

## Experience in Management of Acute Limb Ischemia During the COVID – 19 Pandemic from A Tertiary Centre in Oman

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### ABSTRACT

**Purpose:** The COVID 19 pandemic has an association with coagulopathy the reason for which is still under investigation. During the first wave, centers internationally saw more of venous thromboembolism and during the second wave there was a rise in acute limb ischemia. In this paper we analyze our experience with acute limb ischemia patients who were managed at our tertiary Centre in Muscat, Oman during the first and second waves of the pandemic.

**Methods:** The paper is a observational cohort study based on a single tertiary center, in which data was collected prospectively from the electronic medical records of COVID 19 positive patients who were referred to the vascular surgery unit, during the period of March 2020 to August 2021, the mentioned period involves both the first and second wave spikes of COVID – 19 in Oman. The records were analyzed to assess patient’s demographic data (Age and gender) as well as their co morbidities, current medications and other risk factors including smoking or previous amputations. This study has been approved by the ethics committee of our university hospital.

**Results:** The study had a total of 15 patients of which 10 were male with a range of 38 – 96 years. None of the patients were vaccinated. All had at least 1 co morbidity and 10 were in the COVID intensive care unit. All the patients were on prophylactic enoxaparin at time of referral and had elevated inflammatory markers. Our results show a significant rise in acute limb ischemia during the 2nd wave with 9 of those patients being referred at the above-mentioned time.

**Conclusion:** COVID-19 is strongly associated with an increased incidence of thromboembolic events, secondary to the hypercoagulable state. Our statistics also show the significant increase of ALI occurrence in the second wave of COVID 19 at our center in comparison to the first wave. Managing ALI remains a challenge considering the persistent hypercoagulable state produced by the infection in this subset of patients who are critically ill. Outcomes remain bleak with patients either succumbing to the infection or requiring an amputation.

COVID – 19, a virus which has resulted in a global pandemic, mainly presenting with respiratory symptoms was also found to have a close association with coagulopathies resulting in severe life-threatening complications such as disseminated intravascular coagulation and acute limb ischemia.

The aim of the following study is to recognize the clinical findings and the characteristics of patients infected with COVID – 19 who presented with Acute Limb ischemia at Sultan Qaboos Hospital University Hospital. Furthermore, we are analyzing the statistical differences in the occurrence of ALI during the first and second waves of COVID 19 at the Sultanate of Oman.

The following paper also involves the management of those patients, especially after being referred to the Vascular surgery team in the respective mentioned center.

**Keywords:** Acute limb ischemia; COVID – 19; Pandemic; Coagulopathy; Thrombosis; First wave; Second wave; Management; Outcome

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## **INTRODUCTION**

Studies since January 2020 has shown a direct relation between novel Coronavirus disease and a hypercoagulable state resulting in micro and macrovascular thrombotic complications which may result in severe complications, including acute limb ischemia (ALI).<sup>[1]</sup>

The relation between COVID 19 and ALI remains unexplained and there are multiple hypothesis which include prolonged hospitalizations, ICU admissions, hyperinflammation resulting in a cytokine storm and the possible endothelial injury that occurs during the infection.<sup>[2]</sup> However, published literature suggests that patients with severe Acute Respiratory Distress Syndrome (ARDS) due to COVID pneumonia have significantly deranged coagulation profiles and are at higher risk of developing micro and macrothrombi even though the majorities do start the prophylaxis early on.<sup>[3]</sup>

Our study compares the number of patients that were referred to the Vascular surgery team during the two major waves of the pandemic at our tertiary center.

## **METHODS**

This paper is a retrospective study conducted during the period of March 2020 to August 2021 at our tertiary center, in which data was collected from the electronic medical records of COVID 19 positive patients who were referred to

the vascular surgery unit and it has the approval of our ethics committee. Patients were seen upon referral either from the COVID intensive care unit or the emergency department.

The mentioned duration incorporates both the first and second wave spikes of the pandemic in Oman.

All patients had their basic lab work up, as well as the COVID inflammatory markers sent. This included CBC, CRP, D Dimer, coagulation profile, and LDH.

Patients underwent either an arterial ultrasound duplex and/or a CT angiography (CTA) depending on the clinical status/stability of the limb and the patient.

We also study the co-morbidities of this cohort and whether they were on any prophylactic medications prior to receiving the referral.

### Results (Table 1)

**Table 1:** Demographic Data, co morbidities and other risk factors of the entire cohort (n = 15)

Variable	N,(%)
<b><i>Demographic</i></b>	
M: F	10:05
Age (mean)	63 (38 – 96)
<b><i>Co morbidities</i></b>	
Hypertension	5
AF	1
CKD	2
Previous vascular disease	2
Diabetes	5
Smoker	1
<b><i>Referral pattern</i></b>	
1 <sup>st</sup> wave	6
2 <sup>nd</sup> wave	9

There were a total of 15 patients in our study. Mean age was 63 years (range 38-96 years) and 10 patients were males. 9 of the 15 presented during the second peak of the pandemic.

