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Can haematological parameters be a guide in hospitalization and survive of COVID-19 patients diagnosed at the emergency service?

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Abstract

This study investigates the relationship between hematological laboratory parameters and length of hospital stay in Coronavirus Disease 2019 (COVID-19) patients. Of the possible or suspect COVID-19 cases who applied to our emergency service, those who were diagnosed with Covid were included in the study. Age, mean corpuscular volume (MCV), platelet count (PLT), red cell distribution width (RDW), blood urea nitrogen (BUN) and neutrophil-to-lymphocyte ratio (NLR) values of the patients who resulted with mortality were found to be significantly higher when compared with those of the patients who survived (p<0.001; 72.0 vs 51.0, p=0.007; 86.7 vs 85.4, p<0.001; 223.0 vs 196.0, p<0.001; 306.0 vs 243.0, p=0.009; 14.2 vs 13.9, p<0.001; 21.0 vs 14.0, p<0.001; 5.6 vs 3.0, respectively). According to the results, a positive significant association was found between age, LDH and NLR and hospitalization time (p<0.001; p<0.001and p<0.001 respectively). High level of NLR can help in showing hospital mortality and long hospitalization time in diagnosed COVID 19 cases, while low NLR can help the clinician in deciding on the indication of home treatment.

Keywords: Emergency medicine, Coronavirus Disease 2019, neutrophil-to-lymphocyte ratio, hospitalization time, hemogram

Introduction

Coronavirus called "Severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) has been defined as the causative agent for Coronavirus Disease 2019 (COVID-19) [1,2]. The clinical course of the disease is generally characterized by atypical respiratory symptoms such as fever, shortness of breath and cough; however, in some cases, the disease can progress to severe viral pneumonia and acute respiratory failure that requires intubation [2-4].

The transition of SARS-CoV-2 from human to human has been proven by evidence [5-7] resulting quickly spread from Wuhan. The importance of laboratory results for hospitalized COVID-19 patients, and the need for additional research, has been highlighted in previous studies [2,4].

Hospital admission hematological parameters and their association with length of stay were investigated in this study of COVID-19 patients.

Material and Methods

Ethics Statement

The institutional review board of Bakırköy Sadi Konuk Local Ethics Committee (decision number: 2020.05.1.20.052, date: 15/05/2020) approved this study. Participants provided informed written consent.

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Of the possible or suspect COVID-19 cases who applied to our emergency service between April 1 and May 2020, those who were diagnosed with COVID were included to the study. Patients diagnosed according to Ministry of Health Science Board algorithm were grouped in two as outpatients and hospitalized patients (Figure 1).

