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Utility of Biochemical Markers for Differential Diagnosis of Ascitic Fluid.

KEYWORDS: Cirrhosis, Ascitic fluid cholesterol, Tuberculous peritonitis, Malignant ascites.

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ABSTRACT *Ascites is the accumulation of free fluid in the peritoneal cavity. Differential diagnosis of ascites is a common clinical problem. Less expensive biochemical techniques are required to differentiate ascites with unknown etiology so we undertook this study to evaluate the diagnostic efficiency of ascitic fluid cholesterol, serum ascites albumin gradient (SAAG) and serum ascites cholesterol gradients (SACG) in differentiating non-tuberculous & non-malignant, tuberculous and malignant ascites and to confirm the results of previous studies. 100 patients (Group I 70 patients with hepatic cirrhosis and other non-tubercular and non neoplastic diseases, Group II 20 patients with tuberculosis and Group III 10 patients with malignancy) were evaluated for ascitic fluid total protein, albumin, cholesterol, SAAG and SACG. The mean value of SAAG was significantly higher in Gp. I patients when compared with Gp.II and Gp.III ascitlc patients. The mean ascitic fluid cholesterol was significantly higher in malignant ascites (Gp. III) when compared with Gp.I and Gp.II ascitlc patients. The mean SACG was significantly lower in malignant (Gp.III) compared to Gp.I and Gp.II ascitlc patients. SAAG is a better marker to differentiate cirrhotic ascites from tuberculous and malignant ascites. Ascitic fluid cholesterol and SACG are better markers to differentiate malignant ascites from cirrhotic and tuberculous ascites.*

INTRODUCTION

Ascites is the accumulation of free fluid in the peritoneal cavity[1].It is a common clinical complication of various diseases. The most important causes of ascites is cirrhosis (80%) followed by malignant peritonei (10%), tuberculous peritonitis (2%), congestive cardiac failure, nephrotic syndrome, others (3%)[2,3]. It is one of the most common amongst the various clinical problems confronting a physician, and ascitic fluid analysis is the most effective way to diagnose it[4].

The differential diagnosis of ascites is a common clinical problem and is important for further diagnostic and therapeutic procedures. Several components of ascitic fluid were tested for their differential diagnostic usefulness. Cytologic investigation of ascitic fluid is specific but may produce a large percentage of false-negative results; its sensitivity ranges between 40% and 70%[5,6].

A new physiologically based approach to classify ascites by albumin gradient between serum and ascitic fluid (SAAG) has completely replaced the traditional way of classification as transudate (ascitic fluid total protein ≤2.5gm %) and exudate (ascitic fluid total protein >2.5gm %). A high albumin gradient (≥1.1gm %) is usually associated with increased portal pressure as in cirrhosis and a low gradient (<1.1gm%), in conditions where ascites is not related to portal hypertension, but due to peritoneal chafe- as in malignant peritonei, tuberculous peritonitis, metastatic peritoneal implants etc . In patients with low albumin gradient the ability to differentiate malignant ascites from other etiologies is a major clinical problem[7].

Several studies have proved an elevated ascitic fluid cholesterol levels in patient with malignant Ascites [7]. Ascitic fluid cholesterol level have a diagnostic sensitivity of 89.65% & specificity of 100% . An enhanced movement of plasma lipoproteins into peritoneal cavity could cause the raised cholesterol levels. It has also been suggested that a minor fraction of cholesterol in malignant ascites might be derived from cell membranes and thus contribute to elevated ascitic fluid concentrations in malignant ascites[8]. Along with it, serum ascites cholesterol gradient (SACG) too aids in differential diagnosis of ascites[7]. Only a few studies have related the serum & ascitic fluid total protein, albumin, cholesterol & their gradients (SAAG, SACG) in differential diagnosis of ascites so we undertook this study to evaluate the diagnostic efficiency of ascitic fluid cholesterol, serum ascites albumin gradient (SAAG) and serum ascites cholesterol gradients (SACG) in differentiating non-tuberculous & non-malignant(cirrhotic), tuberculous and malignant ascites and to confirm the results of previous studies.

