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Original article

Study of clinical profile of ascites and its relationwith serum ascites albumin gradient

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Abstract:

Introduction: The serum ascites albumin gradient has been proved in literature to categorize ascites better than either the ascitic fluid total protein or other parameters in ascitic fluid analysis.

Aim: To evaluate the value of SAAG in the etiological diagnosis of ascites.

Materials and Methods: The present observational cohort study was conducted on 100 USG confirmed cases of ascites. The detailed history and physical examination was done on every patient as per the proforma. 10 ml of ascitic fluid was drawn and was sent in two separate bottles for the ascitic fluid analysis. Patients with Ascitic Fluid Total Protein (AFTP) < 2.5 gm/dl were taken to transudative group and > 2.5 gm/dl of AFTP were taken to exudative group. The same The SAAG value distribution in those two groups was also studied.

Results: The mean age of diagnosis of ascites was 49.86±15.88. • The distribution of ascitesamong the males and the females was more or less equal with 52 males and 48 females with a sex ratio of 1.08. The most common cause of ascites among both the males and females was cirrhosis. Though cirrhosis was the common cause in both the genders, it constituted the major cause in males (i.e. 38/52=73.1%). • About 72% of the people were in high SAAG group and the left out 28% were in low SAAG group. According to AFTP value 48% of cases presented as exudative and 52% of cases had transudative ascites. SAAG and AFTP are depicted as sensitivity (94.74% and 83.33%), specificity (91.67% and 63.16%),

Conclusion: The serum ascites albumin gradient (SAAG) is superior to ascitic fluid total protein (AFTP) in the diagnosis of ascites

Keywords: ascites , serum ascites albumin gradient, ascitic fluid total protein

Introduction

Ascites is defined as the accumulation of excess fluid in the peritoneal cavity. This collection is the result of an imbalance when the rate of fluid accumulation from the mesenteries, peritoneum and hepatic surfaces far exceeds its return to the circulation via the capillaries and lymphatics.[1] In health, men have little to no intraperitoneal fluid collections while women may, according to the phase of menstrual cycle, an amount of as much as 20mL in the peritoneal cavity. Collection of significant fluid in the peritoneal cavity is found to have a poor outcome on the mortality in patients. Studies have shown that patients with cirrhotic ascites have a 3-year mortality rate of 50% and those developing refractory ascites, have a 1-year survival rate of less than 50%.[2]

Causes leading to the development of ascites are manifold, of which alcoholic liver disease, intra-abdominal malignancy, non-alcoholic cirrhosis, and malignancy with cirrhosis are the most common.[3] Ascites is one spectrum of liver cirrhosis and portal hypertension. Its presence in a cirrhotic patient signifies decompensation. Once diagnosed, and severity evaluated, cases are managed by a variety of mean, singly or in combination, such as, salt restriction, diuretic therapy, therapeutic paracentesis, or by surgical shunt procedures. [4]

Spontaneous bacterial peritonitis is the most common complication associated with the development of ascites. (ascitic fluid with PMN count of >250 μ L). Close attention to the presence of abdominal tenderness helps to determine the presence of this complication. Studies indicate that in patients with ascites, abdominal pain and abdominal tenderness are more commonly seen in those who develop spontaneous bacterial peritonitis.[5] Patients with ascites and fever should undergo a paracentesis with bedside blood culture inoculation and cell count. Patients with a protein level of less than 1 g/dL in ascitic fluid are at high risk for the development of spontaneous bacterial peritonitis. Prophylactic antibiotic therapy with a quinolone is often recommended.

Acute kidney injury in the setting of ascites and cirrhosis is a medical emergency, requiring prompt diagnosis and multimodal management.[6]

Several gastrointestinal and ovarian malignancies present with ascites, and malignant ascites is a grave prognostic sign of the diseased individual with poor survival.[7,8] In these conditions, ascites develops only as a consequence of the underlying illness. So the evaluation of the patients with ascites requires, that the cause of ascites be established. A proper diagnosis is a prerequisite for the successful management of these patients.

