International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Incidence of Deep Vein Thrombosis in Patients with a Recent History of COVID-19 Infection: A Prospective Observational Study from a Tertiary-Care Centre in Southern India

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Received: 15-06-2026
Accepted: 26-06-2026
Available online: 20-07-2026

ABSTRACT

Background: SARS-CoV-2 infection is associated with a prothrombotic state that persists into the convalescent phase. Data on the incidence of deep vein thrombosis (DVT) in post-COVID-19 patients from Indian tertiary-care surgical practice are limited.

Objectives: To estimate the incidence of lower-limb DVT in patients with a documented preceding COVID-19 illness presenting to KMCRI, tertiary-care general-surgery service, and to characterize associated demographic, clinical, and laboratory factors.

Methods: A prospective observational study was conducted over 18 months in the Department of General Surgery at the Karnataka Medical College And Research Centre, Hubballi. Sixty-six consecutive patients aged ≥18 years with a documented COVID-19 episode within the preceding 90 days and clinical features suggestive of DVT or one or more recognized thrombotic risk factors were enrolled. All underwent bilateral lower-limb venous compression Doppler ultrasonography. Demographic, clinical, and laboratory data were recorded on a standardized proforma. Statistical comparisons used Fisher's exact test and the Mann–Whitney U test, with $p < 0.05$ considered significant.

Results: Eleven of 66 patients (16.7%; 95% CI 8.6–27.9) had ultrasonographically confirmed DVT. Mean age was 55.0 ± 14.4 years and the male-to-female ratio was 1.44:1. The left lower limb was involved in 63.6% of cases, and 45.5% had proximal (iliac/femoral/popliteal) disease. Mean D-dimer was significantly higher in DVT-positive patients (6.06 ± 3.56 vs 1.37 ± 1.41 µg/mL; $p < 0.001$), as was CRP (18.52 ± 15.87 vs 6.64 ± 6.15 mg/L; $p < 0.001$). Hypertension was significantly more common in patients with DVT (45.5% vs 9.1%; $p = 0.008$). Older age, hospitalization during acute COVID-19, prolonged immobilization, and malignancy showed clinically relevant non-significant trends. All confirmed cases were managed with therapeutic anticoagulation; no in-hospital mortality or clinically apparent pulmonary embolism was observed.

Conclusions: The incidence of DVT in post-COVID-19 patients evaluated at this tertiary-care surgical centre was 16.7%, considerably higher than reported incidences for general medical/surgical inpatients in Indian cohorts. Elevated D-

dimer and CRP, together with hypertension, identified patients at greatest risk. These findings support targeted post-discharge surveillance and a low threshold for compression ultrasonography in symptomatic post-COVID-19 patients.

Keywords: *Deep vein thrombosis, COVID-19, SARS-CoV-2, Venous thromboembolism, D-dimer, Compression ultrasonography, India.*

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is now recognized as a multisystem inflammatory illness in which a prothrombotic phenotype is a defining clinical feature. Early observational studies during the first pandemic wave reported strikingly high rates of venous thromboembolism (VTE) in hospitalized patients, with incidences ranging from 7% to over 40% depending on disease severity, diagnostic protocol, and intensity of thromboprophylaxis [1,2]. The pathophysiology is multifactorial and reflects the convergence of Virchow's triad — endothelial injury through direct SARS-CoV-2 invasion of endothelial cells via the ACE2 receptor, venous stasis secondary to immobilization and acute illness, and hypercoagulability driven by a profound systemic inflammatory response with elevated D-dimer, fibrinogen, and interleukin-6 [3].

Although attention initially focused on thrombotic events during the acute hospital phase, subsequent studies have demonstrated that the increased risk of venous thromboembolism — and of deep vein thrombosis (DVT) in particular — extends into the convalescent and post-discharge period. A multicentre prospective Italian study of moderate-to-severe non-ICU COVID-19 pneumonia using serial compression ultrasonography reported a DVT incidence of 13.7% during the first wave [4]. In a later analysis spanning the first and subsequent waves, the same group reported an overall pooled incidence of 8%, with a clear decline over time attributable to earlier and more intensive thromboprophylaxis [5]. In contrast, in critically ill patients with COVID-19, DVT incidence ranged from 7.7% to as high as 46% across European, Brazilian, and North American cohorts [6,7].

