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Original Article

Clinical Presentation of Patients with Hepatocellular Carcinoma in a Tertiary Level Hospital of Bangladesh

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Abstract

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer, accounting for 75% - 86% of all cases. Men are affected approximately two to three times more than women. It is considered as the fifth most common cancer in men and the ninth in women. The prognosis for liver cancer is very poor which has made it globally the second most common cause of death from cancer. The highest liver cancer rates are found in East and Southeast Asia and in Middle and Western Africa. Western world is complaining of rising HCC prevalence as a result of migration from HBV-endemic regions, hepatitis C virus (HCV) infection, alcoholic cirrhosis, and non-alcoholic steatohepatitis associated with the obesity epidemics. The accurate diagnosis of HCC dependent on clinical presentation, biochemical, imaging, cytological and/ or histopathological examination. This was a descriptive study of hepatocellular carcinoma patients those attended Dhaka Medical College Hospital and Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh from September 2006 to march 2008. Thirty (30) consecutive biopsy proven hepatocellular carcinoma patients were enrolled in this study. This study collected data by reviewing Medical records (prescriptions and diagnostic reports) and interviewing patients for various present symptoms/ signs, past complaints (symptoms/ signs) they experienced in different duration and for confirmation of HCC. Among the symptoms almost all 29(96.66%) of the patients had experienced loss of appetite and most of the patients were experienced generalized weakness 28(93.33%) followed by weight loss 24(80%). More than two-third of the patients had complained abdominal pain 22(73.33%), abdominal fullness 21(70%), abdominal mass 20(66.66%) and nausea and vomiting 20(66.66%). Various signs of HCC were found in examination during interview and from their past experience/ reviewing medical record of illness; where most of them 27(90%) had hepatomegaly and half of them 15(50%) had splenomegaly and ascites. Among the others sign of HCC, one-third (33.33%) of them had yellow discolouration of eyes, yellowish urine, jaundice and fever. Several signs were also observed like Leg swelling 9(30%), cough 8(26.66%), alteration of bowel habit 6(20%). Signs like blood vomiting 1(3.33%) and leg oedema 4(13.33%) were also observed. Information regarding clinical presentation from this study may be utilized as indicator for referral, case definition in research works and probable diagnosis of HCC. This clinical presentation may be a strong tool for symptomatic surveillance of HCC and prevention of HCC including chronic hepatitis B and chronic hepatitis C virus infection.

Keywords: *Hepatocellular carcinoma, clinical presentation, loss of appetite, generalized weakness, weight loss.*

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INTRODUCTION

Hepatocellular carcinoma (HCC) is a primary liver malignancy and one of the most common cancers worldwide and is one of the leading causes of cancer-related death.[1–3] HCC is the most common type of primary liver cancer, accounting for 75% - 86% of cases[4]. Men are affected approximately two to three times more than women, with higher incidence and mortality across most countries.[5] It is considered as the fifth most common cancer in men and the ninth in women. The prognosis for liver cancer is very poor which has made it globally the second most common cause of death from cancer.[6]

The highest liver cancer rates are found in East and Southeast Asia and in Middle and Western Africa.[7] This difference in incidence of liver cancer between different geographical regions and countries is mainly attributed to difference in the incidence of underlying risk factors: viral hepatitis, alcohol use, occupational exposure; and

nonalcoholic fatty liver disease (NAFLD).[8–13] HCC is secondary to liver cirrhosis in 80% of patients and is the main cause of death in liver cirrhosis patients in Europe.[14] Additionally, the Western world is complaining of rising HCC prevalence as a result of migration from HBV-endemic regions, hepatitis C virus (HCV) infection, alcoholic cirrhosis, and non-alcoholic steatohepatitis associated with the obesity epidemics.[15] Only 30–40% of patients present with early-stage disease amenable to curative treatments, such as resection or liver transplantation (LT), while others can only undergo local therapies or palliative care.[14] .

Bangladesh is a developing country in Asia with a population of 170 million. It is estimated that more than 8 million people are chronically infected with HBV[16] and about 1 to 2 million with HCV.[17] Khan M et al have detected 18.75% liver cirrhosis patients developed HCC by examining a cohort of 64 patients at Bangladesh in 1997[18]. 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.[19] However, studies from India, a close neighbour of Bangladesh, have reported that about 80% HCC patients are infected with HBV and most of the HCC patients are cirrhotic.[20] These studies indicate that more investigations are required to develop insights about clinical features, etiological agents and epidemiology of HCC at Bangladesh.

