



REVIEW ARTICLE

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Causes, management and complications of ascites: a review

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ABSTRACT

Ascites is the pathological state in which fluid accumulates in the peritoneal cavity. Fluid accumulation may be due to infection and malignancy or due to other diseases like liver disease, heart failure, and renal disease. The ascitic fluid can be graded into Transudative and Exudative fluid based on the serum ascites albumin gradient (SAAG). The prominent cause of ascites is found to be Liver Cirrhosis. The most common symptom of Ascites is recent weight gain, increased abdominal girth and dyspnea. The first line treatment of ascites includes education regarding dietary sodium restriction and oral diuretics. However, other mechanical methods can also be used if the patient is unresponsive to this approach. But, there are some limitations while using these mechanical methods. Ascites is also associated with certain complications like spontaneous bacterial peritonitis, hepatorenal syndrome and dilutional hyponatremia. Ascites itself is not fatal unless it becomes infected. So, early diagnosis and effective treatment should be ensured in order to avoid further complications. This review focuses on the grades, causes, symptoms, management and complications of Ascites.

Key Words: SAAG, causes, cirrhosis, management, diuretics, paracentesis.

INTRODUCTION

Ascites is derived from a Greek term "ASKOS" which refers to a bag or sac. It is the pathological accumulation of free fluid in the peritoneal cavity. The fluid accumulates because of conditions directly involving the peritoneum (infection, malignancy), or due to other diseases remote from the peritoneum (*i.e.*, liver disease, heart failure, hypoproteinaemia). Normally there is no fluid in the peritoneal cavity, however in women a small amount (almost 20 ml) or less than 1 ounce can sometimes (but not often) can be present depending on her menstrual cycle (Ascites-1), but for the confirmation of ascites, it is required that at least 1500 ml of fluid should be present in peritoneal cavity and also detectable by clinical examination but significantly more in obese person (ascites-2) (Muhammed *et al.*, 2012; Al Knawy, 1997).

GRADING OF ASCITES

Ascites exists in three grades namely, grade 1 which is mild, only visible on ultrasound and CT scan, grade 2 which is determined with flank bulging and shifting dullness and grade 3 is directly visible, and is confirmed with the fluid wave/thrill test. Traditionally, ascites was divided into 2 types, transudative and exudative type. This classification was based on the amount of protein found in the fluid. A more meaningful system has been developed, on the basis of amount of albumin in the ascitic fluid in contrast to serum albumin (albumin measured in the blood). This system is called the Serum Ascites Albumin Gradient or SAAG. Ascites due to portal hypertension caused cirrhosis, congestive heart failure or Budd-Chiari has SAAG value generally greater than 1.1. Ascites related to other reasons (malignancy, pancreatitis) has value lower than 1.1. Another grading system adapted from European Association for the study of the liver is given in table 1 (Moore & Wong, 2003).

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PATHOPHYSIOLOGY & CAUSES OF ASCITES

Ascites generally results from portal hypertension and low levels of a protein called albumin. Diseases that can lead to severe liver damage can cause ascites. These diseases include long-term hepatitis C or B infection and alcohol abuse over many years. People suffering from certain cancers in the abdomen may develop ascites. These cancers include colon, ovaries, uterus, pancreas, and liver cancer. Other conditions that can lead to this problem include, clots in the veins of the liver (portal vein thrombosis), congestive heart failure, pancreatitis, thickening and discoloring of the sac like covering of the heart. Kidney dialysis may also be linked with ascites (Runyon, 2009). Table 2 depicts some of the common causes of ascites.

Ascites due to liver cirrhosis

Literature showed that Cirrhosis is the commonest cause of ascites in the Western world (~75%), followed by peritoneal malignancy (12%), cardiac failure (5%) and peritoneal tuberculosis (2%) (Runyon, 1993).

Mechanism of ascites in cirrhosis

The mechanism of ascites in cirrhosis is complex but portal hypertension and renal sodium retention is common. The history shows that cirrhotic ascites progresses from diuretic responsive (uncomplicated) ascites to the development of dilutional hyponatraemia, refractory ascites, and finally, hepatorenal syndrome (HRS). While survival of patients who develop ascites in 1 year is 85%, it declines to 25% once it has progressed to hyponatraemia, refractory ascites or HRS (Planas *et al.*, 2004).

