ORIGINAL ARTICLE

Serum/Ascites Albumin Gradient in Differential Diagnosis of Ascites

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Abstract

Aim
The classification of ascites into ‘transudative’ and ‘exudative’ has recently been challenged. The present study was aimed to differentiate ascites on the basis of serum/ascites albumin gradient, a proposed biochemical criteria for differential diagnosis of ascites and also to compare its diagnostic accuracy with the traditional marker : ascitic fluid total proteins, classifying ascitic fluid into transudate and exudate.

Material & method
Paired ascitic fluid and serum samples from 100 patients were examined with an established method for the diagnosis of cause of ascites. The present study included 76 patients having ascites related to portal hypertension (cirrhosis - 54, cardiac - 10, secondary bacterial peritonitis - 6, liver metastasis - 6), and 24 patients of tubercular ascites not related to portal hypertension.

Results
The diagnostic accuracy of SAAG and AFTP were 96% and 68% respectively.

Conclusion
Differential diagnosis of ascites should be based on the serum/ascites albumin gradient which is a better distinguishing marker for separating ascites related to portal hypertension from all other causes of ascitic fluid collection, irrespective of infection.

Key words
Ascites, Serum/ascites albumin gradient, Ascitic fluid total protein.

Introduction
Ascites is one of the most common amongst the various clinical problems confronting a physician, and ascitic fluid analysis is the most effective way to diagnose it. The traditional classification of ascites into ‘exudative’ and ‘transudative’ involves estimation of ascitic fluid total protein (AFTP), which is high ≥ 2.5 gm/dL in exudate and < 2.5 gm/dL in transudate. This classification, however, is unable to correctly identify the aetiological factors responsible for its causation and has been challenged on various occasions in different clinical conditions especially in cirrhotic patients on prolonged diuretic therapy, cardiac ascites, 1/3rd patients of malignant ascites, spontaneous bacterial peritonitis, and sometimes even in normal ascitic fluid. Moreover, it offers little insight to the pathophysiology of ascitic fluid formation.

Further, these drawbacks led to development of a new approach to classify ascites, based on albumin gradient between plasma and ascites. In presence of portal hypertension, oncotic pressure gradient between plasma and ascitic fluid has to be raised, to counter-balance the high hydrostatic pressure driving the fluid to the intraperitoneal cavity. Albumin being the single most important factor of oncotic pressure generation, the difference between the serum and ascitic albumin concentration (serum/ascites albumin gradient - SAAG) was used to differentiate ascitic fluid into
categories: gradient ≥ 1.1 g/dl in cases with portal hypertension and < 1.1 g/dl in ascites unrelated to portal hypertension. Various studies have demonstrated superiority of SAAG in classifying ascites compared to transudate-exudate concept but with conflicting observations. There have also been reports arguing against superiority of SAAG compared with other markers used for differentiation of ascites into transudate and exudate especially in non-alcoholic liver disease. In view of the above, the present study was undertaken to evaluate the value of SAAG in the differential diagnosis of ascites and also to compare its sensitivity and diagnostic accuracy with that of AFTP.

Material and method

The present prospective study included 100 patients of ascites. In 76 patients the cause of ascites was related to portal hypertension. Out of 54 patients, 29 (53.7%) had post-hepatitic, 9 (16.6%) alcoholic, and 16 (29.6%) cryptogenic cirrhosis. Six patients of cardiomyopathy, 2 each of corpulmonale, and valvular heart diseases contributed to cardiac ascites. While contribution of SBP and malignancy to group I of study was six each. Twenty four patients of tubercular ascites were unrelated to portal hypertension and comprised group II of the study.

Table I: Comparison of AFTP and SAAG in study groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>AFTP (g/dl)</th>
<th>SAAG (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;2.5</td>
<td>≥ 2.5</td>
</tr>
<tr>
<td>Group I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cirrhotics</td>
<td>42</td>
<td>12</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>SBP</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Liver metastases</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Group II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tubercular</td>
<td>0</td>
<td>24</td>
</tr>
</tbody>
</table>

Ascitic fluid was collected in all patients by paracentesis done under sterile condition using 21 gauge needle. The routine testing of ascitic fluid included total protein, albumin and cell count. The same tests were done on blood sample drawn at the time of abdominal paracentesis. The specific investigations like ascitic fluid culture, liver biopsy, upper gastrointestinal endoscopy, lipid profile, echocardiography, etc., were performed as required. The statistical analysis was done using student’s ‘t’ test. The diagnostic accuracy was calculated as the sum of the true positive plus true negative results divided by the total number of cases.

