

Research Article

# To study the demographic profile of HCC patients and the pattern of clinical characteristics in a tertiary care center of north western India

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## Abstract

Hepatocellular carcinoma (HCC) is a prevalent malignancy globally and the fifth most common cancer worldwide. This retrospective study, spanning six years, explores the shifting etiological patterns of HCC in Northwestern India, particularly influenced by factors like Hepatitis B and C endemics, alcohol consumption, and vaccination programs. Data from 164 HCC patients reveal a significant shift, with Hepatitis C surpassing Hepatitis B as the primary etiological factor. The study highlights the distinctive HCC profile in Northwestern India, emphasizing the imperative to address HCV as a silent precursor to HCC and the need for enhanced surveillance and intervention strategies. The findings underscore the significance of controlling alcohol abuse, managing cirrhosis complications, and the urgency for improved diagnostic markers beyond AFP. The study prompts a reevaluation of vaccination interventions and advocates for heightened screening measures to detect and mitigate HCV-related HCC at earlier stages.

**Keywords:** Hepatocellular carcinoma, Etiology, Northwestern India, Hepatitis C, Retrospective Study

## Introduction

Hepatocellular carcinoma (HCC) is one of the most prevalent malignant tumors worldwide and the fifth most common cancer in the world. In nations like India, where endemics of Hepatitis B and C it is extremely common in certain parts, the risk of HCC is particularly high. Also, other risk factors like alcohol consumption are on the rise, and with the vaccination program for Hepatitis B, the demographic profile of etiology is having a shift, especially in the North West region of India<sup>1</sup>.

From a pattern of being Hepatitis B endemic zone and being the most common cause of chronic liver disease in India, Hepatitis C being a hidden factor and presenting as HCC as the only symptomatic presentation is turning heads. The profile of the Northwestern region matches that of the West despite the lifestyle pattern being very different. <sup>2</sup>.

In this study, a retrospective data evaluation for the past six years was studied, and an entirely shifting pattern profile compared to the earlier Indian data was noted. This was to establish the difference in the etiological factor of HCC compared to the rest of the country due to local factors causing the change.

## Methods

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All patients of HCC presenting to the Oncology OPD and IPD of Sri Guru Ram Das Rotary Cancer Hospital, Sri Amritsar, under SRDUHS, Sri Amritsar, a tertiary care Centre in Punjab, Northwestern India, and caters to populations coming from J&K, Punjab, Himachal Pradesh & Haryana; between 2017 – 2022 were included in the study.

### *Study Design*

Patients already diagnosed with HCC and presenting to the Oncology OPD for treatment and those who were diagnosed at our center between 2017-2022 were included in our study, and the data was collected retrospectively from the case records.

### *Patient Evaluation*

The patient was subjected to clinical evaluation, including a detailed history, to list out the presenting signs and symptoms and also make out any causation from the history pattern like alcohol, blood transfusion, IV drug abuse, or other means of unsafe needle use in the periphery.

Laboratory Investigation included routine evaluation -Complete blood counts, liver function tests, renal function tests, and viral markers for HBV and HCV. Serum Alpha-feto-protein (AFP) was estimated using a particle enzyme immunoassay.

Hepatitis viral markers, including HBsAg, IgM Anti HBc, HBV Quantitative DNA, and HCV RNA, were first detected using qualitative PCR, and if they were positive, they were quantitated.

Radiology workup included an Ultrasound abdomen, a Triple Phase CT abdomen was done for all patients, and a PET CT scan was done to ascertain the extent of the disease before instituting therapy.

Diagnosis of cirrhosis was made on the basis of clinical, biochemical, and endoscopic findings. HBV cirrhosis was diagnosed when detectable HBsAg in serum was present. HCV cirrhosis was diagnosed when detectable anti-HCV, HCV RNA, or both were present in serum. Alcoholic cirrhosis was labeled when the patient had a history of alcohol consumption of more than 80 g/day for more than five years. The severity of cirrhosis was graded based on the Child-Pugh classification.

Diagnostic criteria for HCC were any of the following: AFP more than 500 ng/ml or hypervascular liver mass on contrast-enhanced CT abdomen Triple phase or Fine needle aspiration cytology (FNAC). As per the modified European Association for Study of Liver, criteria were followed, which consisted of either FNAC or any 2 of the following: AFP more than 500 ng/ml or arterialization of the mass on TPCT or MRI.

### *Treatment*

Various types of treatment therapies are available at our center. Treatments were given, keeping into account factors like the stage of the disease, the underlying presence of cirrhosis, and its severity. Therefore, findings on TPCT/PET CT indicating tumor burden, portal vein involvement, presence of extra-hepatic disease, or distant metastasis were recorded. The child's score and the PST score of the patient were also noted, and the treatment was then finally decided.

