ORIGINAL ARTICLES

ASSESSMENT OF PATIENTS WITH CHRONIC LIVER DISEASE QUALIFYING FOR LIVER TRANSPLANT

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ABSTRACT

Objective: To determine the frequency, etiology and pattern of patients with chronic liver disease at a tertiary care hospital qualifying for a liver transplant.

Design: Cross-sectional Study

Place and duration of study: Military Hospital Rawalpindi from December 2008 to May 2009.

Patients and Methods: Study included all patients of Chronic Liver Disease, admitted in medical wards. Diagnosis was made on the basis of clinical and ultrasonographic findings suggestive of chronic liver disease. Etiology was identified by serological tests (ELISA or PCR) and immunological tests. Metabolic screening was done for Wilson's disease and haemochromatosis. HCC was diagnosed and staged by biopsy and CT scan. After taking informed consent, detailed medical history, physical examination and required biochemical tests were carried out. All patients of age 12 years and above were evaluated according to Model for End Stage Liver Disease (MELD) and those below 12 years of age were evaluated by Pediatric End Stage Liver Disease (PELD). Milan's Criteria was used for hepatocellular carcinoma and Mayo risk scores (MRS) for patients with Primary Biliary Cirrhosis and Primary Sclerosing Cholangits.

Results: A total of 212 patients suffering from chronic liver disease were included. Out of these, 164 (77.4%) were suffering from chronic hepatitis C, 16 (7.5%) from chronic hepatitis B, 2 (0.9%) from autoimmune hepatitis, 2 (0.9%) from hepatocelluar carcinoma, 1 (0.5%) from alcoholic hepatitis, 2 (0.9%) from Wilson's disease, 1 (0.5%) from haemochromatosis and 24 (11.3%) were Cryptogenic. All these patients were evaluated for liver transplant according to the appropriate criterion. Out of 212 patients, 43 (20.3%) patients had MELD/PELD Score of ≤ 10, 92 (43.4%) patients were in the range of 11-18, 44 (20.8%) patients in range of 19-24, 31 (14.6%) patients were in range of 25-35 and 02 (0.9%) patients were≥36 (79.71). Patients with MELD/PELD score more than 10 are considered for liver transplant but the MELD/PELD score at which a patient will realistically receive a liver varies by region and organ demand as defined by the number of candidates on the waiting list and their blood type.

Conclusion: High frequency of patients of chronic liver disease in our setup qualify for a liver transplant. It provides preliminary data for the need of liver transplant centers in our region.

Keywords: Chronic Liver Disease, Hepatitis C, Liver Transplant, MELD,

INTRODUCTION

Globally 57% of cirrhosis is attributed to either HBV(30%) or HCV(27%). According to 2002 worldwide mortality estimates, 929,000 deaths occurred due to chronic HBV, HCV including 44,600 cirrhotic deaths[1]. In 1998, chronic liver disease (CLD) was classified as the tenth most frequent cause of death in the United States according to the national vital statistics report[2]. In UK cirrhosis related mortality rate has increased steeply during 1990's. Mortality rate more than doubled in men from Scotland and rose by over 69% in England and Wales. In women 46% increase in Scotland and 44% increase in England was observed[3]. A study for prevalence of chronic liver disease in general population of northern Italy found a much higher prevalence of chronic liver disease than reported previously in selected populations from Western countries. Signs suggestive of chronic liver disease were seen in 21.3% of the subjects. The prevalence rates of hepatitis B virus and hepatitis C virus positivity were 1.3% and 3.2%, respectively. Alcohol abuse was the etiological agent in 23%[4].

In a study conducted at Shifa International Hospital, Islamabad twelve months admission data was reviewed from its computerized data

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base and mortality rates for different diseases among the hospitalized patients was observed. Out of 160 deaths related to medical causes from 8529 admissions, 20.6% patients had chronic liver disease of which 70% had hepatitis C virus (HCV) as cause of their liver disease, 12% had hepatitis B virus (HBV) infection, 9% had both hepatitis B C virus infections and 9% had no known cause of their chronic liver disease[5].