MATERIALS AND METHODS

This is a descriptive study with present and prospective documentation of cases. Randomly selected 50 cases of suspected hepatocellular carcinoma those attended the Dhaka Medical College Hospital and Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh, from November 2007 to September 2008 were taken for this study. Finally 30 consecutive biopsy proven hepatocellular carcinoma patients were enrolled in this study.

A questionnaire was prepared with baseline characteristics of the patients with HCC and presenting signs/ symptoms of the patients. This was filled up by asking questions, examination and reviewing record (prescription/ diagnostic report) of the patients. The diagnosis of underlying liver cirrhosis was done on the basis of history, physical examination, endoscopic findings (presence of varices) and radiological features (ultrasonography and computed tomography). HCC was confirmed by liver biopsy. Patients who could not provide a confirmatory histopathological report of HCC were excluded from this study. Data were analyzed by SPSS (Statistical Package for Social Science) software program, version -12.

All data were presented as mean ± SD, and the distribution of data were presented in table and graphical presentation was also displayed.

RESULTS

Table I shows the baseline characteristics of patients of HCC; here, thirty (30) patients were analysed. The mean age of HCC patients was 47.8+SD14.8 years; among the patients male were 23 (76.67%) and male-female ratio was about 3.3:1. About 33.33% of the patients were farmer by occupation and others were Farmer 10 (33.33%), Business 5(16.67%), Housewife 4(13.33%), Service 3(10%), Labor 3(10%), Student 2(6.67%) and Others 3(10%). It was also found that more than 65% patient were attending the hospital from rural areas.

Table-I: Baseline characteristics of patients of HCC in Bangladesh (n=30)

Baseline characteristics of patients		30 patients
Age		
	Mean	47.8+SD14.8 years
	Range	18 - 80 years
Sex		
	Male	23 (76.67%)
	Female	7 (23.33%)
Occupation		
	Farmer	10 (33.33%)
	Business	5 (16.67%)
	Housewife	4 (13.33%)
	Service	3 (10%)
	Labor	3 (10%)
	Student	2 (6.67%)
	Others	3 (10%)

Table II states various symptoms of the patients observed during interview and from their experienced during illness. Common symptoms were loss of appetite, generalized weakness, weight loss, abdominal pain, abdominal fullness and nausea/ vomiting were noted among 29 (96.66%), 28(93.33%), 24(80%), 22(73.33%), 21(70%) and 20(66.66%) of patients respectively. Other symptoms like abdominal mass 20(66.66%), yellow coloration of eyes and urine 10(33.33%), fever 10 (33.33%), leg swelling 9(30%) abdominal swelling 9(30%), blood vomiting 1(3.33%) were also found.

Table-II: Symptoms of patients with hepatocellular carcinoma (HCC) (n=30)

Symptoms	No. of patients	Percentage
Loss of Appetite	29	96.66%
Generalized weakness	28	93.33%
Weight loss	24	80%
Abdominal pain	22	73.33%
Abdominal fullness	21	70%
Nausea/Vomiting	20	66.66%
Abdominal mass	20	66.66%
Yellow coloration of eyes & urine	10	33.33%
Fever	10	33.33%
Leg swelling	9	30%
Abdominal swelling	9	30%
Blood vomiting	1	3.33%

Table III shows the signs of HCC, here, hepatomegaly was 27(90%). Others signs were weight loss 24(80%), ascites 15(50%), splenomegaly 15(50%), jaundice 10(33.33%), testicular atrophy 10(33.33%) ans leg oedema 4 (13.33%),

Table-III: Signs of hepatocellular carcinoma (HCC) (n=30)

Sign	No. of patients	Percentage
Hepatomegaly	27	90%
Weight loss	24	80%
Ascites	15	50%
Splenomegaly	15	50%
Jaundice	10	33.33%
Testicular atrophy	10	33.33%
Palmar erythema	5	16.66%
Clubbing	4	13.33%
Oedema of legs	4	13.33%

Table IV represents the aetiological factors of HCC patients; here evidence of liver cirrhosis was found in 21(70%) of patients by ultrasonography and assessment of liver function test. Regarding etiological factors HBsAg was found in 15(50%) of patients, anti-HCV antibody was detected in 6(20%) patients, cryptogenic was 5(16.66%), autoimmune 3(10%), excessive alcoholic consumption was 1(3.33%).

