https://doi.org/10.48047/AFJBS.6.Si4.2024.764-771

African Journal of Biological Sciences

Diagnostic Efficacy Of Serum Ascitic Cholesterol Gradient And Ascitic Cholesterol In Differentiating Benign And Malignant Ascites-A Cross Sectional Study

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Article History

Volume 6, Issue Si4, 2024
Received: 25 May 2024
Accepted: 15 June 2024
doi:
10.48047/AFJBS.6.Si4.2024.764-771

ABSTRACT

Background: Ascites, the abnormal accumulation of fluid in the peritoneal cavity, can arise from various benign and malignant conditions. The differential diagnosis of ascites is crucial for determining appropriate treatment. This study investigates the diagnostic efficacy of the serum ascitic cholesterol gradient (SACG) and ascitic cholesterol levels in distinguishing between benign and malignant ascites.

Methods: This cross-sectional observational study included 75 patients with ascites at Saveetha Medical College Hospital. Participants were categorized into benign and malignant ascites groups based on clinical, biochemical, and radiographic findings. Serum and ascitic fluid samples were analyzed for albumin and cholesterol levels. The diagnostic efficacy of SACG was compared to serum ascitic albumin gradient (SAAG) and cytology for malignant cells.

Results: The study found significant differences in serum and ascitic fluid cholesterol levels between benign and malignant ascites groups. SACG demonstrated higher sensitivity (94.4%) and specificity (96.49%) compared to SAAG (sensitivity 88.8%, specificity 91.2%) in differentiating malignant from benign ascites. SACG also showed superior diagnostic accuracy.

Conclusion: SACG is a valuable diagnostic tool for distinguishing between benign and malignant ascites, offering higher accuracy compared to traditional markers such as SAAG. Incorporating SACG into routine diagnostic protocols may improve early diagnosis and treatment of malignant ascites.

Keywords: Ascite, Serum Ascitic Cholesterol Gradient (SACG), Serum Ascitic Albumin Gradient (SAAG), Benign Ascites, Malignant Ascites, Diagnostic Efficacy, Cholesterol Levels, Cross-Sectional Study, Cytology, Liver Cirrhosis, Peritoneal Malignancy.

INTRODUCTION

Ascites is the abnormal buildup of fluid within the peritoneal cavity, and it can be caused by conditions either directly involving the peritoneum, like infections or malignancies, or by diseases that are not directly related to the peritoneum, such as liver disease, heart failure, or hypoproteinemia.[1] The majority of its underlying mechanisms involve portal hypertension, which results in sodium retention due to vasodilation and the activation of sodium-retaining systems. These processes play a pivotal and dynamic role in either promoting or hindering fluid transfer into the ascitic space. The components of ascitic fluid and plasma are in constant flux, but the peritoneal cavity can only absorb a limited amount of ascitic fluid daily, typically around 700-900 ml.

The natural progression of ascites involves a disruption of the circulatory system. Initially, ascites may respond to diuretics, but over time, it can become resistant to them. At this stage, patients may develop hyponatremia before potentially progressing to hepatorenal syndrome. Ascites is a common complication that occurs in various clinical conditions, with the highest prevalence seen in liver cirrhosis (around 80%), followed by peritoneal malignancy (approximately 10%), tubercular peritonitis (about 2%), and conditions like congestive cardiac failure and nephrotic syndrome (2%).[2] Due to the diverse causes of ascites, its differential diagnosis poses a common clinical challenge for healthcare providers.[3]

Analyzing ascitic fluid is a valuable method for identifying the underlying cause of ascites. To differentiate between exudate (ascitic fluid with a total protein content greater than 2.5 gm %) and transudate (ascitic fluid with a total protein content of 2.5 gm % or less) in ascites of various origins, multiple variables are employed. These include assessing cholesterol levels, lactic acid dehydrogenase, amylase, fibronectin levels and adenosine deaminase, as well as physically examining the ascitic fluid, evaluating total protein concentration, cell count, cytology and Serum Ascitic Fluid Albumin Gradient (SAAG).[4] Ascites can result from either malignant or non-malignant causes, and distinguishing between these two conditions is crucial for making subsequent diagnostic and treatment decisions.[5,6]