In this cohort, 13 patients had 1 co morbidity and 3 had two. 9 patients were on Enoxaparin, 1 patient on unfractionated heparin both in prophylactic doses and 3 patients were on clopidogrel and/or Aspirin. 1 patient underwent above knee amputation. Two patients underwent successful open surgical thrombo-embolectomy (1 femoral; 1 brachial) with limb salvage. Patient who underwent brachial thrombo-embolectomy re-thrombosed and underwent embolectomy again. He succumbed to his COVID status. One patient left against medical advice from the emergency department.

There was one elective above knee amputation in this study due to delayed presentation and a total of 8 deaths which was secondary to the COVID pneumonia.

## **DISCUSSION**

ALI is commonly associated with high-risk mortality and morbidity such as; amputation, myocardial infarction, decompensated heart failure, renal and respiratory complications. However, better outcomes can be expected if referred, diagnosed and managed early.<sup>[4]</sup>

A systematic review of 157 articles concluded that SARS-CoV2 infection leads to a state of hypercoagulability and hyperinflammation, eventually resulting in ischemic insults to digits and limbs.<sup>[5]</sup> Increasing inflammatory markers such as d-dimer, fibrinogen, total leukocyte count and C reactive protein. Retrospective assessment of patients diagnosed with COVID-19, had fulfilled one or most of the virchow's triad elements, Whether it is the state of hypercoagulability, endothelial injury caused by the COVID cellular infection or the blood stasis due to immobilization noted in patients who were on ventilatory support or intubated. All were factors that increased their chance at developing thromboembolic events. As knowledge grew about the virus, we started treating it as a systemic disease with a very high chance of causing serious threat to the limbs.<sup>[5]</sup>

A similar study which was published in 2020 done by<sup>[6]</sup> and took place in Italy had very similar results to ours, showing that ALI was commoner in the second wave than in the first despite patients being on prophylactic anticoagulation. In our study, ALI associated with COVID-19 was not specific to patients' age, comorbidities or the anticoagulation therapy they were on.

The severe thromboembolic events and development of ischemic limbs was noted from the first wave of COVID 19, however, the aim of our study was to understand the reason behind the numbers of ALI referrals being higher during the second wave. We believe that there are multiple factors that resulted in ALI referrals being higher during the second wave (Figure 1). As shown in Figure 2, during the 1st wave, the maximum number that was recorded per day was 2,000 cases. In the second wave, numbers nearly tripled, with 5,400 cases being recorded daily. Also, numbers of admissions increased, and there was a higher requirement of ICU beds with patients remaining critically ill for longer periods of time. This added burden required the services non-intensivists and paramedical staff not fully trained in intensive care to care for patients in the ICU/COVID wards. In order to reduce exposure of staff to these patients and to optimize use of PPI's, patients were examined twice during each 12 hour shift and PRN.



**Figure 1:** Showing acute limb ischemia of the right hand. Presenting to our centre at emergency.



**Figure 2:** Acute limb ischaemia of the left foot

In our data, 7 of our patients were referred late. The decreased frequency of examination and lack of experience in picking up signs and symptoms of ischemia in critically ill/ventilated patients perhaps led to diagnosis of ALI at an advanced stage.

Secondly, all the cases that were referred during the second wave had a hospitalization stay of more than 20 days, with the majority being admitted in ICU and all of them were in severe cytokine storm with all inflammatory markers worsening either due to ARDS or other factors resulting in their sepsis including the ischemic limb/s itself. Lastly, the COVID – 19 variants during the second wave, such as the delta variant were found to be a lot more aggressive than those found in the 1st wave. This was reported internationally, as admissions in the ICU increased worldwide and management of the cytokine storm became more difficult.

The pattern of thromboembolic events in COVID 19 patients remains challenging and not fully understood. There isn't a protocol that has been formed yet by the WHO in regard to the hyper coagulability state in COVID 19 patients; however, our hospital started all COVID patients regardless of the severity of their condition on prophylactic

enoxaparin during the second wave provided their renal function was normal. For those with abnormal renal function UFH was used subcutaneously.

The subset of patients in our study were critically ill, on inotropes, ventilated and in most cases not stable enough for an endovascular or open surgical procedure. Added to this conundrum were the difficulty of convincing patient family about intervention when the prognosis of limb salvage was guarded and the possibility of re intervention due to the underlying hypercoagulable state.

### **Role of regional anesthesia in management of ALI**

Regional Anesthesia [RA] can help reduce the need for general anesthesia when a patient is taken up for intervention. RA combined with regular paracetamol, NSAID, providing adequate analgesia and reduces use of morphine as a first line drug. Additionally, intra-op systemic steroids reduce the inflammatory response to tissue damage, thereby, improving pain management, reducing stress response, and the incidence of post-op nausea and vomiting.<sup>[7]</sup> However, the only deterrent is the need to have an anesthetist with the required expertise in RA.