Indian data on post-COVID-19 venous thromboembolism remain limited. Even prior to the pandemic, the absolute risk of DVT in Indian hospitalized medical patients was reported as low — approximately 0.8–1.6% — but elevated compared with non-hospitalized individuals [8,9]. The ENDORSE study earlier highlighted major under-utilization of thromboprophylaxis in India (17.4%) compared with the global average of 50.2% [10]. The intersection of post-COVID hypercoagulability with this background of under-prophylaxis raises the possibility of an unrecognized burden of DVT among Indian patients presenting in the recovery phase of COVID-19, particularly to surgical and emergency services.

The present prospective observational study was therefore undertaken at a tertiary-care teaching hospital in Karnataka, India, with the primary objective of estimating the incidence of lower-limb DVT in patients with a documented preceding COVID-19 infection. Secondary objectives included characterization of the demographic, clinical, and laboratory profile of affected patients, identification of associated risk factors, and description of anatomical extent, management, and short-term outcome.

MATERIALS AND METHODS

Study design and setting

This was a single-centre prospective observational study conducted in the Department of General Surgery at the Karnataka Medical College And Reseach Institute, a tertiary-care teaching hospital in Hubballi, Karnataka, India, over an 18-month study period. The institutional ethics committee approved the study protocol, and written informed consent was obtained from each participant prior to enrolment. The study was conducted in accordance with the Declaration of Helsinki and reported in line with the STROBE statement for observational studies.

Participants

Consecutive adult patients (age ≥ 18 years) presenting to the surgical outpatient department, emergency room, or as in-patient referrals were screened for eligibility. Patients were included if they had a documented COVID-19 illness within the preceding 90 days (defined as a positive RT-PCR or rapid antigen test, or a clinically and radiologically compatible illness during a period of locally documented community transmission) and one or more of the following: clinical features suggestive of DVT (unilateral lower-limb pain, swelling, tenderness, or calf girth asymmetry), or the presence of recognized thrombotic risk factors warranting screening (recent hospitalization, prolonged immobilization, recent major surgery or trauma, active malignancy, paralysis or paresis, plaster immobilization of the lower limb, oral contraceptive use, or a strong family history of venous thromboembolism). Patients were excluded if they had a known pre-existing diagnosis of DVT, were on therapeutic anticoagulation for any indication, were pregnant, had a congenital coagulation disorder, were undergoing palliative care for terminal illness, or declined consent.

Data collection and clinical evaluation

All eligible patients underwent a standardized clinical evaluation using a structured proforma. Demographic variables (age, sex, place of residence, socioeconomic status using the modified Kuppuswamy scale, occupation, education, physical activity, and body mass index), COVID-19 history (laboratory confirmation, site of management, severity), and a detailed risk-factor inventory were recorded. Clinical examination included documentation of limb tenderness, edema, calf girth measured at three standardized levels (D1, D3, D5) on consecutive days, and a focused systemic examination. Habits (smoking, tobacco chewing, dietary pattern) and comorbidities (diabetes mellitus, hypertension, cardiac, haematological, and oncological disease) were recorded.

Laboratory investigations included complete haemogram, prothrombin time and international normalized ratio (INR), bleeding and clotting times, C-reactive protein, and quantitative D-dimer (latex-enhanced immunoturbidimetric assay, reported in μg/mL fibrinogen-equivalent units). Bilateral lower-limb venous compression Doppler ultrasonography was performed by a single experienced radiologist using a high-frequency linear probe (5–12 MHz) on a standard duplex ultrasound system. The diagnosis of DVT was made on the basis of established criteria — non-compressibility of the vein, absence of spontaneous and phasic-with-respiration flow, presence of intraluminal echogenic material, and loss of augmentation on distal compression. Thrombus extent was categorized as proximal (iliac, common femoral, superficial femoral, or popliteal veins) or distal (calf veins, posterior tibial, peroneal, or soleal veins).

