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Original Research Article

Study the usefulness of ascitic fluid cholesterol level in diagnosis of malignant related ascites

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ABSTRACT

Background: The differential diagnosis of ascites is a common clinical problem. However, the capability to distinguish malignant from non-malignant causes of ascites using available biochemical techniques would obviate many expensive and time-consuming diagnostic studies on patients presenting with ascites of unknown etiology. Therefore, this study was planned to evaluate usefulness of ascitic fluid cholesterol level in diagnosis of malignant ascites.

Methods: Author conducted an observational study in 80 patients, those admitted and willing to give consent in the department of Medicine, LLR and Associated Hospitals, GSVM Medical College, Kanpur from December 2015 to October 2017. All patient underwent full investigations to make the diagnosis of ascites malignant (20) and non-malignant (n=54), tubercular (7) and non-tubercular (47) groups. Six patients were excluded because the ascitic fluid analysis was suggestive of bacterial peritonitis. The data was processed in MS Excel and analysis was carried out using SPSS (23th version).

Results: Author found that the mean value of ascitic fluid cholesterol in malignant group was 100.85+34.28 vs 6.7+2.5 in non-malignant group (p value <0.01) and the mean value of ascitic fluid cholesterol in malignant group was 100.80+34.28 vs 32.43+15.7 in tubercular group, so ascitic fluid cholesterol is highly specific (100%) and sensitive (65%) at cut off value of 100mg/dl in differentiating benign and malignant cause of ascites.

Conclusions: Ascitic fluid cholesterol having high specificity, can be used for differentiating between non-malignant and malignant ascites. It can also be used to differentiate tubercular ascites from malignant ascites.

Keywords: Ascites, Malignant, Non-tubercular and ascitic fluid cholesterol, Non-malignant, Tubercular

INTRODUCTION

Ascites is the pathological accumulation of fluid within abdominal cavity, which can present a challenging diagnostic problem.[1] Malignant ascites accounts for about 10% of all cases of ascites and is usually caused by ovarian, endometrial, lung, breast, colorectal, pancreatic, hepatobiliary, and primary peritoneal carcinomas.[2,3] The differentiation between malignancy-related ascites (MRA) and non-malignant ascites (NMA) is important for further diagnostic and therapeutic procedures.[4,5]

Cytodiagnostic investigation of ascitic fluid is characterized by a high specificity but a low sensitivity in detecting malignant disease because only a few neoplastic cells are present in the fluid or processing of specimens is suboptimal with lysis of tumour cells.[6,7] To increase diagnostic sensitivity, cytologic evaluation has

been coupled with the analysis in serum and ascitic fluid for total protein, various enzymes, fibronectin, tumor antigens, and lipids.[2,8,9]

Papers about the detection of ascitic cholesterol have been published a lot and they have shown a relatively high diagnostic efficiency in differential diagnosis of MRA.[2,3] However, conflicting results have been reported and the exact role of ascitic fluid cholesterol concentration remains unclear. Therefore, author performed this study to establish the usefulness of ascitic fluid cholesterol level in diagnosis of malignant related ascites.

Aims and objectives of this study was to study the usefulness of ascitic fluid cholesterol level in diagnosis of malignant Related ascites.

METHODS

This prospective study was carried out in the Post Graduate Institute of Medicine, G.S.V.M. Medical College, Kanpur during the period of December 2015 to October 2017. Those patients willing to give consent were admitted in the department of medicine, LLR and Associated Hospitals, GSVM Medical College, Kanpur. Informed consent taken from all patients.

Total 80 patients of ascites were included in this study. Among these 80 patients, 74 were included in the study and 6 excluded because the ascitic fluid analysis was suggestive of bacterial peritonitis. In all patient all related investigations like Complete blood count, liver profile, serum amylase and lipase, serum creatinine Alfa-fetoprotein, CA-125, Prothrombin Time/INR , Lipid profile, Serum CRP, Urine albumin, 24 hours urinary protein and Ascitic fluid examination for the Biochemical analysis for Albumin, Total Protein, Cholesterol, Glucose, Amylase, LDH, CRP and ADA, Cytological Analysis for Cell counts and Differential count, and Microbiological Analysis for gram stain, ZN stain, malignant cells and bacterial culture were performed.

