Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/15415
DOI URL: http://dx.doi.org/10.21474/IJAR01/15415

RESEARCH ARTICLE

ETIOLOGY AND DIAGNOSIS OF ASCITES OF UNDETERMINED ORIGIN IN A DEVELOPING COUNTRY: A PROSPECTIVE STUDY

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Manuscript Info

Manuscript History
Received: 18 July 2022
Final Accepted: 20 August 2022
Published: September 2022

Key words:-
Ascites, Albumin, Undetermined

Abstract

Introduction: Ascites is defined as the pathologic accumulation of free fluid within the abdominal cavity. It is a symptom of numerous medical conditions and has a broad differential diagnosis. The Various etiologies of Ascites of undetermined origin are analysed and presented
Materials And Methods: 30 patients presenting to the hospital with no obvious or identifiable cause of ascites were evaluated between 2019 and 2020. Patients with no obvious cause of ascites onbiochemical, radiological, pathological investigations werestudied and diagnostic laparoscopy with histopathological examination was done.
Results: Tuberculosis was the commonest cause of ascites in 19 patients, Malignancy in 5 patients, Cirrhosis in 3 patients. In 10 patients the cause of ascites could not be ascertained even after extensive investigations.
Conclusion: Tuberculosis continues to remain the leading cause of ascites of undetermined origin followed by malignancy. There is a need for further research as causes of undetermined ascites remain elusive even after exhaustive investigations.

Introduction:-

Ascites is defined as the pathologic accumulation of free fluid within the abdominal cavity. It is a symptom of numerous medical conditions and has a broad differential diagnosis. Ascites has been graded into three types: grade I: mild (<1.5l) and only detectable on abdominal ultrasonography (US) or computed tomography (CT), grade II: manifested with flank bulging and shifting dullness, and grade III: visible and can be confirmed with a fluid thrilling test[1]. Ascites tends to occur in long-standing (chronic) rather than in short-lived (acute) disorders. Ascites is classified according to total protein content of the fluid into transudative and exudative ascites. It is also classified according to serum ascites albumin concentration gradient (SAAG) into high gradient > 1.1 g/dl or low SAAG ascites <1.1 g/dl[2, 3].

Aims And Objectives:-

To ascertain the cause of ascites in patients when biochemical, radiological, pathological interventions are inconclusive, by performing diagnostic laparoscopy with or without biopsy with histopathological examination.

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Materials And Methods:-

Study Design:
It was a hospital based prospective observational study.

• **Sample Size**:
This was a time bound study and was conducted over a period of 2 years from December 2019 to December 2021. The study included a total of 30 Patients.

• **Study Subjects**:
Subjects included the patients who underwent diagnostic laparoscopy for the evaluation of ascites after appropriate clinical, biochemical, radiological examination including CT scan/ USG failed to reveal the cause of ascites.

Sample Collection:
The following exclusion and inclusion criteria were used for the study.

Inclusion Criteria:
• Patients of either sex in the age group of 21 to 90 years with no identifiable cause of ascites were taken for study.

Exclusion Criteria:
• Those with an obvious and identifiable cause of ascites.
• Those with any contraindications for general anesthesia.
• Those with any contraindications for laparoscopy

Observation And Results:-

Age Distribution
The age distribution ranged from 21 to 90 years. Most Common age group in the study was 46-60 years with 12 cases (40%) followed by 61-75 years (23.3%) as shown in Table 1.The mean age in our study was 51.6 years.

Age	Frequency	Percentage
15-30	3	10
31-45	6	20
46-60	12	40
61-75	7	23.3
Above 75	2	6.7

Table 1:- Age distribution.

Sex:
There was male preponderance with Male to Female ratio of 2.3:1. Males constituted 70% (n= 21) and females 30% (n= 9) in our study as shown in Table 2

	Frequency	Percentage
Male	21	70
Female	9	30

Table 2:- Gender Distribution.

CO-Morbidities:
Various comorbidities were identified in our study participants, the most common being Diabetes Mellitus (11, 36.7%) followed by Hypertension (9,30%) and Hypothyroidism (2, 6.7%). There was no comorbidity in 16.7% (5) cases as shown in Table 3.

	Frequency	Percentage
T2DM	11	36.7
HTN	9	30
COPD	1	3.3
Asthma	1	3.3
Hypothyroidism	2	6.7
Dyslipidemia	1	3.3

No Medical Comorbidity	5	16.7

Table 3:- Medical Comorbidity.

