

### **Relationship of C-reactive protein to lymphocyte ratio with prognosis and mortality in Covid 19**

#### **ABSTRACT**

**Background:** The Covid 19 pandemic is a serious disease that has infected millions of people and died tens of thousands. The clinical findings of the disease is observed in a wide range from asymptomatic to death. On the other hand, abnormal pathological variety is findings in laboratory parameters.

**Aims:** In this study, it was aimed to relation laboratory parameters with prognosis and mortality in the admission intensive care.

**Study Design** This study was done in Ersin Arslan Training and Research Hospital Covid Intensive-care unit between July 1, 2021 and September 30, 2021.

**Methodology:** Patients over the age of 18 who were positive Polymerase Chain Reaction test and admitted in the intensive-care unit were included in the study. The data of a total of 197 patients who were compatible with this criteria was retrospectively analyzed. White blood cells, C-reactive protein, procalcitonin and lymphocyte values (within the first 24 hours) of the patients, use history of steroid, and whether they were intubated and their mortality were investigated. The relations of the obtained data with each other were evaluated. Statistical analysis was performed using the Wilcoxon Signed-Rank test.

**Results:** 113 were males (57.3%), and 84 were females (42.7%). The mean age was  $64.6 \pm 2.16$  (21-95) years. Most of the patients (67.5%) were over 60 years old. WBC values of the patients were 46.8% high and 53.2% normal (normal value range 4-10  $\mu$ L). Lymphocyte values were 55.3% lymphopenia, 43.6% normal lymphocytes, 1.1% lymphocytosis (normal value range 0.8-4  $\mu$ L). CRP results were 98.9% high (normal value range 0-5 mg/L). High PCT value was 26.3% of the patients (normal value range 0-0.5 ng/ml). 86.8% of the patients were used steroids. 58.3% intubated (in Intensive-care unit) and 54.8% died of the patients. According to the lower and upper reference values; WBC/Lymphocyte:1-12.5 and CRP/Lymphocyte: 0-6.25 values were accepted normal ranges.

**Conclusion:** Mortality is more often in patients with females and over 60 years of age admitted to the intensive-care unit in Covid-19. If the CRP to Lymphocyte ratio is more than 100, it is related with mortality.

**Keywords:** Covid-19, CRP, laboratory, lymphocyte, mortality

#### **1.INTRODUCTION**

The SARS-CoV-2 virus emerged in China at the end of 2019, it caused the global pandemic called Covid-19 [1]. The clinical findings of the disease is observed in a wide range from asymptomatic to death. Respiratory symptoms are common in this disease. High of C-reactive protein (CRP, 58.3%), lymphopenia (43.1%), leukopenia (18.7%), and leukocytosis (16.8%) were reported in laboratory parameters [2]. Clinical findings and laboratory results are important criteria in the course of the disease. Many parameters, such as exacerbation of respiratory symptoms, hypoxemia, high procalcitonin (PCT) value, diversity of white blood cells (WBC) values, lymphopenia, high CRP values, are decisive in the admission of the patients to the intensive-care unit. In this study, it was aimed to relate WBC, CRP, lymphocyte, procalcitonin values and their ratios with prognosis and mortality in patients in intensive-care unit.

#### **2. MATERIAL AND METHODS**

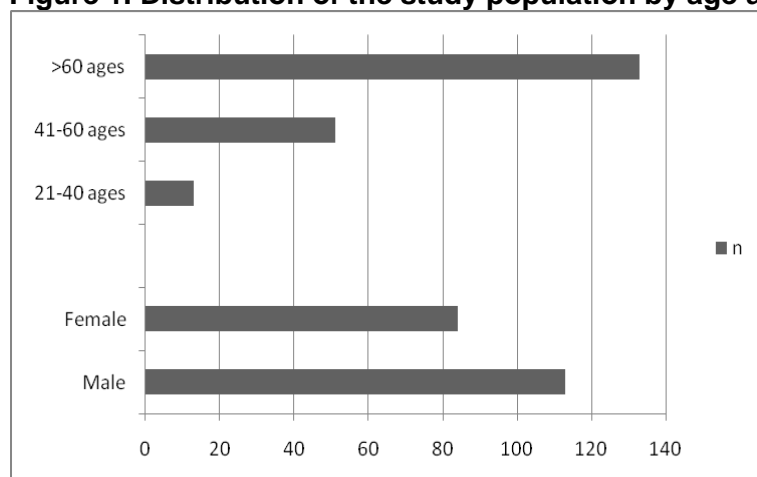
This study was done in Ersin Arslan Training and Research Hospital Covid Intensive-care Unit between July 1, 2021 and September 30, 2021. Patients over the age of 18 who were positive for the Covid-19 Polymerase Chain Reaction (PCR) test and admitted in the intensive-care unit were included in the study.

Patients younger than 18 years of age, with negative PCR tests, and without laboratory results at the first 24 hours in the intensive-care unit were excluded in the study. The data of a total of 197 patients who were compatible with these criteria were retrospectively analyzed. WBC, CRP, PCT and lymphocyte (L) values (within the first 24 hours) of the patients, use history of steroid, and whether they were intubated and their mortality were investigated. The relations of the obtained data with each other were evaluated. Statistical analysis was performed using the Wilcoxon Signed-Rank test.

