Section: General Medicine

Original Research Article

A CLINICAL STUDY TO PROVE THAT SERUM ASCITES ALBUMIN GRADIENT HAS SUPERIOR DISCRIMINATING POWER OVER ASCITIC FLUID TOTAL PROTEIN IN CLASSIFYING PORTAL AND NON PORTAL CAUSES OF ASCITES

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ABSTRACT

Background: To compare the efficacy of serum - ascites albumin gradient (SAAG) to AFTP (ascitic fluid total protein) concept in classification of ascites due to portal hypertension and non-portal hypertension.

Materials and Methods: It is a retrospective study in which total of 100 patients of ascites were studied. 72 patients had ascites due to portal hypertension and 28 patients had non-portal hypertension cause. Patients aged more than 18 years with ascites proved by ultrasound and not treated with diuretic. They were categorised into 2 groups based on the presence or absence of postal hypertension by ultrasound criteria and endoscopy. Ascitic fluid total protein, Serum and Ascitic fluid albumin was done in all patients.

Results: SAAG was in portal hypertensive range in 68 of the 72 patients with portal hypertensive and in non-portal hypertensive range in 26 of the 28 patients in non-portal hypertension causes. AFTP was in portal hypertensive range in 56 of 72 patients hypertension and in non-portal hypertensive range in 25 of the 28 patients non portal hypertension causes. Serum - ascites albumin gradient (SAAG) has efficacy of 94%, and ascitic fluid total protein (AFTP) 81% in classifying ascites of portal hypertension and non-portal hypertension causes. The mean of serum - ascites albumin gradient (SAAG) in portal hypertension is 1.7 and in non-portal hypertension 0.78, and is statistically significant in classifying ascites of portal and non-portal hypertension causes. The mean of ascitic fluid total protein (AFTP) in portal hypertension is 1.90 and in non-portal hypertension 3.41 and is statistically significant but lesser than serum- ascites albumin gradient.

Conclusion: A serum ascites albumin gradient >1.1g/dl does suggest of portal hypertension not only in patient with transudate type of ascites but also in cases with high protein concentration.

Keywords: Serum - ascites albumin gradient (SAAG), Ascitic fluid total protein(AFTP), portal hypertension, Transudate.

INTRODUCTION

Ascites is defined as accumulation of fluid within the peritoneal cavity. The etiological spectrum of ascites is vast and practically includes pathology of all the systems. Careful history taking and clinical examination can provide clue to the etiology of ascites. But paracentesis remains the main stay of the investigation of a new onset ascites. In most cases ascites will appear as a part of a well-recognized illness i.e cirrhosis, congestive heart failure, nephrosis or disseminated carcinomatosis. Few patients have more than one cause for ascites formation.

More than 80% of cases of ascites are due to portal hypertension, mainly as a result of cirrhosis, other subset of cause includes pathology of peritoneum, which are not related to portal hypertension. This classification is important because the mode of evaluation and management is different for these two groups. In past portal hypertension ascites was distinguished from the non-portal hypertension causes by determining whether the fluid is transudate or exudates. This concept assumed that in portal hypertension, protein poor ascitic fluid transudates from the normal peritoneal surface, Whereas in ascites associated with peritoneal diseases protein rich ascitic fluid exudates from the peritoneal surface. Ascitic fluid is termed transudate if AFTP (ascitic fluid total protein) is <2.5g/dl.[1,2]

Currently many problems and exceptions have been noted with this concept. Many infected and malignancy related samples have been reported to have transudate fluid and many samples obtained from patients with cirrhosis or heart failure had exudative ascitic fluid. Hence there is a need for this study to know the efficacy of serum ascites albumin gradient to differentiate ascites of portal and non-portal hypertensive etiology. Recently an alternative method to distinguish ascites associated with portal hypertension from non-portal hypertension is proposed. This method is serum - ascites albumin gradient (SAAG), that is subtracting serum fluid albumin from ascites albumin. This method is physiologically based and is a parameter of oncotic pressure gradient reflecting presence or absence of portal hypertension. Serum ascites albumin gradients is increased in ascites of portal hypertensive etiology and decreased in non-portal hypertensive ascitic causes.[3,4]

Ascites associated with portal hypertension has high gradient serum - ascites albumin gradient i.e. > 1.1 gm / dl, whereas ascites associated with peritoneal inflammation or malignancy has low gradient <1.1gm/dl. In mixed ascites with more than one etiology, serum - ascites albumin gradient is high reflecting the presence of portal hypertension.

