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Original Research Article

Association of Oncogenic Viruses in Liver Cirrhosis: North India

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ABSTRACT

Background/Aim: Chronic infections with hepatitis B virus (HBV) and hepatitis C virus (HCV) are well-recognized risk factors for cirrhosis and liver cancer. Approximately 7% of the world's population is infected with HBV and 3% with HCV. In India it has been reported high prevalence of HBV of 55% and HCV of 25.8% in patients with CLD. The estimates of their contributions to worldwide disease burden have been lacking basically in India. Thus it has great importance to analyze the association of hepatitis viruses (Mainly HBV & HCV) in liver cancer.
Methods: A total of 250 patients of liver cirrhosis were enrolled in our study. These patients were analyzed for hepatitis viruses (B & C) with the help of rapid kit. For the conformation of cancer they must go for the liver function test including α-feto protein as well as by histopathological study for the presence of hepatocellular carcinoma. Results: Hepatitis B and Hepatitis C have been detected in 212 (84.8%) and 38 (15.2%) respectively 250 liver cirrhosis patients. There is no any viruses are found in association of liver cancer. Liver cancer is more common among men than women regardless of race or ethnicity. Conclusions: The study shows that there are HBV infection is more than the HCV infections account for the majority of cirrhosis and primary liver cancer in India, which needs national programs to prevent new infections and provide medical management and treatment for those already infected.

Key words: HCC, HBV, HCV, ALT, AST

INTRODUCTION

There have been a number of other viruses that have been demonstrated to be associated with the aetiology of human cancers after the discovery of Epstein Barr virus (EBV) from Burkitt lymphoma (BL) cells in 1964, (Joseph S et al. 2004). Infectious agents, chiefly viruses, are accepted causes or candidates as causes of diverse malignancies of people world-wide. Human oncogenic viruses belong to different virus families and utilize diverse strategies to contribute to cancer development, they share many common features. One key feature is their ability to infect, but not kill, their host cell. In contrast to many other viruses that cause disease, oncogenic viruses have the tendency to establish long-term persistent infections.

Worldwide, liver cancer is the third most common cause of cancer mortality, with approximately 550,000 annual deaths (Parkin DM et.al. 2001). Globally, as of 2010, liver cancer resulted in 754,000 deaths, up from 460,000 in 1990, making it the third leading cause of cancer death after lung and stomach. (Lozano, R 2010). Hepato cellular carcinoma HCC in India occurs in two peaks, one at a young age between 40 to 55 years and another above 60 years. The two peaks occur because of adapting hepatitis B either in childhood, or in adulthood (Melbye M et al. 1984). The estimated number of cases per year in India is approximately close to 22,000 with a similar mortality (Kumar R et al. 2008).

Geographical correlation exists between the incidence of HCC and the prevalence of chronic hepatitis B and C viruses, suggesting that these two viral infections are the most important risk factors associated with HCC (Levrero M 2006). In India, 70% to 80% of all HCCs are related to the hepatitis B virus (HBV), approximately 15% are related to hepatitis C virus (HCV), and 5% to both HBV and HCV (Kumar R et al.2008).

There is not adequate data regarding the clinical, biochemical, and radiological profiles of HCC cases from India. Thus this study aims to investigate the risk factors of HCC and the clinical, biochemical, and radiological profiles of HCC cases in India.

MATERIALS AND METHODS

A total of 250 HCC cases were included in the study during May 2011 to June 2014. Cases taken from the Gastroenterology OPD of Jeevan Jyoti Hospital Hospital (Allahabad) and from the medicine OPD of Guru Gobind Singh Memorial Vanadana Women's Hospital (Allahabad).

The HCC patients associated with HBV or HCV were included and HCC related with alcohol were excluded from the study. A written informed consent was taken from all the subjects.

