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Indian Journal of Pathology and Oncology

Journal homepage: www.innovativepublication.com

Original Research Article

Analysis of ascitic fluid in differentiating transudate versus exudate - in a tertiary care centre

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ARTICLE INFO

Article history:
Received 31-08-2019
Accepted 22-10-2019
Available online 22-02-2020

Keywords:
Ascitic fluid total protein (AFTP)
Serum Albumin Ascitic Gradient (SAAG)
Paracentesis
Cirrhosis

ABSTRACT

Introduction: Ascites is the accumulation of fluid within the peritoneal cavity. Normally, 5-20ml of peritoneal fluid is found between the layers of peritoneum, acting as a lubricant and reducing the friction of organ movement during digestion and bodily movements. The use of serum ascites albumin gradient has out dated the total protein measurement in differentiating transudate from exudate fluid. Analysis is done in two broad spectrums:
(1) Biochemical analysis (2) Clinical pathology and Cytological analysis
Aim & Objectives: This study was done with the objective to evaluate the ascitic fluid analysis for differentiating transudate versus exudate and also the characteristics of the peritoneal fluid in various causes of ascites.
Materials and Methods: In this study, 100 patients of ascites were evaluated for ascitic fluid total protein (AFTP) and Serum Albumin Ascitic Gradient (SAAG) along with ultrasound and other required investigations. Ascitic fluid was obtained by Paracentesis, an invasive sampling procedure to remove fluid or air from the peritoneal cavity for diagnostic or therapeutic purposes. The fluid obtained is sent for analysis. Ascitic fluid analysis is a group of tests used to diagnose the etiology of fluid accumulation.
Result: Study shows that ascites due to various aetiology is common among 31-50 years of age group with a slight male predominance. The present study suggests that transudative ascites are more common than exudative ascites with a percentage of 52%.
Conclusion: Serum Albumin Ascitic Gradient (SAAG) is much more superior to ascitic fluid total protein (AFTP) in the differential diagnosis of Ascites. Ascitic fluid analysis helps in diagnosing the aetiology of ascites based on the cytological and biochemical parameters. The common aetiology for ascites reported in India is liver cirrhosis. The development of ascites in cirrhotic patients is associated with a mortality of 15% and 44% at one-year and five-year follow-up periods, respectively.

1. Introduction

Ascites is the excessive accumulation of fluid in the peritoneal cavity. The normal peritoneal cavity contains a small amount of fluid (< 50mL) with high protein content. Accumulation of fluid in the peritoneal cavity resulting in ascites has many different mechanisms.[1,2] The most frequent cause of ascites is cirrhosis-related portal hypertension in 85% of cases; 15% of cases are due to intraabdominal noncirrhotic conditions, including malignancies, infections, and cardiac and renal failure.[3]

Under normal circumstances, the amount of peritoneal fluid depends on a balance between plasma flowing into and out of the blood and lymphatic vessels. It is only when this balance has been disrupted or in cases of inflammation or injury, ascites develops. The imbalance in the level of plasma may be due to increased capillary permeability, increased venous pressure, decreased protein (oncotic pressure), or increased lymphatic obstruction.

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https://doi.org/10.18231/j.ijpo.2020.026

Ascites may be broadly classified as (a) Transudate and (b) Exudate

To treat ascites appropriately, it is important to determine its cause. For which the nature of the fluid (i.e. Transudate or Exudate) has to be determined.

1.1. Transudative ascites

It has low protein content. Its most common cause is cirrhosis. The transudate fluid is from normal peritoneal surface and is low in protein and is formed commonly due to increase in portal pressure in accordance with Starling hypothesis. Common conditions that could result in this type of ascites include portal hypertension due to cirrhosis, congestive decompensated heart failure, hypoalbuminemia in nephrotic syndrome.

1.2. Exudative ascites

It has high protein content. E xudates fluid is from the inflamed and tumor laden peritoneal surface hence it is high in protein suggestive of Peritonitis or Malignant ascites.

