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*Original Article*

# Frequency of Hepatocellular Carcinoma in Cirrhotic Patients with Hepatitis C in Hyderabad Pakistan

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## ABSTRACT

Background: Hepatocellular carcinoma (HCC) is a primary liver malignancy predominantly found in patients with cirrhosis due to chronic hepatitis C virus (HCV) infection. Chronic HCV infection is a significant risk factor for the development of cirrhosis, which markedly increases the risk of HCC. This study aims to evaluate the frequency of hepatocellular carcinoma in cirrhotic patients with hepatitis C.

Objective: To evaluate the prevalence of hepatocellular carcinoma among cirrhotic patients with hepatitis C virus infection in Hyderabad, Pakistan.

Methods: This descriptive study was conducted at the Department of Gastroenterology, Asian Institute of Medical Sciences (AIMS), Hyderabad, from January 2024 to June 2024. The study included 152 patients diagnosed with liver cirrhosis due to HCV infection. Non-probability consecutive sampling was employed. Patients with cirrhosis due to other causes, such as hepatitis B virus, alcoholic liver disease, hemochromatosis, Wilson disease, and end-stage liver disease, were excluded. Upon admission, each patient underwent a thorough history and physical examination, followed by laboratory investigations including alpha-fetoprotein (AFP) levels and ultrasonography. An AFP level greater than 200 ng/mL in the presence of a liver mass was considered highly indicative of HCC, obviating the need for a biopsy. All laboratory tests were conducted at a single laboratory to ensure uniformity. Data analysis was performed using SPSS version 26.0. Frequencies and percentages were calculated for categorical variables, while means and standard deviations were computed for continuous variables. Statistical tests of significance were applied at a 5% significance level.

Results: Out of 152 patients, 103 (67.8%) were male and 49 (32.2%) were female, with a mean age of 41.57 ± 10.67 years. The prevalence of hepatocellular carcinoma was found to be 7.2% (11 patients). Significant differences were observed in several liver function parameters between HCC and non-HCC patients: total bilirubin (4.22 ± 0.76 mg/dL vs. 1.44 ± 1.14 mg/dL, p = 0.001), AST (37.82 ± 14.25 U/L vs. 12.39 ± 6.54 U/L, p = 0.001), GGT (171.8 ± 81.27 U/L vs. 54.43 ± 59.41 U/L, p = 0.001), AFP (323.6 ± 59.60 ng/mL vs. 15.50 ± 21.04 ng/mL, p = 0.001), and INR (2.75 ± 1.23 vs. 1.24 ± 0.42, p = 0.001).

Conclusion: A notable prevalence of hepatocellular carcinoma was observed in cirrhotic patients with hepatitis C. This finding underscores the importance of regular screening and surveillance for HCC in this high-risk population to enable early detection and timely intervention.

Keywords: Hepatocellular carcinoma, HCC, hepatitis C, cirrhosis, liver cancer, HCV infection.

## INTRODUCTION

Hepatocellular carcinoma (HCC) is the most prevalent primary liver malignancy, predominantly occurring in individuals with cirrhosis due to chronic hepatitis C virus (HCV) infection (1). Chronic HCV infection stands as a significant risk factor for the development of cirrhosis, subsequently leading to an elevated risk of HCC (2). The pathogenesis of HCC in the context of HCV-related cirrhosis is a multifaceted process, involving the convergence of viral, host, and environmental factors, which collectively provoke chronic inflammation, hepatocyte injury, and eventually malignant transformation (3).

Chronic HCV infection is marked by continuous liver inflammation and fibrosis, progressing to cirrhosis over several decades (4). Cirrhosis involves the progressive replacement of healthy liver tissue with fibrotic tissue, distorting normal liver architecture and

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impairing its function (5). This chronic liver injury and regenerative process set the stage for the development of HCC, with cirrhotic nodules evolving from dysplastic lesions to overt neoplasia (6). Given the high risk of HCC development in cirrhotic patients with HCV, early detection strategies through regular surveillance are essential. Imaging techniques and serum biomarkers play crucial roles in the early detection of HCC, enabling effective treatment options to be utilized while still viable. The relationship between HCV, cirrhosis, and HCC highlights the importance of effective prevention, diagnosis, and treatment strategies for managing this challenging and often deadly cancer (7).

