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RESEARCH ARTICLE

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Could red cell distribution width be used for predicting cardiac injury in neonates with COVID-19?

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Abstract

Background: Coronavirus disease 2019 (COVID-19) can affect people of all age groups and it can occasionally cause life-threatening clinical illnesses in immunologically immature populations, especially in newborns. High red cell distribution width (RDW) values were used as an early prognostic biomarker of some neonatal diseases. We aimed to determine the prognostic value of RDW in severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infected neonates.

Methods: Newborns with positive SARS-CoV-2 *polymerase chain* reaction (PCR) test from a nasopharyngeal swab sample, who had refractory fever (>38°C and lasting more than 24 h during hospitalization), were screened for multisystem inflammatory syndrome in newborns (MIS-N), systemic inflammatory indexes calculated and cardiologic evaluations. Due to troponin levels (high: >45 ng/L and low: ≤45 ng/L) patients were grouped.

Results: Out of the 68 SARS-CoV-2 PCR-positive newborns, 26 patients had refractory fever. Comparison of laboratory findings between the high and low-troponin groups showed that RDW and neutrophil/lymphocyte ratio values were significantly higher in patients with high troponin levels ($p = 0.022$ and $p = 0.030$, respectively). The cut-off values with optimal sensitivity and specificity were determined as 1.00 for neutrophil/lymphocyte ratio ($p = 0.205$) and 16.6 for RDW ($p = 0.014$). None of the patients died.

Conclusions: Neonatal COVID-19 generally has a benign prognosis, but can progress to severe disease and cases of MIS-N are rare. RDW could be prognostic in the diagnosis and management of neonates with SARS-CoV-2 infection with high troponin levels.

KEYWORDS

coronavirus disease 2019 pandemic, inflammation, newborn, red cell distribution width, troponin

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), a potentially fatal infection caused by the novel virus severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), spread rapidly worldwide and was declared a pandemic by the World Health Organization in March 2019. COVID-19 can affect people of all age groups, and case series of multisystem inflammation syndrome in neonates (MIS-N) have been reported.

Although SARS-CoV-2-positive neonates evaluated in the emergency department usually do not present marked symptoms, it can

occasionally cause life-threatening clinical illness in this immunologically immature population. There are many gaps in the literature regarding the causes and severity of clinical symptoms in newborns. The true incidence of serious manifestations such as MIS-N and multisystem inflammatory syndrome in children (MIS-C) remains unclear. After understanding the pathophysiology of these clinical conditions, scores were developed to determine various prognostic factors to monitor their severity, prognosis, and treatment in all age groups, and studies on this are still ongoing.[1,2] Identifying early markers of disease severity will greatly assist in the selection of COVID-19 patients who require more aggressive monitoring and management, as well as facilitate the appropriate use of health resources.

Red cell distribution width (RDW) is determined in standard complete blood count analysis and is a measure of variability in red blood cell (RBC) volume. The potential prognostic role of the RDW in COVID-19 can be explained by multiple mechanisms, some of which are hypothetical. Conditions that may affect RBC biology and contribute to anisocytosis include RBC damage due to hemolytic anemia or intravascular coagulopathy, direct damage due to infection of RBCs or bone marrow precursors, and iron metabolism disorder caused by inflammatory response, but the strongest hypothesis is that anisocytosis occurs due to inflammation.[3,4]

The literature data on RDW and its clinical relevance in newborns are scarce, but there are studies showing that high RDW values may be an early prognostic biomarker for outcomes in neonatal sepsis, transient tachypnea of the newborn, critically ill children, and critical pediatric diseases such as severe bacterial infection.[4–8] RDW assessment has an important role in determining the severity and prognosis of cardiac autonomic dysfunction and cardiovascular disease in adults.[9,10] A number of diseases that are characterized by inflammatory burden are associated with elevated RDW levels, such as autoimmune,[11] gastrointestinal[12] and liver[13] diseases, and malignancy conditions.[14,15] Recent studies have indicated that RDWs are directly associated with morbidity and mortality rates in patients hospitalized for COVID-19.[16–19] This study aimed to determine RDW values in SARS-CoV-2-infected neonates admitted to emergency departments and evaluate the potential role of RDW as a prognostic factor.

