

## STUDY ON ASSOCIATION OF HEPATOCELLULAR CARCINOMA WITH HEPATITIS B VIRUS INFECTION: BANGLADESH PERSPECTIVE

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### Abstract

Hepatocellular carcinoma (HCC) is a common visceral malignant tumour and Hepatitis B virus is considered as an important etiologic agent. HBV is a DNA containing virus. Blood and body fluids are its primary vehicle of transmission. It causes chronic hepatic injury and malignant transformation of hepatocytes by its HBX protein. In our study we have diagnosed 43 cases of HCC out of 79 cases of hepatic mass lesions. The mean age of the patients is 48.55 years with a male predominance. Serum HBsAg positivity was detected in 28 (61.9 %) of HCC cases and 6 (17.64%) in non-HCC cases. The association of HBsAg with HCC cases is statistically highly significant ( $P < .001$ ) when compared with non HCC cases.

### Introduction

The geographical distribution of hepatocellular carcinoma varies in different countries of the world. In countries where HCC is common including parts of Asia and Africa, it is frequently associated with macro nodular cirrhosis of liver and also with hepatitis B virus. The close association between HCC and hepatitis B virus (HBV) suggests a causal relationship between the two<sup>1,2</sup>. In Africa there is also high association with aflatoxin B1.

There are two major types of primary carcinoma of liver, hepatocellular carcinoma arising from hepatocytes and cholangiocarcinoma arising from bile duct epithelium. HCC accounts for more than 90% of all primary liver cancer<sup>3</sup>. Statistically it has been found that hepatitis B carriage correlates with the frequency of HCC throughout the world. In Britain the mortality from primary liver cancer is 1-2 per 100,000 and the carriage rate for hepatitis B

surface antigen is one per 1000 where as in China the primary liver cancer mortality is approximately 17 per 100,000 and the hepatitis B antigen carrier rate is 7.5 to 14%<sup>4</sup>. In Taiwan, the incidence of HCC among carriers of hepatitis B surface antigen (HBsAg) is much higher than among noncarrier<sup>5</sup>. Globally, approximately 3% of world population are infected with hepatitis C virus with 1% to 5% increased risk of HCC<sup>6</sup>. The aim of our study was to explore the correlation of HCC with HBV in Bangladeshi population.

### Materials and methods

This study was carried out in the department of pathology, Bangabandhu Sheikh Mujib Medical University, Dhaka during the period of October, 2001 to November 2002. A total of 79 patients of different age and sex with hepatic masses were collected from BSMMU hospital and Dhaka medical college hospital with an aim to find out the usefulness of FNAC in the diagnosis of HCC and to see the association of HCC with HBV. All necessary and relevant data of the patients were recorded methodically in a data sheet. Before performing FNA from liver, result of prothrombin time, report of USG of whole abdomen and informed written consent of the patients were obtained. Blood of the patients was collected in disposable syringes. After centrifugation serum was preserved in deep refrigerator. The serum was tested for HBsAg in ELISA method.

### Results

As very little epidemiological study on HCC has been conducted in Bangladesh<sup>7</sup>, the purpose of this study was to diagnose hepatic SOL by FNAC and to assess the prevalence of infection by hepatitis B virus in cases of HCC. The cytological diagnosis was correlated with histology, clinical history, physical findings, serum markers, Ultrasound and CT scan report. Out of 79 cases of hepatic masses 43 were HCC, 21 metastatic lesions and the remaining cases were liver abscesses and other lesions. The age range of HCC cases were between 18 to 88 years.

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The mean age was 48.55 years. The number of male patients was 41 and female were 2. The male to female ratio was 20.5:1. The result is shown in table I.

**Table I :** Age distribution of HCC cases (n=43)

Age in years	Number of patients	Percentage	Mean age in years
11-20	01	2.32	48.55
21-30	04	9.30	
31-40	12	27.90	
41-50	10	23.25	
51-60	7	16.27	
61-70	6	13.95	
71-80	0	0	
81-90	2	4.65	

We have taken detail history of present illness and past illness and made meticulous physical examination of the patients. The patients with HCC appeared before us at the advanced stage of the disease with overt signs and symptoms. Their duration of illness varied from I month to I year. They had dull upper abdominal pain, palpable lumps, ascites and jaundice. They had the complaints of fever, loss of appetite and loss of weight. Twenty four patients with HCC had previous history of acute hepatitis. One patient had history of alcohol consumption for prolonged time and two female patients had history of oral contraceptive pills for long period. The presenting clinical features of HCC are shown in table II.

**Table II :** Symptoms & clinical findings of HCC cases (n=43)

Signs & symptoms	Number of patients	Percentage
Pain in abdomen	42	97.67
Lump in abdomen	40	93.02
Ascites	19	44.18
Jaundice	15	34.88
Loss of weight	27	62.79
Loss of appetite	34	79.00

Along with history and physical findings, the ultrasonography report of whole abdomen was also evaluated. The image report described the HCC lesions as single large space occupying lesion, multiple discrete lesions or as diffuse heterogeneous echogenicity. The sonological diagnosis was HCC

including a differential diagnosis of metastatic lesion and vice versa. The ultrasonography findings are shown in table III.

**Table III :** Ultrasonography findings in HCC cases (n=43)

USG findings patients	No of	Percentage	Diagnosis
Single SOL	11	25.58	HCC
Multiple SOL	23	53.48	Metastatic tumor
Diffuse heterogeneity	9	20.93	HCC

SOL: Space occupying lesion.

