



See the commentary by Baradaran et al (J Parathyroid Dis. 2022;10: e11184)



Evaluation of the relation between disease severity with platelet distribution width, platelet large cell ratio, mean platelet volume and red cell distribution width in severe and critically ill hospitalized patients with coronavirus disease 2019

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Abstract

Introduction: Hematological parameters are raised for classification and determining of prognosis in coronavirus disease 2019 (COVID-19).

Objectives: The aim of this study is to determine the relation between severity of the illness and serum level of red cell distribution width (RDW), mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (P-LCR) in patients with COVID-19 focusing on severe and critically ill patients.

Patients and Methods: In this cross-sectional investigation, we examined the correlation between severity of disease and value of RDW, PDW, P-LCR and MPV in hospitalized patients with COVID-19 in Velayat hospital, located in Qazvin province in Iran from November 2020 to March 2021. According to the clinical characteristics, the patients were divided into two group of severe and critically ill. Patients' data including age, gender, and the value of RDW, PDW, P-LCR and MPV were extracted from the health information system of our hospital. Then, these parameters were analyzed and compared among the groups.

Results: The data of 59 patients were evaluated. The mean age of patients was 62.07 years and 59.3% of these patients were female. Around 64.4 percent of the patients were critically ill. The median the value of RDW in the critically ill group was significantly higher than the severe group ($P = 0.009$). The value of RDW had a significant positive correlation with the severity of the disease (correlation coefficient: 0.341, $P = 0.008$).

Conclusion: Our data showed that RDW might be helpful to differentiate the critically ill patient with COVID-19 from severe one.

Keywords: COVID-19, Red cell distribution width, Mean platelet volume, Platelet distribution width, Platelet large cell ratio

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Introduction

Novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused a new sickness called coronavirus disease 2019 (COVID-19) that was first detected in December 2019 by a broke out in Wuhan city, China. Later the World Health Organization (WHO) declared the outbreak a public health emergency of worldwide concern in January 2020 (1).

Laboratory measurement represents a coagulopathy

with about one third of admitted patients with COVID-19 developing thrombotic events (2). Hematological parameters, such as mean platelet volume (MPV), platelet distribution width (PDW) and red cell distribution width (RDW) are extensively studied for classification and detecting of prognosis in COVID-19 (3).

One of the platelet function parameters is MPV that increases with increasing platelet size. The platelets with higher MPV produce more amounts of prothrombotic

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■ Implication for health policy/practice/research/medical education

Red cell distribution might be a diagnostic factor in differentiating the severity of disease in hospitalized patients with coronavirus disease 2019.

factor that may lead to thrombotic complications (4). This platelet function parameter is increased in diseases caused by thrombosis such as stroke, venous thromboembolism and acute coronary syndrome (5,6).

Another parameter of determining platelet function is PDW that represents the variation in the size of platelets. Following increasing the platelet destruction and more alterations in the size of newly built immature platelets, PDW increased (7).

One of the routinely reported parameters of complete blood count is RDW that reflects the red blood cell size diversity (8). This parameter has been affected in hypoxemia, pulmonary embolism and social pneumonia (9-11).

Objectives

In this study, we aimed to determine whether there is a relation between severity of disease in hospitalized cases with COVID-19 and serum levels of the mentioned hematologic parameters focusing on severe and critically ill patients. The results may be helpful for physicians in determining and differentiating the severity of the disease in hospitalized patients with COVID-19 between severe and critically ill groups when making clinical decisions.

Patients and Methods

Study design

In this cross-sectional investigation, we examined the correlation between severity of disease and the value of RDW, PDW, P-LCR and MPV in hospitalized patients with COVID-19 in Velayat hospital, located in Qazvin province (with a population of 1.2 million people) in Iran from November 2020 to March 2021.

Patients

Our target patients were severe and critically ill hospitalized patients with COVID-19. We selected Velayat hospital (as a dedicated hospital for patients with COVID-19 in Qazvin province) as sampled population and finally we collected 128 patients' data during the research period.

Diagnosis of patients was based on a positive reverse transcription polymerase chain reaction (RT-PCR) test of COVID-19 and positive imaging representing SARS-CoV-2.

Patients' information counting age, gender, the value of RDW, PDW, P-LCR and MPV (on the primary day of hospitalization) were extracted from the health data framework of the mentioned hospital. The data in this database is collected from the recorded reports of hospital patients. The investigation period was from November

2020 to March 2021.

