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Portal vein thrombosis in patients with COVID-19: A systematic review

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Title page

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Portal vein thrombosis in patients with COVID-19: A systematic review

Abstract:

Several studies have proven that COVID-19 is linked to a higher incidence of different thrombotic events. Thrombosis of the portal vein can result in portal hypertension and can extend to the mesenteric vein resulting in intestinal ischemia. A search of PubMed, Web of Science, and Scopus for relevant studies revealed an association between PVT and COVID-19. This review is structured according to PRISMA guidelines. Thirty-three studies met the inclusion criteria. Twenty-nine case studies/series and four cohort/cross-sectional studies were included. Age at diagnosis was lower when compared to PVT due to cirrhosis. In cohort/cross-sectional studies, males comprised 54.83% of subjects, whereas in case reports/series, males comprised 62.1%. Obesity, asthma, hypertension, and diabetes were the most common comorbidities identified. The majority of the thrombotic events occurred within two weeks. The treatment aimed to prevent thrombus progression and improve recanalization. According to the evidence, early intervention prevents the poor prognosis of intestinal ischemia and its propagation.

Keywords: COVID-19, portal vein Thrombosis, anticoagulants, comorbidities

1.1 Introduction

Since its breakout in December 2019, coronavirus disease 2019 (COVID-19) has caused significant morbidity and mortality¹. The disease originated as a local ailment in Wuhan and has now spread globally. As of January 2022, there were more than 280 million confirmed illnesses and 5 million fatalities².

The clinical manifestations of COVID-19 vary based on the patient's immune system, gender, and age. Many patients experience general symptoms such as fever, cough, and fatigue, whereas complications such as thrombosis, severe respiratory symptoms, heart, kidney, and multi-organ failure are less common³.

Venous thromboembolism has emerged as a significant side effect. Multiple studies have linked severe COVID-19 to arterial and venous thromboembolic disorders. Additionally, the virus appears to target endothelium cells, resulting in endothelial dysfunction⁴.

Despite extensive research into the relationship between COVID-19 and pulmonary embolism and deep vein thrombosis of the lower limb, other thrombotic events, like splanchnic vein thrombosis, are less well understood. Even in a patient with subclinical infection with COVID-19, there was a reported massive thrombus affecting the portal and superior mesenteric valves⁵.

The etiology of portal vein thrombosis (PVT) CAN be attributed to several causes. By analyzing the current data on PVT associated with COVID-19, we can highlight patient characteristics, clinical presentation, treatment, and potential outcomes.

2.1 Methods

We conducted a systematic literature search for PVT as a complication of COVID-19. The current review is structured according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA 2020 criteria) (supplementary file), and the review protocol was registered in PROSPERO (CRD42022300494).

2.2 Sources and search strategy:

The PICO characteristics of the research question used to develop the search strategy are P: Portal vein thrombosis; I: COVID-19 positive; C: none and O: clinical picture of portal vein thrombosis, diagnostic techniques, treatment methods, and case outcome.

Two independent reviewers conducted a comprehensive literature search of the Databases PubMed, web of science, and SCOPUS. In addition to the reference lists of included articles.

Two independent reviewers conducted the search between 1-1-2022 and 28-2-2022. Until the end of the data extraction period, all published and unpublished studies on PVT among COVID-19 patients were included. Hand-searching bibliography lists from all qualifying publications yielded additional papers potentially suitable for inclusion.

PUBMED Search terms keywords, mesh term as follows:

(("covid 19"[All Fields] OR "covid 19"[MeSH Terms] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH Terms] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR "coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "covid"[All Fields] OR "ncov"[All Fields]) AND ("portal"[All Fields] OR "vein"[All Fields] OR "occlusion"[All Fields] OR "portal vein"[MeSH Terms] OR "Portal vein thrombosis"[All Fields]))

2.3 Article Screening Process

Two independent reviewers conducted and reported the screening results of the title and abstract, as well as the full text. Non-relevant studies were excluded. The consensus was used to settle any disagreements.

2.4 Inclusion and exclusion criteria

Two independent reviewers analyzed studies reporting portal vein occlusion as a complication of COVID-19 with no language or publication date restrictions.

Prospective/retrospective cohort studies, cross-sectional studies, case studies, and case series were included. Studies should include the following: time of portal vein occlusion or thrombosis, clinical presentation, diagnostic studies, image confirmation, and outcome of the PVT. Animal studies, opinions, meeting abstracts, reviews, or studies with irrelevant or insufficient data were excluded. Any Disagreements were resolved by verbal discussion.

