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A Retrospective Study of Surgical Emergencies during COVID-19 Pandemic due to Thrombotic Complications in SVS Institute

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Abstract: ***Background: To know the incidence of thrombotic events leading to surgical emergencies in COVID patients in SVS Medical college and hospital, during COVID pandemic. Methods: A structured retrospective study was conducted during first and second wave of pandemic in our institute. Data of the patients who presented to the casualty with surgical emergencies such as acute bowel ischemia, acute ischemia limb, Deep vein thrombosis, Portal vein thrombosis, was collected and diagnosis was established by consecutive analysis of all investigations performed. Results: Of all the abdominal emergencies eight cases, one case of bilateral lower limb ischemia, one case of unilateral upper limb ischemia, ten cases of Deep vein thrombosis were found to be positive for COVID19. Conclusion: The incidence of surgical emergencies during COVID-19 pandemic due to thrombotic complications in our institute over a period of 2yrs is 3.83%.***

Keywords: COVID19, Thrombosis, surgical emergencies, Abdominal pain, Acute bowel ischemia, Arterial and venous thrombosis, CT Scan, RTPCR, Rapid antigen test for COVID-19, SVS Medical college and hospital.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is commonly complicated with pro thrombotic state and endothelial dysfunction. Excess of venous thromboembolic events such as deep vein thrombosis, pulmonary embolism (PE), portal vein thrombosis have been described in patients suffering from COVID-19. However arterial thrombosis like limb ischemia, mesenteric ischemia are rarely described in the settings and are underestimated.

Here we report our multicentric experience with patients suffering from both arterial and venous thromboembolic events during COVID-19 pandemic in our institution (SVS medical college and Hospital).

Aims and Objectives
To know the incidence of thrombotic events leading to surgical emergencies in COVID patients in our institute during COVID-19 pandemic.

2. Materials & Methods

A structured retrospective study was conducted during first and second wave of pandemic in our institute. Data of the patients who presented to the casualty with surgical emergencies such as Acute appendicitis, Acute intestinal obstruction, Hollow viscus perforation, Deep vein thrombosis, Gangrene of limbs were collected and diagnosis was established by consecutive analysis of CT scan, Rapid Antigen Test for COVID-19/ RTPCR performed. This study was done in the department of general surgery in a tertiary care centre that has round the clock availability of all radiological investigations apart from all other required investigations. This study was performed according to the guidelines of the ethical committee of the institute. The data was tabulated and results were expressed using statistical package for the social sciences (SPSS) software.

3. Design

This was a retrospective study conducted in SVS MEDICAL COLLEGE AND HOSPITAL, Mahabubnagar.

Duration:
The duration of the study was from August 2020 to August 2022.

Inclusion Criteria:
All the patients presenting with surgical emergencies with RAT negative were included in this study.

Exclusion Criteria:
Traumatic emergencies were excluded from the study. Patients who were giving similar complaints in the past before COVID pandemic were excluded from the study.

4. Results

The study sample was taken from the patients who were admitted in the hospital with surgical emergencies. Thorough history was taken from the patients regarding COVID-19 symptoms and past history of exposure to COVID-19 was also noted. As study was conducted during COVID-19 pandemic all the patients who came to the emergency department were screened for COVID-19 using Rapid Antigen Test for COVID-19, RTPCR and HRCT Chest. Those who were negative for COVID-19 with RAT and HRCT Chest were included in the study.

Those patients with sudden onset abdominal pain, fever, vomiting, abdominal distension, gangrene of toes with cellulitis changes, calf muscle tenderness were examined. They were clinically examined for pulse, blood pressure, abdominal distension, tenderness, guarding, rigidity and other clinical signs of peritonitis, symptoms of limb ischemia. After initial assessment and resuscitation, patients were subjected to haematological and radiological investigations.

Patients who were haemodynamically stable were subjected to contrast enhanced computed tomography (CECT) abdomen, Doppler study, CT Angiogram, RTPCTR.

Patients who were haemodynamically unstable or had signs of peritonitis on clinical examination were subjected to laparotomy after confirming the diagnosis with necessary radiological and hematological investigations and RAT/HRCT Chest to rule out COVID-19.

Patients who were haemodynamically unstable or had signs of sepsis on clinical examination were subjected to amputation after confirming diagnosis with necessary radiological and haematological investigations and COVID-19 with RAT/HRCT chest.

In our study,

- A total of 600 patients with surgical emergencies were included.
- Out of 600 patients, 435 were males and 165 were females. Maximum patients were found in the age group of 40-60years. (Table 1).

