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Risk Factors, Clinical Presentation, Diagnosis, and Treatment Outcomes of Portal Vein Thrombosis: A Five-Year Hospital-Based Study From Qatar

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Abstract

Background: There is a lack of robust epidemiological information on portal vein thrombosis (PVT) in Qatar. This study aimed to describe the risk factors, clinical presentation, diagnosis, and treatment outcomes of PVT in patients with and without liver cirrhosis admitted to Hamad General Hospital.

Methods: This retrospective observational study was conducted at Hamad General Hospital, Doha, Qatar. Consecutive patients with PVT between January 1, 2015 and December 31, 2019 were included in this study.

Results: We included 363 cases representing 0.05% of all inpatients admitted to our hospital during the study period. Their mean age was 47.79 ± 14.48 years. There were 258 (71.1%) males and 105 (28.9%) females. Abdominal pain was the most common presenting symptom (160 (44.1%)), while splenomegaly was the most common presenting sign (158 (43.5%)). Liver cirrhosis was the most frequent risk factor for PVT (147 (40.5%)), while no risk factors were identified in 49 (13.5%) patients. Anticoagulant therapy was given to 171/207 (82.6%) patients with acute PVT and 19/156 (12.2%) patients with chronic PVT. The options used for anticoagulation treatment were: low molecular weight heparin (LMWH) or unfractionated heparin alone, LMWH/unfractionated heparin followed by warfarin, and direct-acting oral anticoagulants (rivaroxaban). Out of the 262 patients in whom PVT recanalization was assessed, 43.8% of the cases had recanalization after anticoagulation treatment, while 12.6% of them had spontaneous recanalization without such therapy. A comparison between different anticoagulants used in this study showed no significant difference in the effectiveness of the three regimens used. The 30-day mortality was recorded for 71 patients (19.5%). The major risk factors for 30-day mortality were: age over 45 years, male sex, hepatic failure, malignancies, and bilirubin > 34 µmol/L.

Conclusion: PVT is a rare clinical entity in Qatar with liver cirrhosis being the most common risk factor. Early administration of anticoagulation therapy is associated with a significant recanalization, while age > 45 years, male sex, hepatic failure, malignancies, and bilirubin > 34 µmol/L are independent risk factors for 30-day mortality.

Keywords: Portal vein; Thrombosis; Malignancy; Liver cirrhosis; Thrombophilia

Introduction

The portal vein is formed by the union of splenic and superior mesenteric veins, which drain the spleen and the small intestine, respectively. A total or partial restriction of portal venous blood flow due to the presence of a thrombus in the vein lumen is referred to as portal vein thrombosis (PVT) unrelated to solid malignancy. It is common in patients with cirrhosis but is less often seen in patients without cirrhosis [1]. The clinical presentation, prognosis, and management of PVT vary significantly depending on the underlying etiology, which must be identified as early as possible. Failure to do so can lead to significant morbidity and mortality resulting from a lack of timely diagnosis and/or an inappropriate workup [2].

The prevalence of PVT varies between different clinical studies depending on the types of patients, and the imaging modality used to establish the diagnosis [3]. In a post-mortem study [4], the prevalence of PVT was found to be 1%, whereas in another retrospective study, the prevalence rate of PVT was 3.7 per 100,000 inhabitants [5]. Yet another study from Italy found that the overall incident rates of PVT in a cohort of 3,535 patients were 3.8 per 100,000 inhabitants in males and 1.7 per 100,000 inhabitants in females [6]. Depending on the modality used for diagnosis in different studies, there was an obvious difference in the prevalence rate of PVT. The use of angiography was associated with a prevalence rate of 0.6%

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versus 4.4% for ultrasound and 11% for computed tomography (CT) and magnetic resonance imaging (MRI) [3].

In the state of Qatar, PVT is a recognized clinical entity which has not been studied in detail until now. This study aimed to describe the risk factors, clinical presentation, diagnosis, and treatment outcomes of patients admitted to Hamad General Hospital (HGH) with PVT.