In considering portal hypertension, backflow and stasis of vasodilatory substances, *e.g.*, nitric oxide, begin to aggregate. This causes, amongst other results visceral vasodilation with resultant hypoperfusion of the renal system. Thus by this way renin-angiotensin-aldosterone system (RAAS) is activated leading to aggressive fluid retention. In short, renin is secreted from the renal juxtaglomerular apparatus (JGA) around the proximal nephrons in reaction to changes in vascular pressures, changes in serum sodium, and from activation of the

Table 1: Grading of ascites (Fullwood & Purushothaman, 2014).

Grade	Detection Technique	Abdominal Distension
1	Ultrasound	Absent (<500 ml of fluid)
2	Inspection, palpation and percussion	Moderately distended
3	Inspection, palpation and percussion	Grossly or markedly distended

sympathetic nervous system. In turn, it will change angiotensinogen (made in the liver) to angiotensin-I which is further converted to angiotensin-II by angiotensin converting enzyme (ACE) in the lungs. Angiotensin-II has various important functions that drive fluid accession and retention, including stimulation of the thirst drive, release of aldosterone from the zona glomerulosa of the adrenal cortex, and the secretion of vasopressin from the posterior pituitary. Pathophysiology of ascites is clearly shown in figure 1 (Teirstein *et al.*, 2005; Garcia-Tsao, 2011; Henriksen and Møller, 2005; Llach *et al.*, 1988).

The development of ascites, in cirrhotic patients, marks the transition from compensated to decompensated cirrhosis. Accumulation of ascitic fluid in cirrhosis results from different factors broadly defined in terms of cytokine and hormonal dysregulation and associated volume overload in the context of portal hypertension (Ginés *et al.*, 1987).

The presence of ascites leads to the progression of cirrhosis. It is also the most common cause for hospital admissions and thus increases unpredicted cost; it increases 1-year mortality and functions as a risk for orthotopic liver transplantation (OLT). In portal hypertension, the major cause of ascites is Cirrhosis (85%). Other causes of ascites (non-cirrhotic) can be widely defined as pre- or post-hepatic in origin (Moore and Thiel, 2013).

Extra-hepatic causes of ascites

Although cirrhosis is the main cause of ascites in majority of the patients, however almost 15% have a cause other than liver disease, which can be cancer, cardiac failure, nephrotic syndrome or tuberculosis. Approximately 5% of patients with ascites have mixed ascites demonstrated by 2 or more underlying causes of ascites formation. Such patients have cirrhosis plus 1 other cause *i.e.*, peritoneal carcinomatosis or peritoneal tuberculosis. Many patients with inexplicable ascites are finally found to have 2 or even 3 causes for ascites formation (*e.g.*, heart failure, diabetic nephropathy, and cirrhosis due to non-alcoholic steatohepatitis). In this setting, the aggregate of predisposing factors can lead to sodium and water retention when every individual factor might not be severe enough to cause surplus fluid (Runyon *et al.*, 1992).

Ascites may be due to multiple reasons other than the liver diseases or portal hypertension, thus can be ruled out by the laboratory testing and imaging. As in case of chronic pancreatitis with associated pseudocyst and internal fistulae formation, major fluid can directly enter into the peritoneal cavity and appearing as abdominal distention with pain. In general, raised ascitic fluid amylase level, found on diagnostic paracentesis, is a firm diagnostic for this category. The physician might be troubled with the diagnosis in a patient with a compelling history of steatorrhea, alcohol use and chronic pancreatitis. Particularly, the serum-ascites albumin gradient (SAAG) is a helpful tool for differentiating ascites-associated disease processes caused by portal hypertension (*e.g.* cirrhosis), from the many other nonportal hypertensive

Table 2: Possible causes of ascites (Marthadu, 2014).

Source	Cause
Hepatic Source	Cirrhosis
	Alcoholic Hepatitis
	Budd-Chiari Syndrome
	Sinusoidal Obstruction Syndrome
Extra-Hepatic Source	Heart Failure
	Nephrotic Syndrome
	Pancreatitis
	Myxedema
	Cancer related (peritoneal metastases, massive liver metastases, etc.)
Mixed Source	Ascites that results from combination of 2 or more causes

causes of ascites. A SAAG value ≥ 1.1 g/dL strongly reinforce (97% sensitivity) in the diagnosis of portal hypertension as a cause (Becker *et al.*, 2006).