Table 1: Age distribution of the patients with surgical emergencies

S. No	Age	Male	Female	Total	%
1	<20	35	25	60	10
2	21-40	140	60	200	33.3
3	41-60	190	70	260	43.3
4	>60	60	20	80	13.3

Table 2: Distribution of patients according to cause of surgical emergencies

S.No	Cause	Male	Female	Total	%	COVID +ve with thrombotic complications (RTPCR, RAT +ve)
1	Acute Appendicitis	285	110	399	66.5	3(0.75%)
2	Hollow viscus perforation	52	4	56	9.3	2(3.5%)
3	Acute intestinal obstruction	19	20	39	6.5	3(7.6%)
4	Deep vein thrombosis	34	14	48	8	10(20.8%)
5	Gangrene of limbs	40	17	57	9.5	2(3.5%)
6	Portal vein thrombosis	0	1	1	0.166	1(100%)

Of all abdominal emergencies, **eight** cases were found to be positive for COVID-19 either before or during the disease, among those three were found to be mesenteric arterial thrombosis. **One** case of bilateral lower Limb ischemia due to extensive thrombosis of infrarenal aorta, common and external iliac arteries was found to be COVID positive 1 month before the manifestation.

One case of Unilateral upper limb ischemia due to thrombosis at Axillary artery was found, for which above elbow amputation was done. This patient was positive for COVID-19 and had treatment at government hospital 2months back.

Ten cases of Deep vein thrombosis, **One** case of Portal vein thrombosis were found to be positive for COVID positive

Table 3: Characteristics of 21 patients with thrombotic events :

Characteristics	All(n=21)	Abdominal emergencies(n=8)	Venous Thrombosis (n=11)	Arterial Thrombosis(n=2)
Median Age	62	60	59	65
Male Sex	15	6	7	2
RISK FACTORS				
Hypertension	7	4	2	1
Dyslipidemia	5	3	1	1
DM	4	1	2	1
Obesity	3	0	2	1
Previous DVT	1	0	1	0
PAD	2	0	1	1
Median laboratory values at the time of event				
D-Dimer (mg/ml)	2725	890	4700	3900
CRP (mg/dl)	92(22-146)	26 (16-146)	105(73-127)	114(69-277)
Ferritin (g/l)	1162(848-4163)	689(537-951)	1270(978-2231)	2000(1225-2891)

5. Discussion

1) Pathophysiology:

SARS-CoV-2 is a single stranded RNA virus that belongs to the Cornaviridae family, which it shares with severe acute respiratory syndrome corona virus(SARS-CoV-1)and the Middle East respiratory syndrome coronavirus (MERS-CoV)[1, 4].SARS-CoV-1, MERS, and SARS-CoV-2 all bindto angiotensin-converting enzyme 2(ACE-2), which is a crucial counter regulatory enzyme that converts angiotensin I to angiotensin II[5, 6]. ACE-2 is present in nearly all human tissues, including but not limited to endothelial cells from small and large arteries and veins, type I and type II alveolar epithelial cells in lungs, and in the nasal and oral mucosa and the nasopharynx[6]. SARS-CoV-2 has a higher binding affinity for human ACE-2 compared to SARS-CoV-1, which likely contributes to its increased rate of virulence and transmission[7, 8]. Angiotensin I, when not broken down by ACE-2, promotes an inflammatory state in the body, as well as causing vasoconstriction, sodium retention, and fibrosis throughout the body[9-11]. Besides inhibiting ACE-2, COVID-19 may also cause down regulation of the enzyme, based on data from SARS-CoV-1[12]. This culminates in a diffuse inflammatory state as evidenced by higher plasma levels of cytokines such as IL-2, IL-7, IL-10, granulocyte colony-stimulating factor, IgG induced protein 10, monocyte chemoattractant protein-1, macrophage inflammatory protein 1-alpha, and tumor necrosis factor α[13]. Recent

studies have evaluated the role of inflammation in creating hypercoagulable states, possibly via activation of endothelial cells, platelets, and leukocytes inducing tissue factor (TF), and subsequently triggering the coagulation system through binding to the clotting factor VIIa[14, 15]. This milieu creates hypercoagulability as evidenced by decreased reaction (R) and K values, and increased values of K angle and maximum amplitude (MA) when using thromboelastography (TEG) and the apparent increased incidence of thrombotic events[16]. TEG and rotational thromboelastometry (ROTEM) are viscoelastic assays performed on whole blood that assess time to clot formation, clot strength, and time to clot lysis. These assays are advantageous in that they assess platelets, fibrinogen, and coagulation factors in a single assay. The R value is the time to initial clot formation, the K value and angle reflect the speed of clot formation, and the MA is a measure of clot strength on TEG. Interestingly, an autopsy study of the lungs in 10 patients with COVID-19 found microvascular platelet-rich depositions in the small vessels of the lungs reminiscent of thrombotic microangiopathy.

