0.93	0.44
Protein Glob	100	.10	2.00	0.69	0.39
SR.bil	100	.3	4.6	1.70	0.99
SGOT	100	20.0	140.0	61.94	27.43
SGPT	100	20.0	140.0	58.00	27.98
Sr.Protein Alb.	100	1.8	4.0	2.93	0.54
Sr.Protein GL.	100	2.2	4.8	3.36	0.55
PT(sec)	100	13.6	40.0	22.50	5.31
Valid N (listwise)	100				

Table 15: Biochemical values of descriptive data of study group.

This is the overall descriptive data of biochemical values obtained from the study group.

MODE OF PRESENTATION SBP CASES:

Among the 100 patients studied 18 patients presented with fever, 4 presented with vomiting and 17 patients presented with altered sensorium. In 18 patients who presented with fever, 11 patients were had SBP (61%), 7 patients were having PMN count >250/mm3 (i.e. CNNA) and 1 was culture positive (i.e. MNB).

17 patients presented with altered sensorium all the 13 patients were positive for SBP among the 13 positive cases 10 culture positive (E. coli), MNB was 1 and the other 3 had only PMN count >250/mm^3 (CNNA). In our study, presence of Jaundice had significant correlation with SBP, and also the degree of Jaundice is an indicator of ascitic fluid infection.[12]

Comparing signs & symptoms and incidence of SBP about 21 patients had abdominal tenderness, among these 16 patients were positive for SBP. 3 patients had ascitic fluid neutrophil count >250/mm3 (CNNA) and 1 was culture positive (MNB) without raising PMN cell count.[9] On admission 12 patients had Asterixis, in these 12 patients 9 patients were positive for SBP and rest of the 3 were positive by PMN count >250/mm3 (CNNA). Among the 18 patients who had admitted with fever 10 were positive for SBP, 3 cases had PMN count>250/mm3 (CNNA) and 1 case was culture positive (MNB). In this study 13 patients had Jaundice in which only 16 were diagnosed SBP and 17 patients admitted with altered sensorium, in which 11 were positive for SBP. And 3 were CNNA (PMN count >250/cu.mm).

Serum bilirubin levels in this study patient's valvue ranges from 0.3 to a maximum of 4.6mg/dl MEAN –61.70mg/dl with SD of +0.99. Maximum number of positive individuals for SBP were seen in patients whose total serum bilirubin was more than 2mg/dl. The higher the derangement of Liver function more the chances of getting SBP. Dysfunctional liver is unable to detoxify the toxic organisms and substance, leading SBP and other complication of DCLD.

DISCUSSION

Spontaneous Bacterial Peritonitis is a life-threatening complication in a decompensated liver disease patient that is characterised by an infection of the ascitic fluid by translocation of microbes from GUT. In the absence of any foci of inflammation. So, a prompt diagnosis of the disease is essential as the mortality of the disease is very high if not treated early.[2]

This study conducted in tertiary care medical college hospital in Salem regarding the prevalence, clinical spectrum and risk factors identification in the case of ascites with clinical features of Spontaneous Bacterial Peritonitis was done in a period of 1 year. 100 cases were selected as per the inclusion and exclusion criteria. The samples were analysed sent for analysis and the results were taken for the study purpose with benefit to the patient.

Among the 100 patients studied, majority of the study cases were consisting of males about 95%. Also, it was found that the around 90% of the study group were alcoholics. The duration of cirrhosis was varying from 2 to 10 years and as shown in chart above, the duration of the cirrhosis has no correlation with the occurrence of SBP.

With respect to the cell count, about 14% of the study population has a cell count of more than 250 /cu.mm. The highest value in the study population was 600 / cu.mm. The lowest was 8 cells/HPF. Among the study population only 3% of the patients had Culture Negative Neutrophilic Ascites (CNNA),[32] 11% culture positive ascites, both culture positive and high count in 10% and 1% mono bacterial ascites.

The culture report of the study showed that majority were gram negative bacilli, E.coli is the most common seen on 10 out of the 13 culture positive analysis. 2 were Klebsiella pneumonia and 1 was Streptococcus.

As the case definitive criteria was fulfilled by 16 cases cell count more than 250 /cu.mm or 13 cases were culture positivity, cases fulfilled the criteria. So, the prevalence of Asymptomatic SBP was 16%. Patients coagulation status was assessed by analysing the PT time.

The Child pugh's criteria was calculated by using the multiple parameters and the cases were classified. Most of the cases fit in the Class B with 65 cases. Class A was occupied by 22 cases and Class C by 13 cases.

The bilirubin levels were found to 22 patients showing hyperbilirubinemia and 78 patients with normal bilirubin levels due end stage liver disease like cirrhosis.

Next ascitic fluid protein levels were correlated. As mentioned in the some literatures, the ascitic fluid protein level has a strong predilection for development of ascetic fluid infection due to the reduced action of the reticuloendothelial system due to reduced opsonin level in the ascitic fluid.

