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Acute limb ischemia in COVID-19 subjects

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Abstract---Background: Corona virus disease 2019 (COVID-19) virus has an underlying pathogenesis which causes interaction between multiple systems not just isolated to respiratory system resulting in propagation of immunothrombosis. AIM: To see association of acute limb ischemia with COVID-19. Results: A total of 8 patients have been diagnosed with acute limb ischemia and managed since the outbreak of pandemic. Conclusion: Early evaluation of peripheral vessels in COVID-19 patients who present with any symptoms of pain, parasthesia, poikilothermia, pallor, pulselessness, paralysis should be considered, especially when found to have an elevated D-dimer level as early treatment of thrombosis with anti-coagulants conservatively or surgically by required amputations.

Keywords---Acute limb ischemia, COVID-19, immunothrombosis.

Introduction

A single-stranded ribonucleic acid (RNA) virus is the cause of the novel coronavirus illness 2019 (COVID-19) [1]. Symptoms of coronavirus infection range from mild to moderate, severe to very severe. Common symptoms are fever, anosmia, headache, runny nose, ageusia, body aches, and diarrhea, whereas systemic involvement (including pneumonia, myocarditis, stroke, and other coagulation disorders) is generally more severe. Except for a few patients who had mild complaints of cough and shortness of breath, most of the patients made a full recovery from the viral infection. COVID-19 patients with severe to very severe disease experience substantial lung damage and fibrosis. These are the patients most likely to develop extrapulmonary problems following COVID-19 infection.

Atypical symptoms of the disease may be associated with systemic involvement, as well as hypercoagulability with microangiopathy and macroangiopathy.

Acute limb ischemia is one of the most common symptoms of hypercoagulability. The symptoms can take the form of blisters, acral cyanosis, chilblains, bruise, dry gangrene, or life-threatening acute ischemia of the limbs. Unfortunately, most patients have to undergo an amputation due to a "delay" in the symptoms of the disease or a rapidly progressing illness.

The new coronavirus disease 2019 (COVID-19) is caused by a single-stranded ribonucleic acid virus (RNA) with a positive feeling [1]. The first site discovered in Wuhan, China, in December 2019, the WHO accepted the invitation and declared it a "global pandemic" in March 2020. [2]

The first case in India was discovered in January 2020 in the state of Kerala [3]. Although initially thought to affect only the respiratory system, many types of research, including ours, show extrapulmonary interference. Various studies show that one of the causes of atypical disease manifestations may be due to systemic involvement and hypercoagulable condition with micro- and macroangiopathy [4].

One of the many manifestations of the hypercoagulable condition is acute extremity ischemia [5]. Its presentation can be in the form of bullae, acral cyanosis, bruising, chills, blood bubbles, dry gangrene or life-threatening acute ischemia of the extremities. A few patients who show up early usually recover only with medical supervision. However, most patients need amputation due to a delay in the presentation of the disease or a swiftly progressing disease.

Some patients, at times, also succumbed due to sepsis. Here we present a case series of acute lower limb ischemia following COVID-19 infection and their treatment strategy that follows. Informed consent was taken from all eight of the patients included in this study.

Materials and Methods

The data has been collected from attendants and patients who got admitted with acute limb ischemia and also having COVID -19 positive status presently or 3 months in Krishna Hospital & Medical Research Centre, Karad, Maharashtra.

Demographic variables: Age, sex.

Setting: Krishna Hospital & Medical Research Centre, Karad, Maharashtra.

Population: The accessible population of the study includes COVID-19 patients admitted in Krishna Hospital & Medical Research Centre, Karad, Maharashtra.

Sample:

The patients who fulfil the inclusion criteria will be considered as samples. Sample size according to Convenient Sampling scheme will be used.

Criteria for sample selection:

Inclusion criteria:

All COVID-19 positive status patients with CT/USG DOPPLER diagnosed acute limb ischemia.

