ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 16, Issue 7, 2023

Online - 2455-3891
Print - 0974-2441

Research Article

CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS PRESENTING WITH ASCITES IN A TERTIARY CARE HOSPITAL

SOUMYA DALABEHERA[1], SRIPRASAD MOHANTY[2], BIJAYA KUMAR BEHERA[3]*

[1]Department of General Medicine, Postgraduate Institute of Medical Education and Research and Capital Hospital, Bhubaneswar, Odisha, India. [2]Department of General Medicine, MKCG Medical College and Hospital, Berhampur, Odisha, India. [3]Department of General Medicine, SCB Medical College and Hospital, Cuttack, Odisha, India. Email: drbkbehera@gmail.com

Received: 04 February 2023, Revised and Accepted: 20 March 2023

ABSTRACT

Objectives: Ascites is one of the common clinical problems confronting a physician, with a myriad of causes behind. Early detection and evaluation of the causes of ascites help in effective management and lessens complications. However, there is lack of data regarding the prevalence of causes of ascites in our set-up. Hence, this study was conducted in our tertiary care hospital to study the clinical profiles and etiological factors of patients with ascites.

Methods: This prospective and observational study was carried out in the Department of General Medicine of S.C.B. Medical College and hospital, Cuttack, Odisha, India, from September 2019 to November 2021. Hundred patients of ascites of either sex >18 years of age admitted in the medicine ward fulfilling the inclusion and exclusion criteria were included in this study and were thoroughly evaluated after obtaining informed consent. All the patients were subjected to detailed history taking, thorough physical examination and routine laboratory evaluation such as complete blood count, random blood sugar, liver function test, renal function test, serum protein and albumin, serum electrolytes, prothrombin time, international standardized ratio, hepatitis B surface antigen, and antibody to hepatitis C. Hepatic encephalopathy, when present, was classified into four grades according to West Haven criteria. Ultrasonography of abdomen and pelvis, Digital chest X-ray PA view, and ECG were done in all the patients.

Results: In the present study of 100 patients, major cause of ascites was found to be cirrhosis of liver (64%) followed by tuberculosis (10%), malignancy (9%), heart disease (7%), and nephrotic syndrome (3%). The major cause of the cirrhosis of liver was alcoholism (64%) followed by hepatitis B (15.6%), Non-alcoholic steatohepatitis (14.1%), Hepatitis C (4.7%), and cryptogenic (3.1%). Complications such as hepatic encephalopathy and spontaneous bacterial peritonitis were observed in 17% and 7.8% cases of ascites, respectively.

Conclusion: Cirrhosis of liver was found to be the most common cause of ascites in our study followed by tuberculosis and malignancy. Alcoholism was the most common cause of cirrhosis followed by chronic hepatitis B.

Keywords: Ascites, Peritoneal cavity, Cirrhosis of liver, Nonalcoholic steatohepatitis.

 DOI: http://dx.doi.org/10.22159/ajpcr.2023v16i7.47489. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Ascites, the pathologic accumulation of fluid in the peritoneal cavity, is a commonly encountered condition in clinical practice and is an important clue to an underlying illness. This may be due to a pathology localized to the peritoneal cavity or secondary to an underlying systemic illness [1]. Due to its diverse clinical condition, it is imperative to know the epidemiology of the various causes of ascites prevailing in our set-up which would give important clues to physicians while evaluating and managing a case of ascites. The objective of the study is to assess the clinical and etiological profiles of patients presenting with ascites in a tertiary care hospital.

The underlying mechanism of development of ascites can involve elevated hydrostatic pressure (e.g., cirrhosis and congestive heart failure), decreased oncotic pressure (nephrotic syndrome), increased peritoneal fluid production compared with resorption (neoplasms), or a combination all these factors [2].

The presence of ascites is frequently obvious from the clinical history, physical examination, and is confirmed by abdominal imaging, ultrasonography being the most sensitive and cost-effective [3]. However, it is important to evaluate the patient thoroughly and reach at a definite cause of development of ascites.

The majority (75%) of patients who present with ascites have underlying cirrhosis, with remainder being due to malignancies (10%), heart failure (3%), tuberculosis (2%), pancreatitis (1%), and other rare causes [4]. The rare causes include constrictive pericarditis, inferior vena cava obstruction, hepatic vein thrombosis, sinusoidal obstruction syndrome, portal vein thrombosis, non-cirrhotic portal hypertension, nephrotic syndrome, biliary leak, hypothyroidism, and familial Mediterranean fever.

The etiology of ascites is best determined by a bedside procedure known as "diagnostic paracentesis," which is considered to be a safe procedure with serious complications occurring very rarely. After extracting the ascitic fluid, it should be analyzed for total cell count, differential count, total protein, albumin, and calculation of Serum Ascites Albumin Gradient (SAAG) in all the patients. Tests such as ascitic fluid culture, Gram's stain, staining for acid-fast bacilli, cytology, glucose, lactate dehydrogenase (LDH), amylase, triglyceride, and adensoine deaminase activity are ordered only when indicated in special clinical circumstances [5].

The development of ascites in a patient with cirrhosis is suggestive of progression to a decompensated state and it heralds a very poor prognosis as the survival rate drops significantly [6]. The diagnosis of malignant ascites also carries a grave prognosis with a survival period of only about 20 weeks without intervention [7].

Treatment depends on the underlying cause. Ascites due to portal hypertension typically responds to dietary salt restriction and use of diuretics. When these measures fail, procedures such as large volume paracentesis, transjugular intrahepatic portosystemic shunt, and

peritoneovenous shunt are the next line of management. Ascites unrelated to portal hypertension usually do not respond to low-salt diet and diuretics. These cases need treatment of the underlying cause. When the underlying disease cannot be cured and patient needs symptomatic relief from the discomfort caused by ascites, palliative measures, such as repeated large volume paracentesis, placement of peritoneal drain should be offered.

There is lack of data with respect to etiologies underlying ascites and their correlation with clinical profiles in our set-up. As prognosis and treatment decisions are largely dependent on the underlying etiology, this study is envisioned to evaluate the cases of ascites presenting to our hospital in terms of clinical features, laboratory investigations, and radiological tests as deemed appropriate to reach at a definite cause.

METHODS

A prospective and observational study was designed and conducted in the Department of General Medicine in SCB Medical College and Hospital, Cuttack, Odisha, India, over a period of 2 years from September 2019 to November 2021. Ethical clearance was obtained from the Institutional Ethics Committee before the commencement of the study. A total number of 100 patients of ascites of either sex above the age of 18 years admitted to the Department of Medicine fulfilling the inclusion criteria were taken in this study and were thoroughly evaluated after obtaining informed consent. The study was done in accordance with the guidelines of the Declaration of Helsinki 2008.

Inclusion criteria

The following criteria were included in the study:

- >18 years age
- Patients presenting with ascites confirmed clinically or by ultrasonography.

Exclusion criteria

The following criteria were excluded from the study:

- Pregnant patients
- Those who fail to give consent
- Critically ill patients.

Baseline data including sociodemographic profile, chief complaints, detailed history, and other relevant information of all the patients were collected using a pre-designed semi-structured questionnaire. Appropriate physical and laboratory examinations such as complete blood count, random blood sugar, liver function test, renal function test, serum protein and albumin, serum electrolytes, prothrombin time, international standardized ratio, hepatitis B surface antigen, antibody to hepatitis C, and hepatic encephalopathy, when present, was classified into four grades according to the West Haven criteria. Ultrasonography of abdomen and pelvis, digital chest X-ray PA view, and ECG were done in all the patients. All patients underwent that diagnostic paracentesis and ascitic fluid were analyzed for its gross appearance, total protein, albumin, total cell count, differential count, Gram's stain, Ziehl-Neelsen (ZN) stain, culture, adenosin deaminase (ADA), catridge-based nucleic acid amplification test (CBNAAT), and cytology. SAAG was calculated by subtracting the ascitic fluid albumin from a simultaneously obtained serum albumin. Ascitic fluid measurement of glucose, amylase, LDH, triglyceride was done only in relevant situations. Upper gastrointestinal (GI) endoscopy was performed in all the patients, unless contraindicated.