Diagnostic paracentesis is a rapid and cost effective way for identifying the basic disease process. Before the 1980s, the ascitic fluid total protein [AFTP] concentration was used to classify ascites as either exudative [AFTP>/= 2.5 g/dl] or transudative [AFTP<2.5g/dl].[9] Such a classification has its limitations as it is unable to correctly identify the etiological factor responsible for ascites and only offered very little insight regarding the pathophysiology of the fluid collection. These limitations resulted in the development of a new approach to classify ascites, based on the difference between the serum and ascitic fluid albumin concentration [Serum Ascites Albumin Gradient-SAAG]. Studies had shown that patient who developed portal hypertension had a SAAG >/= 1.1 g/dl (High SAAG Ascites) while those in whom ascites developed ascites unrelated to portal hypertension showed a SAAG < 1.1 g/dl (Low SAAG Ascites). Multiple studies have showed that SAAG ratio helps to better categorize ascites, as compared to the usage of ascitic fluid total protein or other parameters in ascitic fluid analysis. This study was undertaken with the goal of evaluation the value of SAAG, in the etiological diagnosis of ascites.

Methodology:

The study was undertaken following permissions from the institutional ethics committee. Hundred patients who were diagnosed with ascites clinically and confirmed on ultrasonography of the abdomen were chosen. Only those above the age of 12 years, with moderate to gross ascites were included. Pregnant women; those with a history of severe coagulopathy or disseminated intravascular coagulation; those on long term diuretics; and those with a serum albumin of <1.5gm/dl were excluded from the study. Detailed history and

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physical examinations were performed on all the subjects. The patients were subjected for detailed investigations like blood for total WBC count, differential count, ESR, hemoglobin. Blood was drawn for various investigations like random blood sugar, blood urea, serum creatinine and liver function tests which included serum bilirubin, serum total protein, serum albumin, SGOT, SGPT and alkaline phosphatase. The abdominal paracentesis was done in all patients with full aseptic precaution. The location on either flanks two finger breadths cephalad and two finger breadth medial to anterior superior iliac spine was selected for abdominal paracentesis. 10 ml of ascitic fluid was drawn and sent for the ascitic fluid analysis. The samples were collected, handled and transported to the lab according to the guidelines given by clinical and laboratory standard institute.[1,2] The ascitic fluid albumin estimation was done in all patients. SAAG is calculated by subtracting ascitic fluid albumin from serum albumin. Ascitic fluid cell count and differential count was done in all patients. The ascitic fluid cytology for malignant cells done in patients suspected to have malignancy related ascites. The other investigations were done when required to establish a definite diagnosis included ECG in all 12 leads, Chest X-ray PA view, Echocardiography, serum HBsAg, ascitic ADA level. The cirrhosis of liver was diagnosed based on clinical signs of portal hypertension, Laboratory and ultrasonographic evidence.

Patients of each etiology were classified into exudative and transudative groups. Those patients with Ascitic Fluid Total Protein (AFTP) < 2.5 gm/dl were taken to transudative group and > 2.5 gm/dl of AFTP were taken to exudative group. The same patients of all the etiologic groups were divided into patients with portal hypertension and patients without portal hypertension. The SAAG value distribution in those two groups was also studied.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA).

Descriptive statistics included computation of percentages, means and standard deviations were calculated. Statistical test applied for the analysis was Independent sample t-test. The level of confidence interval and p-value were set at 95% and 5%.

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Results

Table 1: Distribution age according to gender of the study population

Age (Years)		Gender		Total	p-value
		Female	Male		
	11-20	4	0	4	0.006 (Sig.)
		8.3%	.0%	4.0%	
	21-30	6	0	6	
		12.5%	.0%	6.0%	
	31-40	10	8	18	
		20.8%	15.4%	18.0%	
	41-50	4	14	18	
		8.3%	26.9%	18.0%	
	51-60	8	10	18	
		16.7%	19.2%	18.0%	
	>60	16	20	36	
		33.3%	38.5%	36.0%	
Total		48	52	100	
		100.0%	100.0%	100.0%	

Test applied: chi-square test

Ascites was found to be more or less equally distributed among males and females (52 males vs. 48 females), with a sex ratio of 1.08. Though the incidence among males and females increased as the age advanced beyond 30 years, it was higher in males when compared to females (p=0.006).