Exclusion criteria:

1. Patients who are unwilling to participate
2. Patients with COVID 19 negative status
3. Patients with previous history of peripheral vascular disease/diabetic foot

Method of data collection

After obtaining permission from concerned authority and informed consent from samples, data from patients has been collected who are CT/USG DOPPLER diagnosed acute limb ischemia with COVID positive status.

Table 1
List of patients included and interventions performed

Age/Gender	Diagnosis of COVID	General condition	Comorbidities	D-dimer level (µg/ml)	Fibrinogen (mg/dl)	Platelet count	intervention
67y/M	RTPCR HRCT	ARDS with O2 on mask	HTN	4.8	1549	2.77 lakh/cu.mm	B-K amputation
72y/M	RTPCR HRCT	ARDS on mechanical ventilation	HTN IHD	2.8	804	90,000/cu.mm	B-K amputation
69y/F	RTPCR HRCT	ARDS on CPAP	HTN Obesity	2.16	1456	3.00lakh/cu.mm	Symes amputation
60y/M	RTPCR HRCT	ARDS with O2 mask	HTN	4.15	1330	2.80 lakh/cu.mm	A-K amputation
75y/F	RTPCR HRCT	ARDS on CPAP	Asthma obesity	3.16	1210	1.21 lakh/cu.mm	B-K amputation
55y/M	RTPCR HRCT	ARDS on CPAP	HTN	2.21	1654	1.8 lakh/cu.mm	Rays amputation
74y/M	RTPCR HRCT	ARDS on O2 mask	obesity	3.79	1290	88,000/cu.mm	B-K amputation
59y/M	RTPCR HRCT	ARDS on high flow o2	HTN	2.68	1380	1.62 lakh/cu.mm	B-K amputation

M: Male F: Female RTPCR: Real-Time Reverse Transcription Polymerase Chain Reaction Assay, HTN: Hypertension, DM: Diabetes Mellitus, IHD: Ischemic Heart Disease, HRCT: High -Resolution Computed Tomography, ARDS: Acute Respiratory Distress Syndrome, B-K: Below Knee, A-K: Above Knee.

