Original Article

Frequency of Hepatitis B and Hepatitis C in Patients with Hepatocellular Carcinoma at Hyderabad

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ABSTRACT

OBJECTIVE: To determine the frequency of hepatitis B and Hepatitis C in patients with hepatocellular carcinoma in two university hospitals of Hyderabad.
STUDY DESIGN: Descriptive observational study.
PLACE AND DURATION: This study was conducted at Liaquat University Hospital Hyderabad and Isra University Hospital Hyderabad from November 2005 to October 2008.
MATERIAL AND METHODS: Clinically diagnosed hepatocellular carcinoma (HCC) cases were confirmed pathologically. Demographic and clinical information was recorded on a predesigned proforma. Serological assessment for hepatitis B, hepatitis C and delta virus was carried out through ELISA.
RESULTS: A total of 200 cases of hepatocellular carcinoma were included in this study. Hepatitis C antibody was present in 145 (72.5%) cases. HBsAg was present in 42 (21.0%) cases. Thirteen (6.5%) cases were infected by multiple viruses. Twenty-one (10.5%) cases were alcoholic as well as infected by hepatitis C and 1 case (0.5%) was only alcoholic. Twelve cases (6.0%) were neither alcoholic nor having any viral etiology.
CONCLUSION: HCV alone was most frequent presentation in cases of HCC followed by HBV, emphasizing their etiological association.

KEYWORDS: Hepatocellular carcinoma, Hepatitis C, Hepatitis B, Alcohol, Cirrhosis.

INTRODUCTION

Hepatocellular carcinoma (HCC) is a primary malignancy of the hepatocytes. It is the fifth most common cancer in men and eighth most common cancer in women world wide. An estimated 600,000 new cases are diagnosed annually of which 82% are from developing countries [1]. It is currently one of the most common world wide causes of cancer death and an estimated 16,780 patients were expected to die of hepatocellular carcinoma in 2007.[2] It has been recognized that the most important risk factor for the development of hepatocellular carcinoma is cirrhosis and about 80% of patient with newly diagnosed hepatocellular carcinoma have preexisting cirrhosis[3]. Major causes of cirrhosis world wide are attributed to alcohol[4],hepatitis B infection[5] and hepatitis C infection.[6] Global incidence of chronic hepatitis B viruses infection is estimated to be 400 million persons[7] and chronic HBV infection is the most common cause of hepatocellular carcinoma world wide[8]. Similarly according to WHO global incidence of chronic hepatitis C is approximately 200 millions [9] and in United States about 30% of hepatocellular carcinoma cases are thought to be related to HCV infection.[10] Roughly 7 million Pakistanis are carriers of Hepatitis B and approximately 10 millions are affected by hepatitis C. [11] Several researchers have found that hepatocellular carcinoma in Pakistan occurs preferentially in middle aged males commonly in hepatitis B or Hepatitis C affected cases.[12]

The role of hepatitis B and hepatitis C in the etiology of hepatocellular carcinoma greatly varies geographically and may also change over time.[13,14] In this context this study was designed to determine the frequency of hepatitis B and hepatitis C in hepatocellular carcinoma patients at Hyderabad, Sindh – Pakistan.

PATIENTS AND METHODS

This descriptive observational study was conducted at two tertiary care university hospitals of Hyderabad, Sindh – Pakistan, Liaquat University Hospital and Isra University Hospital, from November 2005 to October 2008. All diagnosed cases of hepatocellular carcinoma (HCC) were selected for this study. Biopsy samples of clinically diagnosed HCC patients were sent for pathological confirmation. A well-informed consent was obtained from all study subjects. A predesigned proforma was used to collect demographic and clinical information. At the time of diagnosis data were recorded regarding age, sex, presence of ascites, hepatic encephalopathy, serum level of aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, alkaline phosphatase (ALP), gamma glutamyl tranferase (GGT), albumin, prothrombin time (PT), international normalized ratio (INR). Regarding age, subjects were distributed in

three age groups i.e. up to 45-years (young age group), 46-60 years (middle age group) and more than 60-years (old age group).

Presence of underlying cirrhosis was assessed via clinical and radiological evidence (size and consistency of liver, splenomegaly, ascites, low platelets <150,000/microlitre, dilated portal vein) and was categorized according to Child-Turcotte classification modified by Pugh as Child class A, B and C.

Serological assessment was performed in each case using ELISA method and presence of Hepatitis B surface antigen, anti HCV and Delta antibodies were noted. Abdominal CT scan was performed to assess the size, number and location of tumors, and presence of portal vein thrombosis.

Data Analysis:

Descriptive statistics were used to compare the proportion of demographic and clinical factors of the study subjects. Mean±SD age was calculated. Frequencies and percentages were calculated for presence of HCV, HBV and other qualitative variables.

RESULTS

Two-hundred diagnosed cases of HCC were selected for the study. Among them 165 (82.5%) were males and mean±SD age of the study subjects was 53.7±12 years with range of 29-90 years. HCV alone was found to be the major etiological factor present in 145 (72.5%) cases. Cirrhosis was clinically diagnosed in 168 (84%) cases with maximum presentation of Child's class B (82 cases, 41%). Majority (68, 34%) of the tumors was multicenteric. Portal vein thrombosis was present in 36 (18%) cases. These characteristics are detailed in **Table I**. Sex distribution of the causative factors is detailed in **Table II**.

