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Prevalence and Profile of Hepatocellular Carcinoma in Patients of Chronic Liver Disease in a Tertiary Care Centre in Manipur

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Abstract
BACKGROUND*: Hepatocellular Carcinoma(HCC) is a major health problem, being the 5th most common neoplasm in the world and the third most common cause of cancer related deaths. Though cirrhosis of all etiologies may be complicated by HCC, persistent HBV or HCV infections account for over 80% of cases worldwide. However, studies in Italy and United states indicate alcohol as main cause of HCC(32 to 45%).*
AIM AND OBJECTIVE*: To study the prevalence and profile of HCC in patients of chronic liver disease*
MATERIAL AND METHOD*: This study was a cross sectional study conducted in a prospective manner from sep 2017 to june 2019 in consecutive chronic liver disease patients attending liver clinic and inpatients in a tertiary care hospital in Manipur.*
RESULTS*: 300 patients of CLD were screened, of which 45 patients were found to have HCC. Majority of the patients belonged to CTP B- 30(66.7%), while 8(17.8%), 7(15.5%) were in CTP A and CTP B respectively. Most of the patients were in BCLC stage C-15(33.3%) followed bystage B- 13(28.9%), stage A- 10(22.2%) and stage D- 7(15.5%). Alcohol was the most common etiology accounting to about 21(46.7%) patients followedby hepatitis C with alcohol 9(20%)and hepatitis B 8(17.8%). Male and female sex ratio recorded 10.25:1. Around 17(37.7%) patients have alpha feto-protein level > 400ng/ml.*
CONCLUSION: *In this study, the prevalence of HCC is 15% with alcohol being the most common etiology which may be due to increased alcohol consumption in this part of the country.*
Keyword*: Hepatocellular carcinoma, Child-Turcotte-Pugh, Barcelona Clinic Liver Cancer.*

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I. Background:

Hepatocellular carcinoma(HCC) is the most common primary hepatic malignancy. It almost always occurs in a histologically abnormal liver with an overwhelming majority having underlying cirrhosis at the time of diagnosis.[1.]HCC is thefifth most common cancer worldwide in men and the second most frequent cause of cancer death, with annual incidence of 0.5 million worldwide.[.2]

According to the International Agency for Research on cancer(WHO) the age adjusted incidence rate of hepatocellular carcinoma(HCC) in India ranges from 0.7 to 7.5 and for women 0.2 to 2.2% per 100,000 population per year. The male to female ratio of HCC in India is 4:1. The age of presentation varies from 40 to 70 years.[3] The prevalence of HCC in India varies from 0.2 to 1.6%.[4] According to study conducted by verbal autopsy in 1.1 million homes representing the whole country, the age standardized mortality rate of HCC in India for men is 6.8/100,000 and for women is 5.1/100,000.[5] The vast majority of the cases of HCC occur in the setting of liver cirrhosis, and thus the etiologyof HCC mirrors that of chronic liver disease and cirrhosis. The unique geographical, sex and age distribution of HCC are largely a result of the specific patterns of the risk factors, with the majority of cases the sequel of hepatitis B and C viral infection and alcoholic liver disease.[6]

In India, hepatitis B virus infection has been documented as the probable causative agent in majority of HCC patients.[7] India has been placed in the intermediate zone of prevalence by WHO for chronic hepatitis B.[8] Though we do not have a prevalence study on CHB, it is believed that, it's not less than the national average and makes Manipur a fertile ground for liver cancer. The prevalenceof HBV in intravenous drug users(IDU) in Manipur is 10.8%.[9]

The prevalence of chronic hepatitis C in India is between 0.5 and 1.5%.[10] In Manipur the prevalence is 1.52%.[11] Also, Manipur has a very high co-infection rate[12] which predisposes these co-infected person for accelerated fibrosis and cirrhosis and at risk for liver cancer.

