



**ORIGINAL RESEARCH PAPER**

**Paediatrics**

**STUDY OF THE COMPARATIVE UTILITY OF THE SERUM ASCITES ALBUMIN GRADIENT (SAAG) AND THE ASCITIC FLUID TOTAL PROTEIN IN THE DIFFERENTIAL DIAGNOSIS OF ASCITES**

**KEY WORDS:** Ascites , Portal Hypertension , SAAG , AFTP

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**ABSTRACT**

**Background** –The ascitic fluid total protein , cell counts , lactate dehydrogenase activity (LDH) , ascites - to - serum protein and LDH ratios have traditionally been used to classify ascites . However , none of these parameters have been found to be completely discriminating .

**Objective** – In this study we compared the utility of the serum ascitic fluid albumin gradient and ascitic fluid total protein levels in establishing the differential diagnosis of ascites .

**Methodology** - 60 children between the ages of 1- 15 years were included in the study . Paired Serum and Ascitic fluid samples were taken simultaneously .

**Results** – The SAAG had greater Positive and Negative Predictive values as compared to that of AFTP . The 'p' value for SAAG (> 1.1gm %) in detecting portal hypertension was < 0.001 which was highly significant as against that of AFTP , 'p' value < 0.02 .

**Conclusion** – Serum Ascitic fluid Albumin gradient (SAAG) is a better indicator of portal hypertension than the Ascitic fluid Total Protein (AFTP) .

**INTRODUCTION**

Ascites denotes the pathological accumulation of fluid in the peritoneal cavity . It is derived from a Greek word askites meaning bag-like .

Ascites is a manifestation of various systemic as well as local diseases . More than 90% of all cases of ascites are due to portal hypertension usually a consequence of cirrhosis of the liver , half of the remainder i.e. 5% of all cases of ascites are due to peritoneal diseases .

The diagnosis of Ascites is made on the basis of the History and Physical examination - the 4 classical physical signs : a protuberant abdomen / bulging flanks , shifting dullness , fluid thrill and the puddle sign .

According to the Starling's hypothesis , the fluid movement across a capillary membrane is governed by the balance between the hydrostatic and the colloidal osmotic pressures across the membrane . Transudative ascites is the result of increased hydrostatic pressure ( portal venous pressure ) , decreased serum oncotic pressure or both . Exudative ascites results from an alteration in the membrane permeability due to inflammation of the peritoneal membrane or malignancy .

The major difference in their composition is the level of the ascitic fluid total protein . A cut off value of 2.5 gm/dl is widely used where the total protein in transudate is below this limit and exudate is > 2.5 gm/dl .

This however is not completely discriminating . The drawbacks led to the development of a new approach to classify ascites based on the albumin gradient between plasma and ascites . In the presence of portal hypertension the oncotic pressure gradient between the plasma and the ascitic fluid has to be raised to counterbalance the high hydrostatic pressure driving the fluid into the intraperitoneal cavity . Albumin being the single most important factor in oncotic pressure generation , the difference between the serum and ascitic fluid albumin concentration or the serum ascites albumin gradient (SAAG) has been proposed as a biochemical parameter in the differential diagnoses of ascites 1,2 .

SAAG = [Albumin concentration of Serum] - [Albumin concentration of Ascitic fluid] a parameter

reflecting the oncotic pressure gradient between the vascular bed and the interstitial or ascitic fluid ; the two values being measured simultaneously 3 .

The difference between the serum and ascites albumin concentration ( albumin gradient / SAAG ) is thought to directly reflect the colloid osmotic pressure gradient and indirectly , the degree of portal hypertension 4 .

**AIMS & OBJECTIVES :**

1. To compare the utility of the serum ascitic fluid albumin gradient and ascitic fluid total protein levels in establishing the differential diagnosis of ascites .

2. To evaluate the reliability of SAAG for the differential diagnosis of ascites .

**MATERIALS AND METHODS**

The study was conducted in the Department of Paediatrics of Patna Medical College , Patna .

**MATERIALS**

Total 60 patients of ascites were selected amongst the inpatients and the diagnosis was made on the basis of the History and the Clinical features of the patient .

