

## Original Research Article

# Common causes and trends of hepatocellular carcinoma at regional cancer centre Raipur, India

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## ABSTRACT

**Background:** Hepatocellular Carcinoma (HCC) is the most common primary malignancy of the liver and is the third most common cause of cancer related deaths in Asia-pacific region. Representative data on epidemiology of HCC in India is scanty and mostly from urban areas. It is more common in males than female. Hepatitis, alcohol consumption, aflatoxin and other hepatotoxins in diet are common causes. Authors did a study for the common causes and trends of the HCC registered at authors' centre between January 2013 to November 2018.

**Methods:** Authors analyzed their hospital data for the patient registered with the diagnosis of hepatocellular carcinoma at their centre during the study period for age, sex, number and causes.

**Results:** Out of 23,766 patients registered for cancer in study period, 132 (0.55%) patients were of HCC, of which 89 (66.4%) were males and 43 (32.6%) were females, with ratio of 2:1. Commonest age group was between 50-59 years 46 (34.6%) followed by 40-49 years 26 (19.5%). No patients were below 20 years of age. Among the commonest causes were alcohol consumption in 71 (53.4%), hepatitis B in 37 (27.8%), hepatitis C in 10 (7.5%), HIV in 4 (3%) and unknown in 11 (8.3%). There is rising trend in males and declining trend in females.

**Conclusions:** Incidence of hepatocellular carcinoma is low among all cancer but has high mortality rate. Alcohol consumption and hepatitis were the commonest cause. It is common above 40 years specially in males.

**Keywords:** Alcohol consumption, Causes, Hepatitis, Hepatocellular carcinoma, Trends

## INTRODUCTION

All over the world liver cancer is sixth most common cancer and seventh most common cause of cancer related deaths in males with age standardized incidence rate and mortality rate of 15.7% and 9.3% respectively.<sup>1</sup> Hepatocellular carcinoma (HCC) is the predominant primary liver cancer in many countries and is the third most common cause of cancer-related death in the Asia-Pacific region. The incidence of HCC is higher in men and in those over 40 years old. In the Asia-Pacific region, chronic hepatitis B virus and hepatitis C virus infections are the main etiological agents; in particular, chronic hepatitis B infection (HBV) is still the major cause in all

Asia-Pacific countries except in Japan. Over the past two decades, the incidence of HCC has remained stable in countries in the region except for Singapore and Hong Kong, where the incidence for both sexes is currently decreasing. Chronic hepatitis C infection (HCV) is an important cause of HCC in Japan, representing 70% of HCCs. Over the past several decades, the prevalence of HCV has been increasing in many Asia-Pacific countries, including Australia, New Zealand, and India.<sup>2</sup> Existence of chronic liver disease especially cirrhosis represents potential risk for HCC. Cirrhosis mainly caused by hepatitis B Virus (HBV), hepatitis C virus and chronic alcohol consumption. HCV infection and both current

and past HBV infections were more common in cirrhotic than in noncirrhotic patients with HCC.<sup>3</sup>

Hepatitis B virus is known to cause genomic integration in the liver tissue resulting in chromosomal deletions and in turn metaplasia. The p53 tumour suppressor gene can be altered in HCC under the transactivating potential of the HBs protein.<sup>4,6</sup> HCV-related carcinogenesis is possibly related to chronic inflammation and cirrhosis. There is a positive association between HCC and consumption of alcohol in which alcohol works as a cofactor for hepatotoxins and hepatitis viruses.<sup>7</sup> Chronic alcoholism is also on the rise in India. although the possible role of these viral infections and alcohol in the causation of HCC has not been assessed in detail but nearly 25% of all HBV-related chronic liver disease in India is caused by mutant forms of HBV.<sup>8</sup> Alcohol seems to be a cocarcinogen in the pathogenesis of HCC, by inducing cirrhosis, and by increasing the risk of viral infections (HBV and HCV), as well as via its effects on P450 mixed function oxidase system, thus causing enhanced activation of chemical carcinogens.<sup>5</sup> Apart from viral infections and alcohol, obesity (non-alcoholic fatty liver disease), aflatoxin (cofactor with HBV), tobacco, tyrosinosis, hemochromatosis (iron overload),  $\alpha$ 1-antitrypsin deficiency, autoimmune chronic active hepatitis, primary biliary cirrhosis, non-alcoholic cirrhosis, non-alcoholic steatohepatitis, diabetes, viral load, male sex, older age, exposure to aflatoxins, concurrent alcohol abuse are the main risk factors for HCC has been reported by world gastroenterology organization.<sup>9</sup>