Although cytology for the presence of malignant cells is considered the gold standard for diagnosing malignancy, it has limitations, with a diagnostic sensitivity of only 64%. This is because malignant cells may be present in low numbers in the fluid, or the processing of specimens may not be optimal, leading to tumor cell lysis. Numerous new biochemical markers have been explored to differentiate between malignant and non-malignant ascites. Recently, the serum ascitic cholesterol gradient (SACG) has been proposed as a tool to aid in the differential diagnosis of ascites. The breakdown of fragile malignant cells in ascitic fluid releases cholesterol from their cell membranes into the ascitic fluid. Additionally, peritoneal carcinomatosis can lead to an excessive secretion of plasma lipoprotein into the peritoneal cavity.[7,8]

AIM AND OBJECTIVES

1. To study the diagnostic efficacy of serum ascitic cholesterol gradient and ascitic cholesterol in differentiating benign and malignant ascites
2. To compare efficacy of serum ascitic cholesterol gradient compared to serum ascitic albumin gradient in differentiating benign and malignant ascites
3. To compare efficacy of serum ascitic cholesterol gradient compared to ascitic fluid for malignant cells in detecting the malignant ascites at the earliest possible

MATERIALS AND METHODS

This cross-sectional observational study was done on 75 participants who visited General medicine Department, Saveetha Medical College and Hospital. Patients ≥ 18 years of age of either gender diagnosed with ascites and those willing to give written informed consent were included in the study.

The study included patients with biochemical, clinical, and radiographic results relating to chronic liver illness, particularly those with liver ultrasonography showing a coarse echotexture with surface nodularity, who were categorized into the benign ascites group. In this group, patients with ascites resulting from other non-malignant causes such as tuberculosis, nephrotic syndrome, and cardiac failure were also included. Patients diagnosed with malignancy were assigned to the malignant group. Blood samples were collected under strict aseptic conditions, and serum levels of albumin and total cholesterol were measured.

Abdominal paracentesis, a procedure to remove ascitic fluid, was performed following the guidelines recommended by the American Association for the Study of Liver Diseases. The collected ascitic fluid was then analysed, including assessments of cholesterol levels, ascitic fluid albumin, and the presence of malignant cells. The study also noted the time of appearance of the serum ascitic cholesterol gradient, specifically whether it appeared before the detection of malignant cells in the ascitic fluid.

Diagnostic efficacy and specificity of serum ascitic cholesterol gradient and ascitic cholesterol compared to serum ascitic albumin gradient and ascitic fluid for malignant cells were calculated using Inferential Statistics using SPSS v. 21.

RESULTS

The study was done on 75 patients who fulfilled the inclusion criteria and here we present the results of the same. The study participants had a mean age of 53±10.94 years. Majority of the study participants were male (65.3%). Of the study participants only 25.4% had malignant cells in their ascitic fluid as shown in table 1.

Table 1: Baseline characteristics of the study participants

Parameters	Total number of participantsn=75 (%)
Age (mean±SD)	53±10.94
Gender	
Male	49 (65.3)
Female	26 (34.7)
Malignant cells	
Positive	19 (25.4)
Negative	56 (74.6)

Figure 1 illustrates the comparison of serum albumin and ascitic fluid level between two groups. In malignant ascites the serum albumin level was 3.58 ± .748 which is statistically higher (p=0.000) than benign group (2.96 ± .559). The mean ascitic albumin in malignant group was 2.61 ± 1.17 and benign group was 1.68 ± 1.12. It was statistically higher in malignant ascites group.

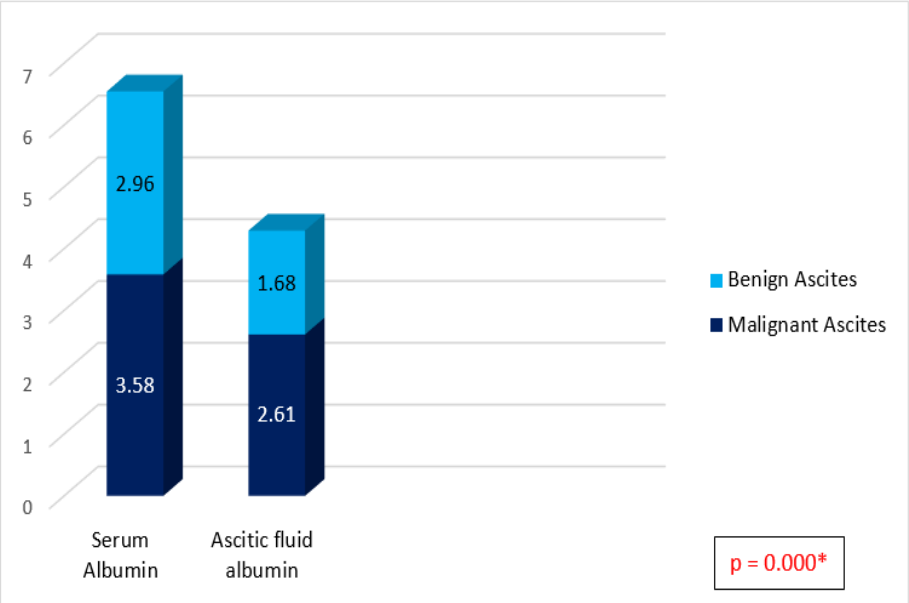


Figure 1: Comparison of Serum albumin and Ascitic fluid albumin levels in patients with Malignant and Benign Ascites

