Original Article

Relationship between the laboratory findings and severity of COVID-19 patients in Bahrami Hospital during 2018 -2019

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ABSTRACT

The covid-19 disease is a systemic and respiratory disease common between humans and animals. It was caused by a virus from the coronavirus family and led to a global pandemic in such a way that it has challenged modern medical science in most aspects. In this study, 200 people were evaluated, and finally, 50 people were included in the study. Patients were divided into mild and severe groups based on the country's protocol. Then demographic information, clinical symptoms, duration between the onset of symptoms and the diagnosis of the disease, duration of hospitalization, and laboratory findings were extracted from the patient files and analyzed. The average number of lymphocytes in the mild group was 2302, and in the severe group was 3699, and there was a significant difference between these two groups. The mean of CRP (C-reactive protein) in the mild group was 32.88, and in the severe group was 13.20, and there was a significant difference between these two groups. In this study, we concluded that there is a direct relationship between the severity of the disease, the number of neutrophils, and the level of CRP, and the number of neutrophils has an inverse relationship, and there is a direct relationship between the severity of the disease, the time of onset of symptoms, and the duration of hospitalization.

Keywords: COVID-19, Laboratory findings, Clinical findings, severe symptoms

Introduction

Coronavirus disease (COVID-19) causes respiratory and systemic disease [1], and according to the isolated causative pathogen, it is named severe acute respiratory syndrome coronavirus 2 (SARS-COV2) [2]. The World Health Organization (WHO) declared this disease a pandemic on March 11, 2020, and the number of infected people and deaths gradually increased, challenging the healthcare system worldwide [3]. Previous studies show that Covid-19 can be transmitted from person to person through droplets and contact [4]. The disease initially affects the respiratory system, but then the course of the disease depends on the individual and can manifest from asymptomatic to severe or fatal [3]. Some cases of infection in children have been reported, which has changed the previous sense that children are not susceptible to Covid-19 [5]. Children and adolescents account for only 1-2% of all cases of Covid-19 worldwide.

The characteristics of Covid-19 in children are different compared to adults; unlike other respiratory viruses, the risk of infection in children is lower than in adults [6], for which an apparent reason has not yet been found [7]. Most conditions seen in children are mild or asymptomatic, with few deaths reported [6]; researchers found that 15.9% of children experienced severe symptoms compared to 18.5% of adults. Infants and toddlers are more vulnerable to moderate infection and dill [8]. However, the severity of fatal cases is expected to continue to increase with the growth of transmission in the community and the current overall prevalence of the disease [9].

Laboratory infections are prominent in controlling viral infections, including pneumonia [10, 11]. Children with Covid-19 have different laboratory findings than adults; for example, lymphocyte reduction is not evident in children compared to adults [12].

No RT-PCR (real-time reverse-transcriptase polymerase-chain-reaction) can give information about the severity of the disease; according to this finding, it can be concluded that there is no clear relationship between the viral load and the individual's clinical phenotype. However, more than diagnosing etiology and disease monitoring, laboratory findings may provide insight into disease severity, prognostic assessment, and treatment monitoring; in addition, laboratory findings may give clues on the body's underlying immunological and pathophysiological response. Present [13].

Considering the relationship between the severity of the disease and the laboratory findings and the necessity of determining the severity of the illness for timely diagnosis and treatment of covid patients, we decided to conduct a study to investigate the laboratory findings of children with covid 19 and its relationship with the severity of the disease.

Materials and Methods

This study is a cross-sectional descriptive-analytical study conducted on patients with covid 19 hospitalized in Bahrami Hospital from March 2018 to March 2019, where the first 200 patients were evaluated, and finally, based on the entry and exit criteria, 50 patients were included in the study. Became The data were collected over one year and were analyzed over two months, and finally, a summary of the information was done within one month. Children 0-18 years who have positive PCR of nasopharyngeal swabs or blood samples (definitive) or children who have negative PCR and CXR involvement in favor of Covid-19 were included in the study. Children with MIS-C (Multisystem *et al*. in Children), any infectious disease At the same time, children with any underlying disease were excluded from the study.

