

Original Research Article

Study of role of amniotic fluid total protein (AFTP) assessment in the diagnosis of tubercular ascites

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ABSTRACT

Background: It is not economically feasible to estimate the serum and ascitic albumin level for calculating Serum Ascites Albumin Gradient (SAAG) in every suspected tubercular ascites patient. Ascites fluid total protein (AFTP) seems a cheaper and viable alternative. Authors attempted to compare the efficacy of Amniotic Fluid Total Protein (AFTP) against Serum Ascites Albumin Gradient (SAAG) in the diagnosis of Tubercular Ascites.

Methods: Patients who were admitted to Medicine Wards, with the complaints of distension of abdomen, proved by ultrasound to have ascites, were included in the study. Total 102 Patients of ascites were included. The incidence of Tuberculous ascites was observed and special features regarding their clinical presentation, ascitic fluid values and imaging studies were noted.

Results: Tubercular ascites was seen in 18 (17.6%) patients out of the 102 subjects studied. In the group of patients having raised ascitic fluid ADA, authors found that the number of patients having raised AFTP (16 cases, 88.88%) was significantly more than the patients having lower SAAG (13 cases, 71.22%) ($p=0.007$).

Conclusions: In the setting where calculating SAAG may prove to be quite expensive, AFTP is a reasonable predictor of Tubercular infection in ascitic fluid.

Keywords: Ascites fluid total protein (AFTP), Tubercular ascites

INTRODUCTION

Ascites literally means 'an accumulation of fluid in the peritoneal cavity, causing abdominal swelling'.¹ One of the most common causes of ascites is cirrhosis of the Liver, leading to portal hypertension which, in turn, causes collection of fluid in the peritoneal cavity.

However; extra hepatic diseases may also lead to ascites, the common causes being infections like Tuberculosis, anemia/hypo-proteinemia, renal diseases, cardiac causes and malignancy.¹ In India, Tubercular ascites occurs quite often. Tubercular Ascites is one of the forms of Extra Pulmonary Tuberculosis, which is often difficult to diagnose.

In clinical practice, a patient of ascites may often present a diagnostic dilemma. The dilemma increases when a patient suffers from two different diseases. Tubercular peritonitis often occurs in a patient of cirrhosis of liver having long standing transudative ascites.

When confronted with such patients, it becomes imperative to properly diagnose the condition, so that the correct line of management may be started. In patients with new-onset ascites of unknown origin, imaging studies like Ultrasound or CT scan of the abdomen should be done and peritoneal fluid should be analysed for cell count, albumin level, culture, total protein, Gram stain, and cytology.

Physical inspection: Most ascitic fluid is transparent and tinged yellow. Cloudy ascitic fluid with a purulent consistency indicates bacterial infection. Tubercular infection may show a coagulum due to high protein consistency.

Cell count: Normal ascitic fluid contains fewer than 250 polymorphonuclear leukocytes (PMNs)/ μL . Any inflammatory condition can cause an elevated white blood cell count. A PMN count of greater than 250 cells/ μL is highly suggestive of bacterial peritonitis. In tuberculous peritonitis and peritoneal carcinomatosis, lymphocytes usually predominate.

Total protein: Previously, the classification of ascites was based on the level of ascitic fluid total protein (AFTP), which divided ascites into two types:²

- Exudative- AFTP >2.5 gm/dL
- Transudative- AFTP <2.5 gm/dL

However, the accuracy is only approximately 56% for detecting exudative causes. The total protein level may provide additional clues when used with the Serum Ascites Albumin Gradient (SAAG). An elevated SAAG and a high protein level are observed in most cases of ascites due to hepatic congestion.

Serum Ascites Albumin Gradient (SAAG)

The SAAG is the best single test for classifying ascites into portal hypertensive (SAAG >1.1 g/dL) and non-portal hypertensive (SAAG <1.1 g/dL) causes.² Calculated by subtracting the ascitic fluid albumin value from the serum albumin value, it correlates directly with portal pressure. The specimens should be obtained relatively simultaneously. The accuracy of the SAAG results is approximately 97% in classifying ascites. The terms high-albumin gradient and low-albumin gradient should replace the terms transudative and exudative in the description of ascites.

Table 1: Classification of ascites by Serum-Ascites Albumin Gradient (SAAG).

