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

Hany Abdelfatah El-hady a, b, *, El-Sayed Mahmoud Abd-Elwahab b, Gomaa Mostafa-Hedeab c, d, Mohamed Shawky Elfarargy e, f

a Department of Surgery, Faculty of Medicine, Jouf University, Saudi Arabia
b Department of Surgery, Faculty of Medicine for Girls, Al-Azhar University, Egypt
c Pharmacology Department, Medical College, Jouf University, Sakaka, Saudi Arabia
d Pharmacology Department, Faculty of Medicine, Beni-suef University, Egypt
e Department of Pediatrics, College of Medicine, Jouf University, Saudi Arabia
f Department of Pediatrics, Faculty of Medicine, Tanta University, Egypt

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.

1. Introduction

Since its breakout in December 2019, coronavirus disease 2019 (COVID-19) has caused significant morbidity and mortality. 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 fatalities.

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 common.

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 endothelial cells, resulting in endothelial dysfunction.

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 valves.

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. 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).

3. 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 COVID-19 patients were included. Hand-searching bibliography lists from all qualifying publications yielded additional papers potentially suitable for inclusion.

4. 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.

5. 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.

6. 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.

7. 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.

9. 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.

10. Results

The database search resulted in the importation of 293 references for screening. After removing duplicates and screening the title and abstract, 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.

11. 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 compromised 62.1% (18 cases), while females compromised 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 (IMV), 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 pneumatosi 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 thrombosis and thrombectomy are used for thrombosis of the mesenteric artery, as reported by DeBarry 2020. 3 Interventional radiology re-cannulates the main portal vein in Petters 2021. 7 Right hepatic vein thrombosis
catheter-directed thrombectomy and thrombolysis in Hussein 2021. 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.

12. Cohort/cross-sectional studies

The four observational studies reporting PVT were 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 53,791 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 (55.5%) and previous Liver disease (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 1.10–1.88, 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).

Munoz et al.’s [17] is a single-cohort retrospective study on 1127 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,
| Study ID | Country in which the study conducted | Age in years | Co-morbidity | Anticoagulant or antiplatelet intake | History of thromboembolic events |
|----------|--------------------------------------|-------------|--------------|-------------------------------------|----------------------------------|
| Ignat 2020 | France | 28 | NIL | NO | NO |
| Rodriguez-Nakamura 2020 | Mexico | 42 | Obesity, ventriculoperitoneal shunt due to a partially resected craniopharyngioma | NA | NA |
| deBarry 2020 | France | 79 | NIL | NA | NA |
| Forlemu 2021 | United states | 39 | Diabetes, hypertension and cholecystectomy | NO | NO |
| Kolli 2021 | United states | 44 | NIL | NO | NO |
| Rehman 2021 | United states | 33 | NIL | NO | NO |
| Rokkam 2021 | United states | 66 | Fibromyalgia, gastroesophageal reflux, traumatic brain injury, anxiety, depression, hypertension, constipation, and acute blood loss anemia, Stool positive for Clostridium difficile infection | NA | |
| DA...lkowski 2021 | Poland | 33 | NIL | NA | NA |
| Low 2020 | United states | 51 | Lower extremity deep vein thrombosis | heparin therapeutic dose for DVT | NA |
| Ofosu 2020 | United states | 55 | Hyperlipidemia | NO | NO |
| Borazjani 2020 | Iran | 26 | Asthma | NO | NO |
| Lari 2020 | Kuwait | 38 | NIL | NO | NO |
| LaMura 2020 | Italy | 72 | Parkinson disease, anxious-depressive syndrome, and mild vascular dementia | enoxaparin prophylactic dose | NO |
| Franco-Moreno 2020 | Spain | 42 | Chronic hepatitis B | NO | NO |
| Abeysekera 2020 | UK | 70 | NIL | NA | NA |
| Vidal 2021 | Italy | 67 | Diabetes, alcohol-related cirrhosis, esophageal varices | NO | NO |
| Miyazato 2021 | Japan | 33 | Chronic tobacco, NO history specific pathological conditions | NO | NO |
| Marsafi 2021 | Morocco | 3 | 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 | NO |
| Petters 2021 | United states | 68 | Coronary artery disease, diabetes, and hypertension, chronic obstructive pulmonary disease, mild Alzheimer's dementia and recurrent urinary tract infection. cholecystitis | Aspirin, heparin prophylaxis | NO |
| Hosoda 2022 | Japan | 51 | NA | NA | NA |
| Jeilani 2021 | UK | 62 | Controlled asthma | low molecular weight heparin (LMWH) | NO |
| Rivera-Alonso 2021 | Spain | 28 | Post C-section | NO | NO |
| Randhawa 2021 | India | 26 | NA | NA | NA |
| Agarwal 2021 | India | 58 | Steroid dependent nephrotic syndrome, morbid obesity, hypertension, and pulmonary embolism (PE) | NO | pulmonary embolism |
| Jafari 2020 | Iran | 38 | NIL | NO | NO |
| Tripolino 2021 | Italy | 40 | NIL | NO | NO |
| Sinz 2021 | Switzerland | 20 | NIL | NA | NO |
| Hussein 2021 | Saudi Arabia | 28 | Steroid dependent nephrotic syndrome, morbid obesity, hypertension, and pulmonary embolism (PE) | NO | NO |
| Sharma 2021 | India | 28 | MALE | NO | NO |
Table 2
Findings in Case studies/case series.

