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Otiginal Article

Liver Cirrhosis Seen in GI Clinics of Ahvaz, Iran

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ABSTRACT

Background:
Liver cirrhosis is an end-stage condition fornumerous chronic liver diseases. Limited data exists on the epidemiology, natural history and complications of liver cirrhosis in Ahvaz, Iran. In a cross-sectional study we have retrospectively evaluated 165 patients from September 1, 1999 until September 1, 2008.

Materials and Methods:
Patients with evidence of cirrhosis of the liver seen on abdominal ultrasound were enrolled. The diagnosis was based on clinical, functional and morphological data.The etiological profile was established by determining viral and autoimmune markers, and by metabolic screening. Patientswho were not confirmed to be cirrhotic were excluded from this study. All cases were studied to determine etiological factors, complications and disease prognosis. Data were recorded on a questionnaire.

Results:
A total of 165 patients were studied, of which there were 114(67%)males and 51(33%) females. The mean age was 47 years. The majority of patients [70 cases (42.4%)] had evidence of HBV infection. Of HBs Ag-positive patients, 31(43.2%) were HDV Ab positive with a mean age of 41.6 years. There wasno significant difference by sex among cirrhotic patients ($p>0.05$).
Other cases included 23 (14%) patients with autoimmune hepatitis (AIH), 15(9.1%)had HCV infection, 2(1.2%) had evidence of Wilson's disease and no etiological factors were recorded in 55 (33.3%) patients. Ascites was present in 32% of cases, splenomegaly in 29%, esophageal varices in 38%, fundal varices in 2%, peptic ulcer in 8%, acute variceal hemorrhage in 8%, various grades of hepatic encephalopathy in 1%, and hepatocellular carcinoma in 6% of patients. When cirrhotic patients were grouped according to Child-Pugh classification,19% were in class A, 30% were in class B, and 51% comprised class C.

Conclusion:
HBV infection was the major risk factor for cirrhosis in this study and ascites was the most common complication. There were more patients with Child-Pugh class C cirrhosis than thoseinclasses B and A. A multidisciplinary approach for the prevention and control of the increase in HBV infection must be adopted in order to inform the public about the seriousness of its complications and possible modes of transmission.

Keywords: Livercirrhosis; Etiology; Clinical profile

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INTRODUCTION

Liver cirrhosis is an important health problem that accounts for significant morbidity and mortality worldwide(1).The epidemiology of liver cirrhosis is characterized by marked differences between ethnic groups and geographic regions. It is also a common cause of mortality amongst the Iranian population and a frequent cause of hospital admissions. Cirrhosis is a consequence of chronic liver disease characterized by replacement of liver tissue with fibrotic scar tissue as

well as regenerative nodules that lead to progressive loss of liver function(2).

There are many causes of cirrhosis, of which alcoholism and hepatitis C are the most common causes of cirrhosis worldwide.However hepatitis B (HBV) and C (HCV) viral infections are leading causes of cirrhosis in Iran. Among the two, HBV has overtaken HCV in the etiogenesis of liver cirrhosis in Iran(3). In 5.9% of cases no cause can be found(4).

Diagnosis of cirrhosis, especially in its advanced stage, means ultimate progression to death due to complications that occurduring the course of the disease. Therefore it is important to establish the main etiologies of this condition in order to avoid or remove them prior to onset of this deadly disease. Cirrhosis can present in many ways depending upon the stage of the disease process (compensated or decompensated cirrhosis).

Portal hypertension, ascites and variceal hemorrhage are common in cirrhotic patients. Esophageal varices have the greatest clinical impact, with a risk of mortality of 17%–42% per bleeding episode(5).Ascites, an important complication of advanced cirrhosis and severe portal hypertension, is sometimes refractory to treatment and complicated by spontaneous bacterial peritonitis and hepatorenal syndrome. Hepatic encephalopathy is another complication, with a mortality of about 30%(6).

About 15% of patients with cirrhosis eventually develop hepatocellular carcinoma(7).