Presenting Complaints

The distribution pattern in descending order of the various presenting complaints was abdominal pain (25 patients, 83.3%); fever (7 patients, 23.3%); abdominal distention, anorexia and weight loss each with 6.6% (2) cases as shown in Table 4

	Frequency	**Percentage**
Abdominal pain	25	83.3
Fever	7	23.3
Abdominal Distension	2	6.6
Anorexia	2	6.6
Weight loss	2	6.6
Both abdominal pain and fever	6	20
Both weight loss and anorexia	2	6.6

Table 4:- Presenting Complaints.

Elicited Signs

On examination ascites was found in 83.3% (25) cases and pallor was present in 16.7% (5) cases. Abdominal tenderness and lymphadenopathy was present in 10% (3) cases each. There were multiple examination findings in 20% (6) cases as shown in Table 5

	Frequency	**Percentage**
Ascites	25	83.3
Fever	0	0
Pallor	5	16.7
Tenderness	3	10
Lymphadenopathy	3	10
Lymphadenopathy+ Ascites	3	10
Abdominal tenderness+ Ascites	3	10

Table 5:- Elicited Signs.

Biochemical Analysis

In biochemistry, anaemia (HB 60 in 23.3% (n=7) and TLC> 11,000/mm3 in 10% (n=3) cases. AFB in sputum was found in 26.6% (n=8) of the cases while the Mantoux Test was positive in 40% (n=12) of the cases. Tumour markers were found to be present in 10% (n=3) of cases as shown in Table 6

	Frequency	**Percentage**
Hb <10 g/dl	10	33.3
ESR >60	7	23.3
TLC >11000	3	10
Positive Mantouex Test	12	40
Positive Sputum for AFB	8	26
Raised Tumour markers	3	10
Both Hb<10, Positive Mantoux test and Positive Sputum for AFB	4	13.3
Both Sputum for AFB and Positive Mantoux Test	1	3.3
Both Positive Mantoux Test and ESR >60	2	6.7
Both Positive Sputum for AFB and ESR >60	1	3.3
Both Positive Sputum for AFB, ESR >60 and Positive Mantoux Test	1	3.3

Table 6:- Biochemical Analysis.

Gross Appearance Of Ascitic Fluid

When the ascites fluid was grossly examined, the colour of the ascitic fluid was serous in 90% (n=27) cases, while it was haemorrhagic in 10 (n=3) cases, as shown in Table 7

	Frequency	Percentage
Serous	27	90
Haemorrhagic	3	10

Table 7:- Gross appearance of ascitic fluid.

Ascitic Fluid Analysis

Analysis of ascites fluid revealed lymphocytosis in 76.7% (n=23) of cases and low SAAG (<1) in 43.3% (n=13) of cases. In culture, MTB was found in 6.7% (n=2) of cases, while malignant cells were detected in 13.3% (n=4) of cases. There were mixed findings in 46.6% of cases (n=14) as shown in Table 8

	Frequency	Percentage
Lymphocytosis	23	76.7
SAAG <1.	13	43.3
Raised ADA levels	3	10
Positive culture for MTB	2	6.7
Malignant Cells	4	13.3
Lymphocytosis, SAAG <1 and Malignant Cells	4	13.3
Lymphocytosis, SAAG<1.1 and ADA levels	2	6.7
Lymphocytosis and SAAG<1.1	6	20
Positive culture for MTB and SAAG<1.1	1	3.3
Positive culture for MTB, ADA levels and Lymphocytosis	1	3.3

Table 8:- Ascitic fluid analysis.

Radiological Findings

In transabdominal ultra-sonography, the most common finding was peritoneal and Omental thickening (73.3%, 22) followed by mesenteric lymphadenopathy (20%, 6). Hepatomegaly and splenomegaly were found in 6.7% (2) cases each as shown in Table 9

	Frequency	Percentage
Peritoneal and Omental Thickening	22	73.3
Mesenteric lymphadenopathy	6	20
Hepatomegaly	2	6.7
Splenomegaly	2	6.7
Both Mesenteric Adenopathy and Peritoneal thickening	1	3.3
Both Splenomegaly and Hepatomegaly	2	6.7

Table 9:- Radiological Findings.

Laparoscopic Findings

On Diagnostic Laparoscopy following findings were noted peritoneal nodules (33.3%, n=10), thickened omentum (36.6%, n=11), adhesions (36.6%, n=11), cirrhosis (13.3%, n=4). There were multiple findings in 26.6% (n=8) cases as shown in Table 10

Table 10:- Laparoscopic Findings.