### **Limitations**

Our small sample size could lead to bias in our results and the study period, follow up was short. The study is a single centre retrospective study and therefore data collection is dependent on accuracy of documentation. Like many other study groups, our study lacks a control group to measure our results against, whereas a COVID diagnosis could merely be an incidental finding without a direct cause and effect analysis.

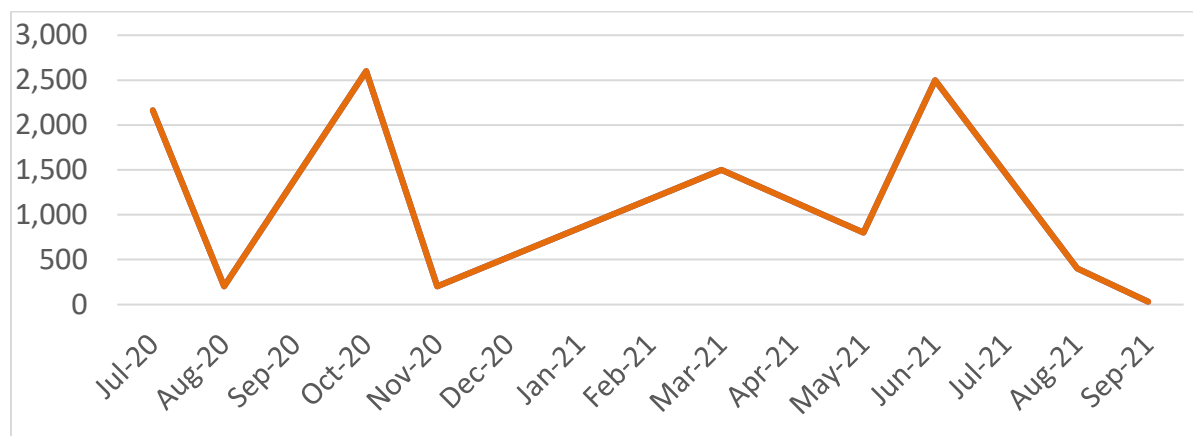
### **CONCLUSION**

In conclusion, COVID-19 is strongly associated with an increased incidence of thromboembolic events, secondary to the hypercoagulable state.

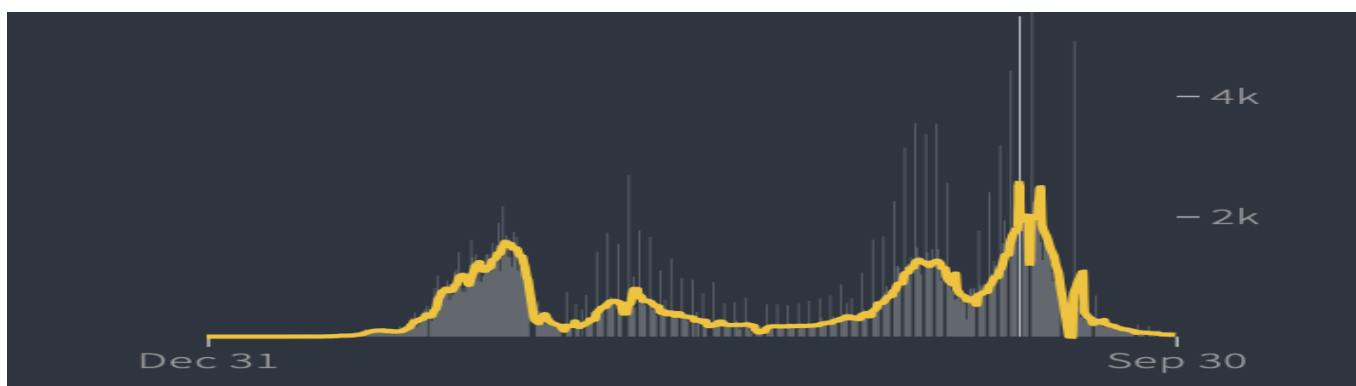
Our statistics also show the significant increase of ALI in the second wave of COVID 19 in comparison to the first wave. Factors contributing to this observation include a more virulent strain of the virus, prolonged hospital stay, higher inotrope use combined with decrease in frequency of examination of patients and medical staff with limited exposure in care of critically ill patients.

Managing ALI remains a challenge considering the persistent hypercoagulable state produced by the infection.

Our primary outcome demonstrated an overall poor prognosis in patients diagnosed with ALI secondary to COVID-19 infection.



**Graph 1:** Showing the peaks of COVID 19 cases in Oman. First peak being between August 2020 and November 2020; and the second being between May 2021 and August 2021.



**Graph 2:** Green arrow showing the number of cases that were recorded during the second wave of COVID 19 reaching up to 5,320 cases/day.

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