Materials and Methods

Study design, population, and setting

This retrospective observational study was conducted at HGH, Doha, Qatar. HGH is a tertiary center that covers all specialties except for hematology-oncology and obstetrics. It includes six intensive care units, which provide a full range of clinical services in different departments of surgery and internal medicine. Consecutive patients with PVT between January 1, 2015 and December 31, 2019 were included in this study, which was approved by the Medical Research Center (MRC) at Hamad Medical Corporation (HMC) (protocol number: MRC-01-19-477).

Data source and patient selection

Patients were identified from the hospital's electronic health records (EHRs) system. All the patients 18 years of age or older, and who had complete data in their records were included in the study. The following detailed information was obtained from the EHRs of the patients: demographic data, clinical presentation, risk factors for PVT, the onset of PVT (acute or chronic), the grouping of patients, laboratory tests, the diagnostic modalities used to confirm the diagnosis, treatment, and outcomes of treatment. The patients under 18 years old or with missing data were excluded from this study.

Definitions

PVT has been classified as acute or chronic. Chronic PVT was considered in the presence of portal cavernoma (the development of myriad collateral vessels in the porta hepatis to bypass the occlusion). Whereas PVT was classified as acute when a recent intraluminal PVT was visualized for the first time with no evidence of chronic PVT [5, 7]. The presence of cirrhosis was acquired from medical records. The primary outcomes in this study involved risk factors and clinical characteristics of PVT, while the secondary outcome was 30-day mortality, which included all cases who died within 30 days following the diagnosis of PVT. Child-Pugh score system was used for stagging of cirrhotic patients.

Data analysis

All statistical analyses were performed using SPSS, version 25.0. Statistical significance was assumed at $P < 0.05$. Data were reported as means ± standard deviation (SD) for quantitative variables, while qualitative variables were described as numbers and percentages. Association between two or more qualitative variables was examined using Chi-square test or Fisher exact test as appropriate. To compare quantitative variables, we applied the unpaired' *t*-test or Mann-Whitney U test as appropriate. Multiple regression analysis was performed to determine independent factors for 30-day mortality.

Results

During the study period, we included 363 patients with PVT for whom detailed demographic and clinical data were available and were analyzed. They constituted 0.05% of total inpatient admission during the study period. Their mean age was 47.79 ± 14.48 (range: 18 - 85 years), with 258 (71.1%) males and 105 (28.9%) females. Four groups of patients were identified: non-malignant non-cirrhotic, non-malignant cirrhotic, malignant cirrhotic, and malignant non-cirrhotic (Table 1).

Clinical presentations and risk factors

Regarding the clinical presentation, the most frequent symptom was abdominal pain (160 (44.1%)), followed by nausea/vomiting (131 (36.1%)), while splenomegaly was the most frequent sign (158 (43.5%)), followed by ascites (127 (35%)). In terms of risk factors, liver cirrhosis was the most common risk factor for PVT (147 (40.5%)), followed by malignancies (108 (29.7%)) (Table 1). Hepatocellular carcinoma was the most common neoplasm, which was present in 60 (16.5%) cases, followed by pancreatic carcinoma (11 (3%)), while coagulation disorders were found in 44 (12.1%) patients (Tables 2 and 3). A single risk factor was found in 134 (36.9%) cases, and an association between more than one risk factor was observed in 180 (49.6%) patients, while no risk factors were identified in 49 (13.5%) patients. Acute PVT was found in 207 (57%) cases, whereas 156 (43%) cases had chronic PVT. Splenic vein thrombosis was observed in 101 (27.8%) patients, while superior mesenteric vein thrombosis was found in 130 (35.8%) cases.