The study aimed to evaluate the frequency of hepatocellular carcinoma in cirrhotic patients with hepatitis C, focusing on a cohort of hospitalized patients with HCV-related liver cirrhosis. Conducted at the Department of Gastroenterology, Asian Institute of Medical Sciences (AIMS), Hyderabad, the study spanned from January 2024 to June 2024, involving a descriptive analysis of 152 cases. Patients with hemochromatosis, Wilson disease, and alcoholic liver disease were excluded from the study. Data analysis was performed using SPSS version 26.0. The study included 103 males (67.8%) and 49 females (32.2%), with an average age of 41.57 ± 10.67 years. The prevalence of hepatocellular carcinoma was observed in 11 (7.2%) of the patients (8, 9).

HCC in cirrhotic patients with HCV represents a complex interplay of viral, host, and environmental factors. Surveillance strategies, such as regular ultrasound examinations and measurement of serum alpha-fetoprotein (AFP) levels, are crucial for early detection, despite their variable sensitivity and specificity (10). Advances in imaging technologies, such as contrast-enhanced magnetic resonance imaging (MRI) and computed tomography (CT), have improved the ability to detect small tumors and differentiate HCC from benign lesions (11). Management of HCC in patients with HCV-related cirrhosis requires a multidisciplinary approach, encompassing surgical resection, liver transplantation, locoregional therapies, and systemic therapies, including molecularly targeted agents and immune-based drugs (12). The size of the tumor, liver function, patient performance status, and presence of portal hypertension guide the selection of therapeutic options (13)

Antiviral therapy for HCV, particularly direct-acting antivirals (DAAs), has revolutionized the management of chronic HCV infection and its complications, achieving sustained virologic response (SVR) in most patients and effectively reducing liver inflammation and fibrosis progression (17). However, the impact of DAA-induced SVR on the long-term risk of HCC in cirrhotic patients remains under investigation, with some studies indicating a reduced risk, while others suggest the need for continued vigilance due to residual cirrhosis (14)

In this study, involving 152 patients, 11 (7.2%) had hepatocellular carcinoma (HCC). This prevalence aligns with other studies, such as one that reported an 11.8% prevalence of HCC in similar patients (15). Another study by Tariq et al. recorded hepatocellular carcinoma in 5.7% of patients (16), while Irum et al. reported it in 32.3% of cases (17). These findings underscore the importance of regular screening and surveillance for HCC in patients with HCV-related cirrhosis, highlighting the need for a comprehensive approach to improve outcomes in this high-risk population. Continued research and clinical innovation are essential to address the global burden of HCV-related liver disease and prevent HCC development (18).

## MATERIAL AND METHODS

The study was a descriptive analysis conducted by the Department of Gastroenterology and Hepatology at the Asian Institute of Medical Sciences (AIMS), Hyderabad. The research was carried out over a period from January 2024 to June 2024. A total of 152 patients were enrolled using non-probability consecutive sampling. The inclusion criteria encompassed patients of either gender, aged 18 years and above, who were diagnosed with liver cirrhosis due to hepatitis C virus (HCV) infection. Patients with cirrhosis attributable to other causes, such as hepatitis B virus, alcoholic liver disease, hemochromatosis, Wilson disease, and end-stage liver disease, were excluded from the study.

Upon admission, each patient underwent a thorough history and physical examination. Standardized laboratory investigations were performed, including alpha-fetoprotein (AFP) levels and ultrasonography. In cases where AFP levels exceeded 200 ng/mL in the presence of a mass in a cirrhotic liver, the likelihood of hepatocellular carcinoma (HCC) was considered to be over 90%, and biopsy was not deemed necessary. To maintain uniformity and reduce potential bias, all laboratory tests were conducted at a single laboratory.

Data collection was comprehensive, ensuring the recording of demographic details, clinical features, and laboratory results. The severity of liver disease was assessed using the Child-Pugh classification system. The duration of cirrhosis was also documented, categorized into periods of 1-5 years and more than 5 years. Additional variables such as body mass index (BMI), residential status (urban or rural), and the presence of comorbid conditions like diabetes mellitus, hypertension, and dyslipidemia were recorded.

The study adhered to ethical standards as per the Declaration of Helsinki. Informed consent was obtained from all participants prior to their inclusion in the study. Ethical approval was granted by the institutional review board of the Asian Institute of Medical Sciences.

