A Review on Ascites: Causes, Diagnosis and Management

Vankodoth Sireesha¹, Sumaya Sumaya², Kompalli Varun³, Y. Pravarsha⁴, Rama Rao Tadikonda⁵

¹Assistant professor, CMR College of Pharmacy, Hyderabad, Telangana.
²Pharm D intern, CMR College of Pharmacy, Hyderabad, Telangana.
³Professor, Principal, Ph. D, CMR College of Pharmacy, Hyderabad, Telangana

Corresponding author: - V. Sireesha
Assistant professor, CMR College of Pharmacy, Medchal, Telangana.

ABSTRACT: Ascites is a condition characterized by abnormal fluid buildup in the peritoneal cavity, primarily caused by cirrhosis of the liver. However, other underlying conditions such as malignant tumors, heart failure, and pancreatitis can also lead to ascites. Patients with ascites may experience symptoms such as abdominal distension, weight gain, and weakness due to fluid accumulation. Diagnosis involves a thorough evaluation, including history, physical examination, and diagnostic abdominal paracentesis to analyze the ascitic fluid. The serum-ascites albumin gradient (SAAG) is a crucial parameter used to determine the cause of ascites. Treatment approaches for ascites depend on its severity and underlying cause. Mild cases may not require specific therapy, while moderate ascites can be managed with dietary salt reduction and diuretics. Severe ascites may necessitate therapeutic paracentesis, followed by sodium restriction and diuretic therapy. Liver transplantation may be considered for patients with refractory ascites. The specific treatment plan is tailored to address the underlying cause, which could include autoimmune hepatitis, chronic hepatitis B, hemochromatosis, or ovarian cancer. Complications of ascites encompass spontaneous bacterial peritonitis, dilutional hyponatremia, hepatorenal syndrome, pleural effusion, and umbilical hernia, each requiring individualized management strategies.

Thus, ascites is a multifaceted condition with various underlying causes. Its diagnosis involves a comprehensive evaluation, and treatment aims to target the underlying cause, alleviate symptoms, and prevent complications. Continued research efforts are essential to advance diagnostic techniques and explore novel therapeutic options for ascites.

KEYWORDS
Diuretics, Therapeutic paracentesis, Sodium restriction, Liver transplantation, Refractory ascites, Albumin supplementation, autoimmune hepatitis.

INTRODUCTION
Ascites is an abnormal build-up of fluid within the peritoneal cavity caused by many disease states. It occurs due to a series of anatomical, pathophysiological, metabolic alterations in the body. The amount of fluid in the abdominal cavity almost exceeds 1 litre.

Etiology
More than 75% of patients with ascites are due to cirrhosis of the liver being the most common cause. The remaining 25% have other causes, such as malignant tumours, heart failure, tuberculosis, pancreatitis, dialysis, or other conditions. So, Ascites-related causes can be categorized as:

• Linked to portal hypertension (cirrhotic ascites)
• Independent of portal Hypertension (non-cirrhotic ascites)

The other causes of ascites include:
1. Intrahepatic portal hypertension due to conditions like Liver cirrhosis, fulminant liver failure, sinusoidal obstruction syndrome
2. Extrahepatic portal hypertension due to various conditions like Hepatic vein occlusion, congestive heart failure.
3. Low albuminemia which occurs in cases like Nephrotic syndrome, protein-losing enteropathy, malnutrition, malignant tumours, trauma, myxoedema, secondary to ovarian tumours,
4. Various diseases like Pancreatic and bile ascites which are usually among the nonperitoneal, malignant primary peritoneal mesothelioma and secondary peritoneal cancer which are usually among peritoneal causes of ascites.

Pathophysiology
The risk factors for liver disease are alcohol consumption, drug addiction, blood transfusions, and prior hepatitis. The earliest indication of liver illness may be ascites. As ascites is a common complication in cirrhotic liver. It develops because of portal sinusoidal hypertension, which results in alterations in intraperitoneal capillary pressure, permeability, and accumulation of retained fluid build-up in the abdominal cavity. This mechanism of fluid accumulation is known as transudation. Effusion or exudation is another mechanism for ascites to develop. Ascites develops secondary to increased vascular permeability brought on by tumor infiltration, inflammatory processes, or mechanical injury to the peritoneum or intraperitoneal organs. In cirrhosis, portal
hypertension results from the combination of increased intrahepatic vascular resistance and increased blood flow through the portal venous system (Fig. 1). In cirrhosis, increased intrahepatic vascular resistance results from an imbalance between vasodilators and vasoconstrictors.\(^5\)