Table 2: Distribution of different etiologies of ascites on the basis of SAAG

Etiology		SAAG		Total	p-value
		≤1.1	>1.1		
	CCF	0	16	16	0.001 (Sig.)
		.0%	22.2%	16.0%	
	Cirrhosis	6	50	56	
		21.4%	69.4%	56.0%	
	Hypothyroidism	0	2	2	
		.0%	2.8%	2.0%	
	Liver metastasis	0	2	2	
		.0%	2.8%	2.0%	
	Nephrotic syndrome	4	0	4	
		14.3%	.0%	4.0%	
	Pancreatitis	2	0	2	
		7.1%	.0%	2.0%	
	Peritoneal Carcinomatosis	6	0	6	
		21.4%	.0%	6.0%	
	Splenic abscess	2	0	2	
		7.1%	.0%	2.0%	
	TB Ascites	8	2	10	
		28.6%	2.8%	10.0%	
Total		28	72	100	
		100.0%	100.0%	100.0%	

Test applied: chi-square test

When comparing the patients based on SAAG ratio, 72% belonged to the high SAAG group and 28% in the low SAAG group. Of those with High SAAG, 50 cases were found to be cirrhotic patients, 16 cases had decompensated heart failure and there were 2 cases each showing evidence of liver metastasis; TB ascites; and hypothyroidism. Low SAAG was also seen in 8 cases of TB ascites, 6 cases of peritoneal carcinomatosis, 4 cases of nephrotic syndrome, 6 cases of cirrhosis and 2 cases each of pancreatitis and splenic abscess.

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Table 3: Distribution of different etiologies of ascites on the basis of Ascitic Fluid Total Protein (AFTP)

Etiology		Ascitic Fluid Total Protein (AFTP)		Total	p-value
		≤2.5	>2.5		
Etiology	CCF	8	8	16	0.002 (Sig.)
		15.4%	16.7%	16.0%	
	Cirrhosis	38	18	56	
		73.1%	37.5%	56.0%	
	Hypothyroidism	0	2	2	
		.0%	4.2%	2.0%	
	Liver metastasis	2	0	2	
		3.8%	.0%	2.0%	
	Nephrotic syndrome	2	2	4	
		3.8%	4.2%	4.0%	
	Pancreatitis	0	2	2	
		.0%	4.2%	2.0%	
	Peritoneal Carcinomatosis	0	6	6	
		.0%	12.5%	6.0%	
	Splenic abscess	0	2	2	
		.0%	4.2%	2.0%	
	TB Ascites	2	8	10	
		3.8%	16.7%	10.0%	
Total		52	48	100	
		100.0%	100.0%	100.0%	

Test applied: chi-square test

When classifying the groups into those with exudative and transudative ascites (taking the cut- off of ascitic fluid total protein as >/=2.5 and <2.5 respectively), 48% of cases were classified as being exudative and 52% cases as transudative.

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Table 4: Comparison between SAAG and AFTP

Parameters	SAAG	AFTP
Sensitivity	94.74%	83.33%
Specificity	91.67%	63.16%
Positive Predictive Value	97.30%	41.67%
Negative Predictive Value	84.62%	92.31%
Accuracy	94.00%	68.00%

The five variables calculated for both SAAG and AFTP are depicted as sensitivity (94.74% and 83.33%), specificity (91.67% and 63.16%), Positive Predictive Value (97.30% and 41.67%), Negative Predictive Value (84.62% and 92.31%), Negative Predictive Value (84.62% and 92.31%) and Accuracy (94.00% and 68.00%).

