ROLE OF SERUM ASCITES ALBUMIN GRADIENT IN THE ETIOLOGIC DIAGNOSIS OF ASCITES

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Abstract

Background: *Classification based on ascitic fluid protein has been challenged on several occasions in diverse clinical situations, including cirrhotic patients on extended diuretic treatment, cardiac ascites, 1/3 individuals with malignant ascites, spontaneous bacterial peritonitis, and even normal ascitic fluid.*

Objective: *The study's objective was to observe the role of serum ascites albumin gradient (SAAG) in diagnosing Ascites.*

Methods: *This cross-sectional observational study was conducted at the Department of Medicine, Sylhet M.A.G. Osmani Medical College Hospital, Bangladesh. with a total of 100 participants with ascites following the inclusion and exclusion criteria of the study.*

Result: *The most prevalent cause of ascites was cirrhosis, observed in 56% of the participants. Among the 56 cirrhosis patients, mean ± S.D. values of AFTP, AFAlb, SAlb, and SAAG were 2.1±1.2, 0.8±0.6, 3.1±0.7, and 2.2±0.7 respective units accordingly. According to ascitic fluid albumin values, a statistically significant relation was observed between cirrhosis and tuberculosis (P<0.01) and cirrhosis vs malignancy (P<0.01) cases. According to serum ascitic albumin gradient values, a similar significant association was also found between cirrhosis vs tuberculosis (P<0.01) and cirrhosis vs malignancy (P<0.01) cases.*

Conclusion: *SAAG is an essential laboratory tool for the correct aetiological diagnosis of ascites.*

Keywords: *Ascites, Cirrhosis, SerumAlbumin, Ascitic fluid Albumin*

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Introduction

The importance of defining the etiologic diagnosis of ascites has been underscored by the fact that many patients with ascites have disorders that may be treatable. However, ascites differential diagnosis remains a clinical issue. For example, despite its excellent specificity, cytological research has been proven inaccurate in many situations due to many false-negative results.[1] measurement of ascitic fluid total protein (AFTP), which is high in exudate (eŠ2.5 gm/dL) and low in transudate (<2.5 gm/dL). This classification faces some trouble in diverse clinical situations, especially in the case of cirrhotic patients on extended diuretic treatment, cardiac ascites, 1/3 individuals with malignant ascites, and spontaneous bacterial peritonitis. However, it offers little insight into the pathophysiology of ascitic fluid formation.[2] Serum-ascites albumin gradient (SAAG) is extensively used in the diagnostic workup of ascites.[3] SAAG is defined as high or low based on ascitic fluid protein concentration. If the SAAG is High when protein is more significant than 1.1 g/dL(11gm/L), and if it is less than 1.1 g/dL(11gm/L), it is termed a "low" SAAG. Portal hypertension, which either liver or heart illness can cause, results in a high SAAG. Total proteins in an ascitic fluid can assist separate cardiac from hepatic causes when the SAAG is more than 1.1 g/dL. The total protein content in ascitic fluid is frequently more than 2.5 g/dL in cardiac illness but less than 2.5 g/dL in liver disease. Carcinoma, T.B.,

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pancreatic ascites, and nephritic syndrome are all linked to a low SAAG. Various studies have demonstrated the superiority of SAAG in classifying ascites compared to the transudate-exudate concept.[3-5] However, the diagnostic value of the SAAG has poorly been evaluated in our population until now. The study aimed to determine the sensitivity, specificity, and accuracy of SAAG in diagnosing ascites.

Methodology:

Type of study:

This cross-sectional observational study was conducted at the Department of Medicine, Sylhet M.A.G. Osmani Medical College Hospital, Bangladesh from January 2013 to December 2013. The sample size was calculated using Cochran's formula considering a 5% level of significance and 5% precision level (marginal error) of 93.39. However, a total of 100 participants were enrolled in the study.

Objectives:

1. To determine the role of serum ascites albumin gradient in the etiologic diagnosis of ascites.
2. To determine the cause of ascites, calculating serum ascites albumin gradient and its role in the differential diagnosis of ascites, as well as determining its sensitivity, specificity and accuracy in determining ascites patients.

Sample selection:

Consecutive purposive sampling was used to select 100 patients with ascites following the inclusion and exclusion criteria of the study. Patients 18 years or older with clinical features of ascites and those whose ultrasonography findings suggested free fluid in the peritoneal cavity were primarily selected for the study.