**INCLUSION CRITERIA :**

1. Patients admitted to indoor wards in Pediatrics department with clinical signs and symptoms of ascites .

2. Those detected incidentally by clinical examination or by ultrasonography

3. Developed ascites during the course of treatment for another disease in ward .

**EXCLUSION CRITERIA :**

1. Patients who had received Diuretic therapy within 3 months prior to admission .

2. Patients who had undergone therapeutic paracentesis within 3 months prior to admission .

**METHODS**

A thorough Clinical examination and relevant history was taken . Ascites was confirmed by diagnostic paracentesis / ultrasonography . Ascitic fluid and serum samples were taken simultaneously 5,6 . Other necessary investigations were done

as follows :

**INVESTIGATIONS**

**A. Routine**

- Complete Hemogram (Hemoglobin, TLC, DLC) and ESR
- Blood Urea and Serum Creatinine, Serum Electrolytes
- Liver Function Tests : Serum Bilirubin (Total, Direct and Indirect fractions), SGPT, SGOT, Alkaline Phosphatase, Serum Total Protein, Albumin, Globulin, A/G Ratio including Prothrombin Time.
- Viral Markers : Hepatitis B Surface Antigen (HBsAg), IgM and IgG anti-HAV, anti-HEV, anti-HCV
- Serum Amylase
- Complete Urinalysis including quantitative estimation of urinary albumin
- Chest X-Ray P.A. view

**B. Abdominal Paracentesis and Analysis of Ascitic fluid 7,8 Position -** The child was placed supine after emptying his/her bladder.

**Site -** Lateral to the Rectus sheath midway between the anterior superior iliac spine and the umbilicus.

**Procedure -** After proper aseptic precautions a 20 G needle attached to a 20 ml syringe was inserted at the proposed site using the Z-technique. About 20 ml fluid was aspirated.

The collected sample was analysed as follows :

- Physical examination : colour, consistency
- Chemical examination : Ascitic fluid total Protein and Albumin, glucose and LDH.
- Cytological examination : Total cell count including differential count and Red blood cell counts
- Bacteriological examination : Gram's Stain and bacterial culture, Ziehl Nielson staining for AFB and culture for Mycobacterium tuberculosis.

The Serum Ascites Albumin Gradient and the Ascitic fluid Total Protein were determined for each patient.

**C. Special Investigations**

- Ultrasonography whole Abdomen and Pelvis
- Stool for Occult blood
- Electrocardiography with standard 12-lead ECG
- Liver Biopsy in cases of cirrhosis of the liver and malignancy
- Barium meal X-Ray
- Upper G.I. Endoscopy .
- Peritoneal Biopsy .

The presence of portal hypertension was suggested by the following :

- History of upper gastrointestinal bleeding as hematemesis, malaena and Jaundice with ascites.
- Clinical features of Splenomegaly and other evidence of portosystemic anatomic shunts (caput medusae, haemorrhoids)

- Ultrasonographic evidence of liver cirrhosis : splenomegaly, ascites, dilated portal vein or splenic vein, coarse echotexture of the liver, venous collaterals, and enlarged left lobe or caudate lobe of the liver.

- Supporting evidences : esophageal varices on upper GI endoscopy and esophageal / fundic varices on barium swallow.

- Confirmation of diagnosis by Liver Biopsy.

Patients were grouped into two major categories - Portal hypertension group of ascites and non-portal hypertension group based on the presence or absence of portal hypertension respectively. This classification was adopted from the study conducted by Hurtado et al, 19919. These major divisions were calculated for each group and the differences analysed for validity and statistical significance using the Chi-Square (X<sup>2</sup>) test.

The sensitivity of SAAG was compared with that of ascitic fluid total protein levels in detecting portal hypertension. Sensitivity, specificity, positive and negative predictive values and percentages of false positives and false negatives were calculated for the above parameters and compared. Meaningful interpretations have been depicted using bar diagrams and pie-charts

**RESULTS AND DISCUSSION**

The Present work "Study of the Comparative Utility of the Serum Ascitic Fluid Albumin Gradient (SAAG) & Ascitic Fluid Total Protein in the Differential Diagnosis of Ascites" was carried out on 60 children.

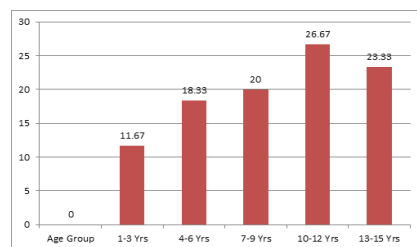
**Table 1 DISTRIBUTION OF THE STUDY POPULATION IN DIFFERENT AGE GROUPS**

Age group	Number of Subjects	Percentage
1 - 3	7	11.67
4 - 6	11	18.33
7 - 9	12	20
10 -12	16	26.67
13 - 15	14	23.33
Total	60	100

The above table shows the distribution of the population in different age groups. Cases were between 1 to 15 years of age .

