



Original Article

Frequency of Portal Vein Thrombosis in Patients with Hepatocellular Carcinoma

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ABSTRACT

The hepatocellular carcinoma (HCC) is a frequent complication of liver. Portal vein thrombosis is common in HCC patients and associated with poor prognosis. But evidence lacks for local population. **Objective:** To assess the frequency of portal vein thrombosis in diagnosed patients of hepatocellular carcinoma presenting at DHQ hospital, Gujranwala. **Methods:** After permission from the ethical committee, this cross sectional study was done at the Department of Gastroenterology, DHQ hospital, Gujranwala from 19-03-2021 to 19-09-2021. Total 125 patients were selected from OPD. Informed consent was taken. All patients underwent Doppler ultrasound to diagnose the portal vein thrombosis. All data was analyzed in SPSS 22. **Results:** Total of 125 patients, 16.8 % (n=21) were in age group of 20-40 years and 83.2 % (n=104) were in age group of 41-60 years. Mean age was 45.52±45.05 years. Distribution of size of hepatocellular carcinoma was 4.03±0.906 cm. There were 72.0 % (n=90) male whereas 28.0% (n=35) were females. According to the type of hepatocellular carcinoma, 64.8% (n=81) had naive and 35.2% (n=44) recurrent hepatocellular carcinoma. Total of 125 patients, 64.0% (n=80) had single and 36.0% (n=45) had multiple hepatocellular carcinoma. Frequency of portal vein thrombosis was 29.6% (n=37) in patients with hepatocellular carcinoma. **Conclusions:** We concluded that portal vein thrombosis is common in patients with HCC. An early diagnosis of Portal vein thrombosis along with the evaluation of the volume of portal vein thrombosis on CT and an early intervention is necessary.

INTRODUCTION

The most frequent primary liver cancer is hepatocellular carcinoma (HCC), which is also the main cause of cancer-related death globally. In the US, HCC is the ninth most frequent cancer-related cause of death. In addition to 21,670 fatalities, 30,640 additional instances of liver and intrahepatic bile duct cancer were predicted to occur in 2013. Males developed HCC more frequently than females (2.4:1), and incidence rates were greater in Melanesia, Micronesia, Southern and Eastern Asia, Middle and Western Africa, and Melanesia [1-3]. The worldwide age distribution of HCC patients is influenced by the incidence of viral hepatitis in core population and the particular age at

which it was contracted. HCC is diagnosed around ten years earlier in high incidence locations where HBV is the most common cause and is transmitted at birth than it is in North America and Europe where the most common cause is HCV acquired later in life. Men are more likely than women to use alcohol, have HBV and HCV infections, and develop HCC. In 80 to 90% of instances, cirrhosis and HCC co-develop [4]. Cirrhosis and/or HCC are two outcomes of persistent viral hepatitis. The two most prevalent types of chronic hepatitis in the world are hepatitis B and C [5]. Portal vein thrombosis is characterized by a blood clot that prevents normal blood flow in the portal vein. Portal vein

thrombosis is most frequently caused by thrombophilic diseases, abdominal inflammation, tumor invasion, and liver cirrhosis. Portal vein thrombosis has been reported less frequently following pancreatic cancer aspiration, radiofrequency ablation for hepatocellular carcinoma, and bariatric surgery [6]. About 35%–50% of individuals develop portal vein tumor thrombosis, and 15%–30% of these cases already involve the main stem at time of identification [7,8]. Portal vein tumor thrombosis prevalence is definitely underestimated, despite the fact that it was accidentally found in 14% of biopsies collected from carcinoma patients and about 62% of autopsied livers [9]. Malignant vascular infiltration may occur in up to 30% of people with known histories of HCC, however this risk drops to 20% in those with recent diagnoses of both thrombosis and HCC [10]. Although there have been numerous studies on this subject, none have been done locally. Consequently, this study will provide us a regional estimation of the prevalence of portal vein thrombosis in people with hepatocellular cancer. The findings of this study will help healthcare professionals and policy maker's better care for patients by identifying the disease burden in our community. To assess the frequency of portal vein thrombosis in patients with hepatocellular carcinoma presenting at DHQ hospital, Gujranwala