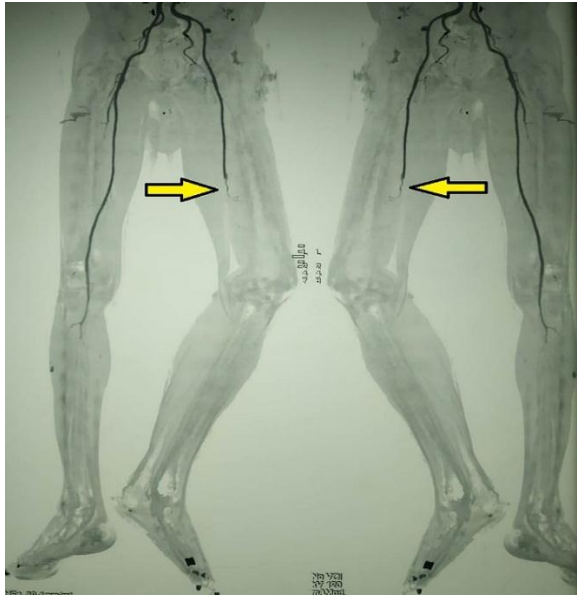


Figure 1 ct angio showing femoral thrombus



Figure 2 ct angio showing block at the level of internal iliac vessel



Figure 3 amputation stump



Figure 4 guillotine above knee amputation



Figure 5 Acute left foot ischemia, patient required b-k amputation



Figure 6 Amputation stump post op

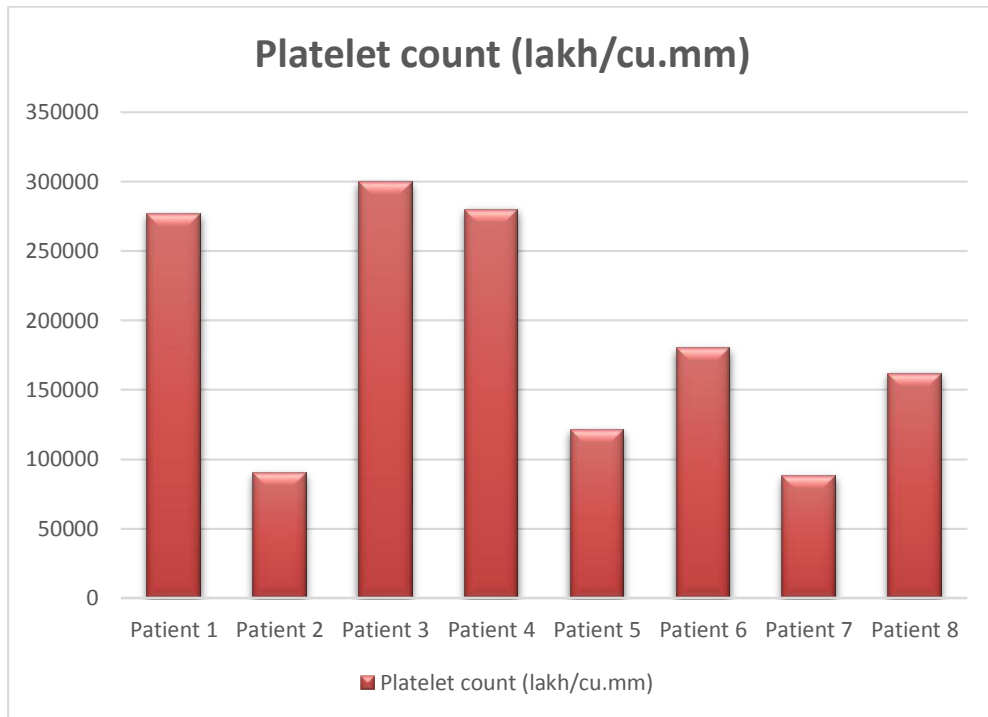


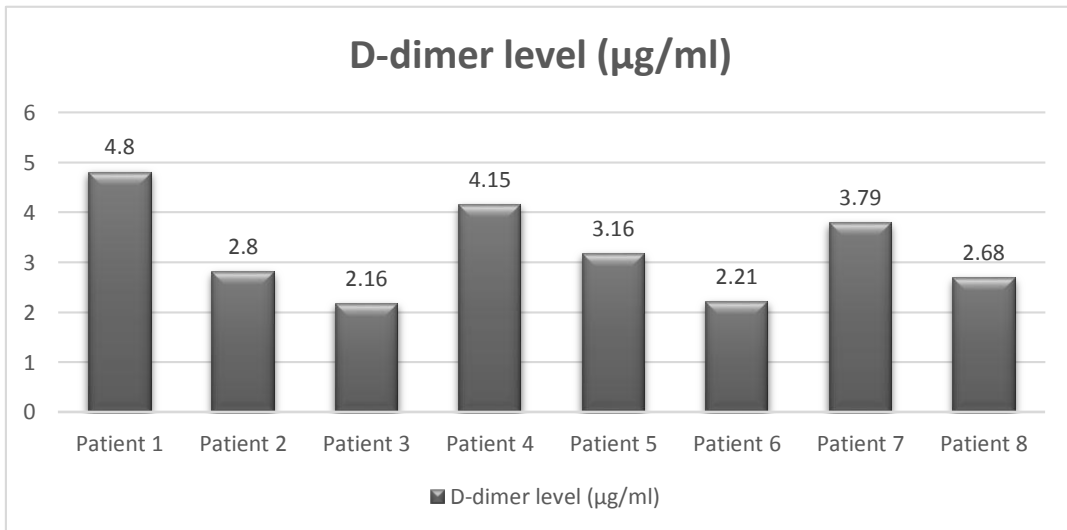
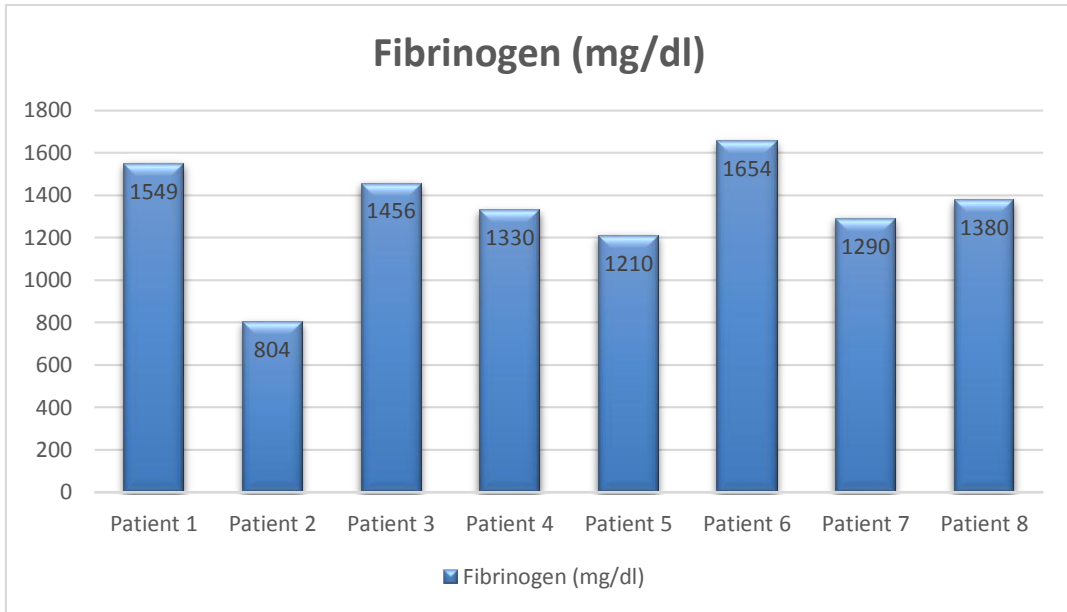
Figure 7 Delayed presentation of ischemic foot post covid required syme's amputation

Results

Age and gender of the patients:

Out of these 8 cases 6 were males (75%) median age of presentation is 68 years. The median age for males is 68years and females were 72 years encountered in the study group.





Mode of diagnosis:

All patients were diagnosed of COVID-19 by both RT-PCR and HRCT. RT-PCR from the nasopharyngeal swab was done. They were also diagnosed based on HRCT on the presence of usual clinical symptoms and bilateral classical ground glass appearance on HRCT chest.

Comorbidities:

Hypertension was the most common comorbidity followed by obesity.

Treatment modality:

5 patients underwent below knee amputations with closure of fascio-cutaneous skewed flaps one underwent syme's amputation one underwent RAYS amputation one patient underwent above knee guillotine amputation after confirming the diagnosis of Acute limb ischemia.

Discussion

Symptoms of coronavirus disease (COVID-19) in 2019 can be segregated as mild to moderate, severe to very severe. While fever, anosmia, ageusia, cough, headache, muscle aches, and diarrhea are mild to moderate in severity, systemic engrossment (such as pneumonia, myocarditis, stroke, and other clotting disorders) puts patients in severe category.

Most patients recover entirely after COVID 19 infection, with the exception of a few who present with coughing or shortness of breath. Patients with severe or very severe disease often suffer from significant lung damage and fibrosis [6]. These are patients at the highest risk of developing extrapulmonary complications after COVID.

There are four mechanisms involved in this complex complex of COVID-19, either alone or in different blends.

First, vascular thrombosis can lead to coagulation disorder (hypercoagulability) due to poor health, endothelial activation, hypoxia, and chronic immobilization.

