SPECTRUM OF HEPATOCELLULAR CARCINOMA AT SHIFA INTERNATIONAL HOSPITAL, ISLAMABAD

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Background: The aim of this study was to review etiological and clinical features of patients with hepatocellular carcinoma (HCC) at a tertiary care centre in past nine years. Relevant data on HCC in other parts of country and world were reviewed. **Methods:** Patients who had biopsy proven HCC were reviewed retrospectively. Demographic features were noted and positivity for serology, presence of cirrhosis, level of alpha-fetoprotein, tumour size and distribution of liver lesions were noted. **Results:** A total of 67 patients were found to have biopsy proven HCC. Mean age was 58.64 ± 12.77 years. Males were 79%. Hepatitis B surface antigen was noted to be positive in 23% of the patients, who were tested and hepatitis C antibody was found to be positive in 67% of the patients who were tested. Alpha fetoprotein level was 632.09 ± 1332.31. Cirrhosis was noted in 69% patients. Tumour size in patients with single lesion was 6.6 ± 1.14 cm. Patients with single lesion had 70% time involvement of the left lobe and 30% times had involvement of the right lobe. Fifty one percent of the patients in this series had multilocular distribution. **Conclusion:** Hepatocellular carcinoma has become a common tumour in Pakistan and studies are showing that this cancer is related to hepatitis C virus infection in majority of the patients. A large number of them have underlying cirrhosis and are multifocal in origin and are presented in an advanced condition.

Key words: Hepatocellular carcinoma, Hepatitis C, Hepatitis B, Alpha fetoprotein, Cirrhosis

INTRODUCTION

Hepatocellular carcinoma (HCC) is a common tumour with world wide distribution and Chronic hepatitis C virus (HCV) infection as a cause of the chronic liver disease and HCC has been on the rise in developed countries.[1] Relationship of HCV infection in hepatocellular carcinoma has been well documented in USA and is expected to increase sharply in the coming years.[2,3] With the rising numbers, the incidence of HCC is expected to reach a peak in the United States around year 2015.[2,3] In developing countries, HCC is a leading cause of death and accounts for between 60% and 90% of all primary liver malignancies.[4]

In Pakistan, many reports of HCC have been published in last 10 years and viral hepatitis and aflatoxins have been its etiology.[5-14] In earlier studies[5,6,10] HBsAg positivity was nearly 60% in cases of hepatocellular carcinoma. However, in latest studies[8,11-13] the positivity for hepatitis C virus infection has been up to 80%. Aetiology, clinical features, and survival of hepato-cellular carcinoma differ among the different countries.[15]

The aim of this study was, therefore, to review the aetiology, clinical features, and management of the hepatocellular carcinoma at our institution in past 9 years. Also reviewed are HCC features from the previously published studies from various parts of Pakistan and around the world.

MATERIAL AND METHODS

Case records for all the patients who were diagnosed HCC histologically at Shifa International Hospital in past 9 years were reviewed. Demographic features were noted. Presence of hepatitis B surface antigen, anti HCV or other features were noted. Radiological features were noted for patients who had ultrasonography or CT scans. Patient who did under go any treatment or if any follow up was available was also recorded.

Published studies from Pakistan on HCC were retrieved from the Medline® and from Pakmedinet.com, which lists local studies not listed in the Medline. Pertinent studies from different regions of world were taken from Medline to compare the findings with local data. Demographic data and other variables are given as mean ± standard deviation. All data was analysed by statistical software, SPSS Version-10 for windows.

RESULTS

There were 67 patients in this study. The age was 58.64 ± 12.77 years, 79% were male. Anti HCV was noted in 67% of patients. Alpha fetoprotein was 632.09 ± 1332.31. Cirrhosis was present in 69% of patients and 51% had multilocular appearance on ultrasonography or CT scan. These data are shown in detail in Table-1.

DISCUSSION

Reviewing the studies from various parts of Pakistan showed that mostly the patient age was from 17–84 years. Up to 89% were male in one study[12]. In earlier studies, hepatitis B surface antigen was positive in 69% of patients.[6] Anti HCV was present in 87% of the patients in one study.[13] Alpha fetoprotein was found to be elevated in 84% of patients, which was the highest number of the patients with elevated AFP.[16] Eighty six percent of the patients were noted to have cirrhosis present in one study.[9] Details of these features are shown in table-2.

