ijlpr 2023; doi 10.22376/ijlpr.2023.13.6.L32-L36

International Journal of Life science and Pharma Research

ISSN 2250-0480

Case Report

Serum Ascites Cholesterol for Diagnosing Malignancy

A Case Report On Diagnosis of Malignancy with Serum-Ascites Cholesterol Gradient

Dr. K. Sumathi[1*], Ms. V.P. Nivedhini[2], and Dr. Jainulavudeen Mohamed Rabeek[3]

[1] *Professor, Department of Biochemistry, Sree Balaji Medical College and Hospital, Bharath institute of Higher education and Research. Chromepet. Chennai. India.*

[2] *Tutor, Department of Biochemistry, Sree Balaji Medical College and Hospital, Bharath institute of Higher education and Research. Chromepet. Chennai. India.*

[3] *Post graduate, Department of Biochemistry, Sree Balaji Medical College and Hospital, Bharath institute of Higher education and Research. Chromepet. Chennai. India.*

Abstract: Ascites are the accumulation of fluid in the Abdomen. It happens due to clinical complications from various diseases that cause signs and symptoms. Cirrhosis, malignant ascites, and abdominal tuberculosis are the most common causes of ascites. The multiple etiologies of ascites make determining the cause difficult. Several techniques can aid in the differential diagnosis of ascites. However, the techniques are more expensive, invasive, and require more time. As a result, a less expensive and faster method of diagnosis, at least as a screening test, would greatly benefit clinicians. Albumin and Cholesterol in serum and ascitic fluid are parameters that would help screen and diagnose cancer. The serum-ascites albumin gradient or gap (SAAG) is a medical calculation that helps determine the cause of ascites. In addition, the serum ascites cholesterol gradient (SACG) aids in the differential diagnosis.The case study aims to evaluate the significance of serum-ascites cholesterol gradient (SACG) in diagnosing ovarian carcinoma. This case report includes a 53-year-old woman who presented to the surgical department with anorexia, indigestion, heartburn, pain or discomfort in the abdominal and pelvic regions, nausea, early satiety, bloating, and weight loss for 1 month. She was diagnosed with ovarian carcinoma. The gradients of serum-ascites albumin and serum-ascites Cholesterol were calculated. Later, the results were compared to Ca-125, an ovarian cancer marker. SAAG showed low sensitivity but high specificity and poor diagnostic performance. Her diagnosis of ovarian carcinoma was confirmed and she was advised to follow up with the oncologist. The current case report will help understand the contribution of the ascitic fluid and serum parameters in a case of ovarian cancer with ascites of unknown etiology.

Keywords: Ovarian cancer, serum-ascites albumin gradient, serum-ascites cholesterol gradient

***Corresponding Author**

Dr. K. Sumathi , Professor, Department of Biochemistry, Sree Balaji Medical College and Hospital, Bharath institute of Higher education and Research, Chromepet, Chennai, India.

Received On 12 September, 2022

Revised On 16 March, 2023

Accepted On 4 April, 2023

Published On 1 November, 2023

Funding This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

Citation Dr. K. Sumathi, Ms. V.P. Nivedhini, and Dr. Jainulavudeen Mohamed Rabeek , A Case Report On Diagnosis of Malignancy with Serum-Ascites Cholesterol Gradient.(2023).Int. J. Life Sci. Pharma Res.13(6), L32-L36 http://dx.doi.org/10.22376/ijlpr.2023.13.6.L32-L36

