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Original Article

# The correlation between cytological examination of ascitic fluid and serum ascites albumin gradient in the differential diagnosis of ascites

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**Abstract**

**Aim:** The accumulation of fluid in pathological quantities in the peritoneal cavity is called ascites. In every newly diagnosed ascites, necessary investigations should be conducted by puncturing ascitic fluid. In this study, we aimed to investigate whether there is any correlation between cytological examination of ascitic fluid and serum ascites albumin gradient (SAAG) in the determination of etiologic causes of ascites.

**Material and Method:** The files of the patients who were admitted to our clinic for the investigation of their ascites etiology between May 2014 and May 2018, were analyzed retrospectively. Pathology reports of the patients whose SAAG was calculated by taking the difference between serum albumin values and simultaneously taken ascitic fluid albumin and whose ascitic fluid cytology examination was performed, were recorded. The data of 248 patients with clinical diagnosis were included in the study. Patients with SAAG <1.1 g / dl and SAAG ≥1.1 g / dl, were divided into two groups.

**Results:** Of the 248 patients included in the study, 114 were female (45.90%) and 134 were male (54.10%) patients. The patients were divided into 2 groups according to SAAG value. In group 1, there were 107 (43.14%) patients with SAAG <1.1 g / dl and in group 2, there were 141 (56.85%) patients with SAAG ≥1.1 g /dl. Group 1: In 70 (28.22%) of 107 patients, positive malignant cytology was consistent with ascites ($p<0.0001$). In 37 (14.91%) patients, benign cytology ascites was present. Group 2: 133 (53.62%) of 141 patients had benign cytology and 8 (3.23%) had malignant cytology.

**Conclusion:** There was a correlation between malignant cytology of ascites with SAAG <1.1.

**Keyword:** Ascites; Malign cytology; SAAG; Bening cytology.

## INTRODUCTION

The accumulation of fluid in pathological quantities in the peritoneal cavity is called ascites (1). In every newly diagnosed ascites, necessary investigations should be conducted by puncturing ascitic fluid (2). The specific etiological diagnosis of ascites is very important, as effective treatment is possible only by this way. The gradient between serum and ascites albumin concentrations (SAAG) is thought to reflect the colloidosmotic pressure gradient directly and the degree of portal hypertension indirectly (3).

It is reported that if SAAG is 1.1 g / dl or more, ascites formation is 97% related to portal hypertension (4). In case SAAG is less than 1.1, non-hypertensive causes should be considered. In the literature, it has been reported that the sensitivity of cytological examination to detect malignant ascites is between 40-75% (5). As the amount of ascitic fluid sample taken for cytology and the rate of transmission to the laboratory increases, the sensitivity of cytology increases up to 97% (6). Malign ascites is an advanced stage malignancy which develops especially in the gastrointestinal system in the abdomen or by extension of tumors belonging to the genital organs to the peritoneum or in tumors of the peritoneum itself (7).

In this study, we aimed to investigate whether there is any correlation between cytological examination of ascitic fluid and SAAG in the determination of etiologic causes of ascites.

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## MATERIAL and METHODS

The files of the patients who were admitted to our clinic for the investigation of their ascites etiology between May 2014 and May 2018, were analyzed retrospectively. Pathology reports of the patients whose SAAG was calculated by taking the difference between serum albumin values and simultaneously taken ascitic fluid albumin and whose ascitic fluid cytology examination was performed, were recorded.

The data of 248 patients with clinical diagnosis were included in the study. Patients with SAAG <1.1 g / dl and SAAG ≥1.1 g / dl, were divided into two groups. These patient groups were also divided into subgroups as positive malignant cytology and benign cytology. The relationship between the cytology results and SAAG values of patients in terms of their clinical diagnosis was examined.

## RESULTS

Of the 248 patients included in the study, 114 were female (45.9%) and 134 were male (54.1%) patients. The patients were divided into 2 groups according to SAAG value. In group 1, there were 107 (43.14%) patients with SAAG <1.1 g / dl and in group 2, there were 141 (56.85%) patients with SAAG ≥1.1 g / dl. Group 1: In 70 (28.22%) of 107 patients, positive malignant cytology was consistent with ascites. In 37 (14.91%) patients, benign cytology ascites was present. Group 2: 133 (53.6%) of 141 patients had benign cytology and 8 (3.23%) had malignant cytology. In Group 1, the most common causes of positive malignant cytology were ovarian cancer (20), gastric cancer (10), colon cancer (9), pancreatic cancer (9) and malignant mesothelioma (8). The most common cause of benign cytology was tuberculous peritonitis which was detected in 17 (6.85%) patients (Table 1).

In group 2, while the most common cause in benign cytology was liver cirrhosis, malignant cytology was detected most commonly in patients with hepatocellular cancer. (Table 2-3). When the results of ascites cytology of all patients were taken into consideration, 170 (68.54%) patients had benign cytology and 78 (31.4%) patients had malignant cytology (Table 3). There was a significant correlation between SAAG <1.1 g / dl and malignant cytology, and SAAG ≥1.1 g / dl and benign cytology (Table 3).