Serological markers of autoimmune hepatitis (anti smooth muscle antibodies, antibodies to liver kidney microsome Type 1, and antinuclear antibodies), serum ceruloplasmin, 24-h urinary copper, slit lamp examination for Kayser-Fleischer ring, serum ferritin, and transferrin saturation were sent, if indicated. All obese patients in whom other causes of ascites were ruled out, non-alcoholic steatohepatitis was presumed to be the cause of cirrhosis. When the etiology of cirrhosis could not be established after these investigations, it was labeled as cryptogenic. CT scan of abdomen and pelvis was done when ultrasound was inconclusive and in patients suspected of intra-abdominal or gynecological malignancies. Colonoscopy was done in selected cases to look for pathologies of rectum and colon. 2D echocardiography was performed when cardiac disease was thought to be responsible for the ascites. When nephrotic syndrome was suspected, serum lipid profile and 24-h urinary protein were measured. Any biopsy specimen obtained was sent for histopathological study. Severity of cirrhosis of liver was assessed using Child-Pugh score (also known as Child-Pugh-Turcotte score) which predicted mortality in these patients.

Statistical analysis

The data were entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for the Social Sciences version 21.0.

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean±SD and median. Normality of data was tested by Kolmogorov–Smirnov test. When the normality was rejected then non-parametric test was used.

Statistical tests were applied as follows:
Quantitative variables were compared using one-way ANOVA/Kruskal–Wallis test (when the data sets were not normally distributed) between groups. Qualitative variables were correlated using Chi-square test/Fisher's exact test. $p<0.05$ was considered statistically significant.

RESULTS

In the present study of 100 patients with ascites, the mean age of the study participants was 45.65±13.28 years with a minimum of 18 years to a maximum of 72 years. Age group-wise distribution suggested that majority belonged to 35–50 years age group (40%) followed by above 50 years (34%) and <35 years (26%). Majority of the study participants were males (62%). The details of age and gender distribution among the study participants are shown in (Table 1 and Figs. 1-3).

According to risk factors for ascites, alcoholism was present in 47% of the subjects while history of multiple sexual partners and contact history with jaundiced patient was observed in 5% of the subjects. Similarly, 5% of the subjects had history of blood transfusion (Table 2 and Fig. 4).

Table 1: Age and gender distribution of the study participants

Variables	Number	Percentage
Age		
<35 years	26	26
35–50 years	40	40
>50 years	34	34
Gender		
Male	62	62
Female	38	38

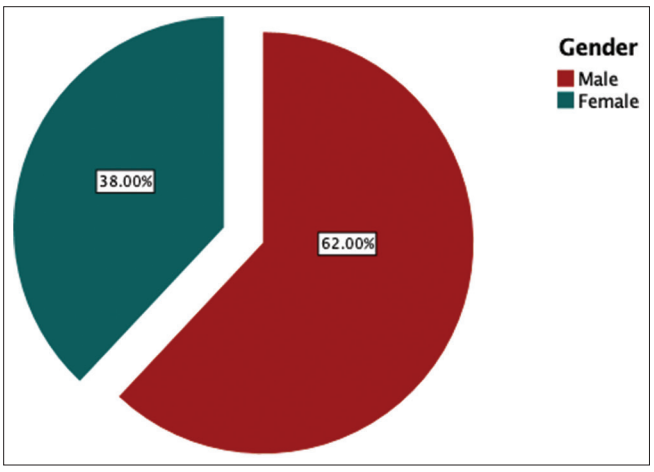

Fig. 1: Gender distribution of the study participants

Table 2: Distribution of risk factors among the study participants

Variables	Number	Percentage
Alcoholism		
Yes	47	47
No	53	53
Multiple sexual partner		
Yes	5	5
No	95	95
Contact history to jaundice patients		
Yes	5	5
No	95	95
History of blood transfusion		
Yes	5	5
No	95	95
Comorbidities		
Diabetes	10	10
Hypertension	9	9
Both DM and HTN	6	6
Old pulmonary TB	3	3
Hypothyroidism	2	2
None	70	70

Table 3: Clinical signs among the study participants

Variables	Number	Percentage
Peripheral edema		
Yes	64	64
No	36	36
Raised JVP		
Yes	8	8
No	92	92
Splenomegaly		
Yes	57	57
No	43	43
Hepatomegaly		
Yes	22	22
No	78	78

With respect to co-morbidities, 10% of the subjects were diabetic while 9% were hypertensive. Both diabetes and hypertension were present in 6% of the subjects. About 3% of patients had a history of pulmonary tuberculosis. Majority of the included patients had no other comorbidities (Table 3 and Fig. 5).

Peripheral edema was observed in 64% of the subjects while raised JVP was found in only 8% of the patients. Splenomegaly (57%) was more common than hepatomegaly (22%) (Table 3 and Fig. 6).

Anemia was highly prevalent among the ascitic patients as 97% were found to be anemic. High leukocyte count was observed in 18% of the subjects while low platelet count observed in 50% of the patients (Table 4 and Figs. 7 and 8).

Raised blood sugar level observed in 20% of the patients. Nearly, equal proportion of patients had increased serum urea (40%) and creatinine (37%) level. Electrolyte imbalances such as hyponatremia (44%), hypokalemia (25%), and hyperkalemia (18%) were also observed among the patients (Table 5 and Fig. 9).

Abnormally high total bilirubin level and direct bilirubin were found in 49% and 53% of the subjects. Liver enzymes such as SGPT (ALT), SGOT (AST), and ALP were increased in 64%, 78%, and 77% of the subjects, respectively. With respect to serum protein and albumin, we observed almost all patients had abnormal albumin levels (99%) while total protein level was deranged in 46% of the subjects. Prolonged prothrombin time was found in 89% of the subjects while prolonged INR was observed in 52% of the subjects (Table 6 and Fig. 10).

Table 4: Routine blood parameters among the study participants

Variables	Number	Percentage
Hemoglobin level		
Anemic	97	97
Non-anemic	3	3
Total leukocyte count		
Normal	82	82
High	18	18
Platelet count		
Low	50	50
Normal	48	48
High	2	2

Table 5: Laboratory parameters among the study participants

Variables	Number	Percentage
Random blood sugar		
Normal	80	80
Raised	20	20
Serum urea		
Normal	60	60
Abnormal	40	40
Serum creatinine		
Normal	63	63
Abnormal	37	37
Serum sodium		
Normal	56	56
Hyponatremia	44	44
Serum potassium		
Normal	57	57
Hypokalemia	25	25
Hyperkalemia	18	18

Table 6: Distribution of liver function test among the study participants

Variables	Number	Percentage
Total bilirubin		
Normal	51	51
Abnormal	49	49
Direct bilirubin		
Normal	47	47
Abnormal	53	53
SGPT		
Normal	36	36
Abnormal	64	64
SGOT		
Normal	22	22
Abnormal	78	78
ALP		
Normal	23	23
Abnormal	77	77
Serum protein		
Normal	54	54
Abnormal	46	46
Serum albumin		
Normal	1	1
Abnormal	99	99
Prothrombin time		
Normal	11	11
Prolonged	89	89
INR		
Normal	48	48
Prolonged	52	52

More than one tenth of the patients (14%) found positive for HbsAg while 5% had anti HCV antibodies (Table 7 and Fig. 11).

Mean ascitic fluid count was 529.50±354.51 leukocytes/μL, while the mean fluid protein level was 2.62±0.81 g/dL. Mean ascitic fluid ADA values were 18.30±14.25 IU/L. Mean SAAG was 1.14±0.29 g/dL (Table 8).

Ascitic fluid cytology was found to be positive for 5% of the subjects while CBNAAT was positive in only 2% of the subjects. High ascitic protein level, that is, ≥2.5 g/dL was observed in 38% of the patients. The SAAG ratio was observed to be ≥1.1 g/dL among 72% of the patients while it was <1.1 g/dL among the rest. None of the patients had a positive ZN stain result. Out of all the patients, 3% had a positive ascitic fluid culture result for *Escherichia coli* and *Streptococcus* (Table 9 and Fig. 12).

The major cause of ascites was found to be cirrhosis of liver (64%) followed by tuberculosis (10%), malignancy (9%), heart disease (7%), and nephrotic syndrome (3%). Other causes included Budd Chiari syndrome, portal vein thrombosis, extrahepatic portal vein obstruction (EHPVO), pancreatic causes, and hypothyroidism (Table 10 and Fig. 13).

