The Implications of COVID-19 Infection on Hematologic Parameters and Coagulation Activity: A Review

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https://dx.doi.org/10.13005/bpj/2522
(Received: 11 October 2022; accepted: 09 November 2022)

Wuhan, China, substantially is the epicenter of the COVID-19 pandemic in December 2019. Coronavirus, the confounder virus, a zoonotic in origin was the causative agent of the disseminated disease worldwide. Structural similarities and convergence points were demonstrated between the coronavirus, SARS, and MERS viruses. Aberrantly, a subset of patients developed a serious acute respiratory distress syndrome or diffuse alveolar injury whereas the rest of the patients encountered mild or no symptoms. The pathological clinical laboratory findings are not only critical in the diagnosis of the COVID-19 infection, on the contrary, but they are also crucial in the prognostic predictions about disease prognosis and therapeutic response. This review aims to give some historical context for the pandemic, demonstrate the laboratory’s important role in the screening of COVID-19 infection, and review the current phase of biomarker examination in COVID-19 infection, focusing on markers derived directly from the hematological laboratory, reflecting the implications of COVID-19 on the hematological system and coagulation pathways. In conclusion, there is a direct significant correlation between infection severity, the death rate in COVID-19 patients, and the low number of either WBCs or a high number of WBCs with a low number of lymphocytes.

Keywords: COVID-19; Coagulation; D-Dimer; Hematology; Lymphopenia.
world, is the gold standard molecular-based test for the identification of COVID-19 in clinical samples from patients with COVID-19-compatible symptoms.\(^7\)-\(^9\) Pathogen identification via RT-qPCR is common because it is rapid duration, high sensitivity, specificity, and additionally the affordability since PCR test cost is almost $51.\(^10\) The test was accomplished by extracting extremely small amounts of RNA from respiratory tract samples such as nasopharyngeal swab/oropharyngeal, tracheal aspirate, sputum, and bronchoalveolar lavage.\(^9\)-\(^20\) Wang et al. highlighted in a study of 1070 samples from 205 patients with COVID-19 in China that the sensitivity of the test is 32%, 63%, 72%, and 93% in the oropharyngeal swab, nasopharyngeal swab, sputum, and bronchoalveolar lavage, respectively.\(^21\)

The clinical manifestations of COVID-19 infections were most commonly incorporated with pneumonia and acute respiratory distress syndrome.\(^22\),\(^23\) There is a scientific agreement on the role of COVID-19 in exerting a multisystem disease in adults and old ages.\(^24\),\(^25\) Controversially, young patients with COVID-19 infections showed asymptomatic or mild-to-moderate illnesses which were rarely fatal.\(^26\),\(^27\) Remarkably, several cases of young patients developed severe symptoms that emanate from death as an end-stage.\(^28\) One of the primary symptoms of COVID-19 is hypoxia and a multi-systemic illness that may be exacerbated by the viral proteins’ modification of Hb. The alteration in Hb conformational shape reduces the fraction of completely functioning Hb in oxygen transportation.\(^29\) In a study of 508 patients conducted by Al-Balas et al., the most commonly reported symptoms in both medically free and medically ill individuals were dry cough, nonspecific malaise, and fever. The average length of hospital stay was shorter in medically free patients than in medically ill patients, and it was shorter in asymptomatic patients than in symptomatic patients.\(^30\),\(^31\) There was a statistically significant link between the presence of long-term illnesses and the onset of symptoms in COVID-19 patients.\(^30\) Noticeably, intensive care was needed more frequently and hospitalization for longer periods for children with the multisystem inflammatory syndrome (MIS-C)\(^32\),\(^33\).

The clinical findings of the complete blood cells (CBC) and coagulopathy were indispensable tests for the prognostic activity of the disease prognosis in COVID-19 patients. For instance, a massive high platelet count in the presence of systemic immunological and coagulation activity is a prognostic of a significant compensatory platelet generation response in these patients.\(^34\) A study conducted on 449 severe COVID-19 patients by Srivastava et al., revealed that fibrinogen and D-dimer degradation products are significantly increased in COVID-19 infections. This escalation is proportionally linked to hypercoagulability throughout the body and repetitive venous thromboembolic complications.\(^35\) Mortality rates among COVID-19 patients are found to be directly correlated to the elevation in D-dimer level.\(^36\) COVID-19 causes not only microvascular thrombotic disorders but also arterial thrombotic events such as strokes and ischemic limbs.\(^37\)

