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Original Research Article

A Hospital-Based Study to Assess the Role and Efficacy of Biochemical Testing in Diagnosing the Cause of Fluid Accumulation

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Abstract

Aim: The aim of the present study was to examine role and efficacy of biochemical testing in diagnosing the cause of fluid accumulation.

Methods: The observational hospital-based study was carried out at Department of Biochemistry, Anugrah Narayan Magadh Medical College and Hospital (ANMMCH) Gaya, Bihar, India for one year. Data was taken from medical records department. All 100 indoor patients who were diagnosed as ascites on the basis of history, physical examination, ultrasonography, and of age >18 years were included in the study after getting the informed consent. Patients who had a diagnostic paracentesis within 2 weeks (cause was already established), secondary cause of peritonitis and unwilling to participate in the study were excluded.

Results: This study included 100 patients with age ranging from 20 to 78 years and majority of patients were aged between 41-50 years (n=24, 24%), only 9 patients 9% admitted with ascites of the age group between 18-30 years. 62 patients (62%) were male and 38 patients (38%). The most common clinical feature was abdominal discomfort, followed by Anorexia, Icterus, Splenomegaly and Hepatomegaly. The most common etiology of Ascites was Liver cirrhosis (39%), followed by Tuberculosis (33%) then Malignancy (9%), and Congestive Heart Failure (6%). The least common etiology of Ascites was Hypothyroidism (3%). 40 of the 60 exudates were detected using the traditional cutoff for cell count greater than 500/mm3, but using the cutoff proposed in the present paper (300 cells/mm3), the detection increased to 49/60. Of the biochemical parameters studied, the AST ratio AF/S (> 0.5) detected the greater number of exudates correctly classified 48/60, while 7 of 40 transudates were falsely classified.

Conclusion: Ascites due to chronic liver disease was the main finding with etiology supported by laboratory findings. Biochemical testing of peritoneal and pleural fluids is carried out widely, although the range of tests likely to be useful is limited in comparison to the repertoire of tests available in a modern biochemistry laboratory.

Keywords: Ascites, Cirrhosis, Portal Hypertension, Serum ascetic albumin gradient, Biochemical Testing

Introduction

The accumulation of fluid in the peritoneal cavity constitutes a peritoneal effusion. This is also termed ascites, which is derived from the Greek askos meaning bladder, belly or bag. [1] Fluids accumulate when pathological processes cause an imbalance between hydrostatic pressure gradients, capillary membrane permeability and lymphatic capacity, resulting in protein-poor transudates or inflammatory exudates. [2] Alcoholic liver disease, intra-abdominal malignancy, non-alcoholic cirrhosis, and malignancy with cirrhosis are common causes in descending sequence. [3] Ascites is one spectrum of liver cirrhosis and portal hypertension. Cirrhotic patients at a time invariably present with ascites and are a marker of decompensation. The use of the physiologically based serum ascites albumin gradient to differentiate ascites caused by portal hypertension from other causes provides a better diagnostic approach. Clinically ascites is detected by the presence of flank dullness to percussion, but is not usually apparent until more than 500 mL of fluid

has accumulated. [4] Radiological techniques, such as rectal or transvaginal ultrasonography, may however be able to detect volumes of less than 50 mL, and may also suggest the cause. [5] Biochemical analysis of pleural and peritoneal fluid samples is widely carried out in clinical laboratories. Usually, the aim is to diagnose the cause of a patient's pleural effusion or ascites, although often tests are requested on repeat samples with limited indication for specific analyses. Fluid samples may or may not resemble plasma in terms of protein and lipid concentrations, and may, at least in principle, be subject to interference because of this matrix difference. [6]

In peritoneal fluid, albumin is the most useful test, for the calculation of the serum-ascites albumin gradient; protein and LDH have a role regarding risk and diagnosis of spontaneous bacterial peritonitis and amylase may be useful in diagnosing fluid accumulation due to pancreatitis. Peritoneal fluid pH and glucose are not indicated analyses. For pleural fluid, protein and LDH are important in distinguishing between transudate and exudate using Light's criteria; albumin and the serum-effusion albumin gradient may have a complementary role in patients already on diuretics. Pleural fluid pH is the most useful marker of infection although LDH and glucose are also used. [7] Pleural fluid amylase is often measured but, if raised, is more likely to reflect a malignant process than pancreatic disease as the former is much more prevalent. Tumour markers in both peritoneal and pleural fluids generally have limited diagnostic accuracy for detecting local malignancy. The value of a cell count and bacterial culture of the ascitic fluid is not disputed, but the role of biochemical testing is less clear.