The diagnoses of HCC were based on morphological and clinical criteria, as well as ultrasound or Computed Tomography (CT), according to standard criteria (Leevy CM et al. 1994). All clinical, biochemical, serological, radiological, and cytohistological details were noted from the case records. The cases were evaluated based on history, physical examination, and liver function profile.

Biochemical examination:

The alanine amino-transferase (ALT), aspartate aminotransferase (AST), albumin, serum bilirubin and α-feto protein (AFP) of the targeted patients was assessed with the help of Kinetic Assay kit (Span Diagnostics Ltd.) following the instruction of the manufacturer. The normal value ranged between 10- 40 U/L, 10- 40 U/L , 3.5 mg/dL, <0.8U/L and 6.0 ng/mL at 37^0 C respectively.

Serological Examination:

Serological tests for the detection of hepatitis B and C by rapid test kit (Transasia Bio-Medicals Ltd.) following instruction of the manufacturer and similarly by ELISA test kit (Span Diagnostics Ltd.) according to the instruction of the manufacturer.

Statistical Analysis:

Data in the text and tables are expressed as mean ± SD by using Microsoft Excel work sheet. The p value was calculated by using ANOVA and was consider significance if $P < 0.05$.

Result

Clinical profiles of HCC cases:

Symptoms like jaundice, nausea and hepatic encephalopathy were present in almost equal proportion in HCC patients with HBV and HCV. Other symptoms such as general weakness (61.5% in HCC with HBV vs. 38.5% in HCC with HCV), abdominal discomfort (52.4% in HCC with

HBV vs. 37.6% in HCC with HCV), and anorexia (41.4% in HBV vs. 58.6% in HCV related HCC) were more frequently noticed in the HCC cases. Among the 250 cases of HCC, 186 (74.4%) had ascites and 38 (15.2%) had hepatomegaly, 26 (10.4%) had splenomegaly.

Biochemical profile of HCC

Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and AFP were significantly increased in HCC. A twofold increase in risk was observed with the increased levels of ALT and AST in the HCC cases. An increased risk of 2.5 times was found in patients with AFP levels between 20 and 400 ng/ mL, while a threefold increase in risk was observed in HCC patients with albumin levels less than 3.5 g/dl(Table.1).

Table.1- Biochemical profile of HBV+ve and HCV +ve HCC patients

Characteristics	HBV+Ve	HCV+Ve	Total	P Value
Sex Male	168	27	195	
Female	44	11	55	
Age	47.12±10.60	46.26±14.84	46.99±10.60	0.102
ALT	121.13±16.26	128.78±16.97	122.30±13.43	0.047
AST	96.61±16.26	80.23±14.14	94.23±13.40	0.035
Serum Bilirubin	5.95±1.27	6.57±1.55	6.05±3.25	0.602
Serum Albumin	3.44±2.33	3.07±0.85	3.38±0.14	0.036
AFP	812.91±17.68	793.18±33.94	809±12.02	0.042

Viral risk factors of HCC

Out of the 250 HCC patients, 84.8% were HBV related and 15.2% were positive for HCV markers. Co-infection of HBV and HCV was observed in 5.3% of the HCC cases. Analysis of the risk factors for HBV markers showed that any marker positivity for HBV increases the risk of developing HCC.

Ultrasonic profile of HCC cases:

Ultrasound images showed that approximately 42% of the cases were hypoechoic, 32.7% were heterogeneous, and 25.3% were hyperechoic.

DISCUSSION

The clinical presentation of the HCC patients in this study was similar to that in previous studies. Both groups (HBV & HCV related HCC) in the present study had a significant number of cases showing signs of ascites, hepatomegaly and splenomegaly. Symptoms such as anorexia, weight loss, weakness, and jaundice were present in more or less similar proportion in both categories. This finding is similar to that reported in an Indian study (Joshi N et al. 2003).

Furthermore, hepatic encephalopathy was observed in a very few cases of HCC this is negligible. This result is similar to that reported by Wong et al. found that Asian-American patients had a significantly lower frequency of hepatic encephalopathy compared with non-Asian Americans (Wong et al. 2011).