Discussion

The management of ascites is based on evaluating its aetiology/pathophysiology. In the present study PHT was found to be the most common pathophysiology in generation of ascites. Patients with PHT need specific treatment to prevent its complications, and similarly patients of ascites with causes other than PHT need further investigations and treatment accordingly. In presence of PHT, osmotic pressure gradient between plasma and AF has to be raised to counterbalance the high hydrostatic pressure driving the fluid into the intra-peritoneal cavity. Albumin being the single most important factor of osmotic pressure generation, the difference between the serum and ascitic fluid albumin concentration (SAAG) is used to differentiate ascites into this two categories - ascites as due to PHT i.e. High SAAG and causes other than PHT i.e. with Low $_{SAAG.}$[10,11]

In the present investigation the mean age of diagnosis of ascites was 49.86±15.88. Majority of the patients were observed in the age group of >60 years (36%) followed by 18% each in 31-40 years, 41-50 years and 51-60 years of age group. The distribution of ascites among the males and the females was more or less equal with 52 males and 48 females with a sex ratio of 1.08. As the age advanced beyond 30 years of age, the incidence increased in both males and females with a maximum of males compared to females. The incidence though increased both in males and females as the age advanced, it was higher in males when compared to females (p=0.006) respectively.

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Studies	Year of study	Total cases	Age and Gender		
			Male	Female	Mean Age (Years)
Khan FY12	2007	104	67.3%	32.7%	52.9±14.8
Nakhale BD et al.[13]	2016	100	74%	26%	42.4±7. 7
Gogoi P et al.[14]	2018	100	69%	31%	-
Gopi & Hanifah[15]	2019	100	74%	26%	51.46±12.84
Present study	2021	100	52%	48%	49.86±15.88

In the present study considering the etiology of ascites in the population studied, cirrhosis of the liver (56 cases) ranked first followed by CCF (16 cases), tuberculous peritonitis (10 cases) and Peritoneal Carcinomatosis (6 cases). The other causes were nephrotic syndrome (4 cases), splenic abscess (2 cases), pancreatitis (2 cases), liver metastasis (2 cases) and hypothyroidism (2 cases).

Studies	Year of study	Total cases	Etiology (%)				
			Cirrhosis	CCF	Peritoneal tuberculosis	Nephrotic syndrome	Malignancy related
Beg M et al.[16]	2001	100	60%	10%	24%	-	6%
Khan FY[12]	2007	104	59.6%	6.7%	7.8%	2.9%	20%
Nakhale BD et al.[13]	2016	100	68%	10%	16%	4%	2%
Gogoi P et al.[14]	2018	100	44%	3%	29%	5%	11%
Present study	2021	100	56%	16%	10%	4%	6%

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In our study 48% of cases presented as exudative and 52% of cases had transudative ascites. Similar findings were shown by a study from Bihar, India.[17] SAAG is the important test in patients in whom cause of ascites is still need to be rectified. SAAG value strongly correlates with the etiology, whether it is due to CLD or other pathology like malignancies and whether the ascites is transudative or exudative.[18]

In the present study the five variables calculated for both SAAG and AFTP are depicted as sensitivity (94.74% and 83.33%), specificity (91.67% and 63.16%), Positive Predictive Value (97.30% and 41.67%), Negative Predictive Value (84.62% and 92.31%), Negative Predictive Value (84.62% and 92.31%) and Accuracy (94.00% and 68.00%). Thus Serum ascites albumin gradient (SAAG) is the single best test against ascitic fluid total protein (AFTP), in the differential diagnosis of ascites.

Studies	**Year of study**	**Total cases**	**Sensitivity**	
			SAAG	**AFTP**
Beg M et al.[16]	2001	100	94.73%	65.62%
Malabu UH et al.[19]	2006	90	96%	73%
Khan FY[12]	2007	104	98.02%	83.54%
Rodríguez *et al.*[20]	2014	116	93%	80%
Nakhale BD et al.[13]	2016	100	92.31%	83.54%
Gogoi P et al.[14]	2018	100	95%	61.66%
Present study	2021	100	94.74%	83.33%

Conclusion

The current investigation came to the conclusion that ascites owing to chronic liver disease was the most common observation, with the aetiology confirmed by test results. Compared to the conventional measure of ascitic fluid total protein AFTP concentration (cut off value 2.5gm/dl), the serum ascites albumin gradient (cut off value 1.1gm/dl) is a superior indication for etiological diagnosis.

Furthermore, in light of the substantial SAAG value, individuals with portal hypertension might be placed on preventive treatment, allowing for a reduction in mortality and morbidity in this population. Further research can be planned to broaden the scope of the application of SAAG to include complications and management of ascites in addition to the differential diagnosis of ascites.

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