

SEROLOGICAL PROFILE OF PATIENTS WITH LIVER CIRRHOSIS IN NORTHERN PAKISTAN

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ABSTRACT

Objective: To evaluate the role of hepatitis B and C in the pathogenesis of liver cirrhosis.

Design: An observational study.

Place and Duration of Study: The present study was conducted in the medical wards of Military Hospital, Rawalpindi from 1st January 2002 to 24th September 2004.

Patients and Methods: Six hundred and fifty patients admitted in the medical wards of Military Hospital Rawalpindi were evaluated for seromarkers of Hepatitis B and C. Viral markers studied were anti HCV, HBs Ag anti HDV, anti HBcIgG, anti HBs, and HBeAg.

Results: One hundred and eighty two out of 650 patients were positive for HBsAg positive and 468 patients were negative for HBsAg. Anti HBcIgG was positive in 345 and anti HBs in 322 of HBsAg negative patient. HBeAg was present in 45 and anti HDV in 26 of HBsAg positive patients. Anti HCV was positive in 455 (70%) patients and no seromarkers were seen in 52 patients.

Conclusion: It was evident from the seromarkers that exposure to hepatitis B and C had occurred but which one was responsible for cirrhosis was hard to determine. In as much as vaccine against hepatitis B is available, mass vaccination in the population may be consideration to prevent cirrhosis due to hepatitis B virus.

Keywords: Liver cirrhosis, vaccination, serology, hepatitis B virus, hepatitis C virus

INTRODUCTION

Cirrhosis is one of the chronic liver diseases characterized by diffuse distinction and degeneration of hepatic parenchymal cells and ultimately results in the disorganization of lobar architecture. The triad of parenchymal necrosis, regeneration & scarring is usually present [1].

In Europe & USA, excessive consumption of alcohol and in Asian countries hepatitis B

(HBV) and C (HCV) are responsible for 75 % cases of liver cirrhosis [2,3]. Hepatitis D is the least common cause of liver cirrhosis [4].

Liver cirrhosis with its attendant complications results in high morbidity & mortality, when caused by HBV and HCV and has high association with hepatocellular carcinoma [5,6]. Earlier work in Pakistan showed hepatic cirrhosis as mostly macro nodular and post necrotic but viral serology was not adequately tested in these studies [7]. Viral markers indicating exposure or active replication are now available for evaluation [8,9].

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In view of evolving therapy in chronic hepatitis a detailed study of serological markers in liver cirrhosis was highly desirable in Pakistan. We therefore evaluated the sera of 650 cirrhotic patients at Military Hospital Rawalpindi to help define the association of serological markers in the diagnosis, monitoring and staging of chronic liver disease.

PATIENTS AND METHODS

All the patients, diagnosed as having liver cirrhosis on the basis of history, clinical features, abdominal ultrasound, radionuclide liver / spleen perfusion scan and liver biopsy (selected cases) and admitted in the medical wards of Military Hospital Rawalpindi, from 1st January 2002 to 24th September 2004 (3 years period) were included in the study. Cirrhotic patients due to causes other than viral infection were excluded. The relevant clinical details were recorded on a performa, designed and filled by the doctors participating in the study. Blood was collected in sterile disposable syringes taking necessary precautions. It was separated into 3 aliquots of sera, labeled and stored in the retrievable fashion until analyzed; one part was used to study viral markers and 2 parts stored for future analysis. Markers studied were anti HCV, HBsAg, HBeAg, Anti HBc IgG, Anti HBsAg and Anti HDV. All tests were done by ELISA (3rd Generation, Abbott Laboratories, Chicago, USA).

RESULTS

In this study out of 650 patients 460 patients (70%) were males while 190 (30%) patients were females. Most of the patients belonged to age group 41 - 60 years. The means age was 47 + 11.1 years. Male to female ratio was 2:1. Median age was 43 years and mode was 41 years. The overall age distribution is given in (table-1).

