Med Discoveries
An open access journal of science and medicine

Article Type: Research Article
Volume 3, Issue 8
Received: Jul 09, 2024
Accepted: Aug 15, 2024
Published Online: Aug 22, 2024

Red Cell Distribution Width as a Diagnostic Clue for Viral Infections among Eastern Sudanese: Outlooks and Challenges

Bashir Abdrhman Bashir Mohammed*

Department Faculty of Medical Laboratory Sciences, Port Sudan Ahlia University, Port Sudan, Sudan.

***Corresponding Author:** Bashir Abdrhman Bashir Mohammed*

Tel: 00249912358772 & 00249 3118 26537; Email: bashirbashir17@hotmail.com

Abstract

Background: Viral diseases continue to be a major threat to global health, so priority is given to limited health care. Red Blood cell distribution Width (RDW), a clue of red blood cell size (anisocytosis), is a potential forecasting sign for the severity of numerous diseases.

Objectives: This study explores RDW as a diagnostic value for viral infections, focusing on hepatitis B, coronavirus disease 2019 (COVID-19), and HIV.

Materials and methods: 176 participants were enrolled in an analytical cross-sectional study. Among them, 44 tested positive for HIV, 44 for COVID-19, 44 for hepatitis B, and 44 were healthy controls. Their red cell indices were examined.

Results: A total of 132 patients were included in this study (mean (SD) age, 45.3(14)). 84(63.6%) were males and 48(36.4%) were females. Excessive RDW values occurred in 39% of the subjects enrolled. In this investigation, there was a statistically significant increase in the rate of morbidity (41.4%, P=0.000) among 24/44 HIV patients with higher RDW values. 18 out of 44 HBV patients (31.0%, P=0.000) showed higher RDW values, indicating liver impairment. Among 10/44 COVID-19 patients, a significantly higher hospitalization rate was noted in those with elevated RDW (17.2%, P=0.000). ROC curves suggest that RDW is the most significant single parameter that predicts high morbidity risk. RDW/HIV (AUC=0.228, sensitivity=21%, specificity=61%, 95% CI 0.128-0.329, and cut-off 14.8%) was anticipated high morbidity risk. RDW/HBV (AUC=0.427, sensitivity=43%, specificity=57%, 95% CI 0.305-0.548, and cut-off 13.7%) was implicated in high morbidity risk. RDW/COVID-19 (AUC=0.418, sensitivity=43%, specificity=59%, 95% CI 0.297-0.539, and cut-off 13.7%) was associated with high morbidity risk.

Conclusion: This study revealed that RDW can be a valuable indicator of viral disease intensity and a marker of morbidity.

Keywords: RDW; Predictive biomarker; Anisocytosis; HIV; Hepatitis B; Sudan.

Introduction

Over the past few years, viruses have become a significant global threat. Some of the viral threats stem from the ability of viruses to mutate frequently and adapt to various hosts [1]. To cope with the threat of viral infections, humanity must effectively identify emerging deadly viruses and anticipate the prognosis of viral disease. Identifying high-risk individuals is crucial in managing viral diseases with limited resources [2]. Differences in red blood cell morphology (size, shape, color, content/inclusion, or distribution) are probably diagnostic markers for pathological features [3]. Generally speaking, there are various qualitative and quantitative measures of red cells, including mass, volume, number, concentration of hematocrit, and hemoglobin. This should be within certain limits for an age group and sex in a given population [4]. Red blood cell Distribution Width (RDW) is a low-cost and easily accessible laboratory test included in a complete blood count with modern hematological

Citation: Mohammed BAB. Red Cell Distribution Width as a Diagnostic Clue for Viral Infections among Eastern Sudanese: Outlooks and Challenges. Med Discoveries. 2024; 3(8): 1203.