MATERIAL AND METHODS

This study was conducted in the Department of Pathology, Shyam Shah Medical College, Rewa during the period from May 2009 to October 2011. The study comprised of 100 patients with different causes of ascites admitted to wards of S.G.M.H. Rewa.

Cases were divided into 3 groups. Groups I consists of 70 patients with ascites due to chronic liver disease and other non-tubercular and non neoplastic diseases. The diagnosis was confirmed by history, abdominal ultrasound scan, altered liver function tests and ascitic fluid findings.

Group II consists of 20 patients with ascites due to tuberculosis, the patients were diagnosed on the basis of history, cytology showing lymphocytes & elevated ADA in ascitic fluid, chest X-ray, ultrasound scan of abdomen and Mantoux test.

Group III consists of 10 patients with ascites due to malignant diseases. The diagnosis was confirmed by positive ascitic fluid cytology or histopathological examination.

An informed consent was taken from all the cases. After detailed clinical history, a detailed clinical examination & a base line investigation were done on all the patients.

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With utmost aseptic precaution, Ascitic fluid and blood samples were taken for biochemical analysis. Estimation of total protein, albumin and cholesterol was done in ascitic fluid and serum. The A/G ratio in serum and ascitic fluid and SAAG were calculated.

The serum total protein was estimated by Biuret method[9] and serum albumin by Bromocresol green method[10]. The serum cholesterol was estimated by enzymatic, CHOD-POD end point assay[11]. The difference between the serum and ascitic fluid albumin concentrations in gm/dl is the serum ascitic albumin gradient (SAAG).

STATISTICAL ANALYSIS

The Statistical software SPSS 16.0 was used for the analysis of the data. Data was expressed as mean ± standard deviation. The data were analyzed by using student's unpaired t test and Pearson's correlation test. P-value of <0.05 was accepted as statistically significant.

RESULTS

Of the 70 patients in group I, 39 were males and 31 were females. Their age groups ranged from 25-60 yrs. In group II, which included 20 patients (age group ranged from 28-48 years) with tuberculous peritonitis, 14 were males and 6 were females and Group III included malignant ascites in which 6 were females and 4 were males, their age group ranged from 35-60yrs. The mean age were 44.38±11.73, 29.90±13.32 and 52.90±11.13 in all three groups respectively.

The results of serum and ascitic fluid analysis in all the three groups have shown in Table 1. The ascitic fluid total protein concentrations were low in gpI when compared to gpII and gpIII patients. The difference between gpI and other two groups was statistically significant.

Serum albumin levels were significantly low in gpI when compared with gpII & gpIII patients. The difference between gpII & gpIII patients was also significant.

Ascitic fluid albumin levels were significantly low in gpI when compared with gpII & gpIII patients.

The difference in the SAAG was significantly higher in gpI when compared with gpII & gpIII patients.

The ascitic fluid cholesterol was significantly elevated in gpIII patients when compared with gpI & gpII patients.

The gpIII patients had lowest SACG when compared with gpI & gpII patients.

DISCUSSION

The differential diagnosis of ascites remains a clinical problem. This study is undertaken to know the levels of different biochemical parameters and their diagnostic efficiency in the serum as well as in the ascitic fluid of 3 group patients.

Our study has reinforced the observations of earlier studies stating a limited value of transudate and exudate concept based on ascitic fluid total protein in differentiating cirrhotic from non-cirrhotic ascites and of no value in differentiating malignant and tuberculous ascites.[12,13,14].

SAAG was adopted as a newer and more physiological approach to classify ascites on the basis of presence or absence of portal hypertension[12,15,16] . Hoefs et.al [17] established a cutoff value of 1.1gm%, it was supported by our and various other studies. Ascites is one of the important sequels of portal hypertension; secondary to cirrhosis. SAAG ≥1.1gm% can differentiate cirrhotic from non-cirrhotic ascites. Similar results were observed in our study, with a critical value of ≥ 1.1gm% SAAG differentiated cirrhotic from non-cirrhotic ascites with a diagnostic accuracy of 95%. Presently SAAG is included in the guidelines of investigations recommended on the management of ascites in cirrhosis by American Association of the Study of Liver Disease (AASLD) and British Society of Gastroenterology[7].

