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Frequency of Hepatocellular Carcinoma in Patients Infected with Hepatitis C Virus visiting a Tertiary Care Hospital in Lahore for Computed Tomographic Evaluation

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Abstract

Background: Hepatitis C virus has been identified as one of the leading causes of chronic liver disease and its complications world-wide. Subsequent development of hepatocellular carcinoma in these patients is a major complication of this infection having serious implications on morbidity and mortality rates. The objective of this study was to find out the frequency of Hepatocellular carcinoma in patients suffering from Hepatitis C visiting Radiology department of a tertiary care hospital for multi-detector computed tomography evaluation.

Methods: This cross-sectional analytical study was conducted at Shalamar Hospital Lahore. A total of 195 patients, suffering from Hepatitis C, visiting Shalamar Hospital, Lahore for evaluation by CT during 6 months study interval were included in this study. Abdominal CT was performed using Triphasic contrast enhancement protocol. All images were interpreted by a senior Radiologist. Frequency of Hepatocellular carcinoma was calculated. Statistical analysis was made using MEDCALC.

Results: Out of 195, 63(32.3%) patients were seen to have hepatocellular carcinoma. This disease was more common in male, 45(34.6%) as compared to female patients 18 (27.7%). The presence of HCC showed statistically significant association with alcoholism, obesity, diabetes mellitus and cirrhosis.

Conclusion: The study concluded that a substantial number of HCV positive patients develop HCC, which is more common in men as compared to women. The presence of HCC is strongly associated with alcoholism, obesity, diabetes mellitus and cirrhosis.

Introduction

Hepatitis C virus (HCV) has been a global concern in recent decades [1]. The virus has been reported to get naturally eliminated from the body within six months of infection in over 30% (15–45%) of infected people without any therapy [2]. The possibility of this clearance has also been linked with certain genetic variations and gender [3]. In other patients, consequences of this infection vary in severity from a mild disease to a serious life-threatening illness, from acute and chronic hepatitis to hepatocellular carcinoma (HCC) if left untreated [1]. Chronic HCV infection will subsequently develop in remaining 70% (55–85%) of people. These patients are considered at risk for developing cirrhosis in 15% to 30% cases within 20 years [2, 4].

Chronic HCV infection is a recognized leading cause of HCC in the modern world [5]. Globally, an estimated 10%–25% of all cases of HCC have been found to be in association with Hepatitis C infection making it the second most common risk factor for HCC [6]. Unlike neighboring countries, where Hepatitis B remains the most common causative factor of HCC, 66–87% of such cases in Pakistan are reported to be in association with HCV [7]. This trend is also seen in developed countries like Japan and USA [5, 6].

HCC can be diagnosed non-invasively using all the imaging modalities including ultrasonography, computed tomography, and magnetic resonance imaging (MRI), each having its own value in terms of diagnostic accuracy. Technological advancements in computed tomography have made scanning faster with advantages of it being more accurate and possibility of image acquisition with uniform hepatic enhancement during each phase of contrast enhanced study [8].

Thanks to these modern diagnostic techniques early detection of HCC has been made possible and its curative resection is being performed in an increasing number of patients. The rate of postoperative recurrence of either intrahepatic metastasis or metachronous multicentric HCC however remains high making it lot more serious complication [9].

The possibility of occurrence of HCC in association with HCV also depends on multiple factors encompassing geographical factors to viral genotype and individual traits of the host such as obesity and alcohol intake [5]. Unfortunately the data published on HCV related HCC in Pakistan is quite old and does not give true picture of the present situation [10, 11]. This study was therefore planned to have an insight on the current disease burden in a big city of Pakistan. Secondly the reported results describe the prevalence of HCV infection among cases who have already developed HCC [10, 11] but we conducted the research in a vice versa fashion to assess the prevalence of HCC in patients infected with HCV.