In our study, it was found that among the 13 positives for SBP 8 had protein level in the ascitic fluid less than 1 g/dl. So, comparing with the protein level of non SBP cases, the values were significant, when compared to other studies.

Next is the Child Pugh's score and its correlation with SBP. As mentioned in various gastroenterology literature, the severity of Child Pugh Turcotte's score has a

strong predilection with formation and worsening of SBP. In our study the cases with Child Pugh's score as Class C were 13. Among the 13, 7cases (53.8%) had SBP, 65 cases were in CPT class B among which 7(10.7%) had SBP.

The 90 % of the population were alcoholics in which about 70-75% had not abstained from alcohol. But there was no significant link between the pathogenesis of SBP or rather the occurrence as the non SBP group population also was having a lot of alcoholics. Alcoholism itself, do not aggravate the risk of development of SBP. But following a binge intake of alcohol, vomiting leads to severe retching leading to Mallory Weiss tear in LES or fundus of the stomach or a bout of hematemesis will lead to SBP. And also, complication of aspiration i.e. pneumonia can precipitate SBP.

High bilirubin levels roughly 80 % of the patients had no direct impact in the SBP population. As the hyperbilirubinemia was also found in patients without SBP too and hence we cannot take this as a significant one. But it has an indirect correlation as incorporated into the Child pugh's criteria.

Now considering about the individual case of SBP i.e. one with cell count more than 250 and those with culture, some more deductions were made. In correlation with the protein level in ascitic fluid, when taking culture alone 8 of the 13 patients were having less than 1 g/dl. But when cell count alone is taken into consideration, 9 out of the 16 patients were having less than 1 g/dl of ascitic fluid cell count.

When both were positive i.e. high count and culture positive, 8 out of 12 cases having ascetic fluid protein less than 1 g/dl.

Next in line of correlation is the Child Pugh's Classification. Among the culture positive, 7 out of 13 were in Class C. In the cell count criteria 8 out of 13 were in class C, but when combined 7 out of the 13 were in Class C.

Among the culture positive, 7 out of 65 were in Class B. In the cell count criteria 8 out of 65 were in class B, but when combined 6 out of the 65 were in Class B.

Bilirubin study revealed that all the 8 out of 13 culture positive patients were having serum bilirubin more than 2, high cell count 8 out of 16 high count patients were showing high bilirubin and when both are positive 8 out of 14 were having hyperbilirubinemia.

Alcoholism and SBP variants were correlated as follows. All the culture positive patients were alcoholic, all high cell count variant patient were alcoholic and when combined again all of them were alcoholics.

There were 12%SBP (culture positive), 3%CNNA (only high cell count), Mono-bacterial ascites was 1% (only organism grown in culture) observed in our study conducted in tertiary care hospitals Salem.

All the patients were started on antibiotics after the paracentesis as the risk of iatrogenic infection was considered. After the results came out, the definitive management was given i.e. Inj. Cefotaxime 2 g iv TDS. The patients drastically improved after antibiotic.

The patients with CPT (Child Pugh's score) as Class C were also given other supportive measures after the samples were taken and then they were administered with clotting factors, albumin infusion and other supportive measures initiated.

As seen in other study, the various other parameters like the transaminases (SGOT and SGPT) had no relation with the disease outcome of this study. In none of the cases, the transaminases were significantly raised. Transaminases are raised only in states of acute liver cell injury and none of the study cases expected to have the same. Other measures like the usage of L-ornithine and L- aspartate and hepatoprotective drugs has been used to prevent complications

All the patients involved in this study were under regular follow up after 2 weeks and so on. None of them had worsened. All the patients improved with the treatment and there was no mortality noted, all were discharged and kept under regular follow up.

SUMMARY

Spontaneous Bacterial Peritonitis is a life-threatening complication of cirrhosis of liver. The main pathophysiology of ascites is attributed to the translocation of the gut microorganisms via the mesenteric lymph nodes that gain access to the peritoneal cavity. SBP was coined by Fennel. One of the most common organisms attributed to the infection is Escherichia coli. In general, Gram-negative bacilli occupy the majority of causative organism with Gram positive cocci like streptococci next and lastly by Anaerobic organism.

The mortality SPB is very high. In hospital mortality generally ranges from 10 to 30 % before the advent of antibiotics, the mortality was as high as up to 90%.

The study was conducted in our hospital in patients admitted in the Medical emergency ward medical IMCU and medical ward. 100 patients were selected after scrutiny.

The ascitic fluid analysis was done after obtaining written consent with the patient and their relatives. Patients were started on prophylactic antibiotics after the procedure. There was no mortality noted in the study group during the study period.

Among the 100 patients only 14 patients were found to have SBP which brings the prevalence up to 14%. The patients with cell count more than 250 cells/cu.mm. were 14 and the culture positive cases were 11 among the population. The Child pugh's scoring was calculated in the patients and it was seen that 65 patients came under the Class B, 13 came under Class C and the rest of the 22 were under Class A.