Outcomes

The primary outcome was the incidence of ultrasonographically confirmed DVT in the study cohort. Secondary outcomes included anatomical extent (proximal vs distal), laterality, association with clinical and laboratory variables, choice of management, and short-term outcome at discharge or first follow-up visit.

Statistical analysis

Categorical data are presented as frequency and percentage; continuous data are presented as mean ± standard deviation (SD) or median with range, as appropriate. Between-group comparisons were performed using Fisher's exact test for categorical variables and the Mann–Whitney U test for continuous variables in view of the modest sample size. The 95% confidence interval for the primary incidence estimate was calculated using the Wilson score interval. A two-tailed p value of < 0.05 was considered statistically significant. Analyses were performed using standard statistical software.

RESULTS

Demographic characteristics

Sixty-six patients fulfilled the inclusion criteria during the study period and were enrolled. The mean age was 55.0 ± 14.4 years (range 18–88), and 39 patients (59.1%) were male, giving a male-to-female ratio of 1.44:1. Forty-two patients (63.6%) were from rural backgrounds, and 28 (42.4%) belonged to the lower socioeconomic stratum. Approximately half (50.0%) reported moderate habitual physical activity, while 28.8% were predominantly sedentary. The mean body mass index was 24.3 ± 3.4 kg/m². Demographic details are summarized in Table 1.

Table 1. Baseline demographic characteristics of the study cohort (N=66).

Variable	Value
Total enrolled (N)	66
Mean age ± SD (years)	55.0 ± 14.4
Age range (years)	18 – 88
Males, n (%)	39 (59.1)
Females, n (%)	27 (40.9)
M:F ratio	1.44 : 1
Rural residence, n (%)	42 (63.6)
Lower SES, n (%)	28 (42.4)
Mean BMI ± SD (kg/m²)	24.3 ± 3.4
Sedentary lifestyle, n (%)	19 (28.8)

COVID-19 history and presenting features

All patients had a documented prior episode of COVID-19. Fifty-two (78.8%) had laboratory-confirmed infection, 8 (12.1%) had a clinically and radiologically compatible illness without laboratory confirmation, and 6 (9.1%) reported contact exposure with symptomatic family contacts. Nineteen patients (28.8%) had been hospitalized during their acute COVID-19 illness, including 4 who had required intensive care. The median interval between recovery from acute COVID-19 and presentation was 24 days (range 6–86 days). At presentation, lower-limb pain was reported by 23 patients (34.8%) and unilateral swelling by 17 (25.8%); fever, breathlessness, tenderness on examination, and pitting edema were present in 18.2%, 19.7%, 24.2%, and 27.3%, respectively. Calf-girth asymmetry exceeding 3 cm was documented in 11 patients (16.7%).

Primary outcome — incidence of DVT

Eleven of the 66 patients had ultrasonographically confirmed DVT, yielding an overall incidence of 16.7% (95% CI 8.6–27.9). The left lower limb was involved in 7 cases (63.6%) and the right in 4 (36.4%); no bilateral involvement was observed. Five patients (45.5%) had proximal disease involving the iliac, common femoral, superficial femoral, or popliteal veins, while six (54.5%) had isolated distal (calf-vein) thrombosis. The detailed anatomical pattern is presented in Table 2.

Table 2. Anatomical extent of confirmed DVT (n=11).

