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Epidemiology, Etiology, Clinical Profile and Treatment of Hepatocellular Carcinoma at a Tertiary Care Institute from Tamilnadu Over 5 Year Follow up - A Retrospective Analysis

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Abstract: ***Background: Hepatocellular carcinoma (HCC) is the most common primary hepatic malignancy. There is huge caveat in the Indian data on HCC. Aim of this study is to study the prevalence, risk factors, clinical profile and treatment of HCC at a tertiary care institute in Chennai, Tamilnadu. Methods: Data analysis of HCC patients enrolled in a teritary care centre from south India between Jan 2017 and Dec 2021. HCC was diagnosed according to AASLD criteria-Triple phase CT of the abdomen and/or serum alpha-fetoprotein and/or histology (Wherever it is indicated). Barcelona Clinic Liver Cancer (BCLC) staging system was used for staging purposes. Results: We registered 104 HCC patients [males 95 (89%), Females 9 (11%) with mean age 58.3± 11.50 years]. The etiology of HCC was: Ethanol induced 32 (30.8%), Hepatitis B virus 29 (27.9%), Hepatitis C virus 9 (8.7%), NAFLD 13 (12.5%), Idiopathic 21 (20.2%). Serum Alph-fetoprotein was >200 ng/ml in (63.5%) and very high AFP (2000-100000) in 37.5%. Typical radiological features on triple phase CT are seen in 72.1 %, Vascular invasion was seen in 46.2 %, Ruptured HCC are seen in 16.3%and distant metastases in 8%. Loss of weight and appetite (71.2) and Abdominal pain (70.2%)are the most common presenting symptoms. Majority of the patients were BCLC stage C (62.5%) followed by stage B (26%). Biochemical: Thrombocytopenia (47.1%), anaemia in (52.8%) and Altered LFT is observed in 38.4%.99 out of 104 patients were treated of which 80.8% are given Sorafenib, 3.8% underwent TACE and 11.5% underwent hepatectomy.38 patients are alive on treatment 36 patients are dead and 30 patients lost to follow up. Conclusions: In our study we observed that Alcohol is the predominant cause for HCC followed by Hepatitis B. Diagnostic range serum alpha-fetoprotein (>200ng/ml) was detected in 63.5% of study patients. Awareness about alcohol abstinence and good healthy life style practices along with Universal immunization with hepatitis B vaccination may reduce the HBV infection rates and in part HCC burden in near future.***

Keywords: Hepatocellular carcinoma, Indian data, epidemiology, risk factors, clinical profile, treatment

1. Introduction and background

Heptocellular carcinoma (HCC) is a global health problem and its prevalence is increasing around the world[1]. HCC is currently the 5th most common cancer in the world[2]. The prevalence of HCC depends on the geographical location as the risk factors for development vary between continents and between countries. In developing countries, the age-adjusted incidence of liver cancer is 2 to 3 times higher than in developed countries. About 80 percent of liver cancers are found in Asia and Africa. The most common type of liver cancer is liver cancer (HCC) and it accounts for about 90% of all liver cancer cases. The most common risk factor for liver cancer is hepatitis B virus infection (HBV) which accounts for about 50% of all liver cancers[3]. Patients with HCV infection have a significantly higher risk of developing liver cancer compared to those who do not have HCV infection but with advent of novel anti HCV antiviral drugs the incidence is substantially reduced compared to previous years[4]. Patients with cirrhosis, however, are still at high risk for developing liver cancer even after clearing HCV. NASH is the fastest-growing aetiology of liver cancer, especially in West[5]. There is huge caveat in the Indian data on HCC hence the aim of this study is to assess the prevalence, risk factors, clinical profile and treatment of HCC at a tertiary care institute in Chennai, Tamilnadu[6, 7].

Aims and objectives:

1) To observe the epidemiological patterns in the incidence of HCC
2) To study the clinical profile and etiological patterns in HCC and to observe the difference from the global trends

