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Clinical Relationship Of D-Dimer Values with Vascular Events in Covid-19 Positive Patients and Its Prognostic Significance

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Abstract

Coronavirus disease 2019 (COVID-19), caused by the acute respiratory syndrome coronavirus 2, is primarily a respiratory illness, it may impact several organ systems. Thrombotic complications and coagulopathies are common in COVID-19, Probably indicating viremia, cytokine storm, or superinfection and organ dysfunction-related activation of the coagulation cascade. In our study of 100 patients, we ascertained that COVID-19 patients had elevated D-dimer levels at the time of admission and these levels were even higher in COVID-19 patients with vascular complications like stroke, myocardial infarction, pulmonary embolism, or mesenteric ischaemia. In the present study, we discovered that 2.07 g/ml was the ideal cutoff value for predicting mortality in COVID-19 participants.

D-dimer levels were higher in patients with vascular event than in patients without vascular complications. In this subgroup, D-dimer level also functions well as a predictor of death. Hence, with the help of structured protocol, biochemical investigations (D-dimer levels) and newer diagnostic modalities we can prognosticate vascular complications and prevent morbidity and mortality in COVID-19 patients.

Keywords: Covid-19, D-dimer, hypercoagulable state

Introduction

The severe acute respiratory syndrome coronavirus 2 that causes coronavirus disease 2019 (COVID-19) was first reported in Wuhan, the capital of China's Hubei province, in December 2019 [1]. Although COVID-19 predominantly affects the respiratory system, it can also have an impact on the digestive, hepatic, cardiac, neurological, and renal systems [1–3]. Disseminated intravascular coagulopathy and other thrombotic consequences are frequent in COVID-19, most likely reflecting activation of the coagulation cascade brought on by viremia or a cytokine storm, but also possibly by superinfection and organ failure [4]. A fibrin breakdown product known as D-dimer is frequently utilized as a biomarker for thrombotic diseases. D-dimer levels rise with age and during pregnancy, with a value of less than 0.5 g/mL often being regarded as normal. D-dimer levels increase as community-acquired pneumonia worsens [5]. D-dimer has been found as a potential indication for COVID-19 patients' prognosis since the COVID-19 pandemic's breakout. In numerous researches, admission day D-dimer level has been demonstrated to be promising for predicting the severity of the ailment [6–9]. The purpose of the study was to investigate the predictive importance of the clinical association between D-dimer readings and vascular evens in COVID-19 positive individuals.

Material And Methods

Study Design: Cross-sectional study.

Study Place: Bharati Vidyapeeth (Deemed to be University) Medical College & Hospital, Sangli.

Study Duration: 8 months

Study Population: All the COVID-19 positive cases above 18 years of age and admitted in Bharati Hospital, Sangli were included in the study.

Study Subject:

1. Cases with Mild symptoms SPO2>94%, RR <24/min were treated as mild cases.
2. Symptomatic cases with SPO2 90-94%, RR > 24/min, Dyspnea were treated as moderate cases.
3. Severe, extensive pneumonia, SPO 2 90% at room air, RR > 30/mins, ARDS were treated as Severe cases.
4. Cases of septic shock, RR > 40/min, SPO2 <90% were treated as Critically ill cases.

Inclusion Criteria: All the COVID-19 positive cases above 18 years of age and admitted in Bharati Hospital, Sangli were included in the study.

Exclusion Criteria:

1. Pregnant women
2. Patients with history of recent trauma or surgery
3. Chronic liver disease

Methodology:

After the appropriate permission from the institution head, each patient was explained about the summary of the research conveying the highlights and consent was obtained. Patients giving the written consent were considered for study. A detail clinical history was taken and a thorough clinical examination was performed. All the relevant investigations were carried out. Care was taken to maintain strict confidentiality and also to maximize the level of comfort while doing the clinical examination and evaluation.

Results And Observations

Among 100 patients hospitalized with COVID-19 positivity, 15 presents with vascular events such as stroke, myocardial infarction pulmonary embolism, mesenteric ischemia (15%). Patients who experienced vascular events had co-morbid conditions like diabetes, vascular disease, congestive heart failure, hypertension, and atrial fibrillation. They were also older (median age, 70 (60-79) vs. 64 (52-75)). Patients presenting with vascular events had higher D-dimer levels at admission [median (IQR), 1.39 (0.70-2.70) g/ml FEU] than patients arriving without vascular events [0.80 (IQR 0.48-1.11) g/ml FEU]. Additionally, individuals who had vascular events had higher peak values [2.86 (IQR 1.03-15.58) vs. 1.0 (IQR 0.56-2.96) g/ml FEU]. Except for neutrophil and white blood cell counts in patients with vascular events, all other lab results comparing patients with and without vascular events at admission were comparable. Less chance of survival exists for patients who have higher peak D-dimer levels exceeding the threshold value. When age, sex, religion or ethnicity, and comorbidities were taken into account, the crude RR was 4.48 (95% CI, 4.12-4.87, p 0.001) and the adjusted RR was 3.00 (95% CI, 2.75-3.28, p 0.001). This study found that elevated peak D-dimer levels above the cutoff value were linked to increased mortality in all COVID-positive patients.