2 | METHODS

2.1 | Study participants

The average number of births in the hospital is 14 000–17 000 per year, and the hospitalization rate is 2.500–3.000 per year. The 150-bed neonatal intensive care unit also has a separate unit where isolation is provided for COVID-19-positive neonates.

This retrospective observational study included a total of 68 patients who presented to the pediatric emergency department of Ankara City Hospital between March 2019 and November 2021 with complaints such as fever, cough, nasal discharge, nasal congestion, wheezing, and reduced feeding had a positive SARS-CoV-2 polymerase chain reaction (PCR) test from a nasopharyngeal swab sample, and were admitted to the neonatal intensive care unit.

2.2 | Data collection

Patients with fever (>38°C) that lasted more than 24 h and was refractory (not falling below 37.5°C within 4–6 h despite cold pack application and nonsteroidal anti-inflammatory drugs) were screened for MIS-N by examining cardiac enzymes (hemogram, troponin, creatine kinase MB [CK-MB], and pro-brain natriuretic peptide [pro-BNP]), liver and kidney function parameters, and ferritin, lactate dehydrogenase (LDH), and D-dimer levels. Intermittent electrocardiogram and echocardiography were also performed.

Absolute neutrophil (N), lymphocyte (L), and platelet (P) count ($\times 10^9$/L) were used to determine the systemic inflammation markers neutrophil-to-lymphocyte ratio (NLR = N/L), platelet-to-lymphocyte ratio (PLR = P/L), and systemic immune-inflammation index (SII = NLR × P).

The patients' demographic, clinical, radiological, echocardiographic, and laboratory data were obtained from the hospital data system and patient records. Infants with a history of neonatal sepsis, meningitis, asphyxia, and low Apgar score at birth, preterm birth, or long-term respiratory support and infants with community-acquired viral and bacterial pneumonia or urinary tract infection were excluded. The study was approved by the institutional review board of the same hospital. The authors have confirmed in writing that they have complied with the World Medical Association Declaration of Helsinki regarding the ethical conduct of research involving human subjects.

2.3 | Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 22.0 (IBM Corp). The data were tested for normal distribution using Shapiro–Wilk test and were analyzed using Student's t test for comparisons of parametric variables, which were mentioned as mean ± SD, Mann–Whitney U test and χ^2 test for comparisons of nonparametric variables, which were mentioned as percentiles, and Pearson's and Spearman's tests for correlation analysis. Receiver operating characteristic (ROC) curve analysis was performed to determine cut-off, sensitivity, and specificity values for statistically significant parameters, and logistic regression analysis was performed to identify independent risk factors. A $p < 0.05$ was considered statistically significant for all tests.

3 | RESULTS

Out of the 68 SARS-CoV-2 PCR-positive patients in this study, 58 had fever, 4 had wheezing and cough, 9 showed reduced feeding activity, 5 had diarrhea, and 2 had drowsiness. Twenty-six patients

with fever lasting more than 24 h during hospitalization were examined for severe illness and multiorgan involvement (Figure 1).

Patients with persistent fever were grouped as those with high (>45 ng/L) and low (<45 ng/L) troponin levels. There were no differences between the two groups in terms of gestational age, sex, birth weight, mode of delivery, or postnatal age at admission (Table 1).

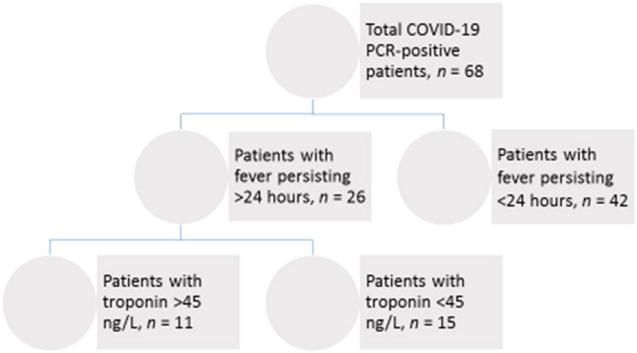

FIGURE 1 Coronavirus disease 2019 (COVID-19) polymerase chain reaction (PCR)-positive patients

Comparison of laboratory findings between the high- and low-troponin groups showed that RDW and NLR values were significantly higher in patients with high troponin levels ($p = 0.022$ and $p = 0.030$, respectively).