Controversially, mild thrombocytopenia is noticed significantly in COVID-19 patients. The cause is attributed to two conditions; firstly, an increase in platelet consumption and, secondly, a decrease in platelet production.\(^38\) Eventually, COVID-19 patients rarely develop disseminated intravascular coagulopathy (DIC) or life-threatening bleeding complications during the infection.\(^39\) The immune system’s cells, specifically lymphocytes, might be affected.\(^40\) Lymphopenia may develop from virus-induced destruction of lymphocytes (especially T lymphocytes) and reduction of lymphocyte proliferation, and recovered lymphocytes may be a prediction of eventual recovery.\(^41\) Eventually, we conducted the current literature review on hematological diversities and coagulopathy in COVID-19 infection, which may help health professionals in COVID-19 management, we have reviewed over 150 relevant articles in the area of the pathological association between Covid-19 infections and coagulopathy disorders published either in Clarivate database or Scopus database.

**The impact of COVID-19 on hematological cellular elements:**

**Platelets**

Platelets, also known as thrombocytes, are small nucleated cellular fragments (2-4 μm) that

originated from megakaryocytes and are released into the bloodstream at maturation. These spherical fragments have a short lifespan of only 8 or 9 days. They act as the first line of defense against vascular injuries and thrombosis by stimulating a cellular response. As already reviewed by M. Yang et al. in the 2003 SARS epidemic, thrombocytopenia affected 20-55% of patients. Meanwhile, a rebound in thrombocyte count was also reported by Giannis et al. after the infection clearance. Based on Wong et al. patients’ encountered acquired thrombocytopenia due to the outbreak of SARS-Cov-1 exposed to a higher risk of mortality. Concomitantly, thrombocytopenia was reported in Middle East Respiratory Syndrome (MERS) infections, another respiratory infection caused by an etiological agent from the coronaviridea family. Additionally, Wool & Miller et al. designated a relevant proportion of 5% to 41.7% of people infected with COVID-19 developed thrombocytopenia, even though, the decrease in thrombocyte number was mild (with counts often falling within the range of 100 to 150 10^9/L). Thrombocytopenia was significantly proportional to the severity of the disease, nine studies in China with 1779 samples of COVID-19 patients administrated by Lippi et al. revealed that platelets count of individuals with severe disease is only 23 10^9/L to 31 10^9/L lower than that of patients with the non-severe disease. This moderate thrombocytopenia has been identified in a proportion of 58-95% of severely infected cases of COVID-19. On the other hand, patients with COVID-19 rarely developed a blended condition of immune thrombocytopenic purpura and severe thrombocytopenia at the same time.

**Erythrocytes and hemoglobin**

Coincided with the emergence of science, red blood cells, also known as RBCs, were designated exclusively as carriers of oxygen and nutrients to the various tissues throughout the body. Recent empirical evidence suggests that RBCs have a substantial role in versatile physiological functions, such as controlling systemic nitric oxide metabolism, blood rheology, redox regulation, and viscosity. In mature RBCs, the nucleus and organelles are abandoned to ameliorate RBCs structure to pertain hemoglobin (Hb), the primary protein responsible for oxygen transport, so that the RBCs can execute their role in oxygen transportation more efficiently.

