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ORIGINAL ARTICLE

Frequency of New Hepatocellular Carcinoma in Patients Suffering from Hepatitis C Virus Infection Related Cirrhosis Exposed to Direct Acting Antiviral-based Therapy

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ABSTRACT

Objective: To find the frequency of hepatocellular carcinoma in patients with hepatitis C virus infection patients on dual antiviral therapy.
Design of the study: Cross sectional study
Settings: Department of Medicine/Division of Gastroenterology, Lahore General Hospital, Lahore.
Duration: 6 months
Sample Size: Sample size of 220 cases was calculated with 95% confidence level and 3.5% margin of error by taking percentage of HCC i.e. 7% in HCV patients on direct acting antiviral-based therapy. Data was analyzed with IBM-SPSS version 21.
Results: In our study the mean age was 37.75±12.08 years. The mean value of duration of HCV therapy of the patients was 8.59±4.023 months. In this study the HCC was noted in 12(5.45%) patients.
Conclusion: The frequency of HCC in patients with HCV infection patients on direct acting antiviral-based therapy is 5.45%.
Keywords: Hepatocellular Carcinoma, Hepatitis C virus, Antiviral Therapy

INTRODUCTION

Hepatitis C virus (HCV) was1discovered to be1the major cause of non-A non-B hepatitis in 1989, in both developed and developing nations, it is now recognized as a main cause of chronic liver disease. Within Europe, sero-prevalence rises with age, peaking in 55–64 year old patients; the highest peak prevalence is seen in1Southern & Eastern Europeans[1,2].

The large number of chronically infected people, the severity of the disease, and the lack of a vaccine, treatment will be an important aspect of disease control. However, because the majority of people who have a chronic infection are unaware of it, screening programmes to detect individuals will be necessary to prevent the disease from progression silently[3,4].

Hepatocellular carcinoma (HCC) is a common cancer globally, that is becoming more common in US. Cirrhosis is the leading cause of HCC, with the hepatitis C virus (HCV) being the common cause. HCC development has been shown to predict death in cirrhotic patients since it hastens decompensation of the liver disease[5]. The history of chronic illness is still a work in progress. It is a condition that progresses slowly and is characterized by prolonged liver inflammation, over the course of 20–30 years of HCV infection, around 10–20 percent of people develop cirrhosis. Overall, yearly, there is a 1–5% risk of HCC after cirrhosis has established[6].

According to one study, HCC was shown to be present in 3.2 percent of HCV patients[7]. Patients were observed for 24 weeks in a recent study, which revealed a 7.6% HCC incidence[8]. The prevalence of HCC among HCV patients was similarly observed to be 8.30% [9]. However, one research found that 21.8 percent of HCV patients on dual treatment developed HCC [10].

The rationale of the study is to find the frequency of HCC in patients with HCV infection patients on direct acting antiviral-based therapy. Literature has showed that HCC is sever complication of HCV, but the varied results have been noticed through literature. Moreover, there is no local evidence available in this regard and the extent of problem in local population is missing. So we are unable to predict the effect of direct acting antiviral based therapy in local population with HCV. So we want to conduct this study to find local evidence and implement the results of this study in future, which could help us in planning better management protocols and early screening of HCC.

MATERIAL AND METHODS

Study Design: Cross sectional study
Setting: Department of Gastroenterology, Lahore General Hospital, Lahore.
Duration: 6 months
Sample Size: Sample size of 220 cases was1calculated1with 95% confidence1level, 3.5% margin of error by taking expected1percentage of HCC i.e. 7% in HCV patients on direct acting antiviral-based therapy.
Inclusion Criteria: Patients between the ages of 18 and 60, of either gender, who have been diagnosed with HCV (on medical record) for more than one year, have a Child-Pugh score of more than 5, and have been on DAA-based therapy for at least one year.
Exclusion Criteria

- HBV, HIV or already diagnosed cases of HCC (medical record)
- Intolerance to treatment (on medical record and history)
- Patients on triple antiviral therapy

Data Collection Procedure: 220 patients were included, through outpatient Gastroenterology department, LGH, Lahore. Informed consent was taken. Basic demographics like name, age, gender, BMI, duration of HCV, genotype and therapy was noted. Blood sample was obtained by using 5cc BD syringe. Sample was sent to the pathology laboratory of the hospital for assessment of AFP level. Meanwhile patients were undergone biphasic CT scan for detection of HCC. All biphasic a single senior radiologist having at least 4-year post-graduation did CT scan. Reports were assessed for AFP and biphasic CT scan and HCC was labeled. All the data was noted on especially designed proforma.
Data Analysis: Data was analyzed with SPSS V21. Age, BMI, duration of HCV, genotype and therapy were presented as mean & SD. Gender & HCC were presented as frequency & percentage. Stratification was used to control effect modifiers such as age, gender, BMI, HCV duration, genotype, and treatment. Post-stratification, chi-square test was applied with $p \leq 0.05$ taken as significant.