| 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        | clinical acute respiratory distress syndrome                                                 | NA                        | Abdominal pain and vomiting.                   | NR                                      | SMV and PV thrombosis                                                                        | Anticoagulant + small bowel resection                                                       | Discharged               |                                                                                        |
| Rodriguez-Nakamura 2020 | 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, enteroenteral manual anastomosis | Death                    | septic shock with renal, cardiovascular, and respiratory failure                       |
| deBarry 2020      | 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-mesenteric trunk, ischemia of the caecum and small intestine and ascites | Laparotomy, necrotic ileum, and right colon were resected. Thrombolyis and thrombectomy of the upper mesenteric artery | Death                    | extended bowel ischemia in addition to severe lung damage caused by COVID-19.           |
| Forlemu 2021      | chest x ray suggestive of SARS-COV2 infection confirmatory testing was positive 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 | 3                         | Abdominal pain                                  | Negative                               | Rt. PVT thrombosis proximal to the bifurcation                                               | enoxaparin and later oral anticoagulants                                                   | Discharged               |                                                                                        |
| Kolli 2021        | 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       | RT-PCR positive FEVER 38. Asymptomatic (COVID-19) and First presentation is abdominal pain | 21                        | Abdominal pain                                  | Negative                               | Rt. PVT thrombosis and acute splenic infarct                                                 | enoxaparin switched to warfarin upon discharge                                           | Discharged               |                                                                                        |
| Rokkam 2021       | RT-PCR positive FEVER 38. Asymptomatic (COVID-19) and First presentation is abdominal pain | 14                        | Watery diarrhea, abdominal pain, mild abdominal distension | NR                                      | Lt. PVT, moderate ascites and colitis                                                        | intravenous unfractionated heparin transitioned to apixaban                              | Discharged               |                                                                                        |
| DA … blokowski 2021 | 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 a non-occlusive thrombus in the right and left portal veins, portal venous gas and gastric pneumonia | low molecular weight heparin                                                              | Discharged               |                                                                                        |
| Low 2020          | NA                                                                                         | NR                        | Hematemesis                                     | NR                                      |                                                                                              |                                                                                              |                                                                                       |                                                                                        |
| Ofosu 2020        | 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    | RT-PCR positive Chest CT scan and x ray: ground glass opacities in both lung fields         | 10                        | Hematemesis, abdominal pain with distension    | Negative                               |                                                                                              | enoxaparin, discharged with oral warfarin                                                  | Discharged               |                                                                                        |