p-value < 0.05 is considered statistically significant

Figure 2 represents the comparison of serum cholesterol and ascitic fluid cholesterol levels between groups. The mean value of serum cholesterol in malignant ascites group was 163.11 ± 17.68 and benign ascites was 129.74 ± 07.43. This value was highly statistically significant (p=0.000). Ascitic fluid cholesterol levels were higher in malignant ascites that is around 121.61 ± 21.76 and in benign ascites it was 44.61 ± 12.79. This was highly statistically significant.

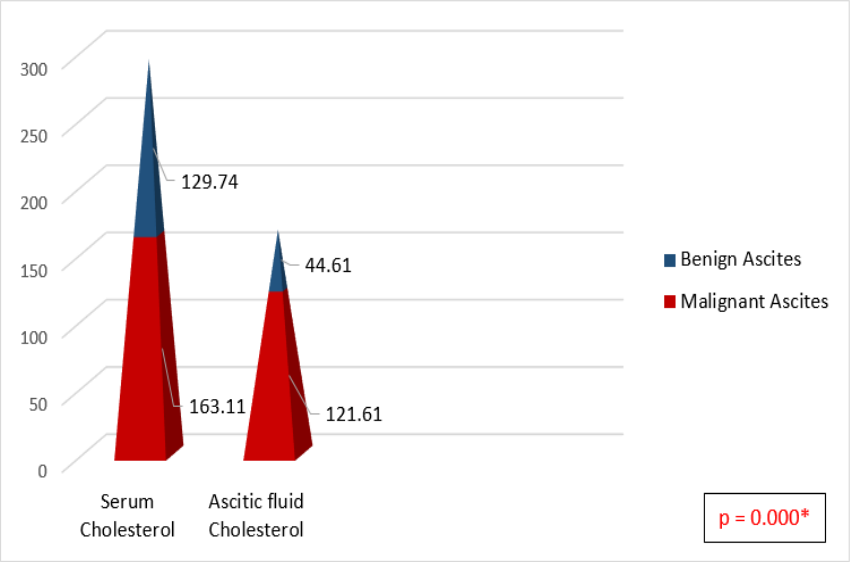


Figure 2: Comparison of Serum cholesterol and Ascitic fluid cholesterol levels in patients with Malignant and Benign Ascites

p-value < 0.05 is considered statistically significant

Figure 3 demonstrates the comparison of SAAG and SACG between groups. The mean SAAG in malignant ascites group was 0.98 ± 0.916 and in benign ascites group 1.44 ± 0.566. It was highly

statistically significant (p=0.000). The mean value of SACG was 41.27 ± 15.50 and in benign group it was 85.12 ± 14.55 with a highly statistically significant p value.