Malignant Ascites

Malignant ascites, which is found in 10% of cases, is commonly because of peritoneal metastasis in neoplastic disease, but it is more common with ovary, breast, gastric, pancreatic, bronchus or colon cancer. Almost in 20% of cases with malignant ascites tumor is of unknown origin and mostly protein content is high in malignant ascites (Becker *et al.*, 2006).

Pathogenesis of Ascites

Besides its well-known demonstration, the pathogenesis of ascites remains unclear and continues to evolve. A hybrid theory currently predominates, which up rise from the “overflow” and “underfill” theories of the past generation. A brief adumbrate of these views suggests that the continuous injury to the liver as a combination of both exogenous factors, like viral or non-alcoholic steatohepatitis (NASH) or chronic alcohol injury; in the setting of an appropriate genetic disposition; and continued micro-processes of inflammation, collagen deposition/regeneration and necrosis, all conspiring to transubstantiate the liver from a low-resistance to a high-resistance system, like a spectrum of fibrosis with vascular smooth muscle dysfunction. These collective processes can lead to increased pressure in the portal vein, leading to portal hypertension (Moore and Thiel, 2013). Sequence of events for the hypothesis of ascites formation can be seen in table 3.

Usually, in rest condition when the peritoneal cavity is relaxed, it has a pressure of about 5-10 mmHg, which has almost 25-50 mL of serous fluid. The serous fluid normally provides a low resistance film over which bowel can move past each other and further hydrates the serosal surfaces maintaining suppleness and haleness. The maximal absorption of fluid out of the peritoneum is approximately 850 mL/d in the most effective circumstances. Peritoneal dialysis works under the theory of selective filtration, and it can be observed effective filtration is altered by modifications in the properties of

Table 3: Sequence of events for the hypothesis of ascites formation (Garcia-Tsao, 2011).

Event	Underfill/ peripheral arterial vasodilatation theory	Overfill theory
Primary event	Vascular	Renal
Secondary event	Renal	Vascular

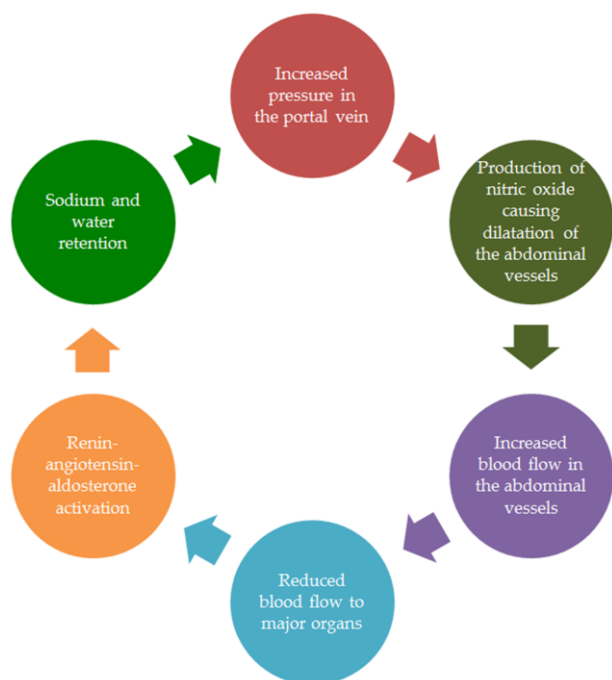


Figure 1: Pathophysiology of ascites (Fullwood and Purushothaman, 2014).

the peritoneal surface area or lymphatic system, either due to fibrotic or infectious, or by some inflammation or mechanical processes. Hence, continued impairment of physiological system can lead to profound ascitic fluid retention (Moore and Thiel, 2013).

DETECTION OF ASCITES

Identification of mild ascites is difficult, but abdominal distension is the clear indication of severe ascites. Patients suffering from ascites generally complaints about pressure and abdominal heaviness, as well as shortness of breath, because of the diaphragm mechanical impingement occur. Physical examination of the abdomen is a useful parameter for determining ascites, as there is visible “flank bulging” and “shifting dullness” in the reclining patient, or “fluid wave” or “fluid thrill” in the massive ascites (Runyon, 2009). Assessment of shifting dullness is also shown in figure 2.