MATERIAL AND METHODS

It is a retrospective study in Patients with ascites admitted to Gandhi Hospital, Secunderabad from Jan 2015 – oct 20016 were included in the study. Total of 100 patients of ascites were studied. 72 patients had ascites due to portal hypertension and 28 patients had non-portal hypertension cause.

Inclusion Criteria: Patients aged more than 18 years with ascites proved by ultrasound and not treated with diuretics.

Exclusion Criteria: Patients with hepatic encephalopathy and acute gastro- intestinal bleeding., with blunt injury abdomen.

All patients with ascites were subjected to detailed history and thorough clinical examination and following investigation were done Ascitic fluid Analysis for Cell count, cytology, Total proteins, Albumin and Malignant cells

Serum and Ascitic fluid were obtained simultaneously for Albumin and total protein estimation, patients should not be on diuretics before Ascitic fluid analysis. Ascitic fluid sample was sent for Biochemical study -total protein and Albumin, cytological examination including malignant cells and Gram stain and ZN-stain. All patients were divided into 2 groups based on the presence or absence of portal hypertension. Diagnosis of portal hypertension was established by ultrasonography of abdomen and portal venous system and upper gastrointestinal tract endoscopic evaluation.

Ultrasonogram diagnosis of portal hypertension is based on demonstration of splenomegaly and dilated portal vein (> 14 mm diameter) and dilated splenic vein. (>12 mm diameter). Endoscopic evidence of esophageal varices, gastric fundal varices and congestive gastropathy was taken as an evidence supporting the diagnosis of portal hypertension.

Among the patients who have ascites due to portal hypertension, etiology was established by history, physical examination and investigations like ascitic fluid analysis, ultrasonogram- abdomen, echocardiogram and liver Biopsy in some cases. In this study ultrasound evidence of altered hepatic echotexture with nodularity in presence of portal hypertension, cirrhosis of the liver was the underlying etiology. In some cases liver biopsy was done for diagnostic confirmation.

Cardiac cause of Ascites was diagnosed on the basis of history, clinical examination and echocardiographic evidence of cardiac failure. Malignancy related ascites was diagnosed with cytological examination of ascitic fluid revealing malignant cells and laparoscopic evaluation and tissue Biopsy. Nephrogenic cause was considered in patients with chronic renal failure as evident by ultrasound showing Bilateral contracted kidney and clinical assessment after ruling out tuberculosis, cirrhosis and cardiac failure.53 Tuberculosis abdomen was considered if history, clinical features and Ascitic fluid showing elevated lymphocyte count.

Statistical Analysis

Parameters used in the study are serum- ascites albumin gradient and ascitic fluid total protein. Descriptive statistics, student -t- test and Screening tests are used for analysis and comparison. In this study indirect evidence of portal hypertension like ultrasound criteria and endoscopy was made use. Portal venous pressure was not measured. So some cases of portal hypertension can be missed by ultrasound and endoscopy.

RESULTS

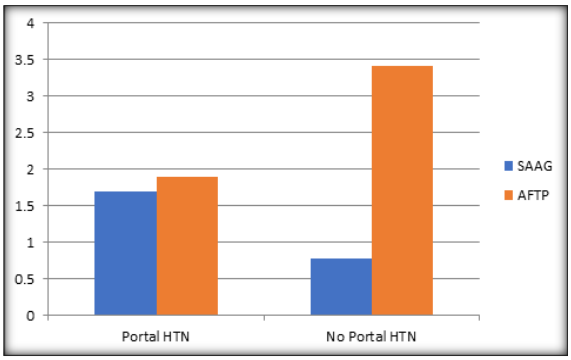

Figure 1: Comparing mean of serum - ascites albumin gradient & AFTP in portal and non-portal hypertension cases.

100 consecutive patients with ascites were taken for the study irrespective of the etiology of ascites during time period from Jan 2015 to Dec 2016.

Of the 100 cases of ascites studied 64 due to cirrhosis ,8 due to cardiac failure ,16 due to tuberculosis abdomen , 8 due to malignancy , 2 due to anemia with hypoproteinemia , 2 due to nephrogenic causes. [Table 1]

The 2 parameters studied Serum – Ascites albumin gradient (SAAG) and Ascitic fluid total protein. The albumin gradient has the highest sensitivity 94.4% followed by AFTP 77.7% .