Area under the curve (AUC) values and 95% confidence intervals in ROC curve analysis are shown in Figure 2 and Table 2. The cut-off values with optimal sensitivity and specificity were determined as 1.00 for NLR ($p = 0.205$) and 16.6 for RDW ($p = 0.014$) (Table 2).

There was no elevation or significant difference in the patients' liver and kidney function parameters. Statistical analysis of parameters such as acute phase reactants, D-dimer, ferritin, LDH, CK-MB, and pro-BNP was not possible due to insufficient data.

One patient with presumed MIS-N developed respiratory distress, abnormal liver function parameters, kidney failure, coagulopathy, arrhythmia (supraventricular tachycardia), and heart failure, and was treated with intravenous immunoglobulin (IVIG), corticosteroid, and inotropic therapy.

TABLE 1 Demographic and laboratory findings of SARS-CoV-2 PCR-positive infants compared based on troponin levels

	High-troponin group ($n = 11$) Mean ± SD	Low-troponin group ($n = 15$) Mean ± SD	p Value
Demographic characteristics			
Gestational age (weeks)	39 ± 1	38 ± 1	0.409
Birth weight (g)	3396 ± 259	3244 ± 297	0.187
Age at admission (days)	14 ± 7	18 ± 7	0.282
Gender (male), *n* (%)	3 (27.3)	7 (46.7)	0.315
Cesarean birth, *n* (%)	5 (45.5)	8 (53.3)	0.691
Laboratory parameters			
WBC (x10^6/L)	9471 ± 4494	8823 ± 3392	0.678
NEU (x10^6/L)	4171 ± 2955	2831 ± 1517	0.144
LYM (x10^6/L)	3433 ± 1708	4019 ± 1673	0.390
HGB (g/dl)	14.8 ± 2.0	13.9 ± 2.1	0.319
HCT (%)	45.0 ± 9.3	42.5 ± 7.3	0.460
RDW (%)	16.8 ± 0.9	15.9 ± 0.8	0.022
MPV (fL)	9.1 ± 1.3	8.8 ± 0.8	0.507
PLT (x10^6/L)	352 909 ± 100 390	405 467 ± 134 961	0.288
PCT (%)	0.31 ± 0.06	0.35 ± 0.10	0.328
NRBC (x10^6/L)	0.1 ± 0.20	0.15 ± 0.30	0.983
LUC (x10^6/L)	0.35 ± 0.18	0.42 ± 0.27	0.434
PLR	134 ± 80	115 ± 57	0.498
NLR	1.43 ± 1.07	0.74 ± 0.38	0.030
SII	475 036 ± 342 228	319 712 ± 239 175	0.185

Abbreviations: HCT, hematocrit; HGB, hemoglobin; LUC, large unstained cells; LYM, lymphocyte; MPV, mean platelet volume; NEU, neutrophil; NLR, neutrophil/lymphocyte ratio; NRBC, nucleated red blood cells; PCT, platelecrit; PLR, platelet/lymphocyte ratio; PLT, platelet; RDW, red cell distribution width; SII, systemic immune-inflamation index; WBC, white blood count.