The appearance of a full, bulging abdomen should lead to percussion of the flanks. One should test for “shifting”, if the amount of flank dullness is higher than usual. Around 1,500 mL of fluid must be present before flank dullness is detected. The patient has less chance of having ascites (10%), if flank dullness is not detected. The fluid wave and puddle sign are not helpful. Ascites due to alcoholic cardiomyopathy can replicate that due to alcoholic cirrhosis. Jugular venous distension is shown in the former but not in the latter. The physical examination for detecting ascites in the obese patient is difficult. An abdominal ultrasound may be needed to determine with surety if fluid is present (Cattau *et al.*, 1982).

Fluid due to portal hypertension can be promptly differentiated from fluid due to other causes. Also, in view of the high incidence of ascitic fluid infection at the time of admission to the hospital, an admission vigilance tap may detect unpredictable infection (Runyon *et al.*, 1992; Pinzello *et al.*, 1983).



Figure 2: Assessment of shifting dullness (Fullwood and Purushothaman, 2014).

SIGNS AND SYMPTOMS OF ASCITES

The most prevalent symptoms are increased abdominal girth (the patient notices tightness of the belt or garments around the waist) and latter weight gain. As fluid continues to amass, it leads to elevation of the diaphragm that result in shortness of breath. Fluid aggregation may also be related with a feeling of satiety and generalized abdominal pain. Ascites can be distinguished from obesity, as the onset of symptoms in ascites is fast, while obesity develops from a period of months to years (Simel *et al.*, 1988).

Depending on the underlying etiology, other signs and symptoms may also be present. For example, patients having ascites as a result of portal hypertension (may be due to fibrosis or cirrhosis of liver) may complain of gynecomastia, hematemesis, leg swelling, bruising or due to encephalopathy mental changes can also occur. Patients complaint of weight loss or chronic fatigue, when the cause of ascites is cancer (peritoneal carcinomatosis). Heart failure may also be a cause of ascites causing exercise intolerance, shortness of breath and wheezing in patients (Warrell *et al.*, 2003).

DIAGNOSIS OF ASCITES

Tests of liver enzymes, coagulation, basic metabolic profile and routine complete blood count (CBC) should be performed for the diagnosis of ascites. Most of the experts suggest that if the ascites is newly developed or if the patient is hospitalized, then paracentesis should be performed as a diagnostic tool. The fluid is then analyzed for its gross appearance, albumin, protein level, and cell counts (red and white) (Warrell *et al.*, 2003).

On the basis of physical examination and history, the assumption is made on the diagnosis of newly onset ascites. Ultrasound and successful abdominal paracentesis then confirms this diagnosis. Physical examination, past record and ascitic fluid analysis determines the cause of ascites formation. Generally, some other tests may also be needed. Moreover, the liver is routinely imaged commonly with ultrasound to in order to make diagnosis for hepatocellular carcinoma, portal vein thrombosis and hepatic vein thrombosis. The most economical and speedy method for diagnosis of etiology of ascites is abdominal paracentesis with adequate ascitic fluid examination (Runyon, 1994; Runyon *et al.*, 2002).

Various Turkish, South African and local studies divulge that the major co-morbid of ascitic patients were fever, abdominal pain, night sweats, weight loss, abdominal swelling, clubbing and palmer erythema (Muhammed *et al.*, 2012)

Table 4: Treatment options for patients with ascites and cirrhosis (Runyon, 2009).

First Line	Second Line	Third Line
<ul style="list-style-type: none"> ➤ Cessation of alcohol use, when present ➤ Sodium restricted diet and diet education ➤ Dual diuretics, usually spironolactone and furosemide, orally with single daily dosing ➤ Discontinue non-steroidal anti-inflammatory drugs ➤ Evaluation for liver transplantation 	<ul style="list-style-type: none"> ➤ Discontinue beta blockers, angiotensin converting enzyme inhibitors and angiotensin receptor blockers ➤ Consider adding midodrine especially in the profoundly hypotensive patient ➤ Serial therapeutic paracentesis ➤ Evaluation for liver transplantation ➤ Transjugular intrahepatic portosystemic shunt (TIPS) 	<ul style="list-style-type: none"> ➤ Peritoneovenous shunt

MANAGEMENT OF ASCITES

Ascites is generally treated while an underlying cause is known, in order to prevent complications, relieve symptoms, and prevent further advancement. In those patients having mild ascites, therapy is usually given as an outpatient. The major aim of the therapy should be weight loss of not higher than 1.0 kg/day for patients having both ascites and peripheral edema and not greater than 0.5 kg/day for patients having ascites alone. In patients with severe ascites causing a tense abdomen, hospital admission is generally imperative for paracentesis (Ginès *et al.*, 1987). Treatment options for patients with cirrhosis and ascites are depicted in table 4.