Other investigations like USG abdomen, upper GI Endoscopy, CT scan abdomen and Pelvis. Echocardiogram, Thyroid Profile, ECG, 2D echo, X ray chest. Upper GI endoscopy, FNAC of the peritoneal nodules and liver biopsy other tumor marker were done in selected cases where it was needed.

Inclusion criteria

- Age>18 yrs.
- Clinical features suggestive of Ascites.

Exclusion criteria

- Age <18 yrs.
- Patient with bacterial peritonitis
- Presence of another co-existing disease/drug therapy that would alter serum cholesterol and CRP levels.
- Those patients who are already on treatment of chemotherapy and or radiotherapy.

Statistical analysis

The data was processed in MS Excel and analysis was carried out using SPSS (23th version). Quantitative variables were analyzed using mean and SD. The results were statistically analyzed by Student 't' test. Two tailed probability values of <0.05 was taken as indicating significance.

RESULTS

In this study, author included 80 patients of ascites. Among these 80 patients, 74 were included in the study and 6 excluded because the ascitic fluid analysis was suggestive of bacterial peritonitis. The patients were divided into two groups malignant(n=20) and non-malignant(n=54). The non-malignant group was further subdivided into two groups tubercular (n=7) and non-tubercular cases(n=47).

Table 1: Distribution of patients according to etiology.

Etiology	Total no. (n=74)	Percentage
Cirrhosis	40	54.05
Tubercular ascites	7	9.45
Decompensated heart failure	4	5.4
Chronic kidney disease	2	2.7
Nephrotic syndrome	1	1.35
Hepatocellular carcinoma	4	5.4
Carcinoma pancreas	2	2.7
Carcinoma prostrate	1	1.35
Carcinoma ovary	8	10.8
Carcinoma bladder	1	1.35
Carcinoma gall bladder	3	4.05
Colorectal carcinoma	1	1.35

Out of 74 patients,40 (54.05%) were diagnosed as cirrhosis and 20 were diagnosed with malignancy. Out of 20 malignant cases, 8 cases were of carcinoma ovary (n=8;40%) (Table 1).

Table 2: Ascitic fluid cholesterol mean value with SD in non-malignant and malignant group.

	Non-malignant* (n=47)	Malignant (n=20)	P value
Ascitic cholester (mg/dl)	6.7±2.5	100.85±34.28	<0.01

*Tubercular cases are not included in the non-malignant group

The mean age of the patients who took part in study was 45.81±12.52 years. The lowest age was 20 years and

highest was 85 years. Among 74 cases, 43 (58%) were males and 31(42%) were females.

For the non-malignant group mean value of ascitic fluid cholesterol (mg/dl) is 6.7+2.5 vs 100.85+34.28 in malignant group. The student t-test is applied, p value is <0.01 indicating that ascitic cholesterol is significantly higher in malignant group (Table 2).

Table 3: Ascitic fluid cholesterol mean value with SD in malignant and tubercular group.

	Malignant (n=20)	Tubercular (n=7)	P value
Ascitic fluid cholesterol(mg/dl)	100.85±34.28	32.43±15.7	<0.01

For the malignant group mean value of ascitic fluid cholesterol (mg/dl) is 100.85+34.28 vs 32.43+15.7 in tubercular group. The student t-test is applied, p value is <0.01 indicating that ascitic cholesterol is significantly higher in malignant group (Table 3).

Table 4: Ascitic fluid cholesterol mean value with SD in non-tubercular and tubercular group.

	Non-tubercular (n=47)	Tubercular (n=7)	p value
Ascitic fluid cholesterol(mg/dl)	6.7±2.5	32.43±15.7	<0.01

For the non-tubercular group mean value of ascitic fluid cholesterol (mg/dl) is 6.7+2.5 vs 32.43+15.7 in tubercular group. The student t-test is applied, p value is <0.01 indicating that ascitic cholesterol is significantly higher in malignant group (Table 4).

DISCUSSION

One of the most common challenges in the treatment of ascites patients is to reveal the cause of the disease as rapidly as possible for an appropriate management. Ascitic fluid can accumulate as an exudate or a transudate, that play a pivotal role in the diagnosis and management of ascites.

The search for novel biochemical markers in the serum and/or ascitic fluid is still under investigation. In this approach, cholesterol have shown to be promising marker.

In this study, author included 80 patients of ascites. Among these 80 patients, 74 were included in the study and 6 excluded because the ascitic fluid analysis was suggestive of bacterial peritonitis. The patients were divided into two groups malignant(n=20) and non-malignant(n=54). The non-malignant group was further subdivided into two groups tubercular (n=7) and non-tubercular cases(n=47).

