Research Article

Evaluation of Ascitic Fluid Cholesterol Level in Diagnosis of Malignancy Related Ascites

Vyankatesh T. Anchinmane[1]*, Shilpa Vijay Sankhe[2]

1. Professor, Department of Pathology, Zydus Medical College and Hospital, Dahod, Gujarat, India.
2. Tutor, Department of Pathology, Zydus Medical College and Hospital, Dahod, Gujarat, India.

***Corresponding author's E-mail:** vyankatesha78@gmail.com

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ABSTRACT

Diagnosis of malignancy related ascites is common clinical problem. The differentiation of unknown etiology ascites, into malignancy and non-malignancy related ascites is very time consuming with existent available methodologies. Ascitic fluid cytology is gold standard method for confirmation of malignancy; however, this method is observer dependent and has low accuracy. The present study objective was, to evaluate the accuracy of ascitic fluid cholesterol level, for diagnosis of malignancy related ascites. Total 50 cases of ascites were included in this study over the period of one year. The 31 were non-malignancy related ascites cases due to etiology of liver cirrhosis, anaemia- hypoproteinemia, chronic renal failure, congestive cardiac failure, tuberculosis etc. The 19 cases were malignancy related ascites. All the cases diagnosis was confirmed with clinical features, laboratory diagnosis and radiological investigations, as necessary for respective cases. Ascitic fluid cholesterol level was estimated for all cases ascitic fluid samples with biochemistry analyzer. The accuracy of ascitic fluid cholesterol was 92 % with cut off of 60 mg % for detection of malignancy related ascites cases. The present study concluded that ascitic fluid cholesterol level is accurate, reliable, rapid diagnostic method for diagnosis of malignancy related ascites.

Keywords: Malignancy, ascites, ascitic fluid cholesterol.

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INTRODUCTION

Rapid accurate diagnosis and accordingly early appropriate management for ascites patients, is a common clinical challenge in any hospital set up. Ascites is the pathological collection of fluid within peritoneal cavity. The differential diagnosis of ascites is common diagnostic problem. The common causes of ascites are liver cirrhosis, anaemia, tuberculosis and malignancy etc. Traditionally, ascitic fluids are categorized into transudates and exudates. Transudates develop commonly due to physiological disturbances of circulation; in view of increase in venous pressure or decrease in plasma oncotic pressure. Transudates are generally associated with chronic cardiac, hepatic or renal disease. The exudates develops due inflammation related increased capillary permeability. Exudates are generally associated with inflammatory conditions like tuberculosis and malignancies of pelvic and abdominal organs. [1, 2]

Ascitic fluid examination is a routine laboratory test, where the ascitic fluid is differentiated into transudate and exudate. The further differentiation of malignancy related ascites cases from other causes ascites is quite often cumbersome; however, it is necessary for further diagnostic and therapeutic procedures.[3]The malignancy related ascites generally accounts for about 10% of all cases of ascites. They are usually related to carcinomas of lung, breast, ovary, endometrium, colo-rectum, pancreas, hepatobiliary organs etc. [4]

Ascitic fluid cytology is the gold standard investigation for confirmation of malignancy related ascites. In the said technology, the detection of malignant cells in the ascitic fluid is done. However, said method has low sensitivity due degeneration/ lysis of malignant cells. [5] Several studies were done in the past to analyse ascitic fluid fibronectin, tumor antigens, lipids etc. for diagnosis of malignant related ascites.[4, 6]Ascitic fluid cholesterol was also analyzed and labeled as more accurate method for diagnosis of malignancy related ascitic fluid. [7] Hence the present study was done, to evaluate the usefulness of ascitic fluid cholesterol level, in diagnosis of malignant related ascites.

MATERIALS AND METHODS

The study was conducted in tertiary care hospital central laboratory for the period from July 2021 to June 2022. The following inclusion criteria were utilized for this study. For liver cirrhosis cases, the clinical history of deranged liver function tests results and radiological investigations were considered. The chronic renal failure diagnosis was confirmed with clinical features and deranged urea/ creatinine results. For the congestive cardiac failure diagnosis; the clinical findings, ECG findings and laboratory results were considered. Anaemia cases were confirmed with hemoglobin estimation results and related clinical

history. Tuberculosis cases were confirmed with clinical features and pathological, microbiological and radiological investigations. Malignancy cases were confirmed with fluid cytology/ FNAC/ histopathology. The cases in which, another co-existing disease or drug therapy altering the serum cholesterol level were excluded from the study.

The semiautomatic biochemistry analyzer was utilized for fluid cholesterol level estimation. Fluid cholesterol level cut off of more than 60 mg % were utilized, to label the case as diagnosis of malignant related ascites. Statistical analyses were done with the SPSS software and fluid cholesterol level accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) was studied for diagnosis of malignant related ascites.

RESULTS AND DISCUSSION

In the total 50 ascites cases, 37 were male and 13 were female. The age range of patients was from 22 years to 61 years. The causes of non- malignant ascites were cirrhosis, anaemia, chronic heart failure (CHF), chronic renal failure (CRF) and tuberculosis. (Table 1) The malignant ascites cases were related to carcinoma liver (4 cases), carcinoma stomach (5 cases), carcinoma ovary (4 cases), carcinoma pancreas (3 cases), carcinoma gall bladder (2 cases) and carcinoma breast (1 case).