First-line treatment

The basic treatment guideline for the patients with ascites and cirrhosis is education with respect to dietary sodium (which should not be more than 2000 mg per day [88 mmol per day]) and oral diuretics. When alacrity of weight loss is less than desired, urinary sodium excretion measurement is a useful parameter to follow (Runyon, 1994; Runyon *et al.*, 2002).

Ascites can be speedily mobilized with severe sodium restriction, but it is not suggested as it is less palatable and may further worsen the malnutrition that is usually present in these patients as weight change and fluid loss are directly linked with the balance of sodium in patients with ascites caused by portal hypertension. Sodium restriction is responsible for weight loss, not fluid restriction, as sodium is followed by fluid passively. Random specimens are less informative in determining the rate of sodium excretion, as compared to twenty-four-hour collections of urine; however, full-day collections are cumbersome. Men suffering from cirrhosis should excrete creatinine not less than 15 mg/kg of body weight per day, and women should excrete not less than 10 mg/kg per day. Less creatinine indicates insufficient collection. In afebrile patients with cirrhosis without diarrhea, the overall sodium excretion (non-urinary) is less than 10 mmol per day. One of the aims of treatment is to enhance excretion of sodium in urine; so that it exceeds 78 mmol per day (if intake is 88 mmol per day then non-urinary excretion should be 10 mmol per day). Only 10% to 15% of patients who are suffering from spontaneous natriuresis exceeding 78 mmol per day can be acknowledged for sodium restriction in diet alone (*i.e.*, without diuretics) (Garg *et al.*, 2011; Eisenmenger *et al.*, 1949).

Fluid restriction is not necessary in treating most patients with ascites and cirrhosis. The chronic hyponatremia usually present in cirrhotic ascites patients is sometimes morbid unless it is immediately corrected at the time of liver transplantation in the operating room. A study of 997 patients with ascites and cirrhosis showed that the sodium level in serum is not greater than 120

mmol/L in only 1.2% of patients and not higher than 125 mmol/L in only 5.7%. In this setting, a try to rapidly correct hyponatremia with hypertonic saline can cause severe complications as compared to hyponatremia itself (Eisenmenger *et al.*, 1950; Abbasoglu *et al.*, 1998).

Salt restriction

The initial treatments in high SAAG ("transudate") are Salt restriction, which allows diuresis (production of urine) as the patient now has more fluid than salt concentration. Salt restriction is fruitful in about 15% of patients (Gatta *et al.*, 1991).

Use of diuretics

As dietary salt restriction is the basic approach in the treatment, and aldosterone is the hormone that tends to increase salt retention, so a medicine that counterbalances aldosterone should be used. Spironolactone is the drug of choice as it blocks the aldosterone receptor in the collecting tubule. This choice has been affirmed in a randomized controlled trial. Dose of diuretics for ascites should be once daily (Fogel *et al.*, 1981).

Diuretic Regimen: Oral Spironolactone and furosemide are given as a single morning doses in the normal diuretic regimen, starting with 100 mg of the spironolactone and 40 mg of furosemide. Formerly, single-agent spironolactone was recommended, but hyperkalemia and the long half-life of spironolactone have limited its use as a single agent only in patients with minimal fluid overload. In a randomized control trial the use of furosemide as a single agent has been demonstrated to be less efficacious than spironolactone. Another randomized trial showed that only spironolactone should be used, while furosemide can be added only when patients are refractory. The time to mobilization of moderate ascites is shortened when initial treatment is given in combination, as demonstrated in another randomized trial. However another randomized trial indicates that initial combination treatment shortens the time to mobilization of moderate ascites. Most patients need combination treatment eventually. A study was performed which is said to be the largest involving a total of 3860 patients with both ascites and cirrhosis, in which combination therapy was given from the beginning. For maintaining normokalemia and achieving rapid natriuresis, the preferred approach was to initiate the therapy with both drugs. Amiloride (10-40 mg per day) can be used in place of spironolactone in patients with tender gynecomastia. Nonetheless, amiloride is more expensive and has been shown to be less effective than an active metabolite of spironolactone in a randomized controlled trial. For the treatment of ascites metolazone, triamterene and hydrochlorothiazide have also been used. While using the combination of spironolactone and furosemide,

Table 5: Complications, symptoms and proposed treatment of ascites (Fullwood and Purushothaman, 2014).

