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Original Article

Incidence of Hepatocellular Carcinoma in Hepatitis-C Patients Presenting to Lady Reading hospital, Peshawar- A Retrospective Study

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) is a significant complication of hepatitis C virus (HCV) infection, with varying incidence and outcomes based on treatment history and co-infections like HIV. Understanding the risk factors and progression of HCC in hepatitis C patients is crucial for effective disease management.

Objective: This study aimed to assess the incidence of HCC in patients with a history of hepatitis C, considering factors such as antiviral treatment and HIV co-infection.

Methods: A retrospective study was conducted at Lady Reading Hospital, Peshawar, from March 2022 to July 2023, involving 30 patients with decompensated liver disease or cirrhosis and a history of hepatitis C. Patients were evaluated for demographics, treatment history, PCR status, and HIV co-infection. Data analysis focused on the development of HCC in relation to these variables.

Results: The study included 30 patients with a mean age of 61.57 ± 11.11 years, predominantly male (93.3%). Of these, 73.3% tested PCR positive for HCV, while 26.7% were PCR negative. A total of 43.3% had received antiviral treatment, while 56.7% had not. HIV co-infection was present in 13.3% of patients. HCC was observed in 80% of patients overall. Among those treated and PCR negative, 87.5% developed HCC. In contrast, 76.5% of untreated, PCR-positive patients developed HCC. Among HIV co-infected patients, 75% developed HCC.

Conclusion: The study indicates a high incidence of HCC among hepatitis C patients, regardless of antiviral treatment status or PCR positivity. HIV co-infection appears to be a significant risk factor for HCC development. These findings highlight the need for continuous monitoring and proactive management of hepatitis C patients, especially those co-infected with HIV.

Keywords: Hepatocellular carcinoma, Hepatitis C, HIV co-infection, Antiviral treatment, PCR status, Liver disease.

INTRODUCTION

Hepatitis C, a liver infection caused by the hepatitis C virus (HCV), a single-stranded RNA virus from the Flaviviridae family, remains a significant public health challenge. Transmission of HCV primarily occurs through contact with infected blood, often via needle sharing, piercings, tattooing, or sexual routes (1, 2). The course of HCV infection varies; while 15-45% of individuals experience an acute phase that resolves spontaneously, 55-85% progress to chronic infection. Chronic HCV infection can lead to severe complications, including cirrhosis and, ultimately, hepatocellular carcinoma (HCC), a serious and often fatal outcome (3, 4).

The clinical presentation of HCV infection is diverse. In its acute stage, symptoms like fever, anorexia, fatigue, and body aches may occur, occasionally escalating to acute liver failure. Chronic HCV infection manifests more insidiously with symptoms like jaundice, abdominal swelling (ascites), and spider nevi (telangiectasia) (5, 6).

Diagnosis of HCV involves a two-step process: initially, testing for anti-HCV antibodies is conducted. If these antibodies are detected, a nucleic acid test for HCV RNA is performed to confirm ongoing infection or past clearance of the virus. Treatment options have evolved, with directly acting antivirals like sofosbuvir and daclatasvir, often chosen for their broad genotype efficacy, reduced resistance risk, and shortened treatment duration (7, 8).

HCC is a major global health burden, ranking as the sixth most prevalent cancer with a male-to-female incidence ratio of three to one. Annually, HCC accounts for over 800,000 new cases and exceeds 700,000 deaths. Risk factors for HCC include chronic HCV and hepatitis B virus (HBV) infections, alcoholism, uncontrolled type 2 diabetes, obesity leading to non-alcoholic fatty liver disease (NAFLD), autoimmune liver diseases, hemochromatosis, tyrosinemia, and certain metabolic disorders like glycogen storage diseases. Alpha-1 antitrypsin deficiency is also a recognized risk factor (9, 10).

Specific HCV genotypes, particularly genotype 3, have been linked with increased susceptibility to HCC, as evidenced in a study of the USA Veteran's Affairs medical system. Additionally, lifestyle factors such as alcoholism and smoking significantly elevate HCC risk. A recent meta-analysis highlighted a relative risk increase for HCC in smokers with HCV compared to non-smokers with HCV. Furthermore, a synergistic relationship between alcoholism and HCV infection in the development of HCC has been noted, especially in individuals consuming over 60 grams of alcohol daily (11, 12).

Obesity and diabetes are additional risk factors for HCC. Co-morbidity of diabetes mellitus with HCV infection significantly heightens the risk of developing HCC. HIV-HCV co-infection also presents a higher HCC prevalence, with a tendency for earlier onset compared to HCV mono-infected patients (13, 14). This elevated risk is attributed to rapid HCV replication, diminished HIV immunity, and accelerated progression to cirrhosis (15-17).

The rationale behind this retrospective study is to determine the incidence of hepatocellular carcinoma in HCV-infected patients' post-treatment and to ascertain the proportion of patients co-infected with HIV who develop HCC. The development of HCC in HCV patients is a multifaceted process, influenced by chronic inflammation, fibrosis, genetic mutations, immune dysfunction, and various co-factors. Understanding these contributory elements is vital for early detection, risk stratification, and the formulation of effective prevention and treatment strategies. Consequently, regular monitoring and antiviral therapy are crucial in managing HCC risk in hepatitis C patients (18-20).