Based on **Table 1** [14], patients were divided into two groups: mild (0,1) and severe (2,3,4) and then demographic information (age and sex), clinical symptoms (fever, cough, sore throat, tachycardia, runny nose) nose, tachypnea, vomiting, fatigue or myalgia, hypoxia, chest pain, and other symptoms), the period between the onset of symptoms and the diagnosis of the disease, the duration of hospitalization and laboratory findings CBC differential (complete cell count), Urea, Cr (Creatinine), CRP, ESR (Erythrocyte sedimentation rate), AST (aspartate aminotransferase), ALT (Alanine transaminase), LDH (Lactate dehydrogenase), Alb (Albumin), BS (blood serum) were extracted from the files of these patients and made into the researcher's checklist. It is registered. To reduce the research bias, one person collected and recorded the study data. The same kit also measured the laboratory data in the relevant hospital. The sample size was considered to be 30 people based on the study of Chao and his colleagues[15]. The mentioned variables were selected for the study due to their availability and low cost for measurement, and also considering that the people being evaluated are children, the laboratory findings mentioned due to the need to draw blood with a smaller volume for size. Finally, the data obtained from the evaluation were analyzed by SPSS statistical software.

The obtained results were analyzed using SPSS version 24 software. Descriptive data were reported using descriptive statistics (mean, standard deviation, frequency, and relative frequency). The normality of quantitative data distribution was checked using the Kolmogorov-Smirnov test. It was inserted to treat the method and by regression of missing data (what is the field or the main) such as height. The analysis did not include LDH, Alb, and ESR variables due to the high number of missed cases (24, 42, and 17, respectively). Outliers or outlier data that change the analysis results were corrected. A significance level of 0.05 was determined.

Table 1. Classification of disease severity based on clinical signs and symptoms

Loading signs and symptoms	asymptomatic	mild	moderate	severe	critical
Cough	-	+	+	+	+
Fever	-	±	+	+	+
Fatigue	-	+	+	NR	NR
Myalgia	-	+	+	NR	NR
Sore throat	-	+	+	NR	NR
Runny nose	-	+	NR	NR	NR
sneezing	-	+	NR	NR	NR
Congestion of the pharynx	-	+	NR	NR	NR
Chest auscultatory	-	-	±	+	+
Nausea	-	+	NR	NR	NR
Vomiting	-	+	NR	NR	NR
Abdominal pain	-	+	NR	NR	NR
diarrhea	-	+	NR	+	NR
Wheezing	-	-	±	NR	NR
Dyspnea	-	-	NR	+	+
Hypoxemia	-	-	-	+	+
Central cyanosis	-	-	-	+	+
Acute respiratory distress syndrome	-	-	-	-	+
Respiratory failure	-	-	-	-	+
Shock	-	-	-	-	+
encephalopathy	-	-	-	-	+
Myocardial injury or heart failure	-	-	-	-	+
Coagulation dysfunction	-	-	-	-	+
Acute kidney injury	-	-	-	-	+
Chest imaging	-	-	+	+	+
SARS CoV-2 PCR	+	+	+	+	+

+ indicates the presence of a symptom, whereas – indicates the absence, ± indicates that symptom may come with other

Results and Discussion

In this study **Figure 1**, 200 patients suspected of having covid were evaluated, 45 of whom were excluded due to having an underlying and infectious disease. PCR of covid was checked in the remaining 155 patients, of which 30 were positive and 125 were negative. , then 125 PCR-negative patients were evaluated in terms of lung involvement in favor of covid, of which 105 people were excluded from the study due to lack of lung involvement in favor of covid. Finally, 50 children from 0 to 18 years old, PCR positive and or negative PCR along with lung involvement in favor of covid, were included in the study; 34 (68%) of these patients were in the mild group, and 16 (32%) were in the severe group. During data analysis, none of the patients were excluded from the study. All patients had Iranian nationality and lived in Tehran.

