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Original Research Article

Study on the clinical and etiological profile of hepatocellular carcinoma in a tertiary care centre in south India: a prospective observational study

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) is the most common primary malignant tumour of the liver occurring in patients with underlying chronic liver disease with high morbidity and mortality with various clinical presentations. This study was conducted to analyse the clinical and etiological profiles of HCC patients in tertiary care liver transplant centre.
Methods: This prospective cross-sectional study was conducted in the department of medical gastroenterology, government Stanley medical college, for one year, with a sample size of 75 patients. Clinical details, demography, laboratory parameters and imaging findings are entered in pre-structured proforma.
Results: Among 75 patients, 69 were males (92%). The mean age of patients was 45.5±10 years. Abdominal pain in 56 (80%) and abdominal distension in 31 patients (44.2%%) was the most common symptom, with underlying cirrhosis in a majority (70.6%). The etiologies include hepatitis B in 25 (33.3%), ethanol in 20 (26.6%), hepatitis C in 8 (10.6%), NAFLD in 8 (10.6%) and cryptogenic in 11 (14.6%) patients. AFP levels >400 ng/ml were observed in 37 cases (49.3%) with a mean value of 6129 ng/ml with normal in 12 (16%) cases. On imaging, multifocal lesions were seen in 24(32%) patients and vascular invasion in 30 (40%) patients. Most of the patients belong to BCLC stage C (54.6%), followed by stage B (30.6%) and stage A (12%) and two patients (2.6%) in stage D. Patients were managed according to institutional protocol with either hepatectomy, TACE, systemic chemotherapy or combination of these modalities.
Conclusions: In our study, HBV (33%) and alcohol (27%) were the most common etiologies, with the majority having underlying cirrhosis.

Keywords: Hepatocellular, Carcinoma, Hepatitis B virus, Alcohol

INTRODUCTION

Hepatocellular carcinoma (HCC) is a primary malignant tumour of the liver that occurs predominantly in patients with underlying chronic liver disease and cirrhosis. According to WHO, it is the fifth most common cancer in the world and the second leading cause of cancer-related mortality.[1] In India, the incidence of HCC in cirrhosis is 1.6% per year and the age of presentation varies from 40 to 70 years. More than 80% of HCC patients have underlying cirrhosis.[2] Thus, any agent leading to chronic liver damage and ultimately causing cirrhosis should be considered a risk factor for HCC.

The major risk factors for HCC include hepatitis B virus (HBV), hepatitis C virus (HCV), alcohol, NAFLD, hemochromatosis, Wilson disease, primary biliary cholangitis and exposure to aflatoxins.[3] The aetiology of HCC varies in different geographical areas. For example, in China, Southeast Asia and Sub-Saharan Africa, hepatitis B is the most common cause. On the other hand, most cases in Japan, Europe and North America are due to chronic hepatitis C. The highest incidence of HCC is in

Asia due to the endemic prevalence of HBV and HCV infections, responsible for 76% of cases worldwide.[4]

The clinical presentation of HCC has significantly evolved over the past few decades. The common presentations include right upper quadrant pain, constitutional symptoms like weight loss, anorexia and malaise, jaundice, ascites, variceal bleeding and hepatic encephalopathy. Rarely paraneoplastic syndromes like diarrhoea, hypoglycemia, hypercalcemia and thrombophlebitis can be a presentation.[5] The diagnosis of HCC is often established based on non-invasive imaging without biopsy confirmation. Even for biopsy, imaging is usually required for guidance. In newly diagnosed patients with HCC, laboratory tests are done to determine the severity of underlying liver disease and to elucidate the aetiology of liver disease.[6] The data on HCC patients in India is important for early detection and management. But there is limited data on the clinical and etiological profile of HCC in the Indian subcontinent. Most of the studies conducted on the profile of HCC are from tertiary care centres with a small sample size. Our hospital being a tertiary care centre and centre for liver transplantation, this prospective cross-sectional study was conducted to study the clinical and etiological profile of HCC patients.

METHODS

This is a prospective cross-sectional study conducted in the department of medical gastroenterology, government Stanley medical college, a tertiary care centre in Chennai, for one year, from January 2021 to December 2021.

Study population

Convenient sample size 75 patients diagnosed with hepatocellular carcinoma by the radiological or pathological analysis were included in the study. Each patient was enquired about with detailed history and subjected to thorough clinical examination. In addition, data on demography, routine lab investigations and radiological imaging were collected. Ethical committee approval has been obtained.

Exclusion criteria

Patients diagnosed with secondary liver and benign focal lesions were excluded from the study.