Serum of all the patients with space occupying lesion was tested for HBsAg by ELISA method. HBsAg was positive in 27(61.9%) cases of HCC and negative in 16(38.09%) cases of patients with HCC. In other lesions HBsAg was positive in 6(17.64%) and negative in 28(82.35%) cases. The association of HBsAg with HCC is statistically highly significant (p<0.001) when compared with non HCC cases. The result is shown in table IV.

**Table IV :** Association of HCC with HBsAg

Nature of the lesion	HBsAg Association (n=43)		Significance
	Positive	Negative	
HCC	27(61.90%)	16(38.09%)	Highly Significant
Others lesions n=34	6 (17.65%)	28(52.35%)	

**Discussion**

On a global basis HCC is the most common visceral malignant tumour with dismal prognosis. Chronic hepatitis B virus and C virus infections are thought to be important etiological factors for its development. B virus is a DNA containing virus with special affinity for liver cells. It causes chronic hepatic injury and cellular transformation. As a South East Asian country Bangladesh is considered endemic for HBV infection.

But a very few studies have been conducted here to judge the association of HBV with HCC.

In our study the average age of the HCC patients is 48.55 years. This result is almost akin to the average age of 49.15 years as reported by Das et al (2000)<sup>7</sup> and as that of cited by Sherlock 1993<sup>4</sup>.

In this study, the mean age of HBsAg positive HCC cases is 41.92 years and that of HBsAg negative cases is 59.87 years. Therefore it appeared that

hepatocellular carcinoma developed in HBV associated patients on an average of 18 years earlier than those of HBsAg negative cases. The present study revealed that 61.9% of HCC cases are associated with HBV infection.

To detect the hepatitis B virus association we have investigated for HBsAg only. If other parameters were included, such as, serum anti HBc, HBeAg, HBV DNA, the result could be higher. The result of association of HBV with HCC observed in the present study is close to the results that were found in India<sup>8</sup> and Pakistan<sup>9</sup>. In India, the prevalence of hepatitis B virus infection in HCC cases ranges from 60% to 71%<sup>10</sup> and in Pakistan, the prevalence is 67% and in Philippines it is 70%<sup>11</sup>.

#### Summary and conclusion

The present study was carried out with the aim of making diagnosis of hepatocellular carcinoma from hepatic space occupying lesions and to estimate the prevalence of hepatitis B virus infection in HCC cases of Bangladeshi populations. Seventy nine cases with hepatic space occupying lesions were included in the study. The predominant type of lesion was hepatocellular carcinoma (n=43, 57.33%). HBsAg was positive in 27 cases (61.90%). In this respect, our findings are nearer to that of our neighboring countries like India and Pakistan. In India, the association of HBV is 60 to 71%<sup>12</sup> and in Pakistan it is 67%<sup>13</sup>. Therefore it is apparent from the study that in Bangladeshi populations HCC has a highly significant association (p<.001) with HBV infection. Moreover, HBsAg positive cases are more likely to develop poorly differentiated hepatocellular carcinoma, liable to follow an aggressive course.

#### References

1. Akagi Go, Fureya K, Otsuka H. Hepatitis B antigen in the liver in hepatocellular carcinoma in Shikoku, Japan. *Cancer* 1982; 49: 678-682
2. Beasley RP. Hepatitis B virus as the etiologic agent in hepatocellular carcinoma-Epidemiologic consideration. *Hepatology* 1982; 2: 215
3. Cotran RS, Kumar V, Collins T, Robbins Pathologic Basis of Disease, 6th edition, Philadelphia, W B Saunders Company, 1999: 846-891
4. Sherlock S, Dooley J. Diseases of the liver and biliary system, 9th edition, Oxford. Blackwell Scientific Publication, 1993: 503-529
5. Beasley RP, Hwang LY, Chin LC, Siang CC. Hepatocellular carcinoma and hepatitis B virus-A prospective study of 22707 men in Taiwan. *The Lancet*; November 1981: 1129-1132
6. WHO Report, 1999. Cited in *Romedica*, April 2002
7. Das JC, Azad AK, Mamun SAA, Rahman MR et al. Clinical presentation and outcome of hepatocellular carcinoma. *Journal of Bangladesh College of Physicians and Surgeons* 2000; 18: 55-60
8. Vogel EL, Anthony PP, Mody N, Barker LF. Hepatitis associated antigen in Ugandan patients with hepatocellular carcinoma, *The Lancet* 1970; 621-624
9. Obata H, Hayashi N, Motoike Y. A prospective study on the development of hepatocellular carcinoma from liver cirrhosis with persistent hepatitis B virus infection. *Cancer* 1980; 25: 741-747
10. Sarin SK, Thakur V, Gupta RC et al. Profile of hepatocellular carcinoma in India, an insight into the possible etiologic associations. *J Gastroenterol Hepatol* 2001; 6: 66-73
11. Lingao AL, Domingo EO, Nishoka K. Hepatitis B virus profile of hepatocellular carcinoma in the Philippines. *Cancer* 1981; 48: 1590-1593
12. Tandon BN, Acharya SK, Tandon A. Epidemiology of hepatitis B virus infection in India, *Gut* 1996; 38: 56-59
13. Mujeeb A, Jamal Q, Khamani R, Iqbal N, Kaher S, Prevalence of hepatitis B surface antigen and HCV antibodies in hepatocellular carcinoma cases in Karachi, Pakistan. *Trop Doct* 1997: 45-46