Comparison of the clinical characteristics, laboratory findings, and outcomes in cirrhotic and non-cirrhotic patients with PVT

Our data showed that in the cirrhotic group, the patient population were slightly older as compared to the non-cirrhotics (54.36 ± 12.99 years vs. 43.62 ± 13.85 years; $P < 0.001$). Furthermore, cirrhotic patients had significantly higher rates of splenomegaly (108/147 (73.5%) vs. 50/216 (23.1%); $P < 0.001$) and ascites (97/147 (65.9%) vs. 30/216 (13.9%); $P < 0.001$) than non-cirrhotic patients. There were also significant abnormalities in liver function tests (albumin, international

Table 1. Demographic and Clinical Characteristics of 363 Patients Involved in This Study

Variables	N (%)
Age	47.79 ± 14.48 (18 - 85 years)
Sex	
Male	258 (71.1%)
Female	105 (28.9%)
Nationality	
Qatari	72 (19.8%)
Non-Qatari	291 (80.2%)
Clinical presentation	
Abdominal pain	160 (44.1%)
Nausea/vomiting	131 (36.1%)
Hematemesis	34 (9.4%)
Rectal bleeding	13 (3.6%)
Melena	38 (10.5%)
Fever	57 (15.7%)
Diarrhea	36 (9.9%)
Splenomegaly	158 (43.5%)
Ascites	127 (35%)
Esophageal varices	137/147
Hepatic failure	36/147
Intestinal ischemia	26 (7.2%)
Others	13 (3.6%)
Risk factors	
Liver cirrhosis	147 (40.5%)
Abdominal infection	69 (19%)
Cardiovascular malformation	2 (0.5%)
Myeloproliferative disorders	17 (4.7%)
Abdominal surgery	47 (12.9%)
Oral contraceptive	5 (1.4%)
Acute pancreatitis	25 (6.9%)
Coagulation disorders	48 (12.1%)
Malignancies	108 (29.7%)
Others	13 (3.6%)
Onset	
Acute	207 (57%)
Chronic	156 (43%)
Group	
Non-malignant-non-cirrhotic	184 (50.7%)
Acute/chronic	136/48
Non-malignant-cirrhotic	72 (19.8%)
Acute/chronic	20/52
Malignant-cirrhotic	75 (20.7%)
Acute/chronic	47/28
Malignant-non-cirrhotic	32 (8.8%)
Acute/chronic	23/9

Table 2. Types of Malignancies as Risk Factors for Portal Vein Thrombosis in Our Study

Tumors	N (%)
Hepatocellular carcinoma	60 (16.5)
Cholangiocarcinoma	7 (1.9)
Pancreatic carcinoma	11 (3.0)
Colon carcinoma	10 (2.8)
Gastric cancer	2 (0.5)
Appendix carcinoma	2 (0.5)
Gastrointestinal stromal tumor	1 (0.25)
Breast cancer	5 (1.4)
Carcinoma of unknown primary	10 (2.8)

normalized ratio (INR), and bilirubin) of cirrhotic patients with significantly high mortality compared to non-cirrhotic patients. On the other hand, non-cirrhotic patients had significantly higher rates of abdominal pain (185/216 (85.6%) vs. 102/147 (69.4%); $P < 0.001$), fever (42/216 (19.4%) vs. 15/147 (10.2%); $P = 0.012$), and diarrhea (29/216 (13.4%) vs. 7/147 (4.8%); $P = 0.004$) than cirrhotics. Table 4 compares cirrhotic and non-cirrhotic patients with PVT in terms of clinical features, risk factors, laboratory findings, and outcomes.

