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Frequency of Portal Vein Tumor Thrombosis among Patients Presented with Hepatocellular Carcinoma

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) is one of the most common types of carcinomas and represents a significant challenge for healthcare providers around the world. Portal vein tumor thrombus (PVTT), seems to be a common complication that continues to be a barrier in the HCC treatments, which is linked to a significant rate of recurrences and a poor prognosis. **Objective:** To determine the frequency of portal vein tumor thrombosis among patients presented with hepatocellular carcinoma. **Study Design:** Descriptive Cross-sectional Study. **Settings:** This study was conducted at the inpatient department of Hepato-gastroenterology, Asian Institute of Medical Sciences, Hyderabad, Pakistan. **Duration:** Six months, from March 2019 to September 2019. **Methods:** All patients who visited to AIMS; Hyderabad were included in the study. Ultrasonography and CT scan imaging, as well as screening for alpha fetoprotein levels, were done to confirm the diagnosis of hepatocellular carcinoma. Laboratory data included hemoglobin, platelet count, AST and ALT levels, serum albumin, total serum bilirubin, gamma glutamyl transpeptidase (GGT), gamma globulin, prothrombin time with an international normalized ratio (INR), and serum creatinine to assess the portal vein tumor thrombosis. All of the information that was gathered was documented by the study's proforma, and then it was analyzed with SPSS version 26. **Results:** The mean age of the patients was 51.4±6.8 years, and the mean BMI was 63.1±7.3 kg/m^2. Out of all males were in majority (70.6%) and females were 29.4%. Portal vein tumor thrombosis was noted in 59 (42.4%) of the patients with hepatocellular carcinoma. The portal vein tumor thrombosis was statistically significant as per age, body mass index, and gender, and the p-values were quite significant (p=<0.05). **Conclusion:** It is to be concluded that portal vein tumor thrombosis is fairly common in HCC patients. Screening detects hepatocellular carcinoma at an earlier stage to reduce the rate of mortality.

Keywords: *HCC, PVTT, Prevalence.*

INTRODUCTION

Hepatocellular carcinoma seems to be the third leading cause of mortality from cancer globally, accounting for approximately 600,000 deaths each year.[1,2] Between 44 and 62% of patients with HCC have been found to have an incidence of portal vein tumor thrombus (PVTT),[3] and anywhere between 10 and 40 percent of patients overall at the time of diagnosis.[4-6]

HCC seems to have a predisposition to infiltrate the portal venous system, that ultimately resulted in PVTT; this would be usually detected with in divisions and trunk of portal vein among the 40 to 90% of individuals whose HCC is progressed at the point of initial assessment.[7] Individuals who have been diagnosed with HCC have a prognosis that is contingent not only on tumor variables but also on hepatic factors.[8] Maximum tumor diameters, the frequency of tumors, the occurrence of macroscopic PVTT, and alpha-fetoprotein concentrations are the factors that contribute to the development of the tumor.[8] Because it reflects tumor aggressiveness (invasion, and the possibilities for

malignant transformation), limits the choices for restorative resection or the transplantation, and thus can become worse residual hepatic physiology, the occurrence of PVTT may have been the single most important factor that contributed to the development of the tumor. It's also believed that approximately to 45% of cases having some kind of macroscopic PVTT.[8-10]

This form of PVTT might be large or macroscopic as indicated on the MRI or the CT scan, or it could be microscopic and will only be demonstrate pathologically. PVTT seems to be a significant determinant of whether an individual will have a relatively low rate of survival.[2,11] It has been stated that the average survival period after such a PVTT diagnosis less than three months if treatment is not administered. The prognosis for these individuals is exceedingly poor, and they have a significant risk of the mortality. If they do not receive treatment, individuals having portal venous invasions have a median survival time of 2.7–4.0 months, according to the publications that have been conducted in the past.[2,12]

Individuals having HCC who have PVTT may have a poorer prognosis as a result of a number of characteristics, such as larger tumors, higher frequent tumors, lower tumor grade, inferior hepatic physiology, as well as elevated serum concentrations of alpha-fetoprotein. It's indeed probable that all of these characteristics are working together to describe the poor hepatic function, tumor aggression, limited chemotherapy sensitivity, and increased risk of complications due to portal hypertension that have been frequently found in HCC cases who have PVTT.[1,13]

PVT's symptoms and manifestations are extremely diverse and also can range from accidental discovery during diagnostic methods for unassociated conditions to serious complications brought on by intestinal infarction or even the emergence of portal hypertension, including such variceal bleeding which can result from gastric fundal or esophageal varices because once splenic vein thrombus is observable.[14] Performing an CT Scan Liver Triphasic will aid the diagnosis and allows for the extension of the thrombosis to be determined. Despite having, high sensitivity for the diagnosis of PVTT on usual imaging, the exact prevalence of PVTT in hepatocellular carcinoma is not well evaluated in Pakistan. Despite the large number of studies on HCC, to date, no local study has evaluated the frequency of portal vein thrombosis in HCC. The aim of this study was to ascertain the frequency of portal vein tumor thrombosis in patients with HCC.