The major cause of the cirrhosis of liver was alcoholism (64%) followed by hepatitis B (15.6%), non-alcoholic steatohepatitis (NASH) (14.1%), hepatitis C (4.7%), and cryptogenic (3.1%) (Table 11 and Fig. 14).

Endoscopic finding was normal in 29% of the subjects while rest had some form of abnormal finding. The major endoscopic finding was severe portal hypertensive gastropathy (PHG) (16%) closely followed by Grade 2 esophageal varices with severe PHG (15%) (Table 12 and Fig. 15).

Table 13 shows the association of sociodemographic factors with etiology of ascites. While ascites due to nephrotic syndrome affects younger age group (100%), the cirrhosis of liver mostly affects older age group (39%). This difference in proportion was statistically significant (p=0.044). Cirrhosis was mostly found in men (75% vs. 25%) while females were more affected by malignancy-related ascites (67%). This difference in proportion was statistically highly significant (p=0.005) (Table 13).

Edema was observed in all forms of ascites but mostly prevalent in heart disease and nephrotic syndrome (100%). Raised JVP was only observed in ascites due to cardiac abnormality (100%). Splenomegaly and hepatomegaly were mostly found in cirrhosis of liver patient. All these observations were statistically significant with p<0.05 (Table 14).

We compared laboratory findings of the patients according to different etiology of ascites. We found a statistically significant difference for anemia, serum urea, serum creatinine, total bilirubin, direct bilirubin, enzymes such as SGPT, SGOT, and serum albumin level (Table 15). Other parameters did not show any significant difference.

Similarly, prothrombin time, and INR had a significant association with etiology of ascites. Ascitic fluid protein was observed to be >2.5 g/dL among majority of patients having various etiological factors except for patients with chronic liver disease and these findings were very highly significant (p<0.001). Universally, all the patients with TB and nephrotic syndrome had SAAG ratio of <1.1 g/dL while majority of patients

Table 7: Distribution of HbsAg and HCV antibody among study participants

Variables	Number	Percentage
HbsAg		
Positive	14	14
Negative	86	86
HCV antibody		
Positive	5	5
Negative	95	95

Table 8: Ascitic fluid parameters among the study participants

Variables	Mean	SD	Range
Ascitic fluid count (leukocytes/μL)	529.50	354.51	50–1400
Ascitic fluid protein (g/dL)	2.62	0.81	0.50–5.80
Ascitic fluid ADA (IU/L)	18.30	14.25	1.9–59.3
SAAG value (g/dL)	1.14	0.29	0.3–2.6
Ascitic fluid amylase (u/L)	192.00	1612.80	3400–15800

SAAG: Serum ascites albumin gradient

Table 9: Ascitic fluid abnormality among the study participants

Ascitic fluid parameters	Number	Percentage
Cytology		
Positive	5	5
Negative	95	95
CBNAAT		
Positive	2	2
Negative	98	98
Protein		
<2.5 g/dL	62	62
≥2.5 g/dL	38	38
SAAG category		
<1.1 g/dL	28	28
≥1.1 g/dL	72	72
ZN staining		
Positive	0	0
Negative	0	0
Culture		
Positive	3	3
Negative	97	97

ZN: Ziehl-Neelsen, CBNAAT: Catridge-based nucleic acid amplification test, SAAG: Serum ascites albumin gradient

Table 10: Distribution of the cause of ascites among the study participants

Etiology of ascites	Number	Percentage
Cirrhosis of liver	64	64
Malignancy	9	9
Tuberculosis	10	10
Heart disease	7	7
Nephrotic syndrome	3	3
Others	7	7

Table 11: Distribution of the cause of cirrhosis among the study participants (n=64)

Etiology of cirrhosis	Number	Percentage
Alcohol	41	64
NASH	8	14.1
Hepatitis B	10	15.6
Hepatitis C	3	4.7
Cryptogenic	2	3.1

NASH: Non-alcoholic steatohepatitis

Table 12: Endoscopic findings among the study participants

Etiology of cirrhosis	Number	Percentage
Mild PHG	4	4
Severe PHG	16	16
Grade 1 esophageal varices	6	6
Grade 2 esophageal varices	5	5
Grade 3 esophageal varices	1	1
Grade 1 EV with severe PHG	9	9
Grade 2 EV with severe PHG	15	15
Grade 3 with severe PHG	8	8
Grade 2 with mild PHG	1	1
Others	6	6
Normal	29	29

PHG: Portal hypertensive gastropathy

Table 13: Association of etiology of ascites with sociodemographic factors

Variable	Cirrhosis n (%)	Malignancy n (%)	TB n (%)	Heart disease n (%)	Nephrotic syndrome n (%)	Others n (%)	p-value
Age (years)							
<35	16 (25)	1 (11)	2 (20)	2 (29)	2 (100)	2 (29)	0.044*
35–50	23 (36)	5 (56)	6 (60)	1 (14)	0 (0)	5 (71)	
>50	25 (39)	3 (33)	2 (20)	4 (57)	0 (0)	0 (0)	
Gender							
Male	48 (75)	3 (33)	4 (40)	1 (14)	2 (67)	4 (57)	0.005**
Female	16 (25)	6 (67)	6 (60)	6 (85)	1 (33)	3 (43)	

*statistically significant (p<0.05), **highly significant (p<0.01)

Table 14: Association of clinical signs with etiology of ascites

Variable	Cirrhosis n (%)	Malignancy n (%)	TB n (%)	Heart disease n (%)	Nephrotic syndrome n (%)	Others n (%)	p-value
Edema	46 (72)	2 (22)	3 (30)	7 (100)	3 (100)	3 (100)	0.001**
Raised JVP	0 (0)	0 (0)	0 (0)	7 (100)	0 (0)	1 (14)	<0.001***
Splenomegaly	55 (86)	0 (0)	0 (0)	0 (0)	0 (0)	2 (29)	<0.001***
Hepatomegaly	15 (23)	0 (0)	0 (0)	5 (71)	0 (0)	2 (29)	0.006**

*statistically significant (p<0.05), **highly significant (p<0.01), ***Very highly significant (p<0.001)

Table 15: Association of laboratory parameters with etiology of ascites

Variable	Cirrhosis	Malignancy	TB	Heart disease	Nephrotic syndrome	Others	P-value
Anemia	63 (98)	9 (100)	10 (100)	7 (100)	2 (68)	7 (100)	<0.001***
High leucocyte count	14 (22)	1 (11)	2 (20)	1 (14)	0 (0)	0 (0)	0.665
Low platelet count	44 (88)	0 (0)	1 (10)	2 (4)	0 (0)	3 (6)	<0.001***
Raised RBS	14 (22)	1 (11)	1 (10)	2 (29)	0 (0)	2 (29)	0.761
High serum urea	33 (52)	1 (11)	1 (10)	5 (71)	3 (100)	0 (0)	0.001**
High serum creatinine	28 (44)	2 (22)	1 (10)	5 (71)	1 (33)	0 (0)	0.024*
Hyponatremia	26 (41)	4 (44)	3 (30)	6 (86)	1 (33)	4 (57)	0.247
Hypokalemia	18 (28)	0 (0)	2 (20)	2 (29)	1 (33)	2 (29)	0.345
Hyperkalemia	14 (22)	0 (0)	2 (20)	2 (29)	0 (0)	0 (0)	0.342
Abnormal total bilirubin	44 (68)	1 (11)	2 (20)	1 (14)	0 (0)	1 (14)	<0.001***
Abnormal direct bilirubin	45 (70)	2 (22)	2 (20)	2 (28)	0 (0)	2 (28)	<0.001***
Abnormal SGPT	49 (77)	5 (56)	5 (50)	2 (29)	1 (33)	2 (29)	0.013*
Abnormal SGOT	58 (91)	6 (68)	6 (60)	3 (43)	0 (0)	5 (71)	<0.001***
Abnormal ALP	49 (77)	7 (79)	8 (80)	7 (100)	2 (68)	4 (57)	0.565
Abnormal serum protein	32 (50)	1 (11)	4 (40)	3 (43)	3 (100)	3 (43)	0.129
Abnormal albumin	64 (100)	9 (100)	10 (100)	6 (86)	3 (100)	7 (100)	0.020*

