

“AN ANALYTICAL STUDY OF SERUM - ASCITES ALBUMIN GRADIENT (SAAG) AND ASCITIC FLUID TOTAL PROTEIN (AFTP) IN CASE OF PORTAL HYPERTENSION AND NON-PORTAL HYPERTENSION ASCITES PATIENTS”

[Original Research Paper]

Authors:

1. DR. C. MOHAMMED ILIYAS

PROFESSOR, DEPARTMENT OF COMMUNITY MEDICINE, DR. S. S. TANTIA MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, SRI GANGANAGAR, RAJASTHAN.

2. DR PAWAN KUMAR SAINI

PROFESSOR, DEPARTMENT OF GENERAL MEDICINE, GOVERNMENT MEDICAL COLLEGE, SRI GANGANAGAR, RAJASTHAN.

3. DR VIKASH KUMAR

ASSISTANT PROFESSOR, DEPARTMENT OF COMMUNITY MEDICINE, LORD BUDDHA KOSHI MEDICAL COLLEGE AND HOSPITAL, BAIJNATHPUR, SAHARSA, BIHAR.

4. DR. MADHAVI MILIND KAMBLE*

ASSISTANT PROFESSOR, DEPARTMENT OF COMMUNITY MEDICINE, AMALTAS INSTITUTE OF MEDICAL SCIENCES, BANGAR, MADHYA PRADESH. E MAIL – MADHAVIKAMBLE1987@GMAIL.COM

***CORRESPONDING AUTHOR**

5. DR. AMRUT ARUN SWAMI

ASSOCIATE PROFESSOR, DEPARTMENT OF COMMUNITY MEDICINE, DR. S. S. TANTIA MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, SRI GANGANAGAR, RAJASTHAN.

Abstract:

Background: We conducted a study to assess the effectiveness of Serum Ascites Albumin Gradient (SAAG) and Ascitic Fluid Total Protein (AFTP) in differentiating between ascites caused by portal hypertension and non-portal hypertension factors.

Methods: This analytical study took place within a hospital setting, specifically among patients admitted to the medicine wards and ICU of a tertiary care hospital. The investigation spanned a 12-month period, running from January 2022 to December 2022. The study delved into the examination of 100 cases of ascites, thoroughly scrutinizing clinical signs and symptoms, ascites classification, and the correlation between Serum Ascites Albumin Gradient (SAAG) and Ascitic Fluid Total Protein (AFTP) levels in ascitic fluid.

Results: The mean age of the patients was 53.41 ± 9.65 years. Out of 100 patients 75% were males. The majority of patients presented with abdominal distension; 94 (94%) cases followed by swelling of limbs in 72 (72%). Most common sign was ascites seen in all cases (100%), followed by splenomegaly in 66 cases (66%) and pedal oedema in 58 cases (58%). We had 16 cases with SAAG of <1.1 gm% (16%) and we had 84 cases with SAAG of ≥ 1.1 gm% (84%).

It was observed that majority of patients with SAAG ≥ 1.1 gm% had portal hypertension related ascites with statistically significant relation. ($P < 0.001$)

The sensitivity, specificity and accuracy of SAAG was 97.3%, 53.85% and 86% respectively. On comparison, we found that the SAAG had better sensitivity, specificity of and accuracy to diagnose it as compared to AFTP.

Conclusion: The results of our investigation indicate that the Serum Ascites Albumin Gradient (SAAG) is a dependable predictor for ascites linked to portal hypertension. Specifically, a SAAG value equal to or exceeding 1.1 gm% exhibits better sensitivity and accuracy in comparison to Ascitic Fluid Total Protein (AFTP).

Keywords: Ascites, Ascitic Fluid Total Protein (AFTP), Portal Hypertension, Non-Portal Hypertension, Serum - Ascites Albumin Gradient (SAAG).