2) Acute Limb Ischemia

Acute limb ischemia (ALI) is an important consideration in patients with COVID-19. There have been over a dozen case reports and case series of ALI described in the literature[17, 18, 19, 20]. These patients often have multiple thromboses involving different vessels throughout their bodies. Many of these patients do not have existing peripheral arterial disease[25]. Acute limb ischemia can even occur among patients already receiving thromboprophylaxis[25]. Symptoms can include acute limb pain, focal hypothermia, skin mottling, absent pulse, or necrosis of the toes. Patients generally have an elevated D-Dimer and may also have an elevated C-reactive protein (CRP)[18]. While a computed tomographic angiogram (CTA) of the extremity is often performed, clinicians should consider adding a CTA of the aorta to evaluate for a concomitant aortic thrombosis. Treatment involves vascular surgery and interventional radiology consultation, as well as empiric systemic anticoagulation. One study of 20 patients found that operative treatment was performed in 17 patients and was able to successfully salvage the limb in 12 (70.6%).

3) Abdominal and Thoracic Aortic Thrombosis:

Acute abdominal and thoracic aortic thrombosis has also been described in patients with COVID-19. Similar to acute limb ischemia, this has been described in patients who are already receiving thromboprophylaxis[21, 22]. This has also been described in a patient with an aortic graft[22].

Symptoms include unilateral distal limb ischemia, bilateral distal limb ischemia[21, 22], bilateral lower extremity weakness, bilateral lower extremity loss of sensation[21], and acute periumbilical abdominal pain. Labs are notable for a markedly elevated D-Dimer level, with a greater than 16-fold increase in one study. An elevated CRP has also been reported. Treatment involves systemic anticoagulation and consultation with vascular surgery or interventional radiology.

4) Mesenteric Ischemia

Mesenteric ischemia is a less common occurrence with significant morbidity and mortality. This has been described in three case reports of patients with COVID-19[23, 24]. Symptoms can include abdominal pain[23, 24], vomitings[23], or diarrhoea[24]. Labs may demonstrate an elevated D-Dimer or an elevated CRP[23, 24]. Imaging should include a CTA of the mesenteric vessels, as a regular CT of the abdomen and pelvis with contrast may not identify this, particularly early in the course of symptoms. Treatment should include systemic anticoagulation and consultation with general surgery, as well as either interventional gastroenterology or interventional radiology.

5) Venous Thromboembolism

As the clinical picture of COVID-19 infection continues to emerge, venous thromboembolism (VTE) is a serious risk, particularly in severe disease. Research has already established that hospitalized patients are prone to deep venous thrombosis (DVT) development. Multiple studies have demonstrated increased rates of DVT in COVID-19 patients. A systematic review and meta-analysis of 20 studies comprising 1988 patients with COVID-19 found a weighted mean prevalence (WMP) of 31.3% for VTE with a WMP of 19.8% for DVT and WMP of 18.9% for pulmonary embolism (PE).

In hospitalized patients not receiving prophylaxis, rates are approximately 0.9% for general admission and 15% to 32% among ICU patients. A German study performed consecutive autopsies of 12 deceased patients with COVID-19, finding bilateral DVTs in 7 (58%) cases, none of which were suspected before death. Another study prospectively analyzed venous ultrasound exams on 34 consecutive patients admitted to the ICU with COVID-19 finding DVTs in 22 patients (65%), with 18 patients having bilateral DVTs. On systematic evaluation 48 h after admission, the authors also found that an additional five developed DVTs despite adequate prophylactic anticoagulation. Another retrospective review of 26 consecutive ICU patients in France found DVTs in 18 patients (69%) receiving anticoagulation.

Patients hospitalized on the general medical floors also demonstrate an increased risk of DVT. A retrospective review of 71 non-ICU patients in France who received systematic lower extremity doppler exams prior to discharge found 16 patients (22%) developed DVT despite thromboprophylaxis with weight-based enoxaparin[26].