Most of patients with liver cirrhosis were grouped into Child-Pugh score B (50%). Sixty percent patients had intermediate stage HCC, according to the grading of BCLC.

Table-IV: Aetiological factors of HCC patients (n=30)

Aetiological factors		No. of patients	Percentage
1.	Hepatitis B virus infection	15	50%
2.	Hepatitis C virus infection	6	20%
3.	Cryptogenic	5	16.66%
4.	Autoimmune	3	10%
5.	Alcoholic	1	3.33%

Table V shows imaging technique revealed space-occupying lesions in all patients with HCC. The number of lesions were single in 21(70%) patients and multiple in 9(30%) patients.

Table V: Ultrasonographic findings of Hepatocellular carcinoma (n=30)

	Lesion(s)	No. of patients	Percentage
Mass	Single	21	70%
	Multiple	9	30%
Echopattern	Hyperechoic	03	10%
	Hypoechoic	17	56.66%
	Mixed	10	33.33%

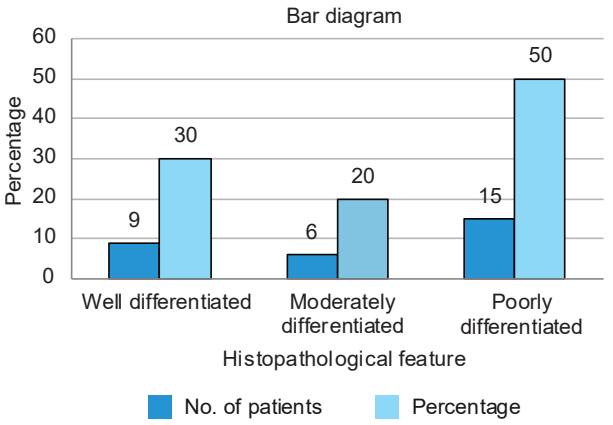

Figure-1: Bardiagram showing histopathological features of hepatocellular carcinoma (n=30)

Figure 1 illustrate the report of histopathological features after percutaneous needle biopsy, where poorly differentiated hepatocellular carcinoma were 15(50%) cases, well differentiated were 9(30%) cases and moderately differentiated were 6(20%)cases.