Introduction:

Ascites is defined by the accumulation of fluid in the peritoneal cavity. A comprehensive examination of medical history and clinical findings provides valuable information about the root causes of ascites. While some cases can be linked to peritoneal issues not associated with portal hypertension, more than 80% are connected to portal hypertension, primarily arising from cirrhosis. The importance of this categorization lies in the fundamental variations in the strategies for assessment and treatment tailored to each specific group. [1]

Historically, ascites related to portal hypertension was often differentiated from non-portal hypertension causes by determining if the fluid is transudative or exudative. The premise was that in portal hypertension, protein-poor ascitic fluid transudes from the regular peritoneal surface, while in ascites linked to peritoneal diseases, protein-rich ascitic fluid exudes from the peritoneal surface. Ascitic fluid is considered a transudate if the Ascitic Fluid Total Protein (AFTP) is less than 2.5g/dl. [2]

Ascites can arise from portal hypertension, such as in cirrhosis, or from conditions affecting the peritoneum independent of portal hypertension, like tubercular peritonitis or peritoneal carcinomatosis. The underlying mechanisms of ascitic fluid formation remain unclear, and the conventional classification based on Ascitic Fluid Total Protein (AFTP) into exudative and transudative ascites does not provide a complete understanding of the pathophysiology. [3]

Clinical situations have made it difficult, particularly in cases of cardiac ascites, malignant ascites, and mixed ascites, such as cirrhotic patients with spontaneous bacterial peritonitis, cirrhotic patients receiving prolonged diuretic therapy, and ascites in the abdomen. In order to categorise ascites into two groups, a new method called SAAG [Serum Ascites Albumin Gradient] has been created – High SAAG ascites with SAAG ≥ 1.1 g/dl in cases with the portal hypertension and the Low SAAG ascites with SAAG < 1.1 g/dl in cases with ascites, that is unrelated to portal hypertension. [3-5]

SAAG indicates the oncotic pressure exerted by serum albumin on ascitic fluid, precisely representing the substantial hydrostatic pressure difference between the portal bed and ascitic

fluid. Consequently, the disparity in albumin concentrations between serum and ascitic fluid directly corresponds to portal pressure. [6,7]

The SAAG classification is highly physiological and aligns effectively with the pathogenesis, even in cases involving diuretic use, cardiac ascites, and mixed ascites. Numerous studies have demonstrated the superior efficacy of SAAG over the transudate-exudate concept for categorizing ascites. [8-10]

Currently, there is an increasing incidence of ascites related to malignancies, posing challenges in diagnosis through routine ascitic fluid analysis. While SAAG effectively distinguishes ascites caused by portal hypertension from other origins, it falls short in discriminating between malignant ascites and tuberculous ascites, as both exhibit a low SAAG (<1.1 gm%). [11]

The sensitivity of fluid cytology for detecting malignancy is relatively low, given the challenge in distinguishing between reactive atypical mesothelial cells and actual malignant cells. [12, 13]

Therefore, this research was undertaken to examine the Serum Ascites Albumin Gradient (SAAG) and Ascitic Fluid Total Protein (AFTP) in instances of portal hypertension and non-portal hypertension ascites. The goal was to assess how well SAAG and AFTP could differentiate between ascites associated with portal hypertension and ascites that had no connection to portal hypertension.

Methodology:

This was a single centre hospital-based cross-sectional study conducted in patients admitted to the tertiary hospital under surgical wards and ICU over a period of 12 months from January 2023 to December 2023. The sample size was 100 cases.

According to Shankar Suman et al, [14] the sensitivity of SAAG is 94% and specificity is 90%. The sensitivity of AFTP is 78% and specificity is 50%. The prevalence of ascites in case of cirrhosis is 50%. Hence, we chose-

$$p = 50\%$$

$$z = \text{standard constant value at 95 CI} = 1.96 \text{ Sensitivity} = 94\%$$

$$d = \text{absolute precision} = 0.07$$

$$N \geq Z^2 \text{ Sensitivity} (1 - \text{Sensitivity}) / d^2 P$$

$$N = 1.96^2 * 0.94 * (1 - 0.94) / 0.07^2 * 0.5$$

Thus,

$$\text{Sample Size} = N = 88$$

Rounding it up to 100, so we included a total of 100 cases in our study.

Patients visiting our Hospital, A tertiary care hospital and a teaching institute were studied. The study included individuals aged 18 years and above, diagnosed with ascites through ultrasound, who provided written informed consent. Exclusions comprised patients with hepatic encephalopathy, acute gastrointestinal bleeding, and those with abdominal blunt injuries. A total of 100 ascites patients underwent comprehensive history-taking, thorough clinical examinations, and detailed investigations. Ethical clearance for the study was taken from institutional ethical committee after discussion of the study protocol with committee.

