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Relationship between Low Eosinophil Level at Presentation and Disease Severity and Mortality in Covid-19 Patients

Elif Çelikel[1], **Afşin Emre Kayıpmaz**[1]

[1]Ankara City Hospital, Department of Emergency, Ankara, Turkey

Elif ÇELİKEL

Afşin Emre KAYIPMAZ

ABSTRACT

Purpose: Early and rapid diagnosis of COVID -19 is vital to reduce mortality. It has been shown that detecting low eosinophil levels at the first application in suspected cases of COVID -19 can be used to diagnose the disease and predict its severity. In the present study, we aimed to determine the usability of this parameter in the early diagnosis of COVID-19 and treatment planning by evaluating at the eosinophil levels.

Methods: As a retrospective study included those who were admitted to the hospital, with the pre-diagnosis of COVID-19. Demographic characteristics, laboratory values, radiological images and clinical follow-up were scanned through the hospital system. All statistical analysis was done using the SPSS v25 software.

Result: Thirty-seven women (30.08%) were included in our study. The average age was 49.13, and we found the most cases in the 26-65 age range. The most common symptoms were cough 51.21%, dyspnea 26.8% and fever 26.39%. Hypertension was detected 21.95% and diabetes 12.19% as comorbid diseases. A computed tomography scan showed viral pneumonia in 50.40% (n:62) of our cases. 49.59% (n: 61) had Polymerase chain reaction positive results and 39.02% (n: 48) of our cases had both viral pneumonia in the CT scan and PCR (+). We found that dead patients had significant lower eosinophil levels.

Conclusion: Eosinophil level may support the diagnosis in suspected cases of Covid-19 and maybe a warning that the clinical picture may progress seriously.

Keywords: Covid-19, Eosinopenia, Severity

Covid-19 Hastalarında Başvuru Anında Düşük Eozinofil Düzeyi ile Hastalık Şiddeti ve Mortalite Arasındaki İlişki

ÖZET

Amaç: Covid-19 tanısının erken ve hızlı tespit edilmesi mortaliteyi azaltmak için önemlidir. Eozinofil düzeyinin Covid-19 şüpheli vakalarda ilk başvuru anında düşük tespit edilmesinin hastalığın tanısını koymada ve ciddiyetini öngörebilmede kullanılabileceği belirtilmiştir. Çalışmamızda vakalarımızın eozinofil düzeyine bakarak bu parametrenin Covid-19 erken tanı ve tedavi planlanmasında kullanılabilirliğini saptamayı amaçladık.

Gereç ve Yöntem: Retrospektif olarak yapılan bu çalışmaya Covid-19 ön tanısı ile yatan vakaları aldık .Hastaların demografik özellikleri, laboratuar değerleri, radyolojik görüntüleri ve klinik takip bilgileri hastane bilgisayar sisteminden tarandı. SPSS 25 programı ile istatistik hesapları yapıldı.

Bulgular: Hastalarımızın 37'si kadındır (%30,08). Yaş ortalaması 49,13 ve en çok vakayı 26-65 yaş aralığında tespit ettik. En sık semptom olarak öksürük %51,21, dispne %26,8 ve ateş %26,39 görüldü. En sık görülen komorbid hastalık hipertansiyon %21,95 ve diyabet %12,19. Vakalarımızın %50,40'ın da (n:62) bilgisayarlı tomografisin de viral pnömoni (konsolüdasyon, buzlu cam opasiteleri), %49,59'unda (n:61) Polimeraz Zincir Reaksiyonu pozitifliği ve %39,02'sin de (n:48) ise hem bilgisayarlı tomografi'de viral pnömoni hem de PCR (+) tespit edildi. Vefat eden vakalarımızda ilk başvuruda eozinofil düzeylerinde düşüklüğü tespit ettik.

Sonuç: Eozinofil düzeyi düşüklüğü Covid-19 şüpheli vakalarda tanıyı destekleyebilir ve klinik tablonun ciddi seyredebileceği ile ilgili bir uyarı olabilir.