Inclusion criteria were the following;

1. Confirmed diagnosis with COVID-19
2. Admitted patients.

Inaccessibility of patient information was exclusion criterion of the study.

Severity

After collecting data, patients were divided into 2 groups of severe and critically ill. According to the interim guidelines issued by the ministry of health, government of Iran, patients with at least one of the following conditions was considered critically ill (the other patients considered severe):

- Systolic blood pressure less than 90 mm of mercury
- Respiratory rate of more than 30
- Oxygen saturation level of less than 90%

Hematological parameters

The value of RDW, PDW, P-LCR and MPV were measured after taking the blood samples from hospitalized cases with SARS-CoV-2 in the first day of admission.

Outcomes

The primary outcome of this study was to evaluate the correlation between severity of disease and serum level of RDW, PDW, P-LCR and MPV in hospitalized patients with COVID-19.

The secondary outcome was to evaluate and compare the median of these hematological factors in severe and critically ill group.

Statistical analysis

IBM SPSS statistics version 22 software was conducted to analyze the data of this study. In our investigation, *P* value less than 0.05 was considered significant. In this study, Spearman's correlation and Mann-Whitney U tests were used.

Results

During the research period, 128 cases with COVID-19 were enrolled. Out of 128 individuals, 69 patients were excluded from the study due to missed information (Figure 1). Finally, the data of 59 patients were considered.

The mean age of patients was 62.07 years and 59.3% of these patients were female. The demographic and clinical characteristics of the patients are presented in Table 1. As shown in Table 1, 64.4% of the patients were critically ill.

The median value of RDW in the critically ill group was considerably greater than in the severe group ($P = 0.009$). The median value of MPV, P-LCR and PDW as they are shown in Table 2, which revealed no significant difference among the groups.

Serum level of RDW had a significant positive correlation with the severity of the disease (correlation coefficient: 0.341, $P = 0.008$). There was no significant

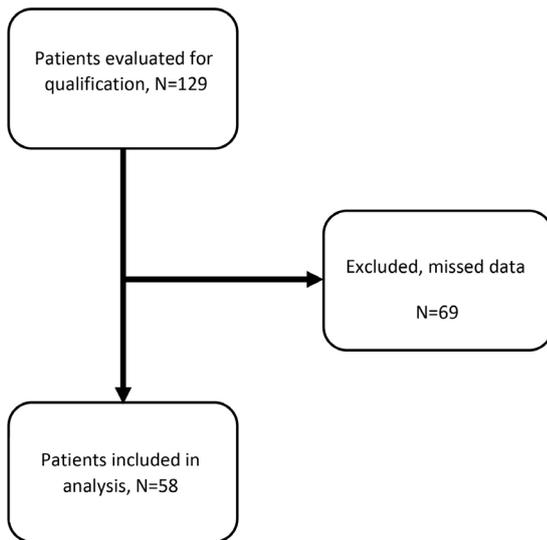


Figure 1. Flow diagram.

correlation between severity of disease with MPV (correlation coefficient: -0.022 , $P=0.870$), PDW (correlation coefficient: 0.043 , $P=0.749$) and P-LCR (correlation coefficient: 0.086 , $P=0.516$).

Discussion

This study was conducted on 59 hospitalized cases with COVID-19 to determine the relation between severity of the illness and the value of RDW, MPV, PDW and P-LCR. Median value of RDW was significantly higher in critically ill group than in severe group. Moreover, it was significantly correlated with disease severity. Unlike RDW, the other parameters of MPV, PDW and P-LCR were not correlated with disease severity.

A study from turkey to evaluate the relationship of disease severity in COVID-19 patients with their MPV

and RDW parameters, showed RDW-CV level was significantly correlated with disease severity, which is in consistent with our results (12). Contrary to our result, their study showed a significant correlation of MPV with disease severity. Maybe this is because of the different methodology of these two studies.

The increase of RDW means increase in anisocytosis that has been reported in several diseases, particularly in nonspecific acute respiratory distress syndrome patients (13,14). However, why this hematological parameter increased in patients with COVID-19 is not completely understood and it is still under evaluation.

Infection with SARS-CoV-2 causes variations in membrane structure of circulating red blood cells including the lipid and proteins (15). Furthermore, bone marrow injury due to SARS-CoV-2 infections is reported (16). These factors may cause a rise in RDW by influencing on RBCs and rising the anisocytosis.

