Investigation of Biochemical Markers of Covid-19 Infected Patients

Nauman Khokkar^a, Muhammad Umer Khan^a*, Muhammad Ahmad Ashraf^a, Muhammad Usman Ghani^b, Saima Younis^b, Iram Amin^c, Muhammad Shahid^c, Inam Ullah^a and Rakhtasha Munir^b

^aInstitute of Molecular Biology and Biotechnology, University of Lahore, Lahore, Pakistan ^bCentre for Applied Molecular Biology, University of the Punjab, Lahore, Pakistan ^cCentre of Excellence in Molecular Biology, University of the Punjab, Lahore, Pakistan

(received October 20, 2023; revised October 9, 2024; accepted October 29, 2024)

Abstract. Covid-19 is a highly contagious viral disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2). The objective of this research was to assess the clinical and hematological parameters of COVID-19-positive patients in order to identify potential biomarkers for the disease. The study included 2661 clinical reports from patients aged 25-90, with 1588 males and 1073 females. Blood samples were analyzed for various parameters and the N gene was targeted for SARS-CoV-2 detection through PCR. Statistical analysis was performed using SPSS 22.0 and presented results with mean values and standard deviations, with significance levels set at P < 0.05. Our study found that 59.7% of patients were male and within the 41-65 age group. Hematological analysis revealed significant associations between RBC levels ($P < 0.001^*$) and normal monocyte levels ($P = 0.04^*$). Additionally, 87% of patients had lymphopenia, 78% had leukocytosis, 84.6% had neutrophilia and 11.3% had thrombocytopenia. Clinical profiles showed elevated levels of CRP (98.9%), LDH (74.2%), ferritin (84.8%), D-dimer (97.8%) and significant association with albumin (<0.01). Finally, variations in urea and creatinine suggested potential renal involvement.

Keywords: COVID-19, C-reactive protein, D-dimer, ferritin, AST, ALT, lymphocyte, neutrophils

Introduction

The COVID-19 illness, stemming from the SARS-CoV-2 virus, is highly transmissible and has been officially designated as a global pandemic by the world health organization (WHO), resulting in far-reaching consequences (Khan et al., 2023). The novel coronavirus, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is highly contagious and has been linked to the emergence of the severe acute respiratory syndrome bat virus. This virus is classified as a positivestranded RNA virus and belongs to the beta-CoV group within the coronaviridae family. It is known to have bats and rodents as its primary reservoirs (Rajnik et al., 2021; Khan et al., 2020). The global spread of the COVID-19 pandemic occurred swiftly (Mir et al., 2022). At the close of 2019, Wuhan, China's industrial hub, encountered a singular coronavirus pandemic that resulted in the loss of over 1800 lives and affected 70,000 individuals within the initial 50 days (Khan et al., 2020). On February 11, 2020, the world health organization (WHO) declared COVID-19 a global public health emergency and as of June 11, 2020, there have been 7,544,790 laboratory-confirmed cases reported worldwide. Additionally, there have been 421,556 fatalities and 3,823,429 individuals have recovered from the virus (Coronavirus, 2020).

Various studies conducted during the tenure pandemic have uncovered specific risk factors that exhibit a direct relationship with severe disease and adverse outcomes. These risk factors encompass gender, age, comorbidities, clinical characteristics and laboratory findings, as well as the type of treatment administered (Williamson et al., 2020; Wu and McGoogan, 2020; Zhou et al., 2020). Research has demonstrated that the intensity and consequences of the disease are influenced by ethnicity. Various ethnic groups exhibit distinct outcomes for the disease, thereby rendering certain ethnicities as a risk factor (Bhandari et al., 2020; Price-Haywood et al., 2020). The initial transmission mode of SARS COV-2 is through close contact and the release of respiratory droplets through coughing and sneezing. The virus primarily attaches to ACE2 (angiotensin-converting enzyme 2) receptors, which are most prevalent in the lungs, kidneys and gastrointestinal tract (Suvvari et al.,

^{*}Author for correspondence; E-mail: muhammad.umer4@mlt.uol.edu.pk

2020). In China, the age group affiliated by novel corona virus range from 10 to 80 years old (Yuan et al., 2024; Wu and McGoogan, 2020; Zhonghua et al., 2019). The mild group of coronavirus symptoms is generally characterized by the absence or mild presence of pneumonia symptoms, while those with moderate or severe symptoms may experience sepsis, severe pneumonia and multiple organ dysfunction syndrome (Rajnik et al., 2021). According to the data, the most frequently reported symptoms at the onset of infection were fever (98.6%), fatigue (69.6%), dry cough (59.4%), muscle pain (34.8%) and dyspnea (31.2%). In addition, headache (6.5%), dizziness (9.4%), abdominal pain (2.2%), diarrhea (10.1%), nausea (10.1%) and vomiting were also reported (Coronavirus 2020; Li et al., 2020). There is considerable evidence to suggest that critically ill individuals frequently exhibit indicators of heightened inflammation, as evidenced by elevated levels of CRP, LDH, D-dimer and Ferritin (Huang et al., 2020). According to the data, the majority of COVID-19 patients exhibited lymphocytopenia (82.3%), thrombocytopenia (36.2%) and leukopenia (33.7%). In contrast, elevated levels of alanine transaminase (ALT), aspartate aminotransferase (AST) and creatinine kinase (CK) were observed at a lower frequency (Rajnik et al., 2021). The significance of CD8+ cell count, as well as other blood cell counts such as platelets, neutrophils and eosinophils has been acknowledged to some extent in the context of severe COVID-19(Velavan and Meyer, 2020).