METHODS

This Cross sectional study was done at the Department of Gastroenterology, DHQ hospital, Gujranwala from 19-03-2021 to 19-09-2021. Total 125 patients were selected, keeping 28% [11]. prevalence of portal vein thrombosis in patients presenting with HCC, 95% confidence interval and 8% margin of error. Patients were recruited by applying Non-probability consecutive sampling. Patients were enrolled if they fall in age range 20–60 years, both genders, presenting with HCC were enrolled. HCC was identified using Triphasic CT. When all of the following characteristics appear on a triphasic CT, hepatocellular carcinoma was deemed positive: Aorta illuminates during the arterial phase when contrast fills the arteries; the IVC and portal vein appear black. When contrast enters the portal vein during this phase, the portal vein becomes as bright as the aorta. In the delayed phase, the contrast drains off, so none of the liver's arteries are illuminated. Since HCCs have a robust arterial supply via the hepatic arterial system, "amplification in arterial phase and rapid contrast washout in portal venous phase are characteristics of HCC (hypodense). Patients having nodular lesion less than 3cm in size, having non-specific vascular profile on USG were excluded from the study. Written consent was obtained. Age, gender, kind, number, and size of HCC, as well as other information, were all

documented in a proforma. For the confirmation of HCC, a thorough medical history and triphasic CT were performed. All patients had USG to determine whether they had portal vein thrombosis. The presence of aberrant intraluminal echoes, which were primarily grey scale echogenic, and the absence of intraluminal color signals during color Doppler ultrasound were regarded positive signs of portal vein thrombosis. SPSS version 22.0 was used to analyze the data. Age and the size of the hepatocellular carcinoma were two quantitative criteria for which the mean and standard deviation were calculated. For gender, kind and quantity of hepatocellular carcinomas, and portal vein thrombosis, frequency and percentage were computed.

RESULTS

Out of 125 cases, 16.8% (n=21) were aged 20–40 years and 83.2% (n=104) were aged 41–60 years, thus the mean age 45.52 ± 5.05 years. Out of 125 cases, 72.0% (n=90) were males whereas 28.0% (n=35) were females. The mean size of HCC mass was 4.03 ± 0.91 cm, with 64.0% (n=80) patients had single lesion but 36.0% (n=45) had multiple lesions. Among 125 cases, 64.8% (n=81) were treatment naïve while 35.2% (n=44) had recurrent HCC Table 1.

Feature	Mean \pm SD, F (%)
Age 20–40 years	21 (16.8%)
Age 41–60 years	104 (83.2%)
Age (years)	45.52 ± 5.05
Gender	
Male	90 (72%)
Female	35 (28%)
Type of HCC	
Treatment Naïve	81 (64.8%)
Recurrent	44 (35.2%)
Number of lesions	
Single	80 (64%)
Multiple	45 (36%)
Number of lesions	
Single	80 (64%)
Multiple	45 (36%)
Size of HCC (cm)	4.03 ± 0.91 cm
3cm–6cm	44 (35.2%)
>6cm	81 (64.8%)

