Original Research Article

A study on ascitic fluid total protein and serum ascites albumin gradient in evaluation of ascites in children

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Abstract

Background: Ascites is the pathologic accumulation of fluid within the peritoneal cavity. Because many diseases can cause ascites, in particular cirrhosis, samples of ascitic fluid are commonly analyzed in order to develop a differential diagnosis. The concept of transudate versus exudate, as determined by total protein measurements, is outdated and the use of serum-ascites albumin gradient as an indicator of portal hypertension is more accurate. **Aim:** To compare the diagnostic value of Serum Ascites Albumin Gradient and the Ascitic Fluid Total Protein concentration in separating exudative and transudative causes of ascites and to study the value of Serum Ascites Albumin Gradient in separation of ascites related to Portal hypertension from ascites not related to Portal hypertension **Methodology:** It was a Hospital based descriptive study carried out at Kamineni Institute of Medical Sciences. We selected 40 patients admitted with clinical ascites. **Results:** Of the patients studied 57.5% cases were females and 42.5% cases were males. Highest number of cases were due to Nephrotic syndrome (37.5%)followed by Cirrhosis of liver (22.5%), Tuberculous ascites (20%) and Cardiac ascites (15%). Ascitic fluid total protein (AFTP) at a cut off of 2.5 g/dl, had a Sensitivity of 82.5%,Specificity of 60%, Positive predictive value of 85.5%, Negative Predictive value of 46.15% and Accuracy of 78% in classifying ascites as 'Transudate' or 'Exudate'. Serum Ascites Albumin Gradient (SAAG) of 1.1g /dl had a Sensitivity of 40%, Specificity of 40%, Positive predictive value of 80%, Negative predictive value of 27.6% and Accuracy of 50% in classifying ascites as 'Transudate' or 'Exudate'. Serum Ascites Albumin Gradient (SAAG) at 1.1 g/dl had a Sensitivity of 100%, Specificity of 93.5%, Positive Predictive valueof 92.5%, Negative predictive value of 100% and Accuracy of 96% in classifying ascites as 'High gradient' (due to Portal hypertension)or 'Low gradient' (non Portal) hypertensive conditions. **Conclusion:** Serum Ascites albumin gradient is found to be superior to ascetic fluid total protein in the diagnosis of ascites and recommended for classification of ascites as 'High-gradient' or 'Low gradient' ascites instead of 'Transudative' or 'Exudative' ascites. SAAG is superior to transudate —exudate concept not only becauseof its high diagnostic accuracy but also because of it being a better approach to the pathogenesis of ascitic fluid collection.

Keywords: Ascitic fluid, Albumin gradiant, Tuberculous ascites, cirrhosis of liver, Specificity

Introduction

Ascites is defined as pathological fluid accumulation within the abdominal cavity[1]. The word ascites is derived from the Greek word '*askos'*, which means a bag or sack[1-3]. Clinically, ascites is a consequence or complication of a number of diseases, including hepatic, cardiac, and renal diseases, infection, and malignancy. Ascites usually carries an unfavorable prognosis. For example, the development of ascites in cirrhotic patients is associated with a mortality of 15% and 44% at one-year and five-year follow-up periods, respectively[4,5]. However, the prognosis largely depends on the underlying cause (*i.e.* the primary disease). Combined analysis of laboratory data of ascitic fluid samples and clinical and pathological data is essential for establishing a differential diagnosis. This review aims to assess critically the value of ascitic fluid analysis in the diagnosis of ascites, especially cirrhotic ascites.

Diagnostic paracentesis (50 to 100ml) should be part of the routine evaluationof the patient with ascites. The fluid should be examined for its gross appearance, protein content, cell count and differential cell count. Grams and Acid Fast stains and Culture to be performed.

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The Ascitic Fluid Total Protein Concentration (AFTP) has been used to classify samples into broad categories of ―Transudate‖ or ―Exudate‖. Samples are traditionally classified as transudates if the AFTP is less than 2.5 g/dl and as exudates if AFTP is greater than 2.5 g/dl.

The exudate —— transudate concept is based on the assumption that fluid formed by exudation from an inflammed or tumor laden peritoneal surface is high in protein. The causes of exudate are bacterial peritonitis, tuberculous peritonitis and intra abdominal malignancies. Fluid that transudates from a normal peritoneal surface due to an imbalance of starling forces as in cirrhosis, heart failure and nephrotic syndrome is assumed to be low in protein[1]. The AFTP concentration in ascites depends on serum total protein concentration and in cirrhosis. It also depends on portal pressure[2].