2.5 Data extraction:

Two reviewers independently extracted study data such as the author's name, the year of publication, and the study's country. In each study, demographic and clinical patient data were also obtained. Patients' extracted data include age, gender, comorbidities, method of COVID-19 diagnosis, time till PVT, presenting symptoms of PVT, CT finding of PVT, site of PVT, treatment, and outcome.

2.6 Study of Quality assessment

The quality of the included studies was determined using the critical appraisal tool for case reports developed by the Joanna Briggs Institute. Two reviewers independently conducted their assessments independently, and any disagreements were resolved through discussion and consensus.

2.7 Statistical analysis:

Data were extracted and entered into Excel sheets. The study's findings were subjected to a meta-analysis based on their quality. Categorical variables were expressed using percentages, while continuous variables were expressed using mean, standard deviation, or range of values.

3.1 Results:

The database search resulted in the importation of 293 references for screening. After removing duplicates and screening the title and abstract have been screened, we assessed 48 studies for full-text eligibility, and we found 33 that met the criteria for inclusion; therefore, they are included in this systematic review Fig (1).

Because of the possibility of study heterogeneity, the findings are presented in a narrative method.

A total of 29 case reports and case series studies (Table 1) (Table 2), as well as four cohort or cross-sectional studies (Table 3), were included in the study.