Results

Ascitic fluid total protein were significantly lower in group I patients (table I and II) compared to the patients of group II. Albumin gradient was ≥ 1.1 gm/dL in 72 patients of group I, while AFTP was < 2.5 gm/dL in 52 patients of this group (table II). All the patients of group II had serum gradient of < 1.1 gm/dL (Table I). Therefore it was observed that the serum albumin ascitic gradient had a diagnostic sensitivity of 94.73% and 96% accuracy compared to AFTP, which is 65.62% and 68% respectively (Table I, II).

Discussion

The results of present study show that the serum/ascitic fluid albumin is a useful marker for the diagnosis of ascites, as it has diagnostic accuracy of 96%. Similar observations have been also reported by other studies. If the gradient is > 1.1 gm/dL, the underlying cause is almost always related to portal hypertension. The application of albumin gradient disregards the concept of transudate versus exudate as it provides a more rational approach, separating ascitic fluid into two categories on the basis of the presence or absence of portal hypertension. The albumin gradient retains its ability even in infected ascites, which is considered exudate according to traditional concept, although it usually develops in patients of cirrhosis, which, owing to the low ascitic fluid total protein concentration, is traditionally labelled as transudative ascites. In
fact, ascites with low protein concentration is more prone to develop infection. The results of the present study reinforce the conclusions of the reports which showed that albumin gradient is superior to the transudate-exudate concept in classifying ascitic fluid collections of varied aetiology. The utility of albumin gradient in non-alcoholic liver disease has been debated. However, in the present study the test was found to have significant diagnostic accuracy in ascites caused by both alcoholic and non-alcoholic liver disease. The high albumin gradients in cardiac failure patients is also a manifestation of an elevated portal pressure due to increased inferior vena cava pressure and also in malignant ascites it is the elevated portal pressure due to metastasis in liver and peritoneum which is responsible for increased albumin gradients. This is explained on the basis of the equilibrium of starting forces, when ascites is related to portal hypertension, this increments of portal pressure should be counter balanced by an increased difference of osmotic forces (and thus albumin concentration) between serum and ascites. Since serum albumin is already low in decompensated liver disease; this lead to the well known very low albumin ascitic fluid concentrations in patients with cirrhosis. High serum/ascites albumin gradients values indicate higher levels of portal hypertension.

Table II: Diagnostic sensitivity and accuracy of SAAG compared to AFP in study groups.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>p value</th>
<th>Diagnostic Sensitivity</th>
<th>Diagnostic Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAAG (gm/dl)</td>
<td>1.41 + 0.65</td>
<td>0.71 + 0.27</td>
<td>&lt; 0.001</td>
<td>94.73%</td>
<td>96%</td>
</tr>
<tr>
<td>AFPT (gm/dl)</td>
<td>1.80 + 1.05</td>
<td>3.8 + 0.93</td>
<td>&lt; 0.001</td>
<td>65.62%</td>
<td>68%</td>
</tr>
</tbody>
</table>

Conclusion

The results of the present study show that the serum/ascites albumin gradient is a test with significant diagnostic accuracy in separating ascites related to portal hypertension from the forms of ascitic fluid collection caused by mechanisms unrelated to portal hypertension. It does not provide exact cause of ascites. The presence of high albumin gradient only means, the presence of portal hypertension. It is superior to previously proposed transudate-exudate concept, not only because of its higher diagnostic accuracy but also because it provides a better approach to pathogenesis of ascitic fluid collection. The transudative-exudative ascites should be replaced with the ascites related to portal hypertension (high gradient) and ascites not related to portal hypertension (low gradient) respectively.

References

7. Runyon BA. Low protein concentration ascitic fluid is