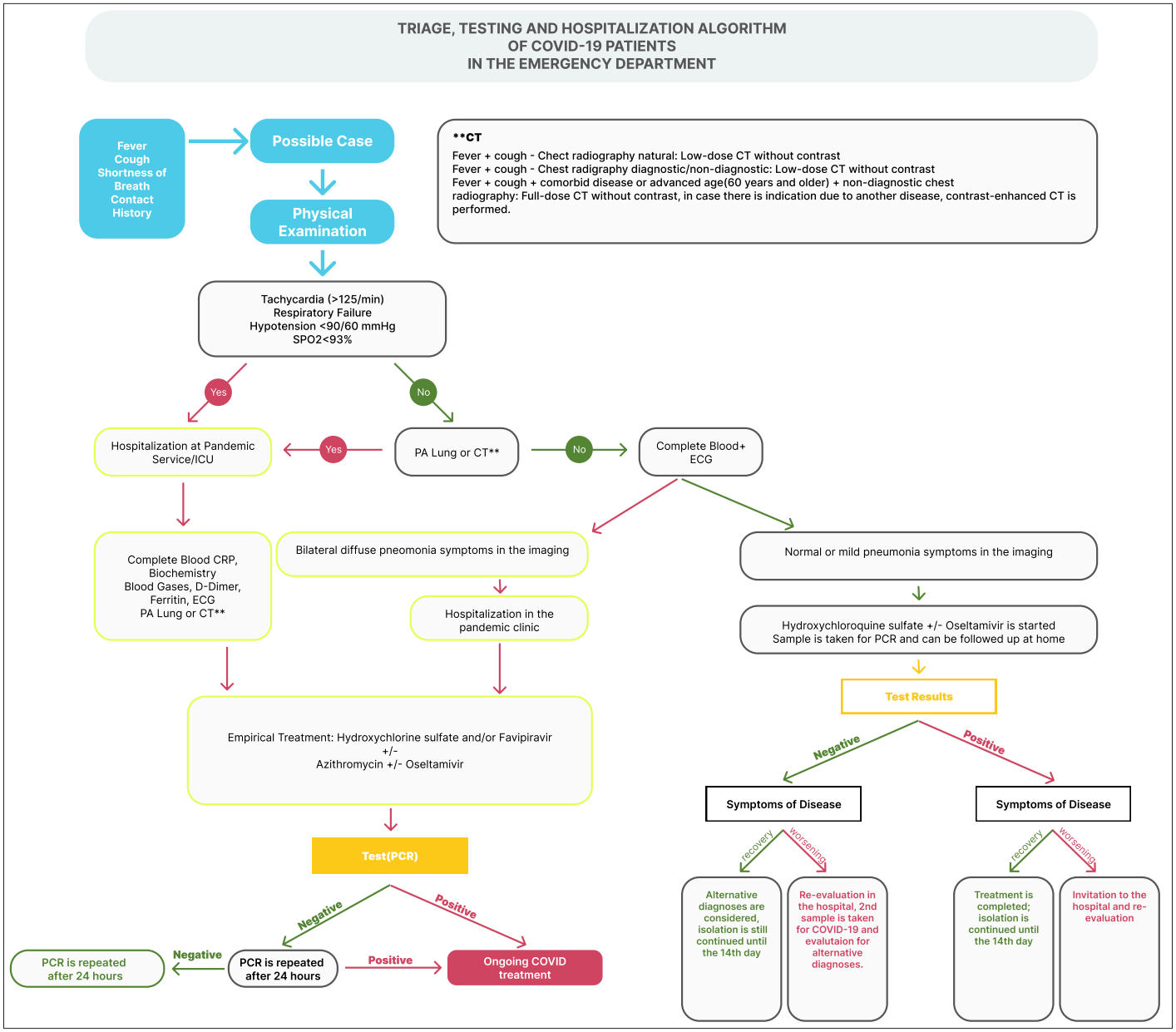

Figure 1. Ministry of Health Science board algorithm

Exclusion Criteria

Patients with missing neutrophil and lymphocyte records or those with chronic haematological disorder were excluded.

Statistical Analysis

In the study, categorical measurements were recorded as number and percentage, continuous variables were reported as mean and standard deviation. We used the Kolmogorov-Smirnov test to check the normality assumption for these continuous variables. In the comparison of values between groups, Student-t test was applied for parameters that followed a normal distribution, whereas the Mann-Whitney U test was utilized for those that did not. Categorical variables were analyzed using the chi-square test. Whether the study parameters were effective in distinguishing between groups was found by calculating the area under the ROC curve and sensitivity and specificity values were calculated. Spearman or Pearson's correlation coefficients were calculated to evaluate relationships between variables. A p value less than 0.05 was considered as statistically significant in our study.

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Results

Of the 4108 patients included in the study, 50.7% (n=2083) female, while 49.3% (n=2025) were male and the median age (quartiles) of the cases was (39.0-65.0) years. It was found that 59.1% (n=2428) of the patients were treated as outpatients, while 40.9% (n=1680) were treated as hospitalized patients. Demographic and laboratory characteristics value of Outpatients or Hospitalized patients are shown in Table 1 and 2. The results of age and laboratory parameters and the final status (survive-mortal) of the patients and the level of significance between these are shown in Table 3.