Data were presented as mean, standard deviation, frequency and percentage. Categorical variables were compared using Pearson chi-square test. Significance was defined by P values less than 0.05 using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Science Inc., Chicago, IL).

RESULTS

Among the 75 patients included in the study, 69 were males (92%), and 6 were females (8%), with an M: F ratio of 11:1. Median age of the patients was 45.5±10 years. Considering the demographic data, around 37 patients (49.3%) were from rural parts of Tamil Nadu, followed by 22 patients (29.3%) from urban areas, predominantly in various parts of Chennai. About 16 patients (21.3%) were from the suburban area. This suggests that our centre being a tertiary care centre, patients from various parts of Tamil Nadu are referred for treatment.

The predominant complaint among HCC patients was abdominal pain/discomfort in 60 patients (80%) and abdominal distension in 35(46.6%) patients, followed by jaundice in p patients (12%). Anorexia and weight loss were invariably present in most cases (86%). The mean symptom duration before the diagnosis of HCC was 1.5 months.

Around 53 patients (70.6%) had underlying cirrhosis. About 32 patients (42.6%) had decompensation from clinically detectable ascites. On clinical examination, around 35 patients (46.6%) had palpable liver (hepatomegaly) with an average life span of 17 cm.

The aetiology includes hepatitis B in 25 (33.3%), ethanol in 20 (26.6%), hepatitis C in 8(10.6%), NAFLD in 8 (10.6%) and cryptogenic in 11 (14.6%), patients, HBV plus alcohol in 2 (2.6%) and HCV plus alcohol in 1 case (1.3%).

AFP levels >400 ng/ml were observed in 37 cases (49.3%) with a mean value of 6129 ng/ml and were normal (up to 7 ng/ml) in 12(16%) cases. The p value was not significant when analysing the correlation of AFP levels with the presence of multifocal lesions. In addition, the correlation of AFP levels with various aetiology for HCC was analysed. Except in patients with cryptogenic HCC ($p<0.001$), the p value was not statistically significant.

Table 1: Baseline characteristics and demographic profile.

Parameters		N	Frequency (%)
Gender	Male	69	92
	Female	6	8
Age (Years)	Mean ± SD	45.5±10	
	Range	28-80 years	
Demography	Urban	22	29.30
	Sub-urban	16	21.30
	Rural	37	49.30
Duration of symptoms before HCC diagnosis	Mean	1.5 months	
Cirrhotic liver		53	70.60
Non-cirrhotic liver		22	29.40

Table 2: Clinical profile of patients.

Parameters	N	Frequency (%)
Abdominal pain/discomfort	60	80
Abdominal distension	35	46.6
Jaundice	9	12
Anorexia and weight loss	65	86
Signs		
Ascites	32	42.6
Icterus	14	18.6
Hepatomegaly	35	46.6
Splenomegaly	11	14.6

Table 4: Tumor characteristics.

Parameters		N	Frequency (%)
AFP levels (ng/ml)	<7	12	16
	7-400	26	34.60
	>400	37	49.30
Number of lesions	Single	51	68
	Multifocal	24	32
Lobar involvement	Right lobe	48	64
	Left lobe	12	16
	Both lobes	15	20
Typical vascular pattern	Present	62	82.60
	Absent	13	17.40
Vascular invasion	Portal vein	22	29.30
	Hepatic vein	5	6.60
	HV + IVC	3	4
CTP score	CTP-A	34	45.30
	CTP-B	25	33.30
	CTP-C	16	21.30
BCLC staging	A	9	12
	B	23	30.60
	C	41	54.60
	D	2	2.60

Table 5: Correlation of AFP levels with aetiology of HCC.

Etiology	Frequency (%)	P value
HBV	25 (33.3)	0.416
Alcohol	20 (26.6)	0.180
Cryptogenic	11 (14.6)	<0.0001
HCV	8 (10.6)	0.570
NAFLD	8 (10.6)	0.552
HBV+ alcohol	2 (2.6)	0.147
HCV + alcohol	1 (1.3)	0.578

Liver lobe involvement was assessed using imaging. The majority of HCC lesions are present in the right lobe in 48 patients (64%), left lobe involvement in 12 patients (16%) and involvement of both lobes in 15 patients (20%). Multifocal lesions were seen in 24 patients (32%). On imaging, the typical vascular patterns of arterial phase enhancement and venous phase washout were seen in 62 patients (82.6%). Tumoral macrovascular invasion into IVC, hepatic vein and portal vein and its branches were seen in 30 patients (40%).

