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Research Article

Etiological factor of ascites and its correlation with serum ascites albumin gradient and cholesterol gradient in patients admitted at rural area

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ABSTRACT

Background: The etiological spectrum of ascites is vast and practically includes pathology of all the systems. In most cases ascites will appear as a part of a well-recognized illness i.e. cirrhosis, tuberculosis, congestive heart failure, nephrosis or disseminated carcinomatosis. Few patients have more than one cause of ascites formation. Majority 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. A portal hypertension ascites was distinguished from the non-portal hypertension causes by determining whether the fluid is transudate or exudate. But many infected and malignancy related samples have been reported to have transudative 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 and serum ascites cholesterol gradient to differentiate ascites of portal and non-portal hypertensive etiology. Ascites associated with portal hypertension has high serum - ascites albumin gradient i.e ≥1.1 gm/dl, whereas ascites associated with peritoneal inflammation or malignancy has low gradient <1.1gm/dl.

Methods: In this study 130 patients of ascites proved by ultrasound were included. They were studied using two parameters – serum ascites albumin gradient (SAAG) and serum ascites cholesterol gradient (SACG). Serum albumin, ascitic fluid albumin, serum cholesterol and ascitic fluid cholesterol was done in all patients.

Results: SAAG was in portal hypertensive range in 96 of the 99 patients with portal hypertension and in non-portal hypertensive range in 24 of the 26 patients in non-portal hypertension causes. SAAG has efficacy of 96.15% in classifying ascites of portal hypertension and non-portal hypertension causes.

Conclusions: The Mean±SD of SAAG in portal hypertension is 1.423±0.188 and in non-portal hypertension is 0.725±0.189 and is statistically significant in classifying ascites of portal and non-portal hypertension causes. A SAAG >1.1 gm/dl is suggestive of portal hypertension not only in patients with transudative type of ascites but also in cases with high protein concentration. The Mean±SD of SACG in malignant ascites is 38.2±10.8 and in non-malignant ascites is 78.1±20.2 and is statistically significant in classifying ascites into malignant and non-malignant etiology.

Keywords: SAAG, SACG, Ascites

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.

In most cases ascites will appear as a part of a well-recognized illness i.e. cirrhosis, tuberculosis, congestive heart failure, nephrosis or disseminated carcinomatosis. Few patients have more than one cause of ascites formation.

84% of cases of ascites are due to portal hypertension mainly as a result of cirrhosis.[1] 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. Currently many problems and exceptions have been noted with this concept. Many infected and malignancy related samples have been reported to have transudative fluid and many samples obtained from patients with cirrhosis or heart failure had exudative ascitic fluid.[2]

In past portal hypertension ascites was distinguished from the non-portal hypertension causes by determining whether the fluid is transudate or exudate. Hence there is a need for this study to know the efficacy of serum ascites albumin gradient and serum ascites cholesterol gradient to differentiate ascites of portal and non-portal hypertensive etiology.

Serum - ascites albumin gradient (SAAG) is derived by subtracting ascitic fluid albumin from serum albumin. The SAAG is accurate in 96.7% cases even in the presence of diuresis, intravenous infusions of albumin. However it is inaccurate in cases of mixed ascites.[3]

In a study, cholesterol concentrations in the ascitic fluid provided the best diagnostic accuracy in the classification of ascitic fluids into exudates and transudates, with a sensitivity of 64.2% and a specificity of 86.7% as compared to SAAG with sensitivity of 86.8% and specificity of 40%.4.

The ascitic fluid cholesterol level is sensitive in diagnosing malignancy related ascites. The high cholesterol level in malignancy related ascites is due to obstruction in lymph flow causing a rupture of lymphatic channel, which leads to secretion of chyle into the peritoneal cavity. Thus there is increased level of cholesterol in ascitic fluid.