1. INTRODUCTION

Ovarian cancer is the third most common cancer found in Indian women. According to estimates, the overall 5-year survival rate for ovarian cancer in India is a dismal 45%. One of the main reasons for such low success rates against this cancer is that it is only diagnosed in the advanced stages. Only in later stages III and IV of the cancer are 56% of ovarian cancer diagnoses made. Bloating, pressure, pain in the stomach, fatigue, feeling overly full after eating a normal meal, frequent bathroom trips, constipation, back pain, and menstrual irregularities are all symptoms of ovarian cancer. The American Cancer Society reported 21,550 cases of ovarian epithelial carcinoma and 14,600 deaths from the disease in 2009, making ovarian carcinoma the gynecologic malignancy with the highest case-to-fatality ratio[1]. Sixty-nine percent of all patients with ovarian carcinoma will die, compared to 19% of those with breast cancer. Most (75%) of patients present at an advanced stage, with the widely metastatic disease within the peritoneal cavity, which explains much of the tumor's high mortality. Ovarian carcinoma spreads through direct extension from the ovarian/fallopian tumor to neighboring organs (bladder/colon) or through the detachment of cancer cells from the primary tumor. It is unclear whether ascites occur when tumor cells first metastasize or if ascites are a sign of a more advanced, high-volume disease, as clinical studies and experience would suggest [2]. A combination of factors can cause ascites formation in ovarian carcinoma. Cancer cells can obstruct subperitoneal lymphatic channels, preventing the physiologically produced peritoneal fluid (1l/day) from being absorbed[3]. The most common causes of ascites are cirrhosis, malignant ascites, and abdominal tuberculosis[4]. Ascites has multiple aetiologies, making determining the cause difficult. Several techniques can help in the differential diagnosis of ascites. The procedures are more expensive, invasive, and time-consuming. As a result, clinicians would benefit greatly from a less expensive and faster method of diagnosis, at least as a screening test. Albumin and cholesterol levels in serum and ascitic fluid are two parameters that can help with cancer screening and diagnosis. The serum-ascites albumin gradient (SAAG) is a medical calculation that aids in the diagnosis of ascites[5]. Furthermore, the serum ascites cholesterol gradient (SACG) assists in the differential diagnosis. This study is aimed to evaluate the significance of serum-ascites cholesterol gradient (SACG) in diagnosing ovarian carcinoma. The study has many objectives to study the role of serum-ascites cholesterol gradient (SACG) in diagnosing ovarian carcinoma, to study the role of serum-ascites albumin gradient (SAAG) in diagnosing ovarian carcinoma, to evaluate the significance of serum-ascites cholesterol gradient (SACG) over serum-ascites albumin gradient (SAAG) in diagnosing ovarian carcinoma.

2. CASE REPORT

A 53-year-old woman presented to the surgical department with anorexia, indigestion, heartburn, pain or discomfort in the abdominal and pelvic regions, nausea, early satiety, bloating, and weight loss for 1 month.

2.1. Medical History

The patient was hypertensive and was on medicines for the same.

2.2. Family History

She had no previous cancers in her family history. Her family history was unremarkable.

2.3. Obstetric History

Her menstrual history included menarche at 13 years of age. She had reached menopause 6 years back at the age of 47. Her menstrual cycle was 28 days. She had dysmenorrhea and menorrhagia.

2.4. Surgical History

She had no surgical history, allergies, or history of alcohol consumption or smoking.

2.5. Observation

Her cervical cytology results were negative every year.

2.6. General Examination

The patient was conscious and oriented on general examination and had no pallor, clubbing cyanosis, or peripheral lymphadenopathy. BP- 130/80mmHg, Pulse rate- 68/min.

2.7. Systemic Examination

Cardiovascular system- S_1S_2 normal, Respiratory system – bilateral air entry present, Abdomen- distended, tenderness in the left iliac fossa. Central nervous system –No sensory and motor deficits.

2.8. Special Tests and Investigations

2.9. Tumour Markers

1. Carbohydrate antigen (CA) 125 = 62 U/mL
2. CA 199 = 14.2 U/mL,
3. Carcinoembryonic antigen (CEA) 0.5 U/mL

Table 1: Serum-Ascites Albumin, Serum-Ascites Cholesterol Gradients

Parameters	Serum value	Ascitic value	Ratios
Albumin (g/dL)	3.74	2.95	serum-ascites albumin gradient (SAAG) = 0.79
Cholesterol (mg/dL)	126.8	82.6	serum-ascites cholesterol gradient (SACG) = 44.2

Her transvaginal ultrasound scan showed left ovarian carcinoma with ascites.