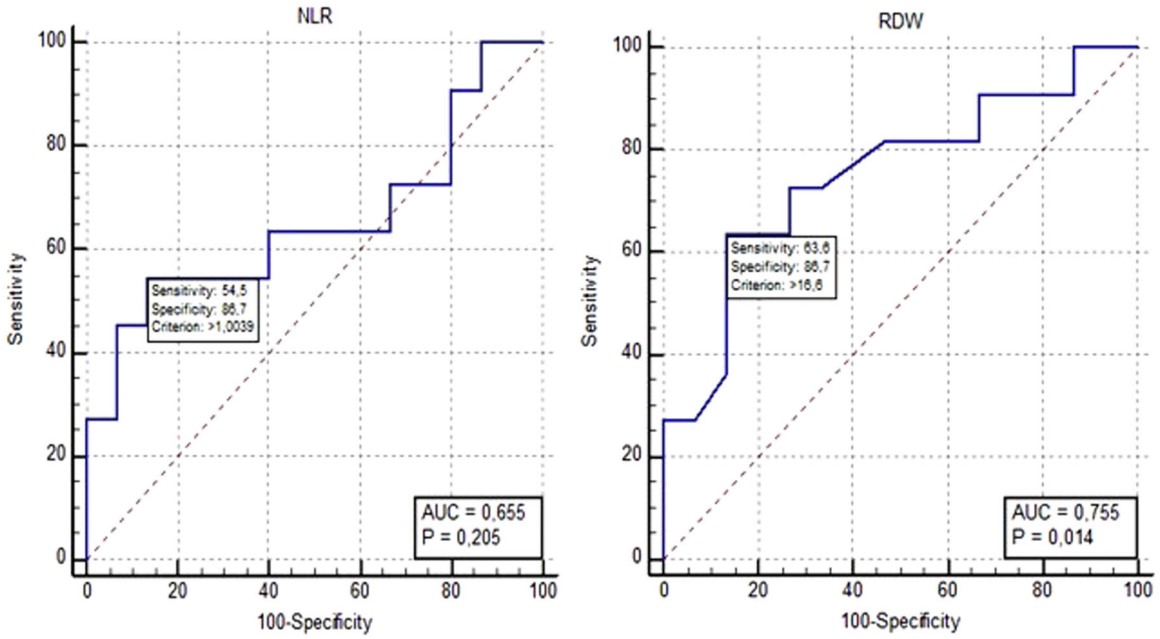

FIGURE 2 Receiver operating characteristic curves for neutrophil/lymphocyte ratio (NLR) and red cell distribution width (RDW). AUC, area under the curve; PCR, polymerase chain reaction.

	Cut-off	Sensitivity	Specificity	AUC	95% CI		*p* Value
					Lower	Upper	
NLR	>1.00	54.5%	86.7%	0.655	0.444	0.828	0.205
RDW	>16.6	63.6%	86.7%	0.755	0.548	0.901	0.014

Abbreviations: AUC, area under the curve; CI, confidence interval; COVID-19, coronavirus disease 2019; NLR, neutrophil/lymphocyte ratio; PCR, polymerase chain reaction; RDW, red cell distribution width.

TABLE 2 Cut-off, sensitivity, specificity, AUC, and 95% confidence interval values of NLR and RDW values of COVID-19 PCR-positive neonates

Except for the patient who developed MIS-N, no clinical or echocardiographic signs of cardiac dysfunction were detected. None of the patients died.

4 | DISCUSSION

This is the first retrospective, cross-sectional study, that evaluated the diagnostic and prognostic value of RDW predicting cardiac injury in neonates with SARS-COV-2 infection. RDW assessed at admission to the emergency department was reported to have strong prognostic power in adults with COVID-19.[16–19] Because most pediatric patients with SARS-CoV-2 infection are asymptomatic or have mild symptoms, blood samples are often not collected. As a result, RDW data are limited for this group. To our knowledge, our study is the first in the literature to investigate this subject in neonatal SARS-COV-2.