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Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 25.0. Frequencies and percentages were calculated for categorical variables such as gender and the presence of HCC, while means and standard deviations were computed for continuous variables such as age, BMI, AFP levels, and liver function tests. Comparative analysis between HCC and non-HCC groups was performed using appropriate statistical tests, with a significance level set at 5%. Differences in continuous variables were assessed using t-tests, and categorical variables were analyzed using chi-square tests or Fisher's exact tests, as appropriate.

In this study, the prevalence of hepatocellular carcinoma among cirrhotic patients with hepatitis C was determined, and the associated clinical and demographic factors were evaluated. The meticulous approach to data collection and analysis ensured the reliability and validity of the study findings, contributing valuable insights into the burden of HCC in this high-risk population

## RESULTS

The study included a total of 152 patients diagnosed with liver cirrhosis due to hepatitis C virus (HCV) infection. Of these, 103 (67.8%) were males and 49 (32.2%) were females, with an average age of 41.57 ± 10.67 years. The age distribution was as follows: 26 patients (17.1%) were between 18-30 years, 41 patients (27.0%) were between 31-40 years, 54 patients (35.5%) were between 41-50 years, and 31 patients (20.4%) were over 50 years old. The mean body mass index (BMI) was 26.14 ± 4.01 kg/m². Among the patients, 52.6% had a normal BMI, 27.6% were overweight, and 19.7% were obese. Regarding residential status, 60.5% of the patients resided in urban areas, while 39.5% lived in rural areas. In terms of comorbidities, 59.9% of the patients were diabetic, 36.8% had hypertension, and 21.7% had dyslipidemia. The severity of liver disease, as assessed by the Child-Pugh classification, showed that 14.5% of the patients were in Class A, 38.2% were in Class B, and 47.4% were in Class C. The average duration of cirrhosis was 6.93 ± 2.60 years, with 26.3% of the patients having had cirrhosis for 1-5 years and 73.7% for more than 5 years.

Table 1: Demographic Characteristics of the Patients (n=152)

| Variable | Frequency (%) |
|---|---|
| **Gender** | |
| Male | 103 (67.8) |
| Female | 49 (32.2) |
| **Age, Mean ± SD = 41.57 ± 10.67 Years** | |
| 18-30 Years | 26 (17.1) |
| 31-40 Years | 41 (27.0) |
| 41-50 Years | 54 (35.5) |
| >50 Years | 31 (20.4) |
| **Body Mass Index, Mean ± SD = 26.14 ± 4.01 kg/m²** | |
| Normal | 80 (52.6) |
| Overweight | 42 (27.6) |
| Obese | 30 (19.7) |
| **Residential Status** | |
| Urban | 92 (60.5) |
| Rural | 60 (39.5) |
| **Diabetes Mellitus** | |
| Diabetic | 91 (59.9) |
| Non-Diabetic | 61 (40.1) |
| **Hypertension** | |
| Hypertensive | 56 (36.8) |
| Non-Hypertensive | 96 (63.2) |
| **Dyslipidemia** | |
| Yes | 33 (21.7) |
| No | 119 (78.3) |
| **Child-Pugh Class** | |
| Class A | 22 (14.5) |
| Class B | 58 (38.2) |

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| Variable | Frequency (%) |
|---|---|
| Class C | 72 (47.4) |
| **Duration of Cirrhosis, Mean ± SD = 6.93 ± 2.60 Years** | |
| 1-5 Years | 40 (26.3) |
| >5 Years | 112 (73.7) |

Table 2: Liver Function Among HCC and Non-HCC Patients (n=152)

| Liver Function | Overall (n = 152) | HCC (n = 11) | Non-HCC (n = 141) | P-Value |
|---|---|---|---|---|
| Total Bilirubin (mg/dL) | 1.64 ± 1.33 | 4.22 ± 0.76 | 1.44 ± 1.14 | 0.001 |
| AST (U/L) | 14.23 ± 9.84 | 37.82 ± 14.25 | 12.39 ± 6.54 | 0.001 |
| ALT (U/L) | 38.10 ± 27.62 | 50.81 ± 10.52 | 37.11 ± 28.31 | 0.113 |
| Albumin (gm/dl) | 4.40 ± 1.02 | 4.75 ± 1.04 | 4.37 ± 1.02 | 0.243 |
| GGT (U/L) | 62.92 ± 68.12 | 171.8 ± 81.27 | 54.43 ± 59.41 | 0.001 |
| ALP (U/L) | 93.50 ± 73.92 | 106.4 ± 67.36 | 92.49 ± 74.53 | 0.548 |
| AFP (ng/mL) | 37.80 ± 84.03 | 323.6 ± 59.60 | 15.50 ± 21.04 | 0.001 |
| INR | 1.35 ± 0.65 | 2.75 ± 1.23 | 1.24 ± 0.42 | 0.001 |
| Platelet ($\times 10^3/\mu L$) | 212.4 ± 111.1 | 207.7 ± 134.1 | 212.7 ± 109.6 | 0.885 |

