Original Research Article

A study on serum ascitic fluid cholesterol gradient in differentiating cirrhotic and malignancy related ascites

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Abstract

Background: Ascites is defined as the collection of excessive amount of free fluid within the peritoneal cavity. For the purpose of lubrication normally at least 50 ml of free fluid is present in the peritoneal cavity.

Objectives: This study was done to investigate the level of efficiency of various conventional parameters in differentiating cirrhotic ascites from malignancy related ascites and to propose serum ascites cholesterol gradient as a new diagnostic parameter.

Materials and methods: This study was conducted among 100 patients of both sexes who have clinically significant ascites admitted in the wards of General medicine, Medical Gastroenterology and medical oncology in Govt. Rajaji Hospital, Madurai. Age group of 20-60 years of both sexes were included.

Results: The mean (±SD) of ascitic fluid cholesterol concentration for cirrhosis group was 56.4 mg% (±7.76) and that for MRA group is 76.26 mg% (±8.27). The p value was <0.001 which was significant. The mean (±SD) of serum ascites cholesterol gradient (SACG) for cirrhosis group was 67.52 (±4.46) and that for MRA group was 60.16 (±3.38). The p value was <0.001 which was significant. The MRA group has low SACG compared to patients with cirrhosis. SACG has shown high specificity in this study which supports the findings of other similar studies.

Conclusion: This study has shown that conventional parameters like ascitic fluid total protein, ascitic fluid albumin, serum ascites albumin gradient are still good at differentiating cirrhotic ascites from

malignancy related ascites. SACG with a cut off level of 62.5 mg% has shown to be a better marker in terms of diagnostic accuracy to differentiate MRA from cirrhotic ascites. Thus ascitic fluid cholesterol level and SACG has been proposed as a new diagnostic marker which are more reliable and cost effective to differentiate MRA from cirrhotic ascites.

Key words

Cholesterol, Exudates, Transudates, Serum ascites cholesterol gradient (SACG), MRA- malignancy related ascites.

Introduction

Ascites is defined as the collection of excessive amount of free fluid within the peritoneal cavity. For the purpose of lubrication normally at least 50 ml of free fluid is present in the peritoneal cavity. But in order to become clinically evident, approximately 1500 ml of free fluid should accumulate. Ascites is a common complication of several diseases. The most important etiology for ascites is cirrhosis (80%) followed by malignant peritonei (10%), tuberculous peritonitis (2%), congestive cardiac failure, nephrotic syndrome, others (3%) [1, 2]. It is a common clinical problem for most of the physicians to make a differential diagnosis of ascites. The traditional way of classification of ascites as transudate (ascitic fluid total protein ≤2.5gm %) and exudate (ascitic fluid total protein >2.5gm %) has now been completely replaced by serum ascites albumin gradient (SAAG) [3-5]. In patients having a low albumin gradient, differentiating malignant ascites from other causes is a major clinical problem. Although cytology for malignant cells is considered a gold standard for malignancy, the diagnostic sensitivity is only 64% [6, 7]. Recently it has been proposed that serum ascites cholesterol gradient (SACG) helps to make a differential diagnosis of ascites [7-9]. Various other studies have shown that in patients with malignancy related ascites the cholesterol levels in ascitic fluid are grossly elevated. This study at present is done to differentiate, ascites that is caused by cirrhosis of liver and that which is caused by malignancy, by estimating, Serum and Ascitic fluid cholesterol gradient (SACG).

Materials and methods

This study was conducted among 100 patients of both sexes who have clinically significant ascites admitted in the wards of General medicine, Medical Gastroenterology and medical oncology in Govt. Rajaji Hospital, Madurai. Age group of 20-60 years of both sexes were included. Patients with spontaneous bacterial peritonitis, nephrotic syndrome, malnutrition, tuberculosis, Budd-chiari syndrome, Mixed causes of ascites (cirrhosis with tuberculosis, cirrhosis with malignancy), heart failure were excluded. The study population was divided into 2 groups A and B.

Group A: Patients with ascites due to cirrhosis of liver in whom malignancy is ruled out by ultrasonogram / CT and cirrhosis diagnosed by ultrasonography.

Group B: Patients with malignancy related ascites diagnosed by ultrasonography/ CT and positive biopsy for malignancy of the respective tissue.

Statistical analysis

All the details obtained from the patients were noted and results were analysed statistically. The 'p' value which was lesser than 0.05 denoted significant one to one relationship.

Results

The mean (±SD) of ascitic fluid total protein concentration in cirrhosis group was 1.71 (±0.23) gm% and that for malignancy related ascites group was 3.76 (±0.25) gm%. The p value was < 0.001 which was significant. Cut off value - 2.5gm%, Sensitivity -82%, Specificity - 94%, PPV - 92%, NPV - 84%, Diagnostic accuracy-88% (**Table – 1**).

Table – 1: Ascitic fluid total protein concentration – Cirrhosis vs MRA.