On the other hand, due to intravascular coagulopathy, micro-thrombi or macro-thrombi is commonly seen in critically ill SARS-CoV-2 cases. This may also cause morphological abnormalities in RBCs by injuring the erythrocytes (17). Thus, this may rise the anisocytosis and the RDW values in critically ill SARS-CoV-2 patients.

The median value of PDW was not significantly different between severe and critically ill groups and it was not correlated with disease severity. Contrary to our result, in another study that evaluated the relation of PDW in cases with SARS-CoV-2 in India, intensive care unit (ICU) patients had significantly higher PDW values than ward COVID-19 patients (18). This disagreement may be due to differences in the classification of the disease severity groups. The mentioned study was performed on wider range of disease severity including mild to severe patients, while in our study, it was focused only on severe and critically ill patients. Therefore, PDW may not be significantly different between severe and critical patients with COVID-19 that further studies are needed to confirm this.

In a study that was carried out on 69 patients who were diagnosed with COVID-19 in China to evaluate the relation between P-LCR and severity of disease, there was a negative correlation between P-LCR severe COVID-19 patients (19). This result is contrary to our result that found no correlation between disease severity and the value of P-LCR in hospitalized individuals with COVID-19. This different result may be due to differences

Table 1. Clinical and demographic characteristics of the patients

Characteristics	
Mean age (SD)	62.07 (17.64)
Female gender (%)	59.3%
Median serum RDW (IQR)	13.7 (12.8-15.4)
Median serum PDW (IQR)	12.0 (11.0-14.0)
Median serum MPV (IQR)	9.60 (10.00-10.60)
Median serum P-LCR (IQR)	23.10 (18.20-29.30)
Critically ill (severity)	64.4%

Table 2. Clinical and demographic characteristics of the patients with severe disease

Characteristics	Severe	Critically ill	P value
Median serum RDW (IQR)	13.30 (12.65-13.90)	14.05 (13.20-15.72)	0.009
Median serum PDW (IQR)	11.70 (10.90-13.45)	12.00 (11.12-14.20)	0.745
Median serum MPV (IQR)	9.50 (8.95-11.05)	9.70 (8.95-10.52)	0.868
Median serum P-LCR (IQR)	23.00 (17.05-30.20)	23.30 (18.92-29.77)	0.511

in the study groups. In the mentioned study the patients were divided into three groups of mild, moderate and severe, while the focus of our study was to determine the relation of P-LCR in severe and critically ill hospitalized cases with COVID-19.

Since a very small percentage of patients with SARS-CoV-2 develop severe or critically ill disease, the sample size of the study was not large. Therefore, the results of this study should be interpreted with caution due to the its sample size. Other studies need to be conducted with larger sample sizes. Likewise, the results of this study cannot be generalized to children because the studied population includes only the adult patients.

This was one of the few studies that its target was evaluating the relation between RDW, DPW, P-LCR and MPV with disease severity in hospitalized patients with COVID-19 focusing on severe and critically ill groups.

The results of this study suggest considering the serum level of RDW may be helpful for physicians in determining and differentiating the severity of the disease in hospitalized patients with COVID-19 between severe and critically ill groups when making clinical decisions.

Conclusion

This study was performed to evaluate the relation between disease severity with serum level of MPV, RDW, PDW and P-LCR in hospitalized patients with SARS-CoV-2 to be used to differentiate the severe patients from critically ill. Our data showed that RDW positively correlated with disease severity and it was significantly higher in critically ill group compared with severe group. This hematological parameter might be helpful for physicians to differentiate the critically ill patient from severe one and making better clinical decisions.

Limitations of the study

This study was conducted on a low-number of patients. Further studies with larger sample size are recommended.

Authors' contribution

Conceptualization: SH, MK, MR; Methodology: SH, MK; Validation: SH, MK; Formal Analysis: ASG; Investigation: SH, MK; Resources: SH, MK; Data Curation: MK, MHA; Writing—Original Draft Preparation: ASG, SH; Writing—Review and Editing: ASG, SH, MK; Visualization: All authors; Supervision: All authors; Project Administration: MR; Funding Acquisition: SH, MK.

Conflict of interest

The authors declare no conflicts of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. This study has been approved by the ethic committee of Qazvin University of Medical Sciences with the ID of IR.QUMS.REC.1400.170. Due to the observational nature of the study, the requirement for informed consent was waived. Patient's characteristics data and information was anonymized and deidentified prior to analysis. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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