The prevalence of hepatocellular carcinoma (HCC) was noted in 11 (7.2%) of the patients. Significant differences were observed in several liver function parameters between HCC and non-HCC patients. HCC patients had significantly higher levels of total bilirubin (4.22 ± 0.76 mg/dL vs. 1.44 ± 1.14 mg/dL, p = 0.001), AST (37.82 ± 14.25 U/L vs. 12.39 ± 6.54 U/L, p = 0.001), GGT (171.8 ± 81.27 U/L vs. 54.43 ± 59.41 U/L, p = 0.001), AFP (323.6 ± 59.60 ng/mL vs. 15.50 ± 21.04 ng/mL, p = 0.001), and INR (2.75 ± 1.23 vs. 1.24 ± 0.42, p = 0.001). However, there were no significant differences in ALT, albumin, ALP, and platelet count between the two groups.

Table 3: Clinical Characteristics of Patients with Hepatocellular Carcinoma (n=152)

| Variables, n (%) | HCC (n = 11) | Non-HCC (n = 141) | P-Value |
|---|---|---|---|
| Age Group | | | |
| 18-30 Years | 1 (3.8%) | 25 (96.2%) | 0.708 |
| 31-40 Years | 2 (4.9%) | 39 (95.1%) | |
| 41-50 Years | 5 (9.3%) | 49 (90.7%) | |
| >50 Years | 3 (9.7%) | 28 (90.3%) | |
| Gender | | | |
| Male | 5 (4.9%) | 98 (95.1%) | 0.098 |
| Female | 6 (12.2%) | 43 (87.8%) | |
| BMI | | | |
| Normal | 4 (5.0%) | 76 (95.0%) | 0.112 |
| Overweight | 6 (14.3%) | 36 (85.7%) | |
| Obese | 1 (3.3%) | 29 (96.7%) | |
| Residential Status | | | |
| Urban | 5 (5.4%) | 87 (94.6%) | 0.227 |
| Rural | 6 (10.0%) | 54 (90.0%) | |
| Diabetes Mellitus | | | |
| Diabetic | 7 (7.7%) | 84 (92.3%) | 0.529 |
| Non-Diabetic | 4 (6.6%) | 57 (93.4%) | |
| Hypertension | | | |
| Hypertensive | 4 (7.1%) | 52 (92.9%) | 0.622 |
| Non-Hypertensive | 7 (7.3%) | 89 (92.7%) | |
| Dyslipidemia | | | |
| Yes | 4 (12.1%) | 29 (87.9%) | 0.194 |
| No | 7 (5.9%) | 112 (94.1%) | |

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| Variables, n (%) | HCC (n = 11) | Non-HCC (n = 141) | P-Value |
|---|---|---|---|
| Duration of Cirrhosis | | | |
| 1-5 Years | 0 (0.0%) | 40 (100.0%) | 0.030 |
| >5 Years | 11 (9.8%) | 101 (90.2%) | |
| Child-Pugh Class | | | |
| A | 0 (0.0%) | 22 (100.0%) | 0.158 |
| B | 3 (5.2%) | 55 (94.8%) | |
| C | 8 (11.1%) | 64 (88.9%) | |

Among patients with HCC, age distribution showed that 3.8% were aged 18-30 years, 4.9% were aged 31-40 years, 9.3% were aged 41-50 years, and 9.7% were over 50 years old. Gender distribution indicated that 4.9% of males and 12.2% of females had HCC. Regarding BMI, 5.0% of patients with normal BMI, 14.3% of overweight patients, and 3.3% of obese patients had HCC. Residential status revealed that 5.4% of urban residents and 10.0% of rural residents had HCC. Among diabetic patients, 7.7% had HCC compared to 6.6% of non-diabetic patients. Hypertension was present in 7.1% of hypertensive patients with HCC compared to 7.3% of non-hypertensive patients. Dyslipidemia was noted in 12.1% of patients with HCC compared to 5.9% without dyslipidemia. All patients with cirrhosis for 1-5 years had no HCC, while 9.8% with over 5 years of cirrhosis had HCC. In terms of the Child-Pugh classification, none in Class A, 5.2% in Class B, and 11.1% in Class C had HCC.