**Clinical Findings**

Abdominal ultrasonography can identify fluid volume of less than 1.5 litres that is asymptomatic. Patients may typically present with progressive abdominal distension which may be painless or associated with abdominal discomfort, weight gain, early satiety, weakness, shortness of breath resulting from fluid accumulation and increased abdominal pressure.\(^7\) Other signs and symptoms include back discomfort, frequent heartburn, changes in bowel habits, swollen limbs, extreme exhaustion and weakness, regular heartburn and feeling full after eating.\(^8\) Patients with advanced liver disease are seen with Jaundice, muscle wasting, gynecomastia. Symptoms such as fever, abdominal tenderness, and confusion can be seen in spontaneous bacterial peritonitis (SBP). Patients with malignant ascites can have symptoms related to malignancy, which may include weight loss. Patients with ascites due to heart failure may represent dyspnoea, orthopnoea, and peripheral edema, and those with chylous ascites report diarrhea, steatorrhea, malnutrition, edema, nausea, enlarged lymph nodes, early satiety, fevers, and night sweats.

**Diagnosis**

Diagnosis of ascites requires knowing a thorough history, performing physical examination and investigation. Diagnostic abdominal paracentesis with the appropriate ascetic fluid analysis is probably the most rapid and effective method to confirm clinical findings of ascites. A needle or small catheter is introduced transcutaneous to take ascetic fluid from the peritoneum during paracentesis, a bedside technique that can be used to diagnose the cause of the ascites. Ascetic fluid protein and albumin are measured with the
serum albumin level to calculate the serum ascites albumin gradient (SAAG). SAAG- >1.1gm/dL indicates existence of portal hypertension. The initial tests performed on the ascitic fluid include a blood cell count, with both a total nucleated cell count and polymorphonuclear neutrophils (PMN) count, and a bacterial culture. The presence of a gradient greater or equal to 1.1 g/dL predicts that the patient has portal hypertension with 97% accuracy. This is seen in cirrhosis, alcoholic hepatitis, heart failure, massive hepatic metastases, Budd-Chiari syndrome, portal vein thrombosis, and portal fibrosis. A gradient less than 1.1 g/dL indicates that the patient does not have portal hypertension and occurs in peritoneal carcinomatosis, peritoneal tuberculosis, pancreatitis, seerosis, and nephrotic syndrome. Liver biochemical testing, serum albumin level measurement, prothrombin time (PT) or INR (normal range – 1.0) are measured for determination to assess hepatic function. Serum amylase and lipase levels should be measured to assess the patient for acute pancreatitis. Additional tests may be required only if a specific diagnosis is clinically suspected. Other tests to consider include amylase (greater than 1000 U/L suggests pancreatic ascites). Mycobacterial culture should be performed only if tuberculosis is strongly suspected. Chest x-ray may reveal elevated diaphragm. Ultrasound is the most sensitive test to detect ascites. CT scan can also be used to detect ascites and may also help determine for presence of any masses. A liver biopsy may be required in some circumstances to confirm. [9]

Complications
Patients with ascites constitute a heterogeneous population with different prognosis depending on the degree of liver insufficiency and circulatory dysfunction, the development of ascites is an ominous sign. The probability of survival of one and five years after the diagnosis of ascites is approximately 50 and 20%, respectively and long-term survival of more than 10 years is very rare. Further, mortality rises to 80% within 6–12 months in patients who also develop kidney failure. In addition of having ascites and cirrhosis, patients are at a higher risk of developing other potentially fatal liver conditions such as refractory ascites, SBP, respiratory distress, poor nutritional status, hyponatremia. [10]

Treatment
The treatment of ascites largely depends on the cause. Thus, figuring out the cause of ascites is important. Treatment of ascites depends on the degree of severity grade of ascites. According to the International Club of Ascites, it is classified into three grades based on severity.

Grade 1: Mild ascites that can only be detected by ultrasonography.
Grade 2: Moderate ascites and moderate distension.
Grade 3: Severe abdominal distension and ascites.

