Research Article

Clinical profile and comparison of SAAG with ascites fluid total protein (AFTP) in cases of ascites at a tertiary referral hospital in Maharashtra

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Abstract

Aims: This observational prospective study was carried out with aims of 1) study various presentations and clinical features in ascites cases, 2) assess different etiological factors, 3) compare serum ascitic albumin gradient **(SAAG)** and ascitic fluid total protein **(AFTP)** in differentiating portal hypertension related causes of ascites from others, 4) study in hospital outcome in cases of ascites**. Material and Methods**: 100 consecutive ascites cases admitted in wards with clinical diagnosis and sonographic confirmation were recruited in the study. After history and detailed clinical examination cases were subjected to ultrasonography and portal vein Doppler to diagnose portal hypertension which was followed by paracentesis. Serum Albumin & total protein, ascitic fluid albumin and total protein, AFTP and SAAG was determined. **Results**: Mean age of diagnosis of ascites was 42.41 ±7.72 years and maximum cases in 30-49 years age group. 68% of cases of ascites had cirrhosis of liver, 16% peritoneal (abdominal) tuberculosis, 10% chronic heart failure (CHF), 4% nephrotic syndrome and 2% had ovarian malignancy. Mean AFTP and Mean SAAG was 1.77±0.73gm% and 2.05±0.52 gm% in 78 cases of portal hypertension related ascites respectively. In normal portal pressure cases (n=22) of ascites it was 3.01±0.37 gm% and 0.72±0.19 gm% respectively. Sensitivity of AFTP and SAAG in differentiating portal hypertension related etiology from other causes was 70.51% and 92.31% respectively .Though sensitivity was less, specificity was equal (95.45%). Eight cases had variceal bleeding, 9 had hepatorenal syndrome and 15 had hepatic encephalopathy. Total 16 cases of liver cirrhosis with ascites died in hospital commonest cause was hepatic encephalopathy and hepatorenal syndrome.

Keywords: Serum ascitic albumin gradient, Ascites, Cirrhosis, Portal hypertension

Introduction

Ascites means the accumulation of fluid in the abdomen was a known physical entity with established therapy by means of paracentesis since 2000 B.C. Ascites may arise in number of clinical settings in addition to cirrhosis and portal hypertension. Although historically ascites was classified as transudative and exudative, similar to ~~the characterization~~ that of pleural fluid, this scheme has limitations. Instead the Serum Ascites Albumin Gradient (SAAG) provides a better classification than total protein content or other parameters [1]. In cirrhosis the serum albumin concentration is usually at least 1gm/dl higher than that of ascetic fluid thus yielding high SERUM-ASCITIC albumin gradient, reflecting the high hydrostatic pressure gradient between portal bed and ascites compartment. Conversely the presence of a low SERUM-ASCITIC albumin gradient (<1.1gm/dl) usually excludes cirrhosis and portal hypertension [2]. Classification of ascites on the basis of high (>1.1gm/dl) SAAG includes cirrhosis, alcoholic hepatitis, cardiac failure, hepatic metastasis, Budd-Chiari syndrome, portal vein thrombosis, fatty liver of pregnancy, etc. Low (<1.1 gm/dl) SAAG is found in peritoneal Tuberculosis, peritoneal carcinomatosis, pancreatic

Manuscript received: 14th Feb 2016
Reviewed: 24th Feb 2016
Author Corrected: 8th March 2016
Accepted for Publication: 18th March 2016

ascites, nephrotic syndrome, serositis, biliary ascites etc [3].

SAAG obtained by subtracting ascetic fluid albumin concentration from serum albumin has been shown to correlate with hepatic sinusoidal pressure. SAAG more than 1.1gm/dl indicate that there is sinusoidal hypertension and hepatic sinusoid as source of ascites. Ascitic Fluid Total Protein (AFTP) and Serum Ascitic Albumin Gradient (SAAG) are two inexpensive tests that taken together are most useful in determining the source of ascites. Hence this study was done at a tertiary teaching hospital in cases of ascites to find etiology and evaluate the significance of ascitic fluid albumin and protein analysis [4,5].