Methods

This cross-sectional study was carried out after the approval of Institutional Review Board of The University of Lahore. It included a total of 195 PCR positive cases of Hepatitis C, both male (n=130) and female (n=65) who visited the Radiology Department of Shalamar Hospital, Lahore during the study duration of 6 months. The mean age of these patients was 60.6 years ± 12.16 with a range of 29-98 years. Convenient sampling technique was used. Pregnant women, those who had a history of allergic reaction to the contrast medium or those with the presence of any known contraindication to use of contrast medium were excluded from the study. The included patients were assessed clinically in detail to assess for the possible associated factors such as alcoholism, obesity, diabetes etc. Siemens Somatom 64 slice CT machine was used for scanning the patients. Triphasic contrast enhanced CT was performed. Plane images were taken first followed by intravenous administration of 100 ml of Ultravist. Images were then acquired for arterial, portal venous and delayed phases at 15-25 sec, 65-70 sec and 5 minutes time intervals post injection, respectively. The scans were then interpreted by a senior Radiologist for the presence or absence of HCC. Frequency of presence of HCC was calculated and Chi Square tests was used to compare the association of host factors with the presence of HCC. MEDCALC was used for statistical analysis.

Results

Out of total 195 patients, 63(32.3%) were diagnosed to have HCC, of which 18(27.7%) were females and 45(34.6%) were males. But this difference in gender was not statistically significant. [Table 1]

Gender	HCC		Total	P Value
	No	Yes		
Female	47(72.3%)	18(27.7%)	65	0.33
Male	85(65.4%)	45(34.6%)	130	
Total	132(67.7%)	63(32.3%)	195	-

Table 1: Shows gender distribution of HCC.

53 of these patients had single, 7 patients had two and 3 patients had three lesions of HCC. The lesions representing HCC (n=76) measured (Anteroposterior × Transverse) 61.3 × 52.26 mm on the average ranging from 11× 7 to 194 × 338 mm.

Of three patients who were alcoholics all were found to have HCC. Among 55 obese patients, 34(61.8%) and of 65 diabetic patients 34(52.3%) had HCC on CT. The association of all these factors with HCC was found to be significant statistically. [Table 2]

Forty-two patients (80.8%) out of 52 patients with cirrhotic liver disease on CT had co-existing HCC. [Table 3] This association of cirrhosis with HCC was also statistically significant.

Variables	Categories	HCC		Total	P Value
		No	Yes		
Alcoholism	No	132(67.6%)	60(31.2%)	192	0.0117*
	Yes	0	3(100%)	3	
Obesity	No	111(79.3%)	29(20.7%)	140	<0.0001*
	Yes	21(38.2%)	34(61.8%)	55	
Diabetes	No	101(77.7%)	29(22.3%)	130	<0.0001*
	Yes	31(47.7%)	34(52.3%)	55	
-	Total	132(67.6%)	63(32.4%)	195	-

Table 2: Shows association of HCC with Alcoholism, Obesity and Diabetes.

Variables	Categories	HCC		Total	P Value
		No	Yes		
Cirrhosis	No	122(85.3%)	21(14.7%)	143	<0.0001*
	Yes	10(19.2%)	42(80.8%)	52	
-	Total	132(67.7%)	63(32.3%)	195	-

Table 3: The cross tabulation shows the association of HCC with cirrhosis.

Mean age of the patients with HCC was 67.34 years while of those without it was 57.38 years. The presence of HCC was also seen to have a significant relationship with advancing age on applying Kruskal- Wallis test with P < 0.000001. [Figure 1]

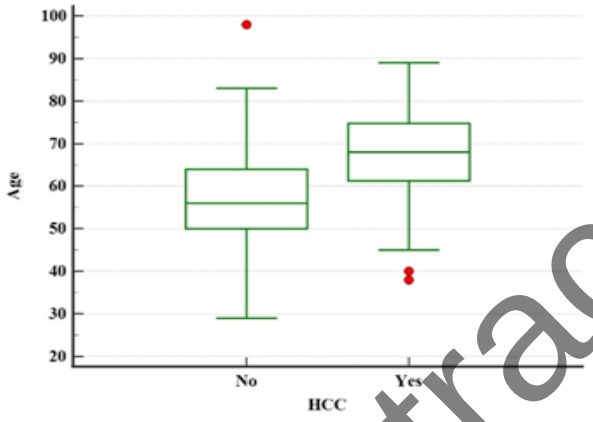

Figure 1: Shows the association of advancing age with the presence and absence of HCC through box and whisker plot. The boxes show upper and lower quartiles and median values of age while the whiskers represent minimum and maximum ages in case of both presence and absence of HCC. The red circles represent the outliers.