#Value in each cell shows number and percentages, *statistically significant (p<0.05), **highly significant (p<0.01), ***Very highly significant (p<0.001)

Table 16: Association of etiology with ascitic fluid parameters and coagulation profile of the study participants

Variable	Cirrhosis	Malignancy	TB	Heart disease	Nephrotic syndrome	Others	p-value
Prolonged prothrombin time (Sec)	64 (100)	6 (67)	6 (60)	5 (71)	1 (33)	7 (100)	<0.001***
Prolonged INR (Sec)	50 (78)	0 (0)	0 (0)	0 (0)	0 (0)	2 (29)	<0.001***
Ascitic fluid ADA							
<40 IU/L	63 (73.3)	6 (7)	0 (0)	8 (9.3)	3 (3.5)	6 (7)	<0.001***
>40 IU/L	01 (7.1)	3 (21.4)	9 (64.3)	0 (0)	0 (0)	1 (7.1)	
Ascitic fluid protein							
<2.5 g/dL	56 (90.3)	0 (0)	0 (0)	1 (1.6)	2 (3.2)	3 (4.8)	<0.001***
≥2.5 g/dL	8 (21.1)	9 (23.7)	9 (23.7)	7 (18.4)	1 (2.6)	4 (10.5)	
SAAG ratio							
<1.1 g/dL	4 (6)	7 (78)	10 (100)	1 (14)	3 (100)	3 (43)	<0.001***
≥1.1 g/dL	60 (97)	2 (22)	0 (0)	6 (86)	0 (0)	4 (57)	
Mean ascitic fluid cell count (Leucocytes/μL)	380.16±230.02	1166.67±139.01	951.11±249.32	488.75±154.49	306.67±197.31	675.71±450.77	<0.001***

#Value in each cell shows number and percentages. SAAG: Serum ascites albumin gradient, ADA: Adenosin deaminase, *statistically significant (p<0.05), **highly significant (p<0.01), ***Very highly significant (p<0.001)

with chronic liver disease (97%) and heart disease (86%) had SAAG >1.1 g/dL. This difference in proportion was very highly significant (p<0.001). The mean ascitic fluid cell count was found highest among those with any form of malignant etiology followed by patients with TB. Least value of mean ascitic fluid cell count was observed among patients with nephrotic syndrome. These findings were very highly significant with p<0.001 (Table 16).

Hepatic encephalopathy and spontaneous bacterial peritonitis were the complications observed among 11 (17.0%) and 5 (7.9%) study

participants, respectively. Majority of patients with liver cirrhosis had Grade 2 hepatic encephalopathy (9.3%) followed by Grade 3 (6.2%). Only 1 (1.5%) patient had developed Grade 4 hepatic encephalopathy (Table 17 and Fig. 16).

The Child's Pugh score used for assessing severity of liver cirrhosis categorized 60.9% and 39.1% of patients under Class B and C, respectively (Table 18 and Fig. 17).

Out of all the patients, 10 had peritoneal TB but upon ZN staining none of them showed a positive result. In contrast, CBNAAT showed a positive test result among 20% of patients of the same group. These findings were very highly significant with p<0.001 (Table 19).

More than half of the patients with one or the other kind of malignancy (55.5%) tested positive upon cytological analysis of ascitic fluid with p<0.001 (Table 20 and Fig. 18).

Out of 5 patients with spontaneous bacterial peritonitis, 3 had a positive result for ascitic fluid culture with *E. coli* as the dominant organism found in 2 and Streptococcus in one of them (Tables 21 and 22, Fig. 19).

Table 17: Complications among patients with liver cirrhosis

Variable	Number	Percentage
Hepatic encephalopathy		
Grade 1	00	0.00
Grade 2	06	9.3
Grade 3	04	6.2
Grade 4	01	1.5
Total	11	17.0
Spontaneous bacterial peritonitis	05	7.9

Table 18: Child-Pugh score among cirrhotic patients

Child-Pugh class	Number	Percentage
Class A (5–6 points)	00	00
Class B (7–9 points)	39	60.9
Class C (10–15 points)	25	39.1
Total	64	100.0

Table 19: Ascitic fluid parameters among patients with peritoneal TB

Ascitic fluid parameters	Peritoneal TB		p-value
	Present n (%)	Absent n (%)	
ZN stain			
Positive	00	00	-
Negative	10 (100)	90 (100)	
CBNAAT			
Positive	02 (20)	00	<0.001***
Negative	08 (80)	90 (100)	

ZN: Ziehl-Neelsen, CBNAAT: Catridge-based nucleic acid amplification test, ***Very highly significant (p<0.001)

Table 20: Cytological analysis of ascitic fluid among patients with malignancy

Ascitic fluid cytology	Malignancy n (%)		p-value
	Present	Absent	
Positive	5 (55.5)	00	<0.001***
Negative	4 (44.5)	91 (100.0)	

***Very highly significant (p<0.001)

Table 21: Ascitic fluid culture among all the study participants

Ascitic fluid culture	Number	Percentage
Escherichia coli	02	2.0
Streptococcus	01	1.0
None	97	97.0
Total	100	100.0

Table 22: Ascitic fluid culture among spontaneous bacterial peritonitis

Ascitic fluid culture	Number	Percentage
Escherichia coli	02	40.0
Streptococcus	01	20.0
None	02	40.0
Total SBP	05	100.0

DISCUSSION

In this prospective study of 100 patients with clinical ascites, the mean age was found to be 45.65±13.28 years. Majority were males (62%) and between 35 and 50 years. In a study conducted by Mehra *et al*. in Rohilkhand region of India, mean age of participants was 45.14 years and 61% were males and majority were in the age group of 31–50 years, similar to our finding [8]. In another study done by Muhie in Ethiopia, the mean age of ascites patients was 43.8 years and 57.7% were males, the values being approximately equal to our study, whereas in studies by Joshi *et al*., Khan, and Kumar *et al*., the mean age of patients were found to be 54.8, 52.9, and 51.5 years, respectively, which are higher than our findings [9-12].

Alcoholism was the most common risk factor in our study, observed among 47% of patients followed by equal proportions of patients with history of multiple sexual partners, blood transfusions, and contact with a jaundiced patient, that is, 5% each. Identical to our finding, alcohol was the dominant risk factor in other similar studies conducted by Muhie in Ethiopia and Kumar *et al*. in Himachal Pradesh [9,12].

Peripheral edema was observed in 64% of the subjects whereas raised JVP was seen in only 8% of cases. Splenomegaly and hepatomegaly were found in 57% and 22% of patients respectively. In the study of Joshi *et al*., hepatomegaly was seen in approximately similar no. of cases, that is, in 25% and 21.9% of patients, respectively [9,10]. Muhie found raised JVP in 26.9% of their patients, much higher than our finding, attributable to the higher number of heart failure cases in their study. Edema (48.1%) was seen in a lesser number of cases by Muhie probably due to higher mean albumin level in their study (2.8 g/dL vs. 2.73 g/dL). Splenomegaly and hepatomegaly were mostly found in cirrhosis patients whereas edema was observed in all the patients of heart disease and nephrotic syndrome and raised JVP was mostly seen in ascites due to cardiac etiology. All these observations were statistically significant with p<0.05.

Taking a note on etiological factors of ascites, the most common cause was cirrhosis of liver (64%). In Western countries, the major causes of ascites are cirrhosis of liver (75%) and malignancies (10%), with the remainder being due to heart failure (3%), tuberculosis (2%), pancreatitis (1%), and other rare causes [4]. As peritoneal TB is more prevalent in developing countries like India, the percentage of patients with ascites due to cirrhosis is lesser in our study compared to Western literature.

In the present study, liver cirrhosis was found to be the dominant cause among males, that is, 75% while malignancy was dominant among females, that is, 67% with p=0.005 which may be due to the fact that cirrhosis of liver, in most cases, is alcohol related and in developing countries like India, alcoholism is chiefly considered to be consumed by males and is still a taboo among females.