Stage A patients were offered surgery if their liver function was good with no clinically relevant portal hypertension. If not, then surgery could not be undertaken, and instead, local ablative therapies were performed.

Local ablative therapies were radiofrequency ablation and were undertaken at our center. RFA was done in those patients who had HCC less than 5 cm and less than 5 in number. Also, Trans Arterial Chemo Embolization was performed.

Surgical Options- included Lobectomy / Hepatectomy depending upon the extent of the lesion.

Oral Chemotherapy options included sorafenib.

Add On Therapy-

All patients with cirrhosis who had evidence of high-risk varices on endoscopy underwent primary prophylaxis with endoscopic variceal banding. Patients who had HBV-related HCC, along with markers of active viral replication, were given antiviral treatment. The other complications of chronic liver disease and HCC were managed with conventional treatment.

### Results

A total of 164 patients with HCC were registered in the liver clinic. The mean age at presentation was  $58 \pm 14.4$  years (range 18–88 years), and 131 (80%) of them were males (Figure 1). Abdominal pain was the predominant symptom in the right upper quadrant or epigastric in location, presenting in 67% of the patients. Patients presenting with complaints of abdominal distention were less than 44%, and about 14% presented with Ascites. Not all patients with ascites complained of abdominal pain, and only half of them complained of associated abdominal pain. Patients presenting with weight loss stood at 21%.

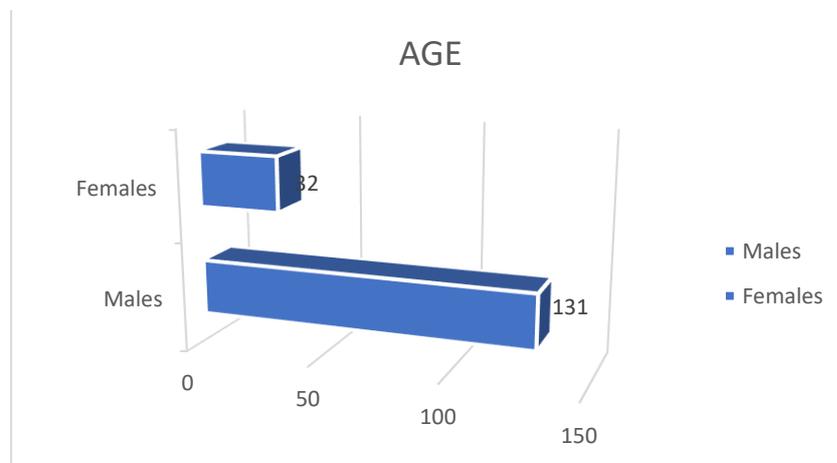


Figure 4 Patients gender

History of episodes of acute hepatitis in 27%, and those with chronic hepatitis stood at 58%. History of significant intake of alcohol was present in 14% with a mean intake of 92 g/day and median duration of 17.5 years (range 0–40).

The association with serum biochemical markers and Child-Pugh score is detailed in the table below.

Table 1. Liver function tests, Child's class (n=164)

PARAMETER	Median(range)
Serum Bilirubin;mg/dl	1.6(0.2-18.11)
Serum Albumin,g/dl	2.8(1.08-4.2)
AST,U/l	76.4(18-466)
ALT,U/l	64.3(11-428)
Child Class A	22(17.7%)
Child Class B	82(66.12%)
Child Class C	20(16.1%)

### *Etiology*

HCV was the most common etiological factor and was detected in 44.6 % of the patients, out of which a significant number was associated with a history of IV drug abuse or a history of blood transfusion in the past. Compared to the Pan India data pattern, where HBV was the predominant factor, HCV was predominant as an etiology in this part of the country (Figure 2).

The Spread of HCV was also related to the past history of blood transfusion and the use of unsafe needles by peripheral practitioners. Alcohol association was present in 16.2% of the patients. The mean age of presentation in HBV patients was significantly lower than HCV-related HCC.