Statistical Analysis:

Information was gathered through a semi-structured pre-tested questionnaire, and data entry was carried out using Microsoft Excel. The data is presented using frequencies, percentages, charts, and graphs. For quantitative variables, the mean and standard deviation are provided. Statistical analyses were performed using SPSS software version 21, applying appropriate tests such as the Chi-square test for association and the student's t-test for comparisons where relevant. Other statistical tests were employed as dictated by the study's needs. A significance level of $p < 0.05$ was considered statistically significant.

Observations and Results:

100 cases of ascites were studied in detail. It was observed that majority of patients were in age group 51-60 years (39%) followed by 41-50 years (29%). More than 60 years were 19 cases (19%) and rest were 31 to 40 years (13%), 3 cases were less than 25 years (3%). The mean age of the patients was 52.1 ± 9.76 years. Out of 90 patients 78% were males and 22% females.

Table 1: Distribution of patients according to Clinical features: Symptoms & Signs:

Clinical features:	No. of Patients (n=100)	Percentage*
Symptoms		
Abdominal distension	94	94%
Alcoholic	64	64%
Swelling of limbs	59	59%
Breathlessness	49	49%
Jaundice	34	34%
Fever	24	24%
H/O Blood transfusion	19	19%
Signs		
Ascites	100	100%
Splenomegaly	64	64%
Pedal Oedema	61	61%

Pallor	52	52%
Icterus	49	49%
Hepatomegaly	34	34%

***(Multiple Responses Present)**

The provided table 1 outlines the distribution of patients based on clinical symptoms and signs. It was noted that the majority of cases, specifically 94%, exhibited abdominal distension, followed by swelling of limbs in 59% and breathlessness in 49%. A predominant portion of the patients, comprising 64%, were identified as chronic alcoholics.

The most prevalent sign observed was ascites, evident in all cases (100%), followed by splenomegaly in 64 cases (64%), pedal edema in 61 cases (61%), pallor in 52 cases (52%), jaundice in 49 cases (49%), and hepatomegaly in 34 cases (34%).

Out of the total 100 cases, 74 exhibited ascites related to portal hypertension (74%), while the remaining 26 cases did not involve portal hypertension (26%). The distribution of study participants showed a significant difference between those with and without portal hypertension-related ascites ($p < 0.0001$).

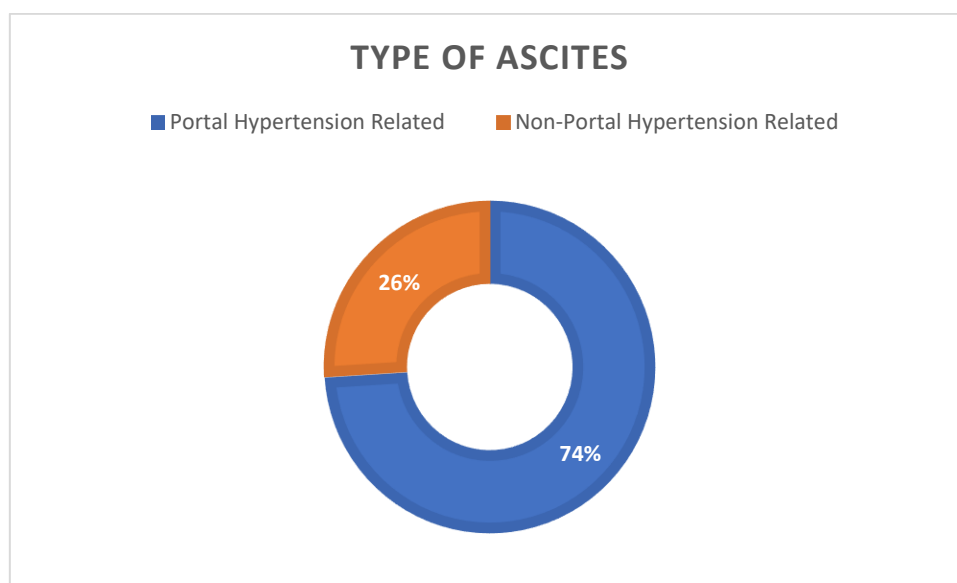


Fig 1. Distribution of cases according to portal hypertension related ascites

We observed that 92 cases survived after treatment (92%) while the rest 8 died (8%). Significant difference was seen in the outcome of the study participants ($p < 0.001$).