High gradient ≥1.1 g/dl (11 g/l)	Low gradient <1.1 g/dl (11 g/l)
Alcoholic hepatitis	Biliary ascites
Budd-Chiari syndrome	Bowel obstruction or infarction
Cardiac ascites	Nephrotic syndrome
Cirrhosis	Pancreatic ascites
Fatty liver of pregnancy	Peritoneal carcinomatosis
Fulminant hepatic failure	Postoperative lymphatic leak
Massive liver metastases	Serositis in connective tissue diseases
“mixed” ascites	Tuberculous peritonitis
Myxoedema	
Portal vein thrombosis	
Sinusoidal obstruction syndrome	

Culture/Gram stain/smear examination

Culture has 92% sensitivity for the detection of bacteria in ascitic fluid, provided that samples are inoculated into blood culture bottles immediately, at the bedside. In contrast, Gram stain is only 10% sensitive for visualizing bacteria in early-detected spontaneous bacterial peritonitis. A smear for acid fast bacilli has a diagnostic sensitivity of only 0-3%.

A definitive diagnosis of TB can be made by culturing Mycobacterium Tuberculosis organisms from a specimen obtained from the ascitic fluid. However, its yield is very low: 30-50%; and it may take 2-8 weeks to receive the results.

Adenosine De-Aminase (ADA) measurement: It is one of the most widely used biomarkers for the diagnosis of Extra Pulmonary Tuberculosis. ADA is an enzyme involved in purine metabolism that is found in many tissues, particularly in lymphocytes of the lymphoid tissue.

Activity of this enzyme increases in TB infection because the Mycobacterial antigens stimulate the T-lymphocytes. It has been proposed to be a useful surrogate marker for TB in body fluids, such as pleural, pericardial, and peritoneal fluid, although possible false-negative and false-positive results should be considered. The sensitivity and specificity for diagnosing Tuberculous peritonitis have been reported to be 100% and 97%, respectively, using cut-off values from 36 to 40 IU/L, with the optimal cut-off point of 39 IU/L. Liao et al suggested that lowering cut-off value to 27 IU/L could increase the sensitivity and specificity to 100% and 93.3%, respectively, in patients with liver cirrhosis, in whom false-negative results are a concern.³ In present setting, authors deal mostly with patients belonging to poor socioeconomic strata.

There is serious dearth of funds, and only few basic investigations are available free of cost to the patients. The estimation of albumin level is an expensive procedure. Hence, it is not economically feasible to estimate the serum and ascitic albumin level for calculating SAAG in every patient. Ascites fluid total protein is a much cheaper alternative. Hence, in this study, authors attempted to compare the efficacy of AFTP against SAAG in the diagnosis of Tubercular Ascites.

METHODS

It was an observational type of study design carried out at Medicine wards at a tertiary care hospital and its duration was 1st February 2014 to 31st January 2017.

Inclusion criteria

- Patients with ascites proved by ultrasound

- Patients aged more than 18 years.

Exclusion criteria

- Pregnancy
- Hemodynamic instability
- Bleeding disorders/prolonged prothrombin time.
- Unwilling to give consent.

Patients who were admitted to Medicine Wards, with the complaints of distension of abdomen, proved by ultrasound to have ascites, were included in the study. Total 102 Patients of ascites were included. The incidence of Tuberculous ascites was observed and special features regarding their clinical presentation, ascitic fluid values and imaging studies were noted.

After obtaining required written informed consent, all patients were subjected to detailed workup as follows:

- Complete Blood Count
- Blood Sugar: Fasting and Post prandial
- Liver Function Tests
- Kidney Function Tests
- Prothrombin Time
- Australia Antigen Test
- Hepatitis C IgG antibody in selected patients
- Ultrasound imaging of abdomen
- Ascitic fluid analysis: Routine and Microscopy – Protein, Sugar, Cells etc, Adenosine De-Aminase (ADA) level estimation.
- X Ray of Chest, PA view.

Definition of Tubercular ascites: The patient was diagnosed as a case of Tubercular ascites when the ADA level was found to be above the cutoff level of 30-45 IU/L. The data were analysed using SPSS (version 17).

RESULTS

As shown in the table below, Tubercular ascites was seen in 18 (17.6%) patients out of the 102 subjects studied. Thus, after cirrhosis of liver (71, 69.6%), tuberculosis of abdomen is the 2nd commonest cause of ascitits amongst present participants (Table 2).