The specificity of serum - ascites albumin gradient is 92.8% and that of AFTP is 89.2% . The positive predictive value of serum - ascites albumin gradient is 97.1 % and that AFTP is 94.9% . The negative predictive value of serum - ascites albumin gradient is 86.6 % and that AFTP is 60.9% .

Efficacy means percentage of all results that are true results . It is expressed as true positive and true negative tests over the number of tests. Efficacy54 for serum - ascites albumin gradient is 94%and that of AFTP is 81%.

The mean value for serum - ascites albumin gradient in portal hypertension is 1.7 , greater that of non-portal hypertension 0.78 . The t value is 12.82 and p value is <0.0001

The mean value for ascitic fluid total protein (AFTP) in non-portal hypertension is 3.41 greater than that of portal hypertension 1.90 . The t value is 3.35 and p <0.001for AFTP.

The P value clearly suggests that serum - ascites albumin gradient is highly effective in classifying ascites of portal and non-portal hypertensive etiology .

In cirrhosis of liver, out of 64 cases, serum - ascites albumin gradient correctly classified it as a portal hypertensive etiology in 60 cases while AFTP (Ascitic fluid total protein) did so in 52 cases .

In cardiac failure , serum - ascites albumin gradient correctly classified it under portal hypertensive etiology in all 8 cases while ascetic fluid total protein (AFTP) did so in only 4 cases .

Table 1: Disease wise distribution of cases

Disease	No. of. Cases
Cirrhosis	64
Cardiac failure	8
Tuberculosis Abdomen	16
Malignancy	8
Anemia with Hypoproteinemia	2
Nephrogenic cause	2
Total	**100**

Table 2: Age wise distribution of cases

AGE (in years)	No. of. Patients
21-30	18
31-40	20
41-50	28
51-60	22
61-70	12

Table 3: Symptomatology of the patients

Disease		Symptoms					
		Distension of abdomen	Fever	Pain abdomen	Loss of appetite	Bowel disturbances	Yellowish discoloration sclera
Cirrhosis (64)		60	12	14	28	16	28
Cardiac failure (8)		4	-	-	2	-	2
Tuberculosis		6	10	8	8	4	-
Abdomen (16)							
Malignancy (8)		4	2	-	6	2	-
Anemia(2)	with	2	-	-	2	-	-
Hypoproteinemia							
Nephrogenic cause (2)		2	-	-	2	-	-

Table 4: Signs of the patients

Diseases	Icterus	Pallor	Hepatomegaly	Ascites	Splenomegaly	Pedal edema
Cirrhosis (64)	40	26	18	64	28	14
Cardiac failure (8)	2	2	8	6	4	8
Tuberculosis Abdomen (16)	-	6	-	4	2	-
Malignancy (8)	2	4	2	6	-	-
Anemia with Hypoproteinemia (2)	-	2	-	2	-	2
Nephrogenic cause	-	2	-	2	-	2

Table 5: Serum ascites albumin gradient in ascitic fluid

	Portal HTN	No Portal HTN	Total
USG	72	28	100
Test positive (High SAAG)	68	2	70
Test negative (Iow SAAG)	4	26	30
Total	72	28	100
Test positive (Low AFTP)	56	3	59
Test negative (High AFTP)	16	25	41
Total	72	28	100

Table 6: Comparing sensitivity, Specificity, Positive and Negative predictive values of the two parameters studied

Variable	erum –ascites albumin gradient (%)	Ascitic fluid total protein(%)
Sensitivity	94.4	77.7
Specificity	92.58	89.2
Positive Predictive value	94.9	97.1
Negative predictive value	60.9	86.6

DISCUSSION

The efficacy of serum - ascites albumin gradient (SAAG) and ascetic fluid total protein (AFTP) to classify portal hypertension and non-portal hypertension etiology is 94% and 81% respectively . These values are comparable to the results obtained by Akrividis EA et al,[7] Goyal A et al,[6] and Runyon B A et al[5] . The serum - ascites albumin gradient correctly differentiated Ascites of portal hypertension and non-portal hypertension causes in 94%of the cases in the present study ,96.7% as studied by Runyon et al,[5] and 97% as studied by Mc Hutchison JG.[8]