In the latter part of 2020, the delta variant of SARS-COV-2 was identified in India and it has since been detected in approximately sixty countries, among them Pakistan (Brown et al., 2021). Delta variant has potentially higher rate of transmission than other variants (Public Health, 2021). As the world grappled with the challenges posed by the Delta variant, another novel variant of concern (VOC) emerged in California in early January 2021. This variant, known as the epsilon variant is characterized by two lineages designated as B.1.427 and B.1.429. Various studies suggested that epsilon variant had moderately high ability of transmission in general population relative to previous variants (Deng et al., 2021). Like numerous countries worldwide, Pakistan witnessed a substantial surge in COVID-19 cases, reaching peak levels. The world health organization (WHO) reported that Pakistan documented 1,085,294 confirmed cases of COVID-19 and 24,187 deaths from January 3, 2020, to August 13, 2021.

As the COVID-19 pandemic persists in causing widespread social, economic and especially medical devastation, there is an urgent need to develop effective methods for identifying predictors of disease progression in a swift, cost-effective and dependable manner. This research aims to emphasize the paramount importance of comprehending the clinical and hematological aspects of COVID-19 in order to identify predictive biomarkers. The primary objective of this study is to investigate variations in various biochemical markers, such as CRP, D-dimer, LDH, ferritin, LFTs, RFTs and CBC parameters, among COVID-19 patients, which can significantly contribute to the accurate diagnosis of the virus. Additionally, the study seeks to identify biomarkers that indicate a poor prognosis and mortality associated with COVID-19.

Material and Method

Sample collection. The present study collected a total of 2661 clinical reports of individuals who tested positive for COVID-19 and fell within the age range of 25-90 years. Of these individuals, 1588 were male and 1073 were female. These patients were admitted to various hospitals across Pakistan. The research was undertaken at the institute of medical laboratory technology, which is a constituent part of the University of Lahore. All individuals who tested positive for COVID-19 through both nasopharyngeal and oropharyngeal swab tests were classified as confirmed cases of the disease. The study encompassed individuals with mild, moderate and severe symptoms. Blood samples were collected from each participant with the aim of examining various parameters. An extensive dataset of COVID-19 patients' clinical information was assembled to investigate the relationship between various parameters, including CBC (HB, RBC, HCT, MCV, MHC, MCHC, PLT, TLC, neutrophils, lymphocytes, monocytes, eosinophils), LFT (total bilirubin, ALT, AST, ALP, total protein, ALB), RFT (urea, creatinine), CRP, ferritin, D-dimers and LDH.

PCR-based analytical detection. Polymerase chain reaction (PCR) was performed for the detection of the N gene as a target for the presence of SARS-CoV-2 in the nasopharyngeal (NP) swab sample. If the presence of the N gene was identified, a PCR assay targeting the RdRp (RNA-dependent RNA polymerase) was employed to validate the sample. Systaaq real-time PCR was used to confirm covid-19-positive samples for the N gene and RdRp (RNA-dependent RNA polymerase) genes.

Statistical analysis. The statistical analysis for this study was carried out utilizing the SPSS software, specifically version 22.0. Descriptive statistics, including mean values and standard deviations, were employed to present the results. To discern potential differences in biochemical data between individuals infected with COVID-19 and a control group comprising healthy individuals, a comparative analysis was performed through mean comparisons. Significance levels were determined by assessing P values, with statistical significance set at a threshold below 0.05.

Results and Discussion

Patients' demographics. The population demographics of COVID-19 patients in this study, comprising a total of 2,662 individuals, exhibit noteworthy trends in relation to age and gender, as depicted in Table 1 and Fig. 1. The age distribution indicates that the greatest number of patients fall within the 41-65 year range, accounting for 49% of all cases, with the 20-40 year range coming in second at 19.2%. Meanwhile, patients aged 65 and above represent 31.8% of the total cases. With regard to gender, the data reveals that a larger proportion of males (59.7%) were affected as compared to females (40.3%).

Distribution of hematological parameters of Covid-19 patients (N=2662). Table 2 in the study under analysis provided insights into potential hematological abnormalities associated with COVID-19 by analyzing the hematological parameters of 2,662 patients. The study assessed various parameters such as hemoglobin (Hb), red blood cell count (RBC), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count, white blood cell count (WBC), neutrophils, lymphocytes, monocytes and eosinophils.

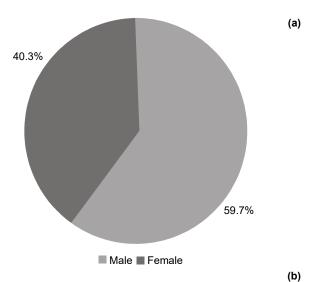
Table 1. Age groups and gender distribution in Covid-19 patients (n=2662)

SARA-COV-	2 group	Frequency	Percentage	
Age groups	20-40 years	512	19.2%	
	41-65 years	1303	49%	
	Above 65 years	847	31.8%	
Gender	Male	1589	59.7%	
	Female	1073	40.3%	
	Total	2662	100%	

The study's results indicate that a considerable proportion of patients (19.2%) had low levels of Hb, whereas the majority (75.7%) had normal Hb levels. Notably, only 5.0% of patients exhibited elevated Hb levels. The P-value associated with these findings is 0.7, which suggests that there is no significant correlation between the variables.

The results of the RBC analysis indicate that 5.0% of patients had elevated RBC levels, while 44.4% of patients had low levels, and 50.5% of patients had levels within the normal range. The P-value associated with these results is <0.001*, suggesting a significant association.

The data pertaining to HCT levels reveals that 29.8% of patients had low levels, while 66.9% had normal levels and 3.3% had higher levels. The associated P-value is 0.7, which suggests that there is no significant association.



