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A Study on Hyponatremia in Decompensated Liver Disease

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Abstract
Background: *Chronic liver disease occurs throughout the world irrespective of age, sex, region or race. Cirrhosis is an end result of a variety of liver diseases characterized by fibrosis and architectural distortion of the liver with the formation of regenerative nodules and can have varied clinical manifestations and complications. Hyponatremia is a frequent complication of advanced cirrhosis related to impairment in the renal capacity to eliminate solute-free water, that causes retention of water which is disproportionate to the retention of sodium, thus causing a reduction in serum sodium concentration and hypo-osmolality. Hyponatremia in cirrhosis is associated with increased morbidity and mortality. There is evidence suggesting that hyponatremia may affect brain functions and predisposes to hepatic encephalopathy. Hyponatremia also represents a risk factor for liver transplantation as it is associated with increased frequency of complications and impaired short-term survival after transplantation.*
Materials and Methods: *This is a prospective study, conducted by Department of general medicine, Kanyakumari Government Medical College. The study period was from jan 2016 to jan 17. Informed consent obtained from the patients regarding the study.*
Observation and Results: *In this study, a total of 100 patients with decompensated liver disease were included. Among the 100 patients, 80 were males and 20 were females. Among this 67% of the patients were Alcoholics. 11 patients found to be HBsAg positive, 7 patients found to be Hep C Positive, 15 were cryptogenic. In this study, 70% of the patients were found to have hyponatraemia.*
Conclusion: *Hyponatremia is very common in patients with cirrhosisand the routine correction of asymptomatic hyponatremia is not recommended. The main indications for correction of hyponatremia are presence of neurologic symptoms that might be due to hyponatremia and serum sodium less than 120 mEq/L. Liver transplantation is the only definitive treatment for end stage liver diseases.*

Introduction

Global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5% of the general population. Hence, we estimate that more than fifty million people in the world, taking the adult population, would be affected with chronic liver

disease. Globally, alcohol, NASH and viral hepatitis currently are the most common causative factors. Hyponatremia is a common finding in patients with decompensated cirrhosis due to an abnormal regulation of body fluid homeostasis. Recent studies extended these observations and showed that hyponatremia is an important marker of prognosis in both the pre transplant and post-transplant setting. Hyponatremia in cirrhosis is currently defined as a decrease in serum sodium below 130mmol/L. The prevalence of hyponatremia, as defined by serum sodium < 130 mmol/L, is 21.6%. If the cut-off level of 135mmol/L is used, the prevalence increases up to 49.4%. Patients with cirrhosis may develop two types of hyponatremia. In some patients, hyponatremia is due to important losses of extracellular fluid, most commonly from the kidneys (because of overdiuresis due to treatment with excessive doses of diuretics) or from the gastrointestinal tract. This condition, known as *hypovolemic hyponatremia*, is characterized by low serum sodium associated with decrease in plasma volume, lack of edema and ascites, signs of dehydration, and prerenal renal failure. Hepatic encephalopathy is a common finding, probably because of the effects of a rapid reduction of serum osmolality on brain function. In contrast to hypovolemic hyponatremia, in most patients with cirrhosis, hyponatremia develops in the setting of expanded extracellular fluid volume and plasma volume with ascites and edema. This condition is known as *hypervolemic* or *dilutional hyponatremia* and is due to a marked impairment of renal solute–free water excretion, resulting in disproportionate renal retention of water with respect to sodium retention. Both conditions differ markedly with respect to volume status. In hypovolemic hyponatremia, the actual plasma volume is reduced, and there is also a reduction in the total extracellular fluid volume with a lack of ascites and edema. In hypervolemic hyponatremia, plasma volume is increased in absolute values but is low with respect to the marked vasodilation of the arterial circulation, a condition known as effective arterial hypovolemia and the total extracellular fluid volume is increased, with as cites and/or edema.

Materials and Methods

In our study, we concentrate on the prevalence and etiopathogenesis of chronic liver disease and hyponatremia. The study was conducted among the patients admitted in the wards of general medicine during jan 2016 – jan 2017.

Results

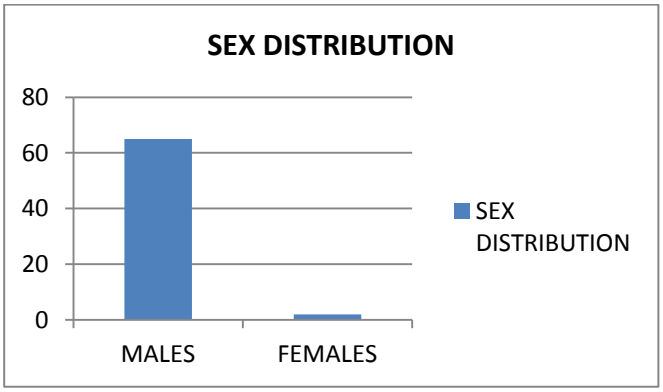
Of the total 100 cases, 80 were males (80%) and 20 were females (20%).