**METHODS**

Authors conducted this study at Regional Cancer Centre (RCC), Pt. J.N.M. medical college Raipur. Total number of patients registered at RCC with the diagnosis of cancer, were taken in the study. Authors analyzed their hospital-based cancer registry data retrospectively for the cases registered as hepatocellular carcinoma. Authors thoroughly analyzed the data for age, sex, age group, type of histopathology or cytology, history of any past illness specially jaundice and its cause. When proven case of viral hepatitis than searched for its type (HBV/HCV), either history given by the patient or confirmed by records of any previous treatment, he had brought with him. History of any addictions specially alcohol consumption, its frequency and duration. Authors also analyzed data for socioeconomic conditions and dietary habits. When no specific cause was found they assigned it as unknown cause. The present study was retrospective study. The study participants were patients registered to RCC Raipur between January 2013 to November 2018.

**Inclusion criteria**

- Patients registered at RCC Raipur
- Both males and females of all ages

- All patients were proven case of liver cancer reported as hepatocellular carcinoma either with histopathology or cytology.

**Exclusion criteria**

- Patients reported for other sites of cancers
- Liver cancers other than HCC.

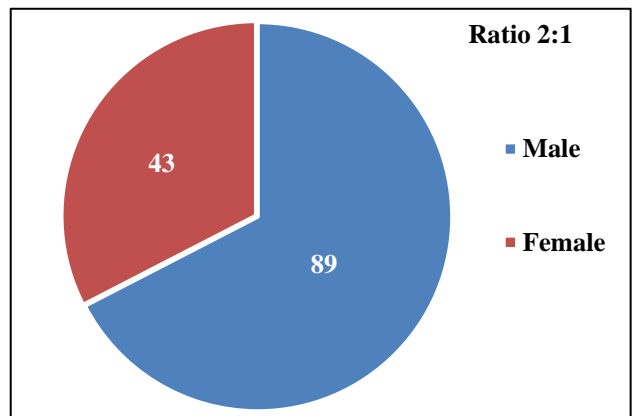
**Statistical analysis**

Analysis done by entering the data in excel sheets and using simple statistical formula. Graphs are plotted with the help of data entered in data sheet.

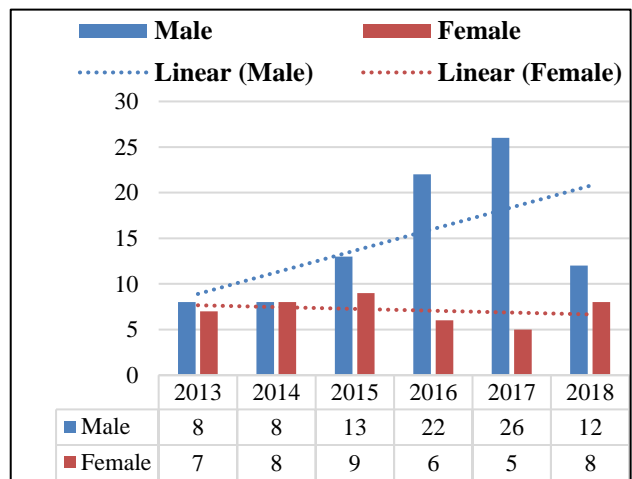
**RESULTS**

**Gender distribution**

Total number of cancer patients registered at RCC Raipur during the study period was 23,766. Out of these patients 132 (0.55%) were reported as hepatocellular carcinoma. Out 132 patients, 89 (67.4%) were males and 43 (32.6%) were females. The number of male patients is higher than females with male to female ratio of 2:1 (Figure 1).



**Figure 1 Male and female distribution.**



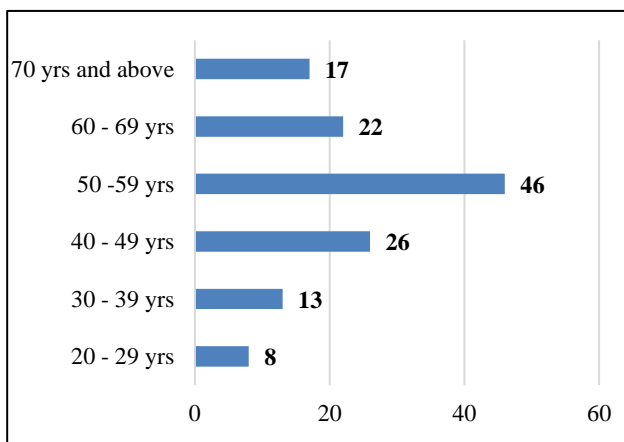
**Figure 2: Sex wise distribution and trend.**

**Trend of HCC in both sexes**

When authors analyzed the trend of HCC in five years, in males only 8 cases were reported in year 2013 whereas 26 cases in 2017. In females 7 cases were reported in 2013, with 5 and 8 cases in 2017 and 2018 respectively. There is increasing trend in male and nearly static to declining trend in female in the study period (Figure 2).