Table 2: Disease wise distribution of study participants (N = 102).

Disease	No. of patients (n=102)
Cirrhosis of liver	71 (69.6%)
Tuberculosis of abdomen	18 (17.6%)
Spontaneous bacterial peritonitis	6 (5.8%)
Anemia with hypoproteinemia	5 (4.9%)
Renal disease	4 (3.92%)
Cardiogenic cause	2 (1.96%)
Malignancy	1 (0.98%)
Pyo-peritoneum	1 (0.98%)

Characteristics of the patients with tubercular ascites were studied further. The age and gender wise distribution of the participants showed equal male to female ratio (9:9).

The 40-60 years was the commonest age group affected (55.55%, males-33.33%, females- 22.22%), followed by 20-40 years age group (33.32%, males- 16.66%, females-16.66%) (Table 3).

Table 3: Distribution of participants with Tubercular Ascites according to age and gender (N=18).

Age group (years)	Male	Female
20-40	03 (16.66%)	03 (16.66%)
40-60	06 (33.33%)	04 (22.22%)
60-80	00 (00.00%)	02 (11.11%)

With respect to clinical features of the patients, distension of abdomen was the most common finding present in all the 18 (100%) patients with tubercular ascites, followed by pallor (15, 83.33%), pedal edema (09, 50.00%), jaundice (05, 27.77%), reduced appetite (05, 27.77%), pain in Abdomen (03, 16.66%) and fever (02, 11.11%).

Table 4: Relationship between Serum-Ascites Albumin Gradient (SAAG), Ascitic Fluid Total Protein (AFTP) and Adenosine De-Aminase (ADA) (N=18).

	SAAG <1.1	AFTP >2.5
Number of patients having ascitic ADA>30-45 IU/L (N=18)	13 (71.22%)	16 (88.88%)

p = 0.007

Thirteen out of 18 patients (71.22%) with ascitic Adenosine De-Aminase (ADA) levels >30-45 IU/L had Serum-Ascites Albumin Gradient (SAAG) levels <1.1; while 16 (88.88%) of them had Ascitic Fluid Total Protein (AFTP) levels >2.5 (Table 4).

DISCUSSION

The diagnosis of Extra Pulmonary TB (EPTB) remains a challenge all over the world, even more so in India. Peritoneal Tuberculosis is the sixth most common site of Extra Pulmonary TB, worldwide and in our country.^{4,5} Peritoneal TB occurs in three forms: wet type with ascites, dry type with adhesions and fibrotic type with omental thickening and loculated asites.⁶

In this study, an attempt was made to diagnose Tuberculous Ascites by the use of three methods: ADA in ascitic fluid, SAAG ratio and AFTP levels in ascitic fluid. ADA level of 30-45 IU/L was taken as the basis for diagnosis of Tubercular Ascites. Out of 102 patients, it was found that 18 (17.6%) patients fulfilled this criterion of TB ascites. The proportion of EPTB cases amongst all

cases of TB varies in different populations all over the world. At present, the current reported rate of abdominal Tuberculosis is around 11% of all EPTB.^{7,8}

In a large series of autopsies conducted in Western India, evidence of abdominal TB was found in 3.72% of cases by Pimparkar et al in the period of 1964 to 1974.⁹ In present study, the incidence of abdominal tuberculosis was found to be higher. The reason could be the different method of diagnosis. Also, there has been a recent increase in the incidence of abdominal Tuberculosis all over the world. The recent increase in the prevalence rate of abdominal TB is believed to be a result of an increased prevalence of HIV infection in the world.¹⁰

The demographic distribution of patients revealed that the disease occurred more commonly in male subjects in the age group of 40-60 years. The common clinical features included distention of abdomen (100%), pallor (83.33%) and pedal edema (50.00%).

In the group of patients having raised ascitic fluid ADA, authors found that the number of patients having raised AFTP (16 cases, 88.88%) was more than the patients having lower SAAG (13 cases, 71.22%). This difference was statistically significant $p=0.007$. This means that raised AFTP was a better means for detecting exudative ascites due to Tuberculous infection in the abdomen than lower SAAG ratio, which corroborates previous similar observations.^{11,12}

CONCLUSION

In conclusion it can be said that; in the setting where calculating SAAG may prove to be quite expensive, AFTP is a reasonable predictor of Tubercular infection in ascitic fluid.

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