Original Article

Value of ascitic fluid cholesterol to differentiate cirrhotic from non-cirrhotic ascites

Syed Abul Foez[1], Md. Ziaur Rahman Chowdhury[2], Md. Abdur Rahim[3], Md. Zia Hayder Bosunia[4], Abul Kalam Mohammed Shoab[5], Sheikh Mohammad Noor-E-Alam[6]

Abstract *This cross sectional study was conducted in the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU) to see the 'value of ascitic fluid cholesterol to differentiate cirrhotic from non-cirrhotic ascites'. A total 80 patients with ascites (40- cirrhotic, 40- non cirrhotic) were enrolled. Most of the cirrhotic patients (35%) were of 41-50 years of age, whereas most of the tubercular patients (36.36%) were of 21-30 years of age, most of the patients with malignancy (38.88%) were of 51-60 years of age. Mean(±SD) age of cirrhotic and malignant patients were 49.55±12.77 and 50.61±13.67 years respectively, whereas in tubercular patients 33.64±15.81 years. Most cirrhotic patients were male (77.5%) whereas in non-cirrhotic cases 52.5% were male, 47.5% were female. HBV was the most common cause of cirrhosis (72.5%) followed by HCV-20% and the remaining 7.5% causes were unknown (NBNC). Among non-cirrhotic ascites 55% cases were due to tubercular peritonitis, 45% due to carcinomatosis peritonii. Most of the cirrhotic patients were in CP stage C (77.5%), 22.5% patients found in CP stage B, none of the patients with cirrhotic ascites found in CP stage A. Ascitic fluid cholesterol in cirrhotic ascites found much lower than non-cirrhotic ascites. Mean(±SD) cholesterol in cirrhotic ascites was 8.425±5.96 mg/dl, whereas in non-cirrhotic ascites was 87.15±26.05 mg/dl and the difference between two groups was highly significant (p<0.001). At a cutoff level of ascitic fluid cholesterol 29 mg/dl; the sensitivity, specificity, PPV, NPV and diagnostic accuracy was 100% to differentiate cirrhotic from non-cirrhotic ascites. Mean(±SD) ascitic fluid cholesterol in malignant ascites was 83.62±26.32 mg/dl, whereas in tubercular ascites was 90.03±26.14 mg/dl and the difference was not statistically significant (p=0.673). In view of the good diagnostic efficiency, easy availability and cost effectiveness, ascitic fluid cholesterol was an excellent parameter to differentiate cirrhotic ascites.*

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Introduction

'ASCITES' describe - pathologic fluid accumulation within peritoneal cavity.[1] Differential diagnosis of ascites is the common clinical problem. The effective way of diagnosis is ascitic fluid analysis. In cirrhosis, there is impaired hepatic lipoprotein synthesis and abnormalities in transcapillary-lymph hydrodynamics results in lower selectivity for the movement of HDL and LDL from plasma to ascites.[2] On the other hand- in the presence of peritoneal disorders such as tubercular peritonitis/carcinomatosis peritonii, there is increase filtration of plasma protein and lipoprotein. Furthermore, in peritoneal carcinomatosis increase vascular permeability, increase cholesterol synthesis and release from neoplastic cells also contribute increase cholesterol in ascitic fluid.[3] Three most important

1. * Assistant Professor, Department of Hepatology, Sylhet MAG Osmani Medical College, Bangladesh.
2. Assistant Professor, Department of Pediatrics, Sylhet MAG Osmani Medical College, Bangladesh.
3. Assistant Professor, Department of Hepatology, Abdul Malek Ukil Medical College, Noakhali, Bangladesh.
4. Assistant Professor, Department of Hepatology, Rangpur Medical College, Bangladesh.
5. Assistant Professor, Department of Neurology, Sylhet MAG Osmani Medical College, Bangladesh
6. Assistant Professor, Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Bangladesh.