Anahtar kelime: Covid-19, Eozinopeni, Mortalite

Correspondence: Elif Çelikel
Ankara City Hospital, Department of Emergency, Ankara, Turkey
Phone: +905058310158
E-mail: drelifkaya@gmail.com

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In December 2019, SARS-CoV-2, an enveloped RNA virus, was detected in China as well as increasing pneumonia cases. The disease caused by this virus was named COVID-19 by the World Health Organization (1). In Turkey, on January 22, 2020, the Ministry of Health COVID-19 Scientific Committee was established, and the encounter measures, infection control-isolation and treatment processes were planned (2). In addition to fever, dry cough, dyspnea and malaise, atypical symptoms such as gastrointestinal system findings and anosmia can also be observed in these patients (3). Besides symptomatic cases, there are also asymptomatic cases (4). Asymptomatic cases may pose a risk for the spread of the disease (5,6). Mortality increases in patients who are 65 years old and above, chronic disease and immune system weakness (7). Hypertension (HT) and diabetes mellitus (DM) are the most common comorbid diseases. Studies have shown that DM increases the need for intensive care follow-up, especially in patients (8,9). It is important to reduce the spread rate of COVID-19, which causes severe respiratory distress and makes an early diagnosis to decrease mortality (10). Studies suggest that hematological parameters can be used for diagnosis and evaluation of the treatment given in these patients (11). It has been stated that detection of low neutrophil, lymphocyte, hemoglobin and eosinophil levels in the complete blood count at the first application of the patient may strengthen the diagnosis of COVID-19 (12). The eosinophil is a hematological parameter used for diagnosis and treatment in many diseases with its pro-inflammatory effect, which is active in the tissue and circulation. The immune-regulatory and antiviral effect of eosinophil has also shown (13,14). Eosinophil level can be measured easily and quickly from a complete blood count. In a study conducted in patients with a diagnosis of COVID-19, it has shown that low eosinophils may be linked to increased inflammatory response and increased viral load may trigger eosinophil granulated protein consumption by reducing the level of IL-5 released from CD8 T cells, leading to low level of eosinophil (15,16). We evaluated the eosinophil levels of patients who hospitalized in intensive care or in service with the diagnosis of COVID-19. We aimed to evaluate the disease's progression by looking at the usability of initial eosinophil levels in early diagnosis and the eosinophil levels after treatment.

MATERIAL AND METHOD

This study was approved by Ethical Committee of Ankara Numune Training and Research Hospital Ethics Committee (No: E1-20-598). We enrolled all cases in Ankara Numune Training and Research Hospital Emergency Department between 15/04/2020 and 22/04/2020. Patients were 18 years old or older with polymerase chain reaction (PCR) positivity and/or lesions compatible with COVID-19 viral pneumonia in computed thoracic tomography. In the present study, we retrospectively scanned the patients' demographic characteristics (age, sex), contact history, smoking situation, symptoms at the time of admission, comorbid diseases, admission information, length of stay, computed tomography (CT) (consolidation, ground-glass opacity), blood and PCR results from the records in the hospital computer system. We analyzed the data using the SPSS v.25 program. Statistical analyzes were performed with a Mann-Whitney U test. Statistical significance was evaluated with a 95% confidence interval. $p < 0.05$ was considered statistically significant.

RESULTS

One hundred twenty-three cases were included in the study. 69.91% of our cases were men. The average age was 49.10. 62.60% of our cases did not contact patients diagnosed with COVID-19 (Table 1). % 60,16 of our patients do not have a chronic disease. % 19,51 of cases smoke. A Mann-Whitney test indicated that eosinophil levels was lower at the first admission for patient who had a positive PCR results (Mdn = 0.5), than for patients who had a negative PCR results (Mdn: 0.7, p=0.05). Even though eosinophils levels were greater for patients who discharged (Mdn = 0.6) than for patients who died (Mdn = 0.4), this difference was not statistically significant (p = .908).In 50,40% (n:62) of our cases, lesions consistent with viral pneumonia (consolidation, ground-glass opacity) were observed on CT. 49.59% (n: 61) were positive for PCR, and 39.02% (n: 48) were both positive for CT, viral pneumonia and PCR. Cough 51.21%, was the most common symptom while dyspnea 26.80% and other symptoms %27,64 (gastrointestinal complaints) were also present. HT 21.95% and DM 12.19% were the most common chronic diseases (Table 2). Those with co-morbid diseases have longer hospital stays (MDN = 10.5, p=0.003). Hospitalization periods were also greater for patients who had a positive PCR results (Mdn = 9) than for patients who had a negative PCR results (Mdn = 7, p=.015) Nevertheless, hospitalization periods were not statistically significant between patients who discharged (Mdn = 8) than for patients who died (Mdn = 6, p=.155). 71.5% (n: 88) of our cases were followed by hospitalization and 28.45% (n: 35) of them in the intensive care unit. = 0.069). In our study patients who died had statistically significant higher neutrophil, D-dimer, ferritin, white blood cell (WBC) and C-reactive protein (CRP) levels than patients who discharged. 91.05% (n: 112) of our cases were discharged. The average age of the discharged cases was 73, and 68.57% (n: 24) were male. The eosinophil levels of

our patients hospitalized in intensive care and died were also low, but when we compared the eosinophil levels of the patients discharged, we found no statistical difference (p: 0, 908) (Table 3).