182 out of 650 patients were positive for HBsAg and 468 patients were negative for

HBsAg. In 114 HBsAg positive patients anti HBcIgG was present , where as 25 patients were also positive for anti HBs. HBeAg was present in 45, anti HDV in 26 and 39 of these patients were also positive for HCV (table-2).

Out of 468 HBsAg negative patients 345 (74%) were positive for anti HBc IgG, 322 (69%) for anti HBs and 7 of these were positive for HBeAg. 52 patients did not have major seromarkers of both HBV and HCV (table-2).

HBeAg was positive in 52 patients, 45 of these were positive and 7 were negative for HBsAg. In 26 patients anti HBs was positive in combination with HBsAg and HBeAg. There were 26 patients with HDV super infection in HBsAg. 5 out of these were additionally positive for anti HCV. Anti HCV was positive in 455 (70%) patients. 39 of these were HBs Ag positive and 416 were HBsAg negative. Anti HBcIgG was detected in 317 (70%) and anti HBs in 305 (67%) of these 455 patients (table-2).

DISCUSSION

Liver cirrhosis is a common condition in Pakistan resulting from Hepatitis B & C [10,11,12]. Evaluation of etiological factors and the diagnosis of disease entity has been the subject of many studies in the past and have also been addressed in the present study.

Majority of the patients (70%) were males and male to female ratio was 2:1. About 170 million people in the world have liver cirrhosis and male predominance has been reported in different studies including the present study as well [13,14,15]. On the other hand female predominance was reported in Soweto Black Children [16]. Male predominance might be due to more no of males reporting for their tests and due to more dynamic and active role of male in our set up. One may not be certain to predict, whether the male predominance is due to

predilections of the gender for disease process or otherwise until a basic sero survey is carried out.

In our study most of the patients 56% were in the 4th & 5th decade of life. A similar age range has been reported from South East Asia although some studies from the west have reported younger and older groups [16,17,18]. The finding of our study are comparable with the recent studies conducted in Pakistan as well [19,20,21]. The disease thus affects the individuals mostly when the community is dependant upon his vigor and enterprise. The deleterious effects are not only in the form of bodily ill health and reduced efficiency but also in the form of expenditures incurred on the tests for monitoring of progression of disease and treatment. These all have their own adverse financial implications and individual at the age is more liable to transmit infection to others.

The study of cases less than 20 years of age was interesting when the possible risk factors in them were sought. All the 13 cases with age less than 10 years were those who had been on multiple blood transfusions. Similarly 15 out of 20 cases in the age group 11 - 20 years were also on multiple blood transfusions, due to bleeding disorders. 4 cases out of remaining 10 cases had either mother or father with hepatitis C where as no risk factor could be evaluated in rest of cases. These were labeled as endemic cases [22].

In this study, viral markers for HBV and HCV were positive in 92 % of patients, this collaborates, with the results reported by Shah et al, as 85 % in chronic liver disease, although, in their report HBV was much higher (66%) than HCV (44.7%), but they only checked the HCV in their HBV negative patients, thus might have missed dual infection cases [23].

The frequency of HBV markers in the sera is related to the prevalence of HBV Infection in the study region and on the

sensitivity of techniques used. In the present study, HBsAg positively was observed in 28% cases which are very similar to 24% in the study by Shah et al [23]. Other has also shown similar results [24,25,26]. Evidence of antecedental hepatitis B virus infection was seen as anti HBcIgG positive cases in 70% cases which is comparable to earlier reports of 80% and 74% by Anwaar et al [27] and Haider et al [28]. Similar results have also been published by Ray and associates [29].

Interestingly 26 cases had both markers for anti HBs and HBsAg positively and 22 of these were additionally positive for HBeAg. This may be interpreted as mutation of HBV, also observed by others [30,31,32]. They also suggested that anti HBS is not formed against the circulating antigen and is not responsible for clearing the antigen [33].

We observed that 25% of the HBsAg positive patients had active replication (HBeAg positive) in contrast to 5% reported earlier in HBsAg positive patients with chronic liver disease [34]. 7 odd cases had positive HBeAg in absence of HBsAg. This variant has also been described from Africa. [35].