At par with our study finding, liver cirrhosis was found to be the leading cause of ascites in studies conducted by Tsega (82%) [13], Malabu

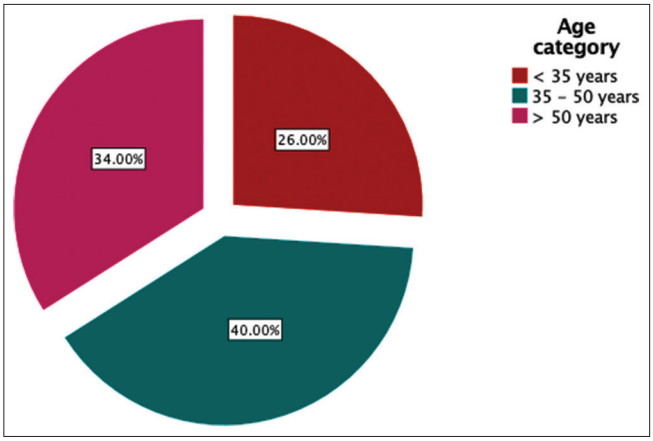

Fig. 2: Age distribution of the study participants

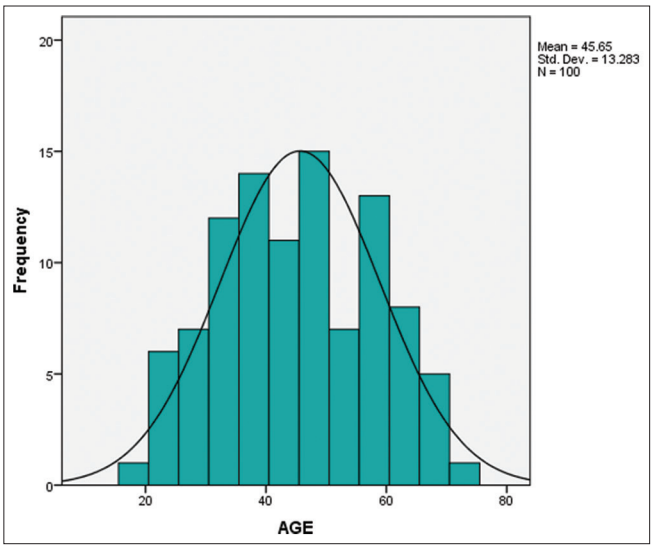

Fig. 3: Age category-wise distribution of the study participants

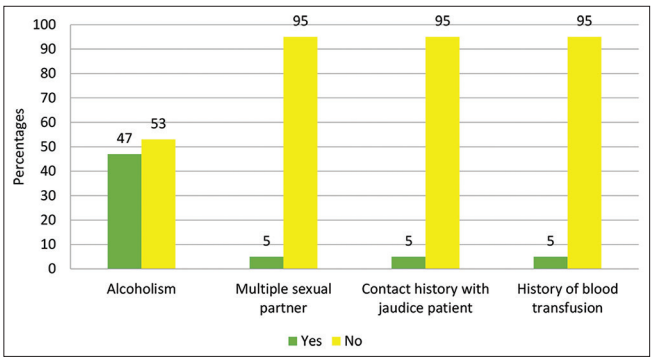

Fig. 4: Distribution of risk factors among the study participants

et al. (44%) [14], Kumar *et al.* (60.7%) [12], Joshi *et al.* (71.05%) [10], Hwangbo *et al.* [15], Muhie (46.2%) [9], Tasneem *et al.* (80%) [16], and Khan *et al.* (59.6%) [11] worldwide.

Tuberculosis was attributable for 10% of cases in our study and was the second most common cause of ascites which is comparable to other developing nations. Kumar *et al.* and Mehra *et al.* found an approximately similar number of cases of peritoneal TB, that is, 13% and 15.68%, respectively, in their study, whereas in the study of Malabu *et al.*, 23% of cases were attributed to TB, much higher than our study.

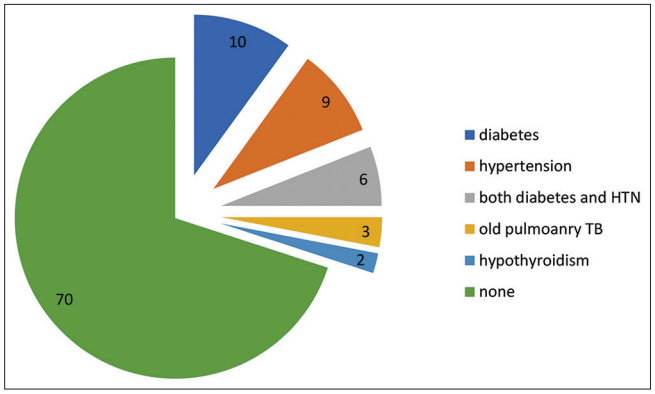

Fig. 5: Comorbidities among the study participants

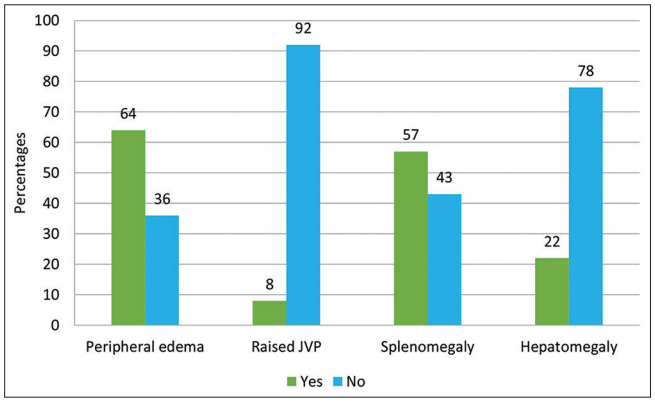

Fig. 6: Bar graph showing clinical signs among the study participants

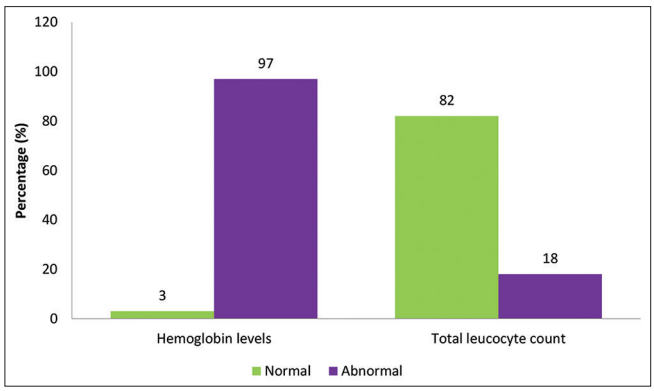

Fig. 7: Bar graph showing routine blood parameters among the study participant

In all these three studies, tuberculosis was found to be the second most common cause of ascites corroborating our finding [8,12,14].

Malignancy and heart diseases were the underlying cause of ascites in 9% and 7% of cases, respectively, in the present study. These two conditions were responsible for approximately 6% of cases each in the study of Mehra *et al.* and 8% of cases each in the study conducted by and Kumar *et al.*, respectively [8,12]. The malignancies responsible for ascites in our study were gastrointestinal malignancies, gall bladder malignancy, carcinoma breast, carcinoma ovary, carcinoma cervix, and non-Hodgkin lymphoma. Gastrointestinal malignancy (44.4%) was the most common cause of malignancy related ascites in our study in contrast to the study of Kumar *et al.* where ovarian carcinoma (53.84%) was the most common cause followed by gastrointestinal malignancy (30.76%) [12]. All the cases of cardiac