Anatomical extent	n (%) of DVT cases (n=11)
Iliac + femoral + popliteal	3 (27.3)
Common femoral to popliteal	1 (9.1)
Popliteal + femoral	2 (18.2)
Femoral vein	1 (9.1)
Calf veins	1 (9.1)
Soleal vein	2 (18.2)
Posterior tibial	1 (9.1)

Comparison of DVT-positive and DVT-negative groups

DVT-positive and DVT-negative patients were compared across demographic, clinical, and laboratory variables (Table 3). DVT-positive patients were on average older (60.7 ± 13.4 vs 53.9 ± 14.4 years, p = 0.15) and more likely to be male (63.6% vs 58.2%), although neither difference reached statistical significance. Hypertension was significantly more common in DVT-positive patients (45.5% vs 9.1%; p = 0.008). Malignancy, prolonged immobilization, hospitalization during acute COVID-19, and smoking each showed clinically relevant but statistically non-significant trends. Mean D-dimer was approximately fourfold higher in DVT-positive patients (6.06 ± 3.56 vs 1.37 ± 1.41 µg/mL; p < 0.001), and CRP was almost threefold higher (18.52 ± 15.87 vs 6.64 ± 6.15 mg/L; p < 0.001).

Table 3. Comparison of clinical and laboratory variables between DVT-positive and DVT-negative groups. *Statistically significant. p-values by Fisher's exact (categorical) or Mann–Whitney U (continuous) test.

Variable	DVT positive (n=11)	DVT negative (n=55)	p
Mean age (years)	60.7 ± 13.4	53.9 ± 14.4	0.15
Male sex, n (%)	7 (63.6)	32 (58.2)	1.00
Hypertension, n (%)	5 (45.5)	5 (9.1)	0.008*
Diabetes mellitus, n (%)	3 (27.3)	15 (27.3)	1.00
Active smoker, n (%)	3 (27.3)	5 (9.1)	0.12
Malignancy, n (%)	2 (18.2)	1 (1.8)	0.07
Prolonged immobilization, n (%)	5 (45.5)	11 (20.0)	0.12
Hospitalized during COVID, n (%)	5 (45.5)	14 (25.5)	0.27
D-dimer (µg/mL), mean ± SD	6.06 ± 3.56	1.37 ± 1.41	<0.001*
CRP (mg/L), mean ± SD	18.52 ± 15.87	6.64 ± 6.15	<0.001*
BMI (kg/m²), mean ± SD	24.7 ± 4.1	24.3 ± 3.3	0.84

Management and short-term outcome

All 11 patients with confirmed DVT were started on therapeutic anticoagulation. Low-molecular-weight heparin (enoxaparin 1 mg/kg subcutaneously every 12 hours) was the initial agent in all cases, followed by a vitamin-K antagonist in 4 patients (36.4%) and a direct oral anticoagulant in 3 patients (27.3%). The remaining patients continued on LMWH at discharge pending overlap with oral therapy. Mechanical measures (limb elevation, graduated compression stockings) were used as adjuncts. At first follow-up (between 2 and 6 weeks), 6 patients (54.5%) had improved clinically and radiologically, 2 (18.2%) remained stable on therapy, 2 (18.2%) had been discharged on oral anticoagulants with planned outpatient review, and 1 (9.1%) was lost to follow-up. No patient developed clinically apparent pulmonary embolism, and there were no major bleeding complications attributable to anticoagulation during the in-hospital phase.

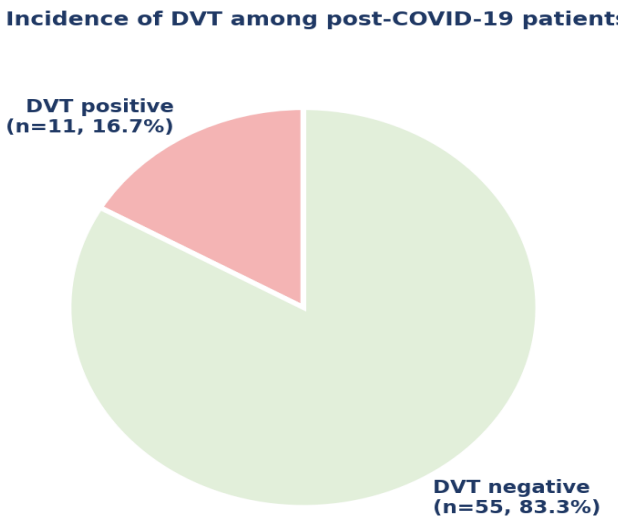

Figure 1. Incidence of DVT among the study cohort (n = 66). Eleven patients (16.7%) had ultrasonographically confirmed lower-limb deep vein thrombosis.