(continued on next page)
| 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 |
|-----------------|---------------------------------|---------------------------|---------------------------|-------------------------------|--------------------------------------|-----------------------------|---------|------------------------|
| Lari 2020       | 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 left and right portal vein hepatic attenuation in the liver segments supplied by thrombosed branches | Jejunal segment resection, heparin anticoagulation, ECMO | Discharged |                        |
| LaMura 2020     | Fever                           | 6                         | Fever, jaundice, mild abdominal pain with bloating and constipation | Negative                      | Abdominal pain                     | Exenaparin                  | NR      |                        |
| Franco-MoreNO2020 | RT-PCR negative, Serological test showed positive IgG and negative IgM, fever and dry cough | 21                        | Diffuse abdominal pain | Negative                      | Abdominal pain                      | Exenaparin                  | After 4 weeks oral anticoagulant | Discharged |                        |
| Abeysekera 2020 | Positive Antibody serology fever and a dry cough | 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     | 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   | Hypoxemia, Fever and respiratory distress | 12                        | NA                        | NR                            | Thrombosis of the PV main trunk extending to SMV intraperitoneal fluid, thrombosis of PV, splenic vein, SMV Thickening, submucosal edema and parietal pneumatosis of the jejunum | Anticoagulant therapy | NR      |                        |
| Marsafi 2021    | RT-PCR positive                 | 7                         | Diffuse abdominal pain | NR                            | Death Intestinal ischemia and secondary short bowel syndrome | Surgical resection of small bowel, anticoagulant therapy | Death | Intestinal ischemia and secondary short bowel syndrome |
| Petters 2021    | RT-PCR positive, Fever and cough | 13                        | Abdominal distention and diarrhea | NR                            | Death Intestinal ischemia and secondary short bowel syndrome | Re-cannulation of the main portal vein by interventional radiology, enoxaparin therapy | Discharged |                        |
| Hosoda 2022     | RT-PCR positive, Fever          | 42                        | Abdominal distension | NR                            | Extensive gastrointestinal necrosis induced by excessive portal and mesenteric vein thrombosis | Fluid resuscitation and vasopressor died within 6 h from the onset of the shock | Death | Extensive gastrointestinal necrosis induced by excessive portal and mesenteric vein thrombosis |
| Jeilani 2021    | RT-PCR positive, Cough          | 9                         | Abdominal pain and distension | Negative                      | PVT and SMV thrombosis, engorgement of small bowel mesenteric vessels. | Low molecular weight heparin | Discharged |                        |
| Author   | Year | Symptoms                                      | Imaging Findings                                      | Treatment                                                                 | Disposition         |
|----------|------|-----------------------------------------------|-------------------------------------------------------|---------------------------------------------------------------------------|---------------------|
| Rivera-Alonso 2021 | Fever Positive for IgG, negative for IgM, First presentation is abdominal pain | Abdominal pain, general discomfort, and fever.       | left portal vein thrombosis impaired liver perfusion in the related segment, mild cholecystitis, PVT, SMV thrombosis With few periportal collaterals. | fondaparinux injection then warfarin | Discharged         |
| Randhawa 2021   | antibody serology was positive chest peripheral ground-glass opacities consistent with COVID-19 infection | Abdominal pain loss of appetite Negative            | the main portal vein was not visualized, gross ascites and bilateral minimal pleural effusion Portal vein thrombosis, intraperitoneal fluid, patchy enhancement of hepatic parenchyma | continuous intravenous heparin infusion | Discharged         |
| Agarwal 2021    | NA   | Acute abdominal pain and distension Negative  | Acute abdominal pain and distension                   | LMWH                                                                      | Discharged         |
| Jafari 2020     | RT-PCR positive respiratory distress and fatigue chest CT scan, including multifocal patchy Consolidations and bilateral pleural effusion | Abdominal pain NR | Acute abdominal pain and distension                   | continuous intravenous heparin infusion | Discharged         |
| Tripolino 2021  | RT-PCR positive fever | Abdominal pain | Abdominal pain | Continuous intravenous heparin Patchy enhancement of hepatic parenchyma | Discharged         |
| Sinz 2021       | RT-PCR negative fever and cough history of flue like symptoms Positive SARS-CoV2 IgM and IgG | Fever and abdominal pain Negative | Fever and abdominal pain | LMWH                                                                      | Discharged         |
| Hussein 2021    | Intermittently positive PCR Anosmia and ageusia Positive Ig M and Ig G | Abdominal pain, Nephrotic syndrome Relapse, anasarca, diarrhea, and | Abdominal pain, Nephrotic syndrome Relapse, anasarca, diarrhea, and | Enoxaparin then switch to Rivaroxaban | Discharged         |
| Sharma 2021     | RT-PCR positive | Abdominal pain Negative | Abdominal pain | right and left PVT, mild HSM and ascites.             | Discharged         |
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 Hassnine12 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 COVID-19, whereas group B included 42 people with hepatic cirrhosis alone as controls. In Group A (liver cirrhosis and COVID-19), 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 Hepato-cellular carcinoma HCC.

13. 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 post-mortem 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.15

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.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 studies.26 In cohort/cross-sectional studies, males compromised 54.83%, whereas in case reports/series, they compromised 62.1%, which is supported by other studies.26

Obesity, asthma, hypertension, and diabetes were found to be the most prevalent comorbidities in this review. Nevertheless, Tomerak et al. 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-19.31 However, in a patient with...
preclinical COVID-19, a sizable thrombus involving the SMV was detected. \(^\text{3,5} \) Thrombosis is a possibility, whatever the severity of COVID-19 is, as this review included four case studies of asymptomatic covid 19 complicated by \(^{32} 33 34 35 \) The time between COVID-19 and PVT in the case/series range between 2 days and 42 and mean 12.32 days. \(^\text{36} \) Most thrombotic events occurred within 2 weeks.\(^\text{35} 36 37 27 38 39 \) 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.\(^\text{41} 42 \) Thrombolytic therapy efficacy was poorer, and the mortality rate was higher when compared to conservative treatment.\(^\text{43} 44 45 46 \)

14. 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 extra pulmonary 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.

15. 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.

16. Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajjspir.2022.11.002.

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