Investigations and treatment

Various imaging modalities were used to diagnose PVT in this study. Doppler ultrasound of the abdomen was used in 187 (51.5%) cases, abdominal CT with contrast in 209 (57.6%), MRI with contrast in 134 (36.9%), and angiography in five cases (1.4%). Of the acute PVT patients, 171/207 (82.6%) received anticoagulants, while 19/156 (12.2%) chronic PVT patients received anticoagulants (Table 5). Treatment regimens included low molecular weight heparin (LMWH) or unfractionated heparin alone, LMWH/unfractionated heparin followed by warfarin, and direct-acting oral anticoagulants (DOACs). These breakdown of these treatment regimens

Table 3. Coagulation Disorders as Risk Factors for Portal Vein Thrombosis in Our Study

Coagulation disorders	N (%)
Factor V Leiden thrombophilia	7 (1.9)
Protein C deficiency	10 (2.6)
Protein S deficiency	12 (3.3)
Antiphospholipid syndrome	5 (1.4)
MUTHFR mutation	2 (0.5)
Prothrombin mutation	2 (0.5)
Jak2 mutation	2 (0.5)
Antithrombin III deficiency	2 (0.5)
Homocysteinemia/B12 deficiency	1 (0.25)
Paroxysmal nocturnal hemoglobinuria	1 (0.25)

Table 4. A Comparison Between Cirrhotic and Non-Cirrhotic Patients With PVT in Relation to Clinical Presentation Laboratory Findings and Outcomes

Variables	Cirrhotic (N = 147)	Non-cirrhotic (N = 216)	P value
Age, years	54.36 ± 12.99	43.62 ± 13.85	< 0.001
Abdominal pain	102 (69.4)	185 (85.6)	< 0.001
Nausea/vomiting	60 (40.8)	100 (46.3)	0.178
Hematemesis	22 (14.9)	12 (5.6)	0.002
Rectal bleeding	5 (3.4)	8 (3.7)	0.561
Fever	15 (10.2)	42 (19.4)	0.012
Diarrhea	7 (4.8)	29 (13.4)	0.004
Splenomegaly	108 (73.5)	50 (23.1)	< 0.001
Ascites	97 (65.9)	30 (13.9)	< 0.001
Intestinal ischemia	5 (3.4)	21 (9.7)	0.016
Splenic vein involvement	25 (17.0)	76 (35.2)	< 0.001
Superior mesenteric vein involvement	27 (18.4)	103 (47.7)	< 0.001
Acute PVT	48 (32.7)	159 (73.6)	<0.001
Abdomen infection	14 (9.5)	55 (25.5)	< 0.001
Myeloproliferative disorder	2 (1.4)	15 (6.9)	0.02
Malignancy	73 (49.7)	36 (16.7)	< 0.001
Coagulation disorder	8 (5.5)	36 (16.5)	0.001
Abdominal surgery	8 (5.5)	39 (18.1)	< 0.001
Acute pancreatitis	2 (1.4)	23(10.6)	< 0.001
Albumen (g/L)	28.18 ± 8.88	33.93 ± 7.45	< 0.001
ALT (U/L)	83.89 ± 213.76	93.30 ± 346.75	0.762
AST (U/L)	159.51 ± 379.08	104.18 ± 497.04	0.253
INR	1.42 ± 0.34	1.23 ± 0.33	< 0.001
Platelets (/μL)	153.44 ± 187.91	264.64 ± 146.83	< 0.001
Hemoglobin (g/dL)	11.18 ± 2.35	12.80 ± 2.50	< 0.001
Bilirubin (μmol/L)	69.83 ± 92.01	32.44 ± 66.13	< 0.001
Mortality	45 (30.6)	26 (12.0)	< 0.001

ALT: alanine transaminase; AST: aspartate aminotransferase; PVT: portal vein thrombosis; INR: international normalized ratio.