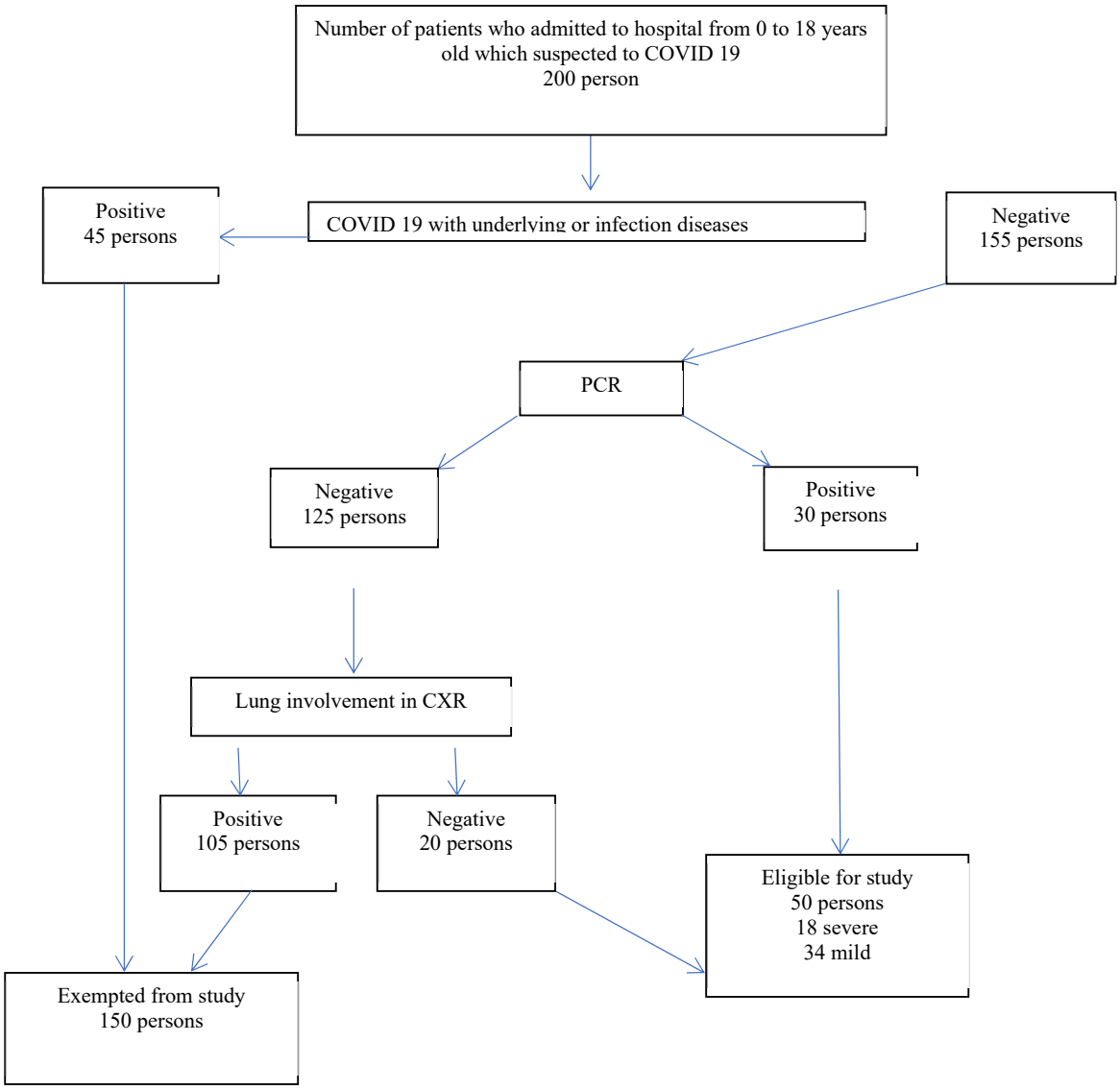


Figure 1. Flowchart of studied patients

In examining clinical symptoms and findings, 48 people had a fever (96%), 25 people had weakness and lethargy (50%), 20 people had vomiting (40%), 13 people had a cough (26%), 11 people had diarrhea (22%), eight people had seizures (16%), six people had dyspnea (12%), five people had tachypnea (10%), five people had decreased appetite (10%), five people had a runny nose (10%), five people had muscle pain (10 %), four people restlessness (8%), four people sore throat (8%), four people abdominal pain (8%), four people abnormal lung auscultation (8%), two people skin rash (4%), two headaches (4%), one nasopharyngeal exudate (2%), one dizziness (2%), one periorbital edema (2%), one cough containing blood vessels (2%) and one melena (2%) had. The demographic findings were evaluated in these two groups, and according to the results, the distribution of gender in the mentioned two groups was the same; the average age and subsequent weight and height in the severe group were higher than in the mild, but there was a significant relationship between them. Did not have **(Table 2)**.

