Original Article

Observation of Serum Ascites Albumin Gradient Values among Children with Ascites

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Most Samsun Nahar Sumi[1*], Nahid E-Subha[2], Farhana Shams[3], Md Ahsan Habib[4], Razia Sultana[5], Mosammat Shameem Ara Begum[6], Sarah Alam[7]

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*Corresponding Author

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ABSTRACT

Introduction: *The serum ascites albumin gradient (SAAG) represents the difference in concentration between serum albumin and ascitic fluid albumin. Various studies have consistently shown a direct correlation between SAAG and portal pressure. A high SAAG value is indicative of portal hypertension.* ***Aim of the study:*** *This study aimed to observe the serum ascites albumin gradient values among children with ascites.* ***Methods and Materials:*** *This cross-sectional study was conducted in the Dhaka Medical College Hospital (DMCH) and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from Jan 2009 to July 2009. A total of 40 consecutive patients with ascites were selected as study subjects using a purposive sampling technique. The data were analyzed using SPSS version 23.0.* ***Results:*** *In this study, 85% of nephrotic syndrome cases had a serum ascites albumin gradient (SAAG) < 1.1 gm/dl, while 15% had SAAG ≥1.1 gm/dl. For chronic liver disease, SAAG was ≥1.1 gm/dl in 92.85% and < 1.1 gm/dl in 7.15%. SAAG was consistently < 1.1 gm/dl in disseminated tuberculosis and protein-losing*

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1. *Assistant Professor, Department of Paediatric Neurology, National Institute of Neuroscience and Hospital, Dhaka, Bangladesh*
2. *Assistant Professor, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical College, Faridpur, Bangladesh*
3. *Assistant Professor, Department of Microbiology, Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh*
4. *Associate Professor, Department of Colorectal Surgery, Dhaka Medical College Hospital, Dhaka, Bangladesh*
5. *Assistant Professor, Department of Paediatric Neurology, Medical College for Women and Hospital, Dhaka, Bangladesh*
6. *Assistant Professor, Department of Pediatrics, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh*
7. *Junior Consultant, Department of Pediatric Neurology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh*

enteropathy but ≥1.1 gm/dl in congestive cardiac failure. Mean SAAG values in nephrotic syndrome, chronic liver disease, disseminated tuberculosis, protein-losing enteropathy, and congestive cardiac failure were 0.72±0.37, 1.63±0.49, 0.68±0.25, 1±0, and 2.30±0, respectively, with highly significant differences (P<0.001). ***Conclusion:*** *The serum ascites albumin gradient (SAAG) demonstrates higher sensitivity and specificity, along with a higher positive predictive value, compared to ascitic fluid total protein concentration in the differential diagnosis of ascites. The SAAG value can serve as a reliable screening test in ascitic patients, with specific tests being conducted as needed for individual patients.*

Keywords: *Serum ascites albumin gradient, SAAG, Ascitic fluid albumin, Nephrotic syndrome, Chronic liver disease, Children*