Second, von willebrand factor(VWF) increased the expression factor in severe COVID-19, leading to endothelial dysfunction thus leading to vascular thrombosis.

Third, the ACE-2 receptor has a broad expression in the cell membrane and provides defense from the development of cardiovascular disease [7]. The ACE-2 is an anti-regulatory peptide that changes angiotensin-II to angiotensin-I, thereby plummeting the biological effects of the anti-thrombin I receptor.

Cell infection leads to the release of proinflammatory cytokines, acute respiratory distress syndrome, myocarditis, and hypercoagulability, an increase in acute coronary syndrome, induction of pulmonary embolism, or prolonged intravascular coagulation.

Fourth, is hematopoietic shock or damage associated with severe COVID-19 annexations that can cause recurrent ischemic organ failure.

One of the ideologies is that the virus affects the heart, kidneys, small intestine, testicles and endothelium via the receptor enzyme angiotensin-2 (ACE-2) receptor [7].

Another group of researchers theorized that the thrombotic condition was directly due to the virus damaging endothelial cells via ACE-2 receptors in the alveoli of the lungs, leading to the activation and disturbance of endothelial cell function [8].

Among the numerous symptoms of COVID-19 infection, it causes damage to the thrombotic effect of this virus globally. Various studies have documented venous thrombo-embolic events and a number of coronary artery diseases, from tapering of the lower extremities to the artery [9]. The coronavirus binds to an excitatory pore that leads to a prothrombotic state, which in turn leads to micro or macrovascular endothelial damage [10]. In addition, inhibition of fibrinolysis increases thrombotic activity. The liver secretes fibrinogen and thrombopoietin by stimulating the hormone interleukin-6 and damaging the endothelium by stimulating the pathway of the coagulation cascade [11].

Dutch studies have shown that critically ill patients diagnosed with COVID-19 had a 31 percent higher risk of developing a thrombotic stroke in hospital and intensive care unit [12]. Several studies have already shown that the patients with severe COVID-19 have a higher risk of thrombotic thrombosis even after anti-thrombotic treatment [13]. One of the patient was diagnosed with ischemia in the leg 15 days after receiving COVID-19 despite receiving antithrombotic medication. Other patients were diagnosed with mild to moderate disease but did not receive antithrombotic treatment. The patient complained of darkening of the lower extremities on day 15 after COVID-19.

Another interesting finding in our subjects was a butter -like sensation in the nerve sheath. An Italian study by Zanin et al. showed that there may be a significant amount of nerve damage caused by the new coronavirus [14]. Our research can be explained or validated in the void.

A research work by Klok et al. had shown the development of coronary heart disease or blood clots approximately 57% [12]. Perini et al. In their study, he reported four patients diagnosed with post-COVID-19 limb ischemia [15].

A further Italian study showed 20 patients diagnosed with ischemia of the body as a “post-COVID-19 extrapulmonary thrombotic complication” [16]. We report these acute post-COVID-19 lower extremity ischemia as a case study in one of the largest hospitals in western India.

Conclusion

All eight cases of lower limb ischemia in our study were cured after initial COVID-19 surgical treatment. The period of home isolation post discharge caused complications. The delay in seeking for medical help had cost the patients their limbs.

There are no definitive guidelines for patients recovering from COVID-19 disease. Therefore, because of the potentially debilitating effects of gangrene, all patients should be treated as soon as they come across any signs or symptoms of ischemia of the legs (pain, pallor, poikilothermia, paraesthesia, pulselessness, paralysis).

Therefore, the history of COVID-19 should be taken into account when studying these patients. No specific guidelines have been industrialized to prevent or manage thrombosis and its problems. The issue of whether or not antibiotics should be used is also an unresolved question. If antithrombotic drugs are to be used, “who shall receive them?” is a critical query. Succeeding studies may shed light on these beguiling questions that remain unanswered.

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