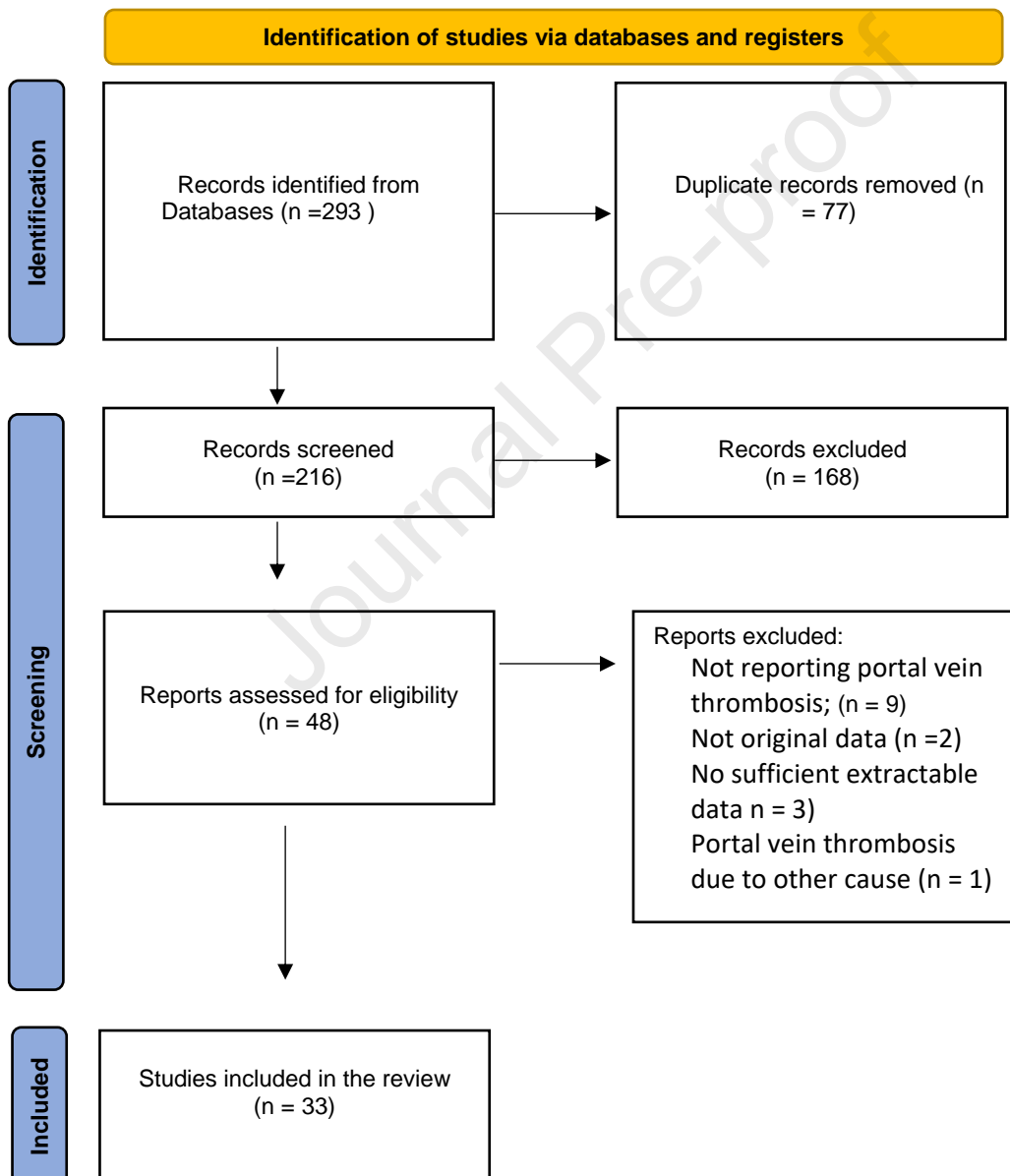


Fig (1). Flow diagram of selected studies

3.2 Case reports/series:

In the included case studies/series, there were 29 cases of PVTC reported from 14 different countries, with the United States accounting for 24.14% of these cases.

Critical appraisal tools were used to evaluate the quality of the included studies. The score ranged from 2 to 7, with a mean of 5.10 and a standard deviation of 1.291. (Supplementary file 1)

The age ranges from 3 to 82 years, with a mean of 45.1 and an SD of 19.68. Males comprised 62.1% (18 cases), while females comprised 37.3% (11 cases). COVID-19 infection was confirmed by RT-PCR, positive serology, or an image finding suggesting COVID-19 infection.

The most common presenting symptom of PVT was abdominal pain (82.76%), followed by distension (17.24%), diarrhea (17.24%), fever (17.24%), vomiting (10.34%), constipation (10.34%), and hematemesis (2 patients) 6.90%. In four cases, abdominal pain was the presenting symptom despite the absence of respiratory or flu-like symptoms. The interval between COVID-19 infections and PVT ranges from 3 to 42 days. Surprisingly, 11 (37.3%) cases have no associated comorbidities. Additionally, 62.07% of thrombophilia profile testing results were negative when investigating a plausible cause for PVT. The test findings were not reported in the other studies. No study revealed a positive test result for thrombophilia.

In addition to PVT, there is an association with the superior mesenteric vein (SMV), inferior mesenteric vein (IVM), or splenic artery thrombosis in some cases.

CT results helped diagnose PVT and other vascular occlusions, in addition to determining the presence of ascites, intestinal wall thickening, or pneumatosis and whether the liver or spleen developed parenchymal changes.

Anticoagulants were the main line of treatment in each case. Low molecular weight heparin (LMWH), enoxaparin, apixaban, rivaroxaban, fondaparinux heparin drip, and coumadin were among the anticoagulants used.

In addition to anticoagulants, intestinal ischemia may necessitate bowel resection, depending on the case. SMA thrombolysis and thrombectomy are used for thrombosis of the mesenteric artery, as reported by DeBarry 2020⁶. Interventional radiology re-cannulates the main portal vein in Petters 2021⁷. Right hepatic vein thrombosis catheter-directed thrombectomy and thrombolysis in Hussein 2021⁸. In three of the 29 cases, the outcome was not reported, and four patients died due to intestinal ischemia, severe necrosis, septic shock, and multi-organ failure MOF.

3.3 Cohort / cross-sectional studies:

The four observational studies reporting PVT were ^{9 10 11 12}, with included 53,913 COVID-19 positive cases complicated by 217 PVT.

Taquet et al.'s [10] research was conducted primarily in the United States, adopting a retrospective cohort analysis using electronic health records. In the two weeks following COVID-19 infection, the absolute risks of cerebral venous thrombosis (CVT) and PVT were examined in 53,7913 COVID-19 confirmed cases and compared to other cohorts of influenza patients and individuals who received an mRNA vaccination for COVID-19.

Out of the 537,913 cases with a COVID-19 verified diagnosis, 211 cases were diagnosed to have PVT. The mean age was 57.2 years. The females were 94 (44.5%), while the males were 117 (55.5%). Significant PVT-related comorbidities include previous PVT 117 (55.5%) and previous Liver disease 148 (70.1%).

After COVID-19, the incidence of CVT and PVT is considerably higher than in matched control cohorts. In the two weeks following COVID-19, the absolute risk of PVT was 392.3 per million (95 percent CI 342.8-448.9). When compared to a matched cohort diagnosed with influenza (N = 393,848 in each cohort, RR=1.43, 95 percent CI 1.101.88, P = 0.0094) or compared to a cohort receiving an mRNA vaccination (N = 388,298 in each cohort, RR = 4.46, 95% CI 3.12-6.37, P < 0.0001).