Among the 100 patients, 67% were Alcoholic liver disease. Among Non-Alcoholic causes, 11% were HBsAg positive cases, 7% were Hep C positive cases and 15% were cryptogenic.

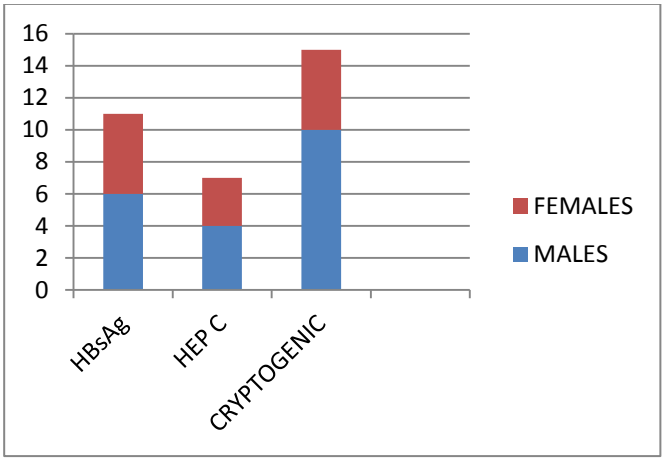
Hyponatremia is found in about 70% of the patients.

Sex Distribution

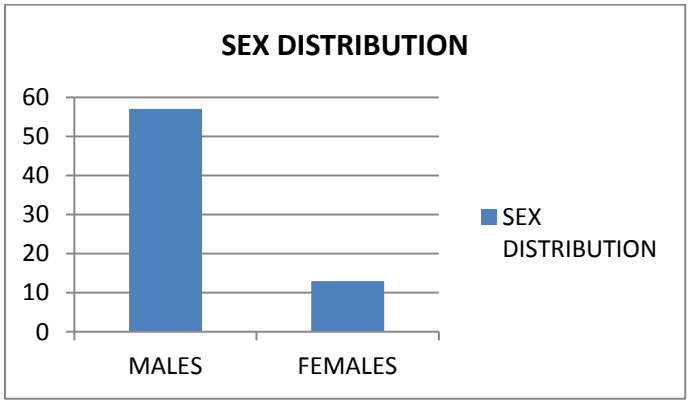
In Alocoholic Liver Disease



In Non-Alcoholic Liver Diseases



Hyponatremia

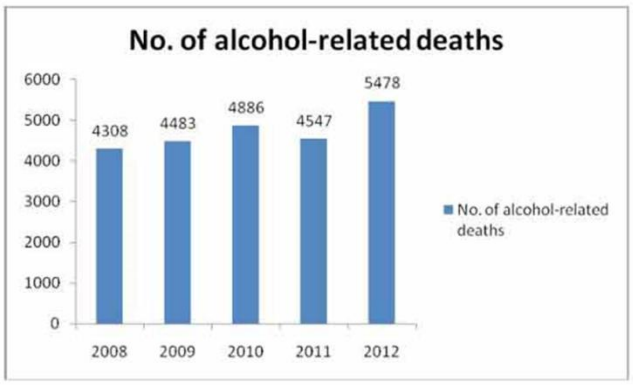


Discussion

Alcohol

According to the WHO, alcohol consumption accounts for 3.8% of the global mortality and 4.6% of DALYs. Liver disease represents 9.5% of alcohol-related DALY's worldwide. In India, alcohol is emerging as the commonest cause of chronic liver disease.

Exhibit 1: Total number of alcohol –related deaths in India



Source: NCRB

Cryptogenic

Most of these patients have underlying diabetes and obesity similar to that of patients with NASH, and represents end-stage NASH. Also, a fraction of cryptogenic cirrhosis cases may represent Autoimmune Hepatitis (AIH) in a "burnt-out" stage.

Viral Hepatitis

Viral hepatitis is a global public health problem, particularly in resource-poor countries. It is estimated that complications of HBV or HCV infection led to nearly 1.4 million deaths in the year 2010. India has "intermediate to high endemicity" for Hepatitis B surface antigen and an estimated 40 million chronic HBV infected people, constituting approximately 11% of the estimated global burden. Population prevalence of chronic HBV infection in India is around 3-4 %.Chronic HBV infection account for 40-50% of HCC and 10-20% cases of cirrhosis in India.