**Table 1. Benign cytology patients**

| Diagnosed Patients (n,%) 170 (68.5) | SAAG<1.1 g/dl Benign cytology (n,%) 37 (14.9) | Diagnosed Patients | SAAG ≥1.1 g/dl Benign cytology (n,%) 133 (53.6) |
|---|---|---|---|
| Tuberculosis | 17 (6.9) | Hepatitis b liver cirrhosis | 59(23.7) |
| Cardiac cirrhosis | 9 (3.6) | Liver cirrhosis due to hepatitis c | 14(5.6) |
| Chronic renal failure | 2 (0.8) | Cryptogenic cirrhosis | 47(18.9) |
| Neuroendocrine tumor | 2 (0.8) | Cirrhosis of the liver due to portal vein thrombosis | 8(3.2) |
| Gastrointestinal Stromal Tumor | 1(0.4) | Liver cirrhosis due to Wilson's disease | 1(0.4) |
| Nephrotic syndrome | 2 (0.8) | Liver cirrhosis due to autoimmune hepatitis | 4(1.4) |
| Pancreatitis | 4 (1.6) | | |

Results are expressed as number of patients and percent

**Table 2. Positive Malign Cytology Patients**

| Diagnosed Patients (n,%) 78 (31.45) | SAAG <1.1 g/dl) Malign cytology (n,%) 70 (28.2) | Diagnosed Patients | SAAG ≥1.1 g/dl Malign cytology (n,%) |
|---|---|---|---|
| Gastric cancer | 10 (4.0) | Hepatocellular cancer | 8(%3.2) |
| Colon cancer | 9 (3.63) | | |
| Gall bladder cancer | 3 (1.21) | | |
| Ovarian cancer | 20 (8.10) | | |
| Pancreatic cancer | 9 (3.63) | | |
| Cholangiocarcinoma | 4 (1.61) | | |
| Mesothelioma | 8 (3.23) | | |
| Liver metastasis | 7 (2.82) | | |

Results are expressed as number of patients and percent

**Table 3. Ascites cytology and SAAG results**

| Ascites cytology (248) (n, %) | Group I (n, %) 107 (43.14) | Group II (n, %) 141 (56.85) |
|---|---|---|
| Benign, 170 (68.54) | 37 (14.92) | Liver Cirrhosis:133 (53.62) |
| Malign, 78 (31.45) | 70 (28.22) | Hepatocellular Cancer : 8 (3.23) |
| P value | (<0.0001)* | (<0.0001)** |

Results are expressed as number of patients and percent
*P < 0.05 versus group II; **P < 0.05 versus group

## DISCUSSION

The most common cause of ascites development is associated with portal hypertension which is related to liver cirrhosis. Although lymphatic obstruction is accepted as the main pathophysiological mechanism behind ascites formation, recent evidences suggest that immunomodulators, vascular permeability factors and metalloproteinases contribute significantly to the process (8). The most important step in the algorithm of etiological evaluation of a patient with ascites is the analysis of ascitic fluid by paracentesis. While defining ascitic fluid, high albumin gradient (≥1.1 g / dl) and low albumin gradient (<1.1 g / dl) replace the terms transudate and exudate respectively (9). According to the etiological investigation of ascites in patients with SAAG ≥ 1.1 g / dl, the most common causes are associated with diseases such as liver cirrhosis with a rate of 97%, Budd-Chiari syndrome, veno-occlusive disease, alcoholic hepatitis and congestive heart failure that cause portal hypertension. In case of SAAG <1.1 g / dl, diseases like malignancy, infectious diseases, nephrotic syndrome and pancreatitis should be considered. Cytological examination of ascitic fluid has an important value in the differential diagnosis. In the literature, it has been reported that the sensitivity of cytological examination in order to detect malign ascites is between 40-75% (5). Malign ascites is an advanced stage finding for many tumors. It is more commonly formed by extension of the intra-abdominal cancers to the peritoneum or in the tumors of the peritoneum itself. The cytology may remain negative unless it is held in peritoneal by primary malignant disease. Therefore, differentiating malign ascites from benign ascites still continues to remain a clinical problem.

In a study conducted by Telfer B. et al., etiology of patients with ascites is formed with 85% cirrhosis, 10% cancers, 3% heart failure, 2% tuberculosis, 1% pancreatitis and other rare causes (10,11). Okten A, et al. detected cirrhosis with 80% as the most common cause during etiological examination of 780 patients with ascites (12). In a prospective study of 132 patients conducted by Bandar A, et al., liver cirrhosis was found to be the most common etiological factor in ascites etiology (13). In the study of Pare et al., patients with SAAG ≥ 1.1 g / dl were found to be portal hypertensive, while patients with gradient <1.1 g / dl were found not to be portal hypertensive with 97% accuracy rate (4). In our study, portal hypertension rate was 94% in patients with SAAG ≥ 1.1 g / dl which is in accordance with the literature. Liver cirrhosis rate was 54% in all ascites patients.

