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Hepatitis B virus related hepatocellular carcinoma is the predominant cause of liver cancer in Bangladesh

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ABSTRACT

Objective: To investigate the etiology and other factor in development of hepatocellular carcinoma (HCC) in Bangladesh. **Method:** Data from past studies were compared with our data to assess the etiology and other factor in development of HCC. Mainly four studies were compared which were done in different time. Ultrasonography was principle modality of primary diagnosis. Fine needle aspiration cytology was done in all cases to have tissue diagnosis. **Results:** Previous studies demonstrate hepatitis B in at least 46.9% cases. Recent studies demonstrate at least 61% association of HCC with hepatitis B infection. Our data which include 39 patients (M: F = 29: 10, Age 22–75 years, mean 51 year) demonstrate HBsAg positivity was present in 16 (41%), Anti HCV positivity in 2 (5%), both negativity in 8 (20.5%) and secondary carcinoma in 13 (33.3%) cases. If only primary HCC is considered then hepatitis B virus (HBV) related HCC constituted 61.5%. Alpha fetoprotein was > 350 ng/mL in 11 out of 26 cases (42.3%). **Conclusions:** Though the study populations are small, they reflect that the prevalence of HBV related HCC correlates with the existing prevalence of HBsAg positivity in general population. Also the etiology has not changed over years and prevalence of hepatitis B related HCC is more or less a static as compared with previous studies.

1. Introduction

Bangladesh lies in the intermediate zone in the world picture of Hepatitis B (HBV) prevalence. The prevalence of hepatocellular carcinoma (HCC) in Bangladesh is 35% among all liver diseases[1]. Here the prevalence of HBsAg positivity in a healthy population is around 5.4%[2]. The prevalence of hepatitis C is quite low (0.8%) in healthy population[3]. So far no large scale study regarding the incidence or prevalence of hepatocellular carcinoma (HCC) done. Small studies or retrospective data shows

predominance of HBV infection as the predominant cause. Our immunization schedule has included HBV vaccination since early 2000. So the result of mass vaccination is yet to come up.

The incidence of HCC in Bangladesh in both male and female is 1.3/100 000/year and autopsy prevalence of 0.2 among 5 450 autopsies[4]. About 35% of patients suffering from chronic liver disease suffer from HCC[5].

2. Materials and methods

Different criteria were followed in small studies done so far. As Bangladesh is a developing country ultrasonographic diagnosis followed fine needle aspiration cytology (FNAC) is the predominant modality of diagnosis. Many of the patients present

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very late. Viral markers are not possible many a times in patients as they are unable to bear the expenses of such an investigation.

Herbal and traditional medicines some time delay the diagnosis. Our data are mainly retrospective or small scale. So many associated inference and observations are missing. Earlier studies did not include Anti HCV as it was not available at that time.

Data of patients seeking the treatment in tertiary center like Bangabandhu Sheikh Mujib Medical University and Dhaka Medical College are presented here. As these two are located in capital city Dhaka, they may represent the national picture.

These data are not randomized rather than on availability of patients. Also only adult data are taken from department of hepatology, Bangabandhu Sheikh Mujib Medical University and department of medicine, Dhaka Medical College Hospital, so paediatric population are not represented. Data are analysed using SPSS statistical software.

3. Result

Results of different studies show predominance hepatitis B as an etiologic factor. However earlier studies did not include evaluation of hepatitis C. Only study from department of pathology included paediatric population. According to that study which 1 patient (2.3%) among 79 patients had hepatocellular carcinoma[6].

Our unpublished data which is done on adult population are from Department of Hepatology, Dhaka Medical College Hospital during January to June 2009. Patients were assessed of their etiology prospectively. 39 patients (M: F = 29: 10, Age 22-75 years, mean 51

year) were included in this study. HBsAg positivity was present in 16 (41%), Anti HCV positivity in 2 (5%), both negativity in 8 (20.5%) and secondary carcinoma in 13 (33.3%) cases. If only primary hepatocellular carcinoma (HCC) is considered then hepatitis B virus (HBV) related HCC constituted 61.5%. Evaluation for NAFLD not done in this study.