Additionally, RBCs are performing a feat role in the microcirculation since they act as sensors of local hypoxia. A study published by Favaron et al. noticed an improved oxygen extraction capability in the microcirculation of COVID-19 patients with severe hypoxia. This was found to be a result of increased RBC availability. However, several studies have demonstrated that patients with COVID-19 have modifications in RBC membrane metabolism and structure. In addition, due to COVID-19 impacts on Hb, COVID-19 has been evaluated as a possible source of acquired acute porphyria. It has been demonstrated that raising Hb F levels in critically sick COVID-19 patients may slow disease progression, reduce morbidity, and improve survival. Commensurately, Russo et al., highlighted the usage of umbilical fetal blood transfusion on COVID-19 patients providing objective confirmation of the role of Hb beta chains in the development of COVID-19. On the bases of wenzhong & hualan revealed that coronavirus can interact with protoporphyrin IX via the spike protein as same as various other viruses. Hemoglobin beta chains, specifically ORF 8, and viral surface glycoproteins show a high affinity to allosteric binding. Liu et al. identified several viral proteins (ORF3a, ORF8a, orf1ab, ORF7a, and ORF10) as possible ligands for the binding of hemoglobin’s 1-beta chains. This binding induces Hb denaturation that hampers viral replication by preventing the cell fusion of COVID-19 through spike protein (as found in other viruses). High-performance liquid chromatography analysis of the serum of 134 COVID-19 patients by San Juan et al., revealed an abundant accumulation of the byproducts of uroporphyrin I, metabolite coproporphyrin III, and coproporphyrin I. According to Shoenfeld et al., COVID-19 and Hb would interact in two locations: erythrocytes, where the virus is delivered intracellularly via the link between Band-3 and spike proteins, and the bone marrow, in which the virus binds with nascent erythroblasts via CD147 and CD26. While in erythroblasts the presence of nuclear material would facilitate viral reproduction and, in this scenario, restrict the normal circulation of red blood cells from the spleen to the bloodstream, causing...
anemia, this is not the case at the erythrocyte level, where the virus penetrates the red blood cell and interacts with the Hb molecule but its replication is blocked by the absence of a nucleus. Anai et al., in a study, revealed that elevated glycosylated Hb levels raise CD147 expression, which in turn raises the likelihood of further problems. Several investigations in individuals with severe COVID-19 disease have reported lower Hb levels, but there is no experimental data to suggest a modification of the oxygen dissociation curve at this time.

**Leukocyte**

Leukocytosis, a high white blood cell count (WBC) is indicative of an active immune response in COVID-19 infections. A Retrospective study of the clinical characteristics of 52 COVID-19 patients demonstrated that asymptomatic people may have been exposed to the virus at a much earlier stage or that they may have compromised IgM production. Complete blood counts demonstrated that asymptomatic patients had higher counts of eosinophils, lymphocytes, and basophils than symptomatic patients, according to these results Han et al. shows that a high number of WBC, especially lymphocytes, is directly linked to a seropositive COVID-19 patient even though there is an absence of symptoms. Compiled data for COVID-19 patients with elevated WBC counts showed that the patients were more likely to develop severe illness and ultimately pass away. Meanwhile, another study has designated a direct significant correlation between infection severity, the death rate in COVID-19 patients, and the low number of either WBCs or a high number of WBCs with a low number of lymphocytes.

L. Yang et al. have established in a meta-analysis study a link between lymphopenia and death rate in COVID-19 patients. Regardless of the severity of the baseline disease a descriptive study of 99 cases of COVID-19 in Wuhan, China revealed that lymphocytes were considerably lower on admission and remained lower during hospitalization in non-survivors, but increased following therapy in survivors. Both human macrophages and monocytes express ACE2, making them susceptible to COVID-19 infections activate and transcribe proinflammatory genes. Fascinatingly, COVID-19 infection appears to dramatically down-regulate the expression of ACE2 in peripheral blood (PB) monocytes. This may be a secondary result of viral binding, we still don’t know if this decrease in ACE2 receptor activity is a proxy for viremia. In addition, ACE2 expression was detected on CD169+ and CD68+ macrophages in the lymph nodes and spleen of COVID-19 patients, suggesting that the COVID-19 virus may specifically target ACE2-positive myeloid cells in these organs. The red pulp of the spleen is a common location for infected CD169+ macrophages. Furthermore, positive tests for viral nucleocapsid protein antigens were more common in macrophage-dense regions of the lymph node periphery. Previous research by Honke et al. has shown that CD169+ macrophages, due to their resistance to type I IFN-dependent activation, are in charge of maintaining a steady state of viral replication in aid of immune development. This suggests that COVID-19 could enter spleens and lymph nodes after infecting CD169+ macrophages. However according to J. Wang et al., there may be more viral replication sites in the body as a result of this, and it may also reduce immunity.

In addition, demographic characteristics such as smoking and blood groups affect the levels of immunoglobulin, Cross-sectional research of 412 Jordanians conducted between September 2021 and January 2022 demonstrated that the enzyme-linked immunosorbent assay approach was used to test total IgG antibodies against COVID-19. The seroprevalence of IgG in the study’s population was 81.8%, with a mean of 15.17 IU/ml. 45.4% of the positive participants had already been infected with COVID-19, while the rest of the study population received vaccination doses.