The Serum -Ascites Albumin Gradient (SAAG)

SAAG defined as the serum albumin concentration minus the ascitic fluid albumin concentration has been used as a physiologically based alternative in the classification of ascites. It is based on oncotic-hydrostatic balance. The difference between serum and ascitic fluid albumin concentration correlates directly with portal pressure[1].

It is also found that in most of the studies, the SAAG cut-off level in classifying ascites was at 1.1 g/dl. Ascites with SAAG greater than 1.1 g/dl is classified as ―High Gradient- ascites and is usually associated with the presence of portal hypertension and those with SAAG less than 1.1 g/dl is classified as ―Low Gradient‖ ascites and there is no portal hypertension[1].

Objectives

To compare the diagnostic value of Serum Ascites Albumin Gradient and the Ascitic Fluid Total Protein concentration in separating exudative and transudative causes of ascites.

To study the value of Serum Ascites Albumin Gradient in separation of ascites related to Portal hypertension from ascites not related to Portal hypertension.

Materials and methods

Place of Study: Kamineni Institute of Medical Sciences

Study Design: Descriptive Study

Period of Study: Nov2018-Oct 2020

Study Population: Hospitalised children of Kamineni Institute of Medical Sciences, Narketpally in the age group of 1 month to 12 yearswho are clinically diagnosed as having ascites

Inclusion Criteria

Children in the age group of 1 month to 12 years clinically presenting with ascitesof various causes such as

- Nephrotic syndrome
- Portal Hypertension
- Tuberculous ascites
- Cardiac ascites
- Malignant ascites
- Spontaneous bacterial peritonitis
- Chylous ascites
- Pancreatic ascites.

Exclusion Criteria

Children presenting with

- Acute fulminant hepatic failure
- Mixed ascites (Patients with portal hypertension due to cirrhosis plus another cause for ascites formation such as tuberculous peritonitis or
- Intra abdominal malignancies, if found out with subsequent investigations
- Dialysis-related ascites.
- Ascites secondary to liver trauma, biliary tract leakage after biliary tract surgery.

Sample Size

Forty patients were recruited for the study.

Description of Manoeuvre

This is a hospital based study carried out in the ward of the Kamineni Institute of Medical Sciences, Narketpally. The children in the age group of 1 month to 12 years satisfying the inclusion criteria were registered. Children having conditions enlisted in the exclusion criteria were carefully excluded.

A detailed history enlisting the presenting complaints, history of present illness, past history, family history, nutritional history and treatment history were noted.

A thorough general examination was done followed by systemic examination with particular emphasis on examination of abdomen and other systems and the findings recorded in a proforma which follows.

Serum and ascitic fluid were obtained simultaneously from the children satisfying the inclusion criteria and separately tested for Total protein concentration by Biuret reaction[29] and Albumin concentration by Bromocresol Green method[29].

Ascitic fluid was studied for its gross appearance, cell count, smear study for Gram stain and Acid fast stain by Ziehl Neelsen's technique. Ascitic fluid culture was done. Other routine investigations on blood and urine were also done.

The Serum-Ascites Albumin Gradient (SAAG) was calculated by subtracting ascitic fluid albumin level from the serum albumin level.

Statistical analysis

The values obtained by biochemical analysis of ascitic fluid namely Ascitic Fluid Total Protein (AFTP), Ascitic fluid Albumin along with Serum Albumin, Serum-Ascites Albumin Gradient (SAAG) and the confirmatory diagnosis as established were entered in the Master Chart.

Protein determination

By the Biuret Reaction[29]

Results

A total of 40 patients were evaluated for the study.

TABLE-5 Etiology of ascites

Total no of cases -40

ETIOLOGY	NUMBER	PERCENTAGE
NEPHROTIC SYNDROME	15	37.5
CIRRHOSIS WITH PORTAL HYPERTENSION	9	22.5
TUBERCULOUS ASCITES	8	20
CARDIAC ASCITES	6	15
PROTEIN ENERGY MALNUTRITION	2	5
TOTAL	40	100

From the above analysis it was found that Nephrotic syndrome ,Portal hypertension, Tuberculosis and Cardiac ascites were the major causes for ascites comprising of 15,9,8 and 6 respectively and only 2 cases of ascites caused by protein energy malnutrition was recorded .