DISCUSSION

Hepatocellular Carcinoma is an important worldwide health issue, particularly in regions where viral hepatitis prevalence is high. This study revealed that HCC was more prevalent in males i.e, male female ratio was 3:1. Previous study conducted by Khan M et al. showed the ratio was 4:1[18], by Mohan das M et al was 3:1[21] by Shawon MA-A et al was 4:1.[22] This is due to the sex-specific differences in exposure to the risk factors, because they are more likely to be infected with HBV and HCV, as well as alcohol consumption, cigarette smoking and food habits. The liver is a hormone-sensitive organ, that's why sex hormones, such as androgen and estrogen, may be an acting factor. It is assumed that androgen promotes HCC development, whereas estrogen plays a protective role.[23-25] The typical age group affected by HCC was 50-59 and 60-69, as we have found most patients corresponded to this age group. In a study performed in Bangladesh, a group found 41 to 50 years as the most common age group to develop HCC.[26] In the United States, from the year 1992 to 2013 the age-specific incidence rate was highest in the age group of 50–69. However, a significant number of patients were also found above the age of 70.[27] The mean age of this study population was 47.8±14.8 years. The study conducted by Gani et al. (2013) comprised 57 HCC patients where the mean age was 45.81 ± 15.31 years.[28] This studt finds that chronic viral hepatitis was the major risk factor contributing to the development of HCC and HBsAg positivity was found in 15(50%) cases. This study suggests that HCC patients show a certain association between the high incidences of HBV infection. In the study by Khan M et al[18], there were 33.3% cases and by Shawon MA-A et al,[22] there were 49% cases of HBsAg positive among Bangladeshi population. Chronic HBV and HCV infection is considered as one of the leading causes of HCC in Bangladeshi population.[29-30] Despite the introduction of vaccination during 2003–2005 into the Expanded Program on Immunization (EPI) in Bangladesh, HBV infection remains abundant in the middle and older age adult population. Chronic HBV infection was the significant risk factor contributing to the development of HCC in our neighboring country India.[1] Although HCV is considered one of the leading causes of liver cancer in many countries,[32-33] in this study, HCV infection was found in 6(20%) of patients. Alcohol consumption is another risk factor of HCC in Western countries.[34-35] But this study finds that alcohol as a risk factor for underlying liver disease has contributed to only minority of patients 1 (3.3%). Alcohol consumption is strictly restricted in Bangladesh by state law and also very much restricted due to socioeconomic conditions and religious restrictions. Here, cirrhosis was found in 21(70%) cases. This study also finds the lesion of HCC at the time of diagnosis, among those single lesions were detected in 70% the cases and multiple lesions in 30% cases.[36-38] Almost all the patients in this study presented in moderate to late clinical stage of the disease. The most common presenting symptoms were loss of appetite in 29 cases (96.66%), generalized weakness in 28 cases (93.33%), weight loss 24 (80%), abdominal pain in 22 (73.33%) cases, fullness of abdomen in 21 (70%) cases, abdominal mass in 20 (66.66%) cases, nausea and vomiting 20 (66.66%) cases .Other complains were yellow coloration of eyes and urine 10 (33.33%), fever 10 (33.33%), leg swelling 9 (30%), abdominal swelling 9 (30%), blood vomiting1 (3.33%) . In previous study conducted by Khan M et al [18] the major symptoms were weight loss74%, abdominal pain 66.3%, loss of appetite78%. In Ayub Al Mamun's study common symptoms were weight loss in 94.3% cases, loss of appetite in 88.6%,abdominal mass 65.7% cases and abdominal pain in 60% cases.[39] Physical signs in this study were hepatomegaly in 27 (90%) cases, weight loss in 24 (80%), ascites 15(50%) splenomegaly 15(50%), jaundice 10 (33.33%), testicular atropy 10 (33.33%), palmer erythmia 5(16.66%), clubbing 4(13.33%), oedema of legs 4 (13.33%). Khan M et al[18] observed weight loss in 74% of patients, hepatomegaly in 66.3% cases, ascites in77.7% cases, jaundice in 37.7% cases. Histopathological features after percutaneous needle biopsy report revealed poorly differentiated hepatocellular carcinoma were 15 (50%) cases, well differentiated 9 (30%) cases and moderately differentiated 6 (20%) cases. In this study, we recorded the first clinical symptoms that have been observed while the patients were admitted in the hospitals. It was evident that every patient came with multiple clinical symptoms which were representative symptoms of HCC. The habit of Bangladeshi patients avoiding clinical checkups and regular screening of disease has become a significant influence on the development of HCC diagnosis of the disease is usually delayed. After being admitted to hospital, different imaging reports such as CT scan, MRI,

ultrasonography, biochemical tests, tumor markers, FNAC or biopsy were used for the detection of HCC.

CONCLUSION

In summary, we believe that our findings are closely representing the actual picture of hepatocellular carcinoma in Bangladeshi patients. Information regarding clinical presentation from this study may be utilized as indicator for referral, case definition in research works and probable diagnosis of HCC. This clinical presentation may be a strong tool for symptomatic surveillance of HCC and prevention of HCC including chronic hepatitis B and chronic hepatitis C virus infection. Early screening and management of chronic viral hepatitis (HBV and HCV) is needed to reduce morbidity and mortality from HCC patients. More research is required to find out clinical presentations that may lead to early diagnosis of Bangladeshi HCC patients for early and better management.

ETHICAL ISSUE

Ethical clearance for the study was taken from the Institutional Review Board of the Bangladesh college of Physicians and Surgeons (BCPS) prior to the commencement of this study (No.CPS-2007, Date-30-10-2007).

CONFLICT OF INTEREST

All authors declare that they have nothing to disclose and have no conflict of interests regarding the publication of this paper.

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