

Original Research Article

Clinicopathological correlation of serum ascites albumin gradient with ascitic fluid total protein in patients of ascites with portal hypertension attending a tertiary care hospital in Eastern Bihar, India

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ABSTRACT

Background: The level of ascitic fluid total protein (AFTP) is used to differentiate between transudative and exudative ascites. Ascites patients having portal hypertension are considered to be transudative in nature. The traditional transudate/exudate system of ascitic fluid classification based on ascitic fluid total protein concentration is sometimes misleading in patients of ascites with portal hypertension. Now a days SAAG (serum ascites albumin gradient) has become more acceptable in differentiating patients presenting with ascites due to portal hypertension. The objective of this prospective study was to correlate serum ascites albumin gradient with ascitic fluid total protein in patients of ascites having portal hypertension.

Methods: 100 cases of ascites are selected randomly. All the provisional diagnosis are confirmed with the help of different biochemical, pathological and radiological investigations.

Results: SAAG (≥ 1.1 gm/dl) was more sensitive and specific (94% and 90% respectively) than ascitic fluid total protein concentration of <2.5 gm/dl (78% and 50% respectively) in detecting portal hypertension and had higher positive and negative predicative values (97% and 82% respectively) compared to AFTP concentration (85% and 38% respectively).

Conclusions: Considering the advantages of measuring the serum-ascites albumin gradient in illuminating the pathogenesis of ascites and the ease with which this test can be done, it is suggested that this parameter should replace the traditional parameter of ascitic fluid total protein level in the routine analysis of ascites fluid and classification of ascites.

Keywords: AFTP, Non-portal hypertension related ascites, Portal hypertension related ascites, SAAG

INTRODUCTION

Ascites is a word of Greek derivation (ASKOS) and refers to a bag or sac. The word is a noun and describes pathologic fluid accumulation within the peritoneal cavity.¹ Normally very little amount of fluid is present within the peritoneal cavity. In pathologic situations, there may be collection of variable amount of excess fluid either due to increased ultrafiltration (transudate) or

as a result of increased permeability of the capillaries, either due to inflammation or malignancy(exudate).² The level of ascitic fluid total protein (AFTP) is used as an easy test to differentiate between transudative and exudative ascites. Ascites in cirrhotic patients are considered to be transudative in nature due to portal hypertension which causes increased ultrafiltration. The traditional transudate/exudate system of ascitic fluid classification based on ascitic fluid total protein

concentration is sometimes misleading. In upto 30% of cases of cirrhotic ascites, the ascitic fluid is exudative in nature.³ Now a days serum ascites albumin gradient (SAAG), which is difference between serum albumin and ascitic fluid albumin has emerged as a more reliable and acceptable indicator for differentiating patients with ascites due to portal hypertension. Patients of ascites having SAAG ≥ 1.1 are considered to be due to portal hypertension. This prospective and correlative study was done in Medicine Department, Katihar Medical College and Hospital from March 2016 to February 2017. In a study of 12 months 100 patients with ascites were studied.

METHODS

The cases were selected randomly as they came to Department of Medicine, Katihar Medical College and Hospital with complains of abdominal distension. A detailed clinical history of these patients was taken. They were evaluated clinically and a provisional diagnosis of ascites was made. Provisional diagnosis of ascites was further grouped into portal hypertension related ascites and non-portal hypertension related ascites. Provisional diagnosis was confirmed on the basis of pathological correlation and special investigations such as ultrasonography and upper gastrointestinal endoscopy and a final diagnosis was made. According to the proforma developed for this study, all data's were entered along with the hospital number of the patients. The informed consent was obtained from the patients before enrolling them for study. The final analysis was done by Microsoft Excel.

Inclusion criteria

- Patients admitted to indoor wards of medicine department with clinical symptoms and signs of ascites
- Detected incidentally by clinical examination or by ultrasonography either before or after admission
- Developed ascites during the course of treatment for another disease in the ward.

Exclusion criteria

- Patients who had received diuretic therapy within 3 months prior to admission
- Patients who had undergone therapeutic paracentesis within 3 months prior to admission.

RESULTS

Out of 100 patients of ascites who participated in this study 80 (80%) were males and 20 (20%) were female. The maximum incidence was in 41-50 years age group (34%), followed by 31-40 years age group (30%). Incidence was less in age group below 20 years (6%) and above 60 years (6%). Out of 100 patients, 72 (72%) had portal hypertension related ascites and 28 (28%) had non-

portal-hypertension related ascites, based on the presence or absence of portal hypertension respectively. Out of 100 patients, 62 (62%) had transudative ascites, whereas 38 (38%) had exudative ascites. An ascitic fluid total protein of 2.5 gm% was taken as a cut off value for differentiating transudative (< 2.5 gm%) from exudative (≥ 2.5 gm%) ascites. In this study SAAG (≥ 1.1 gm/dl) was more sensitive and specific (94% and 90% respectively) than ascitic fluid total protein concentration of < 2.5 gm/dl (78% and 50% respectively) in detecting portal hypertension and had higher positive and negative predicative values (97% and 82% respectively) compared to AFTP concentration (85% and 38% respectively). The significantly small percentage of false negative for SAAG (6%) as against (22%) for AFTP makes this test much better suited than the older ones for mass screening of total population of ascitic patients with portal hypertension. The P value for SAAG (≥ 1.1 gm/dl) in detecting portal hypertension was < 0.001 which was highly significant as against that AFTP (P value < 0.10).