SARS-COV-2 affects organs and tissues directly and indirectly by binding to angiotensin-converting enzyme 2 receptors and can cause a wide range of symptoms in children, from mild illness to MIS-C and death. Children with MIS-C may present with persistent fever, skin rashes, conjunctival hyperemia, mucosal changes, gastrointestinal symptoms (diarrhea and vomiting), cough, nasal discharge, dyspnea, cardiac involvement (arrhythmia, heart failure, and shock), and other signs.[20] MIS-N has similar diagnostic criteria but is extremely rare, reported only in case series.[21]

Multisystem inflammation syndrome in neonates was observed in only one patient in our study and the diagnosis was confirmed according to the Centers for Disease Control and Prevention and American Academy of Pediatrics criteria.[22,23] This patient had fever and circulatory dysfunction at admission and developed multiple organ failure, supraventricular tachycardia, and cardiogenic shock. The ejection fraction was 50%–55% with inotropic support and no signs of coronary dilation. Cardiac function returned to normal within 1 week of treatment with IVIG and corticosteroid therapy.

Other than one case of MIS-N, no organ involvement was observed in the patients in this study. None of the patients died due to COVID-19 or its complications. Therefore, we do not have data on the relationship between RDW and mortality or organ involvement.

Troponin is a protein released into the bloodstream following cell damage and is used as a marker of myocardial damage due to its cardiac specificity. Elevated troponin was also found to be associated

with severe illness and poor prognosis for pediatric COVID-19 and MIS-C.[24,25] Based on this information, although we detected no cardiac dysfunction in our own patient group in clinical examination or echocardiography, we accepted troponin elevation as a marker of cardiac involvement. Therefore, we compared RDW in patients with and without troponin elevation and our statistical evaluation revealed a positive correlation between high RDW and elevated troponin levels. In patients with elevated troponin levels, RDW higher than 16.6% was found to be a significant prognostic marker.

RDW is a measure of RBC size variation (anisocytosis) and is routinely evaluated as part of complete blood count analysis.[5] RDW may increase with inadequate production or increased destruction of RBCs, which usually occur in inflammatory or infectious conditions.[26] For term and late preterm neonates, the reference range for RDW is 15.5% to 20% at birth and does not change in the first 2 weeks.[27] RDW gradually decreases after the 2nd week and reaches normal adult levels (11.5%–14.5%) at around 6 months.[27] In our study, the RDW cut-off value and mean RDW values in the groups were actually within the normal reference range for neonates, which casts doubt on the utility of RDW as a marker of severe illness. When we look at how RDW is used in other diseases in the neonatal literature, it has been recommended as a strong marker in predicting mortality and poor prognosis in neonatal sepsis, with a cut-off value of 17.6%.[6] In transient tachypnea of the newborn, it was associated with severe disease and the need for prolonged respiratory support, and a cut-off value of 17.7% was determined.[5] Similarly, in many neonatal diseases such as asphyxia, bronchopulmonary dysplasia, respiratory distress syndrome, and retinopathy of prematurity, it is used to indicate disease severity and cut-off values appear to be within the normal reference range.

Numerous studies have shown that RDW is an independent prognostic factor for adults admitted to emergency departments.[3,28,29] Contrary to what was observed in adults, no significant relationship has been demonstrated between RDW and hospitalization for COVID-19 or MIS-C in the pediatric age group.[30] The hemopoietic system is affected by aging, especially in terms of bone marrow cellularity, but these effects become apparent after the age of 65 years. This suggests that RDW may be a stronger prognostic factor in COVID-19-infected adults than in infants, whose bone marrow can rapidly replace defective RBCs. The low prevalence of inflammatory and hematological critical disease in children infected with SARS-COV-2 may explain why RDW has not yet been considered a prognostic factor for serious outcomes. The low prevalence of severe disease and limited sample size of pediatric cohorts may also have attenuated the power of RDW as a prognostic factor. Furthermore, as the majority of children infected with SARS-CoV-2 are asymptomatic or present with mild symptoms, blood samples are not always obtained and, therefore, data obtained from blood tests, such as RDW, are not available for all positive children. We determined in this study that troponin level, which is a specific marker of myocardial injury, was elevated and correlated with RDW in some neonates who had no clinical signs of organ involvement. This provides important evidence that RDW may be a prognostic marker.

Studies have revealed a relationship between the severity of COVID-19 illness and lymphopenia in adult patient groups and lymphocytosis in pediatric patients due to immature immune response.[31] There were no differences in WBC and subgroup counts among the patients included in our study.