The serum total bilirubin and the serum transaminases levels showed no correlation with the incidence of SBP in the study population. The protein level in the ascitic fluid and the occurrence of SBP were well correlated in this study. Out of the 14 patients, 8 patients had low ascitic fluid protein level of less than 1 g/dl which has significant correlation. And it was found that there was a strong correlation with the child pugh's criteria and the incidence of SBP. Among the patients 14 patients, 7 were in class C according to the child pugh's criteria. These result were analysed statistically, it showed significance at $p<0.05$.

So, at the end of conclusion, the prevalence of SBP is low in our tertiary care institute and SBP has strong a correlation with low protein levels in ascitic fluid and Child Pugh's criteria.

CONCLUSION

After the analysis, we have come to a conclusion that the prevalence of SBP is very low at **16%** . where as high prevalence of SBP 29% observed in similar study done by Amarapurkar N et.al from india and SBP of 22% observed in Andreu et. Al study

There is also a strong correlation between low ascitic fluid protein level (<1g/dl) and SBP. Like similar study conducted by Amarapurkar DN et. al

Among the study population, the majority of the patients with SBP had Child Pugh's criteria in Class C. This was also correlated well in our study. Like similar study conducted by Jain et.al

So, to conclude

1) The prevalence of Spontaneous Bacterial Peritonitis is low as 16% cirrhotic patients with ascites.
2) Classical SBP 11%, CNNA 3% and MBA1% is seen in patients with ascites.
3) E. Coli is the most common organism, next to that klebsiella pneumonia and streptococcus grown in our study.
4) SBP almost commonly seen in alcoholics.
5) Low levels of ascitic fluid protein, high serum bilirubin and class C CPT score are risk factor for ascites.
6) Fever, asterixis, abdominal tenderness and altered sensorium are common with SBP.

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PATIENT CONSENT FORM

STUDY TITLE:

"A CLINICAL STUDY OF RISK FACTORS AND CLINICAL FEATURES IN PATIENTS OF SBP WITH CIRRHOSIS AND ASCITES IN A TERTIARY CARE HOSPITAL SALEM''

DEPARTMENT OF GENERAL MEDICINE, GMKMCH SALEM

PARTICIPANT NAME : AGE : SEX: I.P. NO :

I confirm that I have understood the purpose of surgical/invasive procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the possible complications that may occur during and after medical/ surgical procedure. I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

I hereby consent to participate in this study for various surgical/invasive procedures and their outcomes.

Time :

Date : Signature / Thumb Impression Of Patient

Place : Patient's name:

Signature of the Investigator : _____

Name of the Investigator _____

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சி தலைப்பு:

பெயர்	:	தேதி	:
வயது	:	உள்நோயாளி எண்	:
பாலினம்	:	ஆய்வு சேர்க்கைஎண்	:

இந்த ஆய்வின் நோக்கம் மற்றும் விவரங்கள் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. இவ்வாய்வில் இருந்து நான் எந்த நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எனக்கு எந்த பாதிப்பும் இல்லை என்பதையும் தெளிவாக புரிந்து கொண்டேன்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆய்வின் போதோ என்னுடைய பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டார்கள் என்பதையும் அறிந்து கொண்டேன்.

இந்த ஆய்வில் எவ்வித நிர்பந்தமும் இன்றி எனது சொந்த விருப்பத்தின் பேரில் நான் பங்கு பெறுகின்றேன்.

நான் சுயநினைவுடனும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் சேர்த்துக்கொள்ள சம்மதிக்கின்றேன்.

ஆராய்சியாளர் ஒப்பம் பங்கேற்பாளர் ஒப்பம்

(அ)

இடது பெருவிரல் ரேகை

PROFORMA

"A CLINICAL STUDY OF RISK FACTORS AND CLINICAL FEATURES IN PATIENTS OF SBP WITH CIRRHOSIS AND ASCITES IN A TERTIARY CARE HOSPITAL SALEM "

PATIENT DETAILS :

- Name :
- Age/sex:
- IP. Number:
- Ward/Unit :
- Date of study :

PARTICULARS:

- Past history
- Complete blood count
- Peripheral smear study
- Blood culture
- Urine culture
- Ascitic fluid analysis for biochemical, cytological and culture & sensitivity
- Renal function test
- Serum electrolytes
- Liver function test
- Urine routine
- USG abdomen

Other investigations like sputum AFB, sputum culture and chest x ray, were done whenever indicated.

KEY TO MASTER CHART

1. PML – Poly Morphonuclear Leucocyte
2. A – Albumin
3. G – Globulin
4. PT – Prothrombin Time
5. Bili – Bilirubin
6. M – Male
7. F – Female
8. CPT – child pugh's Turcotte score