INTRODUCTION

Ascites is a common presentation in secondary care units. Studies conducted over three decades ago in specialist liver centers reported cirrhosis as the predominant etiology in the Western world (80%–85%), followed by malignancy (10%), heart failure (3%), tuberculosis (2%), pancreatitis (1%), and other rare diseases [1,2]. In contrast, in the Middle and Far East, cirrhosis accounted for only 69% of cases [3]. The onset of ascites is considered a significant milestone in the natural history of liver cirrhosis, associated with a median decrease in survival ranging from 12 years to 2 years and a 50% mortality rate over 2 years [4,5]. The key factors contributing to ascites formation involve the activation of the renin-angiotensin-aldosterone (RAAS) and sympathetic nervous systems, leading to renal sodium retention and portal (sinusoidal) hypertension [5,6]. Guidelines for investigating ascites have relied on historical studies from specialized liver centers [2,7]. The prioritization of investigations at the initial presentation of ascites is influenced by the most prevalent underlying cause of the clinical manifestation and the potential diagnostic yield from tests. For instance, the reported diagnostic accuracy of serum ascites albumin gradient (SAAG) at 11 g/L to identify portal hypertension as a cause of ascites is as high as 97% [8]. Kajani et al. demonstrated a significant correlation ($p < 0.05$, $r = 0.624$) between serum ascites albumin gradient (SAAG) and portal hypertension in alcohol-related liver disease (ArLD). However, this relationship was less apparent ($r = 0.398$) in patients with non-alcoholic fatty liver disease (NAFLD) [9]. Notably, SAAG proves to be a poor differentiator between ascites due to heart failure or liver disease. The diagnostic yield with cytology, if performed with all diagnostic paracenteses of ascites, is also low [1]. In contrast, for malignant ascites, the sensitivity of cytology ranges between 57% and 62% for all cancers and reaches 98% for primary peritoneal carcinomatosis [10]. The issue at hand significantly influences clinical decision-making, particularly in terms of the cost implications associated with the yield from different diagnostic tests and the determination of which test should be routinely performed. Inaccurate investigations pose a substantial cost burden on already stretched healthcare services and have the potential to harm patients [11]. Furthermore, imprecise investigations may lead to delays in achieving a definitive diagnosis and initiating appropriate treatments, ultimately impacting patient outcomes [11]. Considering disease-specific risk factors is crucial when requesting diagnostic workups [12]. Prioritizing tests based on pre-test probability can enhance physician productivity [13]. The primary objective of this study was to observe serum ascites albumin gradient values among children with ascites.

METHODS & MATERIALS

This was a cross-sectional study that was conducted at the Department of Pediatrics, Dhaka Medical College Hospital (DMCH) and Bangabandhu Sheikh Mujib Medical University BSMMU, Dhaka, Bangladesh from Jan 2009 to July 2009. The study enrolled a total of 40 consecutive patients with ascites, including 20 cases of nephrotic syndrome, 14 of chronic liver disease, 4 of disseminated tuberculosis, 1 of congestive cardiac failure, and 1 of protein-losing enteropathy. A purposive sampling technique was employed for sample selection, and ethical approval was obtained from the hospital's ethical committee. Properly written consent was obtained from all participants before data collection. The inclusion criteria involved children aged 1 year to 15 years with ascites, while critically ill children were excluded according to the study's exclusion criteria. Demographic and clinical information of the participants was recorded, and data were analyzed using the SPSS version 23.0 program. In statistical analysis, a P value <0.05 was considered indicative of significance.

RESULT

In this study, the distribution of cases included 50% with nephrotic syndrome, 35% with chronic liver disease, 10% with disseminated tuberculosis, and 2.5% each with protein-losing enteropathy and congestive cardiac failure. In the clinical presentation of 40 patients, common features included abdominal distension (100%), weakness (62.50%), edema (62.50%), scanty urine (52.50%), puffy face (55%), anorexia (50%), weight loss (45%), fever (37.50%), jaundice (25%), hepatomegaly (25%), cough (35.50%), splenomegaly (25%), and haematemesis & melena (20%) **(Table I)**.

Table I: Clinical presentations (N= 40)

Features	n	%
Distension of abdomen	40	100%
Weakness	25	62.50%
Edema	25	62.50%
Scanty urine	21	52.50%
Puffy face	22	55%
Anorexia	20	50%
Weight loss	18	45%
Fever	15	37.50%
Jaundice	10	25%
Hepatomegaly	10	25%
Cough	15	35.50%
Pain in abdomen	5	12.50%
Hypertension	2	5%
Dyspnoea	5	12.50%
Splenomegly	10	25%
Pleural effusion	3	7.50%
Haematuria	4	10%
Vascular spider	1	2.50%
Lymph node enlargement	4	10%
Palmer erythema	4	10%
Night sweats	4	10%
Tuberculous patient	4	10%
Palpitation	1	2.50%

Engorged neck veins	1	2.50%
Cardiac murmur	1	2.50%
Haematemesis & melana	8	20%
Testicular atrophy	0	0%
Diarrhoea	1	2.50%
Abdominal tenderness	2	5%

These frequent manifestations highlight the diverse range of symptoms in the patient cohort. In the cases, the distribution of serum total protein (gm/L) revealed the following mean (±SD) values: 41.65 (±5.85) gm/L for nephrotic syndrome, 57.36 (±8.25) gm/L for chronic liver disease, 66.25 (±4.79) gm/L for disseminated tuberculosis, 36.00 (±0) gm/L for protein-losing enteropathy, and 72.00 (±0) gm/L for congestive cardiac failure **(Table II)**.