The aim of this study was to assess the clinical spectrum of cirrhosis in Ahvaz, Iran and to compare the findings with those reported in the literature.

MATERIALS AND METHODS

This descriptive case study was conducted in the Ahvaz Digestive Research Center. We retrospectively analyzed the clinicopathologic characteristics of 165 cirrhotic patients who were admitted to the Gastroenterology Ward or who were seen in outpatient clinics of the Ahvaz Jundishapur University Hospitals (AJSUH) from September 1, 1999 to September 1, 2008.

Patients with evidence of liver cirrhosis were included in the study.The diagnosis of liver cirrhosis was made if patients had advanced fibrosis and regenerative nodules seen on liver biopsy,orimaging evidence of cirrhosis and laboratory evidence that favored chronic liver dysfunction.Those patients who were not confirmed to be cirrhotic were excluded from this study. Patients were carefully examined to determine the etiology of the disease, complication(s) at the time of presentation and disease prognosis. Data were recorded on a questionnaire specifically designed for this purpose. Variables were recorded, analyzed and compared with other studies.

Each patient underwent the following laboratory analyses: full blood count; liver enzymes; liver function tests; serology for hepatitis that included HBsAg, anti-HBs, and antibody to the hepatitis B core antigen (anti-HBc); renal function tests; blood sugar; serum electrolytes; serum albumin and coagulation profile. Blood was also collected for an iron profile study and metabolic disorders that included fasting blood sugar (FBS); total cholesterol; triglycerides; low-density cholesterol (LDL-C) and highdensity cholesterol (HDL-C) to evaluatenon-alcoholic fatty liver disease; anti-mitochondrial antibodies; serum copper and serum ceruloplasmin. PCR was performed to evaluate the presence of HBV and HCV viral infections.

Autoimmune markers of ANA, SMAand anti-LKM1 were tested in all cases. Autoimmune liver disease was diagnosed when one or more of the autoantibodies (ANA, SMA, and anti-LKM-1) were positive according to criteria proposed by the International Autoimmune Hepatitis Group (IAIHG) and used to define an autoimmune etiology in our patients.

Cryptogenic cirrhosis was considered when the clinical history and laboratory data failed to identify any recognizable cause.

Abdominal ultrasound for liver and spleen size, parenchymal echogenicity, portal vein diameter, and ascites was also carried out. MRI of the abdomen was also performed in suspected cases of liver cancer.

In case of ascites, we performed an ascitic tap to look for spontaneous bacterial peritonitis. Any evidence that indicated the presence of other co-existent complications of liver cirrhosis was also recorded.

Patients underwent upper endoscopies for esophageal orgastric varices or portal hypertensive gastropathy was also carried out during the first admission and every one or two years thereafter.

Patients with acute variceal hemorrhage were referred to the Endoscopy Department for endoscopic sclerotherapy or variceal band ligation. The prognosis of the disease was assessed by a modified Child-Pugh classification for grading prognosis in cirrhotic patients. The Child-Pugh classification has scores for five parameters of serum bilirubin, serum albumin,

prothrombin time, ascites and hepatic encephalopathy. The classification grades cirrhosis in three grades: A (scores less than 7); B (scores 7-9); and C (scores more than 9).7 Patients were followed during their hospitalizations and at subsequent follow up visit(s) to determine survival.

RESULTS

In the present study 165 cirrhotic patients were evaluated of which there were 114 (67%) males and 51(33%) females with a mean age of 47 years (SD = 17). There were 70 (42.4%) cases with HBV infection which represented the majority. In HBs Ag positive patients, 54 (77.1%) were male and 16(22.9%) were female; the most frequent age group was 20-40 years (56.4%). The mean age of cases was 37±13.8 (range: 8-72) years. Amongthe HBs Ag positive patients, 31(43.2%) were HDV Ab positive with a mean age of (41.6 years).However, the HDV infection ratios did not differ significantly by sex in cirrhotic patients (p>0.05).