The ascitic fluid cholesterol was compared in malignant and non-malignant (excluding tubercular cases) group. The mean cholesterol level was found to be 100.85mg/dl in malignant group and 6.7mg/dl in non-malignant group with a P-value of <0.01. With a cut off value of ascitic fluid cholesterol 100mg/dl, the specificity was 100% and sensitivity 65%. Rana SV et al also reported that the mean ascitic cholesterol level was significantly higher in malignant ascites than in non-malignant ascites, with a cut off level of 70mg/dl for ascitic fluid cholesterol.[10] The specificity (100%) and diagnostic efficiency (94%) of ascitic fluid cholesterol is better than the 84% specificity and 86% diagnostic efficiency of serum ascitic albumin gradient. The specificity is found to be similar as Rana SV et al and sensitivity is lower than their study because the cut off value of ascitic fluid cholesterol used in this study was higher (100mg/dl vs 70mg/dl).[10]

Almost similar result also reported by Sastry AS et al, the ascitic fluid cholesterol was found higher in malignant ascites (128±8.10) vs 51.40±8.3 in non-malignant cases.[11]

The ascitic fluid cholesterol has sensitivity 88% vs 65% in this study, specificity is 96% vs 100% in this study. Almost similar result was also reported by Bijoor AR et al studied the ascitic fluid and serum concentration of total cholesterol, total proteins and albumin in a group of 45 patients.[12] Non-malignant ascites patients had ascitic fluid cholesterol values of 19.41±8.33 mg/dl, as against the malignancy related ascites patients, who showed levels of 95.87±1.24mg/dl.

Study performed by Vyakaranam S et al also supports the study in which the ascitic fluid cholesterol level above 62mg/dl give the diagnostic accuracy of 96%.[13]

Zhu H et al**,** meta-analysed the literature on using ascitic cholesterol as diagnostic tests to help identify MRA (malignant related ascites).[14] Meta-analysis included 8 studies involving 743 subjects. Summary estimates for ascitic cholesterol in the diagnosis of MRA were as follows: sensitivity, 0.82 (95% CI 0.78 to 0.86); specificity, 0.90 (95% CI 0.87 to 0.93).

In this study author also compared the ascitic fluid cholesterol (mg/dl) between malignant (n=20) and tubercular group of ascites(n=7). The mean level of ascitic fluid cholesterol found in malignant group was 100.85 vs 32.43 in tubercular group which is statistically significant (p<0.01). The similar result was found in a study performed by Sood A et al**,** cholesterol was estimated in ascitic fluid of 44 patients (29 malignant and 15 tubercular).[15] Mean ascitic cholesterol level was significantly higher in malignant ascites (89.52 mg/dl) as compared to tubercular ascites (35.07 mg/dl). Ascitic fluid cholesterol estimation is a reliable and simple test for differentiating malignant ascites from tubercular ascites.

In this study author also compared the ascitic fluid cholesterol(mg/dl) between rest of non-malignant (n=47) and tubercular group of ascites (n=7). The mean level of ascitic fluid cholesterol found in rest of non-malignant group was 6.7 vs 32.43 tubercular group which is statistically significant (p<0.01). This finding needs further studies.

CONCLUSION

Out of 80 patients, 74 patients were included in the study and 6 patients were excluded due to bacterial peritonitis. The lowest age was 20 years and highest was 85 years. The mean age of patients was 45.81+12.52 years. Out of 74 patients 43(58%) were males and 31(42%) were females.

The mean value of ascitic fluid cholesterol in malignant group was 100.85+34.28 vs 6.7+2.5 in non-malignant group (p value <0.01). Ascitic fluid cholesterol is highly specific (100%) and sensitive (65%) at cut off value of 100mg/dl in differentiating benign and malignant cause of ascites. The mean value of ascitic fluid cholesterol in malignant group was 100.80+34.28 vs 32.43+15.7 in tubercular group.

Ascitic fluid cholesterol having high specificity, can be used for differentiating between non-malignant and malignant ascites. It can also be used to differentiate tubercular ascites from malignant ascites. Hence this parameter is being simple and cost effective can be widely used to differentiate non-malignant and malignant ascites, even in small centers with limited diagnostic facilities.

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