SAAG was studied in the study participants, we had 16 cases with SAAG of < 1.1 gm% (16%) and we had 84 cases with SAAG of ≥ 1.1 gm% (84%). Significant difference was seen in the

distribution of the study participants with the SAAG values <1.1 gm% and ≥ 1.1 gm% ($p < 0.001$).

Table 2: Relation of SAAG and portal hypertension related ascites

SAAG	Portal hypertension related ascites	Non-portal hypertension related ascites	P value
≥ 1.1 gm%	72	12	<0.0001 (S)
< 1.1 gm%	02	14	
Total	74	26	

The provided table 2 illustrates the association between SAAG and portal hypertension-related ascites. It was noted that a significant majority of patients, specifically 72 out of 74 individuals, with SAAG ≥ 1.1 gm%, had ascites related to portal hypertension, showing a statistically significant relationship ($P < 0.001$). The sensitivity, specificity, and accuracy of SAAG were 97.3%, 53.85%, and 86%, respectively. The positive predictive value of SAAG was 85.71%, and the negative predictive value of SAAG was 87.5%.

Discussion:

Ascites, a potentially fatal condition with various underlying causes, poses a significant challenge in medical practice worldwide. Early detection is crucial for effective management and prevention of complications. This cross-sectional study conducted at a tertiary institution aimed to assess serum ascites albumin gradient (SAAG) and ascitic fluid total protein (AFTP) levels in patients with portal hypertension and non-portal hypertension-related ascites.

In our study, 100 cases of ascites were evaluated in detail. It was observed that majority of patients were in age group 51-60 years (39%) followed by 41-50 years (29%). More than 60 years were 19 cases (19%) and rest were 31 to 40 years (13%), 3 cases were less than 25 years (3%). The mean age of the patients was 52.1 ± 9.76 years. Out of 90 patients 78% were males and 22% females.

Rinku Joshi et al [15] studied clinical profile of ascites observed mean age of the patients studied was 54.89 ± 12.99 years with the minimum being 16 years and maximum being 82 years. This finding was similar to present study. Nakhale BD et al [16] in a study on clinical profile and comparison of SAAG with ascites fluid total protein (AFTP) in cases of ascites observed 74% were male and 26% were female.

We observed that the majority of cases, specifically 94%, exhibited abdominal distension, followed by swelling of limbs in 59% and breathlessness in 49%. A predominant portion of the patients, comprising 64%, were identified as chronic alcoholics. The most prevalent sign observed was ascites, evident in all cases (100%), followed by splenomegaly in 64 cases (64%), pedal edema in 61 cases (61%).

Nakhale BD et al [16] observed majority of patients had abdominal distension (100%), dyspnea (58%) abdominal pain (35%), 15 cases had altered consciousness (encephalopathy), 8 cases presented with hematemesis. Icterus was present in 30 cases and edema feet in 38. Fever was present in 10 (16%) cases.

Out of the total 100 cases, 74 exhibited ascites related to portal hypertension (74%), while the remaining 26 cases did not involve portal hypertension (26%). The distribution of study participants showed a significant difference between those with and without portal hypertension-related ascites ($p < 0.0001$).

Nakhale BD et al [16] in a study on clinical profile and comparison of SAAG with ascites fluid total protein (AFTP) in cases of ascites observed 78% patients with portal hypertension with ascites. Shanker Suman et al [14] in a study on ascites by estimating Serum Ascites Albumin Gradient (SAAG) and Serum Ascites Cholesterol Gradient (SACG) observed out of 100 patients of ascites, 72 (72%) had portal hypertension related ascites and 28 (28%) had non-portal-hypertension related ascites. This finding was in accordance to present study. AK Seth et al [17] in a study on diagnostic accuracy of serum ascites albumin gradient observed majority of the study subjects were with portal hypertension related ascites. (94.28%)

We observed that 92 cases survived after treatment (92%) while the rest 8 died (8%). Significant difference was seen in the outcome of the study participants ($p < 0.001$).

Touhidur Rahman et al [18] in a study on outcome of the patients with ascites observed 9% patients of this study died during hospital stay, this is in accordance to our study.

SAAG was studied in the study participants, we had 16 cases with SAAG of < 1.1 gm% (16%) and we had 84 cases with SAAG of ≥ 1.1 gm% (84%).

