RESEARCH PAPER | Medical Science | Volume : 4 | Issue : 6 | June 2014 | ISSN - 2249-555X

A Retrospective Study on Clinical Characteristics of Hepatocellular Carcinoma in a Tertiary Care Hospital

KEYWORDS

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ABSTRACT *We performed a single centered retrospective study of clinical characteristics, risk factors of Hepatocellular carcinoma in a tertiary care hospital. We retrospectively analyzed HCC patients for two years 2009 & 2011 in Rajiv Gandhi Govt. General Hospital, Chennai. Demographics, etiology, symptoms, risk factors were collected and diagnosed. The male/ female ratio of the population is 4/1. The mean age of the group is 55 years. 99% of patients were symptomatic among which 92% had abdominal pain. Only 1% was asymptomatic. 71.9% of patients were found to be HBV positive and the highest was observed with alcohol consuming HBV patients. It accounts for about 84.6%. History of smoking was found to play a role as 85% of patients were smokers and further need to be confirmed in future studies.*

Introduction:
Hepatocellular carcinoma (HCC) is a primary malignancy of the liver. The common cancer that occurs in the world is the cancer of liver and Hepatocellular carcinoma is the most commonest. HCC is the leading cause of cancer related death worldwide. It is the 5th most common cancer in the world and the third most common cause of cancer death. Over 5, 00,000 people worldwide are affected and cause one million deaths per annum. The burden of this devastating cancer is expected to increasing further in coming years (Alan *et al,* 2010). The geographic areas most affected are located in South East Asia & Sub-urban Africa (Sameer and David, 2007).

Chronic infection with hepatitis B virus (HBV) and Hepatitis C virus (HCV) are the most important risk factors for the development of cirrhosis. Chronic Hepatitis B and Hepatitis C infections account for an estimated 78% of global HCC cases. Factors other than HBV & HCV include toxins (alcohol consumption) and drugs (aflatotoxin & anabolic steroid use) cigarette smoking, metabolic liver disease (hereditary hemochromatosis & alpha 1- antitrypsin deficiency) & steatosis (El-Sherag *et al,* 2004). Chronic alcohol use of greater than 80g per day for more than 10 years increases the risk of HCC 5 fold (Morgan TK *et al,* 2004). Among these three causes of HCC (HBV, HCV, and alcohol) HBV seems to play a direct role in liver cell transformation (Idleman *et al*, 1998). Unfortunately, as India is being endemic for hepatitis B, the progression of HCC from cirrhosis is around 80% and 60% of those are carriers for Hepatitis B (Kumar *et al*, 2008). 5046352 reported that patients of chronic HBV infection followed by chronic HCV infection were at higher risk of developing HCC in India.

Patients and Methods:
Retrospective analysis of HCC patients treated in the department of Hepatology, Rajiv Gandhi Govt. General Hospital during the year 2009 & 2011 was performed. A diagnosis of HCC was confirmed histopathologically or according to EASL diagnostic criteria (Bruix *et al,* 2000). The patient's records that became unavailable vanished or the patients seen in the Outpatient department were excluded from the study.

The demographics, etiology of liver disease, risk factors, signs and symptoms were captured and noted. The etiology of liver disease was categorized as HBV, HCV, alcoholic liver disease, NAFLD, auto immune hepatitis, primary biliary cirrhosis. No quantitative analysis of alcohol consumption was performed. Assessment of habitual alcohol use and smoking was based on patient self-reporting. The medical records and hospital charts were clearly referred and noted. The various symptoms that were recorded during clinical examination were noted. This includes abdominal pain, anorexia, weight loss, jaundice, anaemic condition, past history of diabetes etc. The changes in the biochemical parameters like AST, ALT, Bilirubin and AFP were monitored and taken into account for further studies. BCLC clinical stage of HCC was also recorded.

Serological Significance:
HBsAg, IgG anti-HBc (TransasiaInstachk Hepatitis B) and Anti HCV (Reliable pro-detect Biomedical Pvt. Ltd) were detected using the commercially available rapid test kit. Samples positive for HBsAg and anti HBc antibodies or both were considered positive for HBV. Liver function tests of all the samples were estimated using an auto-analyzer. Serum AFP, ALT, AST and bilirubin were determined using a fully automated analyzer (ERBA EM-200, India).

Statistical analysis:
All data were entered on to an Excel spread sheet in a flat file and tested for consistence. Outliers were rechecked from case sheet, and where necessary from the individuals. These were then analyzed using SPSS ver.17.