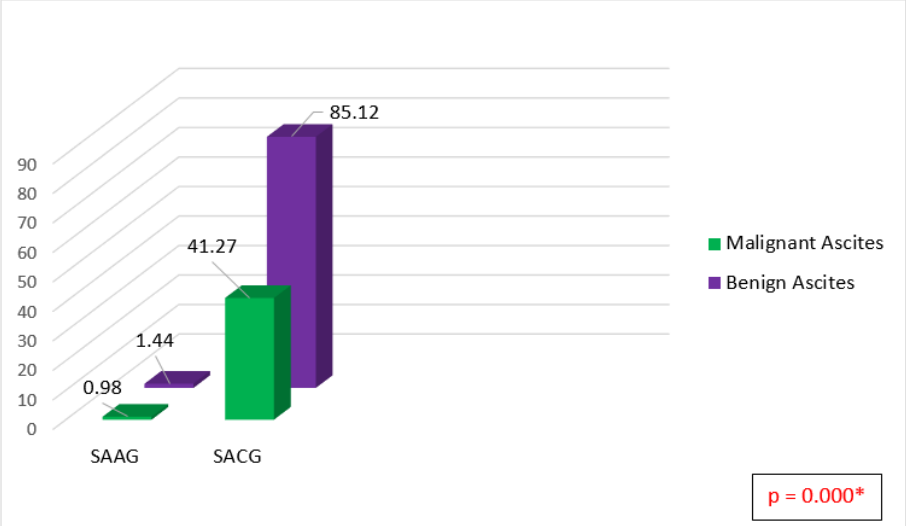
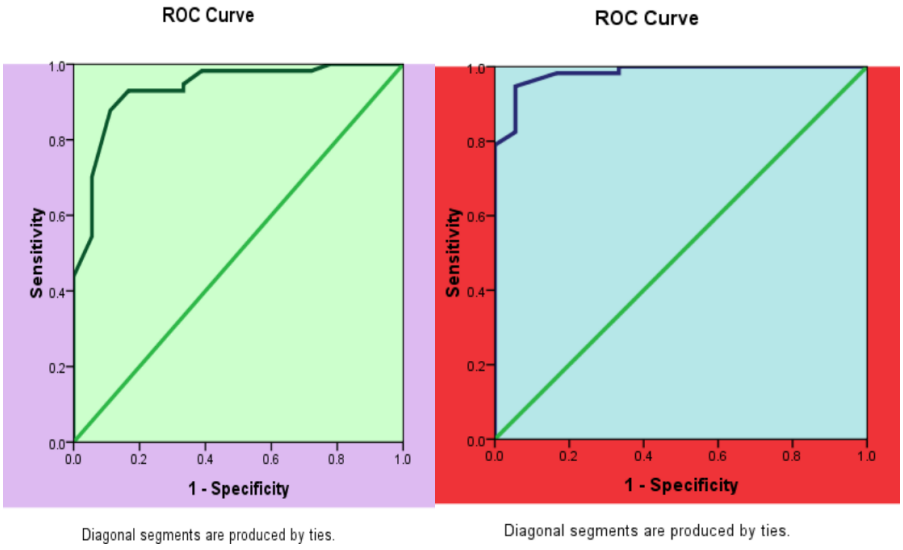


Figure 3: Comparison of SAAG and SACG in patients with Malignant and Benign Ascites p-value < 0.05 is considered statistically significant. SACG – Serum Ascitic Cholesterol Gradient, SAAG – Serum Ascitic Albumin Gradient.



(A) (B)

Figure 4: ROC curve of (A) SAAG and (B) SACG

SAAG – Serum Ascitic Albumin Gradient. SACG – Serum Ascitic Cholesterol Gradient

Figure 4(A) shows the Diagnostic valve of Serum ascitic albumin gradient (SAAG) in separating malignant and Benign Ascites patients is represented in ROC. The sensitivity of SAAG in predicting malignant ascites is 88.8 and specificity is 91.2. The diagnostic accuracy of SAAG in malignant ascites is 90.6. Its overall significance is 0.007. Figure 4(B) represents Diagnostic valve of SACG in malignant and Benign Ascites patients by ROC. The sensitivity was around 94.4 and specificity of SACG was 96.49. The diagnostic value was around 96%.

Comparison of diagnostic value of SACG and ASSG between malignant and Benign Ascites patients is illustrated in figure 5. The sensitivity, specificity, PPV, NPV and diagnostic accuracy were superior in regards to serum ascitic cholesterol gradient when compared to serum ascitic albumin gradient.

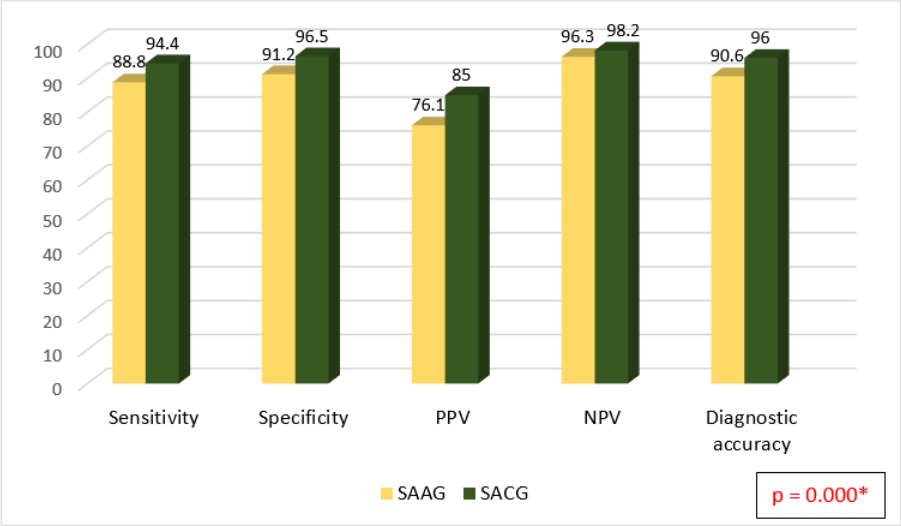


Figure 5: Comparison of diagnostic value of SACG and SAAG between malignant and Benign Ascites patients.

p-value < 0.05 is considered statistically significant. SACG – Serum Ascitic Cholesterol Gradient. SAAG – Serum Ascitic Albumin Gradient. NPV – Negative Predictive Value. PPV- Positive Predictive Value.