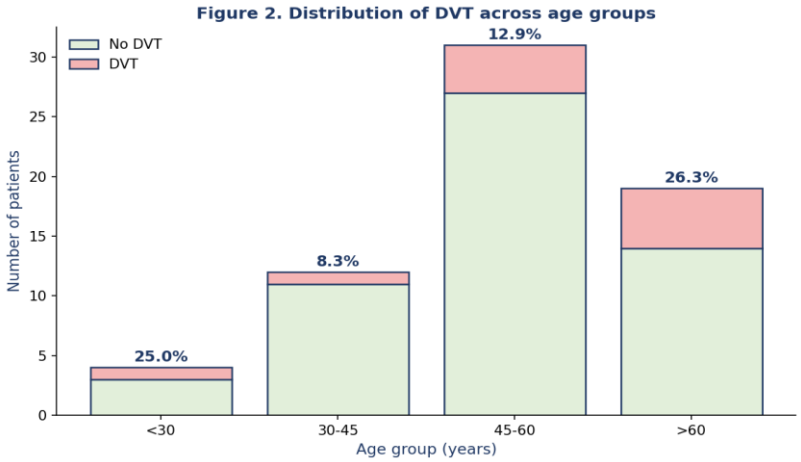

Figure 2. Distribution of DVT across age strata. The highest age-specific incidence was observed in patients older than 60 years.

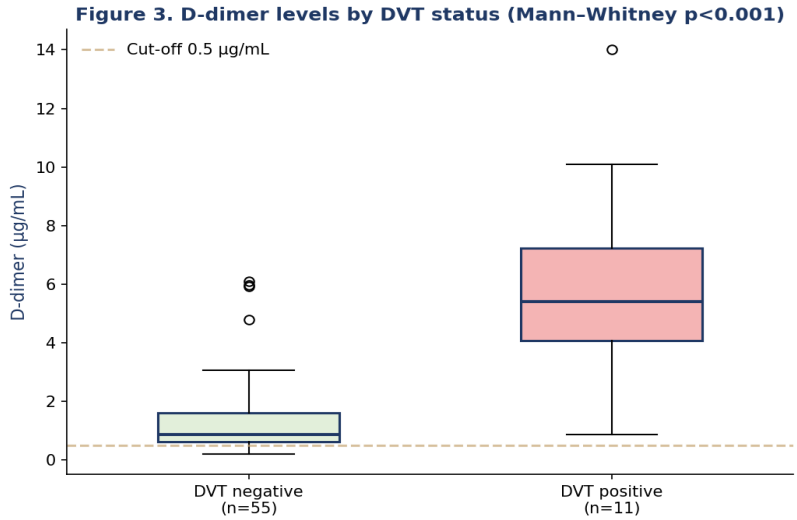

Figure 3. D-dimer levels by DVT status. DVT-positive patients had markedly higher median D-dimer values; horizontal dashed line denotes 0.5 µg/mL conventional cut-off.

