Original Research Article

Clinical profile of hepatorenal syndrome: a prospective study

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ABSTRACT

Background: *Hepatorenal syndrome is the development of renal failure in patients with advanced liver cirrhosis, occasionally fulminant hepatitis, who have portal hypertension and ascitis in the absence of some other kidney disease.*

Objective*: To study the clinical profile of hepatorenal syndrome.*

Methods: *All patients of chronic liver disease with renal involvement were studied and patients fulfilling the criteria of hepatorenal syndrome were recruited in the study. The etiology, clinical presentation, morbidity and outcome of patients were recorded. Various variables were studied between survivor group and non survivor group to detect possible predictors of non survival in hepatorenal syndrome. The data was analyzed using SPSS software.*

Results: *42 patients of hepatorenal syndrome were clinically evaluated. 95% were males and 5% females with mean age of 50.29±8.87 in survivor group and 45.92±10.1 in non survivor group. High level of serum bilirubin, hepatic encephalopathy, decreased level of albumin, hyponatremia and coagulopathy were significant in non survivor group as compared to survivor group.*

Conclusion: *The poor prognostic factors were found to be ascites, severe jaundice, hepatic encephalopathy, alcohol abuse, hypoalbuminemia, progressive renal failure and child pugh score greater than 10. Thus hepatorenal syndrome is decompensated cirrhosis which needs judicious treatment especially using terlipressin and albumin.*

Keywords: *Hepatorenal syndrome, profile, jaundice, child pugh score, ascitis, albumin*

Introduction

Hepatorenal syndrome is a clinical condition that occurs in patients with chronic liver disease, advanced hepatic failure and portal hypertension characterized by impaired renal function and marked abnormalities in the arterial circulation and activity of the endogenous vasoactive system. Frerichi and Flint made the original description of renal function disturbances in liver disease. [1] They describe the development of oliguria in patients with chronic liver disease in the absence of proteinuria and normal renal histology. They proposed, that abnormality in renal function was related to disturbances present in the systemic circulation. In 1950's the clinical description of hepatorenal syndrome by Sherlock, Popper and Vessen emphasized the functional nature of the syndrome; the coexistence of systemic circulatory abnormalities and its dismal prognosis. Renal failure in hepatorenal syndrome was due to extensive vasoconstriction of renal circulation and paved the way to large number of studies assessing the role of vasoactive substances in the pathogenesis of renal hypoperfusion in hepatorenal syndrome. [2] Hepatorenal syndrome occurs in approximately 4% of patients with cirrhosis who are decompensated with a cumulative probability of 8% per year, which increases to 39% at 5 years. In hospitalized patients with ascites, the incidence rate is 7-15%. The incidence of hepatorenal syndrome is similar globally.

[3] People of all races and who have chronic liver disease are at a risk for hepatorenal syndrome. In 1996, the international ascites club in their consensus publication described two different forms of hepatorenal syndrome, type 1 and 2. Although their pathophysiology is similar but their manifestation and outcomes are quite different. Type 1 hepatorenal syndrome is characterized by rapid doubling of serum creatinine to a level greater than 2.5 mg/dl or having the creatinine clearance to less than 20ml/min within two weeks and is precipitated most commonly by spontaneous bacterial peritonitis (SBP). It occurs in approximately 25% of patients with SBP, despite rapid resolution of the infection with antibiotics. Without treatment the median survival rate with type 1 hepatorenal syndrome is less than 2 weeks and virtually all patients die within 10 weeks after the onset of renal failure. Type 2 hepatorenal syndrome is characterized by moderate and stable reduction in the glomerular filteration rate (with serum creatinine increasing to greater than 1.5 mg/dl or creatinine clearance less than 40ml/min). [4, 5] It most commonly occurs in patients with relatively preserved hepatic function. Median survival rate is 3-6 months. Although this is markedly longer than type 1 hepatorenal syndrome; it is still short as compared to patients with cirrhosis and ascites who do not have renal failure.

The data on the profile of hepatorenal syndrome from north India is scanty. In Punjab, the incidence of chronic alcoholism is high and so is the alcoholic liver disease. With the above data in mind the prospective study to evaluate the clinical profile of hepatorenal syndrome was planned.

Material and methods

All patients of chronic liver disease with renal involvement were studied. Only patients fulfilling the criteria of hepatorenal syndrome were studied prospectively to observe clinical outcome after satisfying inclusion and exclusion criteria. Various variables were studied between survivor group and non survivor group to detect possible predictors of non survival in hepatorenal syndrome. The study was approved by institutional ethics committee and written consent was taken from the patients. The hepatorenal syndrome was diagnosed according to the International Ascites club criteria. [1]

Inclusion criteria

- Chronic or acute liver disease with advanced hepatic failure and portal hypertension.
- Low GFR as indicated by serum creatinine greater than 2.5 gm/dl or creatinine clearance <40ml/min.
- Absence of shock, ongoing bacterial infection, or recent treatment with neprotoxic drugs. Absence of excessive fluid lossess including git bleeding.
- No sustained improvement in renal function following expansion with 1.5 litre of isotonic saline.
- Proteinuria <0.5 g/day, and no ultrasonogaphic evidence of renal tract disease.
- The diagnosis for cirrhosis was based on history, examination, liver function test, ultrasound abdomen and endoscopy. In all patients a history of jaundice, fever, abdominal pain, abdominal distension, deceased urine output, git bleeding and altered sensorium was taken.