The differential diagnosis of Ascites remains a clinical problem unless a positive diagnosis of malignancy or infection is confirmed by cytology or culture. Such a definite cause cannot be firmly established by conventional analysis of ascitic fluid Moreover these possibilities may be suspected inappropriately in patients with ascites related to liver diseases. The earlier approach used in the differential diagnosis consisted of separating ascitic fluid based on the concentration of protein. Defining fluid with protein level <2.5or 3g/dl as transudate usually caused by liver diseases and fluid with higher protein level as exudate usually found in neoplasms and tuberculosis or other inflammatory diseases. However high protein ascites occurs in 15-20% of patients with liver diseases.[9]

The present study was undertaken to evaluate the reliability of serum - ascites albumin gradient, a parameter reflecting the oncotic pressure gradient between the vascular bed and the interstitial splanchnic or ascitic fluid. According to starling hypothesis the fluid movement across the capillaries is controlled by the balance of hydrostatic and colloidal osmotic forces across the capillary wall. These forces tend to achieve a dynamic equilibrium so that the increased portal pressure is counter balanced by increased oncotic pressure gradient across the capillary membrane. This physiological event is the basis for postulated serum - ascites albumin gradient as the true indicator of presence or absence of increased portal pressure.[10]

B A Runyon et al,[5] who studied 931 patients with ascites reported accuracy of serum - ascites albumin gradient in 96.7% of the cases and 55.6% for AFTP. Porwal et al,[11] study reported accuracy of 96.1% for serum. In Ascites of liver disease, 30 out of 32 patients of liver diseases serum - ascites albumin gradient was increased, i.e in portal hypertensive range.

This correlated well with the previous studies by Pierre pare, Talbot and Hoefs,[12] who studied 51 patients with Ascites, reported 28 out of 29 patients with liver disease serum - ascites albumin gradient in the predicted range. Eldeeb et al reported increased serum - ascites albumin gradient in 100% of patients with liver diseases and Prediction of Esophageal Varices in Cirrhotic Patients.

In contrast to serum ascites albumin - gradient, AFTP retained accuracy in 26 out of 32 patients (81.2%) with liver diseases. It is due to the fact AFTP is influenced by other factors than portal pressure, serum protein concentration being one. This result correlated with the previous studies, 55.6% patients

had AFTP in transudative range in study conducted by Runyon et al,[5] reported 70% efficacy for AFTP.
In Ascites of congestive heart failure serum - ascites albumin gradient is in the portal hypertension range i.e >1.1gm % in all the 4 Patients studied, whereas AFTP was in transudative range only in two patients. Pierre-pare et al reported 100% accuracy of serum - ascites albumin gradient in these patients. BA Runyon et al,[5] have reported 96.7% accuracy respectively for serum - ascites albumin gradient in cardiac failure.
In tuberculosis serum - ascites albumin gradient placed it under non portal hypertension etiology in all 8 patients where as AFTP in 7 out of 8 patients. Marshal JB,[14] reported SAAG,1.1gm/dl, all in the Non portal Hypertension range in all the patients he studied.
In malignancy related ascites serum - ascites albumin gradient was in non-portal hypertensive range in 3 out of 4 patients, whereas AFTP in exudative range in 3 patients. In Pierre pare et al study serum - ascites albumin gradient retained accuracy in 14 out of 15 patients (93.3%) with malignancy related Ascites. B.A Runyon and kundu et al reported accuracy of 96.7% and 100% respectively for serum - ascites albumin gradient in malignancy related Ascites.
AFTP is in exudative range in malignancies in 55.67% of cases in study by BA Runyon et al and 73.3% of the 15 patients of Pierre pare et al.[12] This study further substantiates that SAAG can be used classify ascites of portal and non-portal hypertensive causes. In this study for diagnostic purpose invasive procedures were not done (liver is peritoneal biopsy), chances of missing ascites of mixed etiology is present. However in ascites of mixed etiology SAAG will be in portal hypertensive range.
Limitations: Portal venous pressure was not measured. So some cases of portal hypertension can be missed by ultrasound and endoscopy.

CONCLUSION

Serum ascites albumin gradient was especially useful in separation of cardiac ascites which usually has high protein concentration. So serum - ascites albumin gradient (SAAG) has superior discriminating power and should replace ascitic fluid total protein (AFTP) in the separation of ascites of portal and non-portal hypertension causes. A serum ascites albumin gradient >1.1g/dl does suggest of portal hypertension not only in patient with transudate type of ascites but also in cases with high protein concentration.

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