

Original Article

HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS: FREQUENCY, SEROPREVALENCE OF HEPATITIS B AND C AND PATIENT PROFILE

Saeed Akhtar Malik, Irfan Ahmad, Muhammad Arif Nadeem and Moazzam Ali Atif

Objective: To find out frequency of hepatocellular carcinoma in cirrhotic patients and to determine seroprevalence of hepatitis B and C and profile of these patients.

Material and Methods: This study was done in Sheikh Zayed Medical College/Hospital, Rahim Yar Khan from February to August 2009. One hundred cirrhotic patients admitted in medical wards were evaluated for demographic and clinical features, seroprevalence of hepatitis B and C and Child Pugh score and class. Those having focal defect in liver on ultrasound were further investigated for serum alphafetoprotein, CT scan abdomen and fine needle aspiration for histopathological examination.

Results: Eighteen patients were found to have HCC with mean age of 53 years, 78% of these patients were male. Eighty three percent were anti-HCV positive, 6% were both HBs Ag and anti-HCV positive and 11% were seronegative. Mean Child score of these patients was 9.16. Main presenting symptoms were massive ascites, hematemesis/melena, hepatic encephalopathy and jaundice.

Conclusion: HCC is a common complication of hepatitis C associated cirrhosis.

Keywords: Hepatocellular carcinoma, cirrhosis, hepatitis B and C.

Introduction

Hepatocellular carcinoma (HCC) is one of the most common causes of worldwide cancer deaths¹ and its cure rate has yet not improved in last 20 years.² Men are far more likely to develop HCC and this difference is more common in high incidence areas, possibly attributable to variations in hepatitis carrier states, exposure to environmental toxins and the trophic effect of androgens.³ In Asia and Western Europe, mean age at presentation is between 50 and 60 years⁴ whereas in sub-Saharan Africa is 33 years. There are also racial and ethnic variations in incidence of HCC,⁵ which are most likely related to the underlying cause of liver disease, genetic and environmental factors.

Risk factors for development of HCC include hepatitis B carrier state, chronic active hepatitis C, hereditary hemochromatosis and cirrhosis of almost any cause.⁶⁻⁷ In chronic hepatitis C and hereditary hemochromatosis, HCC is virtually restricted to patients with cirrhosis or advanced fibrosis.⁸ Compensated cirrhotics have a 3-4% annual incidence of HCC.⁹

Chronic hepatitis C and B are very common in our country, therefore we are seeing more and more HCC patients. The objective of this study was to determine frequency of HCC in cirrhotic patients, to find out seroprevalence of hepatitis C and B in

them and to determine their demographic and clinical characteristics.

Material and Methods

This case series was conducted in departments of Medicine and Radiology in Sheikh Zayed Medical College/Hospital Rahim Yar Khan from February to August 2009. One hundred cirrhotic patients admitted in Medical Department admitted for various complaints related to cirrhosis were included. Cirrhosis was diagnosed on the basis of clinical features, laboratory tests (prothrombin time, serum albumin) and abdominal ultrasound findings.

Detailed history was taken from each patient and thorough examination was done. Investigations like complete blood count, prothrombin time, bilirubin, serum transaminases, albumin and creatinine were evaluated. Child score was calculated and Child class determined. Ultrasound abdomen was carried out to look for coarse or shrunken liver, focal defect in liver, portal vein diameter, splenomegaly and ascites. If any focal defect was found in liver, it was further evaluated by serum alpha fetoprotein, CT scan of abdomen and fine needle aspiration. Diagnosis of HCC was made on basis of focal defect in liver, raised alpha fetoprotein and histopathological examination.

Data was analysed by using SPSS 16.0 version

software. Quantitative data was recorded in mean \pm standard deviation, and compared using student's t test. Qualitative data was recorded as percentage and compared using chi-square test.

Results

Mean age of these 100 cirrhotic patients was 45.54 years (range 15-75 years), (Tables 1, 2). Among these patients, 18 had HCC. Two more patients had focal defects in liver but serum alpha fetoprotein was normal and CT appearance was more in favor of hemangiomas in both patients, so fine needle aspiration was not performed. Both of these patients were female.

Table-1: Baseline characteristics of 100 cirrhotic patients.

Age (Mean\pmSD)		45.54\pm14.15
Gender	Male	68
	Female	32
Viral Profile	Hepatitis C	72
	Hepatitis B	15
	Hepatitis C+B	08
	Negative Hep. serology	05
Child Score		8.73 \pm 2.16
Child Class	A	12
	B	54
	C	34

Table-2: Characteristics of cirrhotic patients with HCC.

Age (Mean\pmSD)		53.11\pm10.9
Gender	Male	14 (78%)
	Female	4 (22%)
Viral Profile	Hepatitis C	15 (83%)
	Hepatitis B	0
	Hepatitis C+B	1 (6%)
	Negative Hep. serology	2 (11%)
Child Score		9.16 \pm 1.72
Child Class	A	1 (6%)
	B	10 (56%)
	C	7 (39%)

Among 18 patients with HCC, 7 presented with resistant or massive ascites, 7 with hematemesis/melena, 2 with encephalopathy and 2 with jaundice. These patients were significantly older than those without HCC (mean age 53 years vs 44 years, $p = 0.011$). Alpha fetoprotein was raised in 17 (94 %) patients and mean serum level was 164 ± 155 ng/ml. Ten (55.55 %) patients had single focal defects and 8 (44.45 %) had multifocal defects. There was no statistically significant difference in Child score (9.16 vs 8.63, $p = 0.34$), portal vein diameter (1.34 vs 1.37, $p = 0.52$) and spleen size (13.44 vs 13.63, $p = 0.84$) between patients with HCC and those without HCC.