Data collection:

Newly diagnosed ascites cases were then informed about the objective of this study, and written consent was obtained from them; Data were collected in a predesigned case record form. Each patient was assessed thoroughly by taking a complete history, including present or previous jaundice, fever, abdominal distension and rapid weight gain, generalized swelling, leg swelling, shortness of breath, puffy face, and scanty micturition. Meticulous clinical examination and necessary investigations were also done to confirm ascites. Finally, informed written consent was taken from each of the patients before taking any interviews.

Further investigations were done to identify the causes of ascites. Finally, the investigator recorded relevant data from history, physical examination, and investigations in a predesigned case record form.

Data analysis:

Data were processed manually and analyzed with the help of SPSS version 16.0 for windows. Quantitative data were presented as a mean and standard deviation, and the student "t" test made comparisons between the groups. Qualitative data were presented as frequency and percentage, and comparison was carried out between two groups by Chi-square ($\chi 2$) or Fisher's Exact Test where necessary. A probability value (p) of <0.05 was considered statistically significant.

Ethical clearance:

Ethical approval was also obtained from the ethical review committee of the study hospital.

Results

The age of the patients ranged from 18 to 71 years with a mean age of 47.3 ± 15.4 years. Among the participants, 62% were male and 38% were female.The mean age of the male was significantly higher than female patients;50.0 ± 15, 042.9 ± 14.3 respectively. (table-I)

Table-I

Significance between gender and mean age among the participants (n=100)

Study Subject	Age in years		*p-value
	Range	Mean ± SD	
Total (n=100)	18-71	47.3 ± 15.4	
Male (n=62)	18-71	50.0 ± 15.0	p<0.05
Female (n=38)	18-70	42.9 ± 14.3	

*student-t test was applied to analyse the data The most common cause of ascites was cirrhosis [56 (56.0%)], and other causes were Abdominal tuberculosis [21 (21.0%)], malignancy [18 (18.0%)], congestive cardiac failure [3 (3.0%)], and nephrotic syndrome [2 (2.0%)].(table-II)

Ascitic fluid albumin values were 0.8 (SD ± 0.6) in cirrhosis, 2.4 (SD ± 0.7) in tuberculous ascites, and 2.6 (SD ± 0.4) in malignancy-related ascites. Ascitic fluid albumin was significantly lower in cirrhosis than tuberculosis (Z=-9.305; p<0.01) and malignancy (Z=-13.302; p<0.01) but not between tuberculosis and malignancy (Z=-0.943; p>0.05)(Table-II)

Ascitic fluid albumin values were 0.8 (SD±0.6)i ncirrhosis, 2.4 (SD±0.7) intuberculous ascites, and 2.6(SD±0.4) in malignancy-related ascites. Association between cirrhosis and tuberculous and cirrhosis and malignancy were significantly significant (p<0.01)but association between tuberculosisand malignancy was not significant (p>0.05). (Table- IV)

Table II

Aetiology of ascities the study participants

Aetiology		
Cirrhosis	56	56
Congestive Cardiac failure	3	3
Abdominal tuberculosis	21	21
Malignancy	18	18
Nephrotic syndrome	2	2

Table III

Characteristics of ascitic fluid in different etiological types of ascites (n=100)

Etiology	Gross appearance				AFTP	AFAlb	SAlb	SAAG
	Straw	clear	Turb	Hemo-rrhagic	Mean (SD)	Mean (SD)	Mean (*SD*)	Mean (SD)
Cirrhosis (n=56)	35	21	0	0	2.1 (1.2)	0.8 (0.6)	3.1 (0.7)	2.2 (0.7)
Congestive cardiac failure (n=3)	0	3	0	0	2.0 (0.0)	0.9 (0.0)	4.5 (0.0)	3.6 (0.0)
Abdominal tuberculosis (n=21)	16	1	0	4	3.8 (1.2)	2.4 (0.7)	3.5 (0.5)	1.0 (0.3)
Malignancy (n=18)	4	2	0	12	4.1 (0.7)	2.6 (0.4)	3.5 (0.4)	0.9 (0.3)
Nephrotic syndrome (n=2)	0	2	0	0	3 (0.0)	2.3 (0.0)	3.8 (0.0)	1.5 (0.0)