Table 5. Treatment and Treatment Outcomes in Patients With Acute and Chronic Portal Vein Thrombosis

Onset of PVT	Treatment received		Recanalization			No recanalization	No follow-up	Death
Acute (N = 207)	Yes	171/207 (82.6%)	106 (61.9%)	Complete	85 (80.2%)	21 (12.2%)	44 (25.9%)	24 (14%)
				Partial	21 (19.8%)			
	No	36/207 (17.4%)	5 (13.9%)	Complete	2 (40%)	21 (58.3%)	10 (27.8%)	10 (27.8%)
				Partial	3 (60%)			
Chronic (N = 156)	Yes	19/156 (12.2%)	9 (47.4%)	Complete	5 (55.6%)	6 (31.6%)	4 (21%)	4 (21%)
				Partial	4 (44.4%)			
	No	137/156 (87.8%)	28 (20.4%)	Complete	19 (67.9%)	66 (48.2%)	43 (31.4%)	33 (24.1%)
				Partial	9 (32.1%)			

PVT: portal vein thrombosis.

Table 6. Distribution of Patients With Respect to the Treatment Received and Comparison Between the Outcomes of the Different Treatment Modalities for PVT Used in This Study

	Heparin alone (N = 51)	Heparin/warfarin (N = 99)	Rivaroxaban (N = 40)	P value
Distributions				
Non-malignant-non-cirrhotic (N = 128)	15 (11.7%)	84 (65.6%)	29 (22.7%)	
Non-malignant-cirrhotic (N = 28)	2 (7.1%)	15 (53.6%)	11 (39.3%)	
Malignant-cirrhotic (N = 10)	10 (100%)	0	0	
Malignant-non-cirrhotic (N = 24)	24 (100%)	0	0	
Outcomes				
Complete recanalization	22 (43.2%)	49 (49.5%)	19 (47.5%)	0.469
Partial recanalization	8 (15.7%)	12 (12.1%)	5 (12.5%)	0.821
No recanalization	14 (27.5%)	10 (10.1%)	3 (7.5%)	
No follow-up	7 (13.7%)	28 (28.2%)	13 (32.5%)	
Mortality	7 (13.7%)	20 (20.2%)	1 (2.5%)	0.027

PVT: portal vein thrombosis.

was as follows: 51 (14.1%) patients received LMWH alone, 99 (27.3%) patients received LMWH/warfarin, and 40 (11%) patients received DOACs (rivaroxaban). All patients who received rivaroxaban were non-malignant cases (11 cirrhotics and 29 non-cirrhotics) (Table 6).

The mean time for the initiation of anticoagulant therapy after diagnosis was 5.83 ± 2.66 days (range: 2 - 16 days). The mean duration of treatment was 5.74 ± 1.55 months (range: 3 - 8 months). Repeat imaging studies were performed within 3 - 10 months of diagnosis to assess portal vein recanalization in 262 (72.2%) patients, of whom 115 (43.8%) cases had recanalization after treatment, while 33 (12.6%) patients showed spontaneous recanalization without anticoagulation therapy. No major bleeding events were reported during anticoagulation therapy. The details of anticoagulant treatment and its outcomes are summarized in Tables 5 and 6. A comparison between different anticoagulants used in this study showed no significant difference in the efficacy of the three regimens (Table 6).

Table 7. Results of Univariate Analysis of Predictors of 30-Day Mortality

Variables	Unadjusted odds ratio (95% CI)	P value
Age > 45 years	4.28 (2.25 - 8.15)	< 0.001
Male sex	1.82 (1.06 - 3.13)	0.03
Presence of ascites	3.27 (1.92 - 5.58)	< 0.001
Hepatic failure	5.15 (2.52 - 10.55)	< 0.001
Liver cirrhosis	3.02 (1.77 - 5.14)	< 0.001
Malignancies	5.07 (2.93 - 8.77)	< 0.001
Low albumen (< 3.5 g/dL)	3.27 (1.74 - 6.13)	< 0.001
Anemia	3.19 (1.83 - 5.56)	< 0.001
Bilirubin > 34 µmol/L)	3.67 (2.14 - 6.27)	< 0.001

CI: confidence interval.