Common conditions that could result in this type of ascites include malignancy, tuberculosis infection, and inflammatory conditions like pancreatitis. In fact, ascites with low protein concentration is more prone to develop infection.[4]

Transudative Ascites based on AFTP is unable to correctly identify the etiological factors and offers little insight to the pathophysiology of ascitic fluid formation. Hence – SAAG [Serum Ascites Albumin Gradient] has been developed as a new approach, to classify ascites into two categories – High SAAG $\geq$ 1.1 g/dl in cases with portal hypertension and Low SAAG $<$1.1 g/dl in cases with ascites, unrelated to portal hypertension. SAAG reflects the oncotic pressure exerted by Serum Albumin over Ascitic fluid Albumin which truly equals the high hydrostatic pressure gradient between the portal bed and the ascitic fluid.

The following research aims at determining the cause of ascites based on laboratory characteristics of the fluid and bring out the diagnostic accuracy of materials used in ascertaining the nature of the fluid to approach a case of ascites.

2. Materials and Methods

This retrospective study was carried out in the Central laboratory and Department of Pathology, Saveetha Medical College and Hospital, Thandalam during the period of July 2018 to December 2018. The study was approved by Institutional Review Board (IRB).

Clinical history, signs and symptoms gave an idea about the etiology and the probable system involved. Further investigations were done through:

1. Plain x ray of abdomen- detection requires at least 500 ml of fluid.
2. Ultrasound (USG Abdomen) - to detect smaller volumes especially if they are adjacent to diaphragm or anterior margin of liver.
3. Computed Tomography- most sensitive for smaller amounts.

Once the provisional diagnosis has been made, the ascitic fluid was drawn for laboratory investigations and analysis by a procedure called peritoneocentesis.

2.1. Indications includes

New onset ascites or ascites of unknown origin, Patients with ascites of known etiology, suspected malignant ascites, peritoneal dialysis patients with fever, abdominal pain or other signs of sepsis

2.2. Contraindications includes

Pre surgical stage, uncorrected bleeding diathesis, previous abdominal surgeries with suspected adhesions, severe bowel distention, abdominal wall cellulitis at the proposed site of puncture

2.3. Procedure: Z- track technique

The insertion sites may be midline or through the oblique transversus muscle, lateral to the thicker rectus abdominus muscles. The patients were made to empty the bladder and then placed in the horizontal supine position, and tilt ed slightly to the side of the collection. Then the hip was slightly rotated, down on the table, on towards the side of needle insertion. A 2-inch needle was then inserted perpendicular to the skin to infiltrate the deeper tissues and peritoneum with local anesthetic. The catheter/introducer was inserted through the skin and the peritoneum was penetrated. Then the syringe was attached and the fluid was drawn into the syringe and remove d in drainage tube and bag. Lavage was done if desired, excess fluid was removed and then RL or saline was infused.

After the procedure was done, the catheter was gently removed and direct pressure was applied to the wound. Then, the characteristics of the fluid obtained was observed, and sent for appropriate studies.

2.4. Gross appearance

The gross appearance of the fluid can provide useful diagnostic information. In most of the cases of cirrhosis, ascitic fluid appeared clear straw-colored. A blood-stained sample was usually due to a traumatic tap and in those cases the fluid tends to clot on standing. Samples which remain homogeneously blood stained throughout the tap could indicate malignancy, pancreatitis, TB, intestinal infarction or recent abdominal trauma.

Around 50 ml fluid would be aspirated and immediately sent for Biochemical Analysis for Albumin, Total Protein, Glucose, Cytological Analysis for Cell counts and Differential count, and Microbiological Analysis for gram stain, ZN stain and bacterial culture.

Serum and Ascitic fluid Albumin were estimated in auto analyzer by Bromocresol green. Total Proteins were estimated in auto analyzer by Biuret methods.