Muñoz et al. ⁹ is a single-cohort retrospective study on 1,127 patients hospitalized at the Infanta Leonor University Hospital. In the study, 6.1%, or 80 thrombotic events, occurred in 69 patients. Positive RT-PCR results were observed in 47 patients (68%), and COVID-19 was clinically diagnosed, and 22 patients (32%) had a clinical diagnosis of COVID-19. The thrombosis population had a median age of 65 years (range 27–96), with 65 percent of men. Venous thromboembolism VTE was the most common thrombosis, involving 71 percent of the patients (49/69) and accounting for 65 percent of the events (52/80; 44 pulmonary embolism (PE), six deep vein thrombosis (DVT), and 2 PVT). One male and one female, aged 27 and 67, were diagnosed with PVT, respectively. They received enoxaparin and were later discharged. Furthermore, despite prophylaxis, 90% of the patients in this study experienced a thrombotic episode.

In the Taya et al. ¹¹ study, imaging abnormalities before and after infection with COVID-19 were compared using contrast-enhanced CT scans of the abdomen and pelvis at a tertiary oncology hospital. The imaging was performed between three and six weeks after the COVID-19 diagnosis. For comparison, a previous CT scan imaging of the pelvis and abdomen was also required. In 63 individuals, it was common to observe new ground glass opacities at the lung bases (34 male, 29 females; mean age, 60.6 years; range, 24.4-85.0 years), accounting for 29/63, 46.0%. In addition, a new PVT (1/63, 1.6%) was discovered. A 67-year-old lady with intrahepatic cholangiocarcinoma was found to have a PVT of a right portal vein branch. Two months earlier, her CT scan was negative for PVT.

A cross-sectional, observational control study By Hassnine ¹² included 70 people with liver cirrhosis divided into two groups with matched individuals in terms of age and sex. Group A included 28 people with liver cirrhosis and COVID19, whereas group B included 42 people with hepatic cirrhosis alone as controls. In Group A (liver cirrhosis and COVID19), PVT was found in 3 cases (10.7%). These cases were not previously known to have PVT. In Group B (liver cirrhosis only), one patient (2.3%) was diagnosed with PVT. This case also has HCC. It was a statistically significant finding comparing PVT in both groups with a p-value (<0.05). The three patients were diabetic, two of them known to have Hepatocellular carcinoma HCC.

4.1 Discussion:

In approximately one-third of patients, the cause of PVT remains unknown. PVT is rare in the absence of cirrhosis. PVT may be caused by concomitant local, acquired, or inherited thrombophilic diseases in non-malignant, non-cirrhotic patients ¹³.

Patients with cirrhosis, hepatobiliary malignancies, infectious or inflammatory gastrointestinal diseases, or hematologic disorders are more likely to develop PVT ¹⁴.

In approximately one-third of PVT cases, the major contributing factor is the cirrhotic liver, accounting for 6 to 64 percent in postmortem studies ¹⁵. PVT has been linked to an uncommon but probable deficiency in protein C and protein S ¹⁵.

Infections such as viral hepatitis, cytomegalovirus (CMV), and Epstein-Barr virus have been proven to increase the incidence of splanchnic vascular thrombosis; as a result, testing for these microorganisms may be tried if no known cause of PVT is discovered. Even in immunocompetent individuals, infections such as CMV have been shown to cause PVT ¹⁴.

Respiratory viruses can influence all components of the coagulation cascade, including primary hemostasis, coagulation, and fibrinolysis, and are linked to coagulation problems and increase the incidence of DVT and PE ¹⁶.

Microvascular changes, increased number of portal vein branches associated with lumen dilatation, partial or total luminal thrombosis of the portal and sinusoidal veins, and portal tract fibrosis were all observed in COVID-19^{17 18}. Consequently, PVT is better explained by systemic inflammation and local microvascular changes in the portal venous system.

In these reviewed PVT cases, most patients had no major predisposing factors such as cirrhosis or malignancy except for a case of alcohol-related cirrhosis and a case of cholangiocarcinoma, even though both were diagnosed with COVID-19 infection. In addition, none of the comorbidities associated with the development of PVT are statistically significant.

The average age of COVID-19 patients who have had thrombotic events was 63.78 years year ^{19 20 21 22 23 24}. In the reviewed cases, PVT presented at a younger age, with the mean age of the included cohort/cross-sectional studies ranging between 57.2 ± 11.5 years in cohort/cross-sectional studies and 45.1 ± 19.68 Years in case reports/series. In addition, the age was younger when compared to PVT associated with cirrhosis ²⁵.

In cohort/cross-sectional studies, males comprised 54.83 % of participants, whereas in case reports/series, males comprised 62.1 % of participants. This finding is consistent with other studies²⁶. In cohort/cross-sectional studies, males comprised 54.83%, whereas in case reports/series, they comprised 62.1%, which is supported by other studies²⁶.