Aims

1) study various clinical presentations in cases of ascites, 2) assess different etiological factors in cases of ascites, 3) compare serum ascitic albumin gradient **(SAAG)** and ascitic fluid total protein **(AFTP)** in differentiating portal hypertension related causes from othes, 4) study in hospital outcome in different cases of ascites.

Material and methods

This hospital based observational study was done in indoor cases of ascites from November 2011 to October 2013 (duration 2 years) at tertiary care medical college in Maharashtra. Study was started after approval from Institutional Ethics committee.

Inclusion Criteria:-

1) Clinical diagnosis of ascites and ultrasonographic confirmation
2) More than 12 years of age
3) Giving informed consent to participate and undergo paracentesis.

Pediatric cases age less than 12 years and cases not willing to participate were excluded.

Study Protocol:-Consecutive cases of Ascites admitted in different Medicine wards were enrolled in the study. Cases satisfying above inclusion and exclusion criteria were recruited in the study. Detailed history was obtained followed by thorough general and systemic examination.

Cases were subjected to detailed abdominal ultrasonographic evaluation, Chest X-Ray and CT abdomen was done when required.

Doppler examination was done 1) portal vein size >13 mm, 2) less than 20% increase in portal vein diameter during full inspiration, 3) congestive index >0.1 [ratio of portal vein cross sectional area cm sq. to mean portal vein flow velocity (cm/sec) normal being 0.07], 4) reversal of portal venous flow and 5) porto-systemic collaterals was suggestive of portal hypertension.

Diagnostic paracentesis was done with prior written consent using 20-22 gauge 2.5 inch disposable needle using sterile precautions. 20 to 50 ml fluid was aspirated and fluid was immediately sent for biochemical analysis Albumin, total protein, Adenosin deaminase (ADA), triglycerides. Fluid was also subjected for microscopy for total and differential leucocyte count, cytological examination, Gm stain and AFB staining. CBC, LFT (includes serum albumin), KFT, HBsAg was also done.

Ascitic Fluid Total Protein **(AFTP)** was calculated by two point method using Colorimeter.
Serum Ascitic Albumin Gradient **(SAAG)=** serum albumin(gm/dl)-ascitic fluid albumin (gm/dl)
SAAG more than 1.1 suggest ascites related to portal hypertension. SAAG less than 1.1 suggest ascites unrelated to portal hypertension.

Results

Total 100 consecutive patients of ascites admitted in medicine wards of our hospital were enrolled in the study irrespective of etiology. Study was carried over period of 2 years (2011-2013). Results were statistically analyzed using Epi-info computer software. P value <0.05 was considered significant.

74% were male and 26% were female with male :female ratio 2.84. Mean age was 42.41 ±7.72 years and maximum cases was in 30-49 years age group. Abdominal distension (100%), dyspnea (58%) abdominal pain (35%), 15 cases had altered consciousness (encephalopathy), 8 cases presented with hematemesis. Icterus was present in 30 cases and edema feet in 38. Fever was present in 10 (16%) of cirrhotic with ascites without SBP and in 4(66.67%) with SBP. Splenomegaly was present in total 42 cases of ascites and hepatomegaly in 6 out of 10 cases of chronic heart failure. 68% of cases of ascites

had cirrhosis of liver, 16% peritoneal tuberculosis,10% chronic heart failure(CHF), 4% nephrotic syndrome and 2% had ovarian malignancy.