In the evaluation of the laboratory findings they were done in two mild and moderate groups. The average number of white blood cells (WBC) was 8779 in the benign group and 10318 in the severe group, and there was no significant difference between these two groups. The average number of neutrophils in the mild group was 4288; in the influential group, 7123, there was a substantial difference in these two groups (p-value: 0.022). The average number of lymphocytes in the mild group was 3699; in the severe group, 2302, there was a significant difference in these two groups (p-value: 0.012). The average hemoglobin was 12.1 in the mild group and 11.6 in the severe group, and there was no significant difference between these two groups. The average number of platelets in the benign group was 283,470, and in the influential group was 285,187, and there was no significant difference between these two groups **(Table 3, Figure 2)**. The average urea in the mild group was 19.91, and in the severe group was 21.56, and there was no significant difference between these two groups. The average creatinine was 0.44 in the mild group and 0.43 in the influential group, and there was no significant difference between these two groups. The average blood sugar was 98.88 in the benign group and 91.88 in the severe group, and there was no significant difference between these two groups. The average CRP was 10.06 in the mild group and 32.88 in the influential group, and there was a substantial difference between these two groups (p-value: 0.004) **(Table 3, Figure 3)** The average AST was 34.44 in the mild group and 34.73 in the severe group, and there was no significant difference between these two groups. The average ALT was 25.25 in the benign group and 27.49 in the influential group, and there was no significant difference between these two groups **(Table 3)**.

It should be noted that LDH, ALB, and ESR variables were not included in the analysis due to the high number of missed cases (24, 42, and 17, respectively) in the study that was conducted at the time of the onset of symptoms and the length of hospitalization of the patients. The average time of onset of symptoms was 1.74 days in the mild group and 2.81 days in the severe group, and there was a significant difference between these two groups (p-value: 0.024). The average duration of hospitalization was 3.59 days in the mild group and 5.44 days in the severe group, and there was a significant difference between these two groups (p-value: 0.054)**(Table 3)**. In the study conducted, there is a direct relationship between the severity of the disease and the number of neutrophils and the level of CRP, and there is an inverse relationship between the severity of the disease and the number of lymphocytes. Also, the findings show a connection between the severity of the disease, the onset of symptoms, and the duration of hospitalization.

There is a direct **(Table 4, Figure 4)**.

Table 2. Demographic information based on disease severity

variables	Severe (16 persons)		Mild (34 persons)	
	average	SD	average	SD
Wight (Kg)	18.225	11.7142	14.976	12.7641
Height (cm)	100.94	27.743	91.76	33.888
Age (month)	51.98	39.109	43.72	50.315
gender	1.31	0.479	1.38	0.493

Table 3. Laboratory results and the time of start of symptoms and duration of hospitalization based on the severity of the illness

variables	Severe (16 persons)		Mild (34 persons)		P value*
	average	SD	average	SD	
WBC	10318.75	5020.520	8779.41	3475.436	0.280
Neutrophil count	7123.06	4154.504	4288.15	2846.703	0.022
Lymphocyte count	2302.56	1334.219	3699.35	2428.661	0.012
Hb	11.694	2.0748	12.147	1.5325	0.444
PLT	285187.50	104308.657	283470.59	93893.310	0.956
Urea	21.56	13.510	19.91	11.968	0.680
Cr	0.438	0.1821	0.441	0.1209	0.942
BS	91.88	22.606	98.88	25.533	0.334
CRP	32.88	25.848	10.06	13.209	0.004
AST	34.73	13.675	34.44	12.991	0.943
ALT	27.49	15.250	25.25	9.497	0.595
Symptoms appearance time	2.81	1.642	1.74	0.963	0.024
Time of hospitalization	5.44	3.286	3.59	2.271	0.054

CBC :Complete Blood Count, WBC : White Blood Cells, Hb : hemoglobin, PLT : Platelet, Cr : Creatinine, BS : Blood Sugur, CRP: C-reactive protein, AST : aspartate aminotransferase, ALT : Alanine transaminase

*independent t test

Table 4. Correlation coefficient of variables with disease severity

Variables	Pearson correlation	P value*
WBC	0.183	0.203
Neutrophil count	0.331	0.019
Lymphocyte count	- 0.212	0.140
Hb	- 0.062	0.670
PLT	- 0.086	0.553
Urea	0.105	0.469
Cr	- 0.034	0.814
BS	- 0.232	0.105
CRP	0.620	0.000
AST	- 0.066	0.651
ALT	0.034	0.815
Symptoms appearance time	0.498	0.000
Time of hospitalization	0.323	0.022