Among surveyed patients, 23(14%) were diagnosed with autoimmune hepatitis (AIH) according to international criteria for type 1 or type 2 AIH. In the AIH group, 13 (56.5%) were female and 10(43.5%) were male with a median age at presentation of 34.8 years (range: 9–62). There were 16 cases that showed complete or partial biochemical responses to standard prednisolone, with or without azathioprine therapy. Four (2.4%) had cholestatic serum biochemistry and biliary changes on liver biopsy with definitive features of primary biliary cirrhosis or primary sclerosing cholangitis. Other causes were HCVin15 (9.1%) cases and Wilson's disease in 2 cases (1.2%).

None of the patients were positive for alpha-1-antitrypsin deficiency or hemochromatosis.

No etiology could be found in 55 (33.3%) patients; therefore they were labeled as either idiopathic or cryptogenic cirrhosis.

Ascites was present in 32% of cases, splenomegaly in 29%, esophageal varices in 38.2%, acute variceal hemorrhage in 8%, different grades of hepatic encephalopathy in 1%,fundalvarices in 2.4%,peptic ulcer in 8.5% and hepatocellular carcinoma in 6% of patients. All patients with acute variceal episodes were adequately and timely treated in the Gastrointestinal Department. When cirrhotic patients were grouped according to Child-Pugh classification, 19% were in class A, 30% were class B, and 51% comprised class C. Tables 1-3 show results of the 165 cases.

Table 1: Age distribution of 165 cases.

Age (years)	Patients (n)	Percent (%)
<20	14	8.5
20-39	35	21.2
40-59	63	38.2
>60	53	32.1

Table 2: Child-Pugh scores and endoscopic findings.

Child-Pugh scores	Patients (n)	Percent (%)
A	66	39.5
B	15	9.3
C	84	51.1
Endoscopic findings		
Esophageal varices	63	38.2
Fundal varices	4	2.4
Peptic ulcer	14	8.5

Table 3: Etiology of liver disease among studied patients.

Etiology	Patients (n)	Percent (%)
HBV infection	70	42.4
Autoimunehepatitis	23	14
HCV infection	15	9.1
Wilson's Disease	2	1.2
Unknown	55	33.3

DISCUSSION

Liver cirrhosis is the end-stage result of various chronic liver diseases. Limited data exists on the etiology and clinical profile of liver cirrhosis in Ahvaz city. The results of the current study have shown that HBV was more common (42.4%) than HCV infection and AIH in patients with cirrhosis who presented to the outpatient clinics at AJSUH. The slight male [114(67%)] predominance seen in this study was similar to that reported both locally and internationally. Ina similar study from Shariati Hospital conducted by Azimi et al., HBV was reported to be the leading etiology (60.6%) of liver cirrhosis in that center(4). This was more or less in accordance with the prevalence of HBV in the reminder of the country(9).

Amongst HBs Ag positive patients, 31(43.2%) were HDV Ab positive with a mean age of 41.6 years. However, the HDV infection ratios did not differ significantly by sex in cirrhotic patients (p>0.05).

We previosly have been shown that these seroprevalence of HDV ininactive chronic HBV carriers is 3.59% in khuzestan province(10).So HDV infection obviosly was more prevalent in our cirrhotic patients than in inactive cariers. The second most common cause of cirrhosis was attributed to AIH(14%) followed by HCV (9.1%). Other causes represented only a minor proportion of cirrhosis patients, accounting for less than 1.5%. None of the patients were positive for alpha-1-antitrypsin deficiency or hemochromatosis. No etiology could be found in 55 (33.3%) patients; therefore they were considered idiopathic.

Recently, the prevalence of cirrhosis due to AIHhas increased to 14%, compared to the reported rate of 8.2% in 1998.4 This contrasted the recent steady decrease in the prevalence of HBV-related cirrhosis following the implementation of vaccination program and potent antiviral therapies in Iran(11-12).

Despite the lack of epidemiological studies in Khuzestan province, it seems that same as other parts of the country , the overall prevalence of HBV-related cirrhosis has decreased whereas the prevalence of HCV-related cirrhosis increased over the past decade(13). This can be explained by the lack of vaccines that target HCV in conjunction with the distinct features of HCV infection characterized by an insidious process but a higher chronicity that leads to an increased number of cases with age. It is anticipated that the proportion of HCV-related cirrhosis will likely increase in the future.