Biochemical profile in cases of ascites:- A) Blood urea and Serum creatinine was raised (>1.5mg%) in 13%(9) cases of ascites with cirrhosis. B) AST(>40IU/L) and ALT (>35 IU/L) was found in 18 and 16 cases respectively out of 68 cases of cirrhosis with ascites. C) Total bilirubin was (>1mg%) in 31 cases. D) Serum total protein was decrease (<6gm%) in 58 cirrhotic, 10 with peritoneal tuberculosis , 5 with chronic heart failure, all 4 cases of nephrotic syndrome and 2 cases of malignancy. E) 2 cases were HBSAg positive. d) Serum Albumin was decreased (<3.5gm%) in 66 cirrhotics, 9 of CHF, 7 of peritoneal tuberculosis, all 4 cases of nephritic syndrome and 2 of malignancy.

Table 1: Microscopic examination of Ascitic fluid with different etiologies

	Cirrhosis without SBP (n=62)	Cirrhosis with SBP (n=6)	Peritoneal tuberculosis (n=16)	Chronic heart failure (n=10)	Nephrotic syndrome (n=4)	Malignancy (n=2)
Mean TLC/mm^3	21.7±8.6	2184±775	419±92	18.9±7.5	20.5±7.9	122±8.4
Neutrophils %	78.7±10	71.5±8.6	15.2±6	79.6±9.7	78.2±14	59±4.2
Lymphocytes%	21.2±10	27.6±10	84.75±6	20.4±9	21.7±14	41±4.2

(TLC—Total leucocyte count)

Mean TLC count was increased in cases of Cirrhosis with Ascites with SBP. Mean neutrophils % was 78.7±10 and Mean lymphocytes % was 21.2±10 in cases of Cirrhosis with Ascites without SBP Mean TLC count was also increased in cases of peritoneal tuberculosis with lymphocytic count of 84.75%. In cases of malignant ascites the mean TLC was 122±8.4 per cu mm.

Table 2: AFTP and SAAG according to different etiologies of Ascites.

	Cirrhosis without SBP (n=62)	Cirrhosis with SBP (n=6)	Peritoneal tuberculosis (n=16)	Chronic heart failure (n=10)	Nephrotic syndrome (n=4)	Malignancy (n=2)
Mean AFTP (gm/dl)	1.87±0.7	0.93±0.1	3.15±0.33	1.64±0.66	2.6±0.14	2.7±0.14
SAAG (gm/dl)	2.12±0.5	1.37±0.1	0.67±0.15	2±0.4	0.88±0.31	0.8±0.14

(AFTP—Ascitic Fluid Total Protein, SAAG—Serum Ascitic Albumin Gradient, SBP—Spontaneous Bacterial Peritonitis)

AFTP <2.5 gm/dl was found in Cirrhosis and congestive cardiac failure. AFTP >2.5 gm/dl was found in Peritoneal TB, Nephrotic syndrome and malignancy.

SAAG ≥ 1.1 was found in Cirrhosis and congestive cardiac failure. SAAG <1.1 was found in Peritoneal TB, Nephrotic syndrome and malignancy.

Table 3: Comparison of mean SAAG with mean AFTP in portal hypertension related etiology from others normal portal pressure cases of Ascites.

	Portal hypertension present (n=78)	Normal portal pressure (n=22)	P value
Mean AFTP (gm/dl)	1.77±0.73	3±0.37	<0.001
Mean SAAG (gm/dl)	2.05±0.5	0.72±0.19	<0.001

78 cases of ascites (68 cases of cirrhosis of liver and 10 of chronic heart failure) were included on basis of Ultrasonographic findings having portal hypertension related etiology and 22 remaining cases of ascites (peritoneal tuberculosis ,nephrotic syndrome, malignancy) were without portal hypertension(normal portal pressure).

Mean **AFTP** in portal hypertension related etiology was **1.77±0.73** gm/dl and **3±0.37** gm/dl in normal portal pressure related Ascites, this difference was statistically highly significant (p<0.001).

Mean **SAAG** portal hypertension related etiology was **2.05±0.5** gm/dl and in normal portal pressure related it was **0.72±0.19** gm/dl ,this difference was statistically highly significant (p<0.001).