Outcomes, and univariate and multivariate logistic regression analysis of factors associated with 30-day mortality

The 30-day mortality was 71 cases (19.5%). Using the univariate analysis, the following variables were found to be probable predictors of 30-day mortality: age > 45 years, male sex, presence of ascites, hepatic failure, liver cirrhosis, associated malignancies, low albumin, anemia, and serum bilirubin level > 34 µmol/L (Table 7). In the multivariate analysis and after adjusting these variables, we found the following as independent risk factors for 30-day mortality: age > 45 years, male sex, hepatic failure, malignancies, and bilirubin > 34 µmol/L (Table 8).

Discussion

There is relative lack of proper studies on PVT in non-cirrhotic patients. Most of the data come from either case reports or small case series. In our current study, we report the frequency, characteristics, and outcomes of PVT in patients with and without cirrhosis in the largest tertiary hospital in Qatar.

The exact incidence of PVT worldwide is not well known. There is a wide variation in the reported prevalence rate reported in different studies. Our results show that PVT is an

Table 8. Results of Multivariate Analysis of Predictors of 30-Day Mortality

Variables	Adjusted odds ratio (95% CI)	P value
Age > 45 years	2.79 (1.39 - 5.59)	0.004
Male sex	2.31 (1.24 - 4.31)	0.008
Malignancies	3.26 (1.78 - 5.98)	< 0.001
Hepatic failure	2.94 (1.31 - 6.60)	0.009
Bilirubin > 34 µmol/L	2.21 (1.19 - 4.08)	0.01

CI: confidence interval.

uncommon clinical entity accounting for 0.05% of the total inpatient admissions in our hospital. There was a significant predominance of male patients in our study which corroborates with figures from other studies [5, 8, 9]. Similarly, our study showed that the age distribution for non-cirrhotic patients was significantly younger than cirrhotics. Our study data showed that the most common predisposing condition for PVT was liver cirrhosis, which is compatible with other reported studies [5, 8-12]. Similarly, our study data highlighted malignancies as the second most common condition associated with PVT, which also corroborates with other published studies [5, 8-11].

The role of inherited or acquired coagulation disorders as a risk factor for PVT has been documented by many authors with variable frequencies [5, 8-17]. In line with Rajani et al [5], we observed that the highest frequency of inherited or acquired coagulation disorders was found among non-cirrhotic patients compared to the cirrhotic group. Nevertheless, we observed a statistically significant difference between the two groups, unlike what's reported by Rajani et al [5].

Many authors [5, 10-13] have reported the presence of more than one risk factors in a high proportion of their patients. This fact was also consistent with our results, which showed an association between more than one risk factors in almost half (49.6%) of the patients. The coexistence of more than one risk factors suggests that PVT may be the result of combined pathogenic mechanisms attributed to these individual risk factors. On the other hand, the literature review showed that in a significant proportion (10-25%) of patients, no risk factor could be identified for PVT [4, 5, 8, 10, 11] which conforms with our study findings, which showed that almost one in seven patients (13.5%) had no identifiable risk factors. The occurrence of cases of PVT with unidentified risk factors in our study may be attributed to the fact that not all patients underwent complete screening for thrombophilia.

Our findings revealed that the clinical presentation of PVT is variable and depends mainly on the type of patients (cirrhotic vs. non-cirrhotic), which is compatible with many studies [5, 8, 9, 12]. In our study, cirrhotic patients were found to have significantly more jaundice, hematemesis, and splenomegaly at presentation compared to non-cirrhotic patients, whereas abdominal pain and fever were found to be significantly more in the non-cirrhotic group compared to the cirrhotics group, which is consistent with some clinical reports [5, 8]. Also, it was found that abdominal pain arises in patients with acute thrombosis, or with involvement of mesenteric veins which causes intestinal ischemia [2], which is consistent with our findings (Table 4). In keeping with Rajani et al [5], we also noticed more patients with ascites in the cirrhotic group than in the non-cirrhotic group (Table 4), although some studies (Al Saeed et al [8]) showed the contrary. As noted in this study and other reports [5-9], the clinical presentations of PVT are variable amongst patients and are usually non-specific. For example, abdominal pain, nausea, and vomiting are extremely common complaints in the emergency department (ED) with a wide differential range and they are not specific to PVT. However, these conditions usually require an abdominal CT scan which results in incidental detection of PVT on a radiological test that was not intended to diagnose PVT. On the other hand, in the absence of abdominal pain upon presentation, it is difficult to relate specific symptoms to PVT, making the diagnosis challenging for clinicians. Therefore, a high index of suspicion is needed especially in cirrhotic patients. Sudden clinical deterioration in a cirrhotic patient, such as the development of hepatic failure, or diuretic-resistant ascites, failure of endoscopic control of variceal bleeding, may be suggestive of the development of PVT and hence should be thoroughly evaluated [2, 3]. Additionally, as per recommended guidelines, the cirrhotic patients should have their livers screened for hepatocellular carcinoma every 6 months, and the portal vein can also be assessed concurrently at no additional expense which can be a prudent and cost-effective way to pick up PVT [18].