Recently, inflammatory markers such as NLR and PLR have been associated with COVID-19 severity, risk groups, and mortality in adults.[31,32] NLR is widely investigated to determine the severity of the diseases such as; thyroid conditions,[33,34] irritable bowel syndrome,[35] SARS-CoV-2 infection in adults.[36] However, we detected no difference in these markers in the patients in our study.

In literature, there is a lack of association between RDW and illness severity.[37,38] But a large number of studies are needed to verify this condition.

Limitations of our study include the small patient sample, retrospective design, incomplete data for other MIS-N parameters, and lack of quantitative antibody analysis. Although neonatal COVID-19 generally has a benign prognosis and cases of MIS-N are rare, larger studies are needed to predict critical disease and research new biomarkers for treatment and follow-up in this patient group, who have inadequate immune responses.

5 | CONCLUSION

In conclusion, in this study, we were able to explain the prognostic role of RDW in neonatal SARS-COV-2 infection as being correlated with elevation of troponin levels which may predict myocardial injury. Using this parameter, clinicians would be able to determine cardiac involvement in the early stages of the disease. Nevertheless, given the ready accessibility and low cost of determining RDW, its prognostic role in adults with COVID-19, and its relationship with other diseases, we believe that RDW may have value in the diagnosis and management of neonates with SARS-CoV-19 infection.

AUTHOR CONTRIBUTIONS

Sarkhan Elbayiyev collated data and wrote the manuscript. Burak Ceran, Mustafa Ş. Akın, H. Gözde Kanmaz, and Fuat E. Canpolat contributed to discussions and reviews. Gülsüm K. Şimşek analyzed data and reviewed/edited the manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Ethical approval was provided by the Institutional Review Board of Ankara City Hospital in advance of implementation (Date: 22/12/2021, number: E2-21-1186). Written informed consent was obtained from the patients/guardians.