Table 1: Age and sex distribution of cases of ascites under study (n=100).

Age group (years)	Number of males (%)	Number of females (%)	Total
11-20	4 (4%)	2 (2%)	6 (6%)
21-30	8 (8%)	2 (2%)	10 (10%)
31-40	24 (24%)	6 (6%)	30 (30%)
41-50	28 (28%)	6 (6%)	34 (34%)
51-60	12 (12%)	2 (2%)	14 (14%)
61-70	4 (4%)	2 (2%)	6 (6%)
Grand total	80 (80%)	20 (20%)	100

Table 2: Distribution of patients (n=100) into portal hypertension related ascites (PHRA) and non-portal hypertension related ascites (NPHRA) group.

Group	No. of patients (%)
Portal hypertension related ascites (PHRA)	72 (72%)
Non-portal hypertension related ascites (NPHRA)	28 (28%)
Total	100

Table 3: Distribution of patients (n=100) into transudative and exudative ascites group.

Group	No. of patients (%)
Transudative ascites	62 (62%)
Exudative ascites	38 (38%)
Total	100

The below table shows that out of 72 patients with portal hypertension related ascites (PHRA), 68 had SAAG ≥ 1.1 gm%, while in the non-portal hypertension related ascites (NPHRA) group, out of 28 patients 10 had SAAG ≥ 1.1 gm% and 18 had SAAG < 1.1 gm%. Hence SAAG ≥ 1.1 gm% was able to identify portal hypertension in 94.44% of cases.

Table 4: Distribution of serum ascites albumin gradient (cut- off value 1.1gm%) in portal hypertension related ascites (PHRA) and non-portal hypertension related ascites (NPHRA) group.

	PHRA	NPHRA	Total
SAAG \geq 1.1gm%	68	10	78
SAAG<1.1gm%	4	18	22
Total	72	28	100

Table 5: Distribution of ascitic fluid total protein (cut-off value 2.5 gm%) in PHRA and NPHRA group.

Ascitic fluid total protein (AFTP)	PHRA	NPHRA	Total
<2.5gm%	56	18	74
\geq 2.5gm%	16	10	26
Total	72	28	100

The above table shows that out of 72 patients with PHRA 56 had AFTP <2.5 gm% and 16 had AFTP \geq 2.5 gm%, while out of 28 patients in NPHRA group 18 had AFTP <2.5 gm% and 10 had AFTP \geq 2.5 gm%. Hence AFTP <2.5 gm% was able to identify portal hypertension in 77.78% of cases.

Table 6: Comparative study of SAAG (\geq 1.1gm%) and AFTP (<2.5gm%) in diagnosing PHRA correctly.

	Correctly diagnosed PHRA	Incorrectly diagnosed PHRA	Total
SAAG \geq 1.1gm%	68	4	72
AFTP<2.5gm%	56	16	72

The above table shows the comparative study of the ability of SAAG in diagnosing portal hypertension with that of AFTP. SAAG was able to identify 94.4% cases of portal hypertension correctly whereas AFTP identified 77.78% cases correctly.

DISCUSSION

In the present study 100 consecutive patients of ascites admitted in the General Medicine wards of Katihar Medical College and Hospital were studied. All the patients were thoroughly evaluated by clinical parameters and investigations including ultrasonography of abdomen, ascitic fluid analysis and upper gastrointestinal endoscopy were done. Patients were first grouped into portal hypertension related ascites (PHRA) and non-portal hypertension related ascites (NPHRA) group. Out of 100 patients, 72 (72%) had PHRA whereas 28 (28%) had NPHRA. These broad divisions were further sub-classified according to aetiology. Out of 72 patients of PHRA, 52 (72.22%) had pure uncomplicated cirrhosis, whereas 20 (27.78%) had cirrhosis with other complications e.g. malignancy in 5 cases, bacterial peritonitis in 2 cases, tubercular peritonitis in 6 cases and

congestive cardiac failure in 7 cases. Out of 28 patients of NPHRA, 8 patients had cardiac disease (28.56%), 6 had tubercular peritonitis (21.42%), 4 had renal disease (14.28%). Rest of the patients consisted of tubercular peritonitis with congestive cardiac failure (2 case), bacterial peritonitis (2 case), malignancy without hepatic involvement (2 case), malabsorption with hypoproteinemia (2 case) and myxedema (2 case). Patients were distributed into exudative and transudative category based on ascitic fluid total protein concentration (cut off 2.5 gm%).