Obesity, asthma, hypertension, and diabetes were found to be the most prevalent comorbidities in this review. Nevertheless, Tomerak et al.¹ found that the comorbidities did not differ significantly between the non-thrombotic and the thrombotic groups. Li et al.²⁷ and Fujiyama et al.²⁸ studies showed higher rates of concomitant diabetes, cardiovascular disease, and hypertension. In these reviewed cases, the most common presentation was abdominal pain followed by distension, diarrhea, and fever. This result aligns with other studies^{29 30 15 14}.

The highest rates of pulmonary thromboembolism, ischemic stroke, acral ischemia, and mesenteric ischemia were observed in patients with severe COVID-19³¹. However, in a patient with preclinical COVID-19, a sizable thrombus involving the SMV was detected³¹. Thrombosis is a possibility, whatever the severity of COVID-19 is, as this review included four case studies of asymptomatic covid 19 complicated by PVT with^{32 33 34 17}. The time between COVID-19 and PVT in the case/series range between 2 days and 42 and mean 12.32+- 8.654. most thrombotic events occurred within 2 weeks^{35 36 37 27 38 39}.

CT scan is considered a preferred diagnostic tool, as it is also used to investigate the presence of signs of bowel ischemia and evaluates the extent of thrombosis in all vessels of the PV system. Other causes of thrombosis can be ruled out by thrombophilia profile testing.

Patients with COVID-19 experience acute PVT and, in most cases, do not have enough time to create adequate collaterals. Early anticoagulation can lead to recanalization in more than 80% of instances¹³. If treatment is started within one week of the onset of acute PVT, the rate of recanalization can reach 70%; however, if treatment is started later, the percentage might drop to 25–30%⁴⁰.

Different anticoagulants are the main standard of care, as evidenced in the cases analyzed. Other interventions are limited to complicated cases such as bowel ischemia. In the case of post-liver transplant PV thrombosis [7], interventional radiology was used to recanalize the PV⁷.

The goal of therapy at the time of presentation is to prevent thrombus progression and improve recanalization. Progressive thrombus propagation into more proximal veins is linked to a higher risk of intestinal ischemia and fatality^{41 42}. Invasive thrombolytic therapy efficacy was poorer, and the mortality rate was higher when compared to conservative treatment^{43 44 45 46}.

5.1 Conclusion

COVID-19 has caused considerable morbidity and mortality not just due to pneumonia and acute respiratory distress syndrome (ARDS) complications but also as a result of various extrapulmonary symptoms. Clinicians should be aware of this potential COVID-19 drawback when managing patients with PVT signs and symptoms. Linking these symptoms to a history of COVID-19 infection could facilitate the early detection of PVT. Critically ill patients with severe abdominal

pain, either as a presenting symptom or while hospitalized, are advised to undergo abdominal imaging, particularly contrast-enhanced scans.

AVAILABILITY OF DATA

The study's data are included in the article/Supplementary Material, and any further queries should be directed to the corresponding author.

Declaration of competing interest: None.

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Table(1)Case studies/case series

Study ID	Country in which the study conducted	Age in years / gender	Co-morbidity	Anticoagulant or antiplatelet intake	History of thromboembolic events
Ignat 2020	France	28 Female	NIL	NO	NO
Rodriguez-Nakamura 2020	Mexico	42 Female	Obesity, ventriculoperitoneal shunt due to a partially resected craniopharyngioma	NA	NA
deBarry 2020	France	79 Female	NIL	NA	NA
Forlemu 2021	United states	39 Female	Diabetes, hypertension and cholecystectomy	NO	NO
Kolli 2021	United states	44 Female	NIL	NO	NO
Rehman 2021	United states	33 Female	NIL		NO
Rokkam 2021	United states	66 Female	fibromyalgia, gastroesophageal reflux, traumatic brain injury, anxiety, depression, hypertension, constipation, and acute blood loss anemia, Stool positive for Clostridium difficile infection		NA
DÄ...bkowski 2021	Poland	33 Male	NIL	NA	NO
Low 2020	United states	51 Male	lower extremity deep vein thrombosis	heparin therapeutic dose for DVT	NA
Ofosu 2020	United states	55 Male	hyperlipidemia	NO	NO
Borazjani 2020	Iran	26 Male	asthma	NO	NO
Lari 2020	Kuwait	38 Male	NIL	NO	NO
LaMura 2020	Italy	72 Male	Parkinson disease, anxious-depressive syndrome, and mild vascular dementia	enoxaparin prophylactic dose	NO
Franco-Moreno 2020	Spain	27 Male	NIL	NA	
Abeysekera 2020	UK	42	chronic hepatitis B	NO	NO