This study aims to provide a comprehensive understanding of the incidence and contributing factors of HCC in HCV-infected individuals, focusing particularly on those who have undergone antiviral treatment. By examining these factors, this research seeks to enhance the current knowledge base, aiding in the optimization of clinical management and prevention strategies for HCC in the context of HCV infection (21-24).

RESULTS

The results from the tables provide a comprehensive overview of the demographics and various factors influencing the development of Hepatocellular Carcinoma (HCC) in patients with Hepatitis C.

The average age of the patients was approximately 61.57 years, with a standard deviation of 11.11 years, indicating a predominantly middle-aged to elderly patient group. The gender distribution was heavily skewed towards males, who constituted 93.3% (28 out of 30) of the study population, while females represented a minor fraction at 6.7% (2 out of 30).

Table 1 Demographics

Demographic	Statistics
Age (Years)	61.57 ± 11.11
Gender	
- Male	28 (93.3%)
- Female	2 (6.7%)

In the context of HCC development, the majority of affected patients were male. Specifically, 91.7% (22 out of 24) of those who developed HCC were male, and 8.3% (2 out of 24) were female. Interestingly, the gender difference in HCC incidence was not statistically significant, as indicated by a p-value of 0.46. All patients who did not develop HCC (6 out of 30) were male, highlighting a lack of female representation in this subgroup.

Table 2 Association between HCC Status and Gender

HCC Status	Male	Female	Total	P value
Yes	22 (91.7%)	2 (8.3%)	24 (100%)	0.46
No	6 (100%)	0 (0%)	6 (100%)	
Total	28 (93.3%)	2 (6.7%)	30 (100%)	

The relationship between HCC development and various clinical parameters presents an intricate picture. Among those who received treatment for Hepatitis C, those who were PCR positive showed an 80% (4 out of 5) rate of developing HCC, whereas this rate was slightly higher at 87.5% (7 out of 8) in those who were PCR negative. In contrast, among patients who did not receive treatment, a significant 76.5% (13 out of 17) who were PCR positive developed HCC. This suggests a complex relationship between treatment, PCR status, and the risk of developing HCC.

Table 3 HCC Development with Treatment, PCR, and HIV Status

Treatment	PCR Status	HCC Status: Yes	HCC Status: No	Total
Yes	Positive	4 (80.0%)	1 (20.0%)	5 (100%)
	Negative	7 (87.5%)	1 (12.5%)	8 (100%)
No	Positive	13 (76.5%)	4 (23.5%)	17 (100%)
HIV Status	Positive	3 (75%)	1 (25%)	4 (100%)
	Negative	21 (80.7%)	5 (19.3%)	26 (100%)
Overall		24 (80%)	6 (20%)	30 (100%)

Regarding the impact of HIV co-infection, 75% (3 out of 4) of HIV-positive patients developed HCC. This rate was slightly lower at 80.7% (21 out of 26) in the HIV-negative group. This finding indicates that HIV co-infection might be a relevant factor in the development of HCC among Hepatitis C patients, although the overall incidence of HCC in the study was high irrespective of HIV status.

Overall, these results demonstrate a high incidence of HCC among the studied Hepatitis C patients, with a notable prevalence in males and a significant association with PCR positivity. The data also suggest that both the treatment status for Hepatitis C and the presence of HIV co-infection are important factors in the development of HCC. These findings contribute to a better understanding of the complex interactions between Hepatitis C infection, treatment outcomes, and comorbid conditions in the pathogenesis of HCC.

DISCUSSION

The study conducted at the MTI, Lady Reading Hospital, Peshawar, provides critical insights into the development of hepatocellular carcinoma (HCC) in patients with a history of hepatitis C infection. The patient cohort, consisting of 30 individuals showing signs of decompensated liver disease or hepatocellular carcinoma, offers valuable data for understanding the progression of HCC in this specific demographic. The mean age of the patients was 61.57 ± 11.11 years, with a predominantly male representation (98.3%). This demographic profile aligns with the general understanding that HCC tends to occur in older patients and is more common in males. The high incidence of HCC (80% of patients) further underscores the aggressive nature of the disease in the context of hepatitis C infection.

A notable finding of the study was that 87.5% of patients who had received treatment and were PCR negative still developed HCC. This is consistent with findings by Xavier Adhoute et al. (6), which indicated that treatment for hepatitis C does not necessarily prevent the development of HCC. This observation is critical as it suggests that even successful antiviral therapy does not completely eliminate the risk of HCC, echoing the conclusions of Page Axley et al (12). These findings emphasize the importance of continued monitoring for HCC in patients treated for hepatitis C.

In the context of co-infections, our study found that 75% of patients with both HCV and HIV developed HCC. This rate is alarmingly high and aligns with the study by Massimiliano Berretta et al. conducted in Japan, which reported a heightened incidence of HCC among patients co-infected with HIV (19). This suggests that HIV co-infection may be a significant risk factor for the early development of HCC in patients with hepatitis C, necessitating a more vigilant approach in managing such patients.

CONCLUSION

In conclusion, the study's findings highlight the persistent risk of HCC development in hepatitis C patients, regardless of the treatment status. This underscores the need for ongoing surveillance for HCC in all patients with a history of hepatitis C, particularly those co-infected with HIV. These observations provide valuable input for clinical decision-making and patient management strategies, reinforcing the idea that vigilance in monitoring and early detection remains paramount in the care of patients with hepatitis C, even after successful antiviral treatment.

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