Discussion

Over 40% cases of HCC occur in China,¹⁰ other areas with high incidence are sub-Saharan Africa, Hong Kong and Taiwan. The prevalence of HCC was low in Pakistan but, as cirrhosis has become highly prevalent in our region, therefore more and more patients with HCC are being diagnosed. Cirrhosis is the most common pathophysiology of hepatocellular carcinoma regardless of its etiology. Cirrhosis is present in 69-86% cases of HCC.¹¹⁻¹⁴ In one of the local studies HCC was seen in 11% of patients with cirrhosis,⁷ while our case series depicted its frequency as 18%. HCC is more common in hepatitis C associated cirrhosis as reflected in the present case series as well as in many other studies.^{11, 13-18} Only one study from INMOL, Lahore showed that hepatitis B was more common cause of HCC (90%) as compared to hepatitis C (78%).¹² One reason of increased frequency of HCC in chronic hepatitis C is probably its increased frequency as a cause of cirrhosis than chronic hepatitis B. Men are far more likely to develop HCC. This disparity is more pronounced in high incidence areas. The ratio decreases as the incidence decreases.³ In various local studies, the mean percentage of men affected with HCC was 77, while it was 78% in the present study.^{11, 13-15} Several large prospective studies conducted in Asia and Western Europe have noted a mean age at presentation between 50 and 60 years.^{4,8} Same finding was seen in our study and other studies done in different areas of Pakistan.^{11, 13-15} In conclusion, HCC is a common complication of cirrhosis; it has strong association with HCV positive cirrhosis; and men in fifth decade of their life are predominantly affected.

Department of Medicine, Sheikh Zayed Medical College/ Hospital, Rahim Yar Khan
theesculapio@hotmail.com
www.sims.edu.pk/esculapio.html

References

1. Parkin DM. Global cancer statistics in the year 2000. *Lancet Oncol* 2001; 2: 533-43.
2. Parvez T, Parvez B, Pervaiz K, Gumgumii AA, Al Ahmadi S, Sabir AA, et al. Screening for hepatocellular carcinoma. *J Coll Physicians Surg Pak* 2004; 14 (9): 570-5.
3. Okuda K. Epidemiology of primary liver cancer. In: *Primary liver cancer in Japan*, Tobe T (Ed). Springer-Verlag, Tokyo 1992: 3.
4. Tsukuma H, Hiyama T, Tanaka S, Nakao M, Yabuuchi T, Kitamura T, et al. Risk factors for hepatocellular carcinoma among patients with chronic liver disease. *N Eng J Med* 1993; 328: 1797-801.
5. Wong R, Corley DA. Racial and ethnic variations in hepatocellular carcinoma incidence within the United States. *Am J Med* 2008; 121: 525-31.
6. Davila JA, Morgan RO, Shaib Y, McGlynn KA, El-Seraj HB. Hepatitis C infection and the increasing incidence of hepatocellular carcinoma: A population based study. *Gastroenterol* 2004; 127: 1372-80.
7. Farooqi JI, Farooqi RJ. Prevalence of hepatocellular carcinoma in patients of liver cirrhosis: An experience in North West Frontier province (NWFP). *J Coll Physicians Surg Pak* 2000; 10 (2): 54-5.
8. Fragon S, Fracanzani AL, Piperno A, Braga M, D Alba R, Ronchi G, et al. Prognostic factors for hepatocellular carcinoma in genetic hemochromatosis. *Hepatol* 1994; 20: 1426-31.
9. Colombo M, de Franchis R, Del Ninno E, Sangiovanni A, De Fazio C, Tommasini M, et al. Hepatocellular carcinoma in Italian patients with cirrhosis. *N Eng J Med* 1991; 325: 675-80.
10. Scolnick AA. Armed with epidemiologic research, China launches programs to prevent liver cancer. *J Am Med Assoc* 1996; 276: 1458.
11. Khokhar N, Aijazi I, Gill ML. Spectrum of hepatocellular carcinoma at Shifa International Hospital, Islamabad. *J Ayub Med Coll Abbottabad* 2003; 15: 1-4.
12. Rahman A, Murad S. Hepatocellular carcinoma: a retrospective analysis of 118 cases. *J Coll Physicians Surg Pak* 2002; 12: 108-9.
13. Chohan AR, Umar M, Khaar B, Khurram M, Zahid M, Shah SF, et al. Demographic features of hepatocellular carcinoma. *J Rawal Med Coll* 2001; 5: 81-3.
14. Butt A, Khan A, Alam A, Ahmad S, Shah S, Shafqat F, et al. Hepatocellular carcinoma: analysis of 76 cases. *J Pak Med Assoc* 1998; 48: 197-201.
15. Sharif S, Burney I, Salam A, Siddiqui T. Hepatocellular carcinoma. *J Coll Physicians Surg Pak* 2002; 12: 264-7.
16. Mumtaz MS, Iqbal R, Umar M, Khaar B, Mumtaz MO, Anwar F, et al. Seroprevalence of hepatitis B and C viruses in hepatocellular carcinoma. *J Rawal Med Coll* 2001; 5: 78-80.
17. Farooqi JI, Farooqi RJ. Relative frequency of hepatitis B and C virus infections in cases of hepatocellular carcinoma in North West Frontier Province, Pakistan. *J Coll Physicians Surg Pak* 2000; 10: 128-30.
18. Kausar S, Shafqat F, Shafi F, Khan AA. The association of hepatocellular carcinoma with hepatitis B and C viruses. *Pak J Gastroenterol* 1998; 12: 1-2.