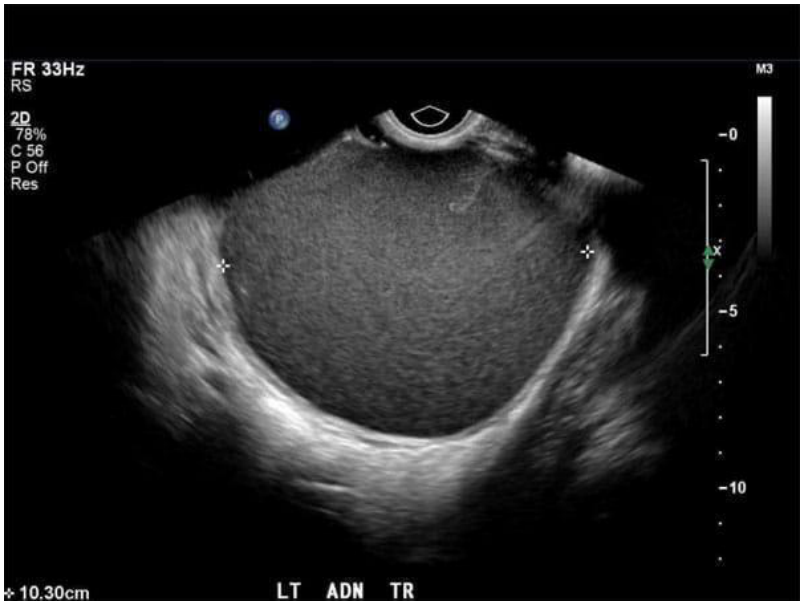

Fig:1 Ultrasound report of the patient with ovarian carcinoma

2.10. Diagnosis

Shewas diagnosed with ovarian carcinoma.

2.11. Treatment

Her diagnosis of ovarian carcinoma was confirmed and she was advised to follow up with the oncologist.

3. DISCUSSION

The above-discussed case is a case of ascites of unknown origin initially. The patient's serum was drawn and ascitic fluid was tapped to reduce the pain. The ascitic fluid was sent to the laboratory to estimate albumin (2.95 g %) and Cholesterol (82.6 mg%). Serum albumin was 3.74 g%, and Cholesterol was 126.8 mg%. From these values, the serum-ascites albumin and serum-ascites cholesterol gradients were calculated (SAAG=0.79 and SACG=44.2), which helped us in diagnosing the etiology of the ascites. A high gradient (>1.1 g/dL, >11 g/L) indicates that the ascites are caused by portal hypertension, either liver-related or not[6]. A low gradient (1.1 g/dL, 11 g/L) indicates causes of ascites that are not associated with increased portal pressure, such as tuberculosis, pancreatitis, infections, serositis, peritoneal carcinomatosis, and pulmonary infarcts. The diagnostic accuracy of AFA is superior to that of SAAG in distinguishing between PH and non-PH ascites, reported a study conducted in Mexican patients with ascites related to portal hypertension[7]. Another study showed that elevated cholesterol levels in the ascites and the albumin gradient in the ascites are excellent indicators of malignant ascites[8]. The Pathogenesis of Ascites is explained by the following parameters which can be applied to calculate the Net filtration across a membrane.

1. Increase in capillary permeability (Lp).
2. Increase in surface area of filtration (S).
1. Increased Hydraulic pressure difference (P).
2. Decreased Oncotic pressure difference (π).

To understand the pathogenesis of ascites, Starling's law of capillary hemodynamics need to be known[9].

Net filtration = LpS [(Pcap - P if) – s (πcap –π if)].

Where Lp- unit permeability of the capillary wall.
S- surface area available for filtration.
s- reflection coefficient of proteins across the capillary wall. (values may vary from 0 to 1).

The two common mechanisms by which cholesterol concentration is increased in ascitic fluid in malignancy are

1. Increase of vascular permeability, synthesis of Cholesterol, and the secretion from the malignant cells implanted on the peritoneum[10].
2. The elevated levels of ascitic fluid Cholesterol are due to the increased movement of plasma HDL and LDL into the peritoneal cavity[11].

At the same time, the patient's serum was also sent to estimate Ca-125, which was found to be elevated- 62 U/ml (Normal: < 35 U/ml). Explaining the reports to the patient and attenders to undergo a transvaginal ultrasound scan (TVUS) confirmed our diagnosis. A variation in the cut-off values was observed in different studies[12], which could be attributed to the serum cholesterol levels, stage of the cancer disease and peritoneal implant extent, and the selection of study patients. Friedman carried out a mouse study and a human Coates study using radiolabelled components[13,14]. They concluded that lymphatic obstruction is closely associated with carcinomatous ascites. SAPG (Serum-ascites protein gradient), with a cutoff value of 4, is one of the best screening tests for distinguishing between cirrhotic and non-cirrhotic ascites compared to SAAG (Serum-ascites albumin gradient). Still, it has a higher sensitivity and lower specificity in distinguishing between malignant and non-malignant disease is a poor parameter with a very low ascites[15]. In his study, Vyakaranam[16] showed that SACG had a sensitivity of 90% and a specificity of 95% with a cutoff value of less than1/2. On the other hand, a similar study by Dharwadkar[17] showed that SACG had 68% sensitivity and 100% specificity with her<100% cutoff value of 95 mg/dL, to