Special investigations like CT scan abdomen and Pelvis, Echocardiogram, Thyroid Profile, Upper GI endoscopy, and biopsy of the peritoneal nodules and liver biopsy were done in selected cases.

3. Result

This retrospective study was performed in Saveetha Medical College. A total number of 100 cases of Ascites in the age group of 11 to 75 were included in the study irrespective of the etiology. The age and gender co-relation has been tabulated for hundred cases of ascites, taking into consideration all the causes of ascites. Maximum numbers of cases were between the age group of 31-50 years accounting for 48% of the total number of cases. Table 1 Age distribution pattern in different etiologies of ascites.

Results showed a male predominance (62%) compared to that of females which was 38%. Refer- Table no. (2) Sex distribution pattern in different etiologies of ascites. Out of 100 cases, the leading etiology of ascites was liver cirrhosis, which accounted for 53 cases. Table 3 Etiological Distribution of the ascitic cases and the typical characteristics of ascites in patients with cirrhosis compared with other diseases are shown in Table 4.

According to the research, the second most common case of ascites was reported in decompensated heart failure patients with about 16% of the total number of cases. There are several reasons why ascites may be common in patients with chronic kidney disease. These include congestive heart failure, fluid overload, an increased risk of infection (Especially tuberculosis), the presence of diseases associated with renal and pleural manifestations (e.g., systemic lupus erythematosus), uremic pericarditis, an increased risk for certain malignancies and pulmonary embolism.

The cases were categorized as Transudate and Exudate. Causes of exudate evaluated on the basis of Differential Cell Count (predominance of white cells). According to the study, transudative ascitEs are more common than exudative ascites with a percentage of 52%. EXudative ascitEs accounts for 48% of the total number of cases. Table 5.

4. Discussion

Peritoneocentesis is a safe procedure without any complications. But there is a need for a noninvasive and rapid tool to determine the cause of ascites as an alternative to invasive

