

# Characteristics Features of Hepatocellular Carcinoma in Bangladesh and their Public Health Implications

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## ABSTRACT

**Background/Objectives:** In spite of being a common cancer, little is known about clinical presentation, etiological factors and prognosis of hepatocellular carcinoma (HCC) in Bangladesh. Accordingly, early detection and efficient management of HCC is not available at this country.

**Materials and methods:** Demographical data, etiological factors and clinical presentations of 57 consecutive patients with HCC were analyzed prospectively at the only medical university of Bangladesh.

**Results:** Ninety-one percent patients with HCC were male. The mean age of HCC patients was 45.8 years (standard deviation: 15.3 years; range: 18-75 years). All patients were symptomatic when they first appeared to the physicians, and many of them were unaware that they had been suffering from liver diseases. Hepatitis B surface antigen was detected in 62% and antibody to hepatitis C virus was found in 6% patients with HCC. Most of the patients with HCC had liver cirrhosis (77%). Single HCC nodule was detected in 61% patients. Sixty-four percent patients had intermediate stage of liver cancer.

**Conclusion:** Containment of HCC-related morbidity and mortality and better prognosis of HCC in Bangladesh depends on early diagnosis of hepatitis viruses.

**Keywords:** Hepatocellular carcinoma, Hepatitis B virus, Hepatitis C virus, Advanced hepatocellular carcinoma.

**How to cite this article:** Gani ABMS, Al-Mahtab M, Rahman S, Akbar SMF. Characteristics Features of Hepatocellular Carcinoma in Bangladesh and their Public Health Implications. *Euroasian J Hepato-Gastroenterol* 2013;3(1):28-30.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION

Primary liver cancer, which consists predominantly of hepatocellular carcinoma (HCC), is the fifth most common cancer worldwide and the third most common cause of cancer mortality.<sup>1</sup> Globally, over half a million people develop HCC each year and an almost equal number die of it.<sup>2</sup> HCC has several characteristics epidemiologic features including dynamic temporal trends; marked variations among geographic regions, racial and ethnic groups, and between men and women; and the presence of several well-documented potentially preventable risk factors. Studies have shown that HCC largely occurs within an established background of chronic liver disease and cirrhosis. Major causes of cirrhosis in patients with HCC include hepatitis B virus (HBV), hepatitis C virus (HCV), alcoholic liver

disease and possibly nonalcoholic steatohepatitis (reviewed in details in reference 3). In addition, hereditary hemochromatosis, alpha-antitrypsin deficiency, autoimmune hepatitis, and some porphyrias have also been associated as minor etiological factors in some patients with HCC.<sup>3</sup> Improved insights about pathogenesis, clinical features, prognosis and interventional strategies have led to develop mechanisms of early diagnosis and improved management against HCC in most developed countries.<sup>4</sup> However, this success has not been duplicated worldwide.<sup>5,6</sup> Although most patients with HCC reside in developing countries of the world, there is lack of information about etiological factors, clinical presentation and management of these patients in the developing countries.

Bangladesh is a developing country in Asia with a population of 140 million. It is estimated that more than 8 million people are chronically infected with HBV<sup>7</sup> and about 1 to 2 million with HCV.<sup>8</sup> However, there are paucity of information about clinical and pathological features of HCC in Bangladesh. Khan et al have detected liver cirrhosis in 18.5% patients with HCC by examining a cohort of 64 patients at Bangladesh in 1997.<sup>9</sup> Another study conducted in United Kingdom, among HCC patients of Bangladeshi origin, has shown that 36 and 56% of these patients have been infected with HBV and HCV, respectively.<sup>10</sup> However, studies from India, a close neighbor of Bangladesh, have reported that about 80% HCC patients are infected with HBV and most of the HCC patients are cirrhotic.<sup>11</sup> These studies indicate that more investigations are required to develop insights about clinical features, etiological agents and epidemiology of HCC at Bangladesh.

The present communication, a prospective study, was accomplished to understand the present status of HCC in Bangladesh. We took elaborative history of HCC patients, and also checked clinical profiles and etiological agents of HCC patients. The findings of this study would be discussed for development a strategy for containment of incidence of HCC and also for better management of these patients in Bangladesh.

## PATIENTS AND METHODS

### Patients

Consecutive 57 patients with HCC those attended the Bangabandhu Sheikh Mujib Medical University, Dhaka,

Bangladesh, in 2008 were enrolled in this study. This is the only Postgraduate Medical University of Bangladesh and acts as a referral center for patients with intractable diseases. The mean age of the patient was 45.8 years (standard deviation: 15.3 years). Fifty-two patients were male (91%) and the rest five were female (9%).