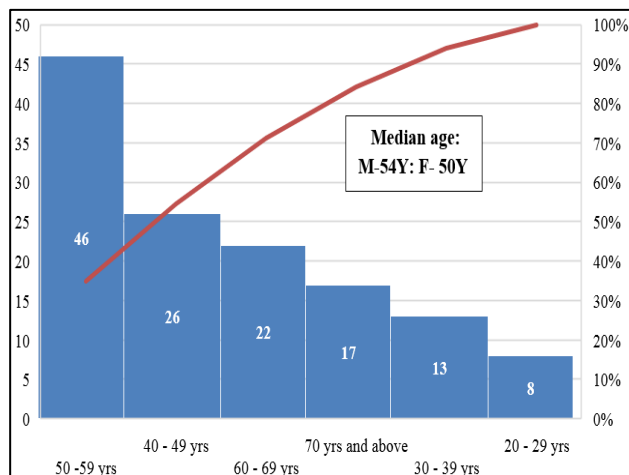
**Age group distribution**

When authors analyzed their data for the age groups, most of the cases were between 40 to 69 years, total 94(71.2%) cases out of 132. The commonest age group affected was 50-59 years, with total number of 46 (34.8%) cases (Figure 3).



**Figure 3: Age group distribution.**

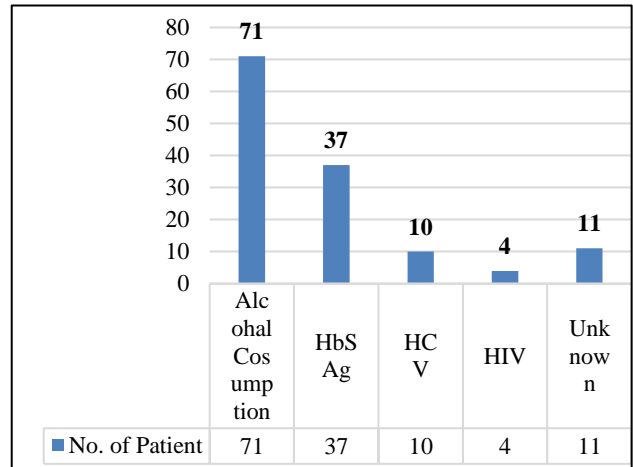
Authors have also plotted their data in descending order of their occurrence. The age group affected in descending order were 50-59, 40-49, 60-69, 30-39, 20-39 respectively, with lowest number below 30years. No cases were reported below 20 years. The Median age in males were 54 and in females 50 years (Figure 4).



**Figure 4: Age wise number of patients in descending order.**

**Major causes**

In present study, the major causes for HCC seen were alcohol consumption in 71 (53.4%), hepatitis B in 37 (27.8%), hepatitis C in 10 (7.5%), HIV in 4 (3%) and unknown in 11(8.3%). Most of the patients were. Among the unknown causes there was no clear-cut history about the dietary habits, addiction, jaundice and or viral hepatitis (Figure 5).



**Figure 5: Major causes of HCC.**

**DISCUSSION**

Hepatocellular carcinoma is primary malignant carcinoma of liver derived from hepatocytes. It accounts for 90% of cases, others being cholangiocarcinoma, hepatoma, and angiosarcoma.<sup>10</sup> At author's centre hepatocellular carcinoma constitutes 80% of all primary tumour of liver.

The information on incidence of HCC in India is inadequate. The autopsy data has been published earlier by Dhir et al, showed an incidence of 0.2 -1.9% of HCC with higher prevalence in south-eastern states.<sup>11</sup> Recent age standardized incidence rates of world for HCC in liver showed an incidence rate of 0.4 - 4.5% in males and 0.1-3.5% in females of India. Lowest incidence rates seen in Kamrup urban district of Assam and Ahmadabad and Dindigul Ambilikikai of Tamil Nadu respectively. Highest incidences rates in both sexes seen in Mizoram.<sup>12</sup> Present data showed incidence of 0.55% HCC among all cancers. Data from 29 hospital based cancer registries shows that liver cancer is not among top ten leading sites of cancers in most of the centres except in Kochi, Silchar, Kottayam in males and only Dibrugarh in females.<sup>13</sup> Data from 27 population-based cancer registries, it is among top 10 leading sites of cancer except in Bhopal, Delhi, Ahmadabad and Cochar PBCR. In north-eastern states its incidence is very high in both males and females.<sup>14</sup>