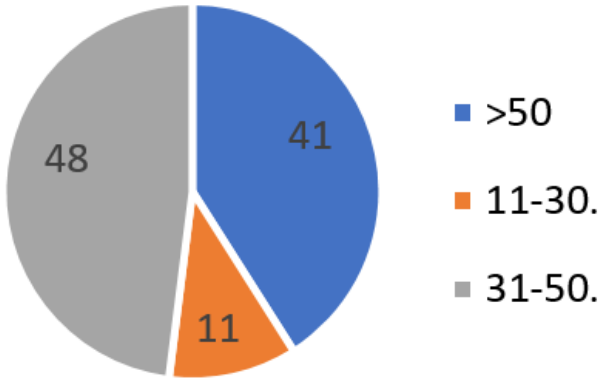

Fig. 1: Age distribution

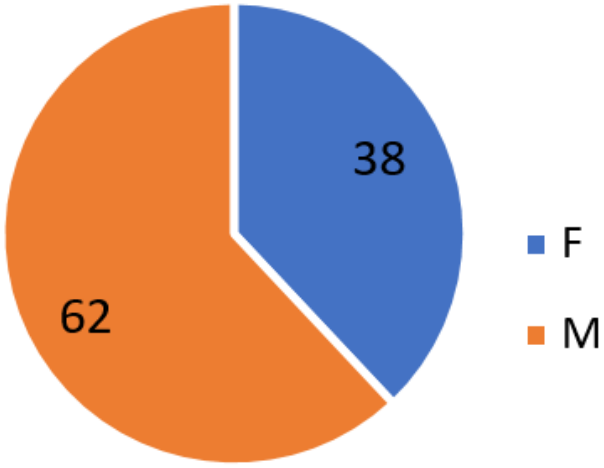

Fig. 2: Sex distribution

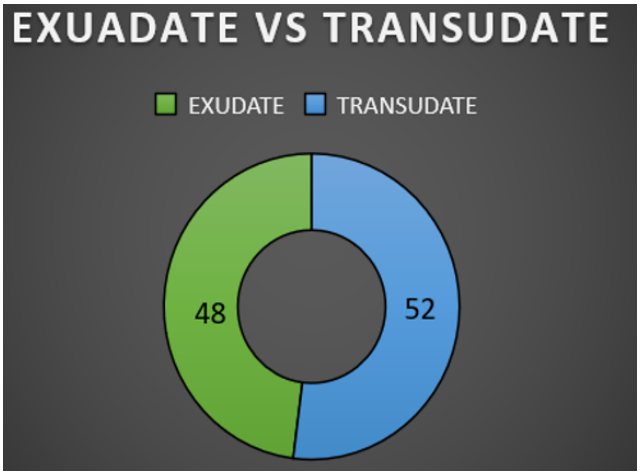

Fig. 3: Count of exudate and transudate

Table 1: Showing age distribution pattern in different etiologies of ascites

S. No	Etiology	No. of cases	Age group			
			0-10	11-30	31-50	Above 50
1.	Cirrhosis	53	0	6	26	21
2.	Decompensated Heart Failure	16	0	2	9	4
3.	Tuberculous Ascitis	8	0	2	3	3
4.	Nephrotic Syndrome	10	0	0	6	5
5.	Malignancy	7	0	0	0	7
6.	Pancreatitis	5	0	1	1	3

Table 2: Sex distribution in different etiologies of ascites

Etiology	Males	Females
Cirrhosis	30	23
Decompensated Heart Failure	8	8
Tuberculous Ascites	5	3
Nephrotic Syndrome	10	1
Malignancy	3	4
Pancreatitis	0	5
Total	56	44

Table 3: Etiological distribution of ascitic cases

Etiology	Total number (n=100)
Cirrhosis-	53
Decompensated heart failure-	16
Tuberculous ascites	8
Nephrotic syndrome-	11
Malignancy	7
Pancreatitis	5

Table 4: Typical characteristics of ascites in patients with cirrhosis compared with other diseases

Causes	Cirrhosis	Decompensated heart failure	Malignancy	Tuberculous ascites	Nephrotic syndrome or sbp	Pancreatitis
Gross appearance	Clear straw or milky	clear to pale yellow	milky or bloody	milky or normal	cloudy or turbid	milky or cloudy or turbid
AFTP	$<$2.5g/dl	$<$2.5g/dl	$\geq$2.5 g/dl	$\geq$2.5 g/dl	$\geq$2.5 g/dl	$\geq$2.5 g/dl
SAAG	$\geq$1.1g/dl	$\geq$1.1g/dl	$<$1.1g/dl	$<$1.1g/dl	$<$1.1g/dl	$<$1.1g/dl
Glucose	Normal	Normal	Reduced	Reduced	Reduced	Reduced
Cell count	$\geq$250/μL or N	-	-	$\geq$250/μL or N	$\geq$250/μL	-

Table 5: Distribution of ascites on the basis of ascitic fluid total protein (AFTP) Distribution

Etiology	Exudative AFTP$\geq$2.5	Transudate AFTP$<$2.5
Cirrhosis	20	33
Decompensated heart failure	8	8
Tuberculous ascites	6	2
Nephrotic syndrome	5	6
Malignancy	4	3
Pancreatitis	5	0
Total	**48**	**52**

paracentesis procedure.[5] Through the analysis of ascetic fluid, it is possible to differentiate between transudative or exudative ascites, and to confirm the etiology behind the diagnosis of ascites. The cytological and biochemical parameters can be a key to a direct diagnosis or can indicate the next step in diagnosis of ascitic etiology.