Out of 100 patients 62 (62%) had transudative ascites while 38 (38%) had exudative ascites. For each aetiology of PHRA and NPHRA group, serum and ascitic fluid total protein and albumin level and serum ascites albumin gradient were tabulated. In this study serum ascites albumin gradient (SAAG) with a cut off value of 1.1gm/dl was used to differentiate portal hypertension related ascites from non-portal hypertension related ascites. This parameter was also compared with the age-old concept of ascitic fluid total protein(AFTP) with a cut off value of 2.5gm/dl to categorize ascites as transudative or exudative. In the present study value of SAAG was 1.54 ± 0.31 gm/dl (mean \pm standard deviation) for patients with portal hypertension related ascites, whereas for non-portal hypertension related ascites excluding cardiac ascites, SAAG was 1.00 ± 0.31 gm/dl. In this study SAAG was more sensitive and specific (94% and 90% respectively) than AFTP (78% and 50% respectively) and had higher positive and negative predictive values (97% and 82% respectively), compared to AFTP (85% and 38% respectively).

The significantly small percentage false negative for SAAG (6%) as against (22%) for AFTP makes this test much better suited than the older ones for mass screening of total population of ascites patients for presence of portal hypertension. The P value for SAAG (\geq 1.1gm/dl) in detecting portal hypertension was (<0.001) which was highly significant as against that of AFTP (p value <0.10).

The traditional transudate/exudate system of ascitic fluid classification based on ascitic fluid total protein concentration is sometimes misleading, as explained below

- The protein concentration in cirrhotic ascites is essentially determined by serum protein concentration and portal venous pressure. A cirrhotic with a relatively high serum protein concentration will have a relatively high ascitic fluid concentration. Because of this almost 20 percent of uncomplicated cirrhotic ascites samples have greater than 2.5gm/dl of protein.
- During a 10kg diuresis, ascitic fluid total protein doubles, such that 67 percent of patients with cirrhotic ascites develop a ascitic fluid total protein level greater than 2.5gm/dl at the end of diuresis

- In patients with malignant ascites due to hepatocellular carcinoma or metastatic carcinoma of liver, about one third of the cases has ascitic fluid total protein less than 2.5gm/dl
- In many cardiac ascites patients, ascitic fluid total protein concentration is greater than 2.5gm/dl
- This classification has no provision for patients with more than one cause of ascites formation.

Therefore, this classification of ascites places many cirrhotic and cardiac ascites patients in the exudative category while many patients with malignant ascites and patients with spontaneously infected ascites are classified in the transudative category.

The results of some of the earlier studies regarding SAAG are as follows

Laudanno et al, found that SAAG classified the causes of ascites correctly in 95.7% of cases compared to AFTP (in 65.6% of cases). They concluded that SAAG was better than the traditional exudate transudate concept in the classification of ascites.⁴

Alba et al, studied the usefulness and diagnostic limitations of SAAG and concluded that SAAG should replace the AFTP concentration as the initial test to classify ascites. They found that an elevated SAAG (≥ 1.1 gm/dl) correlated well with portal hypertension.⁵

Runyon et al, performed a study taking a total of 901 paired serum and ascitic fluid samples from patients with all forms of ascites and found that SAAG correctly differentiated causes of ascites due to portal hypertension in 96.7% of cases from those that were not due to portal hypertension against AFTP (in 55.6% of cases).⁶ They concluded that exudate transudate concept should be discarded in the classification of ascites. The SAAG is far more useful than AFTP as a marker for portal hypertension.

Besides these studies, Pare et al, Marshal et al, in Cabrol et al, Goyal et al.⁷⁻¹⁰ Kajani et al also found similar results.¹¹

The serum ascites albumin gradient (SAAG) classifies ascitic fluid by the presence or absence of portal hypertension. It is physiologically based and intuitive. The SAAG is based on oncotic hydrostatic balance and correlates directly with portal pressure. SAAG is a subtraction, not a ratio. If it is greater than 1.1gm/dl, the patient has portal hypertension and if it is less than 1.1gm/dl, patient does not have portal hypertension with approximately 97 percent accuracy. SAAG does not explain the pathogenesis of ascites formation. It does not explain where the albumin comes from (i.e. liver or bowel). It simply gives indirect index of portal pressure. In the largest series reported (involving 901 paired specimens), accuracy was 96.7 percent. This parameter is accurate despite ascitic fluid infection, diuresis,

therapeutic paracentesis, albumin infusion and aetiology of liver disease. SAAG classifies cardiac ascites in the high serum ascitic fluid albumin gradient category, similar to cirrhotic ascites. The high SAAG of cardiac ascites is presumably due to high right sided heart pressure and the fact that the SAAG measures absolute portal pressure, which is increased when the right sided heart pressure is high. SAAG remains high (≥ 1.1 gm/dl) in mixed ascites, as a reflection of the underlying portal hypertension. Again, substituting low gradient for exudate and high gradient for transudate is not always true e.g. nephrotic ascites is low gradient but not exudative in nature.

CONCLUSION

The serum ascites albumin gradient (≥ 1.1 gm/dl) correlates well with portal hypertension in ascites ($P < 0.001$). The serum ascites albumin gradient (cut off value 1.1gm/dl) is a better indicator of portal hypertension than the traditional parameter of ascitic fluid total protein AFTP concentration (cut off value 2.5gm/dl) ($P < 0.10$).

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