Peritoneal nodules	10	33.3%
Thickened omentum	11	36.6%
Adhesions	11	36.6%
Cirrhosis	4	13.3%
Both Peritoneal nodules and Adhesions	5	16.6%

Both Peritoneal nodules and thickened omentum	2	6.7%
Both thickened peritoneum and omentum	1	3.3%

Post-Operative Diagnosis
(Histo-Pathological Finding)
The post-operative diagnosis was made in 90% (n=27) cases, with Tuberculosis being most common in 63.3% (n=19) cases, followed by malignancy in 16.7% (n=5) and cirrhosis in 10% (n=3) cases. In 10% (n=3) cases, no diagnosis was made as shown in Table 11

Tuberculosis	19	63.3
Malignancy	5	16.7
Cirrhosis	3	10
Inconclusive	3	10

Table 11:- Post Operative Diagnosis.

Discussion:-

Ascites is defined as the pathologic accumulation of free fluid within the abdominal cavity. It is a sign of numerous medical conditions and has a broad differential diagnosis. Ascites tends to occur in longstanding (chronic) rather than in short-lived (acute) disorders.

Etiology Of Ascites
• Normal Peritoneum:
Portal hypertension.
Hypoalbuminemia.
Miscellaneous conditions:
• Chylous ascites
• Pancreatic ascites
• Bile ascites
Nephrogenic ascites
• Uterine ascites
• Ovarian disease
• Cardiac Ascites.
• Diseased peritoneum
Infections:
• Bacterial peritonitis
• Tuberculous peritonitis
• Fungal peritonitis
• HIV associated peritonitis
Malignant conditions:
• Peritoneal carcinomatosis
• Primary mesothelioma
• Pseudomyxoma peritonei
• Hepatocellular carcinoma
Other rare conditions
• Familial Mediterranean fever
• Vasculitis
• Granulomatous peritonitis
• Eosinophilic peritonitis

Pathogenesis Of Ascites
Liver Diseases:
Liver diseases cause cirrhosis which lead to portal hypertension followed by peripheral vasodilatation. The peripheral vasodilatation is associated with retention of sodium & water causing hypervolemia & spill over in to the peritoneal cavity from hepatic sinusoids.

Malignancies:
Peritoneal carcinomatosis appears to cause ascites by exudation of proteinaceous fluid from tumour cells lining the peritoneum, extracellular fluid enters the peritoneal cavity to re-establish oncotic pressure. In patients with massive liver metastasis fluid presumably accumulates owing to portal hypertension. Chylous ascites due to lymphoma appears to be caused by obstruction of the lymph nodes by tumour & rupture of chyle containing lymphatics.

Cardiac Failure:
In heart failure there is decreased effective arterial blood volume. This activates vasopressin, renin, aldosterone & sympathetic nervous system. This leads to renal vaso-constriction and sodium & water retention. Fluid then seeps from the congested hepatic sinusoids as lymph, as in cirrhotic ascites.

Tuberculosis:
Ascites results from exudation of proteinaceous fluid from the tubercles studded over peritoneum.

Pancreatic & Biliary Ascites:
Fluid forms by leakage of pancreatic juice or bile in to the peritoneal cavity and/or by a 'chemical burn' of the peritoneum.

Postoperative:
After abdominal surgery especially extensive retroperitoneal dissection, lymphatics may be transected and lymph leaks for variable period of time

Nephrotic Syndrome:
Loss of protein in urine leads to decreased effective arterial blood volume with activation of vasopressin, Renin-aldosterone, and sympathetic nervous system with resulting renal sodium & water retention.

Diagnoses Of Ascites
History
Patients with ascites should be questioned about the pattern of body weight gain, change in abdominal girth, and ankle oedema. Information about the medical history, medication use, lifestyle, risk factors for liver disease, and infectious disease risk (e.g., migration) are relevant to discover the underlying aetiology.

Physical Examination:
A screening physical exam should be carried out in every patient, with awareness of signs of liver disease (erythema palmare, spider naevi, splenomegaly), heart failure (peripheral oedema, jugular venous distension, third heart sound, pulmonary rales) and malignancy (lymphadenopathy)[4]. The abdomen should be inspected for the presence of bulging flanks and percussion can reveal flank dullness. Complications accompanying ascites such as umbilical, inguinal and other hernias and pleural fluid (hepatic hydrothorax) are particularly common in cirrhotic patients.