Table IV

Mean ascetic fluid albumin level in different type of ascites (n=95)

Ascitic fluid albumin (mg/dl)	Type of ascites			*p- value
	Cirrhosis (n=56)	Tuberculosis (n=21)	Malignancy n=18)	
Mean	0.8	2.4	2.6	C vs M <0.01
Standard				C vs T <0.01
deviation	± 0.6	± 0.7	± 0.4	T vs M >0.05

* ANOVA testwasapplied toanalyzethe data. C=*Cirrhosis*,T=*tuberculosis*, M=*malignant*

Serum-ascitic fluid albumin- gradient was 2.2 (SD ± 0.7) in cirrhosis, 1.0 (SD ± 0.3) in tuberculous ascites, and 0.9 (SD ± 0.3) in malignancy-related ascites. Serum-ascitic fluid albumin- gradient was significantly higher in cirrhosis than in tuberculosis (p<0.01) and malignancy (p<0.01) but not between tuberculosis and malignancy (p>0.05). (table V)

In this study, the sensitivity and specificity of serum-ascites albumin gradient (SAAG) at a cut-off value of ≥11 gm/L in differentiating ascites of cirrhosis from other ascites was 92.9% and 70.5%. Positive and negative predictive values were 80.0% and 88.6% respectively. The overall accuracy was 83.0%.(table VI)

Table V

Mean serum ascitesfluid albumin gradient in different type of ascites (n=95)

Serum-ascitic albumin gradient (mg/dl)	Type of ascites Cirrhosis (n=56)	Tuberculosis (n=21)	Malignancy (n=18)	*p-value
Mean	2.2	1.0	0.9	C vs T <0.01
Standard deviation	± 0.7	± 0.3	± 0.3	C vs M <0.01 T vs M >0.05

* ANOVA testwasapplied toanalyzethe data. C=*Cirrhosis*,T=*tuberculosis*, M=*malignant*

Table VI

Cross-tabulation of serum-ascites albumin gradient at cut-off point 11 gm/L and type of ascites (n=100)

Serum-ascites albumin gradient	Ascites type		Total
	Cirrhotic	Non-cirrhotic	
≥11 gm/L	52 (a)	13 (b)	65
< 11 gm/L	4 (c)	31 (d)	35
Total	56 (a+c)	44 (b+d)	100
Sensitivity	52/ (52+4) *100= 92.9%		
Specificity	31/ (4+31) *100= 70.5%		
Positive predictive value	52/ (52+13) *100= 80.0%		
Negative predictive value	31/ (4+31) *100= 88.6%		
Accuracy	(52+31)/(52+13+4+31) *100= 83%		

Discussion

Currently, the most common cause of ascites was cirrhosis, observed in 56% of cases, abdominal tuberculosis was the cause of cirrhosis in 21%, and malignancy was the cause in18%. Congestive cardiac failure was also observed in 3% and nephrotic syndrome in 2%. The findings of other studies supported these findings.[6,7] These studies suggest that cirrhosis is the most common cause of ascites, as recorded by many global studies. Ascitic fluid total protein values were 2.1 (SD ± 1.2) in cirrhosis, 3.8 (SD ± 1.2) in tuberculous ascites, and 4.1 (SD ± 0.7) in malignancy-related ascites. Ascitic fluid total protein was significantly lower in cirrhosis than in tuberculosis (p<0.01) and malignancy (p<0.01) but not between tuberculosis and malignancy (p>0.05). This result was similar to the study of Sharatchandraetal.[8] In their study, ascitic fluid total protein was significantly lower in cirrhosis than in tuberculosis (p<0.01) and malignancy (p<0.01) but not between tuberculosis and malignancy. It was observed that patients with malignancy as the cause of ascites had higher ascites albumin levels, which was supported by the findings of Khan et al.[9] In this study, the serum-ascitic fluid albumin gradient was 2.2 (SD ± 0.7) in cirrhosis, 1.0 (SD ± 0.3) in tuberculous ascites, and 0.9 (SD ± 0.3) in malignancy-related ascites. Serum-ascitic fluid albumin- gradient was significantly higher in cirrhosis than in tuberculosis (p<0.01) and malignancy (p<0.01) but not between tuberculosis and malignancy (p>0.05). These findings were also following the study by Sharatchandra et al.[8] This result was also supported by Gupta et al. that serum-ascitic fluid albumin gradient was significantly higher in cirrhotic patients with ascites than in malignancy-related ascites.[10] Khan et al. reported that patients with malignancy as the