Table 2. Etiological factors associated with HCC (n=164)

ETIOLOGY	n(%)
HCV	44.6%
HBV	32.4%
Alcohol	16.2%
Unknown	6.8%

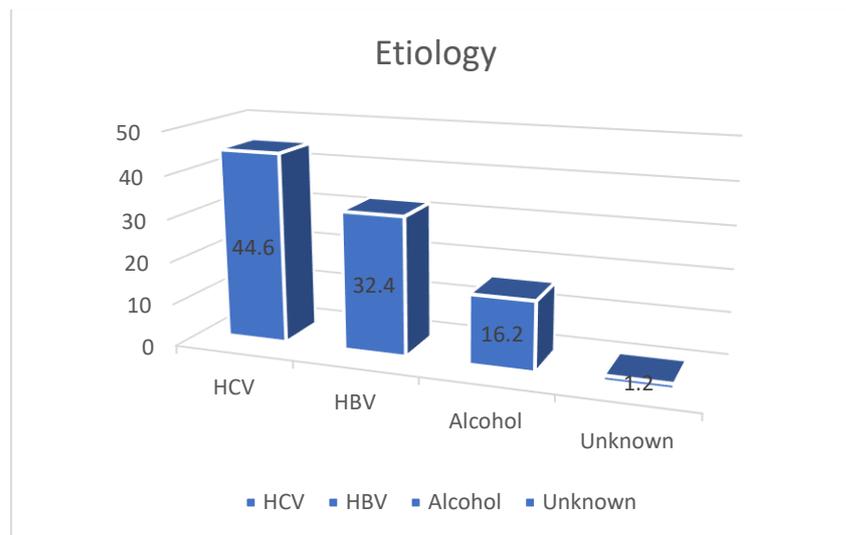


Figure 5 HCC etiological factors in the study

### Tumor Characteristics

In 124 (76%) patients, the largest/ dominant lesion was more than 3.8 cm in size. There was a single lesion identified in 55 patients (34%) and > 5 lesions in 29 (18%). Portal vein involvement as thrombosis partial or complete was identified on imaging in 75 patients (46%). Extra-hepatic metastasis to peri-pancreatic nodes, celiac nodes, inferior vena cava thrombosis, and lungs were seen in 27 (17%) of the patients. The median serum AFP value in the 144 patients in whom it was available was 324 ng/ml (range 1.82– 48,552 ng/ml).

### Treatment pattern

Patient were given all options as per their clinical profile and prognosis. The treatment option sought was biased because of cost constraints and phobia related to surgery and that attached to cancer. A total of 17 patients opted for Radiofrequency Ablation. 6 patients underwent TACE, and 2 opted for Open surgery for liver lobe resection. Rest patients choose Oral chemotherapy regimens, even if they qualified for minimally invasive surgery procedures or surgery was given an option.

## Discussion

This comprehensive study was carried out to understand the profile of patients pertaining to HCC, especially in the North Western region, which is plagued by different risk factors due to the border area profile and peripheral needle abuse profile in the form of drug abuse or use by the quacks.

It was pertinent to see how the etiological factor profile was different from the pattern seen in the rest of the country. Also, the study found that HCC was the final outcome of a silent disease hidden in the form of HCV, and neither any pattern for detecting these silent cases is one to detect and plug the risk factor at an earlier time.

Almost all our patients about (86%) had underlying cirrhosis, and different from the usual profile pattern in the rest of the Indian subcontinent, Hepatitis C was the predominant risk factor. Hepatitis B was seen as the next-in-line etiological factor, and alcohol abuse followed it. The pattern of the etiological factors resembled the West, even though the socio-economic and lifestyle patterns of the two vary a lot.

The mean age of presentation in our study was 58.8, which is more than the age in the earlier series report. The increase in the mean age could be attributed to HCV being the main etiological factor in HBV-related HCC patients in our study presented a decade earlier when compared to HCV-infected HCC patients, the pattern which resembled the earlier studies and with studies describing HBV as the main etiological factor<sup>3</sup>.

HBV also showed a decrease due to increased vaccination patterns of Hepatitis B. The study followed the strong Male preponderance as in earlier studies.

Serum AFP level 500 ng/ml was taken as a conventional diagnostic level for HCC. In this study, AFP was elevated in 84% of patients but was above the diagnostic range in only 44% of patients. Low serum levels may be either because of the smaller size of a tumor or due to the differentiation of masses that do not produce high AFP<sup>4</sup>. The level of AFP did not show any correlation to the number of lesions/ the etiology of HCC/or the presence of malignant spread.

In conclusion, HCV is the most common cause of HCC in this part of the country, followed by HBV infection. Prevention of these etiologic agents is the only realistic means of reducing the morbidity and mortality of HCC. Also, alcohol pattern abuse needs control. The survival of these patients can be improved by aggressively treating HCC complications of cirrhosis and by controlling etiological factors. Serum AFP is not a very sensitive marker for diagnosis or surveillance, and there is an urgent need for better markers and imaging to diagnose smaller tumors. The way vaccine intervention has shifted the etiology profile away from hepatitis B and the factors leading to the spread of hepatitis C need to be looked into. Also, screening for the same at a more significant level could plug the development at an earlier stage.

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