2. Materials and methods

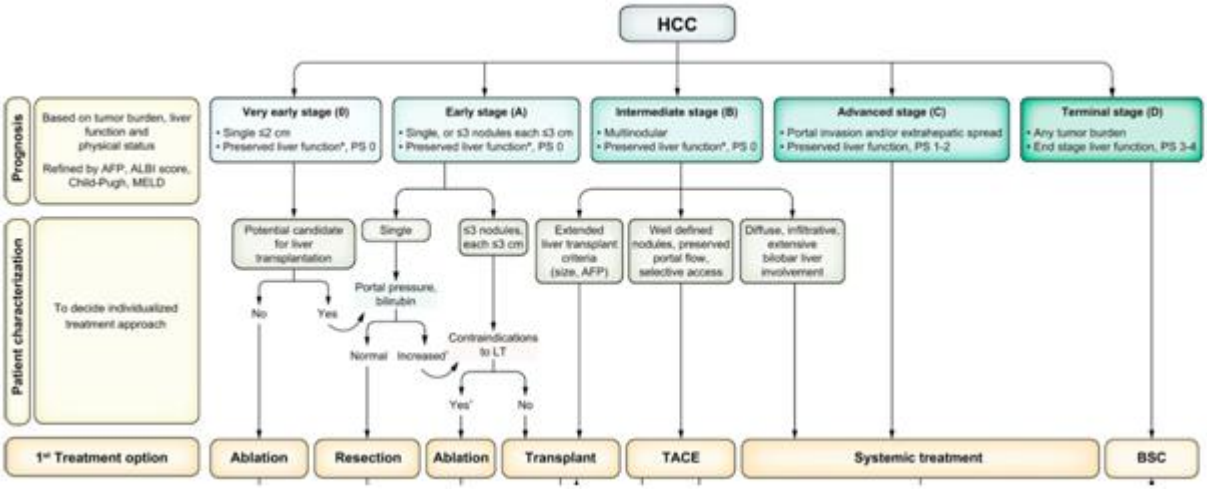
This study is a retrospective observational study conducted in the department of medical oncology, in Government Stanley Hospital, Chennai, for a period of five years (from Jan 2017 to Dec 2021). Approval from the Institutional Ethics Committee was taken for the study. HCC was diagnosed according to AASLD or EASL criteria-Triple phase CT of the abdomen and/or serum alpha-fetoprotein and/or histology (Wherever it is indicated). . Barcelona

Clinic Liver Cancer (BCLC) staging system was used for staging purposes.

AASLD criteria for diagnosis of HCC:
Any lesion of size >2 cm that exhibits both arterial hyper enhancement and venous washout in a single imaging modality concomitant with an AFP >200 ng/mL is sufficient to diagnose HCC.

EASL criteria for diagnosis of HCC:
EASL recommends that lesions that are >2 cm with characteristic radiologic features of arterial hyper enhancement on two different imaging modalities, or on one imaging modality alongside with a serum alpha-fetoprotein (AFP) of 400 ng/dL or more, are diagnostic of HCC.

BCLC staging system:



3. Results

We registered 104 HCC patients [males 95 (89%), Females 9 (11%) with mean age 58.3± 11.50 years].

Etiology: Among all the cases of HCC following etiological causes are observed Ethanol induced 32 (30.8%), Hepatitis B virus 29 (27.9%), Hepatitis C virus 9 (8.7%), NAFLD 13 (12.5%), Idiopathic 21 (20.2%).

Serum AFP: Serum Alph-fetoprotein was >200 ng/ml in (63.5%) and very high AFP (2000-100000) was seen in 37.5%.

Radiological appearance: Typical radiological features on triple phase CT are seen in 72.1 % of the patients where as Vascular invasion was seen in 46.2 %, Ruptured HCC isfound in 16.3% patients and distant metastases are found in 8%.

Clinical features: Loss of appetite (71.2%) and Abdominal pain (70.2%) are the most common presenting symptoms followed by loss of weight (65.3%) and fatigue (58.2%).

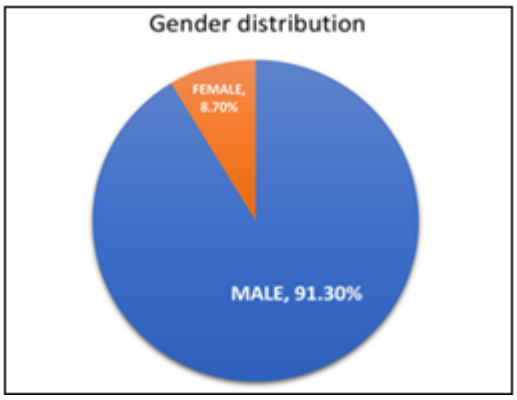
Stage wise presentation: Majority of the patients presented in BCLC stage C (62.5%) followed by stage B (26%), where as stage A & stage D constituted 6.7% & 4.8% respectively. Fifty two patients (50%) had unifocal tumours and rest 50% patients had multifocal tumours.

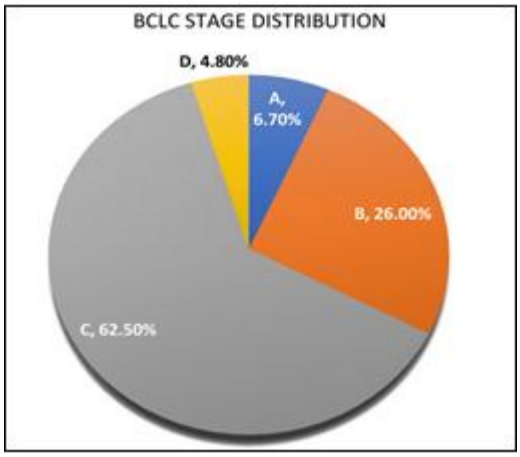
Labaratory Parameters: Thrombocytopenia (47.1%), anaemia (52.8%) are most common abnormalities and Altered LFT is observed in 38.4% of patients.

