

# Cirrhosis of liver: Etiological factors, complications and prognosis

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## ABSTRACT

**OBJECTIVE:** To determine the etiological factors, complication(s) and prognosis of patients suffering from liver cirrhosis in our setup.

**DESIGN:** Cross-sectional study.

**SETTING:** Medical and surgical departments of Liaquat University Hospital Hyderabad/Jamshoro, Sindh – Pakistan, from April 2005 to April 2007.

**METHODS:** Patients having an evidence of cirrhosis of liver on ultrasound examination of abdomen were enrolled. All those patients who were not confirmed to be cirrhotic, excluded from this study. All cases were studied to determine the etiological factors, complications and prognosis of disease. All data were recorded on a proforma. Patients with acute variceal hemorrhage were referred to surgical department for endoscopic sclerotherapy or variceal band ligation.

**RESULTS:** Total 100 patients were studied, 67(67%) males and 33(33%) females. Their mean age was 53.09 with SD= 8.85814 years. Majority of patients, 52(52%) had HCV infection, 16(16%) had HBV infection, 16(16%) had HBV and HCV co-infection, 08(08%) had alcohol abuse, 01(01%) had primary biliary cirrhosis, 02(02%) had Wilson's disease and no etiological factors were recorded in 05(05%) patients. Ascites was present in 59(59%) cases, portal hypertension in 42(42%), esophageal varices in 29(29%), spontaneous bacterial peritonitis in 29(29%), acute variceal hemorrhage in 27(27%), hepatic encephalopathy in different grades in 24(24%), hepatorenal syndrome in 09(09%) and hepatocellular carcinoma in 07(07%) patients. All patients with acute variceal episode(s) were adequately and timely treated in surgical department. When cirrhotic patients were grouped into child-Pugh's classification, 37(37%) were in class 'A' category, 37(37%) in class 'B' category, and 26(26%) in class 'C' category.

**CONCLUSION:** HCV infection is the major risk factor for cirrhosis in our setup. Ascites was the commonest complication. Patients with child-Pugh's class 'A' cirrhosis had significantly longer survival than patients with child-Pugh's class 'B' and 'C'. A multidisciplinary approach for prevention and control of ever increasing HCV infection must be adopted and to make the public awareness through the mass media about its drastic complications, and possible modes of its transmission.

**KEY WORDS:** Liver. Cirrhosis. Viral hepatitis. HCV infection. Ascites.

## INTRODUCTION

Cirrhosis is a serious and irreversible disease. It is a consequence of chronic liver disease characterized by replacement of liver tissue by fibrotic scar tissue as well as regenerative nodules, leading to progressive loss of liver function.<sup>1,2</sup> It is a major cause of mortality and morbidity worldwide.<sup>3</sup> It is also a common cause of mortality amongst Pakistani population<sup>4</sup> and frequent cause of admission in our hospitals.<sup>5</sup> Cirrhosis develops in about 10-20% within 5-30 years. The most common cause being viral hepatitis as compared to West where alcohol is more common.<sup>6,7</sup> Majority of patients (90%) with chronic liver disease had evidence of HBV, HCV or co-infection. Disease is reported more severe in patients with co-infection and cirrhosis is

recorded in 74% of patients.<sup>8,9</sup> HCV is now more common as compared to HBV in our country, and a high frequency of HCV seropositive individuals of both sexes among patients referred for chronic liver disease.<sup>9,10</sup> Portal hypertension, ascites and variceal hemorrhage are common in cirrhotic patients. Esophagogastric varices have the greatest clinical impact, with a risk of mortality of 17–42% per bleeding episode.<sup>5</sup> Ascites, important complication of advanced cirrhosis and severe portal hypertension, is sometimes refractory to treatment and is complicated by spontaneous bacterial peritonitis and hepatorenal syndrome.<sup>11,12</sup> Hepatic encephalopathy is another complication, with a mortality of about 30%.<sup>13</sup> About 15% of patients with cirrhosis will finally develop hepatocellular carcinoma.<sup>6</sup> The prognosis of the disease was as-

sessed by using modified Child-Pugh's classification for grading prognosis in cirrhotic patients. It was devised in 1964 by Child and Turcotte and modified in 1973 by Pugh, et al.<sup>14</sup> We undertook this study to determine the etiological factors, complications and prognosis of patients suffering from liver cirrhosis.