As there is no specific laboratory test for PVT, imaging studies including ultrasound, CT, and MRI are the main tools for the diagnosis of PVT. Although it is operator-dependent, Doppler ultrasound is the first choice as a diagnostic method. It has many advantages to use as it is widely available, is rapid, and has low cost, with high sensitivity and specificity of 89% and 92%, respectively [19]. CT and MRI provide additional information such as an extension of thrombus, evidence of bowel infarction, and status of adjacent organs [18, 19]. In our study, as noted, contrast-enhanced abdominal CT images were used more frequently than Doppler ultrasound. The reason for this behavior is unclear but could be due to the fact that contrast CT was deemed appropriate investigation in ED for patients presenting with non-specific abdmonial symptoms and an unclear diagnois.

Numerous studies have shown varying rates of spontaneous recanalization of the portal vein in non-malignant cirrhotic patients with PVT [20-24]. Our study showed spontaneous recanalization in approximately one in five (19%) of cirrhotic patients who did not receive any anticoagulation therapy. Given these findings and the lack of evidence-based guidelines, the treatment of PVT in cirrhotic patients remains a matter of debate [18]. Although controlled studies have not been conducted, convincing evidence has been obtained from observational studies, including ours, showing that rapid initiation of anticoagulation therapy results in either total or partial recanalization in a significant number of cirrhotic and non-cirrhotic patients with PVT [5, 14, 25, 26]. Moreover, a systematic review showed that more than 80% of acute PVT cases resolved with anticoagulation therapy [27]. Therefore, anticoagulation therapy should be started as early as possible to achieve recanalization and prevent further thrombosis which can lead to serious complications. The important questions to address are: the choice of anticoagulant treatment (based on safety and efficacy) and the duration of treatment.

In non-cirrhotic non-malignant patients with acute PVT, LMWH or unfractionated heparin followed by maintenance warfarin are the preferred agents [2, 5, 27, 28]. DOACs such as rivaroxaban, apixaban, or dabigatran have not been well studied in this patient population. However, a recent systematic review showed that DOACs appear to be a promising choice for the treatment of patients with PVT [29]. Anticoagulation therapy in non-cirrhotic chronic PVT has a controversial role [1-3, 28]. On the other hand, in cirrhotic patients, LMWH is the preferred anticoagulant because of its overall safety and effectiveness in these patients. Warfarin is also an option; however,

achieving and maintaining a target range of INR is the main challenge, as most cirrhotic patients have a prolonged INR due to underlying liver disease [28, 30-32]. In patients with PVT in the setting of malignancy, anticoagulation is a recommended option in most cases, except in cases of minimal thrombotic burden, active bleeding, or severe bleeding risk [33].