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REFERENCES

1. Kilercik M, Demirelce Ö, Serdar MA, Mikailova P, Serteser M. A new haematocytometric index: predicting severity and mortality risk value in COVID-19 patients. *PLOS One*. 2021;16(8):e0254073. doi:10.1371/journal.pone.0254073
2. Obremska M, Pazgan-Simon M, Budrewicz K, et al. Simple demographic characteristics and laboratory findings on admission may predict in-hospital mortality in patients with SARS-CoV-2 infection: development and validation of the Covid-19 score. *BMC Infect Dis*. 2021;21(1):945. doi:10.1186/s12879-021-06645-z
3. Henry BM, Benoit JL, Benoit S, et al. Red blood cell distribution width (RDW) predicts COVID-19 severity: a prospective, observational study from the Cincinnati SARS-CoV-2 Emergency Department Cohort. *Diagnostics (Basel, Switzerland)*. 2020;10(9):618. doi:10.3390/diagnostics10090618
4. Raba AA, Abobaker A, Elgenaidi IS, Daoud A. Novel coronavirus infection (COVID-19) in children younger than one year: a systematic review of symptoms, management and outcomes. *Acta Paediatr (Oslo, Norway: 1992)*. 2020;109(10):1948-1955. doi:10.1111/apa.15422
5. Bolat F, Haspolat NY, Bolat G, Şahin M. Simple hematological markers in predicting the severity of transient tachypnea of newborn: new wine in old bottles. *J Trop Pediatr*. 2021;67(6):fmab100. doi:10.1093/tropej/fmab100
6. Ellahony DM, El-Mekkawy MS, Farag MM. A study of red cell distribution width in neonatal sepsis. *Pediatr Emerg Care*. 2020;36(8):378-383. doi:10.1097/pec.0000000000001319
7. Guo BF, Sun SZ. Diagnostic accuracy of a dynamically increased red blood cell distribution width in very low birth weight infants with serious bacterial infection. *Ital J Pediatr*. 2021;47(1):44. doi:10.1186/s13052-021-00994-w
8. Ramby AL, Goodman DM, Wald EL, Weiss SL. Red blood cell distribution width as a pragmatic marker for outcome in pediatric critical illness. *PLOS One*. 2015;10(6):e0129258. doi:10.1371/journal.pone.0129258
9. Haybar H, Pezeshki SMS, Saki N. Evaluation of complete blood count parameters in cardiovascular diseases: an early indicator of prognosis? *Exp Mol Pathol*. 2019;110:104267. doi:10.1016/j.yexmp.2019.104267
10. Yamada S, Yoshihisa A, Kaneshiro T, et al. The relationship between red cell distribution width and cardiac autonomic function in heart failure. *J Arrhythm*. 2020;36(6):1076-1082. doi:10.1002/joa3.12442
11. Aktas G, Sit M, Dikbas O, et al. Could red cell distribution width be a marker in Hashimoto's thyroiditis? *Exp Clin Endocrinol Diabetes*. 2014;122(10):572-574. doi:10.1055/s-0034-1383564
12. Aktas G, Alcelik A, Tekce BK, Tekelioglu V, Sit M, Savli H. Red cell distribution width and mean platelet volume in patients with irritable bowel syndrome. *Prz Gastroenterol*. 2014;9(3):160-163. doi:10.5114/pg.2014.43578
13. Ustaoglu M, Aktas G, Avcioglu U, Bas B, Bahceci BK. Elevated platelet distribution width and red cell distribution width are associated with autoimmune liver diseases. *Eur J Gastroenterol Hepatol*. 2021;33(1S):e905-e908. doi:10.1097/meg.0000000000002296
14. Aktas G, Sit M, Karagoz I, et al. Could red cell distribution width be a marker of thyroid cancer? *J Coll Physicians Surg Pak*. 2017;27(9):556-558.
15. Yüksel C, Erşen O, Culcu S, Bakırarar B, Unal AE, Demirci S. Prognostic role of red distribution width (RDW) value in gastric cancer. *J Coll Physicians Surg Pak*. 2021;31(1):21-26. doi:10.29271/jcpsp.2021.01.21
16. Foy BH, Carlson JCT, Reinertsen E, et al. Association of red blood cell distribution width with mortality risk in hospitalized adults with SARS-CoV-2 infection. *JAMA Netw Open*. 2020;3(9):e2022058. doi:10.1001/jamanetworkopen.2020.22058
17. Lanini S, Montaldo C, Nicastri E, et al. COVID-19 disease-temporal analyses of complete blood count parameters over course of illness, and relationship to patient demographics and management outcomes in survivors and non-survivors: a longitudinal descriptive cohort study. *PLOS One*. 2020;15(12):e0244129. doi:10.1371/journal.pone.0244129
18. Zinellu A, Mangoni AA. Red blood cell distribution width, disease severity, and mortality in hospitalized patients with SARS-CoV-2 infection: a systematic review and meta-analysis. *J Clin Med*. 2021;10(2):286. doi:10.3390/jcm10020286
19. Aktas G. Hematological predictors of novel coronavirus infection. *Rev Assoc Med Bras (1992)*. 2021;67(suppl 1):1-2. doi:10.1590/1806-9282.67.Suppl1.20200678
20. Fabi M, Filice E, Biagi C, et al. Multisystem inflammatory syndrome following SARS-CoV-2 infection in children: one year after the onset of the pandemic in a high-incidence area. *Viruses*. 2021;13(10):2022. doi:10.3390/v13102022
21. Pawar R, Gavade V, Patil N, et al. Neonatal multisystem inflammatory syndrome (MIS-N) associated with prenatal maternal SARS-CoV-2: a case series. *Children (Basel, Switzerland)*. 2021;8(7):572. doi:10.3390/children8070572
22. Centers for Disease Control and Prevention. Information for healthcare providers about multisystem inflammatory syndrome in children (MIS-C). 2020. Accessed March 2022. https://www.cdc.gov/mis-c/hcp/
23. American Academy of Pediatrics. Multisystem inflammatory syndrome in children (MIS-C) interim guidance. 2020. Accessed March 2022. https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/multisystem-inflammatory-syndrome-in-childrenmis-c-interim-guidance/
24. Abrams JY, Oster ME, Godfred-Cato SE, et al. Factors linked to severe outcomes in multisystem inflammatory syndrome in children (MIS-C) in the USA: a retrospective surveillance study. *Lancet Child Adolesc Health*. 2021;5(5):323-331. doi:10.1016/s2352-4642(21)00050-x
25. Güllü UU, Güngör Ş, İpek S, Yurttutan S, Dilber C. Predictive value of cardiac markers in the prognosis of COVID-19 in children. *Am J Emerg Med*. 2021;48:307-311. doi:10.1016/j.ajem.2021.06.075
26. National Institutes of Health (NIH). Coronavirus disease 2019 (COVID-19) treatment guidelines. 2021. Accessed April 9. https://www.covid19treatmentguidelines.nih.gov/
27. Christensen RD, Yaish HM, Henry E, Bennett ST. Red blood cell distribution width: reference intervals for neonates. *J Matern Fetal Neonatal Med*. 2015;28(8):883-888. doi:10.3109/14767058.2014.938044
28. Bommenahalli Gowda S, Gosavi S, Ananda Rao A, et al. Prognosis of COVID-19: red cell distribution width, platelet distribution width, and C-reactive protein. *Cureus*. 2021;13(2):e13078. doi:10.7759/cureus.13078
29. Lee JJ, Montazerin SM, Jamil A, et al. Association between red blood cell distribution width and mortality and severity among patients with COVID-19: a systematic review and meta-analysis. *J Med Virol*. 2021;93(4):2513-2522. doi:10.1002/jmv.26797