These patients had a variety of clinical signs and symptoms. [Table 4]

Variables	Categories	Frequency (Percentage)
Jaundice	Yes	110(56.4%)
	No	85(43.6%)
Nausea and vomiting	Yes	114(58.5%)
	No	81(41.5%)
Dark colored urine	Yes	127(65.1%)
	No	68(34.9%)
Bloating	Yes	41(21%)
	No	154(79%)

Table 4: Shows frequency of various clinical features

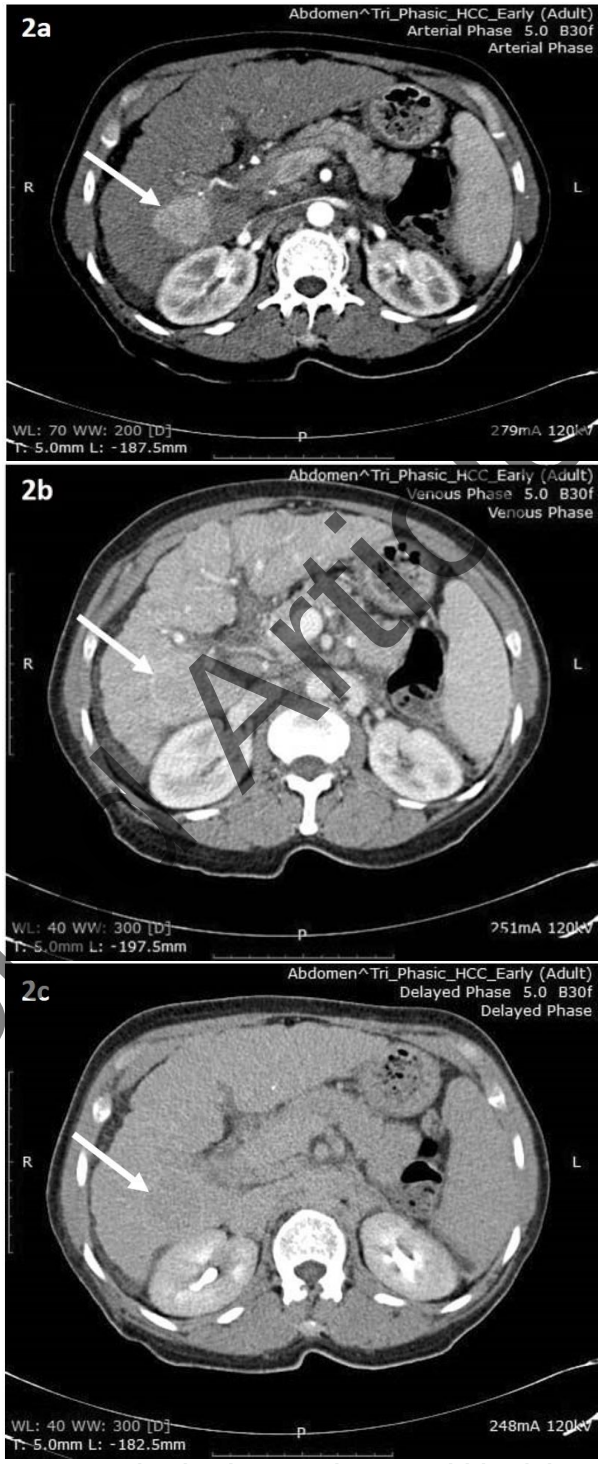

Figure 2: 2a, 2b and 2c show arterial, venous and delayed phases of triphasic CT respectively in a 52 year old, HCV positive woman with evidence of chronic liver disease. HCC is seen at segment VI/VII of the cirrhotic liver. Ascites can also be noted.