Address of Corresponding author:
Dr. Syed Abul Foez,
Asst. Prof., Dept. of Hepatology, Sylhet MAG Osmani Medical College.
Email- asheque151@gmail.com

cause of ascites in our country are – liver cirrhosis (LC), malignancy and tuberculosis (T.B). Differentiation between these are of considerable clinical significance for further diagnostic and therapeutic procedure. In patient with cirrhosis, the development ascites marks the transition from compensated to decompensated cirrhosis. It is the most frequent decompensating event, occuring in 48%.[1] In LC treatment of ascites has not resulted in a significant improvement in survival. However, treating ascites is important, not only because it improves quality of life but because - SBP, a lethal complication of cirrhosis does not occur in the absence of ascites.[5] In developing countries like Bangladesh, due to financial constrain – less expansive and simple biochemical technique is required to differentiate cirrhotic ascites. Since ascitic fluid cholesterol can be determined more easily and cheaply, it may be an excellent parameter to differentiate ascites. Moreover, it become a new tool and by single measurement we can efficiently differentiate cirrhotic ascites from non-cirrhotic ascites.

MATERIALS AND METHODS

This cross sectional study were conducted in department of Hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January 2013 to December 2013. 80 patients were taken and patients were divided into two groups – Group A: consisting of 40 patients with ascites due to cirrhosis of liver and Group B: consisting of 40 patients with ascites due to tuberculosis/malignancy. 40 patients with ascites due to cirrhosis of liver as evidenced by- history and clinical features suggestive of cirrhosis, ultrasonographic evidence of ascites and small size liver with coarse liver echotexure, endoscopic evidence of oesophageal varices, serum ascites albumin gradient (SAAG) > 1.1 g/dl and/or cirrhotic changes in liver biopsy were included. 40 patients with ascites due to tuberculosis/malignancy as evidenced by- history and clinical features suggestive of tubercular peritonitis/malignancy, ultrsonographic evidence of ascites, laboratory investigations suggestive of tuberculosis or malignancy, no clinical/ultrasonographic/endoscopic evidence of liver cirrhosis, SAAG <1.1 g/dl, and/or histopathological examination suggestive of tuberculosis or malignancy. Whereas patient with spontaneous bacterial peritonitis, presence of co-existing disease that would alter serum cholesterol level (e.g. Diabetes mellitus, hypertension, renal failure, familial hypercholesterolemia, thyroid disorder, cardiovascular diseases etc.),. ascites due to nephrotic syndrome, congestive cardiac failure, malnutrition, mixed aeitiology (e.g. cirrhosis with tuberculosis/ malignancy), Budd-Chiari syndrome, fulminant hepatic failure, chemotherapy or radiotherapy already commenced, use of lipid lowering drugs, biliary cirrhosis and chylous ascites were excluded. All the data were checked and edited after collection. It was expressed as Mean ± SD, frequencies or in percentage. Statistical analysis was done using SPSS-16 (statistical package for social sciences) win version 16 software programme.

RESULTS AND DISCUSSION:

In this study Mean (±SD) age of cirrhotic and malignant patients were 49.55±12.77 and 50.61±13.67 years respectively, whereas in tubercular patients 33.64±15.81 years. Most cirrhotic patients were male (77.5%) which was supported by Alam et al. 2008.[6] In non-cirrhotic cases 52.5% were male, 47.5% female. HBV was the most common cause of cirrhosis (72.5%) followed by HCV (20%) and the remaining 7.5% were non-B, non-C (NBNC). Afroz et al. 2007 also found HBV as a leading cause of cirrhosis in Bangladesh.[7] Among non-cirrhotic ascites 55% cases were due to tubercular peritonitis, 45% due to carcinomatosis peritonii. Most of the cirrhotic patients were in Child Pugh (CP) stage C (77.5%), remaining found in CP stage B.

Table 1: Age distribution of study patients (n=80):

Age (Years)	Cirrhotic (n=40)		Non-Cirrhotic (n=40)			
			Tuberculosis (n=22)		Malignancy (n=18)	
	n	%	n	%	n	%
≤20	0	0	5	22.72	1	5.55
21-30	5	12.5	8	36.36	0	0
31-40	4	10	3	13.63	4	22.22
41-50	14	35	2	9.09	3	16.66
51-60	11	27.5	3	13.63	7	38.88
61-70	4	10	0	0	3	16.66
>70	2	5	1	4.54	0	0
Mean±SD (years)	49.55 ±12.77		33.64 ±15.81		50.61 ±13.67	
			41.28±17.01			

Mean (±SD) cholesterol in cirrhotic ascites was 8.425±5.96 mg/dl, whereas in non-cirrhotic ascites 87.15±26.05 mg/dl (p<0.001). The result was consistent with the Bijoor AR et al. 2001, Gerbes AL et al. 1990 and Jungst D et al. 1986.[4,8,9] The optimal diagnostic efficiency of ascitic fluid cholesterol was obtained with a cutoff point of 29 mg/dl by using ROC curve. With this cutoff the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy was 100% to differentiate cirrhotic from non-cirrhotic (T.B/Malignancy) ascites.

