

## Thrombocytopenia and coronavirus: A prognosis and progression of the Coronavirus disease

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### Abstract

Coronavirus pneumonia has been detected in Wuhan City since December 2019. Today, coronavirus 2019 (COVID-19) has become an epidemic worldwide. Although this disease is not fully understood, it can show different symptoms over time. One of the components involved in the body by this virus is platelets that communicate directly with several different types of viruses, including the SARS-CoV virus family, via integrins, P-selectins, and pseudo-receptors. Mechanism of action includes the virus's direct effect on bleeding and maturation of megakaryocytes, increased adhesion and activation of platelets, and platelet consumption in abscesses of damaged lung tissue. Therefore, Covid-19 disease can affect platelet function, which in itself can directly or indirectly affect thrombocytopenia. Pathology of bone marrow aspiration from three patients with Covid-19 thrombocytopenia indicates abnormal megakaryocyte maturation. In addition, it can be associated with the severity and mortality of the disease. In other words, thrombocytopenia can be used as a prognostic factor in patients with progressive Covid-19, which has been reported in 5 to 40% of COVID-19 patients. This study attempts to gather information and recent reports on thrombocytopenia in patients with Covid-19.

**Key words:** Covid-19, Platelets, Thrombocytopenia

### Introduction

Since December 2019, coronavirus pneumonia has been detected in Wuhan City, China, in Hubei Province, China. Over time, the virus has spread worldwide. COVID-19 is a new respiratory disease with various clinical symptoms such as fever, fatigue, dry cough, and shortness of breath. The mechanism of this disease is not fully understood to date, so the symptoms vary from person to person. Some patients have mild symptoms at the onset of the disease. Unusual symptoms include abdominal pain, headache, palpitations, and chest pain. However, changes in blood cells in patients with COVID-19 are common symptoms, including decreased lymphocyte count and platelet count. Thrombocytopenia has been reported in 5 to 40% of COVID-19 patients. Patients with thrombocytopenia

appear to be more severe by Covid-19 disease (1). Studies have shown a significant association between thrombocytopenia and the severity of Covid-19(2). Platelet counts are significantly lower in these patients. Lower platelet counts in patients with COVID-19 were reported in a study of 85 patients with no clinical or radiological improvement after ten days (3).

In another study by Wang et al., Lower platelet counts were reported in severe disease than disease recovery. However, most patients with COVID-19 show only mild thrombocytopenia, even with severe disease. A study conducted in Singapore on Covid-19 patients had only 5% of admitted patients with higher than normal platelets (4). In a study on platelet count in patients with COVID-19, the mean platelet counts in studies reported on platelet count

in COVID-19. According to studies, the mean platelet counts in patients with COVID-19 from  $\sim 160$  to  $215 \times 10^9 / L$  in COVID-19 patients in general to 120 to  $200 \times 10^9 / L$  in high-intensity patients(5). Tang et al. Reported a link between blood clotting and mortality in 183 patients with COVID-19, and out of a total of 21 patients rescued from Covid-19, 12 who did not survive had lower than normal platelet counts(6). As a result, mild thrombocytopenia is a common finding in COVID-19 patients. Platelet counts  $<109/100 L$  are rare, and there is also a link between high platelet counts and a poor prognosis (7). We tried to summarize the causes and reports of thrombocytopenia in patients with Covid-19.

#### **Mechanism of thrombocytopenia COVID-19**

Platelets interact directly with several different types of viruses, including the SARS-CoV virus family, through integrins, P-selectins, and pseudo-receptors, and platelets may be involved in SARS-CoV and MERS-CoV outbreaks (8, 9). In 30 to 50% of patients, thrombocytopenia has been described in patients with SARS and Covid-19(10). The mechanisms of thrombocytopenia in SARS-CoV infection were investigated in 2003 by Young et al. (11). According to their studies, their mechanism of action includes the direct effect of the virus on bleeding and maturation of megakaryocytes and increased adhesion and activation of platelets and platelet consumption in abscesses of damaged lung tissue (11). Activation of platelets in the pulmonary bloodstream can affect the activity of the bloodstream and aggravate damage to the lung parenchyma, causing respiratory failure and frequent need for mechanical ventilation (12, 13), which is described as one of the major conflicts in covid-19 virus (14).

These data open up interesting perspectives on the role of platelet activation and the potential benefits of

antiplatelet agents in COVID-19(15). However, these questions need to be addressed in future research. To the best of our knowledge, no study of platelet activation in patients with COVID-19 has been reported (16).

#### **Platelet gene expression and function in COVID-19 patients**

To solve the thrombotic complications in patients with Covid-19, we must understand the pathogenesis of patients with Covid-19(17). Studies in changes in platelet gene expression in patients with SARS and Covid-19 have shown that RNA sequences in patients with Covid-19 show changes in platelet gene expression that changes. The gene expression is usually associated with altered protein expression, antigen presentation, and mitochondrial dysfunction (18). p Selectin was increased after activation. Platelet activation and accumulation can be partly attributed to MAPK signaling pathway activation and thromboxane production (19). These findings suggested that SARS-CoV-2 infection is associated with platelet hyperactivity, which may contribute to the pathophysiology of COVID-19 (20).