**PATIENTS AND METHODS**

This study was conducted in the medical and surgical departments of Liaquat University Hospital Hyderabad/ Jamshoro from April 2005 to April 2007. Patients having an evidence of cirrhosis of liver on ultrasound examination of abdomen were included in study. All those patients who were not confirmed to be cirrhotic, excluded from this study. These patients were carefully examined to determine the etiology of the disease, complication(s) at the time of presentation and prognosis of the disease. Data were recorded on a proforma specially designed for this purpose. For each patient full blood count, liver function tests, serology for hepatitis, renal function tests, blood sugar, serum electrolytes, serum albumin and coagulation profile were carried out. Blood was also collected for anti-mitochondrial antibodies, serum copper and serum caeruloplasmin. An abdominal ultrasound for liver and splenic size, parenchymal echogenicity, portal vein diameter, and ascites was also carried out. In case of ascites, an ascitic tap was done to look for spontaneous bacterial peritonitis. Any evidence of the presence of other co-existent complications of cirrhosis of liver was also recorded. CT scan of the abdomen was also carried out in suspected eight cases of liver cell mass. Patients with acute variceal hemorrhage were referred to surgical department for endoscopic sclerotherapy or variceal band ligation. The

prognosis of the disease was assessed by using modified Child-Pugh's classification for grading prognosis in cirrhotic patients. Child-Pugh's classification has scores for five parameters i.e. serum bilirubin, serum albumin, prothrombin time, ascites and hepatic encephalopathy. It grades cirrhosis in three grades; Child-Pugh's 'A' grade (score less than 7), Child-Pugh's 'B' grade (score 7-9) and Child-Pugh's 'C' grade (score more than 9).<sup>14</sup> Patients were followed during their stay in the hospital and subsequent follow up visit(s) at hospital and whether they survived or expired. Statistical analysis was performed by using SPSS 13.0.

**RESULTS**

During the study period, 100 patients with a diagnosis of cirrhosis of liver were studied. Majority 67(67%) were males and 33(33%) were females. Their mean age was 53.09 with SD=8.85814 years. Various etiological factors of cirrhosis of the liver are given in **Table I**. **Table II** shows distribution of complications among patients. Using modified Child-Pugh's classification for grading prognosis in cirrhotic patients is shown in **Table III**. In the analysis of laboratory findings, high bilirubin was found in 58%, hyponatremia, and low hemoglobin were found in 68% and 59% patients respectively. In 42% patients, there was high blood urea while creatinine was above normal limits in 18% patients. Hypoalbuminemia (serum albumin <3.3g/dl) was found in 40% patients. Leukocytosis (total leukocyte count >11000/ml) was a feature in the laboratory data of 47% patients. The rest of patients had either normal or low TLC. Coagulation profile was abnormal in a fraction of patients with 54% patients having prothrombin time > 5 seconds. However,

**TABLE I:  
ETIOLOGICAL FACTORS**

Factors	Male		Female		Positive proportion	
	No.	%	No.	%	No.	%
HCV Infection	34	65.4	18	34.6	52	52
HBV Infection	11	68.7	5	31.3	16	16
HBV and HCV co-infection	10	62.5	6	37.5	16	16
Alcohol	8	100	0	0	8	8
Primary biliary cirrhosis	0	0	1	100	1	1
Wilson's disease	1	50	1	50	2	2
Unknown	3	60	2	40	5	5
<b>Total</b>	<b>67</b>	<b>67</b>	<b>33</b>	<b>33</b>		

thrombocytopenia (platelet count <150,000/ml) was a consistent finding in 72% patients. Antimitochondrial antibodies were found positive in one patient, whereas serum copper and serum caeruloplasmin were positive in two patients. An abdominal ultrasound confirmed features of liver cirrhosis in 100% and ascites

complications. In advanced stages of cirrhosis the only option is a liver transplant.<sup>15</sup> Nadeem, et al has reported that cirrhosis of liver is a frequent cause of admission in hospitals and HCV was the most common cause. At least 50% of infected patients, develop

**TABLE II:  
DISTRIBUTION OF COMPLICATIONS**

Complication		Male		Female		Total
		No.	%	No.	%	
Ascites	None	28	68.2	13	31.7	41
	Slight	27	65.8	14	34.2	41
	Mod- Severe	12	66.6	6	33.4	18
Portal hypertension		31	73.8	11	26.2	42
Esophageal varices		22	75.8	7	24.2	29
SBP		20	68.9	9	31.1	29
Encephalopathy	None	53	69.7	23	30.3	76
	Slight- moderate	12	63.2	7	36.8	19
	Mod- severe	2	40	3	60	5
Hepatorenal syndrome		6	66.7	3	33.3	9
Heptocellular carcinoma		4	57.2	3	42.8	7
Hematamesis		21	77.8	6	22.2	27

**TABLE III:  
CHILD PUGH SCORE**

Child Turcutte Pugh Score	Male	Female	Total
A (5-6)	26	11	37
B (7-9)	26	11	37
C (10-15)	15	11	26
<b>Total</b>	<b>67</b>	<b>33</b>	<b>100</b>

in 59% of patients. Ascitic fluid DR and culture and sensitivity showed spontaneous bacterial peritonitis in 29% of patients with cirrhotic ascites. CT scan of the abdomen confirmed hepatocellular carcinoma in 07% of patients. Out of 100 patients, 26% expired including 15 males and 11 females during study period, who were found in class 'C' of Child-Pugh's classification.