### Study Design

A questionnaire was prepared that had two parts: (1) Baseline characteristics of the patients with HCC, and (2) presenting symptoms of the patients. This was filled up by a clinical monitor by asking questions to the patients. The patients were examined by the attending physician. Presence of hepatitis B surface antigen (HBsAg) and anti-HCV antibody was evaluated using commercial kits. The diagnosis of underlying cirrhosis was done on the basis of clinical, endoscopic findings (presence of varices) and radiological features (ultrasonography and computed tomography). The presence of HCC was confirmed by either ultrasound (US), or computed tomography, or magnetic resonance imaging of the abdomen. In some cases, more than one imaging technique was employed. The Barcelona Clinic Liver Cancer (BCLC) staging of HCC were adopted on the basis of clinical and radiological information.<sup>12</sup> The confirmation of HCC was done by cytopathological examination of fine needle aspirates. Patients were excluded from this study if cytopathological study could not provide a confirmatory diagnosis of HCC. The study was conducted according to the ethical guidelines of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, and is in agreement with those set out by the 1975 Declaration of Helsinki as revised in 1983.

### RESULTS

The baseline characteristics of patients with HCC are presented in Table 1. The mean age of HCC patients was 45.81 years, and most of them were male (52 of 57 patients, 91%). About 40% of the patients were farmer by profession. It was also found that more than 60% were attending the hospital of Dhaka from rural areas. Some of the patients travelled more than 300 km to get treatment.

The presenting symptoms of the patients have been shown in Table 2. The patients experienced various symptoms for different duration, but, this was their first consultation with a recognized medical doctor. The symptoms that they experienced before attending this hospital include loss of body weight, pain in the abdomen, ascites and jaundice. Accordingly, all patients with HCC had some symptoms during their first presentation. Some

of the patients had multiple symptoms. Most of the patients had abdominal pain or anorexia as presenting symptoms. About 49% patients felt a palpable mass at the abdomen. Jaundice was detected in 15% patients. When the patients were checked by attending physicians, a palpable liver was found in 74% patients. Ascites were detected in 57% patients. Edema was seen in 23% patients (Table 3).

Imaging technique revealed space-occupying lesions in, all but two patients with HCC (96%, 53 of 55 patients). The numbers of lesions were single in 61% patients and multiple in 39% patients. Evidence of liver cirrhosis was seen in 77% patients by ultrasonography and assessment of liver function test. Most of patients with liver cirrhosis were

**Table 1: Baseline characteristics of patients of HCC in Bangladesh (n = 57)**

Total patients	57 patients
<b>Age</b>	
Mean $\pm$ SD	45.81 $\pm$ 15.31 years
Range	18-75 years
<b>Sex</b>	
Male	9%
Female	9%
<b>Occupation</b>	
Farming	41%
Business	17%
Housewife	10%
Service	9%
Student	9%
Others	14%

Note: Age, sex and occupation of patients with HCC are shown

**Table 2: Presenting symptoms of patients with HCC**

Presenting symptoms	Percentage
Mass in abdomen	49
Pain	79
Weight loss	45
Fever	53
Anorexia	79
Jaundice	15
Cachexia	11
Anemia	32

Note: Some of the patients with HCC had multiple symptoms at first presentation

**Table 3: Clinical features of patients with HCC**

Leukonychia	11%
Edema	23%
Gynecomastia	13%
Spider telangiectasia	32%
Palmar erythema	11%
Palpable liver	74%
Palpable spleen	23%
Ascites	57%
Testicular atrophy	46%
Features of metastasis (lungs)	2%

grouped into Child-Pugh score B (43%). Sixty-four percent patients had intermediate stage of HCC, according to the grading of the grading of BCLC.

Regarding etiological factor, 62% patients were expressing HBsAg in the sera, whereas, anti-HCV antibody was detected in 6% patients. None of the patients has any history of excessive alcohol consumption.

## DISCUSSION

The study presented here has shown that most of the patients with HCC at Bangladesh were infected with the HBV and about 77% of these patients were suffering from liver cirrhosis. Although the results of the present study are not in line with previous publications in 1990s about HCC in Bangladesh,<sup>9,10</sup> the data presented here are in line with that what has been reported by Kumar et al about etiology and cirrhosis of HCC patients in India,<sup>11</sup> a close neighbor of Bangladesh.

In addition, this study revealed that proper screening of liver cirrhosis is absent in Bangladesh. Most of the patients were unaware of their chronic liver diseases before attending the tertiary hospitals. All patients presented with complain like abdominal pain, weight loss, fever, jaundice and palpable mass in the abdomen. The extent of liver cirrhosis was also in progressive state. Unfortunately, most of the patients attended the physicians after development of HCC.

These facts unveil the importance of diagnosis and follow-up of patients with chronic viral liver diseases at an early stage. As most of these patients had advanced HCC, this will comprise their ultimate survival. However, single HCC nodule was detected in 61% patient. If proper interventional strategies can be adopted in these patients, better survival can be expected in these patients.

## CONCLUSION

HCC in Bangladesh occurs at a comparatively earlier age and most of them reside in rural areas. None of these patients had any idea of their liver diseases prior to diagnosis of HCC at tertiary level hospital. When symptoms were developed due to advanced HCC, they came to consult with physicians. As most of the patients had liver cirrhosis, a mechanism should be developed at Bangladesh to properly diagnose chronic hepatitis virus infection and liver cirrhosis. This would lead to better survival of HCC patients.

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