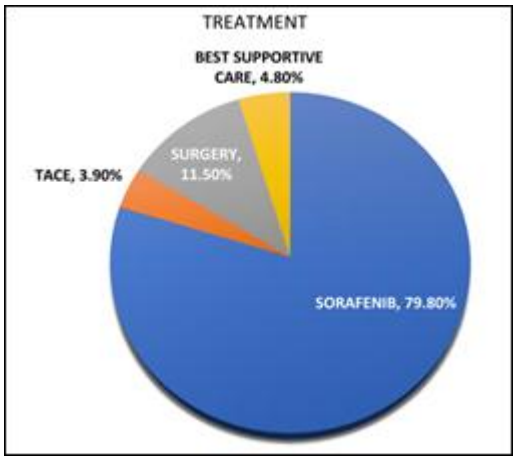
Treatment & Survival: Ninety nine out of one hundred and four patients were treated of which 80.8% are given Sorafenib, 3.8% underwent TACE and 11.5% underwent hepatectomy. Finally thirty eight patients are alive on treatment thirty six patients are dead and thirty patients lost to follow up.

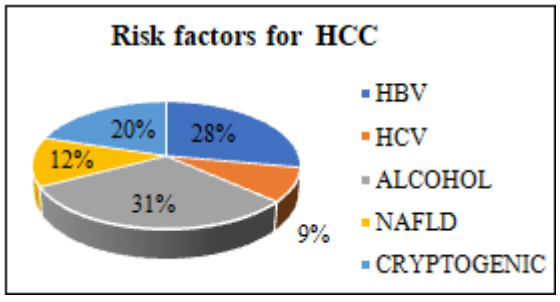
Table 1: Demographic data

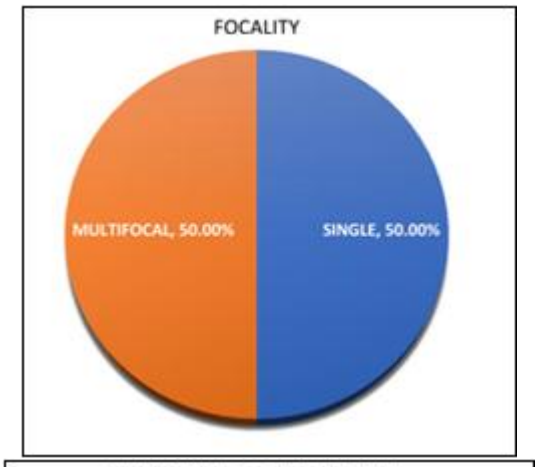
Clinical parameters	Frequency
Age	
Mean age (range)	58 years (36-85)
Gender, n (%)	
Men	95 (89%)
Women	9 (11%)
Typical radiological features n (%)	
Present	75 (72.1%)
absent	29 (27.9%)
Etiology n (%)	
Alcohol	32 (30.8%)
Hepatitis B	29 (27.9%)
Hepatitis C	9 (8.7%)
NAFLD	13 (12.5%)
Idiopathic	21 (20.2%)
BCLC stage n (%)	
BCLC A	7 (6.7%)
BCLC B	27 (26%)
BCLC C	65 (62.5%)
BCLC D	6 (4.8%)
AFP n (%)	
<200 ng/dl	38 (36.5%)
>200 ng/dl	66 (63.4%)
2000-100000 ng/dl (Very high)	11 (15.3%)
Clinical features n (%)	
Loss of appetite	74 (71.2%)
Abdominal pain	73 (70.2%)
Loss of weight	68 (65.3%)
Fatigue	56 (58.2%)

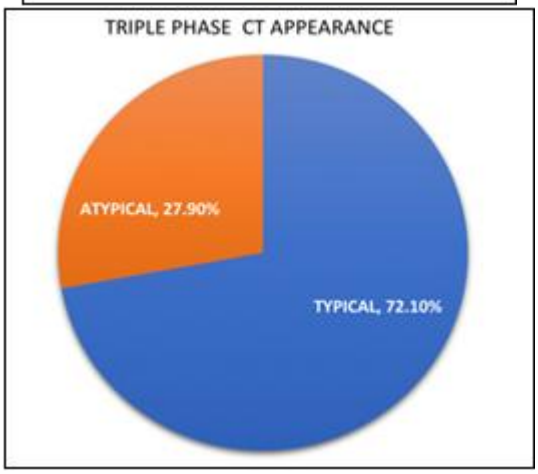












4. Discussion

This is one of the very few studies which tried to comprehensively put forward the five year data right from epidemiology, etiology, presentation to treatment patterns from a teritary care centre in south India. Among the total 104 patients included in our study males constituted the major part (89%) compared to females (11%). This strong male predominance in our study (the male to female ratio was 8-9: 1) is similar to the global trend[8]. The mean age of presentation was 58.3 years which was similar to an earlier series from India[9].