Liver transplantation is considered the standard therapeutic approach for end-stage liver disease[6-9] with a postoperative survival rate increasing to 80% in 5 years[6,10]. In past Child Turcotte-Pugh (CTP) criterion was used to prioritize the patients for liver transplant. CTP score combined a number of clinical and biochemical parameters into an overall score of A, B or C with progression of disease from A to C[11]. In February 2002, the Model of End-Stage Liver Disease (MELD) score was implemented for determining donor liver allocation. The MELD score is a mathematical score determined from the patient's laboratory tests and is highly predictive of short-term mortality[12,13]. Thus, offers an objective measure that is relatively free of bias and directs donor organs to those in greatest need irrespective of waiting time[12]. A separate mortality risk score for pediatric patients, the Pediatric End Stage Liver Disease (PELD) score, was developed using the 3-month mortality risk endpoint[14]. Mayo Risk Score (MRS) was used for the evaluation of patients with Primary biliary cirrhosis and primary sclerosing cholangitis which has been validated using independent data sets at different institutions[15].

There are approximately 140 transplant centers in USA and there is a proper system of organ procurement, retrieval, preservation and transportation. UNOS and local Organ Procurement Organization (OPO) perform these tasks[11]. Pakistan does not have a liver transplant facility, however, the burden of HCV & HBV is tremendous. This study has been carried out to evaluate the number of patients who require transplant at a tertiary care centre.

PATIENTS AND METHODS

This prospective cross-sectional study was carried out at the Military Hospital, Rawalpindi a tertiary care hospital of Pakistan. It was conducted over a period of 6 months from December 01, 2008 to May 31, 2009. It included patients of both genders and all age groups suffering from chronic liver disease, admitted in medical wards. Diagnosis was made on the basis of clinical and ultrasonographic findings suggestive of chronic liver disease. Etiology was identified by serological tests (ELISA or PCR) and immunological tests. Metabolic screening was done for Wilsons disease and haemochromatosis. HCC was diagnosed and staged by biopsy and CT scan. After taking informed consent, detailed medical history, physical examination and required biochemical tests were carried out. Biochemical tests included Serum Creatinine, Total Bilirubin and INR (International normalized ratio).

All patients of age 12 years and above were evaluated according to Model for End Stage Liver Disease (MELD) and those below 12 years of age were evaluated by Pediatric End Stage Liver Disease (PELD). Online UNOS MELD and PELD calculators were used to analyze the data.

MELD Formula used was:

0.957 x Loge (Creatinine [mg/dL]) + 0.378 X Loge (Total Bilirubin [mg/mL]) + 1.120 x Loge (INR)+ 0.643

PELD formula used was:

0.436 (Age Younger Than 1 Year = 1, Older=0) - 0.687 x Loge (Albumin [g/dL]) + 0.480 x Loge (Total Bilirubin [mg/mL]) +1.857 x Loge (INR) + 0.667 (Growth Failure = 1)

Patients of primary biliary cirrhosis and primary sclerosing cholangits were evaluated on the basis of Mayo Risk Scores while in cases of hepatocellular carcinoma, patients meeting United Network for Organ Sharing (UNOS) criteria (1 lesion 2-5 cm or 2 to 3 lesions < 3 cm) were considered eligible for priority listing.

We followed the steps outlined by the United Network for Organ Sharing (UNOS) in the United States. Patients were stratified into 5 UNOS MELD categories according to their

pretransplant MELD scores: ≤10, 11–18, 19–24, 25–35 and ≥36, similar to the MELD categories used by UNOS. Only patients with MELD score more than 10 are considered for a liver transplant.

Data was analyzed using SPSS version 16. Descriptive statistics were used to describe the data i-e frequency and percentages were calculated for qualitative variables.

RESULTS

A total of 212 patients suffering from chronic liver disease were included in the study. Out of these 130 (61.3%) were male while 82 (38.7%) were female. Nine (4.2%) patients were below the the age of 12 years while 203 (95.8%) patients were 12 years or older. Out of 212 patients, 164 (77.4%) were suffering from chronic hepatitis C, 16 (7.5%) from chronic hepatitis B, 2 (0.9%) from autoimmune hepatitis, 2 (0.9%) from hepatocelluar carcinoma, 1 (0.5%) from alcoholic hepatitis, 2 (0.9%) from Wilson's disease, 1 (0.5%) from haemochromatosis and 24 (11.3%) were cryptogenic. Hepatitis C related cirrhosis accounted for the main cause of Chronic Liver Disease in our setup which itself is a preventable disease. Cryptogenic was the second largest group while Hepatitis B related cirrhosis the third largest group (Figure).