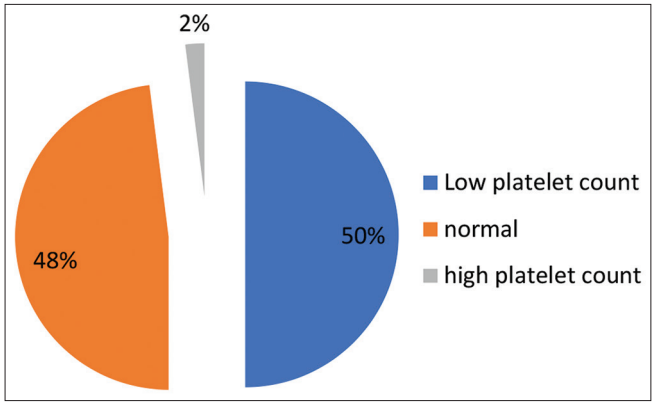

Fig. 8: Pie chart showing total platelet count among the study participants

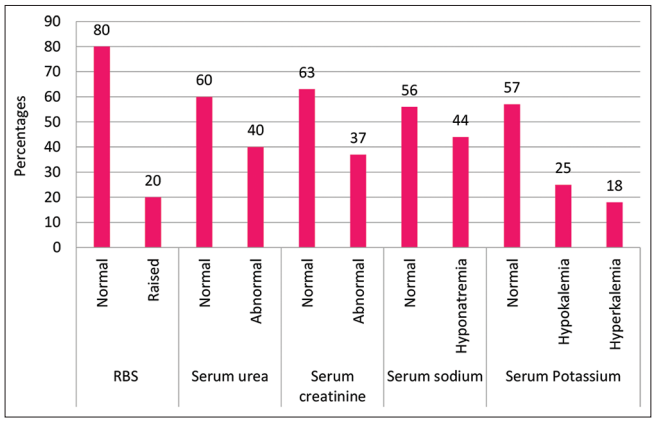

Fig. 9: Bar graph showing laboratory parameters among the study participants

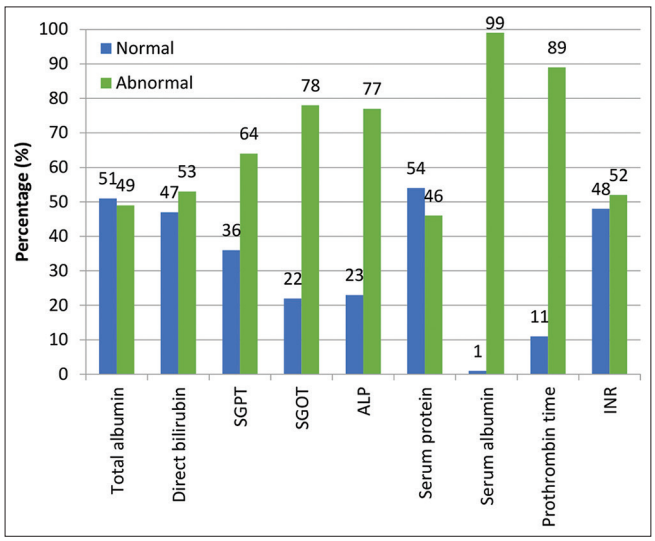

Fig. 10: Bar graph showing liver function tests among the study participants

ascites in our study were due to congestive heart failure in the setting of coronary artery disease and dilated cardiomyopathy in three cases each and rheumatic heart disease in one patient. Other rare causes found in our study included portal vein thrombosis (2%), pancreatic causes (2%), Budd Chiari syndrome (1%), EHPVO (1%), and hypothyroidism (1%).

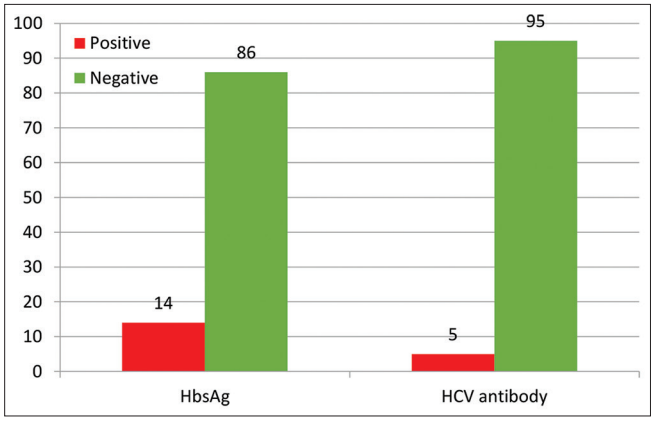

Fig. 11: Bar graph showing HbsAg and HCV antibody of the study participants

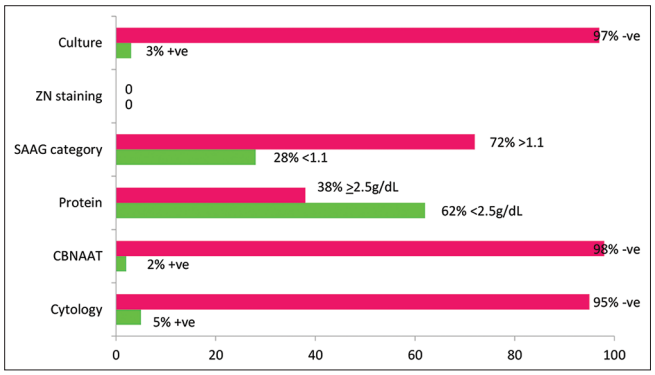

Fig. 12: Bar graph showing ascitic fluid abnormality

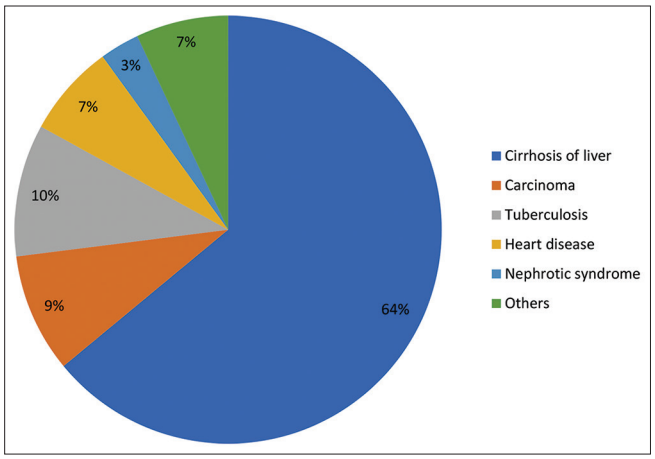

Fig. 13: Etiology of the ascites among the study participants

As far as cirrhosis of liver is taken into account, its leading cause was observed to be alcoholism (64%) followed by hepatitis B (15.6%), NASH (14.1%), Hepatitis C (4.7%), and cryptogenic (3.1%) in our study. Similar to our study, majority cases of cirrhosis were attributed to alcohol in studies conducted by Khan *et al.* (46.7%), Joshi *et al.* (93%), and Kumar *et al.* (73.5%) [10-12]. In contrast to this, studies conducted by Mehra *et al.* and Muhie among ascites patients found Chronic Hepatitis B to be the leading cause of cirrhosis [8,9]. Nine (22.5%) out of 40 patients tested for HbSAg came positive in the study of Muhie, whereas prevalence of HbSAg positivity was 15% in our study explaining the lesser number of HBV related cirrhosis [9]. In a study conducted by Malabu *et al.*, it was observed that as high as 70% of liver cirrhosis cases were attributed to Chronic Hepatitis B infection which is remarkably higher than our finding [14].