cause of ascites were found to have significantly lower SAAGs than other patients (p<0.001).[9] In this study, the sensitivity and specificity of serum-ascites albumin gradient (SAAG) at a cut-off value of <11 gm/L in differentiating ascites of cirrhosis from other ascites was 92.9% and 70.5%. Positive and negative predictive values were 80.0% and 88.6%, respectively. The overall accuracy was 83.0%. The study done by-Knawy et al. supported this result that the efficiency in correctly diagnosing patients with ascites caused by liver disease and those related to non-liver disease (malignancy and peritoneal tuberculosis) was 91% for SAAG at a cut-off value of <11 gm/L.

Limitations of The Study

The study was conducted in one centre with a small sample size. So, the results may not represent the whole community. In addition, this study did not evaluate serum-ascites albumin gradient in the differentiation of ascitic fluid of malignancy and tuberculosis.

Conclusion

The ascitic fluid albumin was lower in patients with liver cirrhosis than in patients with ascites of tuberculosis or malignancy. In contrast, the serum-ascites albumin gradient in patients with liver cirrhosis was higher than in patients with ascites of tuberculosis or malignancy. The efficiency in correctly diagnosing patients with ascites caused by liver disease and those related to non-liver disease was high for serum-ascites albumin gradient at a cut-off value of <11 gm/L, and other studies support this.

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Conflict of interest: None declared

ethical approval: approved by the Institutional Ethics Committee

Recommendation

It can be recommended that Serum-ascites albumin gradient be done in all cases of ascites to differentiate between high and low gradient ascites. In addition, further study should be done to differentiate the causes of low gradient ascites.

References:

1. Habeeb KS, Herrera JL. Management of ascites: paracentesis as a guide. Postgraduate medicine. 1997 Jan 1;101(1):191-200.
2. Runyon BA, Montano AA, Akriviadis EA, Antillon MR, Irving MA, McHutchison JG. The serum-ascites albumin gradient is superior to the exudate-transudate concept in the differential diagnosis of ascites. Annals of internal medicine. 1992 Aug 1;117(3):215-20.
3. Khandwalla HE, Fasakin Y, El-Serag HB. The Utility of Evaluating Low Serum Albumin Gradient Ascites in Patients With Cirrhosis. Am J Gastroenterol 2009; 104:1401-5.
4. Malabu UH, Olubuyide IO, Shaibu ME, Olawuyi F. Ascites in Ibadan, Nigeria–usefulness of albumin gradient in its etiologic diagnosis. Biomedical Research. 2006;17:105-9.
5. Das BB, Purohit A, Acharya U, Treskova E. Serum-ascites albumin gradient: a predictor of esophageal varices with ascites. The Indian Journal of Pediatrics. 2001 Jun;68(6):511-4.
6. Kahn FY. Ascites in the state of Qatar: aetiology and diagnostic value of ascitic fluid analysis. Singapore medical journal. 2007 May 1;48(5):434.
7. Mahmood G, Debnath CR, Mandal AK. Evaluation of 100 cases of ascites. Mymensingh Medical Journal: MMJ. 2009 Jan 1;18(1):62-6.
8. Sharatchandra LK, Ningsen R, Singh Y, Narendra RK, Ranjan S, Singh WG. Serum ascites lipid gradients in alcoholic liver cirrhosis, tuberculosis, and malignancy. Journal, Indian Academy of Clinical Medicine. 2005;6(4):306-11.
9. Khan J, Pikkarainen P, Karvonen AL, Mäkelä T, Peräaho M, Pehkonen E, Collin P. Ascites: aetiology, mortality and the prevalence of spontaneous bacterial peritonitis. Scandinavian journal of gastroenterology. 2009 Jan 1;44(8):970-4.
10. Gupta R, Misra SP, Dwivedi M, Misra V, Kumar S, Gupta SC. Diagnosing ascites: value of ascitic fluid total protein, albumin, cholesterol, their ratios, serum ascites albumin and cholesterol gradient. Journal of gastroenterology and hepatology. 1995 Jun;10 (3):295-9.