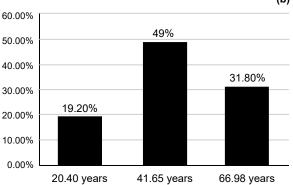


Fig. 1. (a) Distribution of gender and (b) distribution of age groups.

Parameters	Normal range	High % (n=)	Low % (n=)	Normal % (n=)	P-value
Hb	Male 13-16 g/dL	5.0 (n=134)	19.2 (n=512)	75.7 (n=2016)	0.7
	Female 12-15 g/dL				
RBC	Male,4.5-5.5×1012/L	5.0 (n=134)	44.4 (n=1183)	50.5 (n=1345)	<0.001*
	Female, 3.8-4.8×1012/L				
HCT	38-52%	3.3 (n=87)	29.8 (n=793)	66.9 (n=1782)	0.7
MCV	80-90 fL	9.3 (n=248)	20 (n=532)	70.7 (n=1882)	0.8
MCH	27-32 pg	9.0 (n=241)	26.6 (n=708)	64.4 (n=1713)	0.6
MCHC	30-35 g/dL	6.2 (n=167)	8.8 (n=233)	85.0 (n=2262)	0.6
Platelets	$150-450\times10^{9}/L$	5.7 (n=153)	11.3 (n=302)	83.0 (n=2207)	0.9
WBC	$4-11\times10^{9}/L$	78.1(n=2080)	2.7 (n=72)	19.2 (n=510)	0.3
Neutrophils	40-60%	84.6 (n=2252)	1.5 (n=40)	13.9 (n=370)	0.6
Lymphocytes	20-40%	3.7 (n=98)	87.1 (n=2319)	9.2 (n=245)	0.6
Monocytes	2-10%	0.4 (n=10)	3.7 (n=99)	95.9 (n=2553)	0.04*
Eosinophils	1-6%	0.2 (n=6)	7.0 (n=187)	92.7 (n=2469)	0.3

Table 2. Distribution of hematological parameters of Covid-19 patients (N=2662)

Regarding MCV, 9.3% of patients had elevated levels, while 20.0% had low levels and 70.7% had normal levels. The associated P-value is 0.8, which indicates that there is no significant association.

The MCH levels were found to be high in 9.0% of patients, while 26.6% had low levels and 64.4% had normal levels. The associated P-value is 0.6, suggesting no significant association.

Similarly, for MCHC, 6.2% of patients had high levels, 8.8% had low levels and 85.0% had normal levels. The associated P-value is 0.6, indicating no significant association.

Platelets analysis demonstrated that 5.7% had high levels, 11.3% of patients had low platelet levels suggesting thrombocytopenia, while 83.0% had normal levels. The associated P-value is 0.9, suggesting no significant association.

WBC interpretation indicates that 78.1% of patients had high WBC levels suggesting leukoytosis, while 2.7% had low levels and 19.2% had within the normal range. The associated P-value is 0.3, suggesting no significant association.

Neutrophils demonstrated that 84.6% of patients had elevated neutrophil levels indicating neutrophilia, 1.5% had low levels and 13.9% had levels within normal range. The associated P-value is 0.6, indicating no significant association.

Lymphocytes analysis reveals that 87.1% of patients had low lymphocyte levels indicating lymphopenia,

while 3.7% had elevated levels, 9.2 within normal. The associated P-value is 0.6, suggesting no significant association.

Monocytes interpretation indicates that 95.9% of patients had normal monocyte levels, while 3.7% had low levels and 0.4% high levels. The associated P-value is 0.04*, suggesting a significant association.

Eosinophils exhibited 0.2% patients had high levels, 7.0% of patients had low eosinophil levels, while 92.7% had normal levels. The associated P-value is 0.3, indicating no significant association.

Comprehensive clinical profile distribution in Covid-19 patients (n=2662). The clinical profile distribution of 2,662 COVID-19 patients was analyzed in order to understand its impact on various physiological processes, as shown in Table 3 and Fig. 2. The study examined parameters such as C - reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, D-dimer, urea, creatinine, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total protein, albumin and globulin.

The results of CRP interpretation revealed that an overwhelming majority of patients, at 98.9%, had elevated CRP levels (above 5.0 mg/L), while only a small percentage, at 1.1%, had levels within the normal range. The associated P-value for this was 0.9, indicating no significant association.

In regards to LDH levels, the findings suggested that 74.2% of patients had elevated levels (above 480 u/L), while 25.8% had levels within the normal range. The

associated P-value for this was 0.8, further indicating no significant association.

The results of ferritin levels revealed that 84.8% of patients exhibited elevated levels, while only 1.7% had low levels and 13.6% had normal levels. The corresponding P-value for this analysis was 0.9, which suggests no significant association.

Similarly, the analysis of D-dimer levels, a coagulation marker, showed that 97.8% of patients had elevated levels (>0.5 ug/mL), with only 2.2% demonstrating levels within the normal range. The associated P-value for this analysis was 0.7, further indicating no significant association.

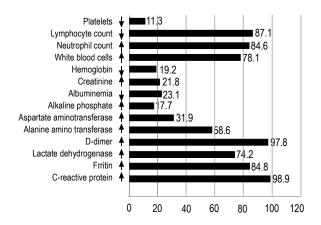


Fig. 2. Distribution of clinically significant parameters in Covid-19 patients.

The results of the urea analysis revealed that 34.4% of patients had urea levels exceeding 50 mg/dL, while 6.5% had levels in the low range and 59.0% fell within the normal range. The calculated P-value for this analysis was 0.9, indicating a lack of significant association.

In the case of creatinine levels, 21.8% of patients had elevated levels, 4.6% had levels in the low range and 73.6% had levels within the normal range. The associated P-value for this analysis was 0.8, suggesting a lack of significant association.