distinguish between ascites in cirrhosis and tuberculous peritonitis. A study by Sastry[18] and Rana[19]to distinguish between malignant and non-malignant ascites showed sensitivities of 90%, 88%, specificity of 97.5%, and 100% cut-off values of >62mg/dl and >70 for Cholesterol in ascites. Gupta showed that ascites cholesterol had a sensitivity of 94% and a specificity of 94% with a cutoff of 55 mg/dl[20]. According to another review study, ascitic fluid cholesterol and SATG were viewed as the more delicate boundaries that would be utilized as an additional biomarker alongside the SAAG for screening and differential finding of malignant ovarian growth to that of liver cirrhosis[21]. Different studies on endothelial penetrability[22] have proposed various mechanisms; crumbling of numerous cells of essential growths which bother peritoneal serosa, prompting expanded penetrability of the carcinomatous film[23]; the expanded degrees of Cholesterol in the stomach liquid concurring upon speculation of blockage lymphatic waste[24] for increased Cholesterol in cases of cancer. These studies were in concordance with the current study.

3. CONCLUSION

From the above case report, the estimation of serum and ascitic cholesterol is a simple and cost-effective laboratory test of high diagnostic accuracy useful in the differential diagnosis of ascites between malignancy and non-malignancy. This study also discovered elevated levels of ascitic fluid .Cholesterol is an excellent predictor of malignant ascites. Its promises to be dependable while remaining simple and cost-effective indicative parameters.

4. ACKNOWLEDGEMENT

We acknowledge the Department of Biochemistry, Department of General Medicine, and Sree Balaji Medical College and Hospital, Chromepet, for supporting us in completing this case report.

5. ETHICAL APPROVAL STATEMENT

The study involved human participants following the ethical standards of the tertiary health care institution where the study was conducted (IHEC Number: 002/SBMC/IHEC/2017/985).

6. AUTHORS CONTRIBUTION STATEMENT

K. Sumathi came up with the ideas presented. V.P.Nivedhini and Jainulavudeen Mohamed Rabeek collected the case details and helped prepare the manuscript. All authors contributed to the discussion and the final manuscript.

7. CONFLICT OF INTEREST

Conflict of interest declared none.