A number of previous workers have shown the relation between high ascitic fluid cholesterol and the occurence of Malignancy related Ascites[1]. Another study by Sood et.al.[18] showed that ascitic fluid cholesterol can also be a good parameter to differentiate malignant and tuberculous ascites. The cut off value was taken as 48mg% [19].The possible reason for the occurrence of higher values of ascitic fluid cholesterol in MRA when compared to NMA may be due to lymphatic obstruction leading to rupture of lymphatic channel, causing increasing exudation of chyle with a relatively high lipid content[20]. In our study ascitic fluid cholesterol concentrations were significantly elevated in malignant ascites when compared to other two group.

Our study showed significantly lower levels of SACG in malignant ascites when compared to cirrhotic and tuberculous ascites. With a critical value of 53mg% SACG differentiated malignant ascites from cirrhotic and tuberculous ascites by a diagnostic accuracy of 93%. Unlike ascitic fluid cholesterol SACG could not differentiate cirrhotic from tuberculous ascites. Only few studies have mentioned the significance of SACG. Our study was consistent with the study done by Ranjith etal [21] and. R.Gupta etal[13].

CONCLUSION

In the present study SAAG differentiated Non-tuberculous and Non-malignant (cirrhotic) ascites from tuberculous and malignant ascites. In view of the good diagnostic efficiency, easy availability and cost-effectiveness, ascitic fluid cholesterol and SACG is an excellent parameter for the diagnosis of malignant ascites.

Table-1 Different biochemical parameters in serum and ascitic fluid

Parameters	Group I (gm%)	Group II (gm%)	Group III (gm%)	P value
Serum total protein (gm%)	5.7±0.63	5.9±0.37	6.01± 0.23	**Gp I Vs II:** >0.01 **Gp I Vs III:** >0.05 **Gp II Vs III:** >0.10
Ascitic fluid total protein (gm%)	1.6514±0.62	3.71±0.44	4.09±0.72	**Gp I Vs II:** <0.0005 **Gp I Vs III:** <0.0005 **Gp II Vs III:** >0.05

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Parameters	Group I (gm%)	Group II (gm%)	Group III (gm%)	P value
Serum albumin (gm%)	2.51±0.75	3.67±0.29	3.84±0.36	**Gp I Vs II:** 0.0001 **Gp I Vs III:** 0.001 **Gp II Vs III:** 0.01
Ascitic fluid albumin(gm%)	1.07±0.33	2.27±0.32	2.3±0.33	**Gp I Vs II**: 0.001, **Gp I Vs III**:0.0001, **Gp II Vs III:** >0.05
SAAG(gm%)	1.66±0.30	0.655±0.23	0.53±0.25	**Gp I Vs II:** <0.0005 **Gp I Vs III:** <0.0005 **Gp II Vs III:** >0.10
Serum Cholesterol(mg%)	166.86±20.73	161.0±17.74	168.86±20.12	**Gp I Vs II:** >0.05 **Gp I Vs III:** >0.05 **Gp II Vs III:** >0.10
Ascitic fluid Cholesterol(mg%)	32.95±7.10	30.05±9.30	74.1±16.17	**Gp I Vs II:** >0.05 **Gp I Vs III:** <0.0005 **Gp II Vs III:** <0.0005
SACG(mg%)	95.52±20.36	89.10±22.75	42.85±17.83	**Gp I Vs II:** >0.05 **Gp I Vs III:** 0.0001 **Gp II Vs III:** 0.001

REFERENCE 1. Bijoor A. R., and Venkatesh T. value of ascitic fluid cholesterol and serum - ascites albumin gradient in differentiating cirrhotic and malignancy related ascites. Indian Journal of Clinical Biochemistry, 2001; 16(1): 106-109. | 2. Runyon BA. Management of adult patients with ascites due to cirrhosis. AASLD Practice Guideline. Hepatology 2004; 39:1-16. | 3. Moore KP, Aithal GP. Guidelines on management of ascites in cirrhosis. Gut 2006; 55 (Suppl. VI):vi1-12. | 4. Rovelstad RA, Bartholomew LG, Cain JC et al. The value of examination of ascitic fluid and blood for lipids and for proteins by electrophoresis. Gastroenterology1958;34: 436-50. | 5. Garrison RN, Kaelin LD, Hauser LS, Galloway RH. Malignant ascites: Clinical and experimental observations. Ann Surg 1986;203: 644-651. | 6. Tomb J.A cytological study on serous fluid in cancer. JMed Liban, 1974;27: 51-58. | 7. Vyakaranam S., Nori S., Sastry M G., et al. Serum- Ascites Albumin and Cholesterol Gradients in Differential Diagnosis of Ascites, NJIRM 2011; 2(3) : 22-28. | 8. Ingle S.B. and Hinge C. utility of ascitic fluid cholesterol levels in malignant ascites. International Journal of Basic and Applied Medical Sciences 2012; Vol. 2 (3):79-82. | 9. Silverman LM, Christenson RH. Amino acids and proteins. Carl A.Burtis, Edward R. Ashwood. Tietz Textbook of Clinical Chemistry, 2nd edition. Philadelphia: Saunders 1993: p696-8. | 10. Doumas BT, Watson W, Biggs HG. Albumin standards and measurement of serum albumin with Bromocresol green Clin. Chem. Acta1971Jan; 31: 86-96. | 11. Carl A Burtis, Edward R, Ashwood, David E, Bruns. Lipid, Apo lipoproteins and other Cardiovascular Risk factors. In: Teitz textbook of clinical chemistry 4th edition. . Philadelphia: Saunders; 26; p 942-943. | 12. Prieto M, Gomez-Lechon MJ, Hoyos M, etal. Diagnosis of Malignant ascites. Comparison of ascitic fibrinonectin, cholesterol, and serum ascites albumin difference. Dig Dis Sci 1988; 33:833-838. | 13. Gupta R, Mishra SP, Dwivedi M,etal. Diagnosing ascites: Value of ascitic fluid total protein, albumin, cholesterol, their ratios, serum ascites albumin and cholesterol gradient. J Gasterol and Hepatol 1995; 10:295-9 | 14. Runyon BA, Montano AA, Akriviadis EA, etal. The serum-ascites albumin gradient is superior to exudates-transudate concept in differential diagnosis of ascites. Ann Intern Med 1992; 117:215-20. | 15. Rector WG, Reynolds TB. Superiority of serum ascites albumin difference over the ascites total protein concentration in separation of transudative and exudative ascites. Am J Med.1984; 77:83-5. | 16. Rector WG. An improved diagnostic approach to ascites. Arch Intern Med 1987; 147: 215. | 17. Hoefs JC. Serum protein concentration and portal pressure determine the ascitic fluid protein concentration in patients with chronic liver disease. J Lab Clin Med 1983; 102:260–73. | 18. Sood, A., Garg, R., Kumar, R., Chinna, R.S., Arora, S., Gupta, R. and Bhatia, K. L., Ascitc fluid cholesterol in malignant and tubercular ascites. J. Assoc. Physicians India 1985;43 (11): 745-747. | 19. Jungst, D.Gerbe, J.D., Alexander, A.L, Robert, Martin, R. Gustav, and G. Paimgartner. Value of ascitic lipids in differentiation between cirrhotic and malignant ascites. Hepatology 1986 ; 6: 239-243. | 20. Runyon B.A., Hoers J.C. and Morgan T.R. Ascitic fluid analysis in malignancy related ascites. Hematology1998; 8, 1104-1109. | 21. Ranjith D, Ranjith MP, Debesh dutta etal. Ascitic fluid lipid profile and albumin level. Bangladesh medical research council Bulletin 2010; 1(36):34-6. |