

GAMUT OF HEPATOCELLULAR CARCINOMA AT ONCOLOGY DEPARTMENT, SHEIKH ZAYED HOSPITAL, RAHIMYAR KHAN

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ABSTRACT

Background: Hepatocellular carcinoma is ranked as third most cause of death from cancer in world. **Objective:** The objective of this study was to review predisposing factors among patients with Hepatocellular carcinoma (HCC) at a tertiary care centre in past two years. **Material & Methods:** This Descriptive study was conducted on patients who had proven HCC by histopathology or tumor marker were reviewed retrospectively and data for January 2009 to December 2010 was included. Demographic features were noted and positivity for hepatitis serology, presence of cirrhosis, level of alpha-fetoprotein, tumour size and distribution of liver lesions were noted. **Results:** A total of 192 patients were found to have histopathology and tumor marker proven HCC. Males were 149 (77.6%) vs females 43 (22.4%). Hepatitis B surface antigen was noted to be positive in 27(14%) patients, and HCV was found to be positive in 138 (72%) patients. Patients with dual hepatitis (HBV+HCV) were 16 (08%) & in remaining 11 (06%) patients the etiology was unknown. Alpha fetoprotein level was highly elevated in 154 (84%) & Cirrhosis was noted in 134 (70%) patients. 117 (61%) patients had multicentric distribution. **Conclusion:** Hepatocellular carcinoma in this area, is related to hepatitis C virus infection in majority of the patients. A large number have underlying cirrhosis, multicentric and advanced disease at presentation. The disease is seen in the 5th and 6th decade & predominantly among males.

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

INTRODUCTION

Hepatocellular carcinoma (HCC) is the fifth most common malignancy and the third most common cause of death from the cancer in the world).¹ Chronic hepatitis C virus (HCV) infection a cause of the chronic liver disease and HCC has been on the rise worldwide.¹ In developing countries, HCC is a leading cause of death and accounts for between 60% and 90% of all primary liver malignancies.²

Approximately, 160 million people are estimated to be infected with HCV as figured out by the World Health Organization, majority of them reside in the developing countries of the world. Even in developed countries, the burden of HCV-related liver disease is increasing so that HCV has become the single most important reason for cirrhosis and Hepatocellular carcinoma.³

In Pakistan, many reports of HCC have been published in the last 10 years, viral hepatitis and aflatoxins have been documented in its etiology.⁴ In earlier studies HBsAg positivity was nearly 60% in cases of Hepatocellular carcinoma.⁵ However, in latest studies the positivity for hepatitis C virus infection has been up to 80%.⁶

Aetiology, clinical features, and survival of hepatocellular carcinoma differ among the different countries.⁷ The objective of this study was to review predisposing factors among patients with Hepatocellular carcinoma (HCC) at a tertiary care hospital.

MATERIAL AND METHODS

This descriptive study was conducted on case records of all the patients who were diagnosed HCC histologically, radiologically and with elevated tumor marker at Clinical Oncology Department, Sheikh Zayed Hospital, Rahimyar Khan in past 2 years were reviewed. Demographic features were noted. Presence of hepatitis B surface antigen, anti HCV antigen or other features were noted. Radiological features were noted for patients who had ultrasonography or CT scans.

RESULTS

Out of the one hundred and ninety two points, 149 (77.6%) patients were male and 43 (22.4%) patients were female. One hundred and twenty one (63%) patients were above the age of 60 years.

Positive HCV serology was present in 138 (72%) of our patients, 27 (14%) patients were HBsAg positive, and in 16 (8%) patients were both HCV & HBV positive. No predisposing cause was found in remaining 11 (6%) patients. Alpha fetoprotein was elevated in 154 (84%) patients. The disease was multicentric in 117 patients (61%)

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These data are shown in detail in Table I.

Table I: Clinicopathological features of HCC Patients (n=192)

Features	Values
Age range	30 - 80 years
Males	149 (77.6%)
Females	43 (22.4%)
HBsAg	27 (14%)
HCV Ab	138 (72%)
Both HBV & HCV	16 (08%)
Unknown aetiology	11 (06%)
AFP elevation	154 (84 %)
Cirrhosis	134 (70 %)
multicentric	117(61 %)

DISCUSSION

The studies from various parts of Pakistan showed the age ranges from 17-84 years. This study shows that the Hepatocellular carcinoma is seen mostly in the 5th and 6th decade, predominantly in males in rural areas of southern Punjab. It was noted that 89% were male in one study. In earlier studies, hepatitis B surface antigen was positive in 69% of patients & Anti HCV was present in 87% of the patients in one study.⁸ In addition to hepatitis C and hepatitis B virus infection, aflatoxin contamination has also been noted in Pakistan and in many other under developed countries of Asia and Africa.⁴ Alpha fetoprotein was found to be elevated in 84% of patients, which was the highest number of the patients with elevated AFP. Eighty six percent of the patients were noted to have cirrhosis present in one study.⁹ Hepatitis C virus infection leads to chronic hepatitis and cirrhosis and eventually to HCC and it takes a long interval between the HCV infection and hepatocellular carcinoma to develop.¹⁰ Hepatitis B has been very much a cause of hepatic carcinogenesis and presence of HBsAg increases the risk manifold.¹¹ Other risk factors noted for hepatocarcinogenesis