Hence the aim of the study was to examine the pathophysiology of peritoneal and pleural fluid formation, the role of biochemical testing in diagnosing the cause of fluid accumulation and the need for, and progress made towards, proper validation of the tests used.

Materials and Methods

The observational hospital-based study was carried out at Department of Biochemistry, Anugrah Narayan Magadh Medical College and Hospital (ANMMCH) Gaya, Bihar, India for one year. Data was taken from medical records department. All 100 indoor patients who were diagnosed as ascites on the basis of history, physical examination, ultrasonography, and of age >18 years were included in the study after getting the informed consent. Patients who had a diagnostic paracentesis within 2 weeks (cause was already established), secondary cause of peritonitis and unwilling to participate in the study were excluded.

The patients included in the study were evaluated by detailed history. Questionnaire regarding risk factors was included in history which included: Alcohol history including amount and duration of alcohol intake, blood transfusion, surgery, needle prick, tattoo, and high-risk behavior. Detailed examination was performed in every case and clinical presentation was recorded. Ascitic fluid paracentesis was done under all aseptic conditions. Ascitic fluid was analyzed for biochemistry, cytology, gram staining, acid fast bacillus staining, malignant cells, culture, and sensitivity. Serum-ascites albumin gradient (SAAG) and adenosine deaminase (ADA) was estimated in all patients. For culture, 10 ml of ascitic fluid was inoculated in two blood culture bottles at the bedside and was sent immediately to the microbiology laboratory. Specific etiology-oriented investigations were carried out. Tubercular ascites was diagnosed on the basis of low SAAG (<1.1), high protein (>2.5), ADA more than 40 IU/L, lymphocytic predominance on cytology, and response to antitubercular therapy. Serological markers such as antinuclear antibodies, an antibody against liver-kidney-microsomes, anti-smooth muscle antibodies, immunoglobulin A, tissue transglutaminase antibody were done on the basis of clinical profile and if indicated. Serum ceruloplasmin, urinary copper levels and slit lamp examination for Kayser–Fleischer ring was done if indicated. All obese patients in whom other etiology of cirrhosis was ruled out were placed under non-alcoholic steatohepatitis as a possible cause for cirrhosis. Ultrasound abdomen was done in all patients followed by computed tomography if the ultrasound was inconclusive or there was evidence of hepatocellular carcinoma. Upper gastrointestinal endoscopy was performed in all patients with cirrhosis unless contraindication was present. Severity of disease was done according to Child-Turcotte-Pugh (CTP) score in cirrhosis patients. The study was approved by Institutional Ethics Committee.

Results

Table 1: Demographic data

Age in years	N	Percentage
18-30	9	9
31-40	18	18
41-50	24	24
51-60	20	20
61-70	18	18
71-80	11	11

Sex		
Male	62	62
Female	38	38

This study included 100 patients with age ranging from 20 to 78 years and majority of patients were aged between 41-50 years (n=24, 24%), only 9 patients 9% admitted with ascites of the age group between 18-30 years. 62 patients (62%) were male and 38 patients (38%).

Table 2: Clinical presentation of patients of Ascites

Sign and symptoms	N	Percentage
Abdominaldiscomfort	90	90
Anorexia	62	62
Icterus	42	42
Abdominal pain	38	38
Nausea and vomiting	37	37
Fever	31	31
Pallor	29	29
Cough	28	28
Weight loss	25	25
Splenomegaly	22	22
Hepatomegaly	20	20

The most common clinical feature was abdominal discomfort, followed by Anorexia, Icterus, Splenomegaly and Hepatomegaly.

Table 3: Distribution of ascites patients based on etiology

Diagnosis	N	Percentage
Liver cirrhosis	39	39
Tuberculosis	33	33
Malignancy	9	9
Congestive Heart Failure	6	6
Chronic kidney disease	6	6
Hypothyroidism	3	3
Viral	4	4

The most common etiology of Ascites was Liver cirrhosis (39%), followed by Tuberculosis (33%) then Malignancy (9%), and Congestive Heart Failure (6%). The least common etiology of Ascites was Hypothyroidism (3%).

Table 4: Percentage of Patients with Transudates and Exudates Related to Cellularity and Biochemical Parameters

	> 300 cells/ mm^3	> 500 cells/ mm^3	PT AF/S >0.5	COL AF/S >0.4	AST AF/S >0.5	LDH AF/S >0.6	ALT AF/S >0.5	SAAG <1.1
E (n = 60)	42	40	45	46	48	49	42	26
T (n = 40)	2	0 (0)	5	7	7	4	8	34
P value	< 0.0001	< 0.0001	<0.0001	< 0.0001	< 0.0001	< 0.0001	0.0001	< 0.0001

40 of the 60 exudates were detected using the traditional cutoff for cell count greater than 500/mm3, but using the cutoff proposed in the present paper (300 cells/mm3), the detection increased to 49/60. Of the biochemical parameters studied, the AST ratio AF/S (> 0.5) detected the greater number of exudates correctly classified 48/60, while 7 of 40 transudates were falsely classified.