Exclusion criteria

- Chronic renal failure was excluded by history, examination and ultrasound showing small kidneys.
- Acute tubular necrosis was excluded from the history, ultrasound and spot urinary sodium.

- Glomerular causes and other tubular causes of ARF were excluded by history and urine routine examination.
- Patients treated with nephrotoxic drugs such as aminoglycosides and NSAIDS.

A detailed record of etiology, duration of liver disease, any precipitating factor for ARF, urine volume status, RFT, morbid events, treatment modality and outcome was recorded in survivor and nonsurvivor group to detect possible predictors of non survival in hepatorenal syndrome. A combination therapy of dopamine (1-5mcg/kg/min), albumin (20%) and Terlipressin (2mg iv 6 hrly) was used in paients of hepatorenal syndrome. Terlipressin was used for at least two days. Patients were followed up till their discharge or death.

Descriptive analysis was used to document the demographic and clinical data of the patients. Data were analyzed using SPSS 19.0. Results expressed as means ± standard deviation. Comparisons between groups were performed by using the Mann-Whitney U-test or two-sided test being appropriate for the detection of statistical significance. Univariate analysis for identifying possible predictors of response to HRS therapy was performed. A value < 0.05 was considered statistically significant.

Results

The study was conducted for 18 months in which 42 patients of hepatorenal syndrome were included. The incidence of hepatorenal syndrome was 0.275% of hospital medical admissions. In present study 95% of male preponderance was seen as compared to females (5%). 17 patients survived and 25 succumbed to hepatorenal syndrome. The mean age of patients was 50.29±8.87 in survivor group and 45.92±10.1 in non survivor group. 33 patients were alcoholic and 9 were non alcoholic having post viral hepatitis. 23.8% had HCV and 4.8% had HBsAg positive viral serology. More than half of the patients were found to be anaemic. All patients in both groups had jaundice, ascites and esopheageal varices. 36(85.7%) patients presented with oliguria, 30(71.4%) with abdominal distension, 26(61.9%) with altered sensorium, 17(40.9%) with fever, 11(26.2%) with pain abdomen, 10(23.8%) with malena and 4(9.5%) with haematemesis.

Table 1: Variables among survivors versus non survivors

Variables	Survivors n=17	Non survivors n=25	P value
Sex Male Female	15(88.24%) 2(11.76%)	25(100%) 0	<0.05*
Ascites	17(100%)	25(100%)	<0.001*
Fever	8(47.06%)	9(36%)	>0.05
Jaundice	17(100%)	25(100%)	<0.05*
Oliguria	12(70.59%)	24(96%)	<0.05*
Encephalopathy	9(52.9%)	21(84%)	<0.05*
Alcoholism	12(70.5%)	21(84%)	>0.05
Esopheageal varices	17(100%)	25(100%)	>0.05
Child Pugh Score	<10	>10	<0.001*
Treatment Dopamine Albumin+Dopamine Albumin+Dopamine + Terlipressin	1(5.8%) 5(29.4%) 11(64.74%)	3(12%) 9(36%) 13(52%)	>0.05 >0.05 >0.05

Table 2: Variables among survivors versus non survivors

Variables	Survivors n=17	Non survivors n=25	P value
Age	50.29±8.87	45.92±10.1	>0.05
Serum creatinine	4.17±1.6	4.8±2.8	>0.05
Blood urea	133.29±89	120.2±65.9	>0.05
Sodium	132.65±7.56	129.36±8.75	>0.05
Potassium	4.76±1.15	4.41±1.03	>0.05
Serum Bilirubin	16.54±12.19	25.09±13.7	<0.05*
SGOT	167.47±124.52	164.40±106.7	>0.05
SGPT	102.24±63.29	96.6±51.34	>0.05
Serum ALP	183.06±114.6	159.24±555.3	>0.05
Serum albumin	2.19±0.53	2.0±0.59	>0.05
Haemoglobin	10.58±2.08	10.58±1.95	>0.05
INR	3.46±4.4	4.16±4.13	>0.05
Serum Osmolality	296±68	260±75	>0.05
Urine Osmolality	845.29±92.5	842.9±167.3	>0.05
Ratio	2.86±1.4	3.24±2.16	>0.05

All the patients on endoscopy showed varices and most of them had grade 2-3 varices. GI bleed was present in 32% of patients.