Complications	Symptoms	Treatments
Spontaneous bacterial peritonitis	Abdominal pain, fever. May be asymptomatic.	Antibiotic administration. Large volume paracentesis should be withheld until infection is treated effectively.
Dilutional hyponatraemia	Increased peripheral oedema and re-accumulation of ascites.	Fluid restriction may be instigated if sodium is <130mmol/L, but should be used with caution
Hepatorenal Syndrome	Reduced renal function, raised creatinine in the absence of infection, shock or use of nephrotoxic drugs.	Administration of the vasoconstrictor terlipressin in combination with albumin. Liver transplantation.
Pleural effusion	Shortness of breath increased respiratory rate, reduced air entry.	Chest drains are contraindicated for this cause of pleural effusion. First-line treatment includes diuretic administration and reduced sodium diet.
Umbilical hernia	Swelling of the area around the umbilicus. May be associated with abdominal pain or discomfort.	May require surgical intervention depending on the severity of the hernia.

hyponatremia can rapidly develop if hydrochlorothiazide is added; so it should either be avoided or used with extreme caution. In the largest, multicenter, randomized controlled trial performed in patients suffering from ascites, dietary sodium restriction and a dual diuretic regimen with spironolactone and furosemide has been shown to be useful in more than 90% of patients in accomplishing a reduction in the volume of ascites to satisfactory levels (Angeloni *et al.*, 2003).

Diuretics and albumin: A non-blinded randomized controlled trial in patients suffering from new onset ascites showed that 25 g infusions of albumin weekly, if given for 1 year preceded by infusions every 2 weeks enhanced survival related to diuretics alone (Wong *et al.*, 2012).

Treatment based on the cause of Ascites

Treatment of ascitic patients depends on the cause of fluid accumulation. The SAAG can be helpful in identifying as well as in ruling regarding treatment. Patients with low SAAG (<1.1 g/dL) ascites normally do not have portal hypertension and, with the omission of nephrotic syndrome, that do not answer to salt restriction and diuretics. In contrast, patients with a higher SAAG (>1.1 g/dL) have portal hypertension and usually are amenable to these measures. Liver injury due to alcohol intake is one of the most volatile causes of liver disease that leads to high SAAG ascites. Stopping alcohol intake is one of the useful steps to treat the underlying cause in this clinical setting. With self-restraint and time ascites may become more responsive to medical therapy (Runyon, 2002; Angeloni *et al.*, 2003).

Mechanical Methods

If a patient is resistance to or shows poor response to diuretic therapy, then ultrafiltration or aquapheresis may be needed to achieve adequate control of fluid retention and congestion. The adoption of aforesaid mechanical methods of fluid removal can produce significant clinical benefits in patients with diuretic resistance and may restore responsiveness to conventional doses of diuretics. Water restriction may be needed if hyponatremia (<130 mmol per liter) develops (Hunt *et al.*, 2005; Ginès *et al.*, 2004).

Therapeutic Paracentesis

In patients having severe (tense) ascites, therapeutic paracentesis may be required. Albumin may sometimes be given intravenously in the amount equal to the proportion of ascites removed, as this method may

decline serum albumin levels in blood (Salerno *et al.*, 1987).

Site for Paracentesis: In the past, the midline was usually selected as the site for paracentesis. Nonetheless, the abdominal wall in the left lower fourth (quadrant), 2 fingerbreadths cephalad and 2 fingerbreadths medial to the anterior superior iliac spine, which has been delineated to be narrow and with a greater pool of fluid as compare to the midline. If the fluid is not easy to localize by examination because of obesity, ultrasonography can be helpful (Sakai *et al.*, 2002).