Table 1: Baseline Characteristics of Patients

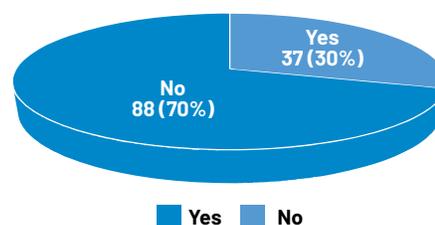


Figure 1: Distribution of portal vein thrombosis

The data was stratified for effect modifiers and it was

observed that in patients aged 20-40 years, portal vein thrombosis was 5 (23.8%) while in patients aged 41-60 years, portal vein thrombosis was 32 (30.8%) and the difference in both age groups was insignificant ($p>0.05$). In males, portal vein thrombosis was 27 (30%) while in females, portal vein thrombosis was 10 (28.6%) and the difference in both genders was insignificant ($p>0.05$). In treatment naïve patients, portal vein thrombosis was 25 (30.9%) while in patients with recurrent disease, portal vein thrombosis was 12 (27.3%) and the difference was insignificant ($p>0.05$). In patients with single lesion, portal vein thrombosis was 24 (30%) while in patients with multiple lesions, portal vein thrombosis was 13 (28.9%) and the difference was insignificant ($p>0.05$). In patients with lesion size ≤ 6 cm, portal vein thrombosis was 17 (38.6%) while in patients with lesion size >6 cm, portal vein thrombosis was 20 (24.7%) and this finding was insignificant ($p>0.05$) Table 2.

	Portal vein thrombosis		p-value
	Yes	No	
Age Group			
20-40	5	16	0.524
	23.8%	76.2%	
41-60	32	72	
	30.8%	69.0%	
Gender			
Male	27	63	0.875
	30%	70%	
Female	10	25	
	28.6%	71.4%	
Type of hepatocellular carcinoma			
Naïve	25	56	0.674
	30.9%	69.1%	
Recurrent	12	32	
	27.3%	72.7%	
Number of hepatocellular carcinoma			
Single	24	56	0.896
	30%	70%	
Multiple	13	32	
	28.9%	71.1%	
Size of hepatocellular carcinoma			
≤ 6 cm	17	27	0.103
	38.6%	61.4%	
>6 cm	20	61	
	24.7%	75.3%	

Table 2: Portal vein thrombosis compared in groups

DISCUSSION

In current study showed that out of 125 patients, 16.8 % (n=21) were in age group of 20-40 years and 83.2 % (n=104) were in age group of 41-60 years. Mean age was 45.52 ± 5.05 years. Distribution of size of hepatocellular carcinoma was 4.03 ± 0.906 cm. Gender distribution of the patients was done, it showed that 72.0 % (n=90) were male whereas

28.0% (n=35) were females. According to distribution of type of hepatocellular carcinoma, 64.8% (n=81) had naïve and 35.2% (n=44) recurrent hepatocellular carcinoma. Total of 125 patients, 64.0% (n=80) had single and 36.0% (n=45) had multiple hepatocellular carcinoma. Distribution of portal vein thrombosis was 29.6% (n=37) in HCC patients. Patients with liver cirrhosis frequently experience this dangerous consequence called portal vein thrombosis. According to one study by Alam et al., 28% of patients with hepatocellular cancer had portal vein thrombosis [11]. When compared to the general population, which has a Portal vein thrombosis, patients with liver cirrhosis have a range of 0.6% to 26%. Portal vein thrombosis has been more frequently detected in liver cirrhosis using non-invasive imaging tools like "ultrasound, computed tomography, or magnetic resonance imaging" due to its peak occurrence during the time of liver transplantation [12]. In addition to surgical options like resection and liver transplantation, non-operative methods like chemo- & radio-therapy, percutaneous ethanol injection, microwave coagulation therapy, trans-arterial chemoembolization, and radio-frequency ablation are included [13]. Another study found that malignant portal vein thrombosis, a frequent HCC consequence, had a poor prognosis. Portal vein thrombosis might be positive in about 10-40% cases at the time of initial identification of HCC. Portal vein thrombosis will be seen in 35-44% of patients with liver cirrhosis at the time of death or liver transplant [14]. In a study by Connoli et al., they observed that in about 24% cases of HCC, portal vein thrombosis developed, who underwent liver transplantation. In their investigation, advanced HCC stage, higher cirrhotic stage, raised blood α -fetoprotein, elevated Bilirubin level, and substantial vascular assault were all indicators of portal vein thrombosis. In non-transplanted patients, Portal vein thrombosis was associated with a significantly worse overall survival rate, and this difference in survival remained even after controlling the stage and Child-Pugh classification [15]. When it comes to cancer-related thrombosis, HCC presents a special set of challenges. Even in cases of cirrhosis without HCC, a sizable portion of patients experience Portal vein thrombosis [16-18]. Cirrhosis and liver failure usually precede the development of HCC, and the risk of thrombosis is frequently believed to be reduced by thrombocytopenia and coagulation abnormalities connected to hepatic failure. Though, it has been found that people with cirrhosis had a 0.5%-1.0% incidence of deep venous thrombosis and pulmonary embolism and according to research, patients with liver failure who have elevated conventional coagulation markers are not protected against thrombotic events. In fact, a lack of the body's natural anticoagulants system in