METHODS

This descriptive cross-sectional study was done at the Department of Hepato-Gastroenterology, Asian Institute of Medical Sciences, Hyderabad. The study duration was six months, from March 20, 2019 to September 19, 2019.

The sample size of 139 patients was calculated according to the formula, by taking expected proportion in population 10%,[4] with margin of error 5% and confidential level 95%.

All patients of liver cirrhosis and HCC, age between 18 years and 70 years and both genders were included.

All the patients with other intrahepatic/extrahepatic cancers, documented histories of congenital coagulation disorders, pregnant women, and those having other gastrointestinal malignancies were excluded.

Each participant was asked to provide written informed permission prior to being enrolled in the project after explaining the risk and benefit of the study. Patient was interviewed in the inpatient and outpatient department of Hepato-gastroenterology of Asian Institute of Medical Sciences Hyderabad. Each study subject underwent clinical and laboratory examinations, as well as ultrasounds and CT scan imaging, as well as screening alpha fetoprotein levels to confirm the diagnosis of hepatocellular carcinoma. Portal vein thrombosis was defined as enhancing thrombus in portal vein in venous phase of Triphasic CT Scan Liver. All the procedures were performed under the supervision of a consultant at least five years of experience. All of the information that was gathered was documented by the study's proforma, and then it was analyzed with SPSS version 26.

RESULTS

A total of 139 patients were included to determine the occurrence of portal venous tumor thrombosis in hepatocellular cancer cases. Out of all study subjects, 98 (70.6%) were males and 41 (29.4%) were females. The mean age of the patients was 51.4±6.8 years, and the mean body mass index (BMI) was 23.4±4.5 kg/m^2. (Table 1)

Table 1: Descriptive statistics of demographic characteristics (n=139)

Variables		Statistics	
Mean age		51.4 ± 6.8 years	
BMI		23.4 ± 4.5 kg/m^2	
Gender	**Males**	98	70.6%
	Females	41	29.4%

Portal vein tumor thrombosis was found to be present in 59(42.4%) patients with hepatocellular carcinoma, as shown in figure 1.

According to the stratification, the frequency of portal vein tumor thrombosis was statistically significant according to gender and BMI (p=<0.05) while statistically

insignificant according to patients' age (p=0.106) as shown in table 2.

Figure 1: Frequency of portal vein thrombosis (n=139)

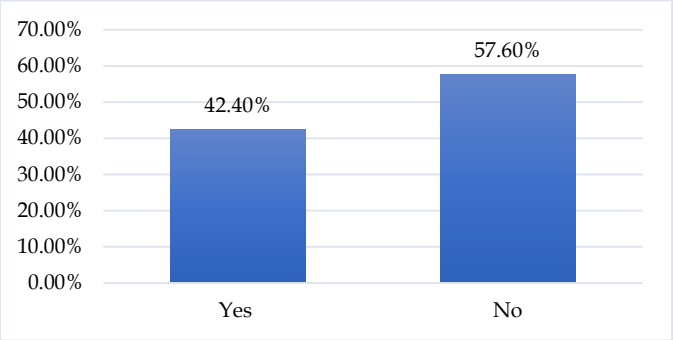

Table 2: Frequency of portal vein tumor thrombosis according to age, gender and BMI (n=139)

Variables		Portal vein tumor thrombosis		p-value
		No	Yes	
Age groups	≤ 40 years	45 (32.4%)	25 (18.0%)	0.106
	> 40 years	35 (25.2%)	34 (24.5%)	
	Total	80 (57.6%)	59 (42.4%)	
Gender	Males	64 (46.0%)	34 (24.5%)	0.004
	Females	16 (11.5%)	25 (18.0%)	
	Total	80 (57.6%)	59 (42.4%)	
BMI	≤ 24 kg/m²	58 (41.7%)	23 (16.5%)	0.001
	> 24 kg/m²	22 (15.8%)	36 (25.9%)	
	Total	80 (57.6%)	59 (42.4%)	