TABLE -6: Sex distribution of cases of ascites

SEX	NEPHROTIC SYNDROME(%)	CIRRHOSIS WITH PORTAL HYPERTENSION (%)	TUBERCULOUS ABDOMEN (%)	CONGESTIVECARDIAC FAILURE (%)	PROTEIN ENERGY MALNUTRITION (%)	TOTAL (%)
MALE	5(33.3%)	5(55.5%)	3(37.5%)	4(66.6%)	0(0%)	17(42.5%)
FEMALE	10(66.6%)	4(44.4%)	5(62.5%)	2(33.3%)	2(100%)	23(57.5%)
TOTAL	**15**	**9**	**8**	**6**	**2**	**40**

The above analysis showed that 23 female were having ascites against 17males comprising of 42.5% and 57.5% respectively.

TABLE-7: Age wise distribution of cases of ascites

AGE (YR)	TUBERCULOUS ABDOMEN	PORTAL HYPERTENSION	NEPHROTIC SYNDROME	PROTEIN ENERGY MALNUTRITION	CONGESTIVE CARDIAC FAILURE	TOTAL
0-1	0	1	1	0	0	2
1-2	0	1	0	0	0	1
2-3	1	0	2	1	0	4
3-4	1	2	2	1	1	7
4-5	1	1	1	0	0	3

5-6	0	0	2	0	1	3
6-7	1	0	2	0	0	3
7-8	1	1	2	0	2	6
8-9	1	1	1	0	1	4
9-10	0	1	1	0	1	3
10-11	1	0	1	0	0	2
11-12	1	1	0	0	0	2
TOTAL	**08**	**09**	**15**	**2**	**6**	**40**

From the above analysis of age wise distribution of cases ,more number cases were recorded between 3 to 9 years comprising of 82.5% and remaining 17.5% of incidence was recorded in the age group of 1 to 3 years and 9 to 12 years.

TABLE-8: Comparsion of a FTP against diagnosis of ascites inclassifying transudates and exudates.

	POSITIVE (TRANSUDATE	NEGATIVE(EXUDATE	TOTAL
AFTP < 2.5g/dl	23(a)	4(b)	27
	7(C)	6(d)	13
TOTAL	**30**	**10**	**40**

Sensitivity = × 100 = 82.5%

Specificity = $\frac{d}{b+d}$ × 100 = 60%

Positive predictive value = $\frac{a}{a+b}$ × 100 = 85.18%

Negative predictive value = $\frac{d}{c+d}$ × 100 = 46.15%

Percentage of false positives = $\frac{b}{b+d}$ × 100 = 40%

Percentage of false negatives = $\frac{c}{a+c}$ × 100 = 23.33%

Accuracy = = 78%

TABLE-9: Comparsion of saag against diagnosis of ascites in classifying transudates and exudates

		POSITIVE (TRANSUDATE	NEGATIVE(EXUDATE	TOTAL
SAAG ≥ 1.1g/dl	POSITIVE	12(a)	3(b)	15
	NEGATIVE	18(c)	7(d)	25
TOTAL		**30**	**10**	**40**

Negative predictive value = × 100 = 27.6%

Percentage of false positives = $\frac{b}{b+d}$ × 100 = 30%

Percentage of false negatives = $\frac{c}{a+c}$ × 100 = 60%

Accuracy = $\frac{a}{a+c}$ = 50%

Sensitivity = $\frac{d}{b+d}$ × 100 = 40%

Specificity = $\frac{a}{a+b}$ × 100 = 40%

Positive predictive value = × 100 = 80%

TABLE-10: Comparsion of SAAG against diagnosis of ascites in classifying high gradient and low gradient ascites

		POSITIVE (TRANSUDATE	NEGATIVE(EXUDATE	TOTAL
SAAG ≥ 1.1g/dl %	POSITIVE	15(a)	2(b)	21
	NEGATIVE	0(C)	23(d)	29
TOTAL		**15**	**25**	**40**

Sensitivity = × 100 = 100%

Specificity = × 100 = 93.5%

Positive predictive value = × 100 = 90.5%

Negative predictive value = × 100 = 100%

Percentage of false positives = × 100 = 6.5%

Percentage of false negatives = $\frac{c}{a+c}$ × 100 = 0%

Accuracy = = 96%

Ascitic fluid total protein is useful in differentiating ascitic fluid into exudates and transudates whereas serum ascites albumin gradient is useful in differentiating portal hypertensive causes (high SAAG) from non portal hypertensive causes (low SAAG).