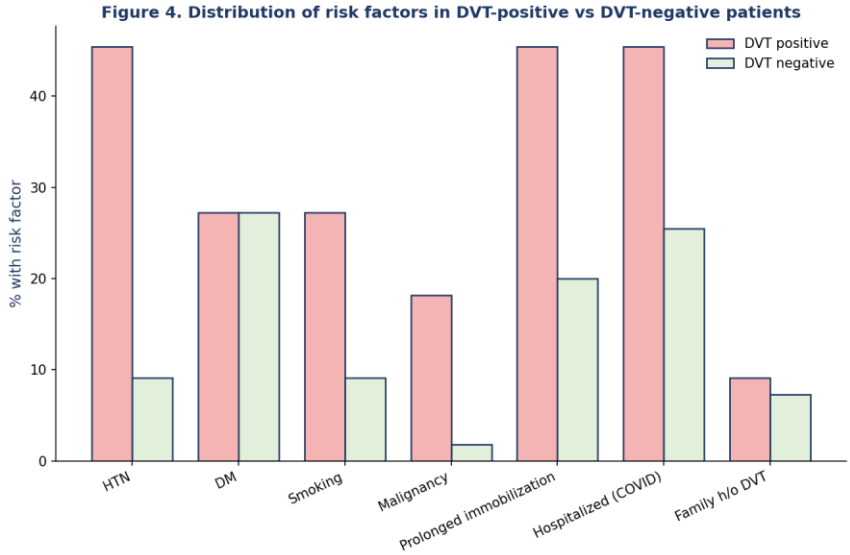

Figure 4. Distribution of selected risk factors in DVT-positive versus DVT-negative patients.

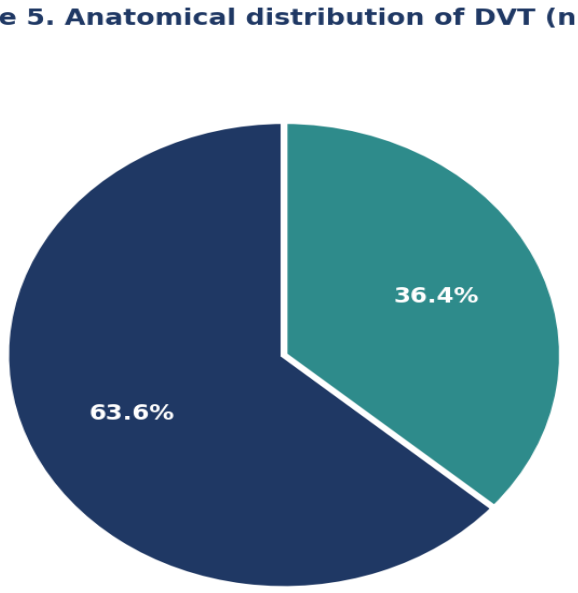

Figure 5. Anatomical distribution of confirmed DVT (proximal vs distal, n = 11).

DISCUSSION

In this prospective observational study from a tertiary-care surgical centre in southern India, the incidence of ultrasonographically confirmed lower-limb DVT in patients with a recent COVID-19 illness was 16.7% (11/66). This incidence is consistent with — though at the higher end of — the range reported in published non-ICU COVID-19 cohorts (8% to 22.5%) [4,5,11], and substantially higher than the 0.8–1.6% incidence reported in pre-pandemic Indian hospitalized medical or surgical patient cohorts [8,9]. Several factors plausibly account for this finding, including the well-documented persistent prothrombotic state in convalescent COVID-19 patients, the underlying under-utilization of pharmacological thromboprophylaxis in Indian practice [10], and the selection of patients at elevated baseline risk through clinical suspicion and risk-factor screening.

The pattern of disease observed — predominance of left-sided involvement, near-equal proportions of proximal and distal thrombosis, and a male preponderance — mirrors that reported in pre-pandemic DVT studies from Indian and international centres [12,13]. The slight excess of left-sided cases is consistent with the well-described anatomical contribution of the May–Thurner phenomenon, in which the right common iliac artery compresses the left common iliac vein. The finding that 45.5% of confirmed cases had proximal disease is clinically important, given the higher risk of

pulmonary embolism associated with proximal thrombosis and the consequent need for prompt initiation of therapeutic anticoagulation.