All these patients were evaluated for Liver Transplant according to the appropriate criterion. Out of 212 patients, 43 (20.3%) patients had MELD/PELD Score of ≤ 10, 92 (43.4%) patients were in the range of 11-18, 44 (20.8%) patients in range of 19-24, 31 (14.6%) patients were in range of 25-35 and 02 (0.9%) patients were ≥36. Patients with MELD/PELD score more than 10 (169 patients i.e 79.7%) were considered for liver transplant but the MELD/PELD score at which a patient will receive a liver varies by region and organ demand as defined by the number of candidates on the waiting list and their blood type.

DISCUSSION

The study was primarily carried out to assess the patients suffering from chronic liver disease for liver transplant. High frequency of

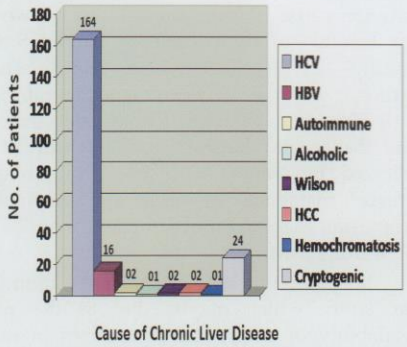

Figure: Causes of Chronic Liver Disease in our region (n=212)

hepatitis B and C viruses has been found among CLD patients in our study. Similar results were presented by other researchers as well[16-19]. Liver Transplant remains a viable option for treatment of patients with CLD and has revolutionized the care of patients with End Stage Liver Disease [20,21] . Unfortunately despite the high morbidity and mortality related to chronic liver disease[5]. in our region no such facilities of liver transplant is present in our country.

In 2006 adults aged 50 and older represented 72% of the waiting list for liver transplant in United States[22]. While in our study 137 patients (64.6%) were aged 50 years and older while 75 patients (35.4%) were below 50 years of age. The proportion of pediatric candidates comprised only 3% of the list in 2006[23] while it constitutes 4.2% of candidates in our study.

At the end of 2006, 73% of all candidates had MELD scores <1522 while in our study only 89 patients (42%) had MELD/PELD score <15 and 123 patients (58%) had a MELD/PELD score >15. This shows the burden of patients requiring liver transplant in our region to be much greater which may be due to increased burden of HCV.

In patients decompensated hepatitis C cirrhosis seems to be the most common cause of CLD which requires liver transplant and it differs from other countries like Singapore

where hepatocellular carcinoma was the most common cause of liver transplant[23]. However our results are comparable to United States waiting list in 2006 where noncholestatic cirrhosis was the largest diagnostic category with 73% of candidates. Cholestatic cirrhosis was the second largest grouping with 10%, followed by 'other' with 9%, while biliary atresia, metabolic diseases and malignant neoplasms each accounted for less than 2% of the waiting list[22].

No patient of PBC or PSC were found in our study which maybe due to the non-availability of diagnostic procedures in most parts of our country and such patients may have remained undiagnosed or labeled as cryptogenic. Similarly very few patients of alcoholic cirrhosis were seen in this study because alcohol is religiously and legally banned in this region and those who do have a history of alcoholism conceal the truth due to social taboos.

Data from this and similar studies show that considerable number of patients in our region suffer from chronic liver diseases for which liver transplant can be done[5,17]. This provides a base line data for the establishment of liver transplant centers in our country. This infact maybe an underestimation of the problem, as those patients who were not admitted may have had a higher score qualifying them for transplant and because they were not admitted were missed. It could be other way also but our study was not a prevalence study and even if admitted patients are considered they at least provide a measure of requirement of transplant for such patients.

No such data is available from our region so more accurate estimates can be done by conducting larger studies involving indoor and outdoor patients and considering deaths attributed to cirrhosis also as these patients would have certainly required transplant.

CONCLUSION

High frequency of patients of chronic liver disease in our setup qualify for a liver transplant. It provides preliminary data for the need of liver transplant centers in our region. It also implies that major cause of chronic liver disease in our patients is hepatitis C which is a preventable disease.

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