Table 1. Comparison of demographic parameters between the patients who were outpatients or hospitalized patients due to COVID 19

	Outpatient n=2428	Hospitalized patients n=1680	P
Mean age, year	48±14	56±17	<0.001
Male/female, %/%	48/52	51/49	0.08
Fever, n (%)	1024 (42)	481 (40)	<0.001
Cough, n (%)	2076 (85)	1365 (81)	<0.001
Dyspnoea, n (%)	1710 (70)	1052 (63)	<0.001
Hypertension, n (%)	221 (10.2)	225 (15.2)	<0.001
Diabetes mellitus, n (%)	166 (7.5)	148 (9.5)	0.03
COPD, n (%)	115 (5.6)	98 (6.2)	0.15
Stroke, n (%)	12 (0.5)	12 (7)	0.41
ARF	42 (1.8)	47 (2.9)	0.03
CRF, n (%)	49 (2.1)	46 (2.8)	0.17
Mortality	12 (0.5)	124 (7.4)	<0.001

N/L: neutrophil/lymphocyte, MPV: mean platelet volume, COPD: chronic obstructive pulmonary disease, ARF: acute renal failure, CRF: chronic renal failure

Table 2. Laboratory characteristics of outpatients or hospitalized patients due to COVID 19

	Outpatient n=2428	Hospitalized patient n=1680	P
Haematocrit, g/dl	37±6.5	39±5	<0.001
RBC	4.26±0.77	4.62±0.60	<0.001
Platelet, x10^3/mm^3	216±93	241±99	<0.001
PDW	17.5±0.79	16.9±0.70	<0.001
WBC, x10^3/mL	7.81 (1.1-36.1)	7.50 (0.5-36)	<0.001
Mean platelet volume, mg/dL	8.45±1.05	8.52±1.52	0.02
Lymphocytes counts,	1.81 (0.1-12.5)	1.49 (0.1-49.1)	<0.001
Neutrophil count	5.20 (0.1-32.7)	5.28 (0.1-27.1)	0.41
Monocyte count	0.59 (0.1-22.9)	0.58 (0.1-23)	0.34
Eosinophil	0.13 (0.6-14.7)	0.09 (0-8.6)	0.10
MCV	85±6	85±6	0.04
MCHC	33±1.1	33±1.1	0.81
PCT	0.17±0.07	0.21±0.08	0.28
RDW CV	15.6±2.6	14.5±2.1	0.91
LDH	270 (96-2544)	293 (96-3474)	<0.001
C-reactive protein	130 (4-520)	137 (4-520)	**0.21**
NLR	4.07 (0.1-94)	5.1 (0.1-94)	**<0.001**

RBC: red blood cells, PDW: platelet distribution width, WBC: white blood cell, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, PCT: procalcitonin, RDW CV: red cell distribution width-coefficient of variation, LDH: lactate dehydrogenase, NLR: neutrophil-to-lymphocyte ratio

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Table 3. Results of age and laboratory parameters according to final states (survival-mortality) and levels of significance between them

	Mortality, median (quartiles) n=135	Survival, median (quartiles) n=3973	P value
Age	72.0 (62.0-80.0)	51.0 (38.0-65.0)	<0.001
MCV	86.7 (83.3-92.1)	85.4 (81.4-89.1)	0.007
MPV	8.5 (7.6-9.6)	8.4 (7.8-9.1)	0.181
PLT	196.0 (153.0-252.0)	223.0 (171.0-283.7)	0.001
LDH	306.0 (226.0-484.0)	243.0 (193.0-315.0)	<0.001
RDW	14.2 (13.6-15.6)	13.9 (13.2-15.1)	0.009
BUN	21.0 (17.0-42.0)	14.0 (10.0-19.0)	<0.001
NLR	5.6 (3.0-7.7)	3.0 (1.9-5.0)	<0.001

MCV: mean corpuscular volume, MPV: mean platelet volume, PLT: platelet count, LDH: lactate dehydrogenase, RDW: red cell distribution width, BUN: blood urea nitrogen, NLR: neutrophil-to-lymphocyte ratio