In our study the ratio of male/ female was 3.55:1 in HCC cases with mean age 46.99±10.60 years, while a study conducted by Manash Pratim Sarma et.al. found that the male/female ratio of the HCC cases was 5.87:1. with the mean age of 40±13.23 years which is likely to be similar with our study. (Manash Pratim Sarma et al. 2012).

In our study different biochemical parameters are as ALT (121.13±16.26 in HBV, 128.78±16.97 in HCV), AST (96.61±16.26 HBV, 80.23±14.14 in HCV), serum bilirubin (5.95±1.27 HBV, 6.57±1.55 in HCV), serum albumin (3.85±2.33 HBV, 3.47±0.85 in HCV) and AFP (812.91±17.68 HBV, 793.18±33.94 in HCV) were significantly increased in HCC. It was

observed that patients with the two to three fold increased levels of ALT, AST are at the risk of HCC if they are infected with HBV are HCV. An increased risk of 2.5 times was found in patients with AFP levels between 20 and 400 ng/mL, while a threefold increase in risk was observed in HCC patients with albumin levels less than 3.5 g/dl. Sarin SK et al. also reported the disturbance in hepatin enzymes. (Sarin SK et al. 2001). Patients having the value of AFP > 400ng/mL is considered as cirrhosis, our study showed the similar result with previous studies which indicate AFP values are higher in patients with cirrhotic changes as compared to those without cirrhosis. Fifty-three percent of cirrhotic patients have values greater than 400 ng/mL compared to 26% of non-cirrhotic patients (Saini N et al. 2006, Collier J et al.1998,Oka H et al.1994).

A strong positive correlation was observed between AST and ALT. This result is similar to the result reported by another Indian study on children (Satapathy SK et al.2006). A total of 208 (83.2%) HCC cases showed raised AFP levels which indicates HCC (>400 ng/ml). This result almost similar with the study of Saini et al. (Saini et al. 2006), where the percentage of HCC cases with raised AFP was 83% (Satapathy SK et al.2006), and 80.96% HCC cases with raised AFP (Manash Pratim Sarma et.al. 2012).

HBV association was found in 84.8% of the HCC cases, whereas HCV association was found in 15.2% of the HCC cases. This finding suggests that most HCC cases were the result of a hepatotropic virus-related chronic liver disease. This result is in accordance to the estimation that HBV is responsible for 55% to 85% of HCC cases worldwide, whereas 15% to 35% of the cases are thought to be caused by HCV infection (Block TM et al. 2003, Anthony PP 2001, Manash Pratim Sarma et al. 2012, Kumar A et al. 1995). A study conducted by Dhir V et al. in showed that in India, 36%–74% of HCC were associated with HBV and about 30% with HCV infection (Dhir V et al 1998).

Several studies reported that the relationship exists between the development of HCC and persistent HBV (Hadziyannis S et al. 1995, Vail Mayans M et al. 1990). While a study conducted by Kumar R et.al. showed HBV accounts for 73% of all cases of HCC and 15% are HCV related HCC. And about 5% patients are co-infected with HBV and HCV (Kumar R et al. 2008).

In our study ultrasound images showed that approximately 42% of the cases were hypoechoic, 32.7% were heterogeneous, and 25.3% were hyperechoic while a study conducted by Manash Pratim Sarma et.al found that 38% of the cases were hypoechoic, 27.7% were heterogeneous, and 25.2% were hyperechoic (Manash Pratim Sarma et al. 2012).

CONCLUSION

HBV and HCV are the major risk factors for HCC in India. Beside HBV and HCV positivity heavy alcohol use significantly increased the risk of developing HCC among cirrhotic patients but alcohol alone is not a risk factor for HCC. The HBV related HCC is more than the HCV. There is no any virus were found to expose the patients of HCC instead the co-infection of HIV in some cases but not any co-infection found in our study. The HCC and primary liver cancer needs national programs to prevent new infections and provide medical management and treatment for those already infected.