The maximum incidence was in the age group 10 - 12 years (26.67 %) followed by 13 - 15 years (23.33%) and then in the 7 - 9 age group (20%). Incidence was lowest in the age group 1 - 3 years (11.67 %) and 4 - 6 years (18.33 %).

**DISTRIBUTION OF THE STUDY POPULATION IN DIFFERENT AGE GROUPS**

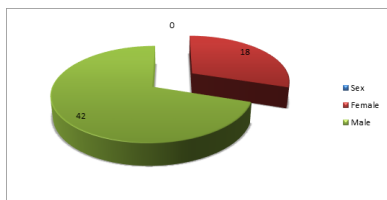


**Table -II DISTRIBUTION OF THE STUDY POPULATION ACCORDING TO GENDER**

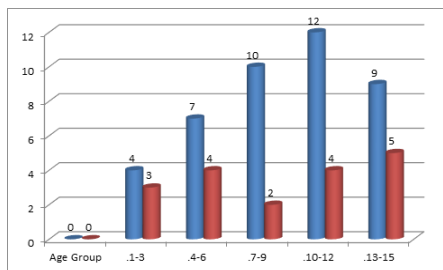
Sex	Number of Subjects	Percentage
Females	18	30
Males	42	70
Total	60	100

Among the 60 subjects 42 (70%) were males and 18 (30%) were females suggesting preponderance of males over females.

Pie-chart Showing distribution of the study population according to gender



**Comparative Bar Diagram Showing Distribution of Age & Sex of the Groups Under study**

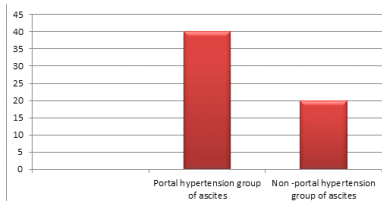


**Table-III DISTRIBUTION OF PORTAL HYPERTENSION AND NON-PORTAL HYPERTENSION GROUP OF ASCITES (n =60)**

Sl no.	Group	No. of Patients (%)
1.	Portal hypertension group of ascites	40 (66.67%)
2.	Non-portal hypertension group of ascites	20 (33.33%)

Out of 60 patients 40(66.67%) were portal hypertension group of ascites and 20 (33.33%) were non-portal hypertension group of ascites, based on the presence or absence of portal hypertension. (n = total number of cases)

**Bar Diagram Showing Relative Distribution of Portal Hypertension & Non- Portal Hypertension**

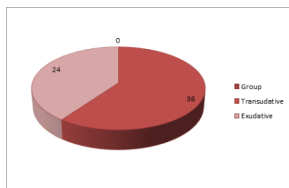


**Table IV DISTRIBUTION OF EXUDATIVE AND TRANSUDATIVE ASCITES**

Sl no.	Group	No. of patients
1.	Transudative	36 (60%)
2.	Exudative	24 (40%)
	Total	60

Out of 60 patients 36(60%) had transudative ascites, whereas 24(40%) had exudative ascites.

PIE Chart Showing Proportion of Exudative Vs Transudative of Ascites



**Table V DISTRIBUTION OF VARIOUS AETIOLOGIES IN PORTAL HYPERTENSION GROUP OF ASCITES**

Sl no.	Aetiology	No. of patients (%)
1.	Cirrhosis (uncomplicated)	36 (90%)
a.	Cryptogenic	15
b.	Viral hepatitis	11
	Hepatitis B	10
	Hepatitis C	1
c.	Idiopathic Hepatitis	6
d.	Wilson's Disease	2
e.	Inborn errors of metabolism (IEMs)	2
2.	Constrictive Pericarditis	3 (7.5%)
3.	Budd - Chiari Syndrome	1 (2.5%)
	TOTAL	40

Out of 40 patients of Portal hypertension group of ascites, 36 patients(90%) had Cirrhosis of the liver whereas rest of the cases were due to post-hepatic causes i.e. Constrictive Pericarditis and Budd - Chiari Syndrome constituting 7.5 % and 2.5 % of cases respectively.

In our study Cirrhosis was of cryptogenic aetiology in 37.5% of the cases. Viral hepatitis constituted 27.5% of the cases of cirrhosis with 25% of the cases due to Hepatitis B and Hepatitis C found only in 2.5% of the cases. 15% of the cases were of Idiopathic Hepatitis with Wilson's disease and IEMs being 5% each.

