Epidemiology of Hepatocellular Carcinoma in India

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Indian data on epidemiology of HCC is not available. Cancer is not a reportable disease in India and the cancer registries in India are mostly urban. National cancer registry program of the Indian Council of Medical Research (ICMR) has been recently expanded to include 21 population based and 6 hospital based cancer registries. The last published registry data by ICMR available in the cancer registry website (www.ncrpindia.org) was in 2008 which provides information on various cancers from 2006 to 2008. The other source of information was the report published by International Agency for Research on Cancer (WHO). According to these available data the age adjusted incidence rate of hepatocellular carcinoma (HCC) in India for men ranges from 0.7 to 7.5 and for women 0.2 to 2.2 per 100,000 population per year. The male:female ratio for HCC in India is 4:1. The age of presentation varies from 40 to 70 years. According to a study conducted by verbal autopsy in 1.1 million homes representing the whole country, the age standardized mortality rate for HCC in India for men is 6.8/100,000 and for women is 5.1/100,000. According to another study the incidence of HCC in cirrhotics in India is 1.6% per year. The unpublished data from various tertiary care centers suggest that the incidence of HCC is increasing in India. There is a need for a multi-centric HCC registry under the aegis of INASL. (J Clin Exp Hepatol 2014;4:S27–S33)

Epidemiology

Hepatocellular carcinoma (HCC) is the most frequent cause of all liver cancers and constitutes 90% of cancers of liver globally.[1] Even though cancers of lungs, breast and large intestine have been identified as three most common cancers, the three leading causes of annual death due to cancers include lungs, stomach and liver.[1] Approximately 7.5 Lakhs of new cases of HCC per year occurs globally which makes HCC as the 5th common cause of cancers effecting human.[1] The mortality in HCC is very high; about 7 Lakhs death due to HCC occur annually and has been estimated to be 3rd common cause of death due to cancers effecting human.[1]

In India, information on HCC is inadequate. From 1988 till December 2012, over two and half decades only 68 publications have been listed in the PUBMED, all from tertiary care center, on select areas and most studies included small samples. The cancer registries in India probably do not provide accurate estimates of HCC prevalence due to its predominant urban locations and the source of information on cancers are from cytology, oncology sites, and municipal registers of death. HCC predominantly is diagnosed and treated by Gastroenterologists/Hepatologist/Transplant Surgeons/G.I. Surgeons. These patients treated by the later doctors are presumably are not being listed in the registries. Further, the diagnosis of hepatocellular cancer is achieved frequently by non-invasive imaging technique rather than by histology/cytological techniques as used in almost all other cancers. Therefore the collated informations from oncology/cytology/pathology departments may not be having the records of a considerable proportion of HCC cases. Lastly cancers are not reportable disease in India.

With these limitations, the specific issues which this review intend to do includes the following:

1. How common is HCC in India?
2. Status of reporting of HCC to cancer registries in India?
3. HCC burden in tertiary care centers?
4. Causes of mismatch of documented and likely actual burden.
5. Regional differences in HCC burden in India.

HOW COMMON IS HEPATOCELLULAR CARCINOMA IN INDIA?

The source of information to assess the frequency of occurrence of HCC in India includes autopsy data, cancer registries and population based surveillance data.

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Abbreviations: AAIR: age adjusted incidence rate; ASMR: age standardized mortality rate; HBCR: hospital based cancer registry; HCC: hepatocellular carcinoma; IARC: international agency for cancer research; ICMR: Indian Council of Medical Research; PBCR: population based cancer registry
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Autopsy Data

The prevalences of HCC described in autopsy series from India are very old and were published between 1966 to 1982.[2,3] The autopsy data has been published earlier by Dhir and Mohandas in 1998,[3] which is depicted in Table 1.

The autopsy data reveals that 0.2–1.9% of autopsy cases had HCC with a higher prevalence of HCC in South-eastern states of India. However, these information have been replaced by cancer registry data in India.