Our study is no exception; the controversy surrounding the treatment of patients with PVT discussed above has been reflected in the practice of our clinicians. We found that 57% of the patients with acute PVT and 12.2% of chronic PVT received anticoagulation therapy (Table 5). However, we were unable to explain why the remaining patients with acute PVT did not receive the treatment and why the patients with chronic PVT received it? Similar to other studies [5, 14, 25, 26], recanalization was observed in a sizable group of our patients. Of the 262 patients investigated for recanalization, 115 (43.8%) cases showed recanalization after receiving different treatment regimens and 33 (12.6%) patients achieved recanalization without anticoagulation therapy (Table 5). An interesting finding of this study was that DOACs were used in our study in 40 patients with a result comparable with that obtained from the utilization of warfarin and LMWH (Table 6). Very few numbers of patients were assessed for recurrence of PVT in our study, therefore, we excluded this variable.

Mortality in patients with PVT varies between 7% and 50% [5, 6, 8, 10, 20, 32, 34, 35]. This variation depends on the type of patient (cirrhotic vs. non-cirrhotic), the follow-up period (long-term vs. short-term), the presence of an associated malignancy, and treatment including liver transplantation. Rajani et al [5] reported a mortality of 43% after a follow-up period of 2.5 years, and Ageno et al [6] reported in-hospital mortality of 7.3%, while Hernandez-Conde et al [35] reported a 30-day mortality of 16.7% after liver transplantation. In our study, the 30-day mortality rate was 19.5%, which falls within the above-mentioned range. It was found that mortality among patients with PVT is related to the underlying cause and less than the consequences of portal hypertension [6, 10, 32].

Ageno et al used multivariate model for assessing the risk factors for in-hospital mortality. The only independent risk factors associated with in-hospital moratlity were age and the presence of non-abdominal solid cancer. In our study, we adjusted many variables such as age > 45 years, male sex, presence of ascites, hepatic failure, liver cirrhosis, associated neoplasm, low albumin, anemia, and high serum bilirubin level. We found that age > 45 years, male sex, hepatic failure, malignancies, and serum bilirubin level of > 34 µmol/L were the most significant independent risk factors for 30-day mortality.

There are some important limitations in our study which must be recognized. Firstly, this was a retrospective analysis with a short follow-up period of the patients. So we were unable to obtain additional information on the recurrence rates of PVT amongst these patients. Secondly, some details on the causes of liver cirrhosis were lacking in the health records perhaps due to incomplete documentation. Thirdly, it was a hospital-based study, therefore we may not be able to generalize our findings to the general population. However, this is the first study to highlight the clinical spectrum of PVT in Qatar, and we believe that our study data will complement the limited data available on PVT in the literature.

Conslusion

In conclusion, PVT is a rare clinical entity in Qatar which primarily affects male patients. Liver cirrhosis is the most common risk factor for PVT in Qatar. The clinical presentations are non-specific and the diagnosis requires a high index of clinical suspicion. Therefore, PVT should be considered in the differential diagnosis of non-specific abdominal pain, especially in patients with risk factors. Early administration of anticoagulant therapy is associated with recanalization in a significant number of patients. Age > 45 years, male sex, hepatic failure, malignancies, and serum bilirubin level > 34 µmol/L are independent risk factors for 30-day mortality. However, further prospective studies are required to support our findings.

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Conflict of Interest

None to declare.

Informed Consent

Not applicable.

Author Contributions

FYK wrote the proposal, analyzed the data, and wrote the final manuscript; EH proposed theidea and review the literature; TOS aided in the data collection and research proposal writing; OAH aided in the data collection and data entry; AA aided in data collection and the first revisionof the manuscript; AK helped in data collection and proposed the idea; MSA helped indata collection and revised the manuscript; MYA proposed the idea and aided in the data collection; YZB aided in the data collection and dataentry; WK aided in the data collection andpreparation and proposed the idea. BM aided in the data collection and data entry; RAA proposed the idea and review the literature. All authors readthe manuscript and agree to publication.

Data Availability

All data are fully available without restriction and from the corresponding author on reasonable request. However, restric-

tions apply to the availability of these data, which are used under license for the current study.

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