Age, mean corpuscular volume (MCV), platelet count (PLT), red cell distribution width (RDW), blood urea nitrogen (BUN) and neutrophil-to-lymphocyte ratio (NLR) values of the patients who resulted with mortality were significantly higher compared with those of the patients who survived (p<0.001; 72.0 vs 51.0, p=0.007; 86.7 vs 85.4, p<0.001; 223.0 vs 196.0, p<0.001; 306.0 vs 243.0, p=0.009; 14.2 vs 13.9, p<0.001; 21.0 vs 14.0, p<0.001; 5.6 vs 3.0, respectively).

The correlation between age and blood count values and hospitalization time is shown in Table 4. According to the results, a positive significant association was found between age and, lactate dehydrogenase (LDH), NLR and hospitalization time (r=0.165, p<0.001; r=0.242, p<0.001; r=215, p<0.001; respectively).

Table 4. The correlation between age and length of hospital stay, blood tests and length of hospital stay

Variables	Correlation coefficient	P value
Age	0.165	**<0.001**
MPV	-0.020	0.411
MCV	0.008	0.750
LDH	0.242	**<0.001**
RDW	-0.040	0.283
BUN	0.039	0.313
N/L ratio	0.215	**<0.001**

MPV: mean platelet volume, MCV: mean corpuscular volume, LDH: lactate dehydrogenase, RDW: red cell distribution width, BUN: blood urea nitrogen, N/L ratio: neutrophil-to-lymphocyte ratio

The results of the univariate and multivariate logistic regression analysis which were applied to find out the independent risk factors in terms of mortality are shown in Table 5. As a result of the multivariate regression analysis, age, gender, neutrophil-to-lymphocyte (N/L) ratio, platelet count parameters were found to be significant predictors for mortality (p<0.001, p=0.001, p<0.001, p=0.006, respectively).

Table 5. Effects of various variables on mortality in univariate and multivariate logistic regression analyses

	Univariate		Multivariate	
Variable	**OR (95% CI)**	**P value**	**Adjusted OR (95% CI)**	**P value**
Age (years)	0.939 (0.928-0.950)	**<0.001**	0.947 (0.935-0.959)	**<0.001**
Gender	0.543 (0.380-0.776)	**0.001**	0.652 (0.441-0.964)	0.032
N/L Ratio	0.919 (0.903-0.936)	**<0.001**	0.945 (0.928-0.964)	**<0.001**
Platelet count	1.003 (1.001-1.005)	**0.006**	1.003 (1.000-1.005)	0.032
MPV	0.875 (0.749-1.022)	0.091	0.985 (0.825-1.177)	0.870

N/L Ratio: neutrophil-to-lymphocyte ratio, MPV: mean platelet volume

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When the cut-off value of N/L ratio level at ROC curve was taken as 4.46 to differentiate patients resulting in mortality, sensitivity was found as 72.2%, while specificity was found as 73.5% (p<0.001, AUC: 0.773, 95% CI: 0.760-0.786) (Figure 2).

