Date of Issue: June-1-2024

Prognostic evaluation of red blood cell distribution width (RDW) in severe and critical COVID-19 patients monitored in the intensive care unit

1. Methodology:

Retrospective, single-center, observational study.

This retrospective study included data from severe and critical COVID-19 patients admitted to the COVID-19 Intensive Care Unit of Ankara University Ibn-i Sina Research and Practice Hospital, Department of Anesthesiology and Reanimation, between June 2020 and May 2024.

---

2. Objective of the Study:

COVID-19 has caused significant morbidity and mortality worldwide, particularly among critically ill patients. Early identification of patients at high risk for poor outcomes is crucial. Red cell distribution width (RDW), a measure of the variation in red blood cell size, has emerged as a potential marker of inflammation and has been associated with adverse outcomes in various medical conditions, including COVID-19.
This study aims to investigate the relationship between RDW and mortality in severe and critical patients admitted to our COVID-19 intensive care unit.

- **Primary Objective:** To determine whether RDW can serve as a prognostic marker for mortality in severe and critical COVID-19 patients admitted to the ICU.
- **Secondary Objective:** To evaluate the association of RDW with adverse outcomes such as invasive mechanical ventilation, duration of intubation, and secondary organ damage in severe and critical COVID-19 patients admitted to the ICU.

---

3. Inclusion Criteria:

- Patients over 18 years of age
- Severe and critical COVID-19 patients (with positive PCR test or diagnosed clinically and radiologically)
- Patients followed in the ICU for at least three days
- Patients without hematological malignancy

COVID-19 severity was classified according to the **Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)** published by the National Health Commission of the People's Republic of China:

- **Severe cases:** Meeting any of the following criteria:
  - Respiratory rate (RR) $\geq$ 30 breaths/min
  - Resting oxygen saturation (finger) $\leq$ 93%
  - Arterial partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) $\leq$ 300 mmHg

    - 50% progression of lung lesions within 24–48 hours on imaging
- **Critical cases:** Meeting any of the following criteria:
    - Respiratory failure requiring mechanical ventilation
    - Shock
    - ICU admission required due to organ failure other than respiratory failure

Reference: National Health Commission & National Administration of Traditional Chinese Medicine. (2020). Diagnosis and treatment protocol for novel coronavirus pneumonia (Trial Version 7). Chinese Medical Journal, 133(09), 1087-1095.

---

4. Exclusion Criteria:

- Patients under 18 years of age
- Patients with hematological malignancies (since RDW levels may be affected)
- Patients who died within three days of ICU admission

---

5. Data Collection:
Patient demographics, clinical features, laboratory results (including RDW), and outcomes will be collected from electronic medical records and patient files.
To ensure patient confidentiality, data will be anonymized. Since all data will be de-identified and analyzed retrospectively, no direct patient contact will be required.

Data to be recorded:

- **Demographics:** Sex, age, body mass index (BMI), number and type of COVID-19 vaccines
- **Comorbidities**
- **Hospitalization data:** Referring department, length of stay, outcome (mortality/discharge), discharge destination
- **At ICU admission:** APACHE II and SOFA scores, days from symptom onset to hospital admission, type of respiratory support, hematological and biochemical laboratory results
- **During follow-up:** Trends in hematological and biochemical laboratory parameters (increase/decrease/normalization), need for invasive/non-invasive mechanical ventilation, duration of intubation, antiviral therapy, development of secondary infections, development of secondary organ failure, mortality/discharge

6. Statistical Analysis

- **Sample Size Calculation**
  The main hypothesis of the study was to investigate whether there is a difference in RDW levels between patients who survived and those who did not. Based on the study by Lorente et al. (2021), which reported RDW values of 13.4 ± 1.5 and 14.5 ± 2.2, an effect size of 0.58 was calculated. At a significance level of 0.05 and a statistical power of 0.80, the required sample size was determined to be 110 patients in total. The sample size calculation was performed using the G*Power software (version 3.1.9.2).

- **Statistical Methods**
  Descriptive statistics will be presented as mean ± standard deviation (min–max) for normally distributed quantitative variables, as median (min–max) for non-normally distributed variables, and as percentages for categorical variables. To compare two independent groups, the *Independent Samples t-test* will be used when assumptions are met, while the *Mann-Whitney U test* will be applied otherwise. Relationships between categorical variables will be evaluated using the *Chi-Square test*, *Fisher's exact test*, or multi-way Chi-Square test, as appropriate. For comparisons involving more than two groups, *One-Way ANOVA* or the *Kruskal-Wallis test* will be applied depending on the distribution of data. All statistical analyses will be performed using SPSS software (version 11.5).

7. Ethical Considerations

- **Confidentiality:** All patient data will be de-identified and securely stored. Access to the data will be restricted to authorized research personnel only. The data will be kept in a secure database with access limited to the research team.
- **Risk to Participants:** Since this is a retrospective study utilizing existing medical records, there is no direct risk to participants. The study does not involve any intervention and does not cause any harm to patients whose records are analyzed.
- **Benefits:** The potential benefits of this study include a better understanding of prognostic markers in COVID-19, which may improve patient care and resource allocation in intensive care units. This could contribute to better patient outcomes and more efficient use of healthcare resources.
- **Informed Consent:** Given the retrospective design of the study and the use of de-identified data, obtaining informed consent from patients was not feasible. Since the study poses no more than minimal risk to participants and does not involve procedures for which written consent is normally required outside the research context, a waiver of informed consent was requested and approved by the ethics committee.