Table II: S. total protein (gm/L) levels

Disease	n	Mean ± SD gm/liter
Nephrotic syndrome	20	41.65□5.85
Chronic liver disease	14	57.36□8.25
Disseminated tuberculosis	4	66.25□4.79
Protein-losing enteropathy	1	36.00□0
Congestive cardiac failure	1	72.00□0

In cases of ascites, the mean (±SD) serum albumin levels were observed as follows: 17.60 (±3.23) gm/L for nephrotic syndrome, 24.64 (±6.81) gm/L for chronic liver disease, 27.75 (±4.5) gm/L for disseminated tuberculosis, 19.00 (±0) gm/L for protein-losing enteropathy, and 35.00 (±0) gm/L for congestive cardiac failure **(Table III)**.

Table III: S. albumin (gm/L) levels

Disease	n	Mean □ SD gm/liter
Nephrotic syndrome	20	17.60□3.23
Chronic liver disease	14	24.64□6.81
Disseminated tuberculosis	2	27.75□4.5
Protein-losing enteropathy	1	19.00□0
Congestive cardiac failure	1	35.00□0

In the analysis of ascitic fluid characteristics, straw-colored ascitic fluid was observed in 40%, while clear fluid was found in 60%. No growth of microorganisms was detected, and both Gram and AFB stains were negative. The mean ascitic fluid protein levels for nephrotic syndrome, chronic liver disease, disseminated tuberculosis, protein-losing enteropathy, and congestive cardiac failure were 1.6 (±0.57), 2.1 (±0.92), 3.7 (±1.1), 2.7 (±0), and 2.2 (±0), respectively. Lymphocytes were abundant in four cases, while others showed mesothelial cells and few lymphocytes **(Table IV)**.

Table IV: Characteristics of ascitic fluid in the study subjects

Diagnosis n (%)	Gross appearance	Protein gm/dl Mean ±SD	Culture	Gram and AFB strain	Cytology
Nephrotic syndrome= 20 (50%)	Straw Color= 4 Clear= 16	1.6±0.57	No growth	No growth	Mesothelial cells occasional-lymphocyte
Cirrhosis of the liver = 4 (35%)	Straw Color= 8 Clear= 6	2.1±0.92	No growth	No growth	Mesothelial cells with few occasional lymphocytes
Disseminated tuberculosis = 4 (10%)	Straw Color= 4 Clear= 0	3.7±1.1	No growth	No growth	Plenty lymphocyte seen
Protein-losing enteropathy = 1 (2.5)	Clear= 1	2.7	No growth	No growth	Mesothelial cells with few occasional lymphocytes
Congestive cardiac failure = 1 (2.5)	Clear= 1	2.2	No growth	No growth	Mesothelial cells with occasional lymphocyte

In the observation of serum ascites albumin gradient (SAAG), it was noted that SAAG was <1.1 gm/dl in 85% (17 cases) and ≥1.1 gm/dl in 15% (3 cases) of nephrotic syndrome. In chronic liver disease, SAAG was ≥1.1 gm/dl in 92.85% (13 cases) and <1.1 gm/dl in 7.15% (1 case) **(Table V)**.

Table V: Distribution of serum ascites albumin gradient (SAAG) in the cases of ascites

Diagnosis	SAAG Group		Total	Mean □SD		P-value
	≥1.1 gm/dl n (%)	< 1.1gm/dl n (%)				
Nephrotic syndrome	3 (15%)	17 (85%)	20	0.72□0.37		<0.001
Chronic liver disease	13 (92.85%)	1 (7.15%)	14	1.68□0.49		
Disseminated tuberculosis	0 (0%)	4 (100%)	4	0.68□0.25		
Protein-losing enteropathy	0 (0%)	1 (100%)	1	1□0		
Congestive cardiac failure	1 (100%)	0 (0%)	1	2.30□0		
Total	17 (42.5%)	23 (57.5%)	40	1.08□0.62		

The mean (±SD) of ascitic fluid total protein (AFTP) in nephrotic syndrome, chronic liver disease, disseminated tuberculosis, protein-losing enteropathy, and congestive cardiac failure was 1.912 (±0.57), 1.82 (±0.82), 3.77 (±1.09), 3.7 (±0), and 2.2 (±0), respectively. The

differences are highly significant statistically (P<0.001) **(Table VI)**.