DISCUSSION

Hepatocellular carcinoma although is one of the most common cancers in world, the incidence of hepatocellular carcinoma varies according to the prevalence of hepatitis B and C infections. Areas such as Asia and sub-Saharan Africa with high rates of infectious hepatitis have high incidence of hepatocellular carcinoma.[15] Hepatocellular carcinoma frequently arises in the setting of cirrhosis, appearing 20-30 years following the initial insult to the liver by the common aetiological agents as hepatitis C infection, hepatitis B infection and alcohol. As the latency period from hepatic damage to hepatocellular carcinoma development is very long, it is necessary to diagnose their aetiological agents earlier so that intervention could be made and thus decreasing the incidence of hepatocellular carcinoma.

In this study it was revealed that hepatitis C virus is the most common risk factor which was present in

TABLE I:
BASELINE CHARACTERISTICS OF PATIENTS OF HEPATOCELLULAR CARCINOMA (n = 200)

Variable		n (%)
Age:		
	Up to 45-years	59 (29.5)
	46-60 years	93 (46.5)
	More than 60-years	48 (24)
Sex:		
	Male	165(82.5)
	Female	35(17.5)
Etiology:		
	HCV	145(72.5)
	HBV	42(21.0)
	HCV & HBV	9(4.5)
	HBV HDV	3(1.5)
	HBV HCV HDV	1(0.5)
	Alcohol	1(0.5)
	alcohol + HCV	21(10.5)
	Others	12(6.0)
Clinical cirrhosis:		
	Yes	168(84.0)
	No	32(16.0)
Child Class:		
	A	41(20.5)
	B	82(41.0)
	C	64(32.0)
Tumor characteristics		
	Single < 5cm	60(30.0)
	Single > 5cm	39(19.5)
	Multicentric all < 5cm	68(34.0)
	Multicentric few > 5 cm	33(16.5)
Portal vein Thrombosis:		
	Yes	36(18.0)
	No	147(73.5)

TABLE II:
SEX DISTRIBUTION OF CAUSATIVE FACTORS IN CASES OF HEPATOCELLULAR CARCINOMA (n = 200)

Causes	Male n = 165(%)	Female n = 35(%)
HCV	117(70.9)	28(80.0)
HBV	38(23.0)	4(11.4)
Multiple viruses	13(7.9)	0
Alcohol + HCV	18(10.9)	3(8.6)
Alcohol	0	1(2.9)
Others	8(4.8)	4(11.4)

72.5% of all cases of hepatocellular carcinoma. Nasir Khokhar et al[15] conducted a similar type of study at Shifa International Hospital Islamabad who found that 67% of all cases of Hepatocellular carcinoma were hepatitis C positive. The study conducted at Aga Khan hospital by Saleem Shariff et al[16] revealed that 41% of cases of hepatocellular carcinoma were seropositive for hepatitis C virus. Similarly a study was conducted at Egypt with high prevalence of Hepatitis C virus by Lehman EM and Wilson ML[17] who found that prevalence of hepatitis C virus in cases of hepatocellular carcinoma was 78.8%. The above mentioned studies show that hepatitis C has become the most common cause of hepatocellular carcinoma world wide and it is also responsible for recent increased incidence in Pakistan. About 13.5% of all Pakistanis are infected with hepatitis C infection [18]. The lifetime risk of hepatocellular carcinoma in patients with HCV is approximately 5% appearing 20–30 years after infection. Recent studies suggest that antiviral treatment of chronic hepatitis C infection may reduce the risk of hepatocellular carcinoma significantly[19].

The other risk factor was Hepatitis B which was present in 21% of all cases of hepatocellular carcinoma in our study while in the studies of Nasir Khokhar [15], Saleem Sharif[16] and Lehman[17] the prevalence rate was 23%, 36% and 25.9% respectively. These studies reveal that chronic hepatitis B is also one of the common causes of hepatocellular carcinoma worldwide. In Pakistan the prevalence of Hepatitis B is 2.6% in healthy population[18] and chronic hepatitis B infection increases the risk of hepatocellular carcinoma in 5 – 10 years after presentation[20]. It is anticipated that with implementation of world wide vaccination, the incidence of Hepatitis B related hepatocellular carcinoma is going to decrease.[21] In our study thirteen cases were infected with multiple viruses and it has been reported that co-infection with HBV and HCV further increases the risk of hepatocellular carcinoma.[22]

It has been observed by Goeser T et al[23] that alcohol use in the setting of chronic HCV doubles the risk of hepatocellular carcinoma compared with HCV infection alone. We have observed in our study that 21 cases of chronic hepatitis C were alcoholics as well; hence prone to develop hepatocellular carcinoma.

Hepatocellular carcinoma although is currently one of the most common worldwide causes of cancer death, a major impact on the incidence of hepatocellular carcinoma should be achieved through current vaccination strategies for hepatitis B virus infection, screening and treatment for hepatitis C virus infection and from the reduction of alcoholic liver disease.

CONCLUSION

HCV alone was most frequent presentation in cases of HCC followed by HBV, emphasizing their etiological association. Hepatocellular carcinoma is one of the most common cancers in the world and liver cancers are strongly linked to hepatitis C virus, hepatitis B virus and alcohol use. The common association of hepatocellular carcinoma with hepatitis B and C suggest that vaccination against Hepatitis B virus on nation wide basis, and early screening and antiviral therapy for hepatitis C virus can decrease the incidence of this life threatening malignancy.

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