analyzers. The RDW measure reflects the extent of anisocytosis, a condition characterized by significant heterogeneity in circulating erythrocyte volume [2]. The RDW may be interrupted by physiological (e.g., pregnancy, aging, or physical exercise) or pathological (e.g., iron deficiency anemia, inflammation, and oxidative stress) factors [5]. Persistent inflammation, which may result from infections, is associated with higher RDW levels [6]. Increased RDW has been proposed as a marker for the severity of the viral disease. However, the exact mechanism by which the viral infections trigger high RDW remains vague. Viral-induced chronic inflammation can disable erythrocyte development, leading to changes in erythropoiesis or underproduction of erythropoietin. This may account for the positive correlation between RDW levels and the seriousness of viral infections [7]. RDW has significant potential for differential determination, morbidity, and mortality forecasts of infectious diseases, including parasitic and bacterial diseases, community-acquired pneumonia, infective endocarditis, sepsis due to Gram-negative bacteria, and viral illnesses. The parameter is progressively picking up consideration as a conceivable, easily available, and cost-effective biomarker for the determination and prognosis of infectious diseases [8]. To this end, it is important to continue researching biomarkers capable of predicting the prognosis of many diseases, including those caused by viruses. This study highlights the points of view and challenges of RDW as an anticipated biomarker for viral diseases, with an accentuation on hepatitis B, COVID-19, and HIV.

Materials and methods

This study was conducted in a single medical center in Port Sudan City using a cross-sectional analytic design. Between January 1, 2021, and December 31, 2022, 132 patients who had 44 confirmed positive COVID-19, 44 confirmed positive hepatitis B, and 44 confirmed positive HIV infections participated in the study. There were 44 healthy subjects without characteristics of interest, serving as a baseline for comparison involved in the study. Using the RDW value, the study cohort was split into two categories (elevated and normal). A cutoff value >14.6%, the top bound of the healthy reference interval, was declared to be elevated RDW [9].

Inclusion and exclusion criteria

All patients who had tested positive for COVID-19, hepatitis B, and HIV were eligible for inclusion. Pregnancy, Anemia (defined as a hemoglobin value below 130 g/L in males and below 120 g/L in females, respectively) [10], comorbidities, and seronegative status for COVID-19, hepatitis B, and HIV or begun treatment were exclusion criteria.

Laboratory method

The semi-automated hematology analyzer (Sysmex KX 21N, Japan) is utilized in analyzing Complete Blood Count (CBC) including RDW-CV.

Statistical analysis

Categorical data are reported as the percentage of composition ratio, whereas continuous variables are expressed as the mean. Student's t-tests were utilized for between-group comparisons. The Shapiro–Wilk test was used to check for the normality distribution of normally distributed data. One-way analyses of variance were applied to the multigroup comparisons, and Tukey-Kramer was employed for the pair-wise comparisons that followed. We compared categorical variables using Pearson's chi-square analysis. Receiver Operating Characteristic (ROC) curves were created to examine how the RDW parameter performed in categorized morbidities. Statistical significance was set up by $P<0.05$.

Ethical approval: This study's procedures for working with human subjects adhered to the Declaration of Helsinki in every way. This study on a single healthcare center in Port Sudan City was approved by the Red Sea Ministry of Health's Ethics Committee [code 44/B/1, January 2021].

Results

The clinical sample of this study consisted of 132 individuals, 44 of whom had COVID-19, 44 had hepatitis B, and 44 had HIV. Moreover, 44 were seemingly healthy subjects as control. It was discovered that 39% (52/132) of the study had excessive RDW values versus 61% (80/132) had normal RDW.

Male patients made up the majority of the study's viral illness patients. The average HB, Hct, MCV, and RBC count values were vastly lower in viral diseases versus the control group ($P<0.000$). Even if it is lower than the group control, the MCH level was only marginally reduced ($P<0.178$). Additionally, the MCHC levels were hardly higher in the viral sickness group than in the control group ($P<0.055$). Interestingly, the RDW values were dramatically elevated in the viral infection group compared to the control group ($P<0.000$). Table 1 provides an overview of the foundational facts.