Table 1: Etiological distribution of Ascites

Disease	Number of cases (n)
Tuberculosis	10
Malignancy	19
Anaemia	05
CHF	02
CRF	02
Cirrhosis	12
Total	50

Table 2: Fluid Cholesterol test evaluation for malignant and non- malignant ascitic fluids

	Malignant ascites	Non- malignant ascites	Total	Predictive value (PV)
Fluid Cholesterol > 60 mg%	17	02	19	**PPV (89.4 %)**
Fluid Cholesterol < 60 mg%	02	29	31	**NPV (93.5 %)**
Total	19	31	100	
	Sensitivity (89.4 %)	**Specificity (93.5 %)**	**Accuracy (92.0 %)**	

The cut off level of 60 mg % was utilized for the evaluation of fluid cholesterol activity in all 50 ascites cases. The fluid cholesterol level 60 mg % and above were considered as malignant ascites positive and fluid cholesterol level less than 60 mg % were considered as malignant ascites negative. With the cut of 60 mg %, the fluid cholesterol showed Sensitivity, Specificity, Accuracy, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of 89.4 %, 93.5 %, 92 %, 89.4 % and 93.5 % respectively. (Table 2) Similar results were obtained in various studies done in the past. Bijoor AR et al showed that malignancy related ascites patient fluid cholesterol levels were of 95.87±1.24mg/dl against the non-malignant ascites patient ascitic fluid cholesterol values of 19.41±8.33 mg/dl. [8]

The different fluid cholesterol cut off was utilized for differentiation of malignant and non-malignant ascitic fluids in many studies in the past. In the studies done by Rana SV et al showed that ascitic fluid cholesterol (with a cutoff of 70 mg / dl) gave sensitivity, specificity and accuracy of 88 %, 100 % and 94 % respectively, with positive predictive values 100 %, for differentiation of malignant and non-malignant ascitic fluids. [4] Garg R et al with fluid cholesterol cut off level of 48 mg / dl, showed sensitivity and specificity as 96.5% and 96.6% respectively, for discrimination of malignant and non - malignant ascites. [9] Sood A et al found the specificity and sensitivity as 100% and 89.65% respectively in differentiating tuberculous from malignant lesions ascitic fluid with fluid cholesterol levels cut off level of 54.5 mg / dl. [10] Vyakaranam S et al found diagnostic accuracy of 96 % with ascitic fluid cholesterol levels cut off level of 62 mg / dl for detection of malignancy related ascitic fluid.[11]Hence, in the present study, fluid cholesterol cut off of 60 mg % was utilized for differentiating malignant and non - malignant ascites.

Albillos A. et al 1990 found values of cholesterol in ascitic fluid 110 and 115 mg/ dl in the two samples of tuberculous peritonitis. [12] Similar findings were found in our study. The two cases of tuberculosis ascites showed fluid cholesterol levels of 76 mg % and 81 mg % respectively and were presented as false- positive cases with fluid cholesterol cut off of 60 mg % for detection of malignant ascitic cases.

The fluid cytology test is gold standard test for confirmed diagnosis of malignant cells in ascites. However, there are several limitations to this diagnostic methodology. The fluid cytology report- negative for malignant cells, do not rule out possibility of malignancy; as blocking lymphatic or blood vessels by tumor or peritoneal inflammation or malignancy without peritoneal metastatic implants, may results into non- shedding of tumor cells in ascitic fluid. Technical accuracy for collection, processing of ascitic fluid sample is very crucial. The skilled trained expert cytopathologist is very much needed for diagnosis of cases.[13] Rana SV et al showed that ascitic fluid cytology has 100 % specificity and

64 % sensitivity for detection of malignancy in ascitic fluid.[4] In the present study, out of 19 malignant cases, the fluid cytology malignancy positive reported cases were 11 and correlates well with the previous studies.

Prieto M et al 1988 postulated that cholesterol is derived from malignant cell membrane. Also, the cholesterol macromolecule sequestration into the peritoneal cavity takes place, in case of blocking of peritoneal lymphatic drainage. [13] Moreover, the fluid cholesterol level detection is simple, cost effective method and can be done with basic laboratory machinery like colorimeter or semi-automatic analyzer. In this study, it is found that the ascitic fluid cholesterol has better accuracy than fluid cytology for detection of malignancy related ascites. The advanced technologies like electron microscopy and immune-histochemistry have upper hand than fluid cytology test; however, they are complicated, costly and cannot be installed at all laboratory centers.

CONCLUSION

The diagnosis of ascitic fluid as malignancy related or malignancy non-related plays a pivotal role in the diagnosis and management of ascites. The search for novel biochemical markers for differentiating malignancy related or malignant non-related ascitic fluid is still under investigation. In this approach, ascitic fluid cholesterol level showed promising results with good accuracy. The estimation ascitic fluid cholesterol level is simple, cost-effective method and can be processed at small centers with limited diagnostic equipment.

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