liver failure can even cause a pro-thrombotic condition [19-20]. For potentially curative ways to cure the HCC including resection, portal vein thrombosis is not the strict contraindication in many Asian guidelines. This most likely occurs as a result of underestimating the detrimental prognostic impact of a mild portal vein tumor thrombosis, at least in part. Portal vein tumor thrombosis is also frequently overlooked in imaging during routine clinical treatment [21].

CONCLUSIONS

In current study, we found that frequency of portal vein thrombosis was 29.6% (n=37) in patients with HCC. We concluded that portal vein thrombosis is common in patients with HCC an early diagnosis of portal vein thrombosis along with the evaluation of the volume of portal vein thrombosis on CT and an early intervention is necessary.

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

- [1] Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *International Journal of Cancer*. 2010 Dec; 127(12):2893-917. doi: 10.1002/ijc.25516.
- [2] O'Connor S, Ward JW, Watson M, Momin B, Richardson LC. Hepatocellular Carcinoma-United States, 2001-2006. *Morbidity and Mortality Weekly Report*. 2010; 59(17):517-20.
- [3] Crissien AM and Frenette C. Current management of hepatocellular carcinoma. *Gastroenterology & hepatology*. 2014 Mar; 10(3):153.
- [4] Mittal S and El-Serag HB. Epidemiology of hepatocellular carcinoma: consider the population. *Journal of clinical gastroenterology*. 2013 Jul; 47 Suppl(0):S2-6. doi: 10.1097/MCG.0b013e3182872f29.
- [5] Balogh J, Victor D 3rd, Asham EH, Burroughs SG, Boktour M, et al. Jr. Hepatocellular carcinoma: a review. *Journal of hepatocellular carcinoma*. 2016 Oct; 3:41-53. doi: 10.2147/JHC.S61146.
- [6] Mantaka A, Augoustaki A, Kouroumalis EA, Samonakis DN. Portal vein thrombosis in cirrhosis: diagnosis, natural history, and therapeutic challenges. *Annals of gastroenterological surgery*. 2018 Jun; 31(3):315-329. doi: 10.20524/aog.2018.0245.
- [7] Manzano-Robleda Mdel C, Barranco-Fragoso B, Uribe M, Méndez-Sánchez N. Portal vein thrombosis: what is new? *Annals of Hepatology*. 2015 Feb; 14(1):20-7.
- [8] Minagawa M, Makuuchi M, Takayama T, Ohtomo K. Selection criteria for hepatectomy in patients with hepatocellular carcinoma and portal vein tumor thrombus. *Annals of surgery*. 2001 Mar; 233(3):379-84. doi: 10.1097/00000658-200103000-00012.
- [9] Zhou Q, Wang Y, Zhou X, Peng B, Yang J, Liang L, et al. Prognostic analysis for treatment modalities in hepatocellular carcinomas with portal vein tumor thrombi. *Asian Pacific journal of cancer prevention*. 2011 Jan; 12(11):2847-50.
- [10] Piscaglia F, Gianstefani A, Ravaioli M, Golfieri R, Cappelli A, Giampalma E, et al. Bologna Liver Transplant Group. Criteria for diagnosing benign portal vein thrombosis in the assessment of patients with cirrhosis and hepatocellular carcinoma for liver transplantation. *Liver Transplantation*. 2010 May; 16(5):658-67. doi: 10.1002/lt.22044.
- [11] Alam S and Pervez R. Validity of colour doppler sonography for evaluation of portal venous system in hepatocellular carcinoma. *Journal of the Pakistan Medical Association*. 2013 Mar; 63(3):365-8.
- [12] Gîrleanu I, Trifan A, Stanciu C, Sfarti C. Portal vein thrombosis in cirrhotic patients - it is always the small pieces that make the big picture. *World Journal of Gastroenterology*. 2018 Oct; 24(39):4419-4427. doi: 10.3748/wjg.v24.i39.4419.
- [13] Cerrito L, Annicchiarico BE, Iezzi R, Gasbarrini A, Pompili M, Ponziani FR. Treatment of hepatocellular carcinoma in patients with portal vein tumor thrombosis: Beyond the known frontiers. *World Journal of Gastroenterology*. 2019 Aug; 25(31):4360-4382. doi: 10.3748/wjg.v25.i31.4360.
- [14] Ashmawy MM, Mahmoud A, El-Masry MA, Abdelaal AA. Risk factors of malignant portal vein thrombosis in cirrhotic patients with hepatocellular carcinoma. *Journal of Current Medical Research and Practice*. 2019 May; 4(2):203.
- [15] Connolly GC, Chen R, Hyrien O, Mantry P, Bozorgzadeh A, Abt P, et al. Incidence, risk factors and consequences of portal vein and systemic thromboses in hepatocellular carcinoma. *Thrombosis research*. 2008; 122(3):299-306. doi: 10.1016/j.thromres.2007.10.009.
- [16] Okuda K, Ohnishi K, Kimura K, Matsutani S, Sumida M, Goto N, et al. Incidence of portal vein thrombosis in liver cirrhosis. An angiographic study in 708 patients. *Gastroenterology*. 1985 Aug; 89(2):279-86. doi: 10.1016/0016-5085(85)90327-0.
- [17] Valla DC and Condat B. Portal vein thrombosis in adults: pathophysiology, pathogenesis and