The data provided indicates that the percentage of patients with elevated total bilirubin levels (>1.1 mg/dL) was 10.9%, while the percentage of patients with low levels was 12.1% and the percentage of patients within the normal range was 77.0%. The associated P-value for this data is 0.8, suggesting no significant association.

Regarding ALT levels, 58.6% of patients had elevated levels (>42 U/L) and 41.3% had levels within the normal range. The associated P-value for this data is 0.5, indicating no significant association.

For AST levels, 31.9% of patients had elevated levels (>45 U/L), while 68.1% had levels within the normal range. The associated P-value for this data is 0.6, suggesting no significant association.

Finally, 17.7% of patients had elevated ALP levels (>305 U/L), 10.7% had low levels and 71.6% had levels within the normal range. The associated P-value for this data is 0.9, indicating no significant association.

Table 3. Allover clinical profile distribution in Covid-19 patients (n=2662)

Parameters	Normal range	High % (n=)	Low % (n=)	Normal % (n=)	P-value
CRP	5.0 mg/L	98.9 (n=2632)	-	1.1 (n=30)	0.9
LDH	Up to 480 u/L	74.2 (n=1974)	-	25.8 (n=688)	0.8
Ferritin	M <25-350 ng/mL	84.8 (n=2257)	1.7 (n=44)	13.6 (n= 361)	0.9
	F <25-250 ng/mL				
D-dimer	<0.5 ug/mL	97.8 (n=2603)	-	2.2 (n=59)	0.7
Urea	20-50 mg/dL	34.4 (n=916)	6.5 (n=174)	59.0 (n=1572)	0.9
Creatinine	M (0.7-1.4 mg/dL)	21.8 (n=581)	4.6 (n=122)	73.6 (n=1959)	0.8
	F (0.4-1.2 mg/dL)				
T. Bilirubin	0.2-1.1 mg/dL	10.9 (n=289)	12.1 (n=322)	77.0 (n=2051)	0.8
ALT	5-42 U/L	58.6 (n=1560)	-	41.3 (n=1102)	0.5
AST	5-45 U/L	31.9 (n=848)	-	68.1 (n=1814)	0.6
ALP	90-305 U/L	17.7 (n=471)	10.7 (n=285)	71.6 (n=1906)	0.9
Total protein	6.4-8.3 g/dL	2.6 (n=68)	23.6 (n=629)	73.8 (n=1965)	0.7
Albumin	3.4-5.4 g/dL	1.5 (n=39)	23.1 (n=615)	75.4 (n=2008)	<0.01*
Globulin	2.5-3.5 g/dL	24.1 (n=641)	21.8 (n=580)	54.1 (n=1441)	0.9

The results of the total protein analysis revealed that 2.6% of individuals exhibited elevated levels of total protein (above 8.3 g/dL), while 23.6% displayed low levels and the remaining 73.8% fell within the normal range. The corresponding P-value of 0.7 indicates a lack of any significant association.

Albumin levels revealed that 1.5% of patients had elevated albumin levels (>5.4 g/dL), 23.1% exhibited low levels and 75.4% within the normal range. The associated P-value is <0.01, indicating a significant association with disease outcome.

Globulin showed 24.1% of patients had elevated globulin levels (>3.5 g/dL), 21.8% exhibited low levels, and 54.1% within the normal range. The associated P-value is 0.9, indicating no significant association.

The COVID-19 pandemic, which has spread globally, has engendered an unprecedented health crisis, exhibiting a diverse range of clinical symptoms and distinct hematological and clinical profiles among the individuals diagnosed with the disease. In light of this, the exploration of biochemical markers assumes considerable significance, as it enables a better understanding of the disease progression. The present study was designed to investigate the levels of various biomarkers in COVID-19 patients, in order to evaluate their impact on the progression of the disease. The comprehensive analysis of the demographic and hematological profiles, along with the clinical parameters, in 2,662 COVID-19 patients provides valuable insights into the various manifestations of the disease. This study aimed to examine the age and gender distribution, as well as the influence of COVID-19 on the physiological, hematological and clinical parameters.

The demographic distribution of COVID-19 cases has revealed a higher incidence in males, which aligns with previous observations and suggests potential gender-based susceptibility. Furthermore, the age distribution highlights a significant impact on middle-aged individuals, emphasizing the importance of targeted interventions for this age group. Numerous studies have consistently reported a higher incidence of infection among men (Aggarwal *et al.*, 2020; Buckner *et al.*, 2020; Docherty *et al.*, 2020; Wang *et al.*, 2020). Previous research has not reported a notable proportion of men being affected but numerous studies have demonstrated an approximate equal gender distribution in COVID-19 infection (Garg *et al.*, 2020; Gupta *et al.*, 2020; Tian *et al.*, 2020; Wan *et al.*, 2020). Our study's average age

of 44.5 years is consistent with the results of studies conducted in China and Pakistan, which reported mean ages of 55 years and 52.58 years, respectively (Tian et al., 2020; Wang et al., 2020). However different studies from China and some from India have portrayed generally that young age group is commonly effected by covid-19 (Docherty et al., 2020; Gupta et al., 2020; Wan et al., 2020). On the other hand, studies published in the UK and the USA highlighted older age group e.g., >65 years (Aggarwal et al., 2020; Buckner et al., 2020; Garg et al., 2020). The explanation may be that the mean age of the European populace is higher than our locality.

The current investigation highlights the possible consequences of COVID-19 on oxygen-carrying capacity through the identification of anomalies in Hb, RBC and HCT. The finding of a substantial association in RBC levels implies potential ramifications for cardiovascular health. Although other hematological parameters exhibited variations, the absence of substantial associations indicates the necessity for additional investigation into the specific underlying mechanisms.