Table-1: Clinicopathological features of HCC at Shifa International Hospital (n=67)

Age ± SD	58.64 ± 12.77 (95% CI 55.52 – 61.75)
Male Sex	79 %
HBsAg (- / + / NA)	30 / 9 / 28 (Positive 23 %)
HCV Ab (/ + / NA)	13 / 26 28 (Positive 67 %)
AFP elevation	80 % 632.09 ± 1332.31 (95% CI 257.37 - 1006.80)
Cirrhosis	69 %
Tumor Size (cm)	6.6 ± 1.14 (95% CI 5.18 – 8.01)
Lobe (Rt/Lt/NA)	3 / 7 / 57
Multilocular	51 %

- = Negative, + = Positive, NA = Not available

This study shows that the hepatocellular carcinoma is seen mostly in the 5th and 6th decade, predominantly in males. Our figures have shown that the anti HCV has been most commonly present in the patients with HCC. In addition to hepatitis C and hepatitis B virus infection, aflatoxin contamination has also been noted in Pakistan[10] and in many other under developed countries of Asia and Africa.[4] Hepatitis C virus infection leads to chronic hepatitis and cirrhosis and eventually to HCC[17] and it takes a long interval between the HCV infection and hepatocellular carcinoma to develop.[18] Hepatitis B has been very much a cause of hepatic carcinogenesis and presence of HBsAg increases the risk manifold.[19] Other risk factors noted for hepatocarcinogenesis are synergism of alcohol with viral hepatitis and diabetes mellitus[29]. Presence of HBsAg in lower socio-economic class has been associated with HCC[21].

Our study showed that alpha fetoprotein was elevated in 67% of patients and the mean level was >500 which is consistent with earlier studies indicating a fairly high likelihood of HCC with levels >400.[15] Although alpha fetoprotein has been noted to be as high as 80% in patients from Germany,[22] there is lack of correlation between alpha fetoprotein and size of the tumour as reported in studies from Pakistan.[23] All the patients in our series were diagnosed on core liver biopsy taken by Menghini needle or by 18-gauge spinal needle,[24] although there is role of targeted fine needle aspiration cytology in these tumours with sensitivity of 75–80%.[25]

Our patients had single lesion in 49% and multiple lesions in 51% cases. A similar presentation has been reported from our institution earlier.[26] Multi focal presentation has ranged from 38% to 56%.[16] Cirrhosis was present in 69% of our patients. This has been associated with significant number of patients with chronic hepatitis C and has ranged from 76% in India[27] to 90% Germany.[22] Along with hepatitis B and C, alcoholism has also contributed to development of cirrhosis which eve-ntually leads to HCC.[28] Various features of HCC in other parts of the world are shown in table-3.

Treatment of hepatocellular carcinoma has ranged from surgery to ablative therapy and chemo-embolization and transarterial embolisation in various regional countries of Asia.[29] Ablative procedures including percutaneous ethanol injection, sclerotherapy radio frequency ablation have also been practiced in many parts of the world.[30] Few of our patients underwent intra lesional alcohol injection but without any significant improvement. However, in some parts of Pakistan, absolute alcohol injection for unresectable hepatocellular carcinoma has given encouraging results[31] and inoperable HCC patients have been given long-acting octreotide injections with improved quality of life.[32] Problem with many patients of hepatocellular carcinoma is their two diseases, one underlying chronic liver disease with cirrhosis and second HCC on top and, therefore, the outcome has not been encouraging in may cases.[33]

CONCLUSION

Our experience with hepatocellular carcinoma in Pakistan indicate that 80% of the patients are male and develop this in 5th and 6the decade of their life. Anti HCV has been present in nearly 80% of the patients with alpha-fetoprotein elevation in 75% of patient. Seventy to eighty percent have underlying cirrhosis and 51% had multilocular presentation. A lot of our patients had presented in advanced stage where surgical and even other ablative treatments have not been possible.

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Table-2: Features of HCC in Pakistan, comparison of various studies

Reference	7	8	9	10	11	12	13	14	15	16	20	24	present study
Age		Mean 52			52±11	51-60		31-61	59		17-84		57±13
Males					86%	2.5:1		89%	66%		5.4:1		79%
HBsAg+	61%	69%	61%	14%	10%	60%		25%	10%	67%		4%	23%
HCV Ab+		13%	76%	68%	75%		77%	54%	87%	33%		78%	67%
Both +		9%	6%		10%			7%		24%			
AFP elevation					142± 155	62%	53%		63%		84%		80%
Cirrhosis Present					86%		70%		80%				69%
Multiloc-ular Feature					46%						38%		51%
No. of patient	100	23	30	56	76	366	118	44	30	54	32	45	67

Table-3: HCC in various countries of world

Country	Japan	Japan	Thai Land	Italy	China	India	India	Indonesia	Germany	USA	Pakistan
Age	62±7	63±9	56±13	64±8	54±13	63±11	49±14	53±14			58±13
Male Sex	65%		76%	81%							79%
HBsAg +	10%	18%	60%	17%	63%	27%	71%	21%	20%	63%	23%
HCV Ab +	83%	70%	28%	87%	4%	53%	4%	40%	53%	24%	67%
AFP elevation	75%		57%	66%					80%		80%
Cirrhosis Present							76%		90%		69%
Multi-locular feature	47%		51%	34%					69%		51%
Treatment options surgery				17							
Chemo embolization		81%			81%						
Tace	8		27	10		13%		26%			
Local ablation	100		2	52							
Chemotherapy	7		13	0							
No. of patients	115	191	51	103	107	15	74	101	100	110	67
Reference	**19**	**40**	**19**	**19**	**40**	**40**	**38**	**40**	**31**	**39**	**Present Study**

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