#### **Immune Thrombocytopenic Purpura in a Patient with Covid-19**

Thrombocytopenic purpura is an immune disease in which the blood doesn't clot normally. This condition is now more commonly known as immune thrombocytopenia (ITP)(21). According to recent reports, deep thrombocytopenia in patients with COVID-19 is caused by immune thrombocytopenic purpura (22). Thrombocytopenia in a patient with COVID-19 includes DIC and sepsis-induced thrombocytopenia. Severe SARS-CoV-2 infection is associated with blood clotting (23).

A case report of a patient with COVID-19 coronavirus showed thrombocytopenic purpura after intravenous immunoglobulin and high-dose dexamethasone (24). The study showed that in the presence of deep

thrombocytopenia in a patient with COVID-19, it is necessary to eliminate the immune response that causes purpura (25). Four patients have experienced symptoms of Purpuric Lesions. On day nine, they experienced symptoms of a cerebral hemorrhage, which could be prevented with early diagnosis and treatment (26). The time sequence, in this case, indicated Covid-19 as a causative agent of thrombocytopenia in the immune system in this patient (27). Although cerebral hemorrhage did not have significant side effects, reports such as these show signs of awareness of Covid-19-related complications (28). Thrombocytopenia was negative, but these patients showed cutaneous and mucosal purpura symptoms, two of whom received intravenous antibody therapy, while one recovered without any treatment (29).

### **Thrombocytopenia as an initial manifestation of COVID-19**

Thrombocytopenia has been a common manifestation in Covid-19 patients since the coronavirus epidemic in 2019(29). The etiology of thrombocytopenia is likely to be very effective in COVID-19. This could be due to the direct effect of Covid-19 on host cells (30). Hematopoietic and stromal bone marrow cells lead to dysfunction of bleeding and inhibition of bone marrow growth or production of cytokines, which leads to the destruction of bone marrow progenitor cells(31). Another mechanism considered is platelet production, which causes thrombocytopenia in the early stages. Platelet depletion can also be due to increased platelet consumption by infection and inflammation, especially in the lungs, which causes damage to pulmonary endothelial cells(32). It activates platelets in the lungs and causes the accumulation and formation of micro thrombosis, which leads to increased platelet consumption (33). In a meta-analysis of 31 studies involving 7613 patients with COVID-19, the results

showed a significant association between thrombocytopenia and patients with severe COVID-19 symptoms admitted to medical facilities(34). However, other clinical, biological, and radiological factors affect the severity and outcome of COVID-19(34).

Thrombocytopenia was reported to be prevalent at the time of admission, while thrombocytopenia is rare in the late stages (14 days after the onset of symptoms)(22). A retrospective study in Wuhan, China, found that delayed-stage thrombocytopenia in COVID-19 was more likely to occur in elderly patients or patients with low lymphocyte counts at admission(2). This type of thrombocytopenia, which occurs in the delayed phase of Covid-19 disease, is associated with an increased length of hospital stay and higher mortality(35). Pathology of bone marrow aspiration from three patients with delayed-stage thrombocytopenia also indicates abnormal megakaryocyte maturation(36). A study at 1476 patients at Wuhan Hospital analyzed platelet counts, and in-hospital mortality showed that thrombocytopenia was common in patients with COVID-19 and increased with increased risk of death(37). The lower the platelet count, the higher the mortality rate. At another treatment center in South Korea, the patient was referred to a medical center without respiratory symptoms with symptoms of thrombocytopenia (38).

### **Delayed-phase thrombocytopenia in patients with coronavirus disease (COVID-19)**

Thrombocytopenia was reported to be prevalent at the time of admission, while thrombocytopenia is rare in the late stages (14 days after the onset of symptoms)(2). A retrospective study in Wuhan, China, found that delayed-stage thrombocytopenia in COVID-19 was more likely to occur in elderly patients or patients with low lymphocyte counts at admission. This type of thrombocytopenia,

which occurs in the delayed phase of Covid-19 disease, is associated with an increased length of hospital stay and higher mortality(2). Pathology of bone marrow aspiration from three patients with delayed-stage thrombocytopenia also indicates abnormal megakaryocyte maturation(36).

### Conclusion

Recent reports of coronavirus showed that patients with thrombocytopenia as one of their clinical symptoms develop the disease more severely. It may be necessary because thrombocytopenia has been reported in 5 to 40% of COVID-19 patients. On the other hand, thrombocytopenia is one of the primary complications of patients with Covid-19 hospitalization and is not usually seen in the delayed stage of the disease.

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### Conflicts of interest:

The authors declare that they have no competing interests.

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