WBC : White Blood Cells, PLT : Platelet, Cr : Creatinine, BS : Blood Sugur, CRP: C-reactive protein, AST : aspartate aminotransferase, ALT : Alanine transaminase

*pearson correlation

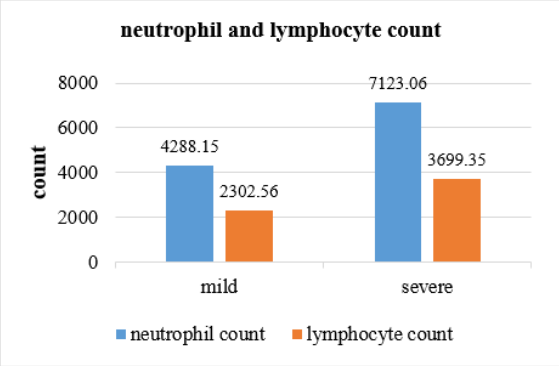
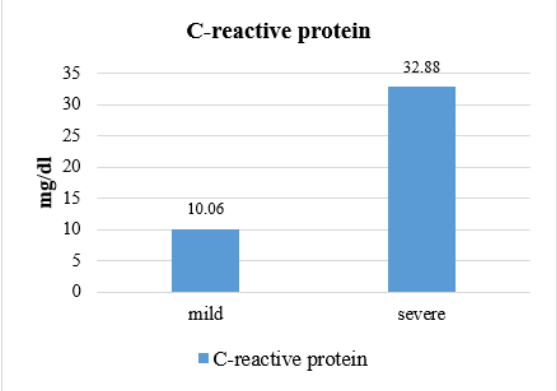


Figure 2. Bar graph of the number of neutrophils and lymphocytes based on the severity of the disease



Fugure 3. Bar chart of CRP level based on disease severity

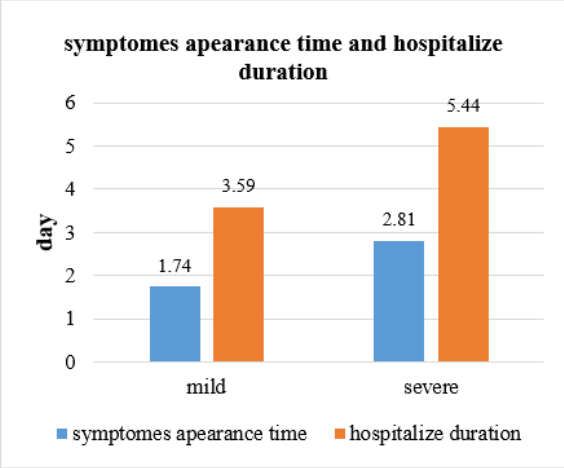


Figure 4. Bar chart of symptom onset time based on disease severity

Covid-19 has taken the whole world in its grip and has become an essential clinical disease. This disease is a threat to the general population and healthcare workers worldwide. Unfortunately, knowledge about the new virus is limited. In the conducted studies, the clinical characteristics of covid 19 have been widely identified, but our understanding of laboratory disorders in patients with covid still needs to be improved.

Because the data of our study was extracted from the patient's files, the incomplete information in the file, the lack of PCR of some patients suspected of having covid, and the lack of measurement of some laboratory data can be stated as limitations of the study. It should be noted that patients with asymptomatic covid could not be evaluated because they did not go to the hospital.