Cancer Registry Data

National cancer registry program was established by Indian Council of Medical Research (ICMR) in 1981.[4] Initially, three hospital-based cancer registries (HBCRs) and three population-based cancer registries (PBCRs) were established. By now, 21 PBCRs and 6 HBCRs have been established. The last published registry data by ICMR available in the cancer registry website (ncrpindia.org) was in 2008 which provides information on various cancers from 2006 to 2008. The present write-up includes the information retrieved from this later report to provide the recent trends of HCC in India, which has been depicted in Table 2.

The summary interpretations of data depicted in ICMR cancer registry are as follows:

a) In 8 of the 23 PBCRs HCC was not included in the first 10 common cancers and in all these centers the age adjusted incidence rate (AAIR) of HCC/100,000 population was between 1 and 1.5. In the remaining PBCRs the AAIR ranged from 2.1 to 7.5 per 100,000 population.

The AAIR for HCC for men ranged from 0.9 to 7.5 and for women it ranged from 0.2 to 2.2 per 100,000 population. The highest AAIR was reported from Sikkim and Mizoram (Table 2). However at Barshi, HCC constituted 7.5% of all cancer and was the most common cause of all cancers recorded in the cancer registry. Table 3 provides the AAIR of HCC in various cancer registries in India as depicted by WHO,[5] which was updated in 2011 and provides similar data on frequency of HCC in India.

IARC–WHO data indicate that Africa and East Asia has the highest frequency of HCC globally with an AAIR of 14–36 per 100,000 people and account for approximately 80% of HCC globally.[5,6]

b) As per cancer registry data,[4] 4–8% of the cancers were due to HCC in at least 13 of 21 PBCRs. At these centers males predominantly had been documented to have HCC with a M:F at 4:1 and the median age ranged from 40 to 70 and the frequency of liver cancers seems to be higher with increasing age.
c) To assess trend of frequency of digestive tract cancer Yeole et al analyzed PBCRs in five sites (Mumbai, Bangalore, Chennai, Delhi and Bhopal) over almost two decades (1980–2003).[7]

The annual percentage change in AAIR for Gut and liver cancer is depicted in Table 4.

The Table 4 indicates that there is a significant increase in liver cancer frequency in Mumbai, Chennai and Bangalore cancer registry over two decades.

Without visible control strategy for HCC, this trend of increase in frequency of occurrence of HCC is likely to continue. Indeed, in 1998 ICMR cancer registry from all sites documented 10,000 HCC cases.[4] In 2002, IARC collated data and reported 13,630 HCC cases from India.[5] In 2009, ICMR cancer registries have documented 25,000 cases of HCC. This would indicates that either HCC frequency is increasing or are being diagnosed more often.

IF approximately we presume that AAIR for HCC in India is about 3–5/100,000 population annually, than in a year, approximately 30,000 to 50,000 HCC would be occurring in India.

Table 1 Autopsy Data on HCC in India.

Place	Autopsies (No.)	HCC (%)
India		
• Mumbai	6000	0.2
• Mumbai	4000	0.2
• Agra	1234	0.7
• Guntur	629	1.1
• Andhra Pradesh	2789	1.6
• Chennai	1218	1.9
Bangladesh	5450	0.2
Denmark	14881	0.3
USA (Boston)	14000	0.6
Japan	401,381	3.1
Hong Kong	1480	6.8

Population Based Surveys

Hepatocellular Carcinoma Related Mortality in General Population

Dixit et al[8] published an important population based survey to identify the cancer related mortality in India.[8] The study was conducted by verbal autopsy study in 1.1 million homes representing the whole country. People who died between 2001 and 2003 were included in the study and the deaths were projected for year 2010. For both sexes and all ages 122,429 deaths occurred in 2001–2003 and 7137 of these were attributable to cancers. In 2010, more than 556,000 cancer deaths were estimated in people of all ages and 72% of these deaths were between 30 and 69 years. In 2010 at all ages, rates of cancer deaths about 59/100,000 for men and about 52/100,000 for women. Among men, the first four causes of mortality included