Alcohol intake has definitely been recognized as a cause of HCC.There have been studies in the United States and in Italy which indicate that alcohol is the main cause of HCC(making up 32 to 45% of HCC).[13]

As Manipur is an endemic zone for CHC, CHB and a lot of alcoholic cirrhosis, screening for liver cancer , would make a lot of difference in management of these cases, as early detection of cancer which are usually asymptomatic can save their lives through definitive treatment. Although there is a paucity of data in Manipur, this study will still try to focus on the different aspects regarding the prevalence of hepatocellular carcinoma in patients of chronic liver disease and try to gain some useful knowledge of the problem in this part of the country.

AIM AND OBJECTIVE: To study the prevalence of HCC in patients of Chronic liver disease.

II. Methods:

The present cross sectional study was conducted from September 2017 to August 2019 at Jawaharlal Institute of Medical Sciences ,Porompat, Manipur, after approval by the institutional ethics committee.

The study population consists of new and previously diagnosed cases of Chronic liver disease of any etiology attending liver clinic and inpatients of Medicine ward in department of Medicine. All patients of Chronic liver disease of any etiology were enrolled into the study after obtaining consent for follow up. Patient with severe comorbidities such as coronary artery disease, chronic renal failure, respiratory disease or any other comorbidities and patient who refuse to follow up or give consent and patient who have allergy to iodinated contrast medium were excluded from the study.

A detailed history and physical examination was obtained from each patient. Investigations included complete blood count, liver function test, kidney function test,viral markers for hepatitis B and hepatitis C, R-antibody, random blood sugar,PT-INR and autoimmune markers. Serum alpha-fetoprotein was estimated by using cobas 6000 technique with normal level <10ng/ml.Fibroscan was assessed by vibration controlled transient elastography(VCTE). Upper GI endoscopy was done by olympus machine.

Radiological investigations:

Abdominal ultrasonogram(US) and triple- phase CT(TPCT) were done at the time of enrolment. US was done by Toshiba Xario 100. Features of chronic liver disease and characteristics of mass lesion if any were noted.TPCT was performed by Toshiba Aquilon MDCT 64 slice machine. The liver was imaged without contrast and with intravenous contrast in three(arterial, portal, venous) phases. If one of the radiological investigations showed a mass lesion, the US and TPCT were interpreted together along with serum AFP levels to arrive at a final diagnosis regarding the presence or absence of HCC.

Triphasic MRI was performed in those selected case in whom the diagnosis remained uncertained even after US and TPCT.

Follow up:

All patients who are being enrolled were followed up using 6 monthly US and TPCT annually to detect early development of any mass lesions.

Sample size:

300 patients.

Defination:

Diagnosis of cirrhosis was done on the basis on clinical, biochemical, endoscopic, imaging and fibroelastography. Biopsy was done in selected cases.

Diagnostic criteria followed for HCC was the European Association for the Study on Liver(EASL) criteria. This consisted of:

1. Either fine needle aspiration biopsy(FNAC)
2. Or any two of the following three criteria: alpha feto-protein level>300ng/ml,arterialization of the mass on TPCT and arterialization of the mass on TPMRI.

HCC staging was done by Barcelona clinic liver cancer(BCLC).

Statistical analysis was done with SPSS version 21 for window. Baseline characteristics were presented as frequency (Percentage) for all variables

III. Results:

During the study period a total of 344 patients of CLD were screened. Of which, 30 patients lost to follow up, 8 had incomplete records and 6 were excluded due to underlying comorbidities.300 patients were available for analysis out of which 45 (15%) were found to have HCC as shown in table no. 1

Table no.1. Distribution of patients by presence of HCC

HCC	No. of patients	Percentage
Yes	45	15%
No	255	85%
Total	300	100%

There were 41 males and 4 females(male: female ratio 10.25:1) with mean age of presentation 54 years. Oldest case of HCC was 85 years and youngest case was 23 years as shown in table no. 2

Table 2.Baseline characteristics of HCC

Characteristics	Values	Percentage
Males	41	91.1%
Females	4	8.9%
Male:female ratio	10.25:1	
Age mean	54 years	
Newly diagnosed cirrhosis	28	62.2%
Known case of cirrhosis	17	38%