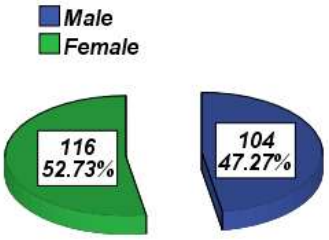
RESULTS

In this study 220 cases were enrolled. The patients mean age was 37.75±12.08 years with minimum & maximum ages of 18 & 60 years.

Table 1:

Age (Years)	n	220
	Mean	37.75
	SD	12.08
	Minimum	18
	Maximum	60

In this study, there were 104(47.27%) male and 116(52.73%) were female. Male to female ratio was 0.89:1. Fig#1



In our study the mean BMI value was 21.144±2.65 kg/m2 with minimum & maximum values of 16.70 & 25.68 kg/m2.Table#2

Table 2: Descriptive statistics of BMI (kg/m2)

BMI (Kg/m2)	n	220
	Mean	21.144
	SD	2.65
	Minimum	16.70
	Maximum	25.68

According to our study the mean value1of duration of HCV of the patients was 8.75±4.155 months with minimum and maximum values 1 & 15 months respectively. Table#3

Table 3: Descriptive statistics1of duration of HCV

Duration of HCV)	n	220
	Mean	8.75
	SD	4.155
	Minimum	1
	Maximum	15

According to our study the mean1value of duration of HCV therapy of the patients was 8.59±4.023 months with minimum and maximum values 1 & 15 months respectively. Table#4

Table 4: Descriptive statistics1of duration of HCV therapy

Duration of HCV Therapy	n	220
	Mean	8.59
	SD	4.023
	Minimum	1
	Maximum	15

In this study genotype two was found in 109(49.55%) patients and genotype one was found in 111(50.45%) patients. Fig#2

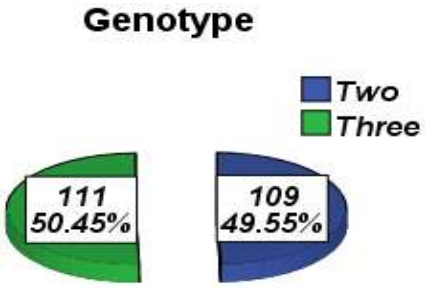


Fig 2: Frequency distribution of genotype

In our study the AFP mean value was 71.87±20.13 with minimum & maximum values of 40 & 147. Table#5

Table 5: Frequency distribution of AFP

AFP	n	220
	Mean	71.87
	SD	20.13
	Minimum	40
	Maximum	147

In our study the HCC was noted in 12(5.45%) patients and it was not found in 208(94.55%) patients. Fig#3

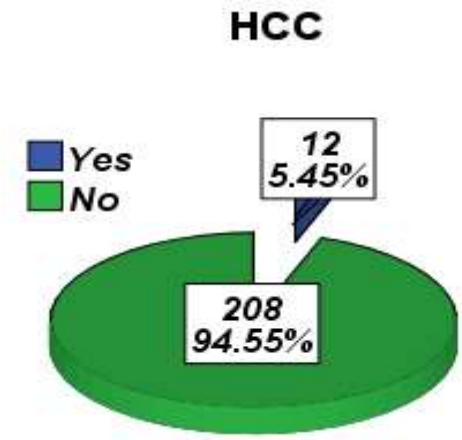


Fig 3: Frequency distribution of HCC

The study found that there were 133 individuals under the age of 40, with four cases of HCC, Similarly, there were 87 individuals over the age of 40, with eight of them having HCC. There was a statistically insignificant difference between HCC and age (p-value=0.067). Table#6

Table 6: Comparison of HCC with age

		HCC		Total	p-value
		Yes	No		
Age (years)	≤ 40	4	129	133	0.067
	> 40	8	79	87	
Total		12	208	220	

According to the findings, there were 104 male patients in this study, with six cases of HCC; Similarly, there were 116 female patients, with six cases of HCC. The HCC with gender had a statistically insignificant difference, with a p-value of 0.846. Table#7

Table 7: Comparison of HCC with gender

		HCC		Total	p-value
		Yes	No		
Gender	Male	6	98	104	0.846
	Female	6	110	116	
Total		12	208	220	