Male predominance is seen in almost all studies in Table 1 and Figure 1[5-7]. One study noted the use of oral contraceptive pills in 58.33% cases in women having no etiologic factor. The average duration of intake of pills was 7.3 years[4]. New etiologic agent like NAFLD is coming up from a recent study. In that study 5% of HCC was diagnosed to be due to NAFLD[7]. So at present scenario NAFLD is may be considered as an etiologic agent. Physical stigmata of cirrhosis of liver were present in only 18.75% cases[4].

Role of aflatoxin has not been evaluated in any studies however its role of is suspected in some cases as food sanitation in our country is not uniformly maintained in our country. Also arsenicosis in rural population is a problem. Paan chewing as a possible etiologic agent has been observed in a number of studies[8].

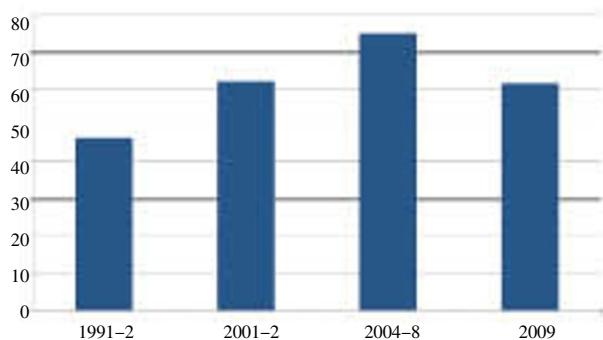


Figure 1. HBsAg positivity in HCC past vs. present.

Table 1

Comparing the patients parameters of different of studies on HCC[5-7].

| | 1991-2 Data | 2001-2 Data | 2004-8 Data | 2009 Data (unpublished data) |
|--------------|---|---|--------------------|---|
| n | 64 | 79 | 976 | 39 |
| Age | 21-75 | 18-88 | - | 22-75 |
| Mean age | 50.1 | 48.5 | - | 51.0 |
| M:F | 81:19 | 97:3 | - | 75:25 |
| HBsAg | +ve 46.9% | +ve 61.9% | +ve 75.0% | +ve 61.5% |
| Anti-HCV | -Not done | -Not done | +ve 17% | +ve 5% |
| Limitations: | Anti-HCV- not done. NAFLD not considered. | Anti-HCV- not done. NAFLD not considered. | Retrospective data | NAFLD not considered. Anti HBe (Total) not done |

The mean age of presentation in all studies is more than 48 years. Alpha feto-protein level was significantly lower in non-cirrhotic patient ($3\ 826 \pm 7\ 852$) ng/mL *versus* ($918 \pm 1\ 823$) ng/mL^[5]. Our study showed alpha feto-protein was > 350 ng/mL in 11 out of 26 cases (42.3%), however co-relation between cirrhotic and non-cirrhotic not done.

In one study the mean age of HCC in HBsAg positive patients was 41.92 years as compared to 59.87 years in non-hepatitis B cases. It appears that HCC appears 18 years earlier than those of non-hepatitis B cases^[6]. Our study shows 47.94 years as mean age in primary HCC.

4. Discussion

In Bangladesh HCC has been neglected as the majority of the patients come from poor or lower-middle class. Second thing that occurs is that time of diagnosis is delayed. This is probably due to awareness, lack of medical facilities, lack of resources and economic reasons. The result of vaccination for hepatitis B through EPI schedule is yet to yield its result. The exact modality of transmission is not identified.

A significant proportion of patients are diagnosed as having HBsAg positivity while medical examination for overseas employment. Several facts emerged from all the studies that is cirrhosis of liver, hepatitis B infection, male sex, middle age are important risk factors for development of HCC in Bangladesh. Less common factor like NAFLD is coming up as the etiologic factor in a recent study^[7-10].

More data could come up if the studies were done prospectively. Though small our study reflects that the prevalence of HBV related HCC correlates with the existing prevalence of HBsAg positivity in general population. Also the etiology has not changed over years and prevalence of hepatitis B related HCC is more or less a static as compared with previous studies.

Conflict of interest statement

The author does not have conflict interest from the present study.

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