More than half of the patients presented with symptom duration<2 months. Majorityhad anorexia 75.5% followed by ascites in 71.1% and pain abdomen in 64.4% as shownin table no. 3

Table 3.Clinical profile of HCC

Symptoms	No. of patients	Percentage
Symptom duration<2months	24	53.3%
Symptom duration>2months	21	46.7%
Abdominal pain	29	64.4%
Ascitis	32	71.1%
Anorexia	34	75.5%
Lower limb edema	24	53.3%
Hepatomegaly	35	77.8%
Constipation	2	4.4%
Upper GI bleed	12	26.7%

The most common etiologic agent was alcohol 46.7% followed by alcohol and hep. C 20% and thereafter hep C 17.8% as shown in table no. 4

Table 4. Showing etiologic studies

Etiology	No. of patients	Percentage
Alcohol	21	46.7%
Alcohol+HVC	9	20%
HBV	8	17.8%
Alcohol+HBV	4	8.9%
HCV	3	6.7%

Severe anemia was present in 15.6%, Serum bilirubin was raised in 12%, AST level of twice the upper limit of normal was seen in 64.4%, Albumin level of < 2.8 in 31.1%. Alpha fetoprotein was raised in 38.7% of the patients with value >400. Lastly, low grade varix 53.3% was the most common finding in upper GI endoscopy as shown in table 5.

Table 5.Haematological, biochemical and endoscopic profile of HCC

Parameter	No. of patients	Percentage
Haemoglobin<7gm%	7	15.6%
Total Bilirubin>2mg	12	26.7%
AST>2*ULN	29	64.4%
ALT>2*ULN	6	13.3%
Serum Albumin		
<2.8gm/dl	14	31.1%
2.8-3.5gm/dl	27	60%
>3.5gm/dl	4	8.9%

Serum Alpha fetoprotein		
<20ng/ml	1	2.2%
20-400ng/ml	27	60%
>400ng/ml	17	37.8%
Upper GI endoscopy		
High grade varices	18	40%
Low grade varices	24	53.3%
Portal hypertensive gastropathy	3	6.7%

HCC was mostly located in the right lobe 55.6% and most of the lesions are multiple 46 % with tumour size >5cms in 51.1%.Extrahepatic manifestations was seen in 31.3% of the patients as shown in table 6.

Table 6.Tumour characteristics

Parameter	No. of patients	Percentage
Distribution of HCC		
Right lobe	25	55.6%
Left lobe	2	4.4%
Bilobed	18	40%
Size of HCC		
<2cms	6	13.3%
2-5cms	16	35.6%
>5cms	23	51.1%
No. of lesions		
One	17	37.8%
Two	7	15.6%
Three or more	21	46.7%
Extrahepatic spread of HCC		
Portal vein	5	11.1%
Retroperitoneal lymphadenopathy	9	20%
Lung + bone	1	2.2%

Most of the patients belonged to child B status 66.7% and BCLC C 33.3% withperformace status 2 40% as shown in table 7.

Table 7.Child pugh score, ECOG PG and BCLC stage

Parameter	No. of patients	Percentage
PS 0	4	8.9%
PS 1	13	28.9%
PS 2	18	40%
PS ¾	10	22.2%
CP A	8	17.8%
CP B	30	66.7%
CP C	7	15.5%
BCLC A	10	22.2%
BCLC B	13	28.9%
BCLC C	15	33.3%
BCLC D	7	15.6%