8. REFERENCES

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin. 2009;59(4):225-49. doi: 10.3322/caac.20006, PMID 19474385.
2. Cannistra SA. Cancer of the ovary. N Engl J Med. 2004;351(24):2519-29. doi: 10.1056/NEJMra041842, PMID 15590954.
3. Hashimoto K, Honda K, Matsui H, Nagashima Y, Oda H. Flow cytometric analysis of ovarian cancer ascites: response of mesothelial cells and macrophages to cancer. Anticancer Res. Jul 2016;36(7):3579-84. PMID 27354626.
4. Vaz AM, Peixe B, Ornelas R, Guerreiro H. Peritoneal tuberculosis as a cause of ascites in a patient with cirrhosis. BMJ Case Rep. 2017 Jul 14;2017: bcr2017220500. doi: 10.1136/bcr-2017-220500, PMID 28710241.
5. Gogoi P, Debnath E, Serum CR/ascites albumin gradient (SAAG), a 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(12):215-9.
6. 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. Ann Intern Med. Aug 1992;117(3):215-20. doi: 10.7326/0003-4819-117-3-215, PMID 1616215.
7. Cervantes Pérez E, Cervantes Guevara G, Cervantes Pérez G, Cervantes Cardona GA, Fuentes Orozco C, Pintor Belmontes KJ et al. Diagnostic utility of the serum-ascites albumin gradient in Mexican patients with ascites related to portal hypertension. JGH Open. 2020 Aug 8;4(5):838-42. doi: 10.1002/jgh3.12404, PMID 33102752.
8. Bijoor AR, Venkatesh T. Value of ascitic fluid Cholesterol and serum-ascites albumin gradient in differentiating cirrhotic and malignancy-related ascites. Indian J Clin Biochem. 2001 Jan;16(1):106-9. doi: 10.1007/BF02867577, PMID 23105301.
9. Rana SV, Babu SGV, Kocchar R. Usefulness of ascitic fluid cholesterol as a marker for malignant ascites. Med Sci Monit. Mon 2005;11(3):CR136-42. PMID 15735567.
10. Jüngst D, Xie Y, Gerbes AL. Pathophysiology of elevated ascites fluid Cholesterol in malignant ascites. Increased ascites to serum relation of proteins and lipoproteins in patients with peritoneal carcinomatosis compared to patients with liver cirrhosis. J Hepatol. 1992;14(2-3):244-8. doi: 10.1016/0168-8278(92)90165-I, PMID 1500688.
11. Vyakaranam S, Nori S et al. Serum – ascites albumin and cholesterol gradients in the differential diagnosis of ascites. NJIRM. 2011;2(3). July- September.22-28.
12. Sood A, Garg R, Kumar R, Chhina RS, Arora S, Gupta R, et al. Ascitic fluid cholesterol in malignant and tubercular ascites. J Assoc Physicians India. 1995;43(11):745-7. PMID 8773030.
13. Feldman GB, Knapp RC. Lymphatic drainage of the peritoneal cavity and its significance in ovarian cancer. Am J Obstet Gynecol. 1974;119(7):991-4. doi: 10.1016/0002-9378(74)90021-0, PMID 4276313.
14. Coates G, Bush RS, Aspin N. A study of ascites using lymphoscintigraphy with 99m Tc-sulfur colloid. Radiology. 1973;107(3):577-83. doi: 10.1148/107.3.577, PMID 4702536.
15. Prabhu M, Gangula RS, Stanley W. Diagnostic utility of serum ascites lipid and protein gradients in differentiating ascites. Int J Hepatol. 2019;2019:8546010. doi: 10.1155/2019/8546010, PMID 31275659.

16. Vyakaranam S, Nori S, Sastry M, Vyakaranam BS, Bhongir AV. 'Serum – ascites albumin and cholesterol gradients in the differential diagnosis of ascites,' NJIRM. Vol. 2; 2011. p. 22-8.
17. Dharwadkar K, Bijoor A. Usefulness of serum ascites cholesterol gradient (SACG), total protein (TP) ratio and serum ascites albumin gradient (SAAG) in differentiating tuberculous ascites and cirrhotic ascites. Int J Med Sci Public Health. 2013;2(4):1068-72. doi: 10.5455/ijmsph.2013.010920134.
18. 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;5(2):429. doi: 10.18203/2320-6012.ijrms20170059.
19. Rana SV, Babu SG, Kocchar R. Usefulness of ascetic fluid Cholesterol as a marker for malignant ascites. Med Sci Monit. 2005;11:136-42.
20. Gupta R, Misra SP, Dwivedi M, Misra V, Kumar S, Gupta SC. Diagnosing ascites: the value of ascitic fluid total protein, albumin, Cholesterol, their ratios, serum-ascites albumin, and cholesterol gradient. J Gastroenterol Hepatol. 1995;10(3):295-9. doi 10.1111/j.1440-1746.1995.tb01096.x, PMID 7548806.
21. Sahithya, Pani, Suseela, Ayesha, Qamar, Srinivasulu, et al. Pasha, MD & Kumar, B & Macherla, Ramana & Reddy. J Clin Diagn Res. 2020. Biochemical Markers of Ascitic Fluid to Differentiate Ovarian Cancer from Liver Cirrhosis Patients;14(3):125-8.
22. Hirabayashi K, Graham J. Genesis of ascites in ovarian cancer. Am J Obstet Gynecol. 1970;106(4):492-97. doi: 10.1016/0002-9378(70)90031-1, PMID 5412843.
23. Cretu AM, Aschie M, Preda G, Rosoiu N. Diagnostic limitations of biochemical evaluation of peritoneal effusions in differentiating malignant and non-malignant pathologies. Ovidius Univ Ann Chem. 2010;21(2):139-46.
24. Mortensen PB, Kristensen SD, Bloch A, Jacobsen BA, Rasmussen SN. Diagnostic value of ascitic fluid cholesterol levels in the prediction of malignancy. Scand J Gastroenterol. 1988;23(9):1085-8. doi 10.3109/00365528809090173. PMID 3247589.