We observed that a significant majority of patients, specifically 72 out of 74 individuals, with SAAG ≥ 1.1 gm%, had ascites related to portal hypertension, showing a statistically significant relationship ($P < 0.001$). The sensitivity, specificity, and accuracy of SAAG were 97.3%, 53.85%, and 86%, respectively. The positive predictive value of SAAG was 85.71%, and the negative predictive value of SAAG was 87.5%

Kanvy BA et al [19] in Saudi Arabia, two other parameters i.e. ascitic fluid lactic dehydrogenase and ascitic to serum ratio of total protein, in addition to SAAG and AFTP were compared. Among all the four highest positive and negative predictive values (80% 98%) against that of ascitic fluid total protein (68% 96%).

M. Beg et al [20] observed the diagnostic accuracy and sensitivity of SAAG were 96% respective values 68% and 66% of AFTP. In the other study, conducted by Gupta R et al [21] Gastroenterology and Pathology, M.L.N Medical college, Allahabad, observed that the diagnostic accuracies of AFTP and SAAG were found to be 88% respectively.

Runyon et al [22] conducted a study among 901 patients in the University of Iowa, Iowa city in the year 1992. The diagnostic accuracy of SAAG and ascitic fluid total protein was 96.7% and 55.6% respectively. In another study conducted among 51 patients by Akriviadis EA et al

[23] in the University of Thressaloniki, Hippocratical Hospital, Greece the diagnostic accuracy of SAAG was found to be 98% when compared to 52%-80%.

Conclusion:

We observed the importance of SAAG evaluation in ascites cases. We found that majority of the ascites cases in our study are due to portal hypertension. There were 4 deaths in our study (mortality 4.44%). Majority of the cases had SAAG of ≥ 1.1 gm%. Our study concludes that SAAG can easily predict portal hypertension related ascites, with SAAG of ≥ 1.1 gm%. The sensitivity, specificity, and accuracy of SAAG were 97.3%, 53.85%, and 86%, respectively. We conclude that SAAG should be calculated in every patient with Ascites and it should be used as a prognostic indicator.

Source of Funding: None

Conflict of interest: None

References:

1. Zhu S, Du L, Xu D, Lu Z, Xu T, Li J, Xu K, Ye J, Song Y. Ascitic fluid total protein, a useful marker in non-portal hypertensive ascites. *Journal of Gastroenterology and Hepatology*. 2020 Feb;35(2):271-7.
2. Selvaraju K, Sridevi M. Analysis of ascitic fluid in differentiating transudate versus exudate-in a tertiary care centre. *Indian Journal of Pathology and Oncology*. 2020;7(1):137-42.
3. Fauci, Braunwald, Kasper, Hauser, Longo, Jameson. *Cirrhosis and its complications, Harrison's principles of internal medicine*, 19th edition. New York, McGraw Hill publications, 2015:2058-67.
4. PASHA MK, KuMaR BR, MacheRla R, REDDY SL, PANI SK, AYESHA Q, SREENIVASALU M, REDDY GM. Biochemical Markers of Ascitic Fluid to Differentiate Ovarian Cancer from Liver Cirrhosis Patients. *Journal of Clinical & Diagnostic Research*. 2020 Jun 1;14(6).
5. Duah A, Agyei-Nkansah A, Duah F, Asafu-Adjaye F, Nartey YA. Causes Of Ascites And Its Correlation With Serum-Ascites Albumin Gradient In Patients Admitted At Medical Wards In A Tertiary Hospital In Ghana. *Postgraduate Medical Journal of Ghana*. 2022 Dec 29;11(2).
6. Duah A, Agyei-Nkansah A, Duah F, Asafu-Adjaye F, Nartey YA. Causes Of Ascites And Its Correlation With Serum-Ascites Albumin Gradient In Patients Admitted At Medical Wards In A Tertiary Hospital In Ghana. *Postgraduate Medical Journal of Ghana*. 2022 Dec 29;11(2).
7. Gogoi P, Debnath E, Changkakati R. Serum/ascites albumin gradient (SAAG), a very cost effective and reliable first-line diagnostic parameter in the differential diagnosis of ascites-a study in a North-East Indian population. *Int. J. Res. Rev*. 2018;5:215-9.
8. Porwal V, Porwal A, Verma A. Etiological factor of ascites and its correlation with serum ascites albumin gradient and cholesterol gradient in patients admitted at rural area. *Int J Adv Med*. 2016 Jul;3(3):573-8.