The child-Turcotte-Pugh score was calculated in all the patients, and 34 patients (45.3%) belonged to CTP class A, 25 patients (33.3%) to CTP class B and 16 patients (21.3%) to CTP class C. On disease staging, using the BCLC system, 41 patients (54.6%) were in BCLC-C, 23 patients (30.6%) in BCLC-B, 9 patients (12%) were in BCLC-A and 2 patients (2.6%) in BCLC-D.

DISCUSSION

This is a prospective observational study conducted in a tertiary care centre in Southern India to study the clinical and etiological profiles of HCC patients. The incidence of HCC increases with age, and the development of HCC is usually rare before the age of 40 years. However, the incidence of HCC by age depends upon the etiological factor and geographic pattern.[7] Our study's median age of patients was 45.5±10 years, with a peak incidence between 50-70 years. This is similar to most studies from the West and India. In addition, the population-based data show a male predominance with a male-to-female ratio of 11:1.

In our study, patients with HBV-related HCC have a lower mean age than other etiologies, consistent with the results of various studies.[8,9] In contrast to HBV-related HCC, HCV-related HCC is seen in the older age group in our study, which is similar to a study from Japan.[10]

In our study, HBV is the most common aetiology responsible for 25 cases (33.3%), consistent with other studies from the Indian subcontinent.[11-13] The aetiology was considered unknown/cryptogenic if the etiological workup was negative for HBV, HCV, alcohol or any etiologic factor, namely metabolic liver disease or Budd-Chiari syndrome. Three (4%) patients had more than one etiological factor, similar to most of the previous studies (9.5-16.5%) in our study. The 70-90% of patients with HCC had underlying cirrhosis in most of the Indian studies similar to our study, where 53 patients (70.6%) had underlying cirrhosis.[14]

The serum AFP is not a good screening test for diagnosis and surveillance of HCC. Measurement of AFP has been used for early diagnosis but with sometimes disappointing results. Its sensitivity ranges from 39-64%, specificity 76-91% and positive predictive value of 9-32%.[15] In one of the studies, despite a cut-off of 100 ng/ml, the sensitivity and specificity of AFP were 21% and 93%. In our study, 37 patients (49.3%) had more than 400 ng/ml AFP and the median AFP value was 6129 ng/ml.

AFP levels have been shown to correlate with tumour size and volume at the time of diagnosis. In a study from Thailand in HCC patients, AFP levels > 400 ng/ml had large tumour size, bilobar involvement, vascular invasion, and decreased survival.[16] In our study, the correlation of

AFP levels with multifocal lesions was not significant. On analysing the AFP levels for the aetiology of HCC, except in cryptogenic HCC, the p value was insignificant.

Most of the patients in our study presented in the advanced stage with large or multicentric tumours where curative therapy could not be offered. The average size of the lesion in our study was 6.2±2.4 cm compared to a previous study by Sarin et al and Butt et al where the average size of the lesion was 6.8±3.4 cm and 7.8±8.1 cm, respectively.[11,16]

We adopted Barcelona clinic liver cancer (BCLC) staging to stage the disease, and patients were managed accordingly. Most patients belonged to BCLC stage C (54.6%), followed by stage B (30.6%) in our study. Triple-phase CT was the imaging modality for diagnosing and looking for tumour characteristics. Most of our patients (68%) had a single lesion involving mainly the right lobe. Multifocal HCC was seen in 24(32%) patients, which is almost similar to the study by Sarin et al (36%) and Paul et al (31%).[11,17] In most studies, vascular invasion is common in HCC, ranging from 10 to 50 percent. Our study showed vascular invasion in the form of IVC, portal vein, or hepatic vein thrombosis is seen in 30 patients (40%), similar to Paul et al, where PVT was reported in 40% of cases.[17]

A rare tumour thrombus involving the portal vein, IVC and extending into the right atrium with pulmonary metastasis was seen in one of our patients treated with oral Sorafenib. Hemoperitoneum due to tumour rupture occurred in three patients (4.8%) in our study who were managed with hepatic resection in two and TACE followed by sorafenib in one.

Limitations

This is a single centre study with relatively small sample size. Involvement of multiple centres with large sample size will help to accurately represent the clinical and etiological profile of HCC patients in our population. Our study lacks long-term follow up of cases, because long-term follow up might help to form surveillance protocols.

CONCLUSION

To conclude, CHB is the most common aetiology for HCC, with underlying cirrhosis in the majority, presenting in the advanced stage. Most of the patients had a single lesion, and vascular invasion was seen in 40%. The mean AFP was 6129 ng/ml. This study shows universal vaccination against Hepatitis B infection will be a single effective and important intervention to prevent HBV-related HCC, apart from the regular screening of patients with underlying cirrhosis, with imaging and tumour markers.

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