**Table-VI DISTRIBUTION OF VARIOUS AETIOLOGIES IN NON - PORTAL HYPERTENSION GROUP OF ASCITES**

Sl no.	Aetiology	No. of Patients(%)
1.	Nephrotic Syndrome	10 (50%)
2.	PEM with Hypoproteinemia	5 (25%)
3.	Tuberculous Ascites	4 (20%)
4.	Protein Losing Enteropathy	1(5%)
	TOTAL	20

Out of a total of 20 cases in this group 10 cases (50%) were of Nephrotic Syndrome and 5 cases(25%) were attributed to ascites due to Protein Energy Malnutrition leading to hypoproteinemia. 4 cases (20%) were of Tuberculous Ascites while one case(5%) was diagnosed as Protein Losing Enteropathy.

**Table-VII SERUM AND ASCITIC FLUID PROTEIN LEVELS IN DIFFERENT ETIOLOGIES OF PORTAL HYPERTENSION GROUP OF ASCITES**

Sl no.	Aetiology	No. of Patients	Serum Protein (gm% )	Ascitic Fluid Protein (gm%)
1.	Cirrhosis	36	5.8(5 - 7.5)	1.7(0.8 - 2)
a.	cryptogenic	15	6.2(5.4 - 7)	1.5(0.6 -2.4)
b.	Viral hepatitis	11	5.6(5.1-6.1)	2.2(1.6-2.8)
	Hepatitis B	10		
	Hepatitis C	1		
c.	Idiopathic Hepatitis	6	5.8(5.2- 6.5)	1.7(1.2-2.2)
d.	Wilson's	2	4.8(4 - 5.5)	1.6(1.2 -2)
e.	IEMs	2	5.2(4.4 - 6)	2 (1.5-2.5)
2.	Constrictive Pericarditis	3	7.6(6.6-8.7)	3.5(3 - 4)
3.	Budd - Chiari Syndrome	1	6.8	4
	Total / Mean	40	5.96	1.89

(For a group consisting of more than one patient, mean was calculated and the range is shown in brackets)

The values for the Serum Total Protein were found to be 5.8 gm% on an average for cases of uncomplicated cirrhosis, 7.6 gm% in cases of Constrictive Pericarditis and 6.8 gm% in case of Budd-Chiari syndrome. In the cirrhosis group the mean Serum Protein was found to be 6.2 gm% in the cryptogenic variety, 5.6 in cases of Viral hepatitis, again 5.8 gm% in idiopathic hepatitis and 4.8 and 5.2 in cases of Wilson's disease and IEMs respectively (Table 7). The mean of the Ascitic fluid Total Protein [AFTP] was 1.7 gm% in cirrhosis, 3.5 gm% in Constrictive Pericarditis and 4 gm% in Budd-Chiari syndrome. The mean Ascitic fluid Total Protein (gm%) in the Cirrhosis group is as follows: 1.5 in Idiopathic Cirrhosis, 2.2 in cases of Viral hepatitis, 1.7 in Idiopathic hepatitis, 1.6 in Wilson's disease and 2 in the IEMs.

The mean Serum and Ascitic fluid Total Protein was found to be 5.96 gm% and 1.89 gm% respectively in the portal hypertension group of ascites.

**Table-VIII SERUM AND ASCITIC FLUID ALBUMIN LEVELS AND THE SERUM-ASCITES ALBUMIN GRADIENT IN THE DIFFERENT AETIOLOGIES OF PORTAL HYPERTENSION GROUP OF ASCITES**

Sl no.	Aetiology	No. of Patients	Serum Albumin (gm%)	Ascitic fluid Albumin (gm%)	SAAG (gm%)
1.	Cirrhosis	36	2.78 (2.2-3.2)	1.34 (0.7-1.9)	1.44 (0.8 - 2.4)
a.	Cryptogenic	15	2.8 (2.2-3.4)	1.5(1.1-2)	1.3 (1.2 -1.6)
b.	Viral hepatitis	11	3.1 (2.8-3.4)	1.5 (1.2-1.8)	1.6 (1.4 - 1.8)
	Hepatitis B	10			
	Hepatitis C	1			
c.	Idiopathic hepatitis	6	3(2.9-3.2)	1.4 (1.1-1.7)	1.6 (0.8 - 2.4)
d.	Wilson's	2	1.4 (1.2 - 1.6)	0.2 (0.1 - 0.3)	1.2
e.	IEMs	2	1.6 (1.2-2)	0.3 (0.2-0.4)	1.3
2.	Constrictive Pericarditis	3	4 (3.5-4.2)	2.6 (2.3- 2.9)	1.4 (1.2 - 1.7)
3.	Budd-Chiari Syndrome	1	4.5	2.8	1.7
	Total / Mean	40	2.91	1.41	1.44