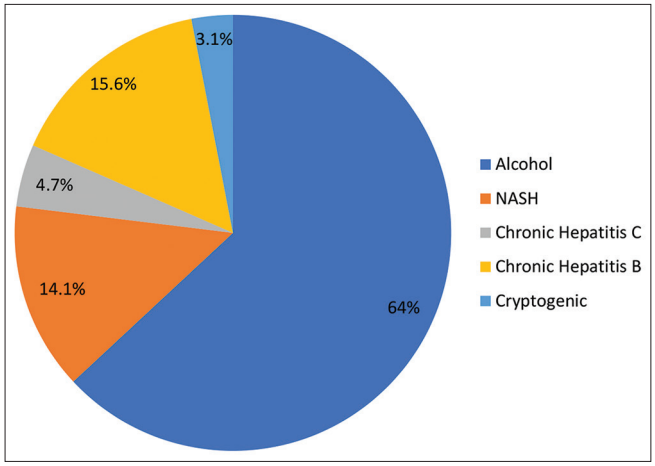

Fig. 14: Etiology of the cirrhosis among the study participants

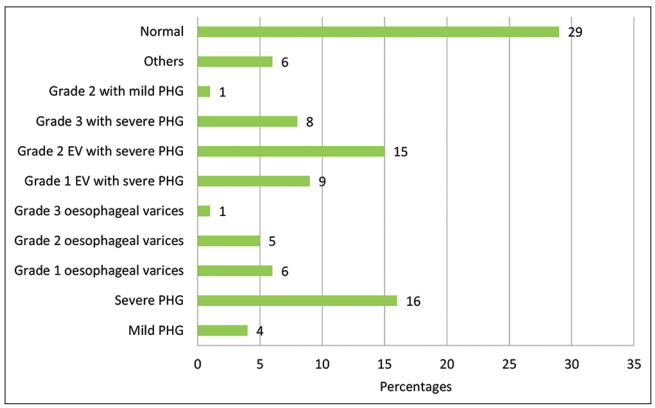

Fig. 15: Endoscopic findings among the study participants

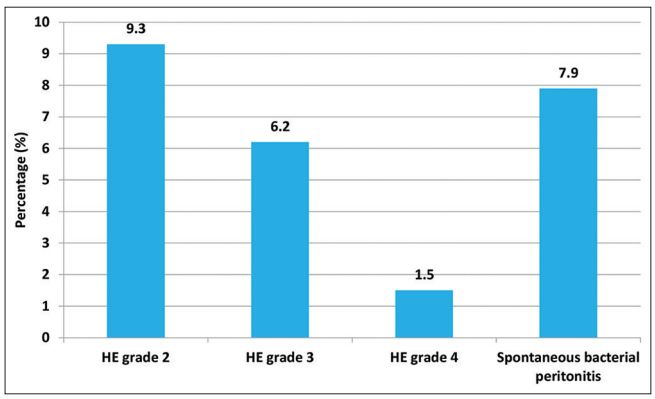

Fig. 16: Complications among patients with liver cirrhosis (n=64)
#HE: Hepatic encephalopathy

In the present study, cirrhosis of liver was observed dominantly among those aged above 50 years with p=0.044 which might be attributed to late age of onset of alcohol-use disorder and the effect of chronic alcoholism on the physiological functions of the body manifesting in later period of life.

About 17% and 7.9% of patients with liver cirrhosis developed hepatic encephalopathy and spontaneous bacterial peritonitis, respectively, in the present study which is lower than the finding of Muhie who found that 20.8% of chronic liver disease (CLD) patients developed hepatic encephalopathy and 20.8% developed spontaneous bacterial peritonitis [9]. In another similar study conducted by Kumar *et al.*, it was observed that out of all the cirrhosis patients, 31.3% developed

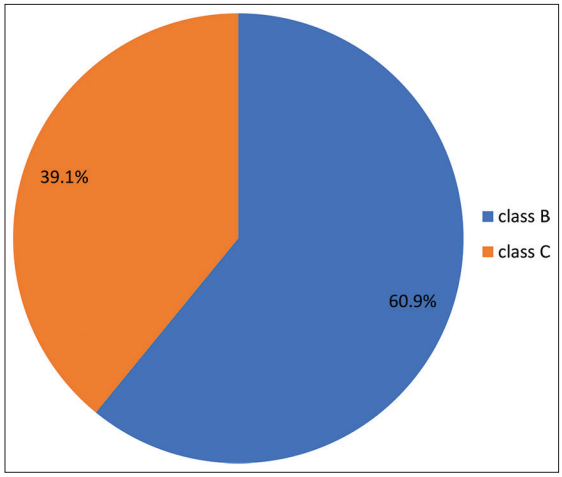

Fig. 17: Child-Pugh score among cirrhotic patients

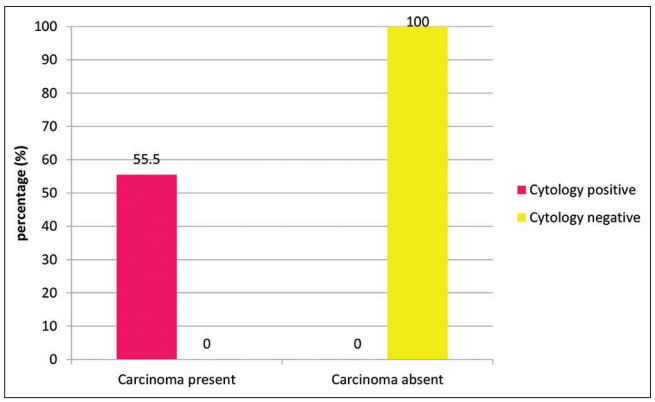

Fig. 18: Cytological analysis of ascitic fluid among patients with malignancy

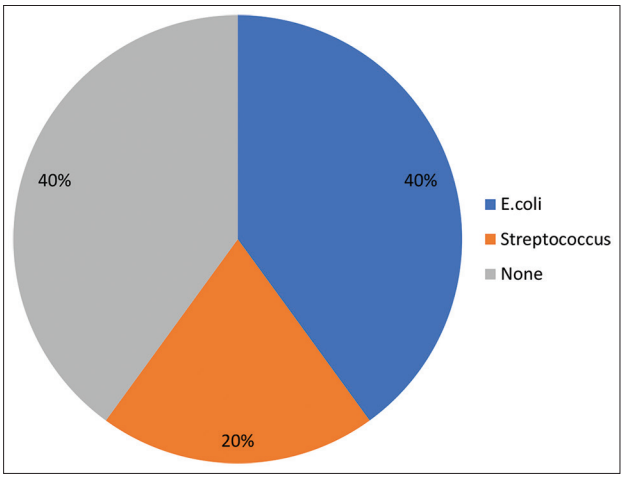

Fig. 19: Ascitic fluid culture among Spontaneous bacterial peritonitis

spontaneous bacterial peritonitis which is very much higher than our finding [12]. In that study, the ascitic fluid culture found the commonest organism to be *E. coli*, similar to our study, both findings being consistent with the previous literature [17].

The Child-Pugh score, used for assessing severity of liver cirrhosis, categorized 60.9% and 39.1% of patients under Class B and C, respectively, which is proximate to the findings of Kumar *et al.*, where

54.9% and 41.9% of patients were classified under Class B and C, respectively [12]. However, in a similar study by Mehra *et al*. on 51 patients of ascites, 48.4%, 19.3%, and 32.2% belonged to Class A, Class B, and Class C, respectively [8]. This finding suggests that majority of cirrhotic patients with ascites are presenting to our hospital in a more advanced stage when prognosis is already poor.

As many as 97% of patients were anemic in our study. High leukocyte count was observed in 18% of the subjects while low platelet count was observed in half of the patients. Raised random blood sugar level observed in 20% of the patients. Almost equal proportion of patients had increased serum urea (40%) and creatinine (37%) level. Electrolyte imbalances such as hyponatremia (44%), hypokalemia (25%), and hyperkalemia (18%) were also observed among the patients. Abnormally high total and direct bilirubin were found in 49% and 53% of the subjects. Liver enzymes such as SGPT, SGOT, and ALP were increased in 64%, 78%, and 77% of the subjects, respectively. Almost all patients had abnormal albumin levels (99%) while total protein level was deranged in 46% of the subjects. Prolonged prothrombin time and prolonged INR were found in 89% and 52% of the subjects, respectively. In a study conducted by Joshi *et al*. in Kathmandu, Nepal, nearly similar findings were observed [10]. They found anemia in 92.1% of the patients which is lower than our finding but a higher percentage (21.05%) showing leukocytosis, raised bilirubin, and SGPT. Lesser number of patients were having deranged PT/INR (64.9% and 50%), hyponatremia (40.35%), raised serum urea (36.8%), high creatinine (31.5%), and hypoalbuminemia (72.8%) as compared with the present study. These alterations in physiological status of the patients of ascites suggest that meticulous attention should be paid towards fluid and electrolyte balance, drug-dose modification and cautious use of diuretics. Furthermore, these patients are at higher risk of bleeding manifestations due to the presence of thrombocytopenia and altered coagulation profile.

Mean ascitic fluid count was 529.50±354.51 leukocytes/μL in our study which is lower than the findings of Muhie, that is, 673±1306.9 leukocytes/μL [9]. Mean ascitic fluid ADA was 18.30±14.25 IU/L and mean SAAG ratio was 1.14±0.29 g/dL.