The present research uncovered the noteworthy participation of monocytes and red blood cells (RBCs) in the progression of COVID-19. Additionally also observed substantial discrepancies in RBC parameters between COVID-19 patients and the control group. Our study revealed significant disparities in monocyte percentages and RBC counts when comparing COVID-19 patients to healthy individuals. Monocytes are crucial for initiating the immune response during infections.

The results, which are consistent with previous findings of altered monocyte levels during COVID-19, provide additional evidence of changes in monocyte levels in COVID-19 patients compared to healthy controls. These findings are consistent with previously published studies (Zhou *et al.*, 2020). Red blood cells (RBCs) have been associated with thrombotic issues and hypoxia in COVID-19 infection. In COVID-19-positive individuals, RBCs have been observed to exhibit increased oxidation of structural proteins and disrupted membrane lipid homeostasis, which may alter RBC deformability and contribute to the thromboembolic complications observed in COVID-19 infection (Thomas *et al.*, 2020).

In several investigations, the documented instances of leukocytosis, leukopenia and thrombocytopenia among patients. Notably, leukopenia, lymphopenia and thrombocytopenia were identified in 9.1-33.7%,

35.3-82.1% and 5.0-36.2% of patients, respectively (Buckner *et al.*, 2020; Tian *et al.*, 2020; Wang *et al.*, 2020). The study revealed that individuals with SARS-CoV-2 infection exhibited reduced lymphocyte counts and elevated neutrophil counts, which are consistent with the findings of (Fan *et al.*, 2020; Guan *et al.*, 2020).

Lymphopenia is most common in 35-83% of patients and is thought to be related to the severity of the infection (Fan, 2020; Guan *et al.*, 2020). Different investigations have reported that anemia is certainly not very significant in COVID-19 (Guan *et al.*, 2020; Huang *et al.*, 2020). In this research did not observe any critical abnormalities in hemoglobin levels. In fact, 75% of patients exhibited normal hemoglobin levels, while only 17.6% showed signs of hemoglobinuria Guan *et al.*, provided a comparative perspective on this issue, which is consistent with findings from Singapore and Wuhan (Guan *et al.*, 2020; Qin *et al.*, 2020).

Hematological abnormalities are frequently documented in COVID-19 patients, carrying both prognostic and therapeutic significance (Terpos *et al.*, 2020). Tracking lymphocyte counts and inflammatory markers (CRP, ferritin, LDH) proved valuable in distinguishing cases from normal conditions. Elevated D-dimer levels were observed in patients with moderate to severe disease, and a rise in D-dimer over the course of the illness served as an indicator of worsening infection (He *et al.*, 2021; Fan, 2020).

The current research has revealed disparities in clinical parameters, with elevated CRP levels in the majority of patients indicating an inflammatory response, consistent with the notion of COVID-19 as an inflammatory disease. Moreover, the elevation of LDH, a marker of tissue damage, underscores the systemic impact. The significant changes in D-dimer levels also suggest potential coagulation abnormalities, raising concerns about thrombotic risks in COVID-19.

In this research, it was observed a direct correlation between elevated levels of serum ferritin and serum CRP and severe disease outcomes. However, studies have produced mixed results regarding the relationship between these biochemical markers and disease severity or mortality. Some studies suggest that high ferritin levels are associated with a more severe disease outcome, while others indicate that elevated levels of inflammatory markers, such as CRP, may even help to moderate disease severity (Chen *et al.*, 2020; Giamarellos-

Bourboulis et al., 2020; Ruan et al., 2020). This study also revealed a significant rise in D-dimer and LDH levels in Covid-19 patients, despite the presence of ferritin and CRP. While D-dimer is primarily utilized for detecting thrombus infection during its initial stages, it is important to note that our results may have implications for the diagnosis and treatment of Covid-19 patients (Yao et al., 2020). Prior research has demonstrated that D-dimer levels are typically elevated in severe illnesses such as pneumonia, as well as obstructive lung disorders, and can function as a prognostic biochemical indicator (Yao et al., 2020; Fruchter et al., 2015). The examination conducted by Chen et al. surmised that many patients had fundamentally elevated LDH (Chen et al., 2020). However, LDH is a glycolytic cytoplasmic catalyst present in basically every tissue. As a general rule, raised LDH indicates tissue injury (Ghamdi et al., 2016; Alsolamy, 2015). Initial level tissue injury was shown by our perception of raised LDH in the beginning phase of outrageous COVID-19 cases.

However the virus attached to the human ACE2 receptor in the lungs (Zhou *et al.*, 2020; Wrapp *et al.*, 2020) which clarifies the reason of lungs susceptibility towards corona virus, various cytokine abnormalities and numerous organ dysfunction can be seen in many severely ill patients, proposing fundamental organ harm brought about by excessive immune system activation (Acharya and Lee, 2020; Shi *et al.*, 2020).

Urea and Creatinine variations indicate potential renal involvement, requiring monitoring for kidney function. The normal levels of *T. Bilirubin* and the majority of liver enzymes suggest a relatively lower impact on hepatic function in this cohort.

The investigation has revealed that while liver parameters are generally minimal, there may be instances where significant abnormalities are present, such as elevated levels of ALT at 58.6%, AST at 31.8%, ALP at 17.7% and total bilirubin at 10.8%. These results align with prior research (Hundt *et al.*, 2020). According to our research, there is a significant increase in the levels of creatinine and urea in COVID-19 patients, with 21.8% and 34.4% respectively. However, two studies conducted by Xiucui Han and Qing Ye, as well as Rajab have reported similar findings regarding creatinine levels (27%), while their results for urea are consistent with ours (Han and Ye, 2021; Mardani *et al.*, 2020).