With all the mentioned interpretations, we finally concluded in our study that there is no significant relationship between the severity of the disease and the amount of WBC, Hb (hemoglobin), PLT, urea, Cr, BS, AST, and ALT. However, we further stated that the higher the severity of the disease, the higher the level of neutrophils and CRP, and conversely, the lower the level of lymphocytes. There is a direct relationship between the severity of the disease and the level of neutrophils and CRP, and there is an inverse relationship between the severity of the disease and the level of lymphocytes. The greater the severity of the disease, the longer the onset of symptoms and the longer the duration of hospitalization. There is a direct relationship between the severity of the patient and the onset of symptoms, and the duration of hospitalization. In a meta-analysis study conducted by Mehta and colleagues in 2021, they concluded that the severity of the disease is more severe in males and that lymphopenia, increased D-Dimer, LDH, and procalcitonin are associated with severe disease [16]. Nizami and his colleagues stated in 2021 that patients with severe and critical Covid-19 had significantly higher LDH, leukocyte, ferritin, and CRP and lower absolute lymphocyte count. Procalcitonin and D-Dimer are significantly increased in the critical group, so the biochemical parameter may be considered a significant predictor for severity assessment in Covid-19 patients [17]. Kara and colleagues 2021 stated that although children are less susceptible to covid-19, comorbidity predisposes children to severe disease, and lymphopenia and high uric acid indicate that covid-19 infection is progressive and severe. He forgives [18].In a study conducted by Alnor and his colleagues on 45 studies in 2020 in Denmark, they showed that the severity of the disease is associated with an increase in WBC, neutrophil count, CRP, LDH, D_dimer, and AST, in addition to a decrease in lymphocyte count, platelet count. Hemoglobin is also related to the severity of the disease. Finally, they concluded that several common laboratory findings are related to the severity of the disease of COVID-19 [19]. Henry and his colleagues, by reviewing 12 articles in 2020 in the USA (United States of America), concluded that the pattern of adaptation of laboratory abnormalities in children with confirmed COVID-19 has not yet been reported, laboratory changes in children with SARS (Severe acute respiratory syndrome) have not been reported to be consistent with early observations of COVID_19, they also recommended that physicians monitor lymphocyte counts and CRP as markers for disease severity and monitor PCT (Procalcitonin) for potential bacterial co-infection as well as IL_6 (Interleukin 6) should be evaluated as a potential prognostic indicator case in severe COVID_19 [7]. Also, Henry and his colleagues reviewed 24 eligible articles in 2020 in the USA, which concluded that there is an inconsistent pattern for changes in leukocyte index in mild and severe cases of children with covid. Specifically, changes in leukocyte counts were seen in only

32% of children with mild disease. In severe diseases, CRP, PCT, and LDH often increase. This study suggests that doctors monitor PCT, LDH, and PCT on an outpatient basis to follow the course of the disease [20]. In a study conducted by Mahmoudi and his colleagues on 55 patients in 2020 in Tehran, they showed that the number of lymphocytes is lower in patients with severe cases, comparing people with mild and moderate pneumonia versus severe pneumonia, increasing the number of CD8+ Tcell and shows a decrease in the percentage of CD4+ Tcell. However, the difference between these two groups is insignificant; interestingly, in the severe group, the ratio of CD4+/CD8+ Tcell is lower compared to the milder group [21].In a study conducted on 2,597 children with Covid-19 in China in 2020, Cui and his colleagues concluded that lymphopenia in children was rare (9.8%), in addition to the increase in CK_MB (Creatine kinase-MB) is more common in children (27%) than in adults, which can be concluded that heart damage is more likely to occur in children [22]. In a study conducted by Qi and his colleagues on 2874 children with Covid from 37 articles with quantitative analysis in 2020 in China, they showed that fever and cough were the most common symptoms of the disease. Asymptomatic infection and severe cases include 27.7% and 1.1% of 1933 patients, respectively. Laboratory findings show that 5.5% of patients are lymphopenic. The prevalence of leukopenia is 7.3%, and the CRP (C-reactive protein) level is above 14%. Finally, they concluded that children with covid have a mild disease, with many asymptomatic infections and a low rate of severe disease [23].In a study conducted by Preston and his colleagues on 2,430 patients with covid in the USA in 2020, they showed that the severity of the covid disease among patients with one or more chronic diseases compared to those without any chronic diseases in children 2-5 years or 6-11 years compared to 12-18 years and increases in males compared to women, also statistically there is no significant relationship between race or type of insurance and the severity of covid 19 disease [24].

Conclusion

Our research has found a significant correlation between the severity of COVID-19, the count of neutrophils, and the levels of CRP. We have found an inverse relationship between neutrophil count and these factors. Additionally, we have observed a positive correlation between disease severity, symptom onset, and hospitalization duration. Therefore, healthcare professionals should consider patients' lab results and symptoms when treating COVID-19 patients. Treatment plans should be customized based on these findings to improve the patient's chances of successful recovery.

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