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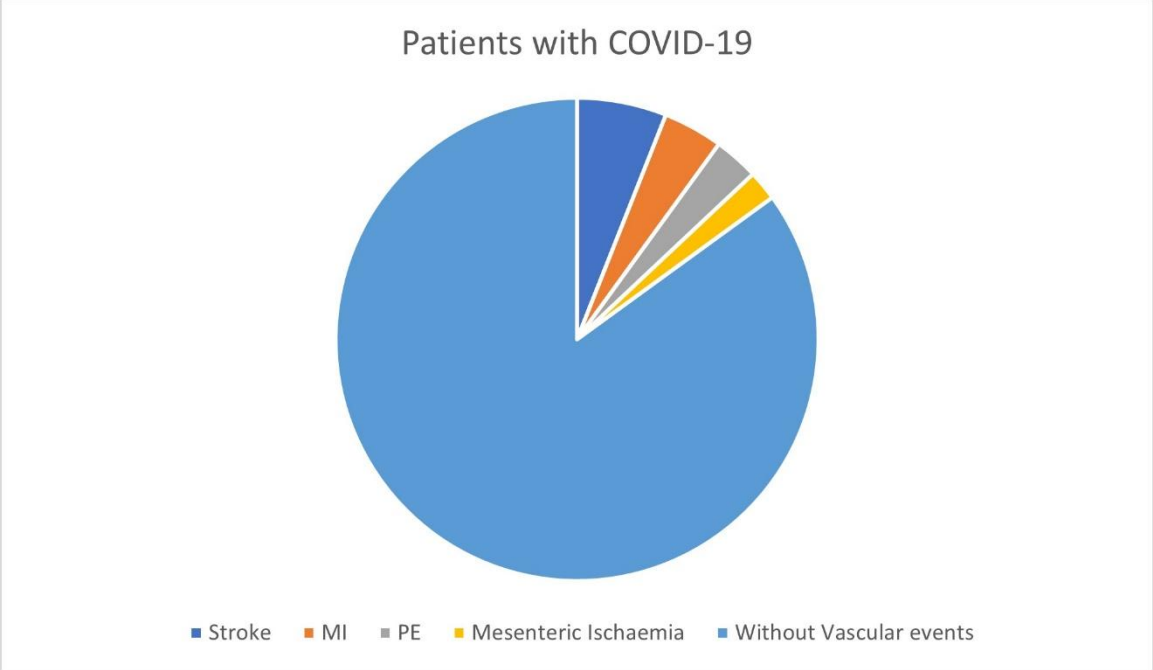
Figure 1: Distribution of vascular events with high D-Dimer levels in COVID-19.



A frequent vascular consequence of severe COVID-19 pneumonia was stroke. In our study 6 out of 100 patients developed stroke (4%). Out of 15 patient who developed vascular complication 6 developed stroke (33.33%). Patients with severe COVID-19 complicated by Myocardial Infarction (4%). 4 patients developed myocardial infarction. Among 100 patients with COVID-19 3 patients developed pulmonary embolism which was radiologically proven. In our study 2 patients out of 100 developed mesenteric ischemia.