REFERENCES

- Anthony PP. Hepatocellular carcinoma: An overview. Histopathology 2001; 39: 109 –118.
- Block TM, Mehta AS, Fimmel CJ et al. Molecular viral oncology of

hepatocellular carcinoma. Oncogene 2003; 22: 5093–5107.
- Collier J, Sherman M. Screening for hepatocellular carcinoma. Hepatology 1998;27:273-8.
- Dhir V, Mohandas KM. Epidemiology of digestive tract cancers in India. III. Liver. Indian J Gastroenterol 1998;17:100–3.
- Hadziyannis S, Tabor E, Kaklamani E, et al. A case-control study of hepatitis B and C virus infections in the etiology of hepatocellular cardnoma. Int J Cancer 1995; 60: 627-631.
- Joseph S. Pagano, Martin Blaser, Marie-Annick Buendia, Blossom Damania, Kamel Khalili, Nancy Raab-Traub, Bernard Roizmang. Infectious agents and cancer: criteria for a causal relation. Seminars in Cancer Biology 14 (2004) 453–471.
- Joshi N, Kumar A, Rani MS, et al. Clinical and aetiological profile of hepatoma at a tertiary care centre. Trop Gastroenterol 2003; 24: 73-75.
- Kumar A, Sreenivas DV, Nagarjuna YR. Hepatocellular carcinoma. The Indian scenario. Indian J Gastroenterol 1995;14:A95.
- Kumar R, Saraswat MK, Sharma BC, et al. Characteristics of hepatocellular carcinoma in India: a retrospective analysis of 191 cases. QJM 2008;101:479-85.
- Leevy CM, Sherlock S, Tygstrup N, et al. (Eds) Diseases of the Liver and Biliary Tract. Standardization of Nomenclature, Diagnostic Criteria and Prognosis. New York: Raven Press 1994; 61–62.
- Levrero M. Viral hepatitis and liver cancer: the case of hepatitis C. Oncogene 2006; 25: 3834-3847.
- Lozano, R "Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010.". Lancet 380 (9859): 2095–128.
- Manash Pratim Sarma, Mohammad Asim, Subhash Medhi, et.al. Viral Genotypes and Associated Risk Factors of Hepatocellular Carcinoma in India. Cancer Biol Med 2012; 9: 172-181.
- Melbye M, Skinhoj P, Nielsen NH, et al. Virus-associated cancers in Greenland: frequent hepatitis B virus infection but low primary hepatocellular carcinoma incidence. J Natl Cancer Inst 1984;73:1267-72.
- Oka H, Tamori A, Kuroki T, et al. Prospective study of alpha-fetoprotein in cirrhotic patients monitored for development of hepatocellular carcinoma. Hepatology 1994;19:61-6.
- Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. Eur J Cancer. 2001;37:S4-S66.
- Saini N, Bhagat A, Sharma S, et al. Evaluation of clinical and biochemical parameters in hepatocellular carcinoma: experience from an Indian center. Clin Chim Acta. 2006; 371: 183-186.
- Sarin SK, Thakur V, Guptan RC, et al. Profile of hepatocellular carcinoma in India: an insight into the possible etiologic associations. J Gastroenterol Hepatol 2001;16:666-73
- Satapathy SK, Garg S, Chauhan R, et al. Profile of chronic hepatitis B virus in children in India: experience with 116 children. J Gastroenterol Hepatol 2006; 21: 1170-1176.

- Vail Mayans M, Calvet X, Bruix J, et al. Risk factors for hepatocellular carcinoma in Catalonia, Spain. Int J Cancer 1990; 46: 378-381.
- Wong PY, Xia V, Imagawa DK, Hoefs J, Hu KQ. Clinical Presentation of Hepatocellular Carcinoma (HCC) in AsianCancer Americans Versus Non-Asian-Americans. J Immigr Minor Health 2011; 13: 842-848. 216.

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