Table 1: Data of gender, age, contact	
Gender	
Male	69,91% (n:86)
Female	30,08% (n:37)
Age	
18-25	13,82% (n:17)
26-45	39,02% (n:48)
46-65	23,57% (n:29)
≥ 65	23,57% (n:29)
Contact	
Yok	62,60% (n:77)
Var	37,39% (n:46)

Table 2: Symptoms and other Diseases	
Symptom	
Cough	51,21 % (n:63)
Other	27,64 % (n:34)
Dyspnea	26,80 % (n:33)
Fever	24,39 % (n:30)
Anosmia	2,40 % (n:3)
Other Diseases	
None	60,97% (n:75)
Hypertension	21,95% (n:27)
Diabetes	12,19% (n:15)

DISCUSSION

Since December 2019, COVID-19 infection has been a cause of rapid mortality worldwide, especially in elderly patients. Admissions to intensive care units with respiratory distress have also increased. Patients hospitalized in intensive care have a high mortality rate (17,18). In this study our patients who were hospitalized in intensive care were mostly old and male. We interpreted this situation in our country that men over the age of 65 are mostly together and outside of the home. In the literature in which there are many male cases in the same situation (19). Our patients are most frequently applied to the emergency department with symptoms such as cough, dyspnea, fever and nausea, vomiting, and diarrhea, which is consistent with other studies (20). To diagnose COVİD-19 patients, thorax CT and PCR test are requested. However, in some cases, CT cannot be taken or an atypical lesion is described. Sometimes the PCR test may be delayed or a repeat test may be required because of insufficient material. We concluded that some people may have had contact with people who were in the early period of the disease or asymptomatic. Catching asymptomatic cases are important to contain the epidemic. Therefore it may be useful to use hematological parameters to detect these patients, especially those in the early stages of infection (21). Eosinophils are produced in the bone narrow and effective immunmodulators in the initiation and spread of some inflammatory processes (22). It has been stated that increased eosinophils in the lung tissue may be a barrier against viral agents (23). In a study suggested that the cause of neutropenia, lymphopenia and eosinopenia is the passage of these cells into the lung tissue, thus causing acute lung injury and ARDS.

Table 3: Relationship between eosinophil ratios and discharged-ex

Discharged* Low Crosstabulation						
			Low	**Normal**	**High**	**Total**
Discharged	**Yes**	**Count**	35	75	1	111
		Discharged	31.5%	67.6%	0.9%	100.0%
		Low	89.7%	92.6%	33.3%	90.2%
		Total	28.5%	61.0%	0.8%	90.2%
	Ex	**Count**	4	6	2	12
		Discharged	33.3%	50.0%	16.7%	100.0%
		Low	10.3%	7.4%	66.7%	9.8%
		Total	3.3%	4.9%	1.6%	9.8%
Total		**Count**	39	81	3	123
		Discharged	31.7%	65.9%	2.4%	100.0%
		Low	100.0%	100.0%	100.0%	100.0%
		Total	31.7%	65.9%	2.4%	100.0%

They stated that the disease might indicate the severity and the monitoring of hematological parameters might be necessary in this case (24). High d-dimer, ferritin, WBC and CRP level can accompany with low eosinophils in COVID-19 (25). Low eosinophil levels may be related to the severity of COVID-19 disease and that eosinophil may be more sensitive than other blood parameters. Besides, studies have demonstrated that decreased eosinophilia levels can support the diagnosis of COVID-19 in cases with typical COVID symptoms and radiologically supported, regardless of lymphopenia (26). It was stated that the increase in eosinophil values with treatment might be beneficial for the progression of the disease (27). In a study, it was shown that the late increase in eosinophil levels, which was low at first in patients with COVID-19, may be determinant for the negative progression of the disease and that we can follow the progression of the disease with serial monitoring of eosinophil levels (28). On the other hand, studies showed that the decrease in eosinophil level will not be associated with adverse clinical progression of the COVID-19 disease. It is said that studies with a large number of cases are needed to evaluate this situation (29).

CONCLUSION

According to our study's data, patients with low eosinophil levels at the beginning were more severe, and we interpreted it as mortality rate. It can be used as a predictive factor for the severity of the Covid-19. This blood parameter can be used to determine the eosinophil level, which can result quickly and diagnose cases suspected to be COVID-19 early and evaluate the treatment process.

Limitation

Our study was done in a single center. We have low number of patients.

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