**DISCUSSION**

Cirrhosis of liver is generally irreversible disease, and treatment focusses on preventing progression and

chronic liver disease and cirrhosis develops in about 10-20% patients within 5-30 years.<sup>5</sup> This study showed that HCV infection was the major etiological factor and was responsible for 52% of the total cases presented with cirrhosis, as observed by Shah, et al that most of their patients with HCV infection, presented with established cirrhosis.<sup>16</sup> We observed 16% of cirrhotic patients with HBsAg infection, similarly Bukhtiari, et al has reported that cirrhosis was present in 74% cases, chronic hepatitis in 18.6% and among the patients with cirrhosis, 28% were HBsAg positive, 55% anti-HBc positive.<sup>8</sup> We observed co-infection of HBV and HCV in 16% of cirrhotics, while Bukhtiari, et al has reported 07% co-infection of anti-HCV and HBsAg as well as 35% of anti-HCV and anti-HBC positive.<sup>8</sup> Farooqui, et al has also reported that anti-HCV was positive in 59% and HBsAg was positive in 32% patients. Both were positive in 03% patients.<sup>9</sup> In contrast, previous studies also included patients with non-viral forms of cirrhosis, mainly alcohol related, where the pathogenesis and pathophysiology of liver damage are quite different.<sup>17-19</sup> Similarly, we observed

ascites and liver related problems among 08% of patients with previous alcohol abuse. In this study, one cirrhotic patient had primary biliary cirrhosis, which is not an uncommon finding as reported in other studies,<sup>20-23</sup> whereas 02% of patients had Wilson's disease, as reported in other studies.<sup>21-23</sup> Surprisingly, in our study the etiological factor was not recognized in 05% of patients and known as cryptogenic cirrhosis as reported by Nadeem, et al.<sup>5</sup> Early studies conducted in which patients recruited at different stages of cirrhosis usually identified portal hypertension and its main clinical consequences (that is, ascites and oesophageal bleeding) as the most frequent causes of transition from compensated to decompensated cirrhosis and of liver related problems. Furthermore such events were reported to have profound effects on survival rates.<sup>24-26</sup> In this study, ascites was recorded as commonest complication of cirrhosis and was present in 59% of patients and to mark decompensation of liver disease as reported in other studies.<sup>24,27</sup> The incidence of SBP in patients with cirrhosis and ascites varies from 7-23% in the West.<sup>28,29</sup> It is around 33% in Pakistan<sup>30,31</sup> and we observed that spontaneous bacterial peritonitis developed in up to 29% of patients with cirrhosis and ascites. In this study, 27% of patients presented with acute variceal hemorrhage, who were referred to surgical department for endoscopic sclerotherapy or variceal band ligation, were adequately treated. The most frequent complication of cirrhosis and portal hypertension with a mortality of 17-42% per bleeding episode is documented in other studies.<sup>24-26</sup> Preventing death from variceal bleeding requires adequate and timely resuscitative measures, specific treatments aimed at arresting the bleeding quickly, and skilled management of the liver disease and secondary complications.<sup>32,33</sup> We observed hepatic encephalopathy in different grades in 24(24%) patients, as reported in other studies that hepatic encephalopathy is a complex neuro-psychiatric syndrome, which may complicate acute or chronic liver failure.<sup>34</sup> The results of this study show that HCC is indeed a major (07%) and early complication of compensated cirrhosis of viral etiology, being the most frequent first complication and cause of death in HCV positive patients, as reported in other studies, conducted in more homogeneous cohorts of cirrhotic patients with initially well compensated "early" cirrhosis of viral etiology have clearly shown that HCC is another important complication that patients may frequently develop in the compensated phase of disease.<sup>35,36</sup> We recorded 09% cases of cir-

rhosis with the hepatorenal syndrome as reported in other studies that hepatorenal syndrome is a progressive disorder associated with advanced cirrhosis and portal hypertension.<sup>37,38</sup> In this study, we evaluated the prognostic staging of patients with cirrhosis on the basis of Child-Pugh's classification and observed 37% had Child-Pugh's 'A' grade of prognosis, 26% had Child-Pugh's 'B' grade of prognosis and 26% had Child-Pugh's 'C' grade of prognosis. Yan, et al has reported that 22% of the patients had cirrhosis of Child-Pugh grade A, 41% of grade B and 36% of grade C.<sup>14</sup> Liver function tests showed a steady decrease from Child-Pugh's grade A to grade B and to grade C. During our study period, 26% of total patients with class 'C' of Child-Pugh's classification, expired as reported in other studies that differences between the three Child-Pugh's grades were significant.<sup>14,39</sup>

## CONCLUSION

We conclude that chronic HCV infection is the major risk factor for cirrhosis in our patients. Ascites is the commonest complication. Patients with Child-Pugh's class 'A' cirrhosis had significantly longer survival than patients with Child-Pugh's class 'B' and 'C'. A multidisciplinary approach for prevention and control of ever increasing HCV infection must be adopted to make the public awareness through the mass media about its drastic complications, and possible modes of its transmission.

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