The study found that people with a normal BMI were 150, with HCC found in seven cases; Similarly, there were 70 patients with an abnormal BMI, with five cases of HCC. The difference between HCC and BMI was statistically insignificant, with a p-value of 0.451.Table#8

Table 8: Comparison of HCC with BMI

		HCC		Total	p-value
		Yes	No		
BMI	Normal	7	143	150	0.451
	Abnormal	5	65	70	
Total		12	208	220	

The study included 101 individuals who had been on HCV medication for less than eight months, with two cases of HCC, Similarly, there were 119 patients who had been on HCV medication for more than 8 months, with 10 of them having developed HCC. There was a significant difference between HCC and HCV treatment duration (p-value=0.041).Table#9

Table 9: Comparison of HCC with duration of HCV therapy

		HCC		Total	p-value
		Yes	No		
Duration of HCV Therapy	≤8	2	99	101	0.041
	>8	10	109	119	
Total		12	208	220	

The study found that individuals with genotype two had 109 incidences of HCC, with 5 cases of HCC, Similarly, there were 111 individuals with genotype three, with seven cases of HCC. The difference between HCC with genotype (p-value=0.575) and HCC without genotype was statistically insignificant. Table#10

Table 10: Comparison of HCC with genotype

		HCC		Total	p-value
		Yes	No		
Genotype	Two	5	104	109	0.575
	Three	7	104	111	
Total		12	208	220	

DISCUSSION

This cross-sectional study was conducted in the Gastroenterology Department, Lahore General Hospital, Lahore, to determine the frequency of hepatocellular carcinoma in HCV infection patients receiving direct acting antiviral medication.

Primary liver cancer is the world's sixth most prevalent malignancy and the third leading cause of cancer-related mortality. Hepatocellular carcinoma (HCC) is the common kind of primary liver cancer, accounting for 85.0 to 90.0% of cases. In the United States, the incidence of HCC is on the increase. Chronic HCV infection is one of the most prominent risk factors for HCC[11].

Hepatocellular carcinoma was shown to be 12 times more common in individuals with HCV infection who were on direct acting antiviral medication in our research (5.44%). The findings of some of the research are discussed below.

According to research by Liu CJ et al [12], the HCV response was sustained in about 97.0% of patients throughout long-term follow-up; Long-term results, including as the development of HCC and death from liver disease, were also improved.

According to one study, HCC was shown to be present in 3.2 percent of HCV patients.7 Patients were observed for 24 weeks in a recent study, which revealed that the incidence of HCC was 7.6% [8].

Chung-Feng Huang et al[13] revealed that 19(2.2%) of the 877.0 patients developed1HCC during 6,963 person-years1of follow-up. HCC occurred in 14 (2.50%) SVR patients and 5 (1.60%) SC patients (P=0.004).

Annual HCC frequency in individuals with severe liver fibrosis or cirrhosis with ongoing HCV infection is estimated to vary from 1% to 8%, with rates decreasing to 0.070 to 1.20% once interferon-based treatments achieve an SVR[14].

The frequency of HCC among HCV patients was similarly observed to be 8.3 percent [9]. However, one research found that 21.8 percent of HCV patients on dual treatment developed HCC[10].

According to Y.-T.H. & C.-L.J[15], the cumulative lifetime frequencies of HCC for men and women positive for both HBV surface antigen (HBsAg) and antibodies against HCV (anti-HCV) were 38.35 percent and 27.40 percent, respectively, for men & women; for those positive for 1HBsAg only, 27.37% and 7.9%; for those1positive for anti-HCV1 only, 23.74% & 16.72%; and1for those positive1for neither, 1.55% & 1.03%.

Although, data were heterogeneous (2 = 59.10), Ashwani K.Singal et al[5] found that pooled data demonstrated lower HCC risk in the treatment group (RR, 0.43; 95 percent confidence interval [CI], 0.33–0.56). Studies having follow-up periods of greater than 5 years added to heterogeneity, according to meta-analysis. Patients with an SVR had a lower risk of HCC, according to an analysis of 14 trials (n = 3310) sustained virological response (SVR) rates with antiviral therapy, compared to non-responses (RR, 0.35; 95.0% CI, 0.26–0.46); Patients on ribavirin-based regimens experienced the greatest benefits (RR, 0.25; 95 percent CI, 0.14–0.46).

CONCLUSION

According to our study the frequency of HCC in patients with HCV infection patients on direct acting antiviral-based therapy is 5.45%.

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