Serum - ascites cholesterol gradient (SACG) is derived by subtracting ascitic fluid cholesterol from serum cholesterol. The cut off value for SACG (serum-ascites cholesterol gradient) is 53mg/dl. If SACG is <53 it is malignant ascites and if SACG is ≥53 it is non-malignant ascites

METHODS

Source of data

Patients with ascites getting admitted to SAMC & PG institute, Gram Bhanwarasala, Indore, were included in the study.

Inclusion criteria

- Patients with ascites proved by ultra sound.
- Patients aged more than 18 years.

Exclusion criteria

- Patients with mixed causes of ascites.
- Patients with blunt injury abdomen.

The study was approved by ethical committee and an informed written consent was obtained from every patient. All patients with ascites will be subjected to detailed history and thorough clinical examination and following investigations will be done.

CBC, serum cholesterol, liver function tests (SGOT, SGPT, serum bilirubin and alkaline phosphatase), blood urea, serum creatinine, routine urine analysis, ultrasound abdomen. Ascitic fluid Analysis: cell count, cell type, total proteins, albumin, cholesterol, malignant cells. ADA, echocardigraphy and upper GI endoscopy (if required). Serum ascitic albumin is measured by BCG method and Serum ascitic cholesterol is measured by enzymatic CHOD-POD method using colorimetry.

Ascitic fluid study

Diagnosis of portal hypertension will be established by ultrasonography of abdomen and portal venous system. Ultrasonogram diagnosis of portal hypertension is based on demonstration of dilated portal vein (>13 mm diameter) with or without splenomegaly. In this study, ultrasound evidence of altered hepatic echotexture with nodularity in presence of portal hypertension, will be considered as cirrhosis of liver.

Cardiac cause of ascites will be diagnosed on the basis of history, clinical examination and echocardiographic evidence of cardiac failure. Malignancy related ascites will be diagnosed with cytological examination of ascitic fluid revealing malignant cells or by imaging techniques or by relevant histopathological examination.

Nephrogenic cause will be considered in patients with albuminuria >3 gm in 24 hours and by clinical assessment after ruling out tuberculosis, cirrhosis and cardiac failure. Tuberculosis abdomen will be considered if history and clinical features are suggestive of tuberculosis and also if ascitic fluid shows elevated lymphocyte count and/or if ascitic fluid ADA >30.

Statistical analysis

Unpaired student 't' test for 2 sample mean was applied to compare the mean values of two groups. Analysis of variance (ANOVA) was applied for comparing mean values of more than 2 groups. Later on post hoc tukey test was applied for comparing individual groups. Statistical software Minitab 17 was used for statistical analysis.

RESULTS

Irrespective of the etiology of ascites, 130 patients with ascites were taken for the study. Table 1 shows out of the 130 cases studied 99 were due to cirrhosis, 10 due to tuberculosis abdomen , 9 due to malignancy, 7 due to pancreatitis, 3 due to DCMP, 1 due to hypoproteinemia with severe anaemia and 1 due to nephrotic syndrome.

Table 1: Disease wise distribution of cases.

Disease	No. of cases
Cirrhosis	99
Tuberculosis abdomen	10
Malignancy	9
Pancreatitis	7
DCMP	3
Hypoproteinemia with severe anemia	1
Nephrotic syndrome	1
Total	130

Table 2: Symptomatology of the patients.

Disease	Symptoms		
	Fever	Pain in abdomen	Loss of appetite
Cirrhosis	3	1	4
Tuberculosis abdomen	10	4	9
Malignancy	0	4	3
Pancreatitis	2	7	2
DCMP	0	0	1
Hypoproteinemia with severe anaemia	0	0	1
Nephrotic syndrome	0	0	1

Table 4 shows that 84 patients from cirrhosis, 6 from pancreatitis, 1 from TB abdomen, 1 from malignancy, 3 from DCMP group had history of alcohol consumption.

Table 6, Figure 6 and 7 shows the values of serum albumin and serum cholesterol in different groups and the value of serum albumin noted is highest in DCMP (Mean±SD of 3.667±0.202) and lowest in pancreatitis (Mean±SD of 1.900±0.105) but the values are not statistically significant. Value of Serum Cholesterol is highest in malignancy (Mean±SD of 132.67±8.44) and lowest in DCMP (Mean±SD of 112.33±10.41) but the values are statistically not significant.