30. Tchidjou Kuekou H, Palandri L, Pouplin S, et al. SARS-COV-2 infection in children and red blood cell distribution width. *Cureus*. 2021;13(9):e17837. doi:10.7759/cureus.17837
31. Henry BM, Lippi G, Plebani M. Laboratory abnormalities in children with novel coronavirus disease 2019. *Clin Chem Lab Med*. 2020;58(7):1135-1138. doi:10.1515/cclm-2020-0272
32. Kosmeri C, Koumpis E, Tsabouri S, Siomou E, Makis A. Hematological manifestations of SARS-CoV-2 in children. *Pediatr Blood Cancer*. 2020;67(12):e28745. doi:10.1002/pbc.28745
33. Afşin H, Aktas G. Platelet to lymphocyte and neutrophil to lymphocyte ratios are useful in differentiation of thyroid conditions with normal and increased uptake. *Ethiop J Health Dev*. 2021;35:1-5.
34. Aktas G, Sit M, Dikbas O, et al. Elevated neutrophil-to-lymphocyte ratio in the diagnosis of Hashimoto's thyroiditis. *Rev Assoc Med Bras (1992)*. 2017;63(12):1065-1068. doi:10.1590/1806-9282.63.12.1065
35. Aktas G, Duman T, Atak B, et al. Irritable bowel syndrome is associated with novel inflammatory markers derived from hemogram parameters. *Fam Med Prim Care Rev*. 2020;22(2):107-110. doi:10.5114/fmpcr.2020.95311
36. Khalid A, Ali Jaffar M, Khan T, et al. Hematological and biochemical parameters as diagnostic and prognostic markers in SARS-COV-2 infected patients of Pakistan: a retrospective comparative analysis. *Hematology (Amsterdam, Netherlands)*. 2021;26(1):529-542. doi:10.1080/16078454.2021.1950898
37. Cakir L, Aktas G, Enginyurt O, Cakir S. Mean platelet volume increases in type 2 diabetes mellitus independent of HbA1c level. *Acta Medica Mediterr*. 2014;30:425-428.
38. Karagoz I, Aktas G, Yoldas H, et al. Association between hemogram parameters and survival of critically ill patients. *J Intensiv Care Med*. 2017;34(6):511-513. doi:10.1177/0885066617703348

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