**Effect of COVID-19 pandemic on hematopoietic organs (bone marrow and spleen)**

In the majority of cases, Hematopoietic stem and progenitor cells (HSPCs) in the bone marrow are responsible for producing a variety of peripheral immune cell subpopulations. There have been some debates about whether COVID-19 affects the HSPC niche directly or indirectly. Research by Zheng et al. conducted immunofluorescence on 33 types of tissues and found that the receptor-binding subdomain 1 of the spike protein of the COVID-19 (RBD-SD1) probe could interact with bone marrow cells...
without the need for ACE2. However, it has been observed that COVID-19 causes a rise in ACE2 expression in human bone marrow primary cells. In a study by Elahi et al., the authors concluded that human bone marrow cells may be susceptible to infection with COVID-19. In concomitant, various stages of specification of human stem cells were used in the experiments of Kucia et al., that has revealed ACE2 and transmembrane serine protease 2 (TMPRSS2) are expressed at the gene and protein levels in a variety of human stem cell lineages, including CD34+CD133+linCD45-cells, which may develop into endothelial progenitor cells (EPCs) and Hematopoietic stem cells (HSCs), CD34+LinCD45+ HSCs, and CD34+CD133+KDR+CD31+EPCs. In addition, pyroptosis in HSCs was found to be triggered by the viral spike protein, which activates the NLRp3 inflammasome. In a series of COVID-19 patients, Varga et al. showed endothelial cell involvement across vascular beds of diverse organs, their results proved further evidence that COVID-19 infections promote endothelial cell damage in COVID-19 patients by targeting ACE2 expressers. This finding is also supported by the fact that ACE2 is shown to be present in a large number of hematopoietic progenitor cells (HPCs) and up to 65% of HSCs deduced from human cord blood.

Debliquis et al. demonstrated that three severely ill COVID-19 patients had an increase in plasma cells, pleomorphic megakaryocytes, macrophages, and hemophagocytosis in their bone marrow aspirates. According to Rapkiewicz et al., increased numbers of megakaryocytes with morphology indicative of active platelet synthesis were discovered in the bone marrow, and electron microscopy of megakaryocytes in bone marrow also revealed the presence of extremely rare virions.

However, in comparison to the lung, heart, and intestines, the spleen has lower levels of ACE-2 receptor expression. On the bases of Feng et al. study, six COVID-19 patients have examined postmortem, and ACE-2 was located in the red pulp and medulla of lymph nodes, indicating that it was expressed in these tissues. In addition, CD169 and CD68 macrophages in the lymph nodes and spleen expressed ACE-2 receptors. The spleen’s red pulp, and only rarely its white pulp, was found to contain viral nucleocapsid antigens. Lymphocyte apoptosis could be triggered by IL-6 secreted by virus-infected macrophages. Pathological abnormalities in the spleen of 10 patients with COVID-19 were evaluated by Xu et al., who found a reduction in T and B lymphocytes, a shrinking and atrophy of lymphoid follicles, a thinning of the white pulp, and an infiltration of neutrophils and plasma cells. In the spleen, Yao et al. discovered a decline in lymphocyte count and evidence of cell degeneration/necrosis.

The implication of COVID-19 Infection on Thrombus Formation

Thrombosis contributes significantly to the devastating consequences of COVID-19 infections such as myocardial infarction and acute respiratory distress syndrome. Fard et al. declared that several pathological modifications such as endothelial cell injury, plaque formation, and oxygen demand injuries are encountered following COVID-19 infection. Congruently, Choudhury & Mukherjee et al. reported hyperactivity of platelets in extremely sick COVID-19 patients, indicating that platelets may play a vital role in the disease progression. Additionally, they revealed that platelets can interact with pathogens through a variety of receptors, including NOD-like receptors, Toll-like receptors (TLRs), the C-type lectin receptor family, and glycoproteins (GPs), including GPαIIbβ3 and GPβa.

Summarizing that platelet activation and thrombosis are directly mediated by platelet TLRs and NOD2. Furthermore, recent in silico studies by Choudhury and Mukherjee et al., demonstrated that the spike protein of COVID-19 could interact with TLRs, particularly TLR-4. Gorog et al. hypothesized putative signaling pathways responsible for the activity of platelets that could be the cause of recurrent thrombosis in COVID-19 patients.