Table 3: Signs of the patients.

Disease	Signs			
	Pallor	Icterus	Hepato megaly	Spleno megaly
Cirrhosis	11	25	3	15
Tuberculosis abdomen	2	0	0	0
Malignancy	1	2	5	1
Pancreatitis	1	1	1	1
DCMP	1	0	3	1
Hypoproteinemia with severe anaemia	1	0	1	1
Nephrotic syndrome	0	0	0	0

Table 4: Alcohol consumption in patients.

Disease	Alcohol consumption
Cirrhosis	84
Tuberculosis Abdomen	1
Malignancy	1
Pancreatitis	6
DCMP	3
Hypoproteinemia with severe anaemia	0
Nephrotic syndrome	0

Table 5: Results of serum analysis.

Parameter	Cirrhosis (n=99)	Tuberculosis (n=10)	Malignancy (n=9)	Pancreatitis (n=7)	DCMP (n=3)
Serum albumin	2.425±0.202	2.778±0.689	2.617±0.419	1.900±0.105	3.667±0.202
Serum cholesterol	114.75±8.15	123.20±8.30	132.67±8.44	126.00±6.14	112.33±10.41

Table 6 shows values of ascitic fluid albumin and ascitic fluid cholesterol in different groups. The value of ascitic fluid albumin was highest in DCMP group (mean±SD of 2.160±0.040) and lowest in cirrhosis group (mean±SD of 1.003±0.029). The value of ascitic fluid cholesterol was highest in malignancy group (mean ± SD of 93.11 ± 9.20) and lowest in cirrhosis group (mean±SD of

36.408±5.527). The values of both were statistically significant.

Table 7 shows the value of SAAG in portal hypertensive causes (mean±SD of 1.423±0.188) and non-portal hypertensive causes (mean±SD of 0.725±0.189) and value of SACG in malignant causes (mean±SD of 38.2±10.8) and non-malignant causes (mean±SD of 78.1 ± 20.2). The p value for SAAG is 0.000, which is highly significant and which clearly suggests that SAAG is highly effective in classifying ascites of portal and non-portal hypertensive etiology. The p value for SACG is 0.000, which is highly significant and which clearly suggests that SACG is highly effective in classifying ascites of malignant and non-malignant etiology.

Table 6: Results of ascitic fluid analysis.

Parameter	Cirrhosis (n=99)	Tuberculosis (n=10)	Malignancy (n=9)	Pancreatitis (n=7)	DCMP (n=3)
Ascitic fluid albumin	1.003±0.029	2.068±0.578	1.853±0.495	1.042±0.113	2.160±0.040
Ascitic fluid cholesterol	36.408±5.527	57.30±6.29	93.11±9.20	55.86±7.67	43.00±2.65

Table 7: Gradients between serum and ascitic fluid.

Parameter	Portal hypertensive causes (n= 104)	Non portal hypertensive causes (n= 26)	P value
SAAG	1.423±0.188	0.725±0.189	0.000
Parameter	**Malignant causes (n= 10)**	**Non malignant causes (n= 120)**	**P value**
SACG	38.2±10.8	78.1±20.2	0.000

Table 8: Sensitivity, specificity, positive and negative predictive values, efficacy of SAAG and SACG.

Parameter	SAAG (%)	SACG (%)
Sensitivity	98.05	75
Specificity	88.88	99.15
Positive predictive value	97.11	90
Negative predictive value	92.30	97.5
Efficacy	96.15	92

DISCUSSION

The efficacy of SAAG in the present study to classify portal hypertension and non-portal hypertension etiology is 96.15%.[6] These values are comparable to the results obtained by Goyal AK et al in 1999 (97%) and Runyon B A et al in 1992 (96.7%).[7,8]

The SAAG correctly differentiated ascites of portal hypertension and non-portal hypertension causes in 96.15% of the cases in the present study, 96.7% as studied by Runyon et al, and 97% as studied by Mc Hutchison JG.