Sensitivity of AFTP is more when compared to SAAG but specificity of SAAG is higher in differentiating exudates and transudates. The overall accuracy is higher for AFTP than SAAG in classifying ascitic fluidinto exudates and transudates.

For ascitic fluid total protein, ascitic fluid having total protein >2.5 g/dl isconsidered as exudate and < 2.5 g/dl is considered as a transudate.

For serum ascites albumin gradient, a value of 1.1 g/dl is taken as cut off mark; ascitic fluid with albumin gradient ≥ 1.1 g/dl as high-gradient ascites which is seen in portal hypertension and < 1.1 g/dl as low gradient ascites seen in non portal hypertensive causes of ascites.

With the above values, ascitic fluid total protein and serum ascites albumin gradient were compared for their sensitivity, specificity, positive predictive value, negative predictive value and accuracy with the following results.

TABLE-11: Mean values of saag and aftp in different conditions

DISEASE	SAAG(G/DL)	AFTP(G/DL)
CONGESTIVE CARDIAC FAILURE	1.76	2.38
NEPHROTIC SYNDROME	0.65	1.3
PROTEIN ENERGY MALNUTRITION	0.7	1.3
CIRRHOSIS WITH PORTAL HYPERTENSION	1.47	2.44
TUBERCULOUS ASCITES	1.00	2.83

The ascitic fluid total protein rightly classified nephrotic syndrome, congestive cardiac failure and malnutrition as transudative causes of ascites (< 2.5 g/dl), but misclassified cirrhosis of liver as an exudate. (> 2.5 gm/dl). This parameter rightly classified the exudates (>2.5 g/dl) with a mean value of 2.83 for tuberculous ascites.

Serum Ascites Albumin gradient rightly classified the causes of ascites with portal hypertension and without portal hypertension at a cut off value of ≥1.1 g/dl included the conditions with portal hypertension viz; cirrhosis of liver with a mean value of 1.47 and congestive cardiac failure with a mean value of 1.86.

Discussion

This study determines the utility value of Ascitic Fluid Total Protein (AFTP) and Serum-ascites Albumin Gradient (SAAG) as diagnostic tests in various causes of ascites in children in the age group of 1 month to 12 years attending Kamineni Institute of Medical Sciences.

It also sheds light on the usefulness of Ascitic Fluid Total Protein, (AFTP) and Serum-Ascites Albumin Gradient (SAAG) in classifying ascites of varied etiology.

A total of 40 children who met the standard of inclusion criteria were studied. Biochemical analysis of ascitic fluid was done for the two parameters namely Ascitic Fluid Total Protein (AFTP) and Serum—Ascites Albumin Gradient (SAAG). The diagnostic tests for various causes of ascites were appropriately done as per the availability in the hospital to confirm the diagnosis.

During the study period, no spontaneous bacterial peritonitis (SBP), malignant ascites, chylous ascites or pancreatic ascites were noted

The most common cause of ascites was nephrotic syndrome (37.5%) followed by cirrhosis with portal hypertension (22.5%) and tuberculous ascites (20%). Cardiac ascites accounted for 15% of cases and malnutrition in 5% of cases.

Tuberculous ascites was mainly diagnosed by taking detailed family history clinical Examination , x ray chest and mantoux and biochemical examination of ascitic fluid The culture was negative in all the cases recorded in the present study.

In the study conducted by Runyon BA et al[1] in Los Angeles, USA. 901 patients with ascites have been studied and the most common cause of ascites was found to be cirrhotic ascites (84.1%). Malignant ascites was encountered in 5% of cases followed by cardiac ascites (2.7%). Tuberculous peritonitis was found in 0.7% and nephrotic syndrome in 0.2% of ascites.

During the present study, nephrotic syndrome was the most common cause in contrast to study population of Runyon BA et al[6] as present only included the pediatric age group. Cirrhotic ascites accounted to 22%, followed by tuberculous ascites which could be due to the high prevalence of tuberculosis in our population.

In a retrospective study conducted at Hadassah university37 in both adults and children with nephrotic syndrome they found that there is a significance difference in the Prevalence of ascites between pediatric (52%) and adult patients (23%). Ascites in nephrotic syndrome is more common in children than in adults.