Table VI: Distribution of ascitic fluid total protein (AFTP) in different types of ascites

Group	AFTP ≥ 2.5 5gm/dl n (%)	AFTP <2.5gm/dl n (%)	Total	Mean □SD	P-value
Nephrotic syndrome	4 (20%)	16 (80%)	20	1.91□0.57	<0.001
Chronic liver disease	5 (35.71%)	9 (64.28%)	14	1.82□0.92	
Disseminated TB	4 (100%)	0 (0%)	4	3.77□1.09	
Protein-losing enteropathy	1 (100%)	0 (0%)	1	2.7□0	
Congestive cardiac failure	0	1 (100%)	1	2.2□0	
Total	14 (35%)	26 (65%)	40	2.16□1.03	

When assessing the comparative effectiveness of individual tests in nephrotic syndrome, it was found that for AFTP, the sensitivity, specificity, positive predictive value, and negative predictive value was 80%, 50%, 61.54%, and 71.43%, respectively. Additionally, for SAAG, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic efficacy were 85%, 75%, 80%, 77.27%, and 83.3%, respectively **(Table VII)**.

Table VII: Comparative effectiveness of individual tests in nephrotic syndrome

Tests	Cut off values	Sensitivity	Specificity	Predictive value		Diagnostic efficacy
				Positive	Negative	
		(%)	(%)	(%)	(%)	(%)
AFTP	2.5g/dl	80%	50%	61.54%	73.43%	35%
SAAG	1.1g/dl	85%	75%	80%	77.27%	83.30%

In the evaluation of the comparative effectiveness of individual tests in chronic liver disease, AFTP demonstrated a sensitivity of 64.29%, specificity of 34.29%, positive predictive value of 45.00%, negative predictive value of 34.62%, and diagnostic efficacy of 64.29%. Meanwhile, SAAG showed a sensitivity of 92.86%, specificity of 84.62%, positive predictive value of 87.50%, negative predictive value of 76.47%, and diagnostic efficacy of 83.3% **(Table VIII)**.

Table VIII: Comparative effectiveness of individual tests in chronic liver disease

Tests	Cut off values	Sensitivity	Specificity	Predictive value		
				Positive	Negative	Diagnostic efficacy
		(%)	(%)	(%)	(%)	(%)
AFTP	2.5g/dl	64.29%	34.29%	45.00%	34.62%	64.29%
SAAG	1.1g/dl	92.86%	84.62%	87.50%	76.47%	95.65%

In the current study as per the comparative effectiveness of individual of individual tests in disseminated tuberculosis, we found that in the case of disseminated tuberculosis sensitivity, specificity, positive predictive value, negative predictive value of AFTP were 100%, 72.22%, 28.57%, 100% and 75% respectively and sensitivity, specificity, positive predictive value, negative predictive value and diagnostic efficacy of SAAG were 100%, 47.22%, 82.66%, 100% and respectively **(Table IX)**.

Table IX: Comparative effectiveness of individual tests in disseminated tuberculosis

Tests	Cut off values	Sensitivity	Specificity	Predictive value		
				Positive	Negative	Diagnostic efficacy
		(%)	(%)	(%)	(%)	(%)
AFTP	2.5g/dl	100%	7.22%	28.57%	100%	75%
SAAG	1.1g/dl	100%	47.22%	82.66%	100%	52.50%