The mean value of the Serum and Ascitic fluid Albumin was 2.78 and 1.34 gm% for the Cirrhosis group, 4 and 2.6 gm% in Constrictive Pericarditis and 4.5 and 2.8 gm% in Budd-Chiari syndrome respectively. The mean values of the Serum and Ascitic fluid Albumin (gm%) in the various aetiologies of cirrhosis is as follows: 2.8 and 1.5 in cryptogenic, 3.1 and 1.5 in viral hepatitis, 3 and 1.4 in idiopathic hepatitis, 1.4 and 0.2 in Wilson's disease and 1.6 and 0.3 in the IEMs respectively.

The average SAAG in the Cirrhosis group was found to be 1.44 gm%. The SAAG values in Constrictive

Pericarditis and Budd-Chiari syndrome was 1.4 gm% and 1.7 gm% respectively. The overall mean Serum Albumin, Ascitic fluid Albumin and SAAG in the Portal Hypertension group of Ascites was 2.91 gm%, 1.41 gm% and 1.44 gm% respectively.

**Table-IX SERUM AND ASCITIC FLUID PROTEIN LEVELS IN DIFFERENT AETIOLOGIES OF NON-PORTAL HYPERTENSION GROUP OF ASCITES**

Sl no.	Aetiology (Non - Portal hypertension)	No. of Patients	Serum Protein (gm%)	Ascitic fluid Protein (gm%)
1.	Nephrotic Syndrome	10	5.45 (5 - 5.9)	3.25 (1.9 - 4.6)
2.	PEM with Hypoproteinemia	5	5.55(5.1 - 6)	1.6 (1.1 - 2.2)
3.	Tuberculous Ascites	4	5.6 (5.2 - 6.0)	2.9 (2.6 - 3.2)
4.	Protein Losing Enteropathy	1	6.1	2.7
	Total / Mean	20	5.54	2.74

Mean value of serum and ascitic fluid total protein for nephrotic syndrome group was 5.45 gm% and 3.25 gm% respectively. For tuberculous ascites 5.6 gm% and 2.9 gm%, 5.55 gm% and 1.6 gm% respectively for Protein Energy Malnutrition with hypoproteinemia and 6.1 gm% and 2.7 gm% respectively for Protein Losing Enteropathy.

Hence the mean Serum Protein and Ascitic fluid Protein in the non-portal hypertension group of ascites was 5.54 gm% and 2.74 gm% respectively (Table 9).

**Table-X SERUM AND ASCITIC FLUID ALBUMIN LEVELS AND THE SERUM ASCITIC ALBUMIN GRADIENT IN DIFFERENT AETIOLOGIES OF NON-PORTAL HYPERTENSION GROUP OF ASCITES**

Sl no.	Aetiology (Non - Portal Hypertension)	No. of Patients	Serum Albumin (gm%)	Ascitic fluid Albumin (gm%)	SAAG (gm%)
1.	Nephrotic Syndrome	10	2.1 (2.0 - 2.2)	1.2 (1.1-1.3)	0.9 (0.9-1.0)
2.	PEM with Hypoproteinemia	5	1.8	0.9	0.9
3.	Tuberculous Ascites	4	2.65 (2.2 - 3.1)	1.67 (1.3 - 2.2)	0.98
4.	Protein Losing Enteropathy	1	2	1	1.0
	Total / Mean	20	2.13	1.21	0.92

The mean values for the Serum Albumin, Ascitic fluid Albumin and the SAAG (Serum Ascites Albumin Gradient) in different aetiologies of the non-portal hypertension group of ascites were 2.1 and 1.2 gm% and 0.9 gm% for Nephrotic Syndrome; 2.65 and 1.67 gm% and 0.98 gm% for patients of tuberculous ascites; 1.8 and 0.9 gm% and 0.9 gm% for children with Protein energy malnutrition and hypoproteinemia and 2 and 1 gm% and 1 gm% respectively in Protein Losing Enteropathy.

Thus the mean Serum Albumin and Ascitic fluid Albumin was 2.13 gm% and 1.21 gm% respectively. The mean SAAG in this group was 0.92 gm/dl.