DISCUSSION

Hepatocellular carcinoma represents one of the commonest forms of cancerous tumors found all over the world. The presence of the PVTT, which occurs in around 35–50% of the individuals, seems to be a strong indicator of a poor prognosis.[15] This is because patients who have PVTT have an elevated risk of tumor dissemination into the bloodstream, which in turn leads to a higher risk of the recurrences.[15] In this study, a total of 139 patients were included to determine the frequency of portal vein tumor thrombosis in patients with hepatocellular carcinoma, and out of all the study subjects, 98 (70.6%) were males and 41 (29.4%) were females, with a mean age of the patients was 51.4±6.8 years and a mean body mass index (BMI) was 23.4±4.5 kg/m².

Consistently Shafqat MN *et al*[16] also conducted the study in order to determine the prevalence of PVT in patients who have been diagnosed with the disease of HCC and they found average age of the patients as 45.52 ± 5.05 years and males were in majority 72.0%, while females were 28.0%. On the other hand, ASMATULLAH UW *et al*[17] also found patients average age as 54.40±3.78 years and males were 62.0%. According to the findings of epidemiological studies, the likelihood of women developing HCC is lower as compared to males.[18] Since the prevalence of HCC is significantly higher in postmenopausal females, those had no history of hormone replacement therapy, this gender imbalance has indeed been related to female sex hormones.[18] On the other hand it has been assumed that the possibility exists that the changes are accompanied of androgen among men, in contrast to the protective effects of oestrogen in the women, contribute to the greater proportion of HCC amongst men as opposed to women.[19]

In this study, portal vein tumor thrombosis was found to be in 59 (42.4% of the patients with hepatocellular carcinoma), which was statistically significant according to gender and overweight (BMI > 24 kg/m²). These findings were slightly higher in contrast to the study of Shafqat MN *et al*[16] as the portal vein thrombosis was found in 37(29.6%) of the study subjects who had hepatocellular carcinoma. Another study reported that the PVT was developed in approximately 24% of HCC patients who had liver transplantation, and according to the findings of their findings, increased HCC stage, increased stage of the cirrhosis, elevated blood alpha-fetoprotein levels, raised levels of bilirubin, and severe vascular assaulting were all predictors of the PVT.[20]

Although Serag WM *et al*[21] reported that, after one year, the prevalence of PVT remained 20% across all patients with cirrhosis, particularly 15% in patients with cirrhosis patients who did not have HCC and at 25% amongst patients with cirrhosis patients who did have HCC. In the study of Samad M *et al*[22] also reported that the individuals who were diagnosed with HCC had a prevalence of portal vein thrombosis 28%. The frequency of portal vein tumor thrombosis was found to be slightly higher as compared to other studies, and this difference may because due to differences in study sample sizes and the severity of the disease. Recently published research evidence has led to the conclusion that PVTT is a complex clinical and the anatomical situation. This condition affects a diverse range of cases, each of whom has a unique prognosis and new treatment options available to them.[15] These factors include the degree to which the portal system is involved, the aggressiveness of the tumor biologically, the participant's clinical characteristics and sensitivity to anti-cancer treatments, the intensity to which the liver is dysfunctional, and the complications that are precipitated by portal hypertension.[15]

In accordance to the Barcelona Clinic Liver Cancer Classification, HCC is classified as having an aggressive form of disease when portal vein tumor thrombosis (PVTT) occurs, and PVTT is a common complication of HCC.[22] Nevertheless, the majority of the studies that have

been published in this field do not distinguish between various PVTT substages, and as a result, they do not take into consideration any potential changes in the individuals' prognoses. It should be noted that CT and MRI scans and procedures have undergone continual improvement, which has resulted in a situation in which it is now simpler to detect tiny PVTT.[23] Investigators should have a significant level of experience in HCC scanning and paid special attention to PVTT identification during their work.

CONCLUSION

It was to be concluded that portal vein tumor thrombosis is fairly common in HCC patients. Males and overweight patients were identified as high-risk cases. Portal vein tumor thrombosis is also a significant source of mortality in HCC patients.

LIMITATIONS

There were various limitations, the most notable of which was that, this was a single-centre analysis with a small sample size and there was also no randomization.

SUGGESTIONS / RECOMMENDATIONS

The results of the current study need to be confirmed by more research, possibly using a bigger sample size as well as more variables across other study centres throughout Pakistan.

CONFLICT OF INTEREST / DISCLOSURE

Authors have stated that there are no conflicts of interest.

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