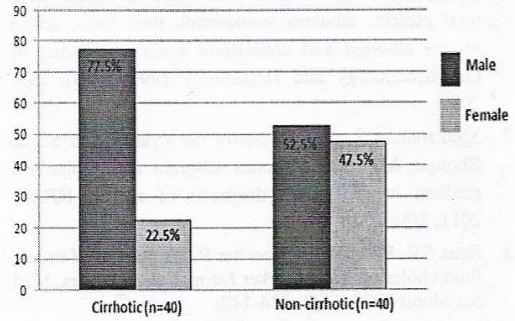

Figure 1: Bar chart showing sex distribution of study patients

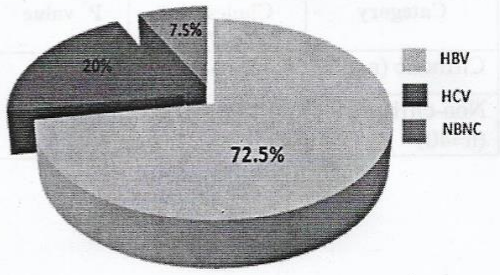

Figure 2: Pie chart showing aetiology of cirrhotic ascites

The result was consistent with the Castaldo G et al. 1994. But a variation in critical value was observed in different studies: Bijoor AR et al 2001 (45 mg/dl), Gupta R et al. 1995 (55 mg/dl), Garg R et al. 1993 (48 mg/dl).[8,10,11] These variations could be attributed to the selection of patients, presence of other co-existing disease that would alter serum cholesterol level. Mean (±SD) ascitic fluid cholesterol in malignant ascites was 83.62±26.32 mg/dl. The result was consistent with the Bijoor AR et al 2001, Gupta R et al. 1995, Garg R et al. 1993, Gerbes AL et al. 1990 and Jungst D et al. 1986.[4,9,10,11] But Vyakaranam S et al. 2011 and Rana SV et al. 2005 found much higher value of ascitic fluid cholesterol in malignant ascites (120.3±36.63 and 117.19±11.34 mg/dl respectively).[12,13] This may be related to the extent of peritoneal implants. In tubercular ascites the value of ascitic fluid cholesterol was 90.03±26.14 mg/dl. The result was consistent with the Gupta R et al. 1995, but not with the Vyakaranam S et al. 2011 who found much lower value (46.66±11.59 mg/dl) and this may be related to the extent of peritoneal involvement.[11,12] The difference of ascitic fluid cholesterol between the tubercular and malignant group was not statistically significant (p>0.05).

Table 2: Ascitic fluid cholesterol in study patients (n=80)

Category	Cholesterol (mg/dl)	P* value
Cirrhotic (n=40)	8.425±5.96	< 0.001
Non-cirrhotic (n=40)	87.15±26.05	

*Mann Whitney U test

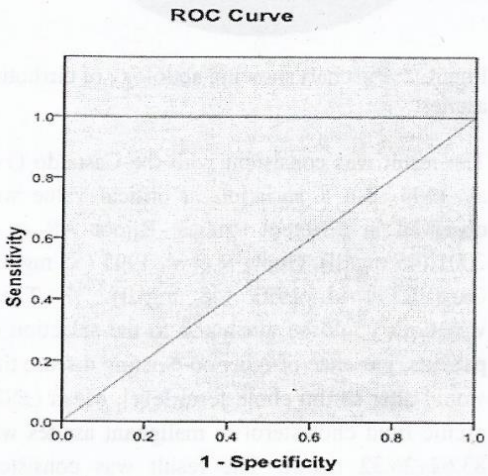

Figure 3: ROC curve for ascitic fluid cholesterol: AUROC (area under ROC curve) = 1

Conclusion

In view of the good diagnostic efficiency, easy availability and cost effectiveness, ascitic fluid cholesterol was an excellent parameter to differentiate cirrhotic ascites. But there were some limitations of this study such as: small sample size, most of the cirrhotic cases were male, patients with tuberculosis were younger than patients with malignancy/cirrhosis.