Table 4: Comparison of Sensitivity and specificity by SAAG and AFTP in differentiating ascites related with portal hypertension from other etiology

	Portal hypertension present(n=78)	**Normal portal pressure (n=22)**
AFTP<2.5 gm/dl	55	1
AFTP>2.5gm/dl	23	21
sensitivity	70.51%	
specificity	95.45%	
	Portal hypertension present (n=78)	Normal portal pressure (n=22)
SAAG≥1.1	72	1
SAAG<1.1	6	21
sensitivity	92.31%	
specificity	95.45%	

Sensitivity of 92.31% by SAAG in differentiating etiology of ascites related to portal hypertension was higher than sensitivity of 70.51% by AFTP. But specificity was similar in both 95.45%.

Table 5: Complications in cases of cirrhosis of liver

Complications in cases of Ascites	**Liver cirrhosis without SBP (n=62)**	**Liver cirrhosis with SBP (n=6)**	**P value**
1) Variceal bleeding	6 (9.6%)	2(33.3%)	0.09
2) Hepatorenal syndrome	7(11.2%)	2(33.3%)	0.13
3)Hepatic encephalopathy	12(19.35%)	3(50%)	0.08
4) Deaths	12(19.35%)	4(66.67%)	0.01

Eight cases had variceal bleeding, 9 had hepatorenal syndrome and 15 had hepatic encephalopathy. Total 16 cases of liver cirrhosis with ascites died. 12 were without SBP and 4 (66.67%) were with SBP. This difference in death was statistically significant P< 0.05.

Hospital outcome in cases of ascites- 16(23.5%) out of 68 cases of liver cirrhosis died and 52 were discharged from hospital after treatment. In most of these cases the cause of death was hepatic encephalopathy (15) and hepatorenal syndrome (9). No in hospital death was observed in cases of peritoneal tuberculosis, chronic heart failure, Nephrotic syndrome. Malignancy cases were discharged and referred to cancer hospital.

Discussion

1) The mean age of diagnosis of ascites was 42.4±7.7 years which was found 8-10 years earlier than studies of Khan FY (2007) 52.9±14.8 years [6] and Hafiz Aslam (2012) 50.7±15.8 years [7].

2) Mean age of occurrence of ascites due to peritoneal tuberculosis was 37.1±5.7 years. In Chow KM (2002) it was 55±18 years [8] and F M Sanai (2005) 35 to 45 years which was comparable with present studies [9].

3) **Comparison of various etiologies of ascites in different studies.**

Studies on Ascites	Year of study	Total cases (n)	Etiology (%)				
			Liver cirrhosis	Peritoneal tuberculosis	CHF	Nephrotic syndrome	Malignancy related ascites
Khan F Y et al[**6]**	2007	104	59.6	7.8	6.7	2.9	20
Adhikari P et al[**10]**	2012	43	48.83	11.62	4.62	-	-
Beg M et al[**11]**	2001	100	60	24	10	--	6
Present study	2013	100	68	16	10	4	2

In present study maximum cases of ascites were of liver cirrhosis, followed by peritoneal tuberculosis cases. The results were comparable with other studies. Only 2 cases of malignancy related ascites were found in our study because many cases with abdominal symptoms or lump were directed to surgery department.