are synergism of alcohol with viral hepatitis and diabetes mellitus.¹² Presence of HBsAg in lower socio-economic class has been associated with HCC. Our study showed that alpha fetoprotein was elevated in 84% of patients. In different studies from Pakistan there is lack of correlation between alpha fetoprotein and size of the tumour as compared to similar study in Germany.¹³ The multicentric tumors were presented in 61%. All the patients in our series were diagnosed on FNAC, Liver Biopsy, radiological findings and elevated tumour marker. Cirrhosis was present in 70% of our patients. This has been associated with significant number of patients with chronic hepatitis C and has ranged from 76% in India¹⁴ to 90% Germany.¹³ Along with hepatitis B and C, alcoholism has also contributed to the development of cirrhosis which eventually leads to HCC.¹⁵ A survey of blood donors in the large urban and rural centers of the country shows that only about 25% of blood and blood product donations were tested for HCV infection. The major reason for not testing Hepatitis C was the higher cost of a test. It can be safely assumed that testing for HCV in rural areas of southern Punjab is less frequent, making blood transfusions still the major cause of HCV transmission in this area.

A number of studies also show the relationship between use of parenteral drug administration by sharing the syringes between patients and transmission of HCV. There is enormous dependence on parenteral therapy for treatment, both in the form of injections and infusion of drips, driven by cultural beliefs in the power of parenteral therapy. Additional risk factors that are peculiar to a developing country and may be important modes of transmission are excessive use of barbers for shaving, ear piercing and non-sterile surgical and dental practices of unqualified health care workers (quacks). However studies are needed in these areas to confirm this fact.

CONCLUSION

Our experience indicates that in HCC patients majority are male and develop this in late age. Anti-HCV has been present in majority of the patients and alpha-fetoprotein elevation in more than 80% of patients. Seventy percent have underlying cirrhosis and 61% had multilocal presentation. Hepatocellular carcinoma is a frequent malignancy in Rahimyar Khan, and HCV is usual underlying cause, however it presents with advanced stage.

REFERENCES

1. Yoshizawa H. Hepatocellular carcinoma associated with hepatitis C virus infection in Japan: Projection to other countries in the foreseeable future. *Oncol* 2002; 62(Suppl): 8-17.
2. Tanaka Y, Hanada K, Mizokami M, Yeo AE, Shih JW, Gojobori T, et al. Inaugural article: A comparison of the molecular clock of hepatitis C virus in the United States and Japan predicts that hepatocellular carcinoma incidence in the United States will increase over the next two decades. *Proc Natl Acad Sci.* 2002; 99: 15584-9.
3. El-Serag HB. Hepatocellular carcinoma and hepatitis C in the United States. *Hepatology* 2002; 36 (5) 74-83.
4. Taseer JH, Malik IH, Mustafa G, Arshad M, Zafar MH, Shabbir I, et al. Association of primary hepatocellular carcinoma with hepatitis B virus. *Bio Medica* 1996; 12: 79-81.
5. Butt A, Khan A, Alam A, Ahmad S, Shah S, Shafiqat F, et al. Hepatocellular carcinoma: analysis of 76 cases. *J Pak Med Assoc* 1998; 48: 197-201.
6. Qureshi H, Zuberi SJ, Jafarey NA, Zaidi SH. Hepatocellular carcinoma in Karachi. *J Gastroenterol Hepatol* 1990; 5: 1-6.
7. Omata M, Dan Y, Daniele B, Plentz R, Rudolph KL, Manna M, et al. Clinical features, etiology and survival of hepatocellular carcinoma among different countries. *J Gastroenterol Hepatol* 2002; 17 (Suppl): 540-9.
8. Chohan AR, Umar M, Khar B, Khurram M, Zahid M, Shah SF, et al. Demographic features of hepatocellular carcinoma: A study of 30 cases. *J Rawalpindi Med Coll* 2001; 5: 81-83.
9. Shah GG, Qureshi IA, Hakim T, Tarin BA, Farooq MA, Qureshi PS. Radiological aspects of hepatocellular carcinoma: A hospital based study. *Pak Armed Forces Med J.* 1999; 49: 54-7.
10. Castells L, Vargas V, Gonzalez A, Esteban L, Esteba R, Guardia J. Long interval between HCV infection and development of hepatocellular carcinoma. *Liver* 1995; 15: 159-63.
11. Yang HI, Lu SN, Liaw YF, You SL, Sun CA, Wang LY, et al. Hepatitis Be antigen and risk of hepatocellular carcinoma. *N Eng J Med* 2002; 347: 168-74.
12. Wang BE, Ma WM, Sulaiman A, Noer S, Sumoharjo S, Sumarsidi D, et al. Demographic, clinical and virological characteristics of hepatocellular carcinoma in Asia: Survey of 414 patients from four countries. *J Med Virol* 2002; 67: 394-400.
13. Petry W, Heintges T, Hensel F, Erhardt A, Wenning M, Niederau C, et al. Hepatocellular carcinoma in Germany. Epidemiology, etiology, clinical aspects and prognosis in 100 consecutive patients of a university clinic. *J Gastroenterol* 1997; 35: 1059-67.
14. Sarin SK, Thakur V, Guptan RC, Saigal S, Malhotra V, Thyagarajan SP, et al. Profile of hepatocellular carcinoma in India: An insight into possible etiologic associations. *J Gastroenterol Hepatol* 2001; 16: 666-673.
15. Hwang SJ, Tong MJ, Lai PP, Ko ES, CO RL, Chien D, et al. Evaluation of hepatitis B and C viral markers: Clinical significance in Asian and Caucasian patients with hepatocellular carcinoma in the United States of America. *J Gastroenterol Hepatol.* Oct. 1996, 11(10) 949-54