Ascites with high protein content ($\geq$ 25 g/L) indicated an exudate that could be due to malignant ascites or infection, whereas low protein content ($<$ 25 g/L) suggested benign ascites (transudate).[6] However, 15 – 20% of patients with cirrhotic ascites have elevated protein levels, consistent with an exudate.[6] To identify cirrhotic ascites with an elevated protein level, the SAAG is currently used, where gradient values of greater than or equal to 11 g/L are classified as portal hypertension – related (benign-transudate) ascites, and values less than 11 g/L are classified as non – portal hypertension ascites, with causes including malignant exudative ascites. Using the SAAG method, diagnosis of portal hypertension – associated ascites in patients with cirrhosis can be made with 97% accuracy.[7]

Ascites can be a consequence or complication of many primary diseases and carries an unfavorable prognosis that largely depends on the underlying causes. Cirrhotic ascites accounts for most of the ascites and it can be complicated by subsequent infections that can lead to ascites. In selected cases, special investigations like CT scan abdomen and Pelvis, echocardiogram, Thyroid Profile, Upper GI endoscopy, and FNAC of the peritoneal nodules and liver biopsy were done.

The American Association of the Study of Liver Disease (AASLD) and British Society of Gastroenterology has included SAAG in the guidelines of investigations for ascites caused by cirrhosis.[8,9]

4.1. Transudate vs Exudate

According to the present study, transudate (AFTP $<$2.5) was predominate to exudate (AFTP $\geq$2.5) with the former having a percentage 52% and the latter with 48%. This is comparable with the previous studies, all of which comment that exudative ascites are more common than the transudative type.

In a research conducted by Sastry AS et al[10] - the transudate was predominant to exudate with the former having a percentage 72% and the latter with 26%

According to the present study, the portal hypertension related etiology was predomina nt in comparison to non-portal causes with the former having a percentage 56% and the latter with 44%.

In a research conducted by Anand Sankar Sastry et al.[10] the portal hypertension related etiology was predominating in comparison to non-portal causes with the former having a percentage 70% and the latter with 30%.

Another prospective study done by M Beg, S Husain et al[11] and they were observed that the serum albumin ascitic gradient had a diagnostic sensitivity of 94.73% and 94% accuracy compared to AFTP, which is 65.62% and 68% respectively.

Various studies have challenged accuracy of traditional exudates-transudate concept which does not truly reflect the pathophysiology.

Again, the relationship between ascitic protein concentration and character as transudate or exudates does not hold true in many conditions as it does not take the value of serum albumin into account.

For example, Sampliner and Iber[12] showed that 12% of unselected patients with chronic liver disease (CLD) had an ascitic fluid protein $>$30 g/L. A similar proportion (17%) was reported by Boyer et al.[13] and moreover, in 12% the ascitic fluid, protein concentration was 40 g/L. Conversely, two of 14 patients in this study with proven malignant ascites had a TP $<$ 30 g/L. Use of ascitic fluid protein/serum protein ratio was of minimal extra value.

In the study of Rector and Reynolds[14] patients with 'transudative' (chronic heart failure and cirrhosis) ascites had lower fluid TP concentrations, but there was considerable overlap with 'exudative' (largely malignancy) ascites, particularly in those with congestiv cardiac failure. This may relate to diuretic use.

5. Conclusion

Diagnosis begins with the clinical history, physical examination, and is followed by paracentesis when appropriate. To conclude the study, paracentesis followed by ascitic fluid analysis using Serum Ascitic Albumin Gradient is the best method to diagnose the underlying etiology.

The presence of high SAAG indicates portal hypertension even in presence of high ascetic fluid protein. It is superior to previously proposed transudate-exudate classification, because of its higher diagnostic accuracy and it provides a better approach to pathogenesis of ascitic fluid collection.

6. Funding

No funding sources

7. Limitations

SAAG is not able to differentiate between malignant ascites and tuberculous ascites as both are having low SAAG. Transudative Ascites based on AFTP is unable to correctly identify the etiological factors and offers little insight to the pathophysiology of ascitic fluid formation.

8. Conflicts of interest

No potential conflict of interest, relevant to this article has been reported.

9. Ethical approval

Not required since it is a retrospective study.

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Cite this article: Selvaraju K, Sridevi M. Analysis of ascitic fluid in differentiating transudate versus exudate - in a tertiary care centre. *Indian J Pathol Oncol* 2020;7(1):137-142.