In the study of Karaaslan Y, et al., SAAG was found to be lower than 1.1 g / dl in 80% of patients with malignant ascites, and SAAG was above 1.1 in 96.2% of the patients who developed non-malignant ascites. Among the primary causes of ascites in the malignant ascites group, ovarian tumors were predominant in 44% and stomach tumors in 20%. (14). In a study conducted by Garison RN, et al., pancreas (20 patients), ovary (18 patients) and colon (18 patients) were the most commonly seen tumors in 107 patients with malign ascites. In cytological evaluations of ascitic fluid, 57% of cases had positive malign cytology and 65% had SAAG <1.1 g / dl (15). In a prospective study conducted by Runyon BA, et al., 45 of 448 patients had malignancy-associated ascites and 53.3% of these patients with ascites had positive malign cytology and SAAG <1.1 g / dl (6). Also in our study, 70 of 78 patients with malignant ascites had SAAG <1.1 g / dl and the most common causes consistent with literature were ovarian tumors 20 (8%), gastric cancer 10 (4.0%), pancreas 9 (3.63%) and colon cancer 9 (3.63%). 8 (3.22%) patients with SAAG ≥ 1.1 mg / dl had positive malign cytology, however, these patients were hepatocellular cancer patients with portal hypertension.

## CONCLUSION

As a result, in our study, we detected that there was a correlation between malignant cytology and SAAG in 70 (28.22%) out of 107 (%43.14) patients with SAAG <1.1 g/dl (p< 0.001). A significant correlation was found between negative cytology and SAAG in 133 of 141 patients with SAAG ≥ 1.1 g / dl (p<0.0001). As a result of our comparisons with these data and other studies, we think that in all new patients diagnosed with ascites, ascites cytological examination should be definitely performed simultaneously with SAAG.

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## REFERENCES

1. Zeybel M, Çolakoğlu Ö, Uğur F. Assit, In: Ünsal B. Editör. Portal hipertansiyon ve komplikasyonları, 1.baskı. İzmir. Meta Basım 2003;123-59.
2. Runyon BA. Management of adult patients with ascites due to cirrhosis: an update. Hepatology 2009;49:2087-107.
3. Hoefs JC. Serum protein concentration and portal pressure determine the ascitic fluid protein concentration in patients with chronic liver disease. J Lab Clin Med 1983;102:260-73
4. Runyon BA, Montana AA, Akriviadis EA, et al. The serum-ascites albumin gradient is superior to exudate-transudate concept in differential diagnosis of ascites. Ann Intern Med 1992;117:215-20.
5. Gerbes AL, Jüngst D, Xie Y et al. Ascitic fluid analysis for the differentiation of malignancy-related and nonmalignant ascites. Proposal of a diagnostic sequence. Cancer 1991;68:1808-14.
6. Runyon BA, Hoefs JC, Morgan TR. Ascitic fluid analysis in malignancy-related ascites. Hepatology 1988;8:1104-9.
7. Castaldo G, Oriani G, Cimino L, et al. Total discrimination of peritoneal malignant ascites from Cirrhosis-and hepatocarcinoma-associated ascites by assays of ascitic cholesterol and lactate dehydrogenase. Clin Chem 1994;40:478-83.

8. Parsons SL, Watson SA, Steele RJ. Malignant ascites. Br J Surg 1996;83:6-14.
9. Pare P, Talbot J, Hoefs JC. Serum ascites albumin concentration gradient: a physiological approach to the differantial diagnosis of ascites. Gastroenterology 1983;85:240-4.
10. Reynolds TB. Ascites. Clin Liver Dis 2000;4:151-68.
11. Moore KP, Wong F, Gines P, et al. The management of ascites in cirrhosis: report on the consensus conference of the International Ascites Club. Hepatology 2003;38:258-66.
12. Ökten A, Mungan Z, Çakaloğlu Y, et al. Assit: Tanı-Ayırıcı tanı, klinik özellikler: Gastroenterohepatoloji. Nobel Tıp Kitapevleri, 2001:345-68.
13. Al-Knawy BA, Etiology of ascites and the diagnostic value of serum-ascites albumin gradient in non-alcohol liver disease. Ann Saudi Med 1997;17:26-8.
14. Karaaslan Y, Gürel S, Dolar ME, et al. Diagnostic value of tumor markers in malignant ascites. Turkiye Klinikleri Journal of Gastroenterohepatology 1999;10:12732.
15. Garrison RN, Kaelin LD, Galloway RH, et al. Malignant ascites. Clinical and experimental observations. Ann Surg 1986;203:644-51.