IV. Discussion:

There is a paucity of data on HCC from northeastern part of India. This study aims to provide the prevalence of HCC in patients with chronic liver disease in a tertiary care hospital in Manipur, JNIMS. This study highlights some distinct regional differences in the etiological profile, clinical presentation and tumour characteristics. Out of the 300 patients studied 45 patients were found to have HCC of various etiology giving a prevalence rate of 15%. There are few studies from India regarding the prevalence of HCC. One of the autopy data published earlier by Murugavel KG et[14] al in 1998 shows 0.2 to 1.9% with a higher prevalence in South eastern India.Another study conducted by PS Mukherjee et al[15] recorded that prevalence of HCC was highest in north 5% and lowest in western and southern regions 1.1% and 1.4%. There was also another study conducted in AIIMSwere the prevalence of HCC was 35.5%.[16]Inthis study, the mean age of presentation was 54 years. This finding was similar to the study conducted in India, in which the mean age of presentation was 54.6, 55.1 and 52.1 years.[17,18,19] Male to female sex ratio was 10.25:1. Other studies from India have also reported a male preponderance[17]. The high male preponderance may be due to difference in lifestyle of males who indulge in alcohol consumption. The most common clinical manifestations was anorexia 75.5% followed by ascites 71.1%

and abdominal pain 64.4%. Anorexia 88% was the dominant symptom in one of the study from eastern India[17]. Another study from North India also reported weakness and anorexia as the main presenting feature[20]. Symptom duration was 1 to 3 months which is seen in most of the Indian studies.[17,19] In prevalence of HBV positivity in India HCC Patients ranges between 36-74%.[17] However a major difference in the etiological profile of HCC was observed in our study, in which alcohol consumption accounted for more than half of the cases of HCC.This difference in the etiological profile in this region of India can be partly explained by the difference in prevalence of HBV and HCV infection and majority around 88.6% of chronic liver disease patients are alcoholic with daily intake in cirrhotic range. There is a difference in etiology depending on regional variation in India with alcohol being the most common etiology of chronic liver disease in north eastern india as compared to other states where viral CHB or CHC virus was the most common.[21] But, our study findings were similar in accordance to study conducted by Premaletha Narayanan et al[17] were alcohol was the most common etiology seen in 57.14% of the patients. Similar findings were also seen in a study conducted by T Goetzeet al[22]. Serum alpha fetoprotein was >400 in 37.8% 0f the patients. Most of the lesions were located in the right lobe 55.6% with multiple lesions 46.7% and more than half of the patients have tumour>5 cms. Majority belonged to Child B status, BCLC stage C with performance status 2.

V. Conclusion:

In our study the prevalence of HCC in patients of chronic liver disease was 15%. The most common etiology being alcohol which being different from the rest of the Indian studies, which may be due to wide geographical variations in the etiology followed by alcohol with hepatitis C infection. Lifestyle modification is very much needed in order to reduce the burden on HCC. Public awareness regarding the direct and indirect carcinogenic effect of alcohol should be created. Since the prevalence of HCC is very high we recommend entire screening of cirrhotic patients with TPCT at the enrolement and monitor USG whole abdomen and SAFP 6 monthly.

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References:

[1]. Liovet JM, Burroughs A, Bruix J. Hepatocellular carcinoma. Lancet 2003;362;1907-17.
[2]. Wands JR, Blum HE. Primary Hepatocellular Carcinoma. N Engl J 1991;325(10):729-31.
[3]. Bray F, Colomet M, Mery L, Pineros M, Znaor A,Zanetti R, et al. Cancer Incidence in Five Continents, Vol. XI. International Agency for Research on Cancer, 2017. Available at http://ci5.iarc.fr/CI5-XI/Default.aspx/. Accessed Juy 28,2019.
[4]. Jayant K, Rao RS, Nene BM, Dale PS, Thorat RV, Khan FY. Rural cancer trends in worldwide epidemiology, risk factors, diagnosis and therapeutics. Hepat Med 2012;4:19-37.
[5]. Dikshit R, Gupta PC, Ramasundarahettige C, Galalakshmi V, Aleksandrowicz L, Badwe R, et al. Cancermortality in India: a nationally representative survey. Lancet 2012;365(12):1118-27.
[6]. Tinkle CL, Haas-Kogan D. Hepatocellular carcinoma: natural history, current management and emerging tools.Biologics 2012;6:207-19.
[7]. Acharya SK. Epidemiology of hepatocellular carcinoma in India. J ClinExpHepatol 2014;4(Supppl3):27-33.
[8]. Bhaumik P. Epidemiology of Viral Hepatitis and Liver Disease in India. Eurosian J Hepatogastroenterol 2015;5(1):34-36.
[9]. Devi KS, Singh NB, Mara J, Singh TB, Sigh YM. Seroprevalence of hepatitis virus and hepatits C virus among hepatic disorders and injecting drug users in Manipur- A preliminary report. Indian J Med Microbiol. 2004;22(2):136-37.
[10]. Puri P, Anand AC, Saraswat VA, Acharya SK, Dhiman RK, Aggarwal R, et al. Consessus statement of HCV Task Force of Indian National Association for the study of the Liver(INASAL). Part 1: Status report of HCV infection in India. J ClinExpHepal 2014;4:106-16.
[11]. Lalhriatpuii ST, Sharma AB, Singh AM, Singh KR, Devi KM, Khetrimayum P. Hepatitis C virus Seroprevalence among Blood Donors in Tertiary Hospital in Manipur. Inter J Innov RES Dev 2014;3(1):190-92.
[12]. Kermode M, Nuken A, Medhi GK, Akoijam BS, Sharma HU, Mahanta J. Indian J Med Res 2016;143(3):348-56.
[13]. Kew MC. Hepatocellular carcinoma: epidemiology and risk factors. J Hepatocell Carcinoma 2014;1:115-25.
[14]. Murugavel KG, Naranatt PP, Shanker EM, Mathews S, Raghuram K, Rajasambandam P, et al. Prevalence of aflatoxin B1 in liver biopsies of proven hepatocellular carcinoma in India determined by an in-house immunoperoxidase test. J Med Microbiol 2007;569110:1455-59.
[15]. Mukherjee PS, Vishnubhalta S, Amarpurkar DN, Das K, Sood A, Chawla YK, et al. Etiology and mode of presentation of chronic liver diseases in India: A multicentric study. PLoS One (Serial online).2017;12(10):e0187033. Availablefrom:https://www.ncbi.nlm.nih.gov/pubmed. Assessed July 12,2019.
[16]. Paul SB, Sreenivas V, Gulati MS, Madan K, Gupta AK, Mukhopadhyay S, et al. Incidence of hepatocellular carcinoma among Indian patientswith cirrhosis of liver: an experience from a tertiary care centre in northern India. Indian J Gastroenterol2007;(6):274-78.
[17]. Narayanan P, Ashraf AAS, Phillip A. Hepatocellular Carcinoma Profile in Tertiary Care Centre. J. Evid. Based Med. Healthc 2017;4(92):5564-66.
[18]. Nagaich N, Sharma R, Katiyar P, Nagaich Y, Sharma I, Nijihawan S. Spectrum of Hepatocellular Carcinoma: Study from a Tertiary Care Centre. J Cancer PrevCurrRes(Serial online). 2016;4(6):00141. Available from: http://medcraveonline.com/JCPCR/JCPCR-04-00141. Assessed July 25,2019.

[19]. Nandennavar MI, Karpurmath SV, Mandakalatur G, Prasad AE. Clinical profile of hepatocellular carcinoma and experience with sorafenib from a tertiary care centre in Southern India. Int J Med SCI 2017;5(2):379-83.
[20]. Kumar R, Saraswat MK, Sharma BC, Sakhuja P, Sarin SK. Characteristics of hepatocellular carcinoma in India: a retrospective analysis of 191 cases. QJM 2008;101(6):479-85.
[21]. Mukherjee S, Dhar K, Dtta S, Mukerjee AK. Hepatocellular Carcinoma in eastern India, a detail analyticalreport from a tertiary care hospital 2015;1(11):69-7.
[22]. Goetze T, Schuette K, Bornschein J, Kipper M, Mohnike K, Malfertheiner P, et al. Epidemiology and clinical characterizationof HCC in a tertiary centre. J. Evid. Based Med. Healthc2017;4(92):5564-66.

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