Conclusion

In summary, study involving 2,662 COVID-19 patients, offers a comprehensive perspective on the disease's hematological and clinical manifestations. The demographic analysis, which reveals a male predominance (59.6%) and a median age of 41.5 years, serves as a foundation for a nuanced exploration. The hematological examination uncovers prevalent lymphopenia (87%), leukocytosis (78%),84.6% neutrophilia and thrombocytopenia (11.3%). Moreover, it was observed noteworthy associations in RBC and monocyte levels, emphasizing the importance of personalized interventions for the diverse hematological profiles identified. The clinical profile analysis highlights elevated levels of CRP, D-dimer, ferritin and LDH, underscoring the systemic impact of COVID-19. Particularly, the discovery of elevated albumin levels (<0.01) as a significant predictor of disease outcome adds a crucial dimension to our understanding. Urea and creatinine variations indicate potential renal involvement, requiring close monitoring for kidney function. Overall, findings emphasize the multifaceted nature of COVID-19, underscoring the need for a comprehensive approach to effective management based on nuanced hematological and clinical insights.

Conflict of Interest. The authors declare that they have no conflict of interest.

References

- Acharya, D., Lee, K., Lee, D.S., Lee, Y.S., Moon, S. 2020. Mortality rate and predictors of mortality in hospitalized COVID-19 patients with diabetes. *Healthcare*, **8:** 338.
- Aggarwal, S., Garcia-Telles, N., Aggarwal, G., Lavie, C., Lippi, G., Henry, B.M. 2020. Clinical features, laboratory characteristics and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19): early report from the United States. *Diagnosis*, 7: 91-96.
- Alsolamy, S. 2015. Middle east respiratory syndrome. *Critical Care Medicine*, **43:** 1283-1290.
- Bhandari, S., Singh, A., Sharma, R., Rankawat, G., Banerjee, S., Gupta, V., Dube, A., Kakkar, S., Sharma, S., Keswani, P., Agrawal, A., Tak, A., Nawal, C.L. 2020. Characteristics, treatment outcomes and role of hydroxychloroquine among 522 COVID-19 hospitalized patients in Jaipur city:

- an epidemio-clinical study. PubMed, 68: 13-19.
- Brown, C.M., Vostok, J., Johson, M., Burns, R., Gharpur, S., Sami, R.T., Sabo, N., Hall, A., Forman, Sehubert, P.L. 2021. Outbreak of SARS-COV-2 infections including Covid-19 vaccine break though infections associated with large public gathering Brensistable country Massachuests. *Mosbidity and Morality Weekly Report*, 70: 1059.
- Buckner, F.S., McCulloch, D.J., Atluri, V., Blain, M., McGuffin, S.A., Nalla, A.K., Huang, M., Greninger, A.L., Jerome, K.R., Cohen, S.A., Neme, S., Green, M.L., Chu, H.Y., Kim, H.N. 2020. Clinical features and outcomes of 105 hospitalized patients with COVID-19 in Seattle, Washington. Clinical Infectious Diseases, 71: 2167-2173.
- Chen, G., Wu, D., Guo, W., Cao, Y., Huang, D., Wang, H., Wang, T., Zhang, X., Chen, H., Yu, H., Zhang, X., Zhang, M., Wu, S., Song, J., Chen, T., Han, M., Li, S., Luo, X., Zhao, J., Ning, Q. 2020. Clinical and immunological features of severe and moderate coronavirus disease 2019. *The Journal of Clinical Investigation*, 130: 2620-2629.
- Chen, N., Dong, X., Qu, J.F., Gong, Y., Han, Y., Qiu, Y., Wang, J., Liu, Y., Wei, Y. 2020. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*, **395**: 507-513.
- Coronavirus, E. 2020. 13,968 Cases and 223 deaths, Retrieved August 21, 2023 from https://www.worldometers.info/coronavirus/country, 2020.
- Deng, X., Garcia-Knight, M.A., Khalid, M.M., Servellita,
 V., Wang, C., Morris, M.K., Sotomayor-González,
 A., Glasner, D.R., Reyes, K.R., Gliwa, A.S., Reddy,
 N.P., Martin, C.S.S., Federman, S., Cheng, J.,
 Balcerek, J., Taylor, J., Streithorst, J.A., Miller, S.,
 Sreekumar, B., Chiu, C.Y. 2021. Transmission,
 infectivity and neutralization of a spike L452R
 SARS-CoV-2 variant. Cell, 184: 3426-3437.
- Docherty, A.B., Harrison, E.M., Green, C.A., Hardwick, H.E., Pius, R., Norman, L., Holden, K.A., Read, J.M., Dondelinger, F., Carson, G., Merson, L., Lee, J., Plotkin, D., Sigfrid, L., Halpin, S., Jackson, C., Gamble, C., Horby, P.W., Nguyen-Van-Tam, J.S., Semple, M.G. 2020. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO clinical characterization protocol: prospective observational cohort study. *British Medical Journal*, 30: 396.
- Fan, B.E. 2020. Hematologic parameters in patients

with COVID-19 infection: a reply. *American Journal of Hematology*, **95:** 1442-1453.