Serum Biochemistry:
It is recommended to assess serum levels of creatinine, urea, electrolytes, prothrombin time and liver function tests and to order a complete blood cell count[5].

Abdominal Ultrasound:
Abdominal ultrasound is the first-line imaging method to confirm the presence and quantity of ascites[6]. Additionally, ultrasound can provide crucial information about the cause of ascites, detect signs of portal hypertension (splenomegaly and portosystemic collaterals), and offer guidance during paracentesis.

Abdominal Paracentesis:
Abdominal paracentesis is the most important step in the diagnostic workup. It is indicated in every patient with new-onset ascites, patients with known ascites and clinical deterioration or a new presentation to an emergency department. Paracentesis is usually performed in the left lower quadrant, 3 cm cranially and 3 cm medially from the anterior superior iliac spine. Other sites include the right lower quadrant and the midline Linea alba between the umbilicus and the pubic bone[7].

Ascitic Fluid Analysis:

Inspection

Inspection of the ascitic fluid can show a milky, cloudy, bloody, straw coloured or clear appearance. Chylous (Milky) ascites can result from malignancy, trauma, liver cirrhosis, infection, pancreatitis, congenital disease and more uncommon causes[8]. Cloudy ascites may indicate peritonitis, pancreatitis or a perforated bowel. Bloody ascites is often associated with malignancies or results from traumatic paracentesis, whereas straw coloured or clear ascites is common in liver cirrhosis[9]. The first impression of the appearance of ascites is non-specific, but can steer the direction of diagnosis

Biochemical Testing

Serum-ascites albumin gradient:

The serum-ascites albumin gradient (SAAG) is the most sensitive marker to distinguish between ascites due to portal hypertension/hepatic congestion and other causes, with an accuracy of 97%. A value ≥ 1.1 g/dl (or 11 g/l) indicates underlying portal hypertension or hepatic congestion; a value < 1.1 g/dl indicates aetiologies not due to portal hypertension, such as malignancy, pancreatitis or infection[10.]

Total protein:

Traditionally, this was thought to indicate the aetiology of ascites according to the transudate-exudate concept, but this approach is now generally considered inferior. The total protein concentration does have prognostic value as concentrations lower than 15 g/l are associated with an increased risk for spontaneous bacterial peritonitis (SBP) in cirrhotic patients.

Amylase:

The amylase concentration in ascitic fluid should be measured in particular when pancreatic disease is considered. An amylase ascitic fluid/blood serum concentration ratio of 6.0 is indicative for pancreatic disease, considering that a ratio of 0.4 is normal in non-pancreatic ascites[11]. However, high levels of amylase have also been detected in patients with malignancy and other conditions making it a rather non-specific finding.

Triglycerides:

A concentration of triglycerides in the ascitic fluid that exceeds the blood serum level (2.2 mmol/l) indicates chylous ascites. Previous abdominal surgery, pancreatitis, trauma and retro-peritoneal lymphoma are among the main causes[12].

Adenosine deaminase activity:

The activity of adenosine deaminase (ADA), an enzyme of purine metabolism, is a reliable marker to differentiate tuberculous ascites from other aetiologies. An ADA cut-off value between 36 to 40 IU/l has a high sensitivity (100%) and specificity (97%) for diagnosing abdominal tuberculosis[12]. Glucose, LDH, Urea and Creatinine of the ascitic fluid should also be measured.

Cytology:

Ascitic fluid cytology should be performed in case of suspicion of malignant ascites or when the underlying aetiology is in doubt. A positive cytology is highly indicative for peritoneal carcinomatosis.

Imaging:

The imaging includes USG and CT scan of the abdomen that may also be utilised for diagnosing ascites. Peritoneal and omental thickening, liver cirrhosis, mesenteric lymphadenopathy and hepatosplenomegaly can be identified.