Oliguria (96%) and hepatic encephalopathy (84%) was more predominant in the non survival group. Serum creatinine values were found to be insignificantly higher in non survival group. Serum bilirubin levels were found to be significantly higher in non survival group as compared to survival group. Hypoalbuminea, hyponetremia and Coagulopathy were more pronounced in non survival group. Ratio of urine osmolality and serum osmolality was higher in non survival group. Significant number of patients had history of alcohol abuse among the non survivals. SGOT, SGPT and serum alkaline phosphatase were almost similar in both groups. Child pugh score was more than 10 in non survival group. 57% of patients were treated with combination of dopamine infusion (1-5mcg/kg/min), albumin (20%) and terlipressin (2mg iv 6 hrly) 33.33% were treated with dopamine and albumin and rest with dopamine alone.

Jaundice, renal failure, hepatic encephalopathy, ascites and Child pugh score of more than 10 were found to be poor prognostic factors with significant p value. (Table: 1, 2) The mortality rate was found to be 60% and survival rate 40% approximately. The patients who left against medical advice and were terminally ill with poor prognosis were included among non survivors.

Discussion

Forty two patients of hepatorenal syndrome diagnosed on the basis of international ascites club criterion admitted to the tertiary care hospital were studied prospectively. Butt AK, [6] Gerald Y et al, [7] Salerno F et al, [8]

reported 65%, 67%, and 73% of male patients in their respective studies. There was male preponderance (95%) as compared to females in our study. Alcoholic liver disease being predominantly a disease of males in north India seems to be the reason for male preponderance. The commonest clinical symptoms of the patients of hepatorenal syndrome were jaundice (100%), followed by oliguria (85.7%), abdominal pain (71.4%), altered sensorium (61.9%), fever (40.9%), and git bleed (33.3%) in both the groups. The common clinical signs of patients of hepatorenal syndrome were the presence of ascites (100%), icterus (100%), followed by flaps (74.4%) and edema feet (57.1%) in both the groups. Salerno F et al demonstrated that all the patients of HRS presented with ascites, jaundice, hepatic encephalopathy and in renal failure. [8] Watt K et al, observed that most of the patients with HRS present with oliguria, high coloured urine, ascites change in mental status, nausea, vomiting and GI bleed. [9]

The liver function test show jaundice in all patients with mean serum bilirubin of 21.36+13.63mg/dl. SGOT and SGPT were raised in more than 90% of the patients. Serum alkaline phosphatase was raised in 69%. 97% had hypoalbuminemia in the range of 0.9-3.3mg/dl. Coagulopathy was present in more than 90% of the patients with mean INR of 4.14±4.34. All patient had bland urine sediment with a urinary spot sodium of <20meq/l. The ratio of urine osmolality and serum osmolality was found to be greater than 1. The renal profile showed mean blood urea of 125.50+75.4mg/dl and mean serum creatinine of 4.6+2.4 mg/dl. Two third of patient had hyponatremia. High level of serum bilirubin, hepatic encephalopathy, decreased level of albumin, hyponatremia and coagulopathy were significant in non survivor group as compared to survivors. Our findings are similar to other studies. [3, 6, 7, 8, 10]

A retrospective case series of cirrhotic patients treated with terlipressin suggested that 20.0% of acute kidney failure in cirrhotics was due to type 1 HRS, and 6.6% was due to type 2 HRS. [11] Twelve out of seventeen patients amongst the survival group were treated with albumin, dopamine and terlipressin and this therapy was successful in 64.7% of the patients in survivor group. These patients had a child pugh score of less than 10. 52% of patients in non survivor group did not improve with this therapy. These patients had a child pugh score of greater than 10. Moreau R et al, [11] in their study in patients with cirrhosis and type 1 hepatorenal syndrome found improved renal function in 58% of the patients after administration of terlipressin and child pugh score < 11 at inclusion were independent predictive factors of survival.

In our study the poor prognostic factors in non survival group were found to be presence of ascites, severe jaundice, hepatic encephalopathy, alcohol abuse, hypoalbuminemia, progressive renal failure and child pugh score greater than 10. The child pugh score of less than 10, and serum bilirubin were found to be independent predictive factor for survival in our study. Three independent risk factors for the development of HRS in cirrhotics have been identified as liver size, plasma renin activity, and serum sodium concentration by Gines et al. [3]

Thus hepatorenal syndrome in decompensated cirrhosis is not that uncommon and judicious treatment helps in saving a significant number of patients. Once considered fatal with mortality of greater than 90% in hepatorenal syndrome, there is improved prognosis of the entity with novel therapies including

terlipressin, dopamine and albumin infusion. This study observed 40% survival in patients of hepatorenal syndrome. However to decrease the incidence of this fatal disease, the emphasis should be to educate the society about abstinence from alcohol and prevention of hepatotropic viral infection.

The most important aspect in the management of hepatorenal syndrome is to prevent its recurrence. The latter is achieved by avoidance, prophylaxis, early recognition and treatment or removal of precipitating factors. Many treatment options are now showing promise for patients with hepatorenal syndrome.

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