Complications of Mechanical Methods: Even though older published series indicated a relatively high disease rate, and even death rate, when trocars were used for paracentesis, while in the recent studies no deaths or infections caused by paracentesis has been documented as the complication of paracentesis in patients with ascites. Although 71% of the patients show abnormal prothrombin time, however, in only 1% of the patients, complications were detected. Although more serious complications (hemoperitoneum or bowel entry by the paracentesis needle) occur, they are sufficiently bizarre (<1/1,000 paracenteses) that they should not diminish performance of this procedure. It is the common practice of some physicians to administer routinely blood products to cirrhotic patients with coagulopathy before performing paracentesis. This practice is not evidence-supported. The costs and risks of preventative transfusions surpass the benefit (Runyon, 1986; Webster *et al.*, 1996).

Contraindications for performing Paracentesis: There are few contraindications while performing paracentesis. Coagulopathy should prevent paracentesis exclusively when there is clinically noticeable fibrinolysis or clinically obvious distributed intravascular coagulation. These situations occur in less than 1 per 1,000 procedures. There is no evidence-supported shut-off of coagulation parameters beyond which paracentesis should be prevented (Runyon, 1986).

Use of Shunts

In small number of patients suffering from advanced cirrhosis and have recurrent ascites, shunts may be used. Commonly used shunts are peritoneovenous shunt, portacaval shunt, and the transjugular intrahepatic portosystemic shunt (TIPS). Nevertheless, none of these shunts has been shown to extend life assurance, and are considered to be the link to liver transplantation. A meta-analysis of randomized controlled trials by the interna-

tional Cochrane Collaboration agreed that "TIPS was more effective at removing ascites as compared with paracentesis, nonetheless, TIPS patients establish hepatic encephalopathy significantly more often" (Saab *et al.*, 2006).

Culturing bacteria for infection detection

Bacterial culture should be performed if ascitic fluid infection is suspected *i.e.*, fever, unexplained encephalopathy or abdominal pain. To identify neutrophils urine dipstick can also be used which hardly takes 90 seconds to minutes. Manual cell count can be replaced by automated cell counting in order to have more accurate and speedy results (Castellote *et al.*, 2003; Eisenmenger *et al.*, 1950).

It has been concluded from multiple prospective trials that when the polymorphonuclear leukocyte (PMN) count was more than or equal to 250cells/mm³ in the ascitic fluid was cultured by previous method, then the bacterial growth occurs in almost 50% of the cases in comparison to the ascitic fluid being inoculated into blood culture bottles at the patient's bedside was 80% (Angeloni *et al.*, 2003).

Usefulness of Baclofen

Baclofen has been shown in a randomized trial, which included only patients with alcoholic liver disease, to decrease alcohol craving and alcohol consumption; it can be given at a dose of 5 mg orally *tid* for 3 days and then 10 mg *tid*. Ascites in decompensated hepatitis B cirrhosis and autoimmune hepatitis can also have a dramatic response to specific treatment. Liver diseases other than alcohol-related, hepatitis B and autoimmune hepatitis are less reversible; by the time ascites is present, these patients may be perfect served by referring for liver transplantation opinion rather than protracted medical treatment (Bruce *et al.*, 2009; Addolorato *et al.*, 2007).

Use of vaptans

Vaptans are a relatively new class of drugs (the vasopressin receptor antagonists) and have been studied predominantly in heart failure but also in the setting of cirrhosis. The most recent oral agent, satavaptan, was especially studied to find its efficacy in treating ascites rather than hyponatremia and was found to be "not clinically useful in the long-term treatment of ascites in cirrhosis" in a study including 1200 patients having cirrhosis. Satavaptan was also associated with higher mortality in comparison to placebo. These drugs can raise thirst (Sterns, 1987; Wong *et al.*, 2003).

Bed rest

Unfortunately, many drugs that have theoretical promise in managing ascites, *e.g.*, angiotensin-converting enzyme inhibitors, have been shown to exacerbate hypotension and have not been clinically helpful. Severe hyponatremia does ensure fluid restriction in the patient with cirrhosis and ascites; nonetheless, there is no evidence-supported specific threshold for initiating fluid restriction and no data-supported level of restriction. Although it is traditional to recommend bed rest (based on extrapolation from heart failure), this is illogical and there are no controlled trials to support this practice. Upright posture may worsen the plasma renin elevation found in patients with cirrhosis and ascites. Theoretically, this may increase sodium cupidity. This theoretical interest would have to translate into clinically relevant outcomes before bed rest could be advised (Schrier *et al.*, 2006).