Among the variables examined, D-dimer was the single strongest discriminator between DVT-positive and DVT-negative patients in our cohort, with mean values approximately four times higher in the former group ($p < 0.001$). This is in keeping with multiple published reports in COVID-19, where D-dimer cut-offs ranging from 0.5 µg/mL to 3.0 µg/mL have been proposed for risk stratification [11,14]. C-reactive protein was also significantly elevated in DVT-positive patients, reinforcing the concept of immunothrombosis — the close coupling of inflammation and coagulation in COVID-19 pathophysiology [3]. Hypertension emerged as the only categorical risk factor that reached statistical significance in our univariate analysis ($p = 0.008$); while hypertension is a less well-established predictor of DVT than age, immobilization, or malignancy in classical risk models, its association with endothelial dysfunction may be particularly relevant in the post-COVID setting.

Other recognized risk factors — advanced age, malignancy, prolonged immobilization, and hospitalization during the acute COVID-19 illness — showed clinically meaningful but statistically non-significant differences between groups. These findings should be interpreted in the context of the modest sample size of 11 events, which provides limited power to detect moderate associations and precludes meaningful multivariable adjustment. The observed direction and magnitude of these associations are nevertheless concordant with the international literature and support a prudent threshold for screening in patients with one or more of these risk factors.

The clinical implications of these findings are several. First, in regions where thromboprophylaxis is under-utilized, post-discharge patients with recent COVID-19 represent an under-recognized population at risk of late-presenting DVT. Second, a normal D-dimer in this setting retains a high negative predictive value and may safely permit a watch-and-wait approach in low-risk patients, whereas an elevated D-dimer combined with persistent inflammation should prompt prompt compression ultrasonography. Third, the absence of in-hospital mortality and the favourable short-term outcome with therapeutic anticoagulation reinforce the value of early detection — a point of particular relevance to surgical services, which may be the first point of contact for patients presenting with non-specific limb symptoms in the convalescent phase.

This study has several limitations. It was conducted at a single tertiary-care centre and therefore may not be generalizable to community settings. The sample size of 66 patients limits the statistical power for risk-factor analysis. Patients were enrolled on the basis of clinical suspicion or risk-factor presence and not on a universal screening protocol, which may have overestimated incidence compared with population-based estimates but conversely may have missed asymptomatic cases in low-risk individuals. Follow-up was limited to the short term, and longer-term outcomes such as post-thrombotic syndrome and recurrence were not assessed. The single-radiologist Doppler protocol provides consistency but limits inter-observer assessment. Finally, the COVID-19 vaccination status of patients was documented but the study was not powered to evaluate its independent effect on DVT incidence.

Notwithstanding these limitations, the strengths of the study include its prospective design, the use of a standardized proforma, systematic compression ultrasonography, and a representative south-Indian tertiary-care population. To our knowledge, this is among the first prospective studies from southern India to specifically address the incidence of DVT in the post-COVID-19 surgical-referral population. Future research should focus on larger multicentre cohorts, incorporation of universal screening protocols for high-risk subgroups, formal evaluation of extended post-discharge thromboprophylaxis, and longer-term follow-up for post-thrombotic complications.

CONCLUSION

In this prospective study of post-COVID-19 patients evaluated at a tertiary-care general-surgery service, the incidence of lower-limb deep vein thrombosis was 16.7%. Elevated D-dimer, elevated CRP, and a history of hypertension were significantly associated with the diagnosis. The findings support a high index of suspicion, routine D-dimer measurement, and a low threshold for compression ultrasonography in post-COVID-19 patients presenting with limb symptoms or with established thrombotic risk factors. Larger multicentre studies are required to validate these observations and to inform evidence-based post-discharge thromboprophylaxis strategies in the Indian context.

Acknowledgements

The authors gratefully acknowledge the Department of Radiodiagnosis and the Central Clinical Laboratory at KIMS, Hubballi, for their support in performing and reporting the imaging and laboratory investigations included in this study.

Author contributions

All authors contributed substantially to the conception and design of the study, data acquisition, analysis and interpretation, drafting and critical revision of the manuscript, and approved the final version submitted.

Conflicts of interest
None declared.

Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical approval and informed consent
The study protocol was reviewed and approved by the Institutional Ethics Committee, KIMS, Hubballi. Written informed consent was obtained from all participants.

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