Grade 1 ascites is not currently recommended for therapy, while grade 2 ascites can be controlled with dietary salt reduction and diuretics. Massive abdominal puncture can be used as the first step in treating grade 3 ascites, which is then followed by sodium restriction and diuretics. [11]

Appropriate treatment of ascites depends on the cause of fluid retention. The goals of therapy in patients with ascites are to minimize the ascitic fluid volume and decrease peripheral edema, without causing intravascular volume depletion. Sodium restriction and diuretics form the basis of treatment. A low-salt sodium diet up to 2000 mg, diuretics (spironolactone to furosemide) and liquid drainage are common forms of treatment. Paracentesis is usually performed in patients with ascites or to relieve from symptoms. In-order to avoid hypotension, albumin supplements must be given at the same time. Instead of albumin, Terlipressin is recommended. It is possible to implant a TIPS, although there are risks involved. [12] TIPS is an effective treatment for patients who do not respond to diuretics. Ascitic patient with treatable liver condition like autoimmune hepatitis, chronic hepatitis B, and hemochromatosis must be prescribed with specific therapy for these diseases. Cirrhotic ascites patients may be better done with liver transplantation than with medical therapy. Non-ovarian peritoneal carcinomatosis patients usually presents with ascites with a low-albumin gradient, so paracentesis is usually beneficial for these patients. Chemotherapy and surgical de bulking may be beneficial for ovarian cancer patients with ascites. Anti-tubercular drugs are used for the treatment of TB peritonitis, however pancreatic ascites may go away on their own. Doxycycline is used to treat Chlamydia peritonitis, while glucocorticoids are effective in treating ascites due to lupus serositis. [13] Attempts to treat the underlying cause is to perform liver transplant. Peritoneal venous shunt therapy is third-line treatment.

Refractory Ascites
As Refractory ascites is characterized by ascites that does not respond to a low-sodium diet and high-dose diuretics, or returns quickly following therapeutic ascites paracentesis. So, liver transplantation should be a possibility for patients with refractory ascites. [14]

Diuretic Treatment
Diuretic therapy management is aided by the measurement of 24-hour urine sodium excretion. When sodium excretion is less than intake (e.g., 80 mmol/day), it suggests that the dose of the diuretic is insufficient in the absence of renal impairment. Diuretic therapy for cirrhotic ascites mostly consists of aldosterone antagonists (such as spironolactone) and loop diuretics (such as furosemide, torsemide, and bumetanide). Spironolactone’s initial dose is 100 mg per day and it can be gradually increased to maximum dose of 400 mg per day. The dosage should be gradually increased over intervals of at least 72 hours. The initial dose of furosemide is 40 mg/day and can be increased to 160 mg/day. Low dosages of aldosterone antagonists plus high doses of loop diuretics are frequently used to treat ascites patients with chronic kidney disease.

In patients with cirrhosis and ascites, nonsteroidal anti-inflammatory medications, ACE inhibitors and angiotensin receptor blockers should be avoided. In case of bacterial infections aminoglycosides should be avoided. [15]
We thank the management, staff, faculty and friends of CMR College of Pharmacy for helping us in this review study.

References

17. Pharmaceutical journal 2015, 4 (3),370 -377

<table>
<thead>
<tr>
<th>Complications</th>
<th>Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>Abdominal pain,fever</td>
<td>Antibiotic administration,large volume paracentesis should be withheld until infection is treated effectively</td>
</tr>
<tr>
<td>Dilutional hyponatremia</td>
<td>Increased peripheral edema and reaccumulation of ascites</td>
<td>Fluid restriction may be instigated if sodium is less than 30mmol/l but should be used with caution</td>
</tr>
<tr>
<td>Hepatorenal syndrome</td>
<td>Reduced renal function, raised creatinine in the absence of infection</td>
<td>Administration of the vasoconstrictor terlipressin in combination with albumin. Liver transplantation</td>
</tr>
</tbody>
</table>

Table: 1 Various Complications and treatment associated with ascites[16]

CONCLUSION
In conclusion, ascites is a complex condition characterized by fluid accumulation in the abdominal cavity. It is primarily associated with advanced liver disease but can have other underlying causes. Diagnostic imaging and paracentesis play important roles in evaluating ascites. Management involves addressing the underlying cause, controlling symptoms, and preventing complications through diuretic therapy and lifestyle modifications. However, refractory cases may require more invasive interventions. Ascites remains challenging, and further research is needed to improve diagnostic techniques and explore new treatments. A multidisciplinary approach is crucial for optimal patient care.

ACKNOWLEDGEMENTS
We thank the management, staff, faculty and friends of CMR College of Pharmacy for helping us in this review study.
18. Elisa M. Aponte; Shravan Katta; Maria C. O’Rourke, Paracentesis, Updated 2022 Sep 5, StatPearls, Treasure Island (FL) StatPearls Publishing; 2022 Jan.