Laparoscopy

In cases where diagnosis cannot be confirmed, laparoscopy can be performed to identify lesions, take biopsies and thus reach a diagnosis. Since the causes of ascites are multiple and varied, so it may be important to find the cause and thus treat accordingly. The usual set of tests to assess the cause include laboratory examinations (cell count, albumin level, total protein gram stain, culture and cytology) and imaging investigations (chest and plain abdominal films, ultrasound and computed tomography scans. The cause of ascites can be identified in the majority of patients by clinical and conventional laboratory examinations but occasionally it cannot be determined without subjecting the patient to further investigations. Thus, ascites of undetermined origin is defined as the ascites in which the aetiology cannot be determined after conventional laboratory examinations and further imaging investigations

Diagnostic laparoscopy is a cost-effective procedure with overall accuracy of 97% as lesions are seen under direct vision with magnification. Lesions less than 1 mm can be identified[13]. Moreover, directed biopsies can be obtained with very low risk of complications

Thus, Diagnostic laparoscopy is indicated for accurate diagnosis of ascites when abdominal ultrasonography, CT abdomen and diagnostic paracentesis have failed to determine the cause of ascites[14]. It is very sensitive for small malignant or benign peritoneal implants. Biopsy of these peritoneal implants can be obtained and sent for histopathological diagnosis.

However, since diagnostic laparoscopy is an invasive procedure there are certain complications reported with this procedure e.g., haemorrhage, perforation, and air embolism.

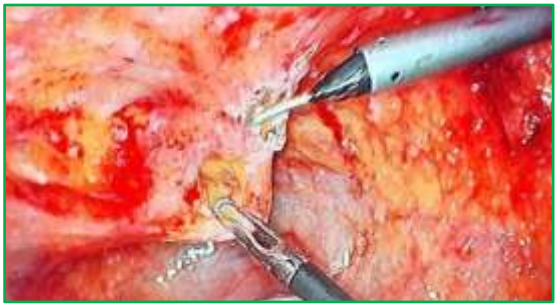
Conclusion:-

Tuberculosis continues to remain the leading cause of ascites of undetermined origin with Low SAAG in developing countries. Further research is needed as even after thorough investigations some cases remain undiagnosed.

Pictures

Peritoneal Nodules and Serous Ascitis

Adhesions of thick omentum with peritoneal wall



Biopsy Being Taken from the Thickened Peritoneum

Nodules Present on the Gut, Omentum and Peritoneum

Serous Ascites Present in the General Peritoneal Cavity

Biopsy being taken from the Falciform Ligament

References:-

1. Moore KP, et al. The management of ascites in cirrhosis: Report on the consensus conference of the International Ascites Club. Hepatology. 2003;38(1):258-266
2. Runyon BA, Montano AA, Akriviadis EA, Antillon MR, Irving MA, McHutchison JG (August 1992). Ann. Intern. Med. 117 (3): 215–20. doi:10.7326/0003-4819-117-3-215. PMID 1616215.
3. Ascites". The Lecturio Medical Concept Library. Retrieved 1 July 2021.
4. Caldentey G, Khairy P, Roy D, et al. Prognostic value of the physical examination in patients with heart failure and atrial fibrillation: insights from the AF-CHF trial (atrial fibrillation and chronic heart failure). JACC Heart Fail. 2014;2:15-23.
5. Moore KP, Aithal GP. Guidelines on the management of ascites in cirrhosis. Gut. 2006;55 Suppl 6:vi1-12.
6. European Association for the Study of the Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. J Hepatol. 2010;53:397-417.
7. Runyon BA, Committee APG. Management of adult patients with ascites due to cirrhosis: an update. Hepatology. 2009;49:2087-107.
8. Steinemann DC, Dindo D, Clavien PA, Nocito A. Atraumatic chylous ascites: systematic review on symptoms and causes. J Am Coll Surg. 2011;212:899-905 e1-4.
9. McHutchison JG. Differential diagnosis of ascites. Semin Liver Dis. 1997;17:191-202.
10. Runyon BA, Montano AA, Akriviadis EA, Antillon MR, Irving MA, McHutchison JG. The serum-ascites albumin gradient is superior to the exudate-transudate concept in the differential diagnosis of ascites. Ann Intern Med. 1992;117:215-20.
11. Haas LS, Gates LK, Jr. The ascites to serum amylase ratio identifies two distinct populations in acute pancreatitis with ascites. Pancreatology. 2002;2:100-3.
12. Laterre PF, Dugernier T, Reynaert MS. Chylous ascites: diagnosis, causes and treatment. Acta Gastroenterol Belg. 2000;63:260-3.
13. M.P. Sharma, Vikram Bhatia. Abdominal tuberculosis. Indian J Med Res 120, October 2004, 305-315.
14. J Hossain, A K Al-Aska, Al Mofleh Laparoscopy in tuberculous peritonitis Journal of the Royal Society of Medicine Volume 85 February 1992, 89.