GLOBOCAN data 2018 showed an incidence rate of 4.7% and mortality rate of 8.2% all over the world, with highest incidence rate in Asia 72.5%, followed by Europe

and Africa, 9.8% and 7.7% respectively. Highest incidences seen in Eastern Asia in males (26.8%) and females (8.7%) with Male to female ratio is 3:1.<sup>15</sup> Age adjusted Incidence rates among population-based registries of India was highest in Papumpure district and Nahrlagun of Arunachal Pradesh, 38 and 21.4 per 100000 respectively. Lowest incidence reported at Cachar District of Assam (1.2/100000).<sup>16</sup> Yang, JD et al, in their study reported that globally, the rate of men suffering from HCC is higher than women, with the male to female ratio ranging from 2:1 to 4:1, the difference being much greater in high-risk areas. In the Asia-Pacific region (especially North and South Korea, Indonesia, and Vietnam), the rate of HCC in men is greater than 4 folds than that of women.<sup>17</sup> At author's institute, with highest incidence seen in males 67.4% and 32.6% in females. Male to female ratio is 2:1.

Present study data suggests that there is rising trend of HCC in males and static to declining trend in females in the study period. Achararya SK et al, had also reported rising trend in males in his study with a male to female ratio of 4:1.<sup>18</sup> Yeole BB et al, observed an increasing trend in the incidence of liver cancer in the both the sexes in Mumbai.<sup>19</sup>

Bergsland EK et al, in his study reported an increased incidence of HCC in Japan, UK, USA, and several Nordic countries noticeably over the past two decades and has become progressively associated with younger age groups. The highest age-specific rates were in people aged beyond 75. The age-specific rates of men in high-risk African populations tend to peak between 60 to 65 age group, while that of women peak between 65 and 70 years of age.<sup>20</sup> In present study the highest incidence were seen in age group 50-59 years (34.84%) followed by 40-49 and 60-69 years, 19.7% and 16.7% respectively, which is similar to above study. These variations of age-group patterns are likely related to the differences in the dominant hepatitis virus in the population, the age at viral infection as well as the existence of other risk factors like alcohol, dietary habits and food culture. No cases of HCC reported below 20 years of age. Major histo-pathologies below 20 years were secondary adenocarcinomas. Hepatoblastoma were seen below 10 years of age (4.8% of all liver neoplasms).

Among the major causes reported in present study were alcohol consumption found in 53.8%, hepatitis B in 27.8%, hepatitis C in 7.5%, HIV in 3% and unknown in 8.3%. Alcohol consumption may be associated with hepatitis viral infection, but due to poor health seeking behaviour in the region and illiteracy may remain undiagnosed. Among the unknown causes, obesity (non-alcoholic fatty liver disease), diabetes, aflatoxin, tobacco, tyrosinosis, hemochromatosis, autoimmune chronic hepatitis may be the cause.

In the study by Dhir V et al, Hepatitis B surface antigen positivity in Indian HCC varies from 36% to 74%, with

an average of 47%. There are no good case control studies on HCC from India.<sup>11</sup> In present study due to improper reporting for HBV and HCV positivity, the number of cases of HCC due HBV and HCV were less.

In the study by Akinyemiju et al, for global burden for liver cancer and etiologies, highest incident cases and death reported in East Asia. Most common cause being HBV. Because of demographic changes of population there is an increase in number of cases of HCC due to both HBV and other causes, more pronounced for other causes, 42% and 56% respectively. Within high income Asia-pacific region like Japan 67% of cases were due to HCV infection.<sup>21</sup>

Marrero JA et al, in their study were also reported that alcohol, tobacco and obesity are independent risk factors for HCC and has synergistic effect to other causes of liver cirrhosis. They increased the risk for HCC by 6-fold, 5-fold and 4-fold respectively.<sup>22</sup>

## CONCLUSION

Data from present study indicates that, incidence of hepatocellular carcinoma is low at authors' centre. Regarding the causes, alcohol consumption is commonest cause followed by hepatitis. More information is needed for viral and other unknown causes, like testing for surface markers to ascertain specific virus and proper investigations for unknown causes. A properly designed case-control study is also needed.

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