Bibliography

1. Runyon BA. Management of adult patient with ascites due to cirrhosis, an update: AASLD practice guideline. Hepatology 2004; 39(3): 841-853.
2. Pare P, Talbot J & Hoefs JC. Serum ascites albumin gradient- A physiological approach to differential diagnosis of ascites. Gastroenterology 1983; 85(2): 240-244.
3. Hoefs JC. Serum protein concentration and portal pressure determine the ascitic protein concentration in patient with chronic liver disease. J Lab Clin Med 1983; 102(2): 260-273.
4. Jungst D, Grebes AL, Martin R & Paumgartner G. Value of ascitic lipid in differentiation between cirrhotic and malignant ascites. Hepatology 1986; 6(2): 239-243.
5. Jungst D, Xie Y & Gerbes AL. Pathophysiology of elevated ascitic fluid cholesterol in malignant ascites. Journal of Hepatology 1992; 14(3): 244-248.
6. Alam S, Ahmad N, Mustafa G, Alam K & Khan M. Characteristics of treatment naive chronic hepatitis B in Bangladesh: Younger populations are more effected; E antigen negatives are more advanced. Saudi J Gastroenterol 2008; 14(1): 15-19.
7. Afroz S, Mahtab MA, Rahman S & Khan M. Hepatitis B virus is the leading cause of cirrhosis of liver in Bangladesh. Hepatol Int 2007; 1(1): 120.
8. Bijoor AR & Venkatesh T. Value of ascitic fluid cholesterol and serum ascitic albumin gradient in differentiating cirrhotic and malignancy related ascites. Indian Journal of Clinical Biochemistry 2001; 16(1): 106-09.
9. Gerbes AL, Xie YN, Mezger J & Jüngst D. Ascitic fluid concentration of fibronectin and cholesterol: comparison of differential diagnostic value with the conventional protein determination. Liver 1990; 10(3): 152-157.
10. Garg R, Sood A, Arora S, Bhatia KL, Chawla AS, Gupta R & Chawla LS. Ascitic fluid cholesterol in differential diagnosis of ascites. J Assoc Physicians India 1993; 41(10): 644-646.
11. Gupta R, Misra SP, Dwivedi M, Misra V, Kumar S & Gupta SC. Diagnosing ascites: value of ascitic fluid total protein, albumin, cholesterol, their ratio, serum ascites albumin and cholesterol gradient. Journal of Gastroenterology and Hepatology 1995; 10(3): 295-299.
12. Vyakaranam S, Nori S, Sastry G, Vyakaranam SB & Bhongir AV. Serum ascites albumin and cholesterol gradient in differential diagnosis of ascites. NJIRM 2011; 2(3):22-28.
13. Rana SV, Babu SV & Kocchar R. Usefulness of ascitic fluid cholesterol as a marker for malignant ascites. Med Sci Monit 2005; 11(3):136-142.

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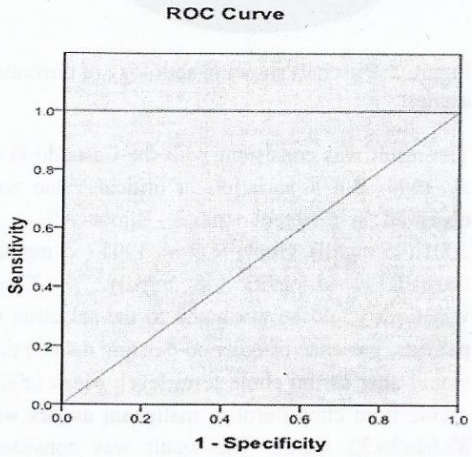

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Bibliography

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2. Pare P, Talbot J & Hoefs JC. Serum ascites albumin gradient- A physiological approach to differential diagnosis of ascites. Gastroenterology 1983; 85(2): 240-244.
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4. Jungst D, Grebes AL, Martin R & Paumgartner G. Value of ascitic lipid in differentiation between cirrhotic and malignant ascites. Hepatology 1986; 6(2): 239-243.
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7. Afroz S, Mahtab MA, Rahman S & Khan M. Hepatitis B virus is the leading cause of cirrhosis of liver in Bangladesh. Hepatol Int 2007; 1(1): 120.
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