Results:
Among a total of 1,18,724 patients admitted in the Department of Hepatology during the year 2009, 44 were diagnosed as HCC and similarly among the 1,12,526 patients admitted in the year, 42 patients were diagnosed as HCC. A total of 86 patients were identified to be having Hepatocellular Carcinoma with a percentage of 0.37 each year. Based on the assessment of the etiology, clinical profile, BCLC clinical stage of HCC 18 patients were excluded and 68 patients were further observed.

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Table.1: Census in the Department of Hepatology, Rajiv Gandhi Govt. General Hospital, Chennai

S. No	Total number of cases	2009	2011
1.	O.P cases	29,14,650	29,04,590
2.	I.P cases	1,18,724	1,12,526
3.	I.P cases with viral hepatitis (HBV&HCV)	281	302
4.	I.P cases with liver disease (other than HBV &HCV)	938	1005
5.	I.P cases with HCC	44	42

In this study, the male/female ratio was 4/1. The mean age of the group is 55years. Approximately 99% of the observed HCC cases were symptomatic and only 1% of patients diagnosed without having any symptom. Among the symptomatic, 92% had abdominal pain, 87% had anaemia, 55% had fever. Nausea with vomiting was observed in about 44% of the study group. Among the selected study group, 45% had diabetes mellitus and 33% had systemic hypertension.

Table.2: Clinical profile of patients with HCC

Symptoms	Percentage (%)
Symptomatic	99
Abdominal pain	92
Anaemia	87
Fever	55
Nausea with vomiting	44
Diabetes Mellitus	45
Systemic Hypertension	33
Asymptomatic	1

Regarding the risk factors, 71.9% of the patients were found to be positive for HBV, 10% with HCV. About 7% of the cases were observed to be co-infected with HBV and HCV. Of all the patients with HCC 84.6% had history of alcohol consumption, 85% had smoking history, 76% had liver cirrhosis, co-morbid diseases. Significant differences in the biochemical parameters were observed in the group. The level of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and bilirubin were significantly increased in HCC. The AFP level was elevated in 76% of the patients which is considered to be significant for HCC diagnosis in patients with liver cirrhosis.

Table 3: Associated risk factors with HCC

Risk factors	Percentage
HBV positive	71.9
HCV positive	10
HBV & HCV co-infection	7
Alcohol consumption	84.6
Smoking history	85
Liver cirrhosis	76

HCC cases were staged according to Barcelona Clinic Liver Cancer (BCLC) scoring system. According to the BCLC scoring system, 3% cases were classified as stage B, 90% as stage C and 6% as stage D.

Discussion:

The growing importance of epidemiology in modern medicine has been evident since the mid 1900s (Rothman KJ *et al).* Hepatocellular cancer is a major health problem more than half a million cases are reported yearly worldwide. The collection and analysis of epidemiologic HCC data will play a critical role in guiding future disease prevention strategies and optimizing patient management. The male dominance observed in the present study is similar to that reported by many other studies from India and rest of the world. Males are affected more commonly than females usually common between the age of 30 and 50 (Kumar *et al*, 2003). Levrero *et al* (2006) studied in India the mean incidence of HCC in four population based registries has been reported to be 2.77% for males and 1.38% for females. Overall, the prevalence of HCC in India varies from 0.2% to 1.6%. Similarly in the present study conducted in a tertiary care hospital the prevalence of HCC was 0.37%.

Our study shows that liver cirrhosis is the prime risk factor for hepatocarcinogenesis. However, the very high proportion of hepatitis virus related HCC, in particular the high proportion of HBV infections, contradicts the common view that alcohol is by far the most important etiological factor for Hepatocellular carcinoma. History of smoking also contributed to be one of the major risk factors in our finding which needs to be further studied. In India, around 70 to 80% of HCC cases are caused due to Hepatitis B and Hepatitis C causes for around 15% and 5% due to co-infection, alcohol also accounts to cause HCC, for about 10% (Sarin *et al,* 2007). Levrero *et al* (2006) reported that the prevalence of chronic hepatitis B and C viruses are the most important risk factors associated with HCC. HCC is common in the areas where Hepatitis B and C are endemic. In India, there is no comprehensive analyzed data for HCC. Vaccination against Hepatitis B and antiviral for hepatitis B & C in chronic state, screening program for early diagnosis are the challenging task in Hepatology for developing countries. With the consideration of available data, prevention and control of major co-factors of alcohol consumption, diabetes, and smoking might reduce the incidence of HCC apart from the main factors HBV and HCV infections.

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