Table 5: Sensitivity, Specificity and Efficiency for Each Biochemical Parameter

Proposed parameter	Sensitivity (%)	Specificity (%)	Efficiency (%)	P
> 300 cells/mm^3	78	97	85	< 0.0001
> 500 cells/mm^3	57	100	79	< 0.0001
AST AF/S > 0.5	80	85	81	< 0.0001
LDH AF/S > 0.6	78	90	83	< 0.0001
PT AF/S > 0.5	72	85	78	< 0.0001
COL AF/S > 0.4	70	85	75	< 0.0001
ALT AF/S > 0.5	70	81	74	0.0001

The AF/S of LDH (> 0.6), PT (>0.5), COL (> 0.4), and ALT (> 0.5) correctly detected 78%, 72%, 70%, and 70% of the exudates, respectively.

Discussion

The term "ascites" is derived from the Greek word Askitos meaning bladder or bag. Ascites is the pathologic accumulation of fluid within the peritoneal cavity. [8] It is not actually a disease but a symptom. Normally, there is just enough free fluid in the peritoneal cavity to lubricate the peritoneal surfaces. Ascites occurs when there is an imbalance of factors that favour the flow of fluid from vascular space and/or when there is exudation of fluid through infection or malignant implantation on the peritoneum. Ascitic fluid may accumulate rapidly or gradually depending upon the cause. Mild ascites may not produce any symptoms. Moderate ascites may just produce an increase in abdominal girth and weight gain. Large amounts of fluid can produce abdominal discomfort, appearance of hernias, particularly umbilical hernias and hinder the mobility of the patient. Elevation of diaphragm and restriction of its movements can produce breathlessness.

Many studies were concentrated on the analysis of ascitic fluid to solve the problem of differential diagnosis and discover some reliable cytological and biochemical markers. [9-12] Pare P et al., found Serum Ascitic Albumin Gradient (SAAG) better for discrimination of portal hypertension than ascitic fluid protein concentration [11]. SAAG is considered a useful clinical tool for diagnosis of ascites. [13] SAAG is generally high (≥1.1 g/dL) in portal hypertension related ascites (liver cirrhosis or congestive heart failure [14-17] and low (<1.1 g/dL) in ascites not due to portal hypertension as in cases of infection or malignancy. The accuracy of the SAAG is approximately 97% in classifying ascites related to portal hypertension whereas only 55% was identified using ascitic total protein concentration. [12] British and American guidelines have adopted SAAG as an initial testing strategy for the differential diagnosis of ascites. [18]

This study included 100 patients with age ranging from 20 to 78 years and majority of patients were aged between 41-50 years (n=24, 24%), only 9 patients 9% admitted with ascites of the age group between 18-30 years. 62 patients (62%) were male and 38 patients (38%). The most common clinical feature was abdominal discomfort, followed by Anorexia, Icterus, Splenomegaly and Hepatomegaly. The most common etiology of Ascites was Liver cirrhosis (39%), followed by Tuberculosis (33%) then Malignancy (9%), and Congestive Heart Failure (6%). The least common etiology of Ascites was Hypothyroidism (3%). 40 of the 60 exudates were detected using the traditional cutoff for cell count greater than 500/mm3, but using the cutoff proposed in the present paper (300 cells/mm3), the detection increased to 49/60. Of the biochemical parameters studied, the AST ratio AF/S (> 0.5) detected the greater number of exudates correctly classified 48/60, while 7 of 40 transudates were falsely classified. Ascitic fluid analysis can be helpful and give clues in diagnosing certain disease entities. In our study, the incidence of ascitic fluid effusion was found more in males as compared to females. This sex wise distribution has also been recorded by Filik & Unal, Khan & Mahmood et al. [19-21] The relative frequency of normal straw coloured fluid was greater as compared to abnormal ones. This has also been documented by Barmeir et al. [22] Atalli et al found that cirrhotic ascitic fluid has higher pH than that of malignant and tubercular ascitic fluid and this corresponds with present study. [23] In the study by Gerbes AL et al., showed, cholesterol is a sensitive parameter for the differential diagnosis of malignant ascites. [24]

Conclusion

Ascites due to chronic liver disease was the main finding with etiology supported by laboratory findings. Biochemical testing of peritoneal and pleural fluids is carried out widely, although the range of tests likely to be useful is limited in comparison to the repertoire of tests available in a modern biochemistry laboratory.

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