Girardin et al. proposed a provision concerning the critical role of platelets in hemostasis, thrombosis, and immune response. Additionally, they highlighted Nucleotide Binding Oligomerization Domain Containing 2 (NOD2) activation in COVID-19 infections implication on the pathophysiology, thrombotic consequences, and treatment of inflammation in COVID-19 disease.
CD62P, is an integral protein that serves as a cell adhesion molecule on the surfaces of activated endothelial cells and active platelets, allowing them to adhere to neutrophils and monocytes. Interestingly, Larsen et al. in a study demonstrated that P-selectin stimulates monocytes to secret tissue factor (TF), the primary activator of the extrinsic coagulation cascade. Noticeably, P-selectin-mediated recruitment of leukocytes into the lungs occurs during ARDS, and that infusion of anti-P-selectin (a monoclonal antibody) reduces the severity of ARDS. According to Mulligan et al. and Neri et al. studies, soluble P-selectin levels are increased in ARDS cases compared to the control group, as well as in non-survivors compared to survivors. Klok et al., in a study of 184 patients with confirmed cases of COVID-19 pneumonia who were being treated in the intensive care unit (ICU), 23 had passed away (13%), 22 had been successfully discharged (12%), and 139 (76%) were still being treated there as of April 5, 2020. Patients were given at least the minimum necessary doses of thromboprophylaxis. Their study revealed that COVID-19 patients are more likely to have problems with blood clots, and P-selectin may play a role in starting intravascular coagulation.

In a normal scenario, platelets are responsible for preserving the integrity of the alveolar capillaries. However, in pathologic situations, platelets may be a contributing factor in the development of lung injury. Furthermore, according to Zarbock et al., platelet-leukocyte aggregation and platelet-endothelial interactions have a role in the pathophysiology of acute lung damage. Hottz et al. demonstrated that in the case of viral infections, interactions with leukocytes, thrombocytopenia, and platelet secretion can all have either protective or harmful effects on the immune system.

A retrospective cohort study of a total of 383 COVID-19 patients at Wuhan’s Central Hospital was assessed by Liu et al., together with their respective clinical and laboratory data, to determine a definitive outcome by March 1, 2020. Those patients showed an increase in platelets per 50x10^9/L was related to a 40% reduction in mortality. Their study concluded that the thrombocytopenia rate in COVID-19 patients is predicted to be 5-41.7%, with a moderate form (100-150 x10^9/L) being the most common. A meta-analysis of 7,613 COVID-19 patients by Jiang et al. revealed that platelet counts were observed to be significantly lower in severe and critical disease.

![Fig. 1. Possible thrombotic mechanism during Covid-19 infection and suggested treatment strategies](image-url)
non-survivor patients as compared to those in non-severe and survivors, respectively, Figure 1\textsuperscript{123}.

As a result of Q. Li et al., 2020 studies, low platelet count in COVID-19 patients may be due to platelet consumption and associated with an increased risk of mortality. However, it has not been established as a predictive factor for this disease’s mortality \textsuperscript{124}. According to Thach et al., patients who have a temporal tendency to a lowered platelet count may have a devastating thrombotic complication, and the lower platelet counts are also connected to an increased mortality rate \textsuperscript{125}.

Furthermore, Vice et al. research revealed that hypoxia and sepsis can independently enhance platelet aggregation via the release of von Willebrand factor, which is elevated in the entire blood of COVID-19 patients in the intensive care unit (ICU) \textsuperscript{126}. On the bases of Langer et al. and Yau et al. studies, the significant activation of coagulation in severe COVID-19 infection is most likely connected to the persistent inflammatory response caused by the virus’s strong cytokine production \textsuperscript{127,128}. However, increased levels of D-dimers, thrombocytopenia, a prolonged prothrombin time (PT), and an activated partial thromboplastin time (aPTT) are all indicative of the severity of the disease and have been linked to a poor prognosis and a higher mortality rate in COVID-19 patients \textsuperscript{127,128}.

According to Sui et al., showed that 119 COVID-19 patients, were hospitalized in the intensive care unit. A total of 67.2\% of patients (80/119) had abnormally high levels of fibrinogen \textsuperscript{130}. However, fibrinogen levels were linked to disease severity and inflammatory markers, but not to the cardiac injury biomarker high sensitivity troponin I. The study concludes that patients with COVID-19, especially those with severe disease, had increased levels of fibrinogen which means fibrinogen levels were high in all patients at entry \textsuperscript{130}. Patients with COVID-19 who have elevated fibrinogen levels also tend to have increased inflammation, and more severe illness and require hospitalization to the intensive care unit \textsuperscript{130}. Additionally, Ranucci et al. concluded that fibrinogen, D-dimer, and IL-6 levels were evaluated in COVID-19 patients with ARDS who required mechanical ventilation \textsuperscript{131}. Tang et al. found the fact that increased IL-6 levels were associated with increased fibrinogen levels demonstrated and confirmed the relationship between procoagulant and inflammation alterations; all patients had raised IL-6 levels on admission \textsuperscript{132}.