None of the current study patients were positive for alpha-1-antitrypsin deficiency or hemochromatosis.In Iran, secondary hemochromatosis is not uncommon and is usually seen in patients with thalassemias, but recently one case of hereditary hemochromatosis (HH) has been reported(14).In our study alcoholic liver disease was not an etiology, whereas in another local study (4)it was seen in 6 (3.5%) cases. This was either because it was undetermined by the physicians or patients denied alcoholic consumption.

No etiology could be found in 55 (33.3%) patients; therefore they were labeled idiopathic. This high frequency of idiopathic liver cirrhosis in our study reflects our financial restrictions as well as limited availability of advanced and specific diagnostic tools to determine other underlying causes ofchronic liver disease(CLD). The frequency of idiopathic CLD also varies in different areas of the world. In the United Kingdom it is about 5%-10%, whereas other areas such as France and urban parts of the United States where alcoholism is prevalent have a lower proportion of idiopathic CLD(15).

With the increase in specific diagnostic facilities, there will be a decrease in the percentage of idiopathic CLD.However better designed prospective studies are needed to investigate the precise causes of idiopathic CLD in our area.

These overall findings provide strong evidence that the etiology of cirrhosis in Khuzestan Province continues to change. A larger survey of the current epidemiological status of cases from Khuzestan Province with liver cirrhosis is greatly needed because the etiology of cirrhosis varies widely with socioeconomic, regional and educational variables.

Progressive worsening of hepatic function in cirrhosis increases the risk of serious and potentially life-threatening complications, including ascites, portal hypertension, variceal hemorrhage, spontaneous bacterial peritonitis, hepatic encephalopathy and hepatorenal syndrome. Among these complications, varices and ascites are the most common.

Edema and ascites (32%) were the major presenting symptoms in the present study; the high incidence of edema and ascites in our study indicated fairly advanced disease with decompensation. The incidence of hepatocellular carcinoma (6%), bleeding varices, peptic ulcer, varying grades of hepatic encephalopathy, and splenomegaly (29%) in the present study were similar to that reported in other studies(16).All patients with acute bleeding episodes (8%) were adequately and timely treated in the Gastrointestinal Department. Patients with acute bleeding episodes were noted to have esophageal (38%) and fundal varices (2%).Another cause of bleeding was attributed to peptic ulcers.

The Child-Pugh classification is a simple, convenient prognostic measure in patients with liver cirrhosis that has been repeatedly shown to be useful in this assessment. Whenthe current study patients were grouped into the Child-Pugh classification, 19% were assigned to class A, 30% were considered as

class B and 51% were in class C.

Recently, the MELD score has been shown to be superior to the Child-Pugh score in ranking patients according to the severity of liver disease and risk of dying .The MELD score is considered to be more reproducible than the Child-Pugh score because it does not include subjective variables such as encephalopathy(6-16).

A major short coming of this work was the number of our cases. Further investigations with larger sample numbers are necessary to determine the causes and various clinical complications. We have to implement a prospective study to follow these cases for a longer time to define the outcome.

In summary, this study has provided preliminary data about the clinical profile and etiology of liver cirrhosis in Ahvaz,that will be helpful for the appropriate management of liver cirrhosis and its complications.

We found that HBV infection is the most common etiology of liver cirrhosis; therefore, early detection and treatment of HBV infection should be conducted, particularly in all high risk individuals .In order to prevent the spread of infection, HBV-infected persons should be advised not to share toothbrushes and dental or shaving kits. Public awareness regarding the spread of the disease and avoidance of risk factors is strongly needed. Furthermore our patients with cirrhosis present with a fairly advanced stage of the disease.

Early detection of cirrhosis has led to a genuine survival benefit. Further studies are necessary to address the importance of other potential causes of chronic liver disease such as nonalcoholic fatty liver disease ,celiac disease and so on .

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