

# What Do You Know So Far about the D-dimer Levels in COVID-19?

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## Abstract

The severe Acute Respiratory Syndrome caused by coronavirus 2 (SARS-Cov-2) is capable of triggering important systemic and laboratory changes, which may include elevations in the D-dimer levels and the expression of Von Willebrand Factor. Thus, we present a mini-review, based on the database of the National Library of Medicine (PubMed) on the association of these laboratory parameters and changes in coagulation, with infection by this new human coronavirus. Although studies point to evidence of this association, we emphasize the importance of conducting multicenter studies, with larger samples and in different populations, to better understand COVID-19 as a whole.

**Keywords:** Hemostasis; Coronavirus; von Willebrand Factor; Laboratories

## Introduction

The Severe Acute Respiratory Syndrome, Coronavirus 2 (SARS-Cov-2), was first linked to cases of pneumonia of unknown cause in which they began to be reported in Wuhan, China [1-3]. This represents a major threat to global health, and by the end of June, about 503 thousand deaths worldwide were found due to this disease [4]. Coronaviruses are known for their great potential to cause systemic diseases, including changes in coagulation [5,6]. Although it is still uncertain, studies point to the existence of a relationship between the severity of the case and the laboratory alterations that include the elevations in the levels of D-dimer and Von Willebrand Factor (vWF) [5,7].

This paper was based on the National Library of Medicine's (PubMed) database, which revealed that there are just over 10 published studies relating to the 2019 coronavirus (Covid-19) to changes in D-dimer and vWF levels.

## Methodology

We performed a research in the National Library of Medicine's (PubMed) database by using the MeSH terms "D-dimer" "Von Willebrand Factor", "Covid-19" and "Sars-

Cov-2". In this brief review we chose as criteria: English studies published since December 2019 until July 2020 and the following types of study: cohort, retrospective and case report studies. Thus, we selected 6 studies in total, that satisfactorily addressed the possible associations between the D-dimer and vWF levels in the SARS-Cov-2 infection, which were included and read in their entirety.

## Discussion

The D-dimer consists of the final product of the fibrinolysis process, through plasmin-mediated fibrin degradation and, therefore, is an important biomarker for the assessment of the presence of thromboembolic events [8,9]. A study carried out at Wuhan Asia General Hospital analyzed 343 patients diagnosed with Covid-19 and with elevated D-dimer levels [10]. Through data analysis, it was observed that patients with parameters greater than 2 µg/mL had a higher mortality rate and, therefore, the high D-dimer would be a good predisposing factor for hospital mortality from infection, despite important limitations, such as the fact that this is a retrospective and single-center study. Tang et. al [11] studied 183 cases of pneumonia caused by the virus, among which 21 died, 18 of which were associated with high levels of D-dimer. Interestingly, in the group of non-survivors, 70% of the cases were

diagnosed with Disseminated Intravascular Coagulation (DIC), an important life-threatening condition of the patient, following the criteria of the International Society for Thrombosis and Hemostasis (ISTH) [12]. Unlike the first study, Tang classified values above 3 µg/mL as high for the parameter, however, even so, the mortality rate in this group of patients was higher, at approximately 11%. Yu, et al. [13] published a cohort retrospective study with meta-analysis, showing the association between high levels of this parameter and the severity of sars-cov-2 infection, by analysis of 1561 patients.

Although thromboembolic events are associated with changes in the D-dimer Test, this association with infection with the new coronavirus remains uncertain. Virus infection initiates an inflammatory process mediated by the host's innate immunity, which in turn activates the coagulation system and initiates thrombin production [14]. Thus, changes in this marker would be much more associated with the inflammatory process in the body of the patient affected by the disease, than necessarily a hemostasis disorder [8].

On the other hand, the Von Willebrand factor is a protein released by endothelial cells in response to inflammation, acting in the acute phase of the response. It also plays an important role in situations of endothelial injury. In a case report of 3 patients by Breakey et al. [14], patients with a mean vWF: activity, 348.3% (42–168) drew the team's attention when compared to ICU patients, without SARS-CoV-2. These results are similar to those presented by Escher et al. [15], they also found persistently high values of vWF in their report. The high level of vWF is directly associated with macrovascular thrombotic complication, thus, the hypothesis of a secondary pro-thrombotic coagulopathy was questioned, due to the interaction of SARS-CoV-2 with endothelium. This can be understood as the cause of mortality in cases complicated by the disease. [15,16].

## Conclusion

In conclusion, our brief review of the laboratory findings at SARS-Cov-2 revealed that although there are indications of an association between D-dimer and Von Willebrand's Factor with the severity of the case, there are still limitations, especially regarding the studies design's. With that, we emphasize the importance of more studies that attest to this relationship and the main mechanism involved. Thus, our brief review represents an incentive for future works and with more content to be carried out. Still, the medical team must pay attention to an increased risk of CID in patients who have changes in laboratory parameters, since this is configured as a disease that considerably increases the morbidity and mortality rates of patients.

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