COMPLICATIONS

However, some patients with cirrhosis and ascites also have hepatic encephalopathy, gastrointestinal hemorrhage, bacterial infection, hypotension, azotemia, and/or hepatocellular carcinoma, and may need hospitalization for determinate diagnosis and management of their liver disease as well as management of their fluid overload. Diuretics should be retained in the setting of active gastrointestinal bleeding, hepatic encephalopathy or renal dysfunction. Frequently, intensive education is required to ensure patient understanding that the diet and diuretics are actually effective and worth the effort. There is no limit to the daily weight loss of patients who have significant edema. Once the edema has resolved, 0.5 kg is probably a sensible daily maximum. In the past, patients with ascites frequently occupied hospital beds for prolonged periods of time because of confusion regarding diagnosis and treatment and because of iatrogenic problems (Angeloni *et al.*, 2003).

As, the ultimate aim is to have no clinically identifiable fluid in the abdomen; but it is not significant for getting discharge from the hospital. Patients, who are now stable, with ascites as their main problem, can be released from the clinic after it has been found that they are responding to their medical regimen. Liver transplantation should be considered in the treatment options of patients with ascites. Once patients become fractious to routine medical therapy, 50% die within 6 months and 75% die within 1 year. Referral should not be delayed in patients with refractory ascites (Angeloni *et al.*, 2003).

In patients with ascites possible associated complications are spontaneous bacterial peritonitis (a life-threatening infection of the ascites fluid), hepatorenal syndrome (kidney failure), weight loss and protein malnutrition, mental confusion, coma (hepatic encephalopathy) or change in the level of alertness, and other complications related to liver cirrhosis (Mehta and Rothstein, 2009). Table 5 highlights some of the complications of ascites.

The most frequent decompensating event is the development of ascites in cirrhosis. Splanchnic and peripheral vasodilatation is the most common etiological factors causing ascites and leading to a decrease in effective volume of blood. When talk about the usual development of ascites, it is firstly a compensated event, in which patient responds to diuretics, then becoming resistant to its use, developing hyponatremia and finally leading to hepatorenal syndrome. Most patients respond to diuretics. Patients who no longer react should be managed with repeated large - volume paracenteses. Transjugular intrahepatic portosystemic shunt (TIPS) should be considered in those requiring frequent paracenteses. Fluid restriction is suggested in patients with hyponatraemia. Vasoconstrictors may revert hepatorenal syndrome and are useful as a bridge to liver transplantation. Ascites itself is not lethal unless it gets infected (spontaneous bacterial peritonitis). Infection often increases the hepatorenal syndrome leading to mortality. Antibiotic preventability is indicated for secondary prophylaxis of spontaneous bacterial peritonitis and in high - risk patients (Garcia-Tsao, 2011).

CONCLUSION AND RECOMMENDATIONS

Ascites is a lethal disease, which is common all over the world. Its early detection is required to ensure effective management without any complications. It may be due to hepatic or extra-hepatic causes. Treatment depends upon the cause of the ascites. Dietary sodium restriction and

diuretics remains the first line therapy for its management. Ascites itself is not fatal, unless it becomes infected. So, awareness regarding this disease should be provided to the people.

Recommendations:

- Dietary salt should be restricted to a no-added salt diet of 90 mmol salt/day (5.2 g salt/day)
- Proper prognosis should be made before starting the treatment, in order to get optimal therapeutic outcome.
- In renal compromised patients, before performing dialysis certain hygienic parameters should be kept in mind by the patients like to wash hands (including fingernails), before touching the catheter. Cleaning the skin around the catheter daily. Following doctor's instructions regarding the care and storage of medical supplies.
- Treatment must begin promptly after diagnosis in order to avoid serious and potentially fatal complications.
- Laboratory examinations should be performed on periodic basis to check the disease progression and therapeutic effectiveness.
- Due to compromised liver function unnecessary medications should be avoided
- Therapeutic drug monitoring (TDM) should be performed for the drugs having narrow margin of safety
- Pharmacist should counsel the patients regarding the potential side effects of the therapy, proper use and duration of therapy for the optimal outcome.
- Pharmacist should counter check the prescription before handing to the patient.
- Pharmacist should actively participate in patient awareness programs regarding Ascites.

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