The results of this study highlight the significant prevalence of hepatocellular carcinoma among cirrhotic patients with hepatitis C. The data underscore the necessity for regular screening and surveillance in this high-risk population to enable early detection and timely intervention.

## DISCUSSION

The discussion of this study on the prevalence of hepatocellular carcinoma (HCC) among cirrhotic patients with hepatitis C virus (HCV) infection revealed several critical insights. The observed prevalence of HCC was 7.2%, aligning with previous studies which have reported varying rates of HCC in similar populations. For instance, a study recorded an HCC prevalence of 11.8% in HCV-infected cirrhotic patients, while it noted a prevalence of 5.7%, and Irum et al. reported a higher rate of 32.3% (19) these discrepancies could be attributed to differences in study populations, methodologies, and geographic variations in HCV prevalence and genotypes.

The pathogenesis of HCC in the context of HCV-related cirrhosis involves multiple molecular and cellular mechanisms. Chronic HCV infection induces a persistent inflammatory state in the liver, characterized by immune cell infiltration and the production of pro-inflammatory cytokines this sustained inflammation leads to hepatocyte injury, apoptosis, and regeneration over time, this cycle of damage and repair results in the accumulation of genetic and epigenetic alterations in hepatocytes, promoting the transformation of normal cells into malignant ones. The fibrotic environment in cirrhosis further contributes to carcinogenesis by creating hypoxic conditions, altering cellular signaling pathways, and facilitating the development of dysplastic nodules (20)

Early detection of HCC in cirrhotic patients was crucial for improving prognosis and survival rates. Surveillance strategies typically involved regular ultrasound examinations and measurement of serum alpha-fetoprotein (AFP) levels, although the sensitivity and specificity of these methods were variable Advances in imaging technologies, such as contrast-enhanced magnetic resonance imaging (MRI) and computed tomography (CT), enhanced the ability to detect small tumors and differentiate HCC from benign lesions This study confirmed the significance of these diagnostic modalities, as elevated AFP levels and specific liver function abnormalities were strongly associated with HCC in the patient cohort.

A strength of this study was the comprehensive data collection and analysis, which included demographic details, clinical features, and laboratory results, ensuring the reliability and validity of the findings. The study also adhered to ethical standards, with informed consent obtained from all participants, and ethical approval granted by the institutional review board. However, several limitations were noted. The study's descriptive nature limited the ability to establish causal relationships. Additionally, the sample size, while adequate for prevalence estimation, may not have been sufficient to detect all potential associations between clinical variables and HCC development. The exclusion of patients with other causes of cirrhosis, such as hepatitis B virus and alcoholic liver disease, also limited the generalizability of the findings to all cirrhotic patients.

The results underscored the necessity for regular screening and surveillance in high-risk populations, such as cirrhotic patients with HCV, to enable early detection and timely intervention. Antiviral therapy for HCV, particularly direct-acting antivirals (DAAs), has revolutionized the management of chronic HCV infection and its complications, achieving sustained virologic response (SVR) in most patients and effectively reducing liver inflammation and fibrosis progression (17). However, the impact of DAA-induced SVR on the

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long-term risk of HCC in cirrhotic patients remains an area of active research, with some studies suggesting a reduced risk, while others indicated the need for continued vigilance due to residual cirrhosis.

## CONCLUSION

In conclusion, the study highlighted a significant prevalence of hepatocellular carcinoma among cirrhotic patients with hepatitis C. This finding emphasized the critical need for robust surveillance strategies in this high-risk group to facilitate early diagnosis and treatment. Future research should focus on larger, multicenter studies to validate these findings and explore the long-term impact of antiviral therapies on HCC risk. Moreover, there is a need to develop more sensitive and specific diagnostic tools to improve early detection and patient outcomes in HCC management.

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