Study ID	Country in which the study conducted	Age in years / gender	Co-morbidity	Anticoagulant or antiplatelet intake	History of thromboembolic events
		Male			
Vidali 2021	Italy	70 Female	NIL	NA	NA
Miyazato 2021	Japan	67 Male	diabetes, alcohol-related cirrhosis, esophageal varices	NO	NO
Marsafi 2021	Morocco	33 Male	chronic tobacco, NO history specific pathological conditions	NO	NO
Peters 2021	United states	3 Female	liver transplant recipient for treatment of Caroli disease - post liver transplant right hepatic artery and portal vein thrombosis persistent Epstein-Barr virus (EBV) DNAemia,	enoxaparin prophylactic dose	Post-transplant hepatic artery thrombosis and portal vein thrombosis
Hosoda 2022	Japan	82 Male	Coronary artery disease, diabetes, and hypertension.	Aspirin, heparin prophylaxis	NO
Jeilani 2021	UK	68 Male	chronic obstructive pulmonary disease, mild Alzheimer's dementia and recurrent urinary tract infection.	NO	NO
Rivera-Alonso 2021	Spain	51 Male	cholecystitis	NO	NO
Randhawa 2021	India	62 Female	NA	NA	NA
Agarwal 2021	India	28 Female	Post C-section	low molecular weight heparin (LMWH)	NO
Jafari 2020	Iran	26 Male	controlled asthma	NO	NO
Tripolino 2021	Italy	58 Male	NIL	NO	NO
Sinz 2021	Switzerland	38 Male	NIL	NA	NO
Hussein 2021	Saudi Arabia	20 Male	Steroid dependent nephrotic syndrome, morbid obesity, hypertension, and pulmonary embolism (PE)	NO	pulmonary embolism
Sharma 2021	India	28 MALE	NIL	NO	NO

Findings in Case studies/case series

Table (2)

Study ID	Method of diagnosis of COVID 19	Days till symptoms of PVT	Presenting symptoms of PVT	Thrombophilia profile testing	Image finding of the abdomen (ULS /CT)	Treatment of PV thrombosis	outcome	Possible cause of death
Ignat 2020	<ul style="list-style-type: none"> clinical acute respiratory distress syndrome 	NA	Abdominal pain and vomiting.	NR	SMV and PV thrombosis	Anticoagulant + small bowel resection	Discharged	
Rodriguez-NAkamura 2020	<ul style="list-style-type: none"> Negative RT-PCR test Dyspnea CT scan displayed typical signs of COVID-19 pneumonia 	9	abdominal pain and constipation	NR	CT: thrombosis of portal and mesenteric veins , abdominopelvic collection containing gas	exploratory laparotomy, jejunal perforation, Loop resection, entero-enteral manual anastomosis	Death	septic shock with renal, cardiovascular , and respiratory failure
deBarry 2020	<ul style="list-style-type: none"> Negative RT-PCR Fever and dyspnea CT scan displayed typical signs of COVID-19 pneumonia 	8	Fever, abdominal pain and diarrhea	NR	Rt. PV , SMV thrombosis extending to the spleno-mesaraic trunk, ischemia of the caecum and small intestine and ascites	Laparotomy, necrotic ileum, and right colon were resected. Thrombolysis and thrombectomy of the upper mesenteric artery	Death	extended bowel ischemia in addition to severe lung damage caused by COVID-19.
Forlemu 2021	<ul style="list-style-type: none"> chest x ray suggestive of SARS-COV2 infection confirmatory testing was positive 	3	Abdominal pain	Negative	Rt. PVT thrombosis proximal to the bifurcation	enoxaparin and later oral anticoagulants	Discharged	
Kolli 2021	<ul style="list-style-type: none"> Her COVID-19 test performed during her admission returned positive after she was discharged. Dry cough after discharge as a late presentation of her COVID-19 	14	Abdominal pain, abdominal bloating, and chest discomfort	Negative	PVT	heparin drip and coumadin on discharge	Discharged	
Rehman 2021	<ul style="list-style-type: none"> RT-PCR positive FEVER 38. 	Asymptomatic (COVID-19) and	Abdominal pain	Negative	Rt. PVT thrombosis and acute splenic infarct	enoxaparin switched to warfarin upon discharge	Discharged	