- Fruchter, O., Yigla, M., Kramer, M.R. 2015. D-dimer as a prognostic biomarker for mortality in chronic obstructive pulmonary disease exacerbation. *The American Journal of the Medical Sciences*, **349**: 29-35.
- Garg, S., Kim, L.M., Whitaker, A., Halloran, O., Cumming, C., Holstein, R., Holstein, M., Prill, S.J., Chai, P., Kirley, D., Alden, N.B. 2020. Hospitalization rates and characteristics of patients hospitalized with laboratory confirmed coronavirus disease 2019-COVID-NET, 14 States. *Morbidity* and Morality Weekly Report, 69: 458.
- Ghamdi, M.A., Alghamdi, K.M., Ghandoora, Y., Alzahrani, A., Salah, F., Alsulami, A., Bawayan, M.F., Vaidya, D., Perl, T.M., Sood, G. 2016. Treatment outcomes for patients with middle eastern respiratory syndrome coronavirus (MERS CoV) infection at a coronavirus referral center in the kingdom of Saudi Arabia. *BMC Infectious Diseases*, 16: (open access).
- Giamarellos-Bourboulis, E.J., Netea, M.G., Rovina, N., Akinosoglou, K., Antoniadou, A., Antonakos, N., Damoraki, G., Gkavogianni, T., Adami, M., Katsaounou, P., Ntaganou, M., Kyriakopoulou, M., Dimopoulos, G., Koutsodimitropoulos, I., Velissaris, D., Koufargyris, P., Karageorgos, A., Katrini, K., Lekakis, V., Koutsoukou, A. 2020. Complex immune dysregulation in COVID-19 patients with severe respiratory failure. *Cell Host and Microbe*, 27: 992-1000.
- Guan, W., Ni, Z., Hu, Y., Liang, W., Ou, C., He, J., Liu, L., Shan, H., Lei, C., Hui, D.S., Du, B., Li, L., Zeng, G., Yuen, K., Chen, R., Tang, C., Wang, T., Chen, P., Xiang, J., Zhong, N. 2020. Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine, 382: 1708-1720.
- Gupta, N., Agrawal, S., Ish, P., Mishra, S., Gaind, R., Usha, G., Singh, B., Sen, M.K., Group, S.H.C.2.W. 2020. Clinical and epidemiologic profile of the initial COVID-19 patients at a tertiary care centre in India. *Monaldi Archives for Chest Disease*, 90: (https://doi.org/10.4001).
- Han, X., Ye, Q. 2021. Kidney involvement in COVID-19 and its treatments. *Journal of Medical Virology*, **93:** 1387-1395.
- He, X., Yao, F., Chen, J., Wang, Y., Fang, X., Lin, X., Long, H., Wang, Q., Wu, Q. 2021. The poor

- prognosis and influencing factors of high D-dimer levels for COVID-19 patients. *Scientific Reports*, **11:** 1830.
- Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y.,
 Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu,
 T., Xia, J., Wei, Y., Wu, W., Xie, X., Yin, W., Li,
 H., Liu, M., Cao, B. 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet, 395: 497-506.
- Hundt, M.A., Deng, Y., Ciarleglio, M.M., Nathanson, M.H., Lim, J.K. 2020. Abnormal liver tests in COVID-19: a retrospective observational cohort study of 1,827 patients in a major U.S. hospital network. *Hepatology*, 72: 1169-1176.
- Khan, M.U., Khokhar, N., Ashraf, M.A., Ghani, M.U., Younas, S., Amin, I., Shahid, M., Ullah, I., Munir, R., Ahmed, S. 2023. Association between COVID-19 infection susceptibility and ABO blood groups and rhesus antigen. *Pakistan Journal of Health Sciences*, 4: 46-50.
- Khan, S., Siddique, R., Shereen, M.A., Ali, A., Liu, J., Bai, Q., Bashir, N., Xue, M. 2020. Emergence of a novel coronavirus, severe acute respiratory syndrome coronavirus 2: biology and therapeutic options. *Journal of Clinical Microbiology*, 58: 87-90.
- Li, Q., Guan, X., Wu, P., Wang, X., Zhou, L., Tong, Y., Ren, R., Leung, K.S., Lau, E.H., Wong, J.Y., Xing, X., Xiang, N., Wu, Y., Li, C., Chen, Q., Li, D., Liu, T., Zhao, J., Liu, M., Feng, Z. 2020. Early transmission dynamics in Wuhan, China, of novel Coronavirus—infected pneumonia. New England Journal of Medicine, 382: 1199-1207.
- Mardani, R., Vasmehjani, A.A., Zali, F., Gholami, A., Nasab, S.D.M., Kaghazian, H., Kaviani, M., Ahmadi, N. 2020. Laboratory parameters in detection of COVID-19 patients with positive RT-PCR: a diagnostic accuracy study. *Directory of Open Access Journals*, 8: 43.
- Mir, I., Aamir, S., Shah, S.R.H., Shahid, M., Amin, I., Afzal, S., Nawaz, A., Khan, M.U., Idrees, M. 2022. Immune-related therapeutics: an update on antiviral drugs and vaccines to tackle the COVID-19 pandemic. Osong Public Health and Research Perspectives, 13: 84-100.
- Price-Haywood, E.G., Burton, J., Fort, D., Seoane, L. 2020. Hospitalization and mortality among black patients and white patients with Covid-19. *New England Journal of Medicine*, **382**: 2534-2543.