DISCUSSION

In our study, the age range was 1 to 15 years, with the majority (45%) falling in the 5 to 9 years group. In a study by Edmund et al., ascites cases had an age range of 30 days to 15 years [14]. Our study found the lowest serum albumin in nephrotic syndrome cases (mean: 17.60 gm/L). Chronic liver disease and protein-losing enteropathy cases also showed low serum albumin (means: 24.64 gm/L and 19 gm/L, respectively), while congestive cardiac failure and disseminated tuberculosis cases had normal serum albumin levels. The study aligns with Hanif. M et al. and Das. B. et al. [15,16]. In our study, SAAG accurately classified ascites in chronic liver disease patients with a high gradient in 92.85% of cases and nephrotic syndrome patients with a low gradient in 85% of cases. SAAG also correctly classified ascites in disseminated tuberculosis as a low gradient in 100% of cases, protein-losing enteropathy as a low gradient in 100% of cases, and congestive cardiac failure as a high gradient in 100% of cases, consistent with findings by Das B et al. and Shakil. A et al. [16, 17]. AFTP identified 80% of nephrotic syndrome and 64.28% of chronic liver disease cases as transudative but misclassified 100% of protein-losing enteropathy cases as exudative. These findings align with Shakil. A et al. and Runyon B et al. [17, 18]. In another study by Subhani, Mohsan, et al., they reported that 54.9% (n 90) of ascites cases were accounted for, followed by malignancy (29.3%) and cardiac failure (6.1%) [19]. SAAG directly correlates with portal pressure, while AFTP is influenced by serum protein concentration and portal pressure. High SAAG indicates portal hypertension, while AFTP, directly related to serum protein concentration, is inversely related to portal pressure. The high protein level in ascites in chronic liver disease may be attributed to a high total serum protein concentration a relatively low degree of portal hypertension, or both. In our study, to detect ascites due to nephrotic syndrome, SAAG demonstrated a sensitivity of 85%, specificity of 75%, positive predictive value of 80%, negative predictive value of 77.27%, and diagnostic accuracy of 83.3%. In comparison, AFTP showed a sensitivity of 80%, specificity of 50%, positive predictive value of 61.54%, negative predictive value of 71.43%, and diagnostic accuracy of 65%. These findings align with Das B et al. [16]. For ascites due to chronic liver disease, AFTP exhibited a sensitivity of 92.86%, specificity of 84.62%, positive predictive value of 87.50%, negative predictive value of 76.47%, and diagnostic efficacy of

95.65%. The specificity, positive predictive value, negative predictive value, and diagnostic efficacy of AFTP for ascites due to chronic liver disease were 64.29%, 34.29%, 45.00%, and 64.29%, respectively. Bandan et al. conducted a study with 121 patients having ascites, revealing positive predictive values for AFTP and SAAG in detecting liver disease at 68% and 80%, respectively [20]. Negative predictive values were 96% for AFTP and 98% for SAAG. For detecting ascites due to disseminated tuberculosis, SAAG exhibited a sensitivity of 100%, specificity of 47.22%, positive predictive value of 82.66%, negative predictive value of 100%, and diagnostic accuracy of 52.5%. In contrast, AFTP showed a sensitivity of 100%, specificity of 72.22%, positive predictive value of 28.57%, negative predictive value of 100%, and diagnostic efficacy of 75%. These results differ from Shakil. A et al.'s study, where SAAG had a sensitivity of 68%, specificity of 38%, positive predictive value of 61%, and negative predictive value of 45%, while AFTP had a sensitivity of 82%, specificity of 15%, positive predictive value of 55%, and negative predictive value of 40% [17]. These disparities may arise from the present study's small sample size and differences in the study population.

LIMITATION OF THE STUDY

The study encountered limitations stemming from a small sample size, a brief duration, and its execution in a tertiary referral center equipped with Pediatric Gastroenterology and Pediatric Nephrology Units. These factors may impact the generalizability of the findings, and caution should be exercised when extrapolating the results beyond the specific context of this specialized center.

CONCLUSION

The serum ascites albumin gradient (SAAG) demonstrates satisfactory sensitivity and specificity in detecting nephrotic syndrome, chronic liver disease, and ascites due to disseminated tuberculosis. Notably, it surpasses ascitic fluid total protein concentration in terms of sensitivity, specificity, and positive predictive value for the differential diagnosis of ascites. The SAAG value proves to be a valuable screening test for ascitic patients, offering a reliable initial assessment. However, when necessary, specific tests should be conducted for individual patients to further refine the diagnosis. This approach allows for a more targeted and precise diagnostic process, enhancing the overall accuracy of ascites etiology determination. The utilization of SAAG as a screening tool, coupled with targeted confirmatory tests, supports a comprehensive and efficient diagnostic strategy in the evaluation of patients with ascites.

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CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee

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