- management. *Journal of hepatology*. 2000 May; 32(5):865-71. doi: 10.1016/s0168-8278(00)80259-7.
- [18] Ogren M, Bergqvist D, Björck M, Acosta S, Eriksson H, Sternby NH. Portal vein thrombosis: prevalence, patient characteristics and lifetime risk: a population study based on 23,796 consecutive autopsies. *World Journal of Gastroenterology*. 2006 Apr; 12(13):2115-9. doi: 10.3748/wjg.v12.i13.2115.
- [19] Northup PG, McMahon MM, Ruhl AP, Altschuler SE, Volk-Bednarz A, Caldwell SH, et al. Coagulopathy does not fully protect hospitalized cirrhosis patients from peripheral venous thromboembolism. *American journal of gastroenterology supplements*. 2006 Jul; 101(7):1524-8; quiz 1680. doi: 10.1111/j.1572-0241.2006.00588.x.
- [20] Caldwell SH, Hoffman M, Lisman T, Macik BG, Northup PG, Reddy KR, et al. Coagulation in Liver Disease Group. Coagulation disorders and hemostasis in liver disease: pathophysiology and critical assessment of current management. *Hepatology*. 2006 Oct; 44(4):1039-46. doi: 10.1002/hep.21303.
- [21] Mähringer-Kunz A, Steinle V, Kloeckner R, Schotten S, Hahn F, Schmidtman I, et al. The impact of portal vein tumor thrombosis on survival in patients with hepatocellular carcinoma treated with different therapies: A cohort study. *PLoS One*. 2021 May; 16(5):e0249426. doi: 10.1371/journal.pone.0249426