In the present study, patients with greater RDW values had a higher frequency of anemia than patients with lower RDW values. High rates of anemia were reported in patients with increased RDW values (odds ratio 6.6). It was observed that men had higher odds of having increased RDW values with an odds ratio of (0.57). According to this study, the most common viral infections that promote anemia are HIV and HBV, which account for 63.6% and 43.2%, respectively ($P<0.000$). While the COVID-19 infection had a slight risk of causing anemia 34.0%, it did so extensively.

Table 2 displays the study's conclusions. The difference was statistically significant (41.4% vs. 16.9%, $P=0.000$) in favor of the 24 HIV patients with greater RDW values because they experienced a higher rate of morbidity. A significant difference has also existed between the 18 HBV patients with increased RDW values and those with typical RDW values (31.0% vs. 22.0%, $P=0.000$) which may imply liver impairment. The likelihood of hospitalization was considerably higher in 10 COVID-19 patients with elevated RDW versus those with normal RDW (17.2% vs. 28.8%, $P=0.000$). Diagnostically, it was discovered that anemia in viral infections with raised RDW was substantially linked to a higher risk of pathology.

ROC curve estimation and calculation of AUC for HIV, HBV, and COVID-19 were performed to propose the risk of high morbidity (Figures 1-3). In this current study, ROC curves suggest that RDW is the most significant single parameter predicting high morbidity risk. RDW/HIV (AUC=0.228, sensitivity=21%, specificity=61%, 95% CI 0.128-0.329, and cut-off 14.8%) was anticipated high morbidity risk. RDW/HBV (AUC=0.427, sensitivity=43%, specificity=57%, 95% CI 0.305-0.548, and cut-off 13.7%) was implicated in high morbidity risk. RDW/COVID-19 (AUC=0.418, sensitivity=43%, specificity=59%, 95% CI 0.297-0.539, and cut-off 13.7%) was associated with high morbidity risk. Eventually, ROC indicates that the results align with RDW elevation and anemia intensity.

Table 1: The research population's foundation.

Characteristics	HIV (n=44)	COVID-19 (n=44)	HBV (n=44)	Control (n=44)	P. value
Age					
years	33.0±11.1	62.0±13.2	40.9±17.8	24.3±9.2	0.000
range	18 - 65	29 - 80	3 - 70	18 – 76	
Sex					
male	30(68.2%)	28(63.6%)	26(59.1%)	34(77.3%)	0.312
female	14(31.8%)	16(36.4%)	18(40.9%)	10(22.7%)	
Red cell indices					
HB g/dl	11.5±1.9	12.5±1.7	11.8±2.9	14.1±0.88	0.000
Hct %	32.1±4.6	36.0±4.7	34.1±8.1	42.7±5.7	0.000
MCV fl	79.6±8.5	86.7±4.7	82.2±8.0	90.3±10.6	0.000
MCH pg	28.7±4.4	36.0±35.0	28.7±3.8	30.3±3.5	0.178
MCHC %	35.6±2.3	33.5±6.9	34.8±2.3	33.6±3.8	0.055
RBCs µl	4.05±0.65	4.11±0.55	4.19±1.1	4.74±0.60	0.000
RDW-CV %	16.0±3.0	14.3±1.6	14.8±2.8	13.9±1.6	0.000

HB: Hemoglobin; Hct: Hematocrit; MCV: Mean Cell Volume; MCH: Mean Corpuscular Hemoglobin; NCHC: Mean Corpuscular Hemoglobin Concentration; RBCs: Red Cell Counts; RDW-CV: Red Cell Distribution Width-Coefficient of Variation.

Table 2: Outcome data of studied parameter to their RDW value.

Variables	Elevated RDW	Normal RDW	P. value
HIV (n=44)	24(41.4%)	20(16.9%)	<0.0001
HBV (n=44)	18(31.0%)	26(27.0%)	<0.0001
COVID-19 (n=44)	10(17.2%)	34(28.8%)	<0.0001
Control (n=44)	6(10.3%)	38(32.2%)	–
Anemia (n=62)	37(63.8%)	25(21.2%)	<0.0001

HIV: Human Immunodeficiency Virus; HBV: Hepatitis B virus; COVID-19: Coronavirus Disease 2019; RDW: Red Cell Distribution Width.