Among the risk factors ethanol related decompensated liver disease (DCLD) was the most common cause accounting to 30.8% of the cases which is usually not the case especially in countries like India where hepatitis B associated HCC are more common and this difference could be possibly because of effective vaccination strategies and awareness programs which are being implemented on a larger scale covering the major sections of population. Another reason could be due to widespread use of alcohol irrespective of socioeconomic status leading to alcohol induced cirrhosis thereby HCC. HBV was the second most common cause constituting 27.9% of cases which was still significant, where as NAFLD and HCV constituted 12.7% & 8.7% respectively which is on par with global data where NAFLD is most commonly seen in western countries compared to developing countries and the prevalence of HCV in India is about 0.8-1.5% of the general population and it has been implicated as the causative agent in 14-26% of chronic liver disease[10, 11].

Around 20% of the patients had no identifiable cause for HCC.

In the terms of clinical presentation anorexia (71%) followed by right upper quadrant abdominal pain (70%) were the most common symptoms which is the usual presentation. Many studies have highlighted the importance of symptomatology (weight loss, anorexia and abdominal pain) as markers for HCC[12].

The majority of the HCC patients who presented to our hospital were in BCLC stages C and B [65 (62.5%) and 27 (26%), respectively] and almost all of these were symptomatic at their first presentation, suggesting that there is denovo advanced disease.99/104 patients received treatment either by surgery, TACE, sorafenib or combination of both, but only 38 patients (36.5%) were alive suggesting the aggressive nature of the disease and lower survival due to advanced disease presentation. One of the most important and less discussed challenges is improper treatment compliance and loss to follow-up which constituted around 29% of the total patient population which can significantly affect the treatment outcomes and disease specific survival. This problem is more common among the low socioeconomic group where there is a knowledge gap, lack of awareness, apprehensions regarding the disease and also the treatment and inclination towards alternative treatments (ex: Native herbal treatment).

Serum AFP level >200ng/ml is taken as a conventional diagnostic level for HCC. In this study, AFP was elevated above the diagnostic range in only 63.5% of patients. Low serum levels may be because of either smaller size of tumors or due to better differentiation of masses which did not produce high AFP[13]. The level of AFP did not show any correlation to the focality of tumors or to the risk factors of HCC. Very high AFP (>2000ng/dl) was seen in 37.5% of the patients and majority of these patients (97%) had advanced stage disease (i. e BCLC C & D).

Anemia and thrombocytopenia were found in 52.8% and 47.1% respectively, anemia could be due to multiple factors like nutrition deficiencies due to poor intake and poor liver function, anemia of chronic disease due to malignancy, blood losses (Melena, hematemesis) probably due to underlying cirrhosis which can affect the quality of life and overall disease outcomes. Thrombocytopenia is mostly due to the underlying cirrhosis and splenomegaly, nonetheless few cases could be due to paraneoplastic manifestation. Deranged liver function was seen in 47.1% of the patients which could be due to DCLD, HCC or both.

Finally regarding the treatment aspects 80.8% of the patients received oral VEGF tkisorafenib which is suggestive of advanced disease in majority of patients. Patients who underwent hepatectomy were 11.5% and patients who underwent TACE were 3.8%. There are limitations in the study of which the major limitation was that its a single institution retrospective study another limitation was the study sample which was not very huge, although all the patients were included in a 5 year time span, and another limitation is resource limitations in the form of lack of immunotherapy, lack of ablative techniques like radiofrequency ablation/ microwave ablation.

5. Conclusion

In our study we observed that Alcohol is the predominant cause for HCC followed by Hepatitis B. Diagnostic range serum alpha-fetoprotein (>200 ng/ml) was detected in 63.5% of study patients. Awareness about alcohol abstinence and good healthy life style practices along with Universal immunization with hepatitis B vaccination may reduce the HBV infection rates and in part HCC burden in near future. Also more studies addressing the knowledge gap regarding the epidemiological, clinico-pathological and treatment patterns and survival of various malignancies especially from teritary care centres across all the states and districts are of great importance for understanding the actual presentation of the disease and its comparison with real world data.

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Conflict of interest
No conflict of interest

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