In the study by Runyon BA et al[6],the compatibility of AFTP at a cut off value Of 2.5 g/dl was 55.6% in differentiating transudative and exudative ascites and the compatibility of SAAG at a cut off value of 1.1g/dl was 96.7% in differentiating portal hypertensive and non portal hypertensive causes of ascites.

The compatibility of AFTP was greater in present study (78%) at a cut off level of 2.5g/dl than by Runyon BA et al[6] (55.6%).This was due to the inclusion of numerous causes of ascites in their study .

During the study AFTP at a cut off level of 2.5 g/dl had a sensitivity of 82.5%, specificity of 60%, positive predictive value of 85.18%, negative predicitive value Of 46.15%and with an accuracy of 78% in discriminating "Transudative" and "Exudative" ascites.

Gupta R et al[7] had shown that AFTP at a cut — off level of 2.5 g/dl had an accuracy of 88% to differentiate cirrhotic and non cirrhotic (malignant and tuberculous) ascites. This differed during the present study, the accuracy of AFTP being 78% at a cut — off level of 2.5 g/dl.

Gotyo et al[8] found that AFTP at a cut-off level of 2.5 g/dl had an accuracy of 79.4% in classifying ascites as transudate or exudate which was similar to the accuracy of present study of 78% at a cut-off level of 2.5 g/dl.

In the present study SAAG at a cut-off level of 1.1 g/dl had a sensitivity of 100%, specificity of 93.5% with a predictive value of 90.5%, negative predictive value of 100% and an accuracy of 96% in differentiating ascites as ―High Gradient ascites and ―Low Gradient‖ ascites

Gupta R et al[7] found that SAAG at a cut—off level of 1.1 g/dl had an accuracy of 92% in distinguishing cirrhotic ascites from tuberculous and malignant ascites which was similar to this study.

Das et al[10] found that SAAG at a cut-off level of 1.1 g/dl had an accuracy of 93% similar to present study in differentiating ascites high gradient and low gradient ascites.

In the study by Runyon BA et al[6] 40 patients with cardiac ascites and cirrhotic ascites were studied and the SAAG was ≥ 1.1 g /dl in all the 40 patients. This is in corelation to the present study in which the SAAG is high in cardiac ascites (mean 1.47 g/dl.)

In the study conducted by et al. 42 SAAG was large in patients with transudative ascites (1.6 ± 0.5 g/dl) and small in patients with exudative ascites (0.6 ± 0.4 g/dl). SAAG was especially useful in the separation of cardiac ascites, which often has a high total protein concentration, from high protein exudative ascites.

The findings in the present study concurred with those of Younus et al[11] in case of cardiac ascites, in which, even though there is an elevated ascitic fluid total protein in some patients, as the SAAG was high (1.86 ±0.5 g/dl) in all the cases.

In present study, the findings were similar with 100% sensitivity and 96% accuracy for SAAG and 82.5% sensitivity and 78% accuracy for AFTP. In the present study, SAAG had similar accuracy of 96% in classifying ascites due to portal hypertensive and not due to portal hypertension. But AFTP had a greater accuracy of 78% in classifying ascites into transudates or exudates.

Conflict of Interest: Nil
Source of support:Nil

In the study conducted by Boyer et al[9] ascites due to liver diseases had a higher SAAG (1.7 ± 0.61) and lower AFTP (1.98 ± 1.5 g/dl) when compared to 1.01 g/dl tuberculous peritonitis which has lower SAAG (0.6 ± 0.3) and higher AFTP (4.77 ± 2.05 g/dl). Patients with congestive cardiac failure showed high SAAG (1.12 g/dl) and nephrotic syndrome had lower SAAG. (0.8 g/dl). The observations were similar to present study. In tuberculous ascites, the observed low SAAG with a mean of 1.01 g/dl and a higher AFTP with a mean of 2.83 g/dl. In cirrhotic ascites, the SAAG was high with a mean of 1.47 g/dl, but AFTP was higher with a mean of 2.44 g/dl, which differed from the study by Boyer et al[9].

Conclusion

The above study reinforces the superiority of SAAG to AFTP in diagnostic accuracies of evaluating the etiology of ascites. The utility of SAAG in non-alcoholic liver disease is debatable and needs further studies. The SAAG entity should replace the traditional concept of transudative and exudative ascites as the former classifies the ascites much more physiologically than the later.

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