Study ID	Method of diagnosis of COVID 19	Days till symptoms of PVT	Presenting symptoms of PVT	Thrombophilia profile testing	Image finding of the abdomen (ULS /CT)	Treatment of PV thrombosis	outcome	Possible cause of death
		First presentation is abdominal pain						
Rokkam 2021	<ul style="list-style-type: none"> RT-PCR positive 	14	Watery diarrhea, abdominal pain. mild abdominal distension	NR	Lt. PVT ,moderate ascites and colitis	intravenous unfractionated heparin transitioned to apixaban	Discharged	
DÄ...bko wski 2021	<ul style="list-style-type: none"> clinical fever, headache, and anosmia 	21	Severe abdominal pain, vomiting	Negative	dilated portal vein and the absence of blood flow extending to splenic and SMV	low molecular weight heparin	Discharged	
Low 2020	NA	NR	Hematemesis	NR	a non-occlusive thrombus in the right and left portal veins, portal venous gas and gastric pneumatosis	intravenous heparin	Discharged	
Ofosu 2020	<ul style="list-style-type: none"> RT-PCR positive Fever shortness of breath, and altered mental status. CT scan and x ray: ground glass opacities 	3	Fever shortness of breath, and altered mental status.	Negative	right portal vein thrombus and liver wedge shaped peripheral defect suggestive of ischemia	apixaban	Discharged	
Borazjani 2020	<ul style="list-style-type: none"> RT-PCR positive Chest CT scan and x ray: ground glass opacities in both lung fields 	10	Hematemesis, abdominal pain with distension	Negative	Rt., Lt. portal vein was not opacified and hypo perfused areas in the Rt. And Lt. liver lobes	Enoxaparin, discharged with oral warfarin	Discharged	
Lari 2020	<ul style="list-style-type: none"> RT-PCR positive 	2	Abdominal pain, nausea, vomiting and shortness of breath	Negative	Thrombosis of the portal, splenic ,superior and inferior mesenteric veins. pulmonary embolism	jejunal segment resection, heparin anticoagulation, ECMO	Discharged	
LaMura 2020	<ul style="list-style-type: none"> Fever 	6	Fever, jaundice, mild abdominal pain with bloating and constipation	Negative	left and right portal vein hepatic attenuation in the liver segments supplied by thrombosed branches	enoxaparin	NR	

Study ID	Method of diagnosis of COVID 19	Days till symptoms of PVT	Presenting symptoms of PVT	Thrombophilia profile testing	Image finding of the abdomen (ULS /CT)	Treatment of PV thrombosis	outcome	Possible cause of death
Franco-MoreNO 2020	<ul style="list-style-type: none"> RT-PCR negative Serological test showed positive IgG and negative IgM. fever and dry cough Chest radiography and CT image shows bilateral consolidations with ground-glass surrounding in both inferior lobes. 	21	Abdominal pain	Negative	right branch of the portal vein thrombosis	enoxaparin After 4 weeks oral anticoagulant	Discharged	
Abeysekerara 2020	<ul style="list-style-type: none"> Positive Antibody serology fever and a dry cough Positive image finding 	14	Abdominal pain	Negative	entire length of PV and mid SMV thrombosis, mural edema of the distal duodenum, distal small bowel and descending colon.	apixaban	Discharged	
Vidali 2021	<ul style="list-style-type: none"> RT-PCR negative IgG positive 	7	Abdominal pain and absence of bowel movements for 8 days	Negative	Thrombosis of PV, splenic vein, SMV and IMV. splenic artery occlusion with splenic infarction	low molecular heparin (LMWH)	NR	
Miyazato 2021	<ul style="list-style-type: none"> Hypoxemia, Fever and respiratory distress 	12	NA	NR	Thrombosis of the PV main trunk extending to SMV	anticoagulant therapy	NR	
Marsafi 2021	<ul style="list-style-type: none"> RT-PCR positive 	7	Diffuse abdominal pain	NR	intraperitoneal fluid, thrombosis of PV, splenic vein, SMV Thickening, submucosal edema and parietal pneumatosis of the jejunum	surgical resection of small bowel, anticoagulant therapy	Death	Intestinal ischemia and secondary short bowel syndrome
Petters 2021	<ul style="list-style-type: none"> RT-PCR positive Fever and cough Chest radiograph demonstrated bilateral scattered lung opacities within the lower chest. 	13	Abdominal distention and diarrhea	NR	complete occlusion of the extrahepatic portal vein	re-cannulation of the main portal vein by interventional radiology, enoxaparin therapy	Discharged	