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. Accordingly fluid with protein level <2.5 g/dl was termed as transudate which is usually caused by liver diseases and fluid with protein level >2.5 g/dl was termed as exudate which is usually found in neoplasms and tuberculosis or other inflammatory diseases. However high protein ascites occurs in 15-20% of patients with liver diseases.[9]

Since there was only 1 patient of hypoproteinemia with severe anaemia and 1 patient of nephrotic syndrome, statistics cannot be applied to these patients, so their values of SAAG and SACG are not included in the study.

The present study was undertaken to evaluate the reliability of SAAG, 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 who studied 931 patients with ascites reported efficacy of serum - ascites albumin gradient in 96.7% of the cases. Kundu et al studied 51 patients and reported efficacy of 97.8% for serum - ascites albumin gradient. In a study done by Lauden DM et al the efficacy was 95.7% for serum - ascites albumin gradient.

In Ascites of liver disease, 96 out of 99 patients of liver diseases serum - ascites albumin gradient was increased, i.e in portal hypertensive range. This is correlated well with the previous studies by Pierre pare, Talbot and Hoefs who studied 51 patients with ascites in which 29 patients had liver disease out of which serum - ascites albumin gradient was in the predicted range in 28 patients.[12]

In the present study, in all the 3 patients of DCMP, serum - ascites albumin gradient is in the portal hypertension range i.e >1.1 gm%. Pierre-pare et al reported 100% efficacy of serum - ascites albumin gradient in cardiac failure patients. BA Runyon et al and Kundu et al have reported 96.7% and 97% efficacy respectively for serum - ascites albumin gradient in cardiac failure.

In tuberculosis serum - ascites albumin gradient placed it under non-portal hypertension etiology in all 10 patients. Marshal JB reported SAAG <1.1 gm/dl in the non-portal hypertension range in all the patients he studied.[13] In the present study in malignancy related ascites, serum - ascites albumin gradient is in the non-portal hypertensive range in all 9 patients studied.

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 efficacy of 96.7% and 100% respectively for serum - ascites albumin gradient in malignancy related Ascites.

This study further substantiates that SAAG can be used classify ascites of portal and non- portal hypertensive causes. The efficacy of SACG in the present study to classify ascites into malignant and non-malignant etiology is 92%. The sensitivity of SACG in the present study is 75%.

In this study it is found that the value of SACG in malignant causes is 38.2±10.8 and in non-malignant causes is 78.1±20.2 and the p value is 0.000 which is highly significant which clearly suggests that SACG can be used as a measure to differentiate ascites into malignant and non-malignant etiology. Similar results were found by Sharatchandra LK et al in which the SACG values in cirrhosis, tuberculosis and malignancy were 99.2±27.8, 54.16±36.26 and 50±23 respectively with a sensitivity of 80%.

CONCLUSION

In this study 130 patients of ascites proved by ultrasound were included. They were studied using two parameters – SAAG and SACG. Serum albumin, ascitic fluid albumin, serum cholesterol and ascitic fluid cholesterol was done in all patients. SAAG was in portal hypertensive range in 96 of the 99 patients with portal hypertension and in non-portal hypertensive range in 24 of the 26 patients in non-portal hypertension causes. SAAG has efficacy of 96.15% in classifying ascites of portal hypertension and non-portal hypertension causes.

The Mean±SD of SAAG in portal hypertension is 1.423±0.188 and in non-portal hypertension is 0.725±0.189 and is statistically significant in classifying ascites of portal and non-portal hypertension causes. A serum ascites albumin gradient >1.1 gm/dl is suggestive of portal hypertension not only in patients with transudative type of ascites but also in cases with high protein concentration. The Mean±SD of SACG in malignant ascites is 38.2±10.8 and in non-malignant ascites is 78.1±20.2 and is statistically significant in classifying ascites into malignant and non-malignant etiology.

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