**Table-XI DISTRIBUTION OF ASCITIC FLUID TOTAL PROTEIN**

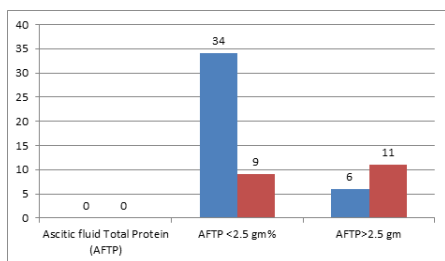
**(CUT-OFF VALUE 2.5 gm %) IN PORTAL HYPERTENSION GROUP AND NON - PORTAL HYPERTENSION GROUP OF ASCITES**

Sl no.	Ascitic fluid Total Protein (AFTP)	Portal Hypertension	Non – portal Hypertension	Total
1.	AFTP < 2.5 gm %	34	9	43
2.	AFTP > 2.5 gm %	6	11	17
	Total	40	20	60

The above table shows that out of 40 patients of portal hypertension group of ascites 34 had AFTP < 2.5 gm% and 6 had AFTP > 2.5 gm % ; while out of 20 patients in non-portal hypertension group of ascites 9 had AFTP < 2.5 gm % and 11 had AFTP > 2.5 gm % . AFTP < 2.5 gm % was able to identify portal hypertension in 85 % of the cases.

X2 value = 10.51  
P = < 0.02

**Bar Diagram Showing Distribution of Ascitic Fluid Total Protein In Portal Hypertension Group and Non Portal Hypertension Group of Ascites**



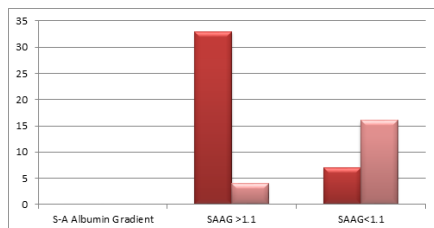
**Table- XII DISTRIBUTION OF THE SERUM ASCITES ALBUMIN GRADIENT (SAAG) CUT-OFF VALUE > 1.1 gm % IN PORTAL HYPERTENSION AND NON - PORTAL HYPERTENSION GROUP OF ASCITES**

Sl no.	S – A Albumin Gradient	Portal Hypertension	Non – Portal Hypertension	Total
1.	SAAG > 1.1	33	4	37
2.	SAAG < 1.1	7	16	23
	Total	40	20	60

The above table shows that out of 40 patients of portal hypertension group of ascites 33 have SAAG > 1.1 gm % and 7 have SAAG < 1.1 gm % ; while in the non – portal hypertension group of ascites 4 have SAAG > 1.1 gm % whereas 16 have SAAG < 1.1 gm % . SAAG > 1.1 gm % was able to identify portal hypertension in 82.5 % of cases

P = < 0.001

**Bar Diagram Showing Distribution of Serum Ascites Albumin Gradient (SAAG) in the two groups**



**Table- XIII SIGNIFICANCE AND VALIDITY VALUES OF DIFFERENT PARAMETERS**

Sl no.	Parameter	Cutoff value	Sensitivity	Specificity	PPV	NPV	'p' value
1.	SAAG	1.1gm%	82.5%	80 %	89%	69%	<0.001
2.	AFTP	2.5gm%	85 %	55 %	79%	65%	< 0.02

where, PPV is the Positive Predictive Value and NPV the Negative Predictive Value of the test.

**CONCLUSION**

In this study the sensitivity of SAAG (82.5%) was comparable to that of the Ascitic fluid Total Protein (AFTP) 85%. However in detecting Portal Hypertension SAAG had a greater specificity 80% as compared to the AFTP which had a specificity of only 55%. The SAAG had greater Positive and Negative Predictive values 89.19% and 69.56% respectively as compared to that of AFTP which had Positive and Negative Predictive Values of 79.06% and 64.71% respectively. The 'p' value for SAAG (> 1.1gm %) in detecting portal hypertension was < 0.001 which was highly significant as against that of AFTP, 'p' value < 0.02.

The SAAG is based on oncotic hydrostatic balance and correlates directly with the portal pressure. The data from various studies 10,11 support the conclusion that the Serum Ascitic fluid Albumin gradient (SAAG) is a better indicator of portal hypertension than the Ascitic fluid Total Protein (AFTP).

The Serum – Ascites Albumin Gradient (SAAG), should replace the traditional parameter of Ascitic fluid Total Protein in the routine analysis of ascitic fluid and in the classification of ascites.

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