Similar to DVT, studies have also demonstrated a high rate of PE occurrence in patients with COVID-19. Post-mortem examination of 21 consecutive patients in Switzerland found PEs in four (19%) of the patients. A similar autopsy study in Germany found PE was present in 42% of deceased patients, with PE being the cause of death in onethird of patients. Multiple studies have also demonstrated a high prevalence of PE in ICU patients hospitalized with COVID-19. A study of 184 consecutive ICU patients with COVID-19 demonstrated confirmed VTE in 27% of patients by CTPA or compression duplex ultrasonography. The majority (81%) of VTE were PE despite standard pharmacological thromboprophylaxis. Another review of 150 ICU patients found the most significant thromboembolic complication among patients was PE (16.7%)[2]. This same study compared a subgroup of patients with COVID-19 acute respiratory

distress syndrome (ARDS) to non-COVID-19 ARDS and found PE rates were significantly higher in the COVID-19 ARDS group, 12% and 2%, respectively[8]. A case series of 107 consecutive patients admitted to the ICU in France demonstrated a PE rate of 20.6%[3]. The authors retrospectively reviewed ICU patients during the same period from the previous year and found a PE rate of 6.1% suggesting patients with severe COVID-19 infections are at higher risk than other non-COVID-19 critically ill patients[3].

Outside of the ICU, studies have demonstrated PE rates of 10% to 22%[26]. A retrospective chart review of 327 general floor patients noted 44 patients were tested for VTE with an overall positive rate of 6.4%. A retrospective review of 71 non-ICU COVID-19 patients in France revealed a PE rate of 10% despite receiving adequate thromboprophylaxis. The authors noted a d-dimer threshold of 10, 000 µg/L was only moderately predictive of VTE (negative predictive value 90%, positive predictive value 44%)[26]. Another retrospective chart review found d dimer levels of greater than 2660 µg/L had a 100% sensitivity and 67% specificity for PE. A retrospective chart review of 100 patients hospitalized for COVID-19 who received CTPA found a PE rate of 23%, with a higher prevalence in ICU patients (74% vs 29%). It is unclear if these patients were receiving anticoagulation. Pre-existing cardiovascular disease was associated with higher incidence of PE. More studies are needed to determine the utility of d-dimer levels for risk stratification of VTE in COVID-19 patients. There is limited data regarding PE prevalence among COVID-19 patients treated in the outpatient setting. However, one recent study in the ED found that among patients receiving a CTPA to evaluate for PE, the positivity rate was similar between COVID-19 patients and those without COVID-19.

When testing for PE in COVID-19 patients, CTPA is the test of choice. If CTPA is contraindicated (e.g., renal failure, severe contrast dye reaction), only the perfusion scintigraphy of the ventilation-perfusion scan should be performed to minimize aerosolization of secretions.

The American Society of Hematology and the American College of Chest Physicians recommend routine pharmacologic prophylaxis for VTE in patients hospitalized with COVID-19 unless there are preexisting contraindications. Low molecular weight heparin is preferred over unfractionated heparin to reduce healthcare worker exposure to infected patients. If heparin-induced thrombocytopenia develops, fondaparinux should be used. Although some authors have advocated for intermediate or therapeutic dosing, both societies endorse standard prophylaxis dosing until more data is available. A review of 150 ICU COVID-19 patients demonstrated a low rate (2.7%) of bleeding complications among patients receiving prophylactic or treatment-based pharmacologic antithrombotic therapy. Although limited, this suggests anticoagulation is relatively safe in COVID-19 patients who do not meet exclusion criteria. A retrospective study of 449 patients with severe COVID-19 infection found an improved 28-day mortality in patients receiving enoxaparin (40–60 mg daily) than those not receiving enoxaparin. Some authors also advocate for the anti-inflammatory role of heparin in severe COVID-19 infection. Heparin is known to decrease inflammation by inhibiting neutrophil activity, expression of inflammatory mediators, and the proliferation of vascular smooth muscle cells. Admitted patients boarding in the emergency department should at minimum receive pharmacologic antithrombotic therapy with a low threshold for additional VTE testing if new symptoms develop.

6. Conclusion

The incidence of surgical emergencies during COVID-19 pandemic due to thrombotic complications in our institute over a period of 2 years (August 2020-August 2022) is **3.83%.** However so far it is difficult to establish whether these manifestations are either due to direct consequences of COVID-19 infection or coincidental findings in infected patients. But we can conclude that there is increased incidence of thrombotic complications in patients with COVID-19 infections.

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