Ascitic fluid protein was observed to be >2.5 g/Dl among majority of patients having various etiological factors such as peritoneal TB, malignancy-related ascites, and cardiac ascites, except for patients with chronic liver disease where it was <2.5 g/dL in 87.5% of cases and these findings were statistically significant ($p<0.001$). These findings are at par with the study of Joshi *et al*. in which 64.2% CLD cases had ascitic protein <2.5 g/dL [10].

The SAAG ratio was observed to be >1.1 g/dL among 72% of the patients in our study, almost similar (70.1%) to the finding of Joshi *et al*. [10]. All the patients with TB (100%) and nephrotic syndrome (100%) and majority of patients with malignancy (77.8%) had a SAAG ratio of <1.1 g/dL while majority of patients with chronic liver disease (97%) and heart disease (86%) had SAAG >1.1 g/dL. This difference in proportion was statistically very highly significant ($p<0.001$). Similar findings were observed in other studies conducted by Kumar *et al*. where, 97% of cirrhosis patients had SAAG >1.1 g/dL. In Malabu *et al*. study, 97.5% of cirrhosis patients had SAAG >1.1 g/dL, 100% of peritoneal TB and 90% of malignant ascites had SAAG <1.1 g/dL and in Pare *et al*. study, 97% of cirrhosis patients had SAAG >1.1 g/dL, and 93% of malignant ascites had SAAG <1.1 g/dL [12,14,18]. These findings suggest that SAAG value is very helpful in discriminating the causes of ascites.

The yield of organisms on smear is low for tubercular bacilli. Staining for AFB is positive in <3% of cases. Out of all the patients in our study, 10 had peritoneal TB but upon ZN staining, none of them showed a positive result, consistent with the findings of Muhie [9]. However, 9.0% of patients of peritoneal TB demonstrated a positive ZN stain in the study of Kumar *et al*. [12].

ADA has a high sensitivity (100%) and specificity (97%) for peritoneal TB when a cutoff value of 36–40 IU/L is used [19]. All cases of peritoneal TB (100%) in our study demonstrated an ADA of >40 IU/L.

Amylase values in the ascitic fluid are typically above 1000 IU/L in pancreatic ascites [20]. Both the cases of pancreatic ascites in our study demonstrated a very high ascitic fluid amylase with a mean ascitic amylase of 192.00±1612. 80 IU/L.

The sensitivity of ascitic fluid approaches 100% in peritoneal carcinomatosis but the overall sensitivity for detection of malignancy-related ascites is 58–75% cases as all the cases are not associated with peritoneal carcinomatosis [21]. The ascitic fluid cytology was found to be positive in 55.5% of patients with malignancies in our study. This is much higher in comparison to the results of Malabu *et al*., where cytology was positive in 22.7% cases out of all malignancy-related ascites [14]. This disparity might be explained by the difference in number of cases with peritoneal carcinomatosis in the two studies.

CONCLUSION

Cirrhosis of liver was found to be the most common cause of ascites in our study followed by tuberculosis and malignancy. Alcoholism was the most common cause of cirrhosis followed by chronic hepatitis B. Complications such as hepatic encephalopathy and spontaneous bacterial peritonitis were observed in 17% and 7.8% cases of ascites, respectively.

Preventive measures like protection of healthy individuals from alcohol abuse and dependence, screening for hepatitis B in high-risk subjects and hepatitis B vaccination, rapid and early diagnosis, treatment, and care of tuberculosis are the needs of the hour. Although there has been a substantial improvement in care of patients with cirrhosis, including those with ascites, prompt evaluation of cases to determine the etiology is very helpful in formulating the treatment strategy to prevent complications and reduce mortality.

AUTHORS' CONTRIBUTIONS

The authors declare that all the named authors have contributed equally to this article.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

FUNDING

No funding sources

REFERENCES

1. Rudralingam V, Footitt C, Layton B. Ascites matters. Ultrasound 2017;25:69-79. doi: 10.1177/1742271X16680653, PMID 28567101
2. Hernaez R, Hamilton JP. Unexplained ascites. Clin Liver Dis (Hoboken) 2016;7:53-6. doi: 10.1002/cld.537, PMID 31041029
3. Chiejina M, Kudaravalli P, Samant H. Ascites. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2021. Available from: www.ncbi.nlm.nih.gov/books/NBK470482/ [Last accessed on 2021 Aug 11].
4. Moore KP, Aithal GP. Guidelines on the management of ascites in cirrhosis. Gut 2006;55(Suppl 6):vi1-12. doi: 10.1136/gut.2006.099580, PMID 16966752
5. Corey KE, Friedman LS. Abdominal swelling and ascites. In: Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. Vol. 20. United States: McGraw Hill; 2018. p. 281-5.
6. D'Amico G, Garcia-Tsao G, Pagliaro LL. Natural history and prognostic indicators of survival in cirrhosis: A systematic review of 118 studies. J Hepatol 2006;44:217-31. doi: 10.1016/j.jhep.2005.10.013, PMID 16298014
7. Garrison RN, Kaelin LD, Galloway RH, Heuser LS. Malignant ascites. Clinical and experimental observations. Ann Surg 1986;203:644-51.

doi: 10.1097/00000658-198606000-00009, PMID 3718029
8. Mehra D, Thakur D, Agarwal G, Kumar A, Sultania S, Chaturvedi A. Etiology of ascites in adults living in Rohilkhand region, India: A hospital-based study. Int J Appl Res 2016;2:1-4.
9. Muhie OA. Causes and clinical profiles of ascites at university of Gondar hospital, Northwest Ethiopia: Institution-based cross-sectional study. Can J Gastroenterol Hepatol 2019;2019:5958032. doi: 10.1155/2019/5958032, PMID 31360695
10. Joshi R, Shrestha DB, Pande R, Maharjan S. Clinical profile of ascites based on presentation and laboratory findings: An institutional experience from Kathmandu, Nepal. J Med Res Innov 2018;2:e000101. doi: 10.15419/jmri.101
11. Khan FY. Ascites in the state of Qatar: Aetiology and diagnostic value of ascitic fluid analysis. Singapore Med J 2007;48:434-9. PMID 17453102
12. Kumar B, Sharma B, Raina S, Sharma N, Gupta D, Mardi K. Etiology of ascites in adults living in the Hills of Himachal Pradesh, India: A hospital-based study. CHRISMED J Heal Res 2016;3:41. doi: 10.4103/2348-3334.172398
13. Tsega E. Laparoscopic evaluation of ascites and other abdominal conditions in Ethiopia. Trop Geogr Med 1989;41:341-5.
14. Malabu UH, Olubuyide IO, Shaibu ME, Olawuyi F. Ascites in Ibadan, Nigeria-usefulness of albumin gradient in its etiologic diagnosis. Biomed Res 2006;17:105-9.
15. Hwangbo Y, Jung JH, Shim J, Kim BH, Jung SH, Lee CK, *et al*. Etiologic and laboratory analyses of ascites in patients who underwent diagnostic paracentesis. Korean J Hepatol 2007;13:185-95. PMID 17585192
16. Tasneem H, Shahbaz H, Sherazi BA. Pharmacoepidemiology of ascites and associated complications in hospitalized patients: Descriptive observational study. Int Curr Pharm J 2015;4:343-6. doi: 10.3329/icpj.v4i2.21482
17. Akriviadis EA, Runyon BA. Utility of an algorithm in differentiating spontaneous from secondary bacterial peritonitis. Gastroenterology 1990;98:127-33. doi: 10.1016/0016-5085(90)91300-u, PMID 2293571
18. Pare P, Talbot J, Hoefs JC. Serum-ascites albumin concentration gradient: A physical approach to the differential diagnosis of ascites. Gastroenterol 1983;85:240-4.
19. Tarn AC, Lapworth R. Biochemical analysis of ascitic (peritoneal) fluid: What should we measure? Ann Clin Biochem 2010;47:397-407. doi: 10.1258/acb.2010.010048, PMID 20595402
20. Runyon BA. Amylase levels in ascitic fluid. J Clin Gastroenterol 1987;9:172-4. doi: 10.1097/00004836-198704000-00012, PMID 2437177
21. DiBonito L, Falconieri G, Colautti I, Bonifacio D, Dudine S. The positive peritoneal effusion. A retrospective study of cytopathologic diagnoses with autopsy confirmation. Acta Cytol 1993;37:483-8. PMID 8328242