Anti HCV was positive in 455 (70%) of our patients. Most of these had evidence of exposure to HBV. Seroprevalence studies have shown that dual infection with HBV and HCV is not uncommon in Asia [36,37], as well as in western countries [38,39]. The reported prevalence is approximately 10-15% in patient with chronic HBV infection [40] which is comparable to 10 % in present study as well.

Most of our patients with dual infection were negative for HBsAg, only 39 were positive for HBsAg and of these 4 were additionally positive for HBeAg. HCV infection has a suppressive effect on the HBV, where it causes progression of Inflammation and necrosis as a long lasting agent. Other clinical studies have shown a low HBV DNA

polymerase activity or HBV DNA level in patients who have chronic infection due to HBV and were also anti HCV positive [36,38].

Gradual loss of HBV DNA, with subsequent HBeAg and HBsAg clearance has been observed in acute HCV super infection [36,38]. However recently it has been reported that occult HBV Infection occurs in chronic hepatitis C, by using PCR in the liver and serum sample of HBsAg negative patients. The authors suggestive role of dual infection as significant factor in the development of cirrhosis and hepatocellular carcinoma in HCV infection [40].

Super infection with delta virus (anti HDV positive) was seen in 26 (14%) of the HBsAg positive patients, this association is well known [41] Shah et al reported anti HDV positively in 17.6 % of HBsAg positive patients with chronic liver disease. Interestingly 5 out of these 26 patients were also positive for anti HDV. The significance of this pattern (anti HDV, anti HCV and HBsAg) to our best of knowledge has not been reported in previous studies, although infection by multiple hepatotropic viruses such as, HAV, HBV and HDV is well known [42]. Further the detection of anti HDV indicates the possibility of chronic HDV agent infection followed by super infection by HCV, possibly occurring through the use of contaminated blood. Co-infection with HCV cannot be excluded, but this needs the development of specific testing which can differentiate between recent and past HCV infection [43]. In such cases we propose that HCV and HDV may synchronize their harmful effect on liver. Also the presence of HBsAg is due to the fact that HDV is a defective virus and depends upon HBV for its survival [44].

CONCLUSION

We concluded from this study that HCV is the leading cause of cirrhosis in our set up. It also signifies the changing epidemiological

Table-1: Distribution of 650 cases of liver cirrhosis according to age and sex.

Age in years	Males	Females	Total
0 - 09	12	1	13
10 - 19	18	4	22
20 - 29	20	12	32
30 - 39	65	24	89
40 - 49	90	45	138
50 - 59	145	75	220
60 - 69	75	20	95
70 - 79	32	18	42
Age Range	460	190	650

Table-2: Seromarkers for HBV, HCV and HDV in patients with liver cirrhosis (n=650).

Major Seromarkers (HBsAg & Anti HCV)	Anti HBcIgG	Anti HDV	HBeAg	Anti HBs
HBsAg (n = 143)	102	21	41	18
Anti HCV (n = 416)	305	-	-	297
HBs Ag & Anti HCV (n = 39)	12	5	4	8
Both negative (n = 52)	40	-	7	25

pattern of chronic liver diseases from HBV to HCV which is a matter of concern for the health community, the health professionals and the epidemiologists , due to the fact that no effective vaccine has been developed against the HCV.

RECOMMENDATIONS

Preventive measures should be adapted to oblivate liver cirrhosis which has serious economic and social implications, for the individual, family and national exchequer.

Vaccination against HBV at birth, screening of blood donor for HBsAg and anti HCV, strict use of the disposable syringes must be observed.

It is also important to educate the tattooists and practitioners of the traditional or alternative medicine about ways to minimize the blood contamination. This involves the sterilization techniques for procedures that involve skin penetration or break to the mucosal surfaces.

Resources should be identified to provide the people of the region with cost effective

measures of prevention of the Hepatitis B & C.

Public health measures should involve not only education of health and allied health professionals but also opinion leaders, politicians and wider community.

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