- Public Health, E. 2021. SARS-CoV-2 variants of concern and variants under investigation in England. Technical Briefing, Retrieved July 25, 2023 from https://www.gov.uk/government/publications/investigation-of-sars-cov-2-variants-technical-briefings.
- Qin, C., Zhou, L., Hu, Z., Zhang, S., Yang, S., Tao, Y., Xie, C., Ma, K., Shang, K., Wang, W., Tian, D. 2020. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. Clinical Infectious Diseases, 71: 762-768.
- Rajnik, M., Cascella, M., Cuomo, A., Dulebohn, S.C., DiNapoli, R. 2021. Features, Evaluation and Treatment of Coronavirus (COVID-19), 235 pp. Academica Press, USA.
- Ruan, Q., Yang, K., Wang, W., Jiang, L., Song, J. 2020. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Medicine*, 46: 846-848.
- Shi, J., Li, Y., Zhou, X., Zhang, Q., Ye, X., Wu, Z., Jiang, X., Yu, H., Shao, L., Ai, J., Zhang, H., Xu, B., Sun, F., Zhang, W. 2020. Lactate dehydrogenase and susceptibility to deterioration of mild COVID-19 patients: a multicenter nested case-control study. *BMC Medicine*, **18:** 168.
- Suvvari, T.K., Kutikuppala, L.V.S., Babu, G.K., Jadhav, M. 2020. Understanding the unusual viral outbreak: coronavirus disease 2019. *Journal of Current Research in Scientific Medicine*, 6: 3.
- Terpos, E., Ntanasis-Stathopoulos, I., Elalamy, I., Kastritis, E., Sergentanis, T.N., Politou, M., Psaltopoulou, T., Gerotziafas, G., Dimopoulos, M.A. 2020. Hematological findings and complications of COVID-19. American Journal of Hematology, 95: 834-847.
- Thomas, T., Stefanoni, D., Dzieciatkowska, M., Issaian,
 A., Nemkov, T., Hill, R.C., Francis, R.O., Hudson,
 K.E., Buehler, P.W., Zimring, J.C., Hod, E.A.,
 Hansen, K.C., Spitalnik, S.L., D'Alessandro, A.
 2020. Evidence of structural protein damage and
 membrane lipid remodeling in red blood cells from
 COVID-19 patients. *Journal of Proteome Research*,
 19: 4455-4469.
- Tian, S., Hu, N., Lou, J., Chen, K., Kang, X., Xiang, Z., Chen, H., Wang, D., Liu, N., Liu, D., Chen, G., Zhang, Y., Li, D., Li, J., Lian, H., Niu, S., Zhang, L., Zhang, J. 2020. Characteristics of COVID-19 infection in Beijing. *Journal of Infection*, 80: 401-406.

- Velavan, T.P., Meyer, C.G. 2020. Mild versus severe COVID-19: laboratory markers. *International Journal of Infectious Diseases*, **95:** 304-307.
- Wan, S., Xiang, Y., Fang, W., Zheng, Y., Li, B., Hu, Y., Lang, C., Huang, D., Sun, Q., Xiong, Y., Huang, X., Lv, J., Luo, Y., Shen, L., Yang, H., Huang, G., Yang, R. 2020. Clinical features and treatment of COVID-19 patients in northeast Chongqing. *Journal* of Medical Virology, 92: 797-806.
- Wang, W., Xu, Y., Gao, R. Lu, R., Han, K., Wu, G., Tan, W. 2020. Detection of SARS-CoV-2 in different types of clinical specimens. *Journal of American Medical Association*, 323: 1843-1844. doi:10.1001/jama.2020.3786.
- Wang, Z., Yang, B., Li, Q., Wen, L., Zhang, R. 2020. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. Clinical Infectious Diseases, 71: 769-777.
- Williamson, E.J., Walker, A.J., Bhaskaran, K., Bacon, S., Bates, C., Morton, C.E., Curtis, H.J., Mehrkar, A., Evans, D., Inglesby, P., Cockburn, J., McDonald, H.I., MacKenna, B., Tomlinson, L., Douglas, I.J., Rentsch, C.T., Mathur, R., Wong, A.Y.S., Grieve, R., Goldacre, B. 2020. Factors associated with COVID-19-related death using (open safely). Nature, 584: 430-436.
- Wrapp, D., Wang, N., Corbett, K.S., Goldsmith, J.A., Hsieh, C., Abiona, O., Graham, B.S., McLellan, J.S. 2020. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science*, 367: 1260-1263.
- Wu, Z., McGoogan, J.M. 2020. Characteristics of and important lessons from the coronavirus Disease 2019 (COVID-19) outbreak in China. *JAMA*, **323**: 1239
- Yao, Y., Cao, J., Wang, Q., Shi, Q., Liu, K., Luo, Z., Chen, X., Chen, S., Yu, K., Huang, Z., Hu, B. 2020. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. *Journal of Intensive Care*, 8: 1-11, 49. (open access).
- Yuan, S., Huang, Y., Xie, P., Li, P. 2024. A case of severe rhabdomyolysis, acute myocardial damage and multi-organ dysfunction syndrome in a patient with novel coronavirus Pneumonia. *Emergency Medicine*, 16: 19-28. (open access).
- Zhonghua, L., Xing, B., Zhi, Z. 2019. Novel coronavirus pneumonia emergency response epidemiology team. The epidemiological characteristics of an outbreak. *China CDC Weekly*, **41:** 145-151.

Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., Xiang, J., Wang, Y., Song, B., Gu, X., Guan, L., Wei, Y., Li, H., Wu, X., Xu, J., Tu, S., Zhang, Y., Chen, H., Cao, B. 2020. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*, 395: 1054-1062.

Zhou, P., Yang, X., Wang, X., Hu, B., Zhang, L., Zhang, W., Si, H., Zhu, Y., Li, B., Huang, C., Chen, H.,

Chen, J., Luo, Y., Guo, H., Jiang, R., Liu, M., Chen, Y., Shen, X., Wang, X., Shi, Z. 2020. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, **579**: 270-273.

Zhou, Y., Fu, B., Zheng, X., Wang, D., Zhao, C., Qi, Y., Sun, R., Tian, Z., Xu, X., Wei, H. 2020. Pathogenic T-cells and inflammatory monocytes incite inflammatory storms in severe COVID-19 patients. *National Science Review*, 7: 998-1002.