Ascitic fluid total protein concentration – Cirrhosis vs MRA

Ascitic fluid Total protein(gm%)	Mean	SD	p value	significance
Cirrhosis	1.71	0.23		
MRA	3.76	0.25	< 0.001	Significant

The mean (±SD) of ascitic fluid albumin for patients in cirrhosis group was 1.21 gm% (±0.18) and that for patients in MRA group is found to be 2.99 gm% (±0.21). The p value is <0.001 which was significant. Cut off value - 1.89 gm%, Sensitivity - 78%, Specificity - 94%, PPV - 92.4%, NPV- 81.3%, Diagnostic accuracy- 86% (**Table – 2**).

Table – 2: Ascitic fluid albumin concentration – Cirrhosis vs MRA.

Ascitic fluid albumin concentration – Cirrhosis VS MRA

Ascitic fluid Albumin (gm%)	Mean	SD	p value	significance
Cirrhosis	1.21	0.18		
MRA	2.99	0.21	< 0.001	Significant

The mean (±SD) of SAAG for cirrhosis group was 1.27 (±0.24) and that for MRA group was 0.74 (±0.12). The p value was <0.001 which is significant. Cut off value - 1.1 gm%, Sensitivity - 82%, Specificity - 100%, PPV - 100%, NPV - 78%, Diagnostic accuracy - 90% (**Table – 3**).

Table – 3: Serum ascites albumin gradient.

Serum ascites albumin gradient

SAAG (gm%)	Mean	SD	p value	significance
Cirrhosis	1.27	0.24		
MRA	0.74	0.12	< 0.001	Significant

The mean (±SD) of ascitic fluid cholesterol concentration for cirrhosis group was 56.4mg% (±7.76) and that for MRA group was 76.26mg% (±8.27). The p value was <0.001 which is significant. Cut off value - 65.2 mg%, Sensitivity - 84%, Specificity - 89%, PPV - 90%, NPV - 82%, Diagnostic accuracy - 86% (**Table – 4**).

Table – 4: Ascitic fluid cholesterol concentration – Cirrhosis vs MRA.

Ascitic fluid cholesterol concentration – Cirrhosis vs MRA

Ascitic fluid cholesterol(mg%)	Mean	SD	p value	significance
Cirrhosis	56.4	7.76		
MRA	76.26	8.27	< 0.001	Significant

The mean (±SD) of serum ascites cholesterol gradient (SACG) for cirrhosis group was 67.52 (±4.46) and that for MRA group was 60.16 (±3.38). The p value was <0.001 which was significant. Cut off value - 62.5 mg%, Sensitivity - 88%, Specificity - 98%, PPV - 96%, NPV - 83%, Diagnostic accuracy - 91% (**Table – 5**).

Table – 5: Serum Ascites Cholesterol Gradient.

Serum Ascites Cholesterol Gradient

SACG(mg%)	Mean	SD	p value	significance
Cirrhosis	67.52	4.46		
MRA	60.16	3.38	< 0.001	Significant

Discussion

Ascites due to any cause is one of the valuable clinical findings. Its critical evaluation is important to diagnose the disease at the background causing the ascites and for its appropriate management. Very often patients with cirrhosis and malignancy are so much debilitated to undergo various invasive investigations. It may be seen with several tumors including malignancies of Breast, Ovary, Colon, Lung, Pancreas, Liver, Uterine cancers, GIT cancers such as stomach and intestinal cancers.

Ascites usually develops in late stages of cancer and it is a grave prognostic sign. Malignant

ascites contributes to 10% of all cases of ascites [10]. It is due to the tumor causing peritoneal carcinomatosis. Survival is very poor for patients in these groups, but their quality of life can be improved by palliative therapy [11]. The mechanism of ascites formation in malignancy related ascites [12] is multifactorial. It is mainly due to two main factors, Increased vascular permeability, Blockade of lymphatic drainage. Compared to patients with cirrhosis, the capillary endothelial permeability is increased in patients who have malignancy related ascites, mainly due to the presence vascular endothelial growth factor (VEGF) , a vascular permeability factor [13, 14] which allows movement of micro and macromolecules into the peritoneal cavity. The peritoneal carcinomatosis, caused by the primary tumor, leads to the blockage of draining lymphatics which also contributes to the malignant ascites. The MRA group has low SACG compared to patients with cirrhosis. SACG has shown high specificity in this study which supports the findings of other similar studies. So this study has reinforced that SACG can be proposed as a new diagnostic parameter to differentiate MRA from cirrhotic ascites malignancy related ascites [15, 16].

Conclusion

This study has shown that conventional parameters like ascitic fluid total protein, ascitic fluid albumin, serum ascites albumin gradient are still good at differentiating cirrhotic ascites from malignancy related ascites. Ascitic fluid cholesterol level is significantly increased in patients with malignancy related ascites. Serum ascites cholesterol gradient (SACG) is low in patients with malignancy related ascites compared to patients with cirrhosis. SACG with a cut off level of 62.5 mg% has shown to be a better marker in terms of diagnostic accuracy to differentiate MRA from cirrhotic ascites. Thus ascitic fluid cholesterol level and SACG has been proposed as a new diagnostic marker which are more reliable and cost effective to differentiate MRA from cirrhotic ascites.

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