Concomitantly, in a study of 1,099 Chinese patients with COVID-19, Guan et al. showed that 260/560 (46\%) had an increased D-dimer (>0.5 mg/L) \textsuperscript{133}. According to the findings of Han et al., patients with COVID-19 have higher
levels of D-dimer and fibrinogen than healthy controls. Also, significant elevations in fibrinogen degradation products (FDP) were observed. While the fibrinogen level remained high, the levels of D-dimers and FDP continued to rise with the severity of COVID-19 (Figure 2).

Additionally, elevated D-dimer levels at admission, as well as increasing D-dimer levels throughout time, are both related to an increase in COVID-19 mortality. Patients who develop septic shock and septic physiology are at an increased risk of death. Patients who acquire DIC, even if it develops in the absence of sepsis, are also at an increased risk of death. The mechanisms that cause coagulation in COVID-19 infection are not clear and confounder at this time, but the scientific society confirms an augmented role for inflammatory responses in the devastating cellular injuries rather than viral features.

Patients diagnosed with COVID-19 pneumonia showed coagulation abnormalities, namely, an escalation in levels of fibrinogen and D-dimer combined with mild thrombocytopenia. Higher mortality rates were proportionally correlated with elevated D-dimer levels. Additionally, PT and aPTT times were abnormally short in COVID-19 patients which can lead to activation of clot formation events. Consequently, shortened aPTT is directly linked to elevated levels in the acute-phase protein Factor VIII (FVIII). Meanwhile, in patients with severely advanced states, a condition mimicking DIC can develop especially in conditions of prolonged PT and aPTT readings. Moreover, D-dimer levels are aberrantly elevated in an extraordinary ratio with no correlation with any abnormalities detected in the PT/INR, aPTT, fibrinogen level, or platelet count nor these findings are unusual for DIC. Dissimilar to the pattern demonstrated in conventional DIC caused by traumatic origin or bacterial sepsis, COVID-19 patients show a minimal prolongation in aPTT and/or PT, and thrombocytopenia is mild (a platelet count of 100–150 ×10^9 /L). The coagulopathy associated with COVID-19 extensively illustrates the spectrum of coagulation stages related to COVID-19 patients. Three stages have been demonstrated for COVID-19-associated coagulopathy: stage 1 D-dimer levels are extremely elevated, in stage 2 the elevated D-dimer levels are combined with mild thrombocytopenia and mild prolongation in PT/INR and aPTT, and eventually, stage 3 show classic DIC scenario.

Eventually, Tsoupras et al., declared that COVID-19 coagulopathy is not been directly linked to severe bleeding as demonstrated in RNA-type viruses related to hemorrhagic symptoms, such as Ebola and some other hemorrhagic fever viruses.

**CONCLUSION**

COVID-19 is a causative agent of a severe acute respiratory syndrome. Several cases of young patients developed severe symptoms that emanate from death as an end-stage. There is a statistically significant link between the presence of long-term illnesses and the onset of symptoms in COVID-19 patients. Patients who encountered acquired thrombocytopenia due to the outbreak of SARS-Cov-1 were exposed to a higher risk of mortality. Thrombocytopenia was significantly proportional to the severity of the disease COVID-19 and Hb would interact in two locations: erythrocytes, where the virus is delivered intracellularly via the link between Band-3 and spike proteins, and the bone marrow. Complete blood counts demonstrated that asymptomatic patients had higher counts of eosinophils, lymphocytes, and basophils than symptomatic patients. There is a direct significant correlation between infection severity, the death rate in COVID-19 patients, and the low number of either WBCs or a high number of WBCs with a low number of lymphocytes. Additionally, fibrinogen levels were linked to disease severity and inflammatory markers, but not to the cardiac injury biomarker high sensitivity troponin I. Inflammatory markers such as fibrinogen, D-dimer, and IL-6 levels showed evaluations in COVID-19 patients with ARDS who required mechanical ventilation. Eventually, significant elevations in fibrinogen degradation products were reported in severe patients, concomitantly with high levels of fibrinogen and D-dimers that continued to rise with the severity of COVID-19.

**ACKNOWLEDGMENT**

The authors would like to thank M Mansour Albalbaki for assistance with data collection and extraction.
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