Study ID	Method of diagnosis of COVID 19	Days till symptoms of PVT	Presenting symptoms of PVT	Thrombophilia profile testing	Image finding of the abdomen (ULS /CT)	Treatment of PV thrombosis	outcome	Possible cause of death
Hosoda 2022	<ul style="list-style-type: none"> RT-PCR positive Fever 	42	Abdominal distension	NR	Rt and left portal vein thrombosis, portal venous gas, severe bowel dilatation, extensive pneumatosis intestinalis	fluid resuscitation and vasopressor died within 6 hours from the onset of the shock	Death	extensive gastrointestinal necrosis induced by excessive portal and mesenteric vein thrombosis.
Jeilani 2021	<ul style="list-style-type: none"> RT-PCR positive Cough Image finding consistent with COVID-19 pneumonia 	9	Abdominal pain and distension	Negative	PVT and SMV thrombosis, engorgement of small bowel mesenteric vessels.	low molecular weight heparin	Discharged	
Rivera-Alonso 2021	<ul style="list-style-type: none"> RT-PCR negative Fever Positive for IgG, negative for IgM, 	Asymptomatic (COVID-19) and First presentation is abdominal pain	Abdominal pain, general discomfort, and fever.	NR	left portal vein thrombosis impaired liver perfusion in the related segment, mild cholecystitis,	anticoagulant therapy	Discharged	
Randhawa 2021	<ul style="list-style-type: none"> antibody serology was positive chest peripheral ground-glass opacities consistent with COVID-19 infection 	14	Abdominal pain loss of appetite	Negative	PVT, SMV thrombosis With few periportal collaterals.	fondaparinux injection then warfarin	Discharged	
Agarwal 2021	NA	NA	Acute abdominal pain and distension	Negative	the main portal vein was not visualized, gross ascites and bilateral minimal pleural effusion	LMWH	Discharged	
Jafari 2020	<ul style="list-style-type: none"> RT-PCR positive respiratory distress and fatigue chest CT scan, including multifocal patchy Consolidations and bilateral pleural effusion 	7	Abdominal pain	NR	Portal vein thrombosis, intraperitoneal fluid, patchy enhancement of hepatic parenchyma	continuous intravenous heparin infusion	Discharged	

Study ID	Method of diagnosis of COVID 19	Days till symptoms of PVT	Presenting symptoms of PVT	Thrombophilia profile testing	Image finding of the abdomen (ULS /CT)	Treatment of PV thrombosis	outcome	Possible cause of death
Tripolino 2021	<ul style="list-style-type: none"> RT-PCR positive fever 	Asymptomatic (COVID-19) and First presentation is abdominal pain	Fever and abdominal pain	Negative	portal vein occlusion extended to superior mesenteric vein	Enoxaparin then switch to Rivaroxaban	Discharged	
Sinz 2021	<ul style="list-style-type: none"> RT-PCR negative fever and cough history of flue like symptoms Positive SARS-CoV2 IgM and IgG 	14	Abdominal pain nausea and diarrhea.	Negative	extensive portal vein thrombosis mesenteric venous stasis and enhanced small bowel segments in the left abdomen	ICU admission, continuous intravenous unfractionated heparin discharged on oral anticoagulant	Discharged	
Hussein 2021	<ul style="list-style-type: none"> Intermittently positive PCR Anosmia and ageusia Positive Ig M and Ig G 	21	Abdominal pain, Nephrotic syndrome Relapse, anasarca, diarrhea, and	Negative	portal, splenic, mesenteric, and right hepatic veins thrombosis with bowel congestion and small ascites	heparin, discharged on oral prednisone and rivaroxaban Readmission, Catheter directed thrombectomy and thrombolysis. Emergency laparotomy, bowel resection for intestinal infarction	Discharged	
Sharma 2021	<ul style="list-style-type: none"> RT-PCR positive 	Asymptomatic (COVID-19) and First presentation is abdominal pain	Abdominal pain	Negative	right and left PVT, mild HSM and ascites.	LMWH then apixaban	Discharged	

(Table 3): Cohort / cross-sectional studies

	Year	Country	Age	Male	Female	Type of study	Method of diagnosis	Number of covid cases	Number of pvt	Outcome
Muñoz-Rivas 2021	2021	SPAIN	NA	One 27 y Healthy	One 67 y hypertensive	Single-cohort retrospective study	RT-PCR] of nasopharyngeal swabs) or diagnosed on clinical grounds according to the European Centre for Disease Prevention and Control (eCDC) criteria	1127	2	discharged
Taquet 2021	2021	USA	mean (SD), y 57.2 (14.6)	117	94	retrospective cohort study	CONFIRMED	537913	211	NA
Hassnine 2021	2021	EGYPT	NA	NA	NA	cross sectional, observational control study	NA	28	3	
Taya 2021	2021	USA	76		one female 67-year-old with intrahepatic cholangiocarcinoma	retrospective cross-sectional study	NA	63	1	Discharged
Total				119	95			539131	217	
%				54.8 %	43.7 %					