DISCUSSION

The primary challenge in diagnosis is identifying the cause of ascites. In developed countries, approximately 80% of patients are found to have underlying cirrhosis, while about 10% have malignant causes. Ascites is highly prevalent, affecting up to 75% of patients with liver cirrhosis, whereas malignancy-related ascites constitutes roughly 10% of cases.[9] The origins of malignant ascites are typically cancers such as endometrial, ovarian, breast, lung, pancreatic, colorectal, primary peritoneal carcinomas and hepatobiliary. Despite cytology being considered the gold standard for diagnosing malignancy, it exhibits a sensitivity of only 64%. As a result, new biochemical markers have been explored to distinguish between malignant and non-malignant ascites. One such marker, Serum Ascites Albumin Gradient (SAAG), has demonstrated promise in differential diagnosis.[10]

The objective of our study was to assess the role of ascitic fluid lipids, the serum ascites lipid gradient, and diagnostic indicators in distinguishing between malignant and benign ascites in patients with cirrhosis.

In this research, we observed that patients with malignant ascites were, on average, older than those with benign ascites. Out of a total of 75 patients with ascites, 49 were male and 26 were female, with approximately 76% falling into the benign category. A majority of males (80%) had benign ascites, whereas 69% of females had benign ascites.

When it comes to albumin levels, malignant ascites had serum albumin levels that were considerably greater than those of benign ascites. In our study, the serum albumin level in malignant ascites was 3.58 ± .748, significantly higher than the benign group (2.96 ± .559). Serum albumin is considered an independent prognostic factor for malignant ascites. The mean ascitic albumin in the malignant group was also statistically higher than in the benign group.[11,12]

Consequently, SAAG was found to be a valuable marker for differentiating between benign and malignant ascites. The mean SAAG was lower in the malignant group, indicating less difference between serum and ascitic albumin levels in these patients. This suggests increased permeability

of albumin to the malignant peritoneum in malignant ascites. Our study demonstrated high sensitivity, specificity, and diagnostic accuracy for SAAG in predicting malignant ascites.

Cholesterol levels, both in serum and ascitic fluid, were substantially greater in malignant ascites compared to benign ascites. Increased vascular permeability, accelerated cholesterol synthesis, and the release of cholesterol from malignant cells implanted on the peritoneum are all implicated for the elevated cholesterol found in malignant ascites. Ascitic cholesterol exhibited good sensitivity and specificity for diagnosing malignant ascites.[13]

Furthermore, the serum ascitic cholesterol gradient (SACG) was superior to SAAG in distinguishing between malignant and benign ascites. The mean SACG was lower in the malignant group and demonstrated a high sensitivity, specificity, and diagnostic accuracy for identifying malignant ascites. In all aspects, SACG outperformed SAAG in diagnosing malignant ascites from benign ascites.[14]

CONCLUSION

The diverse range of causes for ascites often leads to confusion in its differential diagnosis. Distinguishing between malignant and benign origins of ascites using available biochemical methods could prevent the need for many costly and time-consuming diagnostic tests. It also allows physicians to promptly administer suitable treatment, potentially enhancing patient prognoses. The use of serum ascitic cholesterol gradient in conjunction with serum ascitic albumin gradient represents promising biomarkers for predicting malignancy. Thus, incorporating ascitic fluid cholesterol gradient analysis alongside standard investigations can aid in early diagnosis and appropriate treatment.

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FINANCING

The authors did not receive financing for the development of this research.

CONFLICT OF INTEREST

The author declare that there is no conflict of interest.

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3. Format Analysis:Fathima Nilofar, Lakshmipriya kalidindi
4. Acquisition of funds: none
5. Research:Fathima Nilofar, Lakshmipriya kalidindi
6. Methodology: Fathima Nilofar, Lakshmipriya kalidindi
7. Project Management: Fathima Nilofar,Lakshmipriya kalidindi
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