9. Porwal V, Porwal A, Ajnar Y, Verma A, Pandey P. Estimation of serum ascitic albumin gradient (saag) and serum ascitic cholesterol gradient (sacg) in different causes of ascites. *Çağdaş Tıp Dergisi*. 2016 Oct 10;6(3):150-6.
10. Sastry AS, Mahapatra SC, Dumpula V. Ascitic fluid analysis with special reference to serum ascites cholesterol gradient and serum ascites albumin gradient. *Int J Res Med Sci*. 2017 Feb;5(2):429.
11. Sharma V, Sharma R, Sharma S, Goyal N. CLINICOPATHOLOGICAL CORRELATION OF ASCITES WITH SPECIAL REFERENCE TO SERUM ASCITIC FLUID ALBUMIN CONCENTRATION GRADIENT (SAAG)--A STUDY IN A TERTIARY CARE CENTRE OF GAJRAULA, UTTAR PRADESH. *Journal of Evolution of Medical and Dental Sciences*. 2019 May 6;8(18).
12. Dubey TN, Dawane S. Diagnostic value of serum ascites lipid gradients in patients with ascites. *International Journal of Contemporary Medical Research*. 2016 Sep;3:2572-7.
13. Pande G, Hatti M, Rai MK, Rai P, Kumar K, Vp K, Nehra A, Kumar S, Ranjan Rout S, Mishra SK, Kumar D. Response guided slow infusion of albumin, vasoconstrictors and furosemide improves ascites mobilization and survival in acute on chronic liver failure: a proof-of-concept study. *Journal of Inflammation Research*. 2022 Jan 1:5027-39.
14. Suman S, Jyoti D, Agrawal PK, Bhattacharya BK. Clinicopathological Correlation of serum ascites albumin gradient with ascitic fluid total protein in patients of ascites with portal hypertension attending a tertiary care hospital in Eastern Bihar, India. *Int J Adv Med*. 2017 May 23; 4(3):842.
15. Joshi R, Shrestha DB, Pande R, Maharjan S. Clinical Profile of Ascites Based on Presentation and Laboratory Findings: An institutional experience from Kathmandu, Nepal. *Journal of Medical Research and Innovation*. 2018 Jan 2;2(1):101-4.
16. Nakhale BD, Dube AH, Bhagat JP, Ingole R, Patil M, Clinical profile and comparison of SAAG with ascites fluid total protein (AFTP) in cases of ascites at a tertiary referral hospital in Maharashtra: *Int J Med Res Rev* 2016;4(4):512-518.
17. Seth AK, Rangarao R, Pakhetra R, Baskaran V, Rana P, Rajamani S. Accuracy of serum-ascites albumin gradient in the aetiological diagnosis of ascites. *Medical Journal Armed Forces India*. 2002 Apr 1;58(2):124-6.
18. Rahman T, Alam SR, Haque S, Nasreen H, Sultan MM. Aetiology, Clinical Presentation and Outcome of Patients with Ascites in Medicine Unit of Chittagong Medical College Hospital: A Study of 100 Cases. *IAHS Medical Journal*. 2021;4(1):56-62.
19. Al-Kanvy BA. Etiology of ascites and the diagnostic value of serum-ascites albumin gradient in non-alcohol liver disease. *Annals of Saudi medicine*. 1997 Jan;17(1):26-8.
20. Beg M, Husain S, Ahmad N, Akhtar N. Serum/Ascites Albumin Gradient in Differential Diagnosis of Ascites. *J Indian Acad Clin Med*. 2001;2(1):51-4.
21. Gupta R, Misra SP, Dwivedi M, Misra V, Kumar S, Gupta SC. Diagnostic ascites: Value of total protein albumin, cholesterol their ratios serum ascites albumin and cholesterol gradient. *J Gastroenterol Hepatol*. 1995;10(3):295-9.
22. Runyon BA, Montano AA, Akriviadis EA, Antillon MR, Irving MA, McHutchison JG. The serum-ascites albumin gradient is superior to the exudate-transudate concept in the

- differential diagnosis of ascites. *Annals of internal medicine*. 1992 Aug 1;117(3):215-20.
23. Akriviadis EA, Kapnias D, Hadjigavriel M, Mitsiou A, Goulis J. Serum/ascites albumin gradient: its value as a rational approach to the differential diagnosis of ascites. *Scandinavian journal of gastroenterology*. 1996 Jan 1;31(8):814-7.