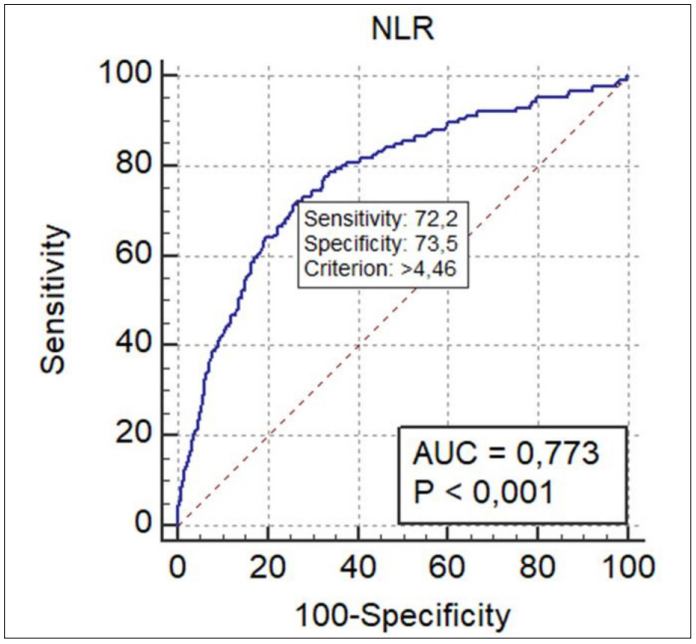

Figure 2. Cut-off value of N/L ratio level at ROC curve

Creatinine, BUN, Urea, estimated Glomerular Filtration Rate (eGFR), Haematocrit, lymphocyte-monocyte-neutrophil count, platelet distribution width (PDW), red blood cells (RBC) estimated Glomerular Filtration Rate (CRP) and serum LDH levels were different among the groups and they were entered into linear regression in a stepwise method.

Discussion

As in SARS and Middle East respiratory syndrome (MERS) [8,9], COVID-19 patients also have significant changes in circulating cells, including anomalies lymphocyte levels and their activity. The patients presented with lymphopenia on admission and this rate varies between 36.9% and 83.2% [10,11]. It has been reported that the immune system is affected, featuring lymphopenia, an imbalance in lymphocyte sub-groups, and a cytokine storm in individuals with COVID-19 and the degree of discomfort can be related to the severity of COVID-19 [3,12,13]. In our study, statistically significant differences were identified about lymphocytes levels in the differentiation of both survival and hospitalization and outpatient groups.

NLR has become an important laboratory parameter of COVID-19 patients because lymphocyte levels have changed characteristic. NLR is used as an indicator for evaluating the progression of infection and prognosis in patients with tumors, and elevated NLR has been found to show poor prognosis [14-16]. Elevated NLR on admission is an independent risk factor for severe COVID-19 and increased mortality. [17,19]. Ding X et al. found only age was associated with the length of hospital stay with multivariate analysis [19]. In our study, while elevated NLR was associated with mortality, low NLR was associated with being outpatient. While age, gender, NLR and thrombocyte were found to be statistically significantly effective on mortality with univariate logistic regression analysis, N/R and age were found to be statistically significantly effective on mortality with multivariate logistic regression analysis. In addition to age in Ding X et al.'s study [19]. NLR was also found to be significantly effective on hospitalization time in our study. In addition, with ROC analysis, when cut-off value of N/L ratio level was taken as 4.46 in the differentiation of patients who resulted with mortality, sensitivity was found as 72.2%, while specificity was found as 73.5%.

As reported in SARS patients, a decrease in thrombocyte count was associated with more severe cases of COVID-19 [20,21] and thrombocytopenia has been found as an indicator of hospital mortality [22]. It has been suggested that lymphocyte count and thrombocyte count combined with IL-6 function as indicators for potential progress to critical disease [23]. In our study, low thrombocyte levels were found to be associated with poor prognosis.

Study Limitations

This research reveals various limitations that should be taken into account when analyzing the results. Because of its retrospective design, the research is vulnerable to biases related to analysis and data collecting. Second, the study population was drawn from a specific geographical area and limited to a defined time period during the pandemic. This limitation could affect the generalizability of the results across different groups or regions with differing demographics, healthcare systems, or COVID-19 management protocols. Additionally, while the study focused on haematological parameters, it did not consider other potentially significant clinical factors that could influence hospitalization and mortality, such as comorbidities, imaging results, or treatment interventions. The absence of these variables may affect the comprehensiveness of the analysis.

Conclusion

As a conclusion, we think that high level of NLR, which can be tested in each emergency in routine hemogram parameters, can help in showing hospital mortality and long hospitalization time in diagnosed COVID-19 cases, while low NLR can help the clinician in deciding on the indication of home treatment.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
The institutional review board of Bakırköy Sadi Konuk Local Ethics Committee (decision number: 2020.05.1.20.052, date: 15/05/2020) approved this study.

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