Importance of Hyponatremia

Hyponatraemia has been shown to be an independent predictor of poor outcomes in cirrhosis and is often associated with refractory ascites, spontaneous bacterial peritonitis, and hepatic encephalopathy[1]. The most important factor in determining the severity of neurologic symptoms in patients with hyponatremia is the sudden onset of fall in the serum sodium rather than the absolute reduction of serum sodium level. Hence, patients with cirrhosis and hyponatremia are less likely to have severe neurologic symptoms. However, hyponatremia may also cause cerebral edema and astrocyte swelling, along with increase intracellular glutamine concentration, thereby precipitating hepatic encephalopathy[8].

Low serum sodium has been shown to have a negative impact on the quality of life in patients with cirrhosis and ascites. A recent cross-sectional study of 523 patients with cirrhosis complicated by ascites demonstrated that health-related quality of life (HRQL) was significantly decreased in patients with hyponatraemia and serum sodium less than 130 mEq/L[7].

Serum sodium and the Model for End-stage Liver Disease (MELD) score have both been shown to predict mortality in patients with advanced cirrhosis on the liver transplant waiting list. Combining serum sodium with MELD (MELD-Na) was shown to more accurately predict mortality on the waiting list, compared with MELD score alone. This was particularly true in patients with lower overall MELD scores[3]. Patients awaiting liver transplant with hyponatraemia have also been shown to have poorer outcomes when compared with normonatremic controls. Using data derived from the Organ Procurement

and Transplantation Network, Kim *et al.* developed and validated a survival score that included serum sodium in the model for end-stage liver disease (MELD-Na). Serum sodium was found to independently predict mortality with an HR of 1.05 per mmol decrease in serum sodium between 125 mmol/L and 140 mmol/L[3,5].

Spontaneous bacterial peritonitis (SBP) is often associated with significant morbidity, including renal failure, and has a high mortality rate in published series[2]. Patients with hyponatraemia at diagnosis of SBP are at much higher risk for development of hepatorenal syndrome and death. Hepatic encephalopathy has been shown in several studies to be worsened by the presence of hyponatraemia. The brain is uniquely adapted to counteract the effects of hyponatraemia. In situations of low extracellular osmolality, water will flow from the extracellular compartment down the osmotic gradient into astrocytes, causing oedema. This depleted state may predispose patients to worsening hepatic encephalopathy and astrocyte swelling with oxidative stress in the setting of hyponatraemia[9]. Other studies have also identified hyponatremia to be a risk factor for increased morbidity and mortality after liver transplantation.

The first step in management should be to identify and correct the underlying cause of hyponatraemia, which includes holding diuretics and addressing gastrointestinal losses. Hypovolemic hyponatremia should be treated with fluid resuscitation to restore the circulatory volume and withdrawal of the precipitating factor. Rapid correction of serum sodium may lead to serious neurological complications such as central pontine myelinolysis or seizures. Treatment for hyponatremia is indicated when the serum sodium is less than 120 meq/L or the patient has neurologic symptoms that might be due to hyponatremia.

Patients who are found to be hypovolemic should be adequately resuscitated with intravenous crystalloid or albumin infusion[4,6]. Fluid restriction should be considered if the patient has neurologic symptoms that might be due to hyponatremia or when the serum sodium is less than 120 mEq/L, which occurs in about 1% of patients with cirrhosis.

Hypertonic saline

In the setting of severe hyponatraemia with symptoms such as seizure, one must consider correction to a safe level, so as to prevent recurrence and neurological injury. This is the one situation where the administration of hypertonic saline is advised, with care taken to avoid overly rapid correction. However, the use of hypertonic saline in cirrhotic patients can lead to worsening ascites and oedema secondary to the sodium avid state that exists in the nephron, and should be used only in acute situations.

Conclusion

Low serum sodium is a poor prognostic indicator in both the pre- and post-transplant patient population and has been shown to increase the risk of early mortality and complications that include infections, renal failure, and encephalopathy. Hyponatremia is very common in patients with cirrhosis and the routine correction of asymptomatic hyponatremia is not recommended. The main indications for correction of hyponatremia are presence of neurologic symptoms like seizures etc., and serum sodium less than 120 mEq/L. Administration of hypertonic saline may be considered in a monitored setting to correct profound hyponatremia (serum sodium < 110 mEq/L) and in the immediate pre-liver transplant period to prevent the risk of osmotic demyelination syndrome. Liver transplantation remains the only definitive treatment for end-stage liver disease complicated by hyponatraemia.

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