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### RESEARCH ARTICLE

#### VENOUS GANGRENE - AN INSTITUTIONAL EXPERIENCE

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#### Abstract

Venous gangrene represents the most severe manifestation following deep venous thrombosis (DVT), and presents as acral ischaemic necrosis. The pathophysiology is driven by an acquired coagulopathic state leading to microvascular thrombosis; outcomes are generally poor. This study was aimed at analysing the outcomes in these rare group of patients who presented with venous gangrene at a single institution during a two year period.

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#### Introduction:-

Venous gangrene represents the most severe manifestation following deep venous thrombosis (DVT), and presents as acral ischaemic necrosis [1]. Even though incidence is relatively rare with paucity of large studies, prognosis is considered poor. This study was aimed at analysing the outcomes in these rare group of patients who presented with venous gangrene at a single institution during a two year period.

#### Methods:-

We collected data from our in-patient register for patients who presented to our institution with venous gangrene of the lower limbs from September 2018 to September 2020 retrospectively. The patient characteristics were analysed with regard to age, sex, side of the involved limb, associated co-morbidities, and presence of active malignancy. Outcomes studied were clinical, and included limb salvage, major amputation rates and mortality. Follow-up till one month was recorded for all patients, patients who were lost to follow-up before this period was also recorded.

#### Inclusion criteria:

We included all patients who presented to us with established clinical gangrene of the lower limbs and documented deep vein thrombosis by ultrasound duplex study.

#### Exclusion criteria:

We did not include patients presenting with pregangrenous stages like phlegmasia alba dolens or phlegmasia cerulea dolens, as these group of patients did not fulfil the clinical diagnosis of gangrenous tissue changes secondary to deep venous thrombosis.

#### Results:-

A total of 12 patients presented with the predetermined diagnostic criteria of venous gangrene. 4 patients were male, and 8 female (Table 1). Most patients had some baseline co-morbid conditions (Table 2). 3 patients had documented malignancy (1 gastric, 2 endometrial). All patients had undergone some form of surgical intervention; 3 patients underwent surgical venous thrombectomy, and the remaining 9 primary amputation. Overall mortality rate was 40% (5 patients) during the post operative period. 3 patients were lost to follow-up (Table 3).

**Discussion:-**

Venous gangrene is one of the rare clinical scenario in the field of vascular surgery where tissue necrosis occurs in the presence of palpable distal pulses or documented patent arteries [1]. This condition primarily occurs in the setting of deep vein thrombosis of the proximal veins of the lower limb in patients with pre-existing comorbidities.

Previously accepted paradigm was that the venous obstruction resulted in an increased interstitial pressure, which in turn resulted in constriction of the nutrient vessels when the closing pressure was exceeded [2].

However now it is understood to be primarily due to an acquired severe prothrombotic state occluding the microvasculature. This state is very often associated with conditions like malignancy [3], heparin induced thrombocytopenia (HIT) [4], warfarin administration [5], antiphospholipid syndrome [6] etc. Three of our patients had active malignancy, of which 2 had endometrial cancer and one had gastric malignancy.

Venous gangrene can be prevented in a subgroup of patients if warfarin is avoided in those presenting with thrombocytopenia or coagulopathy secondary to suspected malignancy. Warfarin should also be avoided in patients presenting with heparin induced thrombocytopenia, keeping with American College of Chest Physicians (CHEST) 2016 10th Edition of Antithrombotic Guideline (AT 10) consensus. In addition, low molecular weight heparin is superior to warfarin in patients presenting with malignancy [7]. Inferior vena cava filter insertion should be avoided in hypercoagulable conditions as this can induce venous thrombosis and gangrene, this includes patients with heparin induced thrombocytopenia and malignancy [2].

Early standard anticoagulation with emergent surgical intervention is considered the best strategy available. As mentioned earlier, most of these patients have some or the other underlying prothrombotic syndrome which drives this escalating catastrophe. Urgent recognition of this specific state in a given patient, and strategies directed at early mitigation and reversal of these inciting and aggravating factors is crucial and cannot be over emphasised.

In patients who present with prolonged international normalised ratio (INR) following vitamin K antagonist (e.g. Warfarin) administration, use of intravenous vitamin K along with suspension of Warfarin is the first step required as part of emergent management [5]. Often additional doses of vitamin K may be required, depending on the normalisation of the INR following the previous dose(s). In this setting even though INR is supratherapeutic, this actually is due to depression in levels of protein C, thus resulting in the prothrombotic state and venous gangrene.

Full therapeutic anticoagulation should be instituted keeping with the CHEST 2016 AT 10 consensus guidelines [7] for deep vein thrombosis. However, there are several caveats that are crucial for proper management. In HIT-associated venous gangrene, any form of heparin is contraindicated and therapeutic anticoagulation is required with either a direct thrombin inhibitor or a direct Xa inhibitor [4]. In patients with malignancy low molecular weight heparin (LMWH) is preferred over other agents, and vitamin K antagonists are actively contraindicated as they result in an exaggerated prothrombotic state [7].

The role of newer modalities of treatment like mechanical thrombectomy have been tried [8] but their specific role is undefined as of today. Well designed, good quality studies comparing this to standard treatment are lacking.

A large proportion of the patients who presented to us unfortunately had advanced tissue necrosis and precluded any possibility of limb salvage, and this mandated primary amputation.

The role of fasciotomy is controversial as pure mechanical increase in interstitial pressure is not the driving pathophysiological force, rather microvascular thrombosis is. Historically early fasciotomy was commonly used to relieve tissue pressure, however successful elimination of large vein thrombosis via percutaneous mechanical or surgical means almost immediately and dramatically reduces distal venous pressure [9] thus rendering the role of fasciotomy obsolete.

In spite of aggressive management the prognosis of venous gangrene is generally poor, as in our series with a mortality rate of 40%. Indeed longitudinal data on the outcomes of patients presenting with this rare syndrome in deep vein thrombosis is either lacking or disheartening.

**Conclusion:-**

Venous gangrene indicates soft tissue necrosis in a limb with large burden proximal DVT, and is a grave and extreme manifestation of the disease. The pathophysiology is driven by an acquired coagulopathic state leading to microvascular thrombosis; outcomes are generally poor. Appropriate decision making and intervention can potentially reduce mortality and amputation rates.

**Table 1:-**

Sex	n = 12	Side	n = 12
Male	4	Left	8
Female	8	Right	4

**Table 2:-**

Comorbid illness	Malignancy	Diabetes	Hypertension	Previous VTE
	3	5	2	1

**Table 3:-**

Outcomes	Primary amputation	Surgical venous thrombectomy	Mortality	Lost to follow-up
n = 12	9/12	3/12	5/12 (2 amputation group 3 thrombectomy group)	3/12 (2 amputation group 1 thrombectomy group)

**Figure 1:-** Patient presenting with venous gangrene complicating left lower limb iliofemoral DVT.**References:-**

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