### 3. RESULTS

A total of 197 patients, 113 were males (57.3%), and 84 were females (42.7%). The mean age was  $64.6 \pm 2.16$  (21-95) years. Most of the patients (67.5%) were over 60 years old (figure 1). WBC values of the patients were 46.8% high and 53.2% normal (normal value range 4-10  $\mu$ L). Lymphocyte values were 55.3% lymphopenia, 43.6% normal lymphocytes, 1.1% lymphocytosis (normal value range 0.8-4  $\mu$ L). CRP results were 98.9% high (normal value range 0-5 mg/L). High PCT value was 26.3% of the patients (normal value range 0-0.5 ng/ml). 86.8% of the patients were used steroids. 58.3% intubated (in Intensive-care unit) and 54.8% died of the patients. According to the lower and upper reference values; WBC/Lymphocyte (W/L): 1-12.5 and CRP/Lymphocyte (CRP/L): 0-6.25 values were accepted normal ranges.

**Figure 1. Distribution of the study population by age and gender**



As a result, males and older than 60 years of patients were more often admitted in Covid intensive-care unit. However, male gender ( $p < 0.2$ ) was not related with mortality. Females ( $p < 0.04$ ) and older than 60 years ( $p < 0.01$ ) of patients were related with mortality. The age range of 21-40 ( $p < 0.8$ ) and 41-60 years ( $p < 0.1$ ) were not related with mortality. Leukocytosis and lymphocytosis were not significantly related with mortality ( $p < 0.1$ ). High PCT value was related significant with mortality ( $p < 0.0001$ ). High ( $p < 0.1$ ) or low ( $p < 0.7$ ) WBC to lymphocyte ratio (WBC/L) was not related with mortality (normal ranges of WBC/L: 1-12.5). If the CRP to lymphocyte ratio (CRP/L, normal ranges of CRP/L: 0-6.25) was more than 100, it was related with mortality in patients who received treatment of steroid ( $p < 0.0001$ ) and did not steroid ( $p < 0.06$ ) treatment (table 1).

**Table 1. Statistical analysis results of the study**

	n	SD	95% CI	
<b>Gender</b>				
Male	113	0.49	±0.06	
Female	84			
<b>Ages</b>	64.6 (21-95)	15.3	±2.16	
<b>Mortality</b>				
Paramaters	n	z	p<	ODDS
<b>Gender</b>				
Male	113		<b>0.2</b>	
Female	84	-2.043	<b>0.04</b>	0.842
<b>Ages</b>				
>60	133	2508	<b>0.01</b>	2.590
41-60			<b>0.1</b>	
21-40			<b>0.8</b>	
High PCT	52	-5.070	<b>0.0001</b>	1.812
High WBC/L	100		0.1	
Low WBC/L	7		0.7	
<b>History of steroids (Yes)</b>				
CRP/L > 100	171	-4.862	<b>0.0001</b>	1.623
<b>History of steroids (No)</b>				
CRP/L > 100	26	-1.867	<b>0.06</b>	1.444

\*WBC/L: WBC/Lymphocyte, CRP/L: CRP/Lymphocyte, PCT: Procalcitonin

#### 4. DISCUSSION

Covid-19 is a serious disease that often affects the respiratory system, spread rapidly worldwide [3] and causes millions of deaths. The spectrum of this disease can range from asymptomatic to life-threatening complications [4]. During the course of the disease, laboratory tests such as WBC, CRP, PCT may be ordered by physicians [5]. Eosinopenia and lymphopenia were reported in study in Covid 19. The reason for this may be the distribution variety of white blood cells as a result of cytokine storm by T cells [6,7]. In our study, although eosinopenia was rare, lymphopenia was more often. It has been reported that 77.8% of the patients are between the ages of 30-69 and 2.4% younger the age of 18 in Covid 19 [8]. In this study, 67.5% of the patients were older than 60 years and the median age was 67 years (21-95). As in this study, lymphopenia has been reported to be related with mortality in other study [9]. CRP values are very important parameter in detecting infection and response of treatment [10], and that is increase almost in many diseases. Decrease of CRP is related with good clinical course. We found that 98.9% of the patients

admitted in the Intensive care unit had high CRP values in the first 24 hours. Laboratory markers related with increased disease severity include lymphopenia, neutropenia, and CRP [11]. In this study, almost all of the patients who were intubated (58.3%) and died (54.3%) were related with high CRP values. No significant relationship was found between neutrophilia and neutropenia with mortality. PCT value is among the sepsis diagnostic criteria. It was more than normal in 88.8% of Covid 19 patients admitted in the intensive-care unit. Steroids are used in the treatment of Covid-19 due to their anti-inflammatory effect. Systemic corticosteroids are probably slightly reduce (moderate-certainty evidence) all-cause mortality in symptomatic Covid-19 [12]. In our study, it was observed that the use of steroids remission the clinic. Mortality was more often with a history of steroids in patients. However, there were not found statistically significant relationship with mortality in patients using and not using steroids. Laboratory markers are among important criteria for physicians to evaluate response to treatment. Therefore, the relationship of all parameters in this study with mortality was analyzed. Markers other than PCT and CRP alone were not related with mortality. The laboratory markers of that day were important criteria in the patients who were admitted to the intensive-care unit. In order to determine good or poor prognostic factors for Covid-19, which is a deadly disease, the ratios of these parameters with each other were analyzed. The ratios of WBC, lymphocyte and PCT were not statistically significant with mortality. However, it was found that the ratio of CRP to lymphocyte was significantly related with mortality.

#### 4. CONCLUSION

Mortality is more often in patients with females and over 60 years of age admitted to the intensive-care unit in Covid-19. If the CRP to Lymphocyte ratio is more than 100, it is related with mortality.

#### ETHICAL APPROVAL

Republic of Turkey Ministry of Health 2021-09-18T22\_38\_39 numbered and Gaziantep University Medical Ethics Committee 2021/322 numbered approval have been received.

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