Discussion

By having an affinity for the ACE2 receptors located in the lungs, heart, kidneys, and small bowel, SARS-CoV-2 induces clinical COVID-19. The vascular endothelium also contains a lot of these receptors [10], This infection causes a lymphocytic "endotheliitis," which has been hypothesized to be one of the bases for the thrombotic consequences of this infection [11]. Varga et al., reported viral inclusions in endothelial cells of the kidneys, heart, lungs, and small bowel along with extensive endothelial dysfunction and apoptosis in a recent pathological examination in individuals with COVID-19 infection (2 autopsy and 1 surgical biopsy) [11]. The multiorgan failure that distinguishes COVID-19's severe cases may have its roots in a virus-induced condition of systemic decreased microcirculatory performance in many arterial beds, according to the scientists. A systemic immunological response to the infection (a "cytokine storm") as well as a direct local action of SARS-CoV-2 on the ACE2 receptors in the vascular endothelium may cause vessels to become inflamed. Patients of COVID-19 are more likely to experience vascular complications, however it can be challenging to distinguish between those who are more likely to get PE since COVID-19 and PE (Pulmonary Embolism) symptoms often overlap. Clinical judgement along with radiological evidence can be helpful to identify vascular complications. It is critically necessary to develop straightforward, minimally invasive diagnostic algorithms that can safely rule-out PE in patients with COVID-19. As a result, we read the recent research published in the European Respiratory Journal by Mouhat and colleagues with interest. 162 hospitalized patients with severe COVID-19 who had computed tomography pulmonary angiography (CTPA) as the gold standard for PE were analyzed retrospectively for variables related to PE by the authors. They found that D-dimer testing and not receiving anticoagulant medication had a statistically significant relationship with vascular complications. It is necessary to find a D-dimer cut-off value to best predict occurrence of vascular complication. For the diagnosis of PE, D-dimer testing is not reliable enough to be utilized

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alone. [13] As a result, diagnostic algorithms have been created, such the Wells' rule and FAST score, which use the D-dimer as a triage test. [14,15] Vascular complications in patients with low D-dimers and limited clinical evidence can be ruled out. In contrast, additional radiological testing must be done on people whose D-dimers are higher than the threshold. With the COVID-19 infection, a pro-inflammatory hypercoagulable condition has been well-documented [17,18]. In COVID-19 individuals with coagulopathy, higher D-dimer levels have been discovered, and multiple observational studies found that an elevated D-dimer level was a reliable indicator of ICU admission or hospital death [19,20,21]. Additionally, D-dimer has been recognized as a biomarker for vascular complications and linked to the severity of stroke in the past [20,22]. D-dimer levels may be independently raised in COVID-19 individuals who present with AIS (Acute Ischaemic Stroke), which could change the predictive significance of D-dimer in those patients. Our research demonstrated that COVID-19 patients had higher D-dimer levels at admission [0.95 (0.56-1.83) g/ml FEU (Fibrinogen Equivalent Unit)] Patients with COVID-19 who presented with vascular complications had concentrations that were higher than usual (0.5 g/ml FEU) [1.42 (0.76-3.96) g/ml FEU] [23,24]. We discovered that 2.07 g/ml was the ideal cutoff value for predicting mortality in COVID-19 participants. Similar to earlier findings, the cutoff value of 2.07 g/ml FEU applies to all hospitalized COVID-19 patients. D-dimer levels > 2.14 mg/l on admission were reported by Yao et al. as a predictor of death, while Zhang et al. reported an ideal cutoff value of 2.0 mg/ml within 24 hours of hospital admission [19,25]. The clinical presentation and laboratory characteristics of the CVST (Cerebral Venous Sinus Thrombosis) cases were comparable to those observed in Europe [26-28]. According to a diagnostic investigation, all hospitalized patients with COVID-19 and radiological signs of PE had plasma D-dimer values of 0.05 g/mL or above. Setting higher D-dimer limits resulted in better specificity but at the expense of a higher false-negative rate that could pose an unacceptable danger to patient safety [29]. AMI (Acute Mesenteric Ischaemia) might be suspected if the gut is thick-walled, edematous, and dilated (>3 cm) on a CT scan. When intestinal pneumatosis or portal venous gas are present, bowel ischemia is likely. However, the appearance of pneumatosis in patients with severe COVID-19 should be read cautiously because it may be there as a result of mechanical ventilation. Bowel infarction is indicated by non-enhancing thick bowel. Frank perforation manifests as a discontinuity in the intestinal wall and a modest accumulation of air [30].

Conclusion

When it is not properly recognized and treated, systemic thrombosis frequently affects critically ill COVID-19 patients and can have deadly consequences. Thrombotic risk frequently continues even after anticoagulation is started. Providers should weigh the pros and cons of preventive vs therapeutic anticoagulation based on a variety of patient-specific factors, such as laboratory results, imaging, clinical suspicion, and a comprehensive comparison of the risks of thrombosis and bleeding. D-dimer levels are higher in patients with vascular complications like myocardial infarction, stroke, mesenteric ischemia, and pulmonary embolism than in patients without vascular complications. Although the threshold for predicting this outcome is much higher, D-dimer performs well as a predictor of mortality in this subgroup. In COVID-19, anticoagulation will be crucial in the management of vascular events. It is vitally needed to conduct larger, well-designed prospective trials to better understand the best management approaches to reduce the thrombotic risks related to COVID-19.

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