Discussion

Multiple studies suggest a strong association of HCC with HCV [5, 12-14]. While most of the reports [5, 10, 15-

17] from Pakistan till now report the incidence of HCV positivity as compared to other viral or non-viral causes among HCC patients, our study intended to find out the vice versa i.e. the incidence of HCC in the patients who were HCV positive.

The incidence of development of HCC in HCV patients have been variable across the globe. The results of a study conducted in Japan reported the incidence of HCC as 10.5%, on follow up of 5.5 to 7.75 years, among patients who were HCV positive and were non-cirrhotic at the time of start of the study [18]. In other studies conducted only in cases who had already developed cirrhosis this was found to be 20.5% [19], 7% [20] and 12.2% [21]. The results of our study showed a very high prevalence of HCC among HCV positive patients as compared to all of these reported results. The reason might be manifold. All of these studies have been carried out in diverse ethnicities at different stages of infections and obviously the predominant genotype of the HCV might also have been different in all these studies. Our study included all the patients who presented in the hospital with various complaints related to chronic liver disease. In contrast the study conducted by Takano et. al. [18] excluded all the patients who were either cirrhotic or had any sign and symptom suggestive of chronic liver disease.

In addition, as already mentioned, the genotype of the HCV is also a very important factor determining the possibility of occurrence of HCC. According to Haqqi A et. al. and Idrees M et. al. Pakistani population infected with HCV has the highest prevalence of HCV genotype 3a followed by genotype 3b [22, 23]. Multiple other studies from Pakistan also reported the same genotype, 3a, to be the most prevalent one. This genotype is associated with the development of HCC compared to the other types [24-26]. Unfortunately we could not get the data on the genotyping of the HCV in our patients but based on the results of previous studies it can be assumed that these patients will also be predominantly having genotype 3a which is also the genotype found to have a strong correlation with the development of HCC. This could also be the cause of higher HCC prevalence in our study population as compared to the other studies from other parts of the world.

Host factors including male gender, advanced age, alcohol consumption, diabetes mellitus and obesity have been reported to influence disease progression and development of HCC [11, 20, 23, 27]. Our study also showed the same trend for all of these factors in our study population.

We found a significantly higher prevalence of HCV related HCC in cirrhotic livers which is also in accordance with the previously published data [7, 11, 15, 19, 20].

The importance of the study lies in the fact that it reflects burden of HCC resulting from HCV infection in local population of Pakistan. Pakistan is the sixth most populous country in the world [7]. The HCV associated HCC has been seen to increase substantially over the last few decades which is an alarming indicator for a fragile healthcare system like ours [12]. The strategies are needed to be adopted to deal with this situation. Masses should be educated about the avoidance of repeated use of disposable syringes and unnecessary injections as well as about the use of new razor for each person at the barber shop etc.

We have already mentioned one of the limitations of our study which is the lack of data about the genotype of the HCV in our patients. In addition our study would also have been stronger if we had also included patients with Hepatitis B virus infection. This would have given us a clearer picture of HCC burden in Pakistan related to both of these viruses. The study concluded that a substantial number of HCV positive patients develop HCC, which is more common in men as compared to women. The presence of HCC is strongly associated with alcoholism, obesity, diabetes mellitus and cirrhosis.

Competing Interests

The author declares that there is no conflict of interest regarding the publication of this paper.

Author Contributions

Data collection and manuscript preparation: Nozaina Iram, Amna Akhtar, Sidra Mehmood, Saliha Tariq, Fakher Un Nisa Bhatti, Rija Zaigham.

Supervision of the data collection procedure, literature search: Imran Yousaf

Muhammad Yousaf Farooq: Statistical analysis, manuscript preparation

Conceived and designed the study, manuscript review and corrections: Zareen Fatima, Muhammad Zakir.

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