4) **Comparison of SAAG and AFTP with different etiologies for ascites.**

Etiologies of Ascites	Mean ascitic fluid total protein (AFTP) (gm/dl)		Mean serum ascitic albumin gradient (SAAG) (gm/dl)	
	Khan F Y et al (2007) [6]	Present study (2013)	Khan F Y et al (2007) [6]	Present study (2013)
Liver cirrhosis without SBP	1.6± 1.44	1.87 ±0.73	2.9± 2.25	2.12± 0.51
Liver cirrhosis with SBP	2.1± 2.16	0.93± 0.11	1.60± 0.17	1.37± 0.16
Peritoneal tuberculosis	2.76± 0.40	3.15 ±0.33	0.56± 0.32	0.67± 0.15
Chronic heart failure	1.2± 3.22	1.64± 0.66	2.8± 2.25	2.03± 0.42
Nephrotic syndrome	2.5± 0.65	2.6± 0.14	0.7± 0.23	0.88 ±0.31
Malignancy related	2.5± 0.65	2.7± 0.14	0.90± 0.75	0.8± 0.14

The findings were comparable with Khan et al study (2007).Both AFTP and SAAG values were comparable. The mean AFTP in SBP cases was low as compared with Khan et al. But in another study by Ali Saqib et al in 2011 on cases of cirrhotic ascites[12], the mean ascitic fluid protein concentration in SBP patients was low (0.86 gm/dl) as compared to mean ascitic fluid total protein concentration in non SBP patients (1.7 gm/dl), $p < 0.001$.

In present study ascitic fluid total protein concentration in liver cirrhosis with SBP cases was 0.93± 0.11gm/dl and without SBP cases was 1.87±0.73 gm/dl, ($p < 0.001$).

5) **Comparison of sensitivity of SAAG and AFTP in differentiating ascites related to portal hypertension with other studies**

Study	Year of study	Total cases (n)	Sensitivity of SAAG	Sensitivity of AFTP
Beg M et al **[11]**	2001	100	94.73%	65.62%
U. H. Malabu et al **[13]**	2006	90	96%	73%
Khan F Y et al **[6]**	2007	104	98.02%	83.54%
Present study	2013	100	92.31%	**70.51%**

Sensitivity was less than SAAG method and comparable with other studies. But specificity was 95.45% and equal to SAAG.

6) Mean ADA levels in cases of tubercular ascites was 59.5±10.02 U/L and comparable to the findings of Black J (1982) [14] and Agrawal S (2011) studies.[15]

7) In the present study the mean TLC count and lymphocyte % was 419 ± 92.88 cells/cumm and 84.75 ±6.05% respectively which is comparable to 680.46±348.69 and 77.9±23.10% in Agrawal et al (2011).[15]

8) In cases of liver cirrhosis with ascites the mortality was 23.52% . The mortality was 13.3% and 43.78% in R Maskey et al [16] and S K Sarin et al [17] respectively.

Conclusions

1. The mean of serum-ascites albumin gradient (SAAG) in portal hypertension related etiology (2.05±0.52 gm/dl) was significantly (<0.001) higher than in normal portal pressure etiology (0.72±0.19 gm/dl). Hence, SAAG was useful in classifying ascites due to non portal and portal hypertension etiology.
2. The mean of ascitic fluid total protein (AFTP) in portal hypertension related etiology (1.77±0.73 gm/dl) was significantly ($p < 0.001$) lower than in normal portal pressure etiology (3.01±0.37 gm/dl). Hence, AFTP was also useful and equally specific in classifying ascites due to non portal and portal hypertension etiology.
3. Serum-ascites albumin gradient (SAAG > 1.1gm/dl) had sensitivity of 92.31%, and ascitic fluid total protein (AFTP < 2.5gm/dl) had sensitivity of 70.51% in diagnosis of etiology due to portal hypertension. Hence the sensitivity of SAAG was higher than ascites fluid total protein AFTP in diagnosis of ascites due to portal hypertension from other etiology.

Funding: Nil,
Conflict of interest: None.
Permission of IRB: Yes

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How to cite this article?

Nakhale BD, Dube AH, Bhagat JP, Ingole R, Patil M, Clinical profile and comparison of SAAG with ascites fluid total protein (AFTP) in cases of ascites at a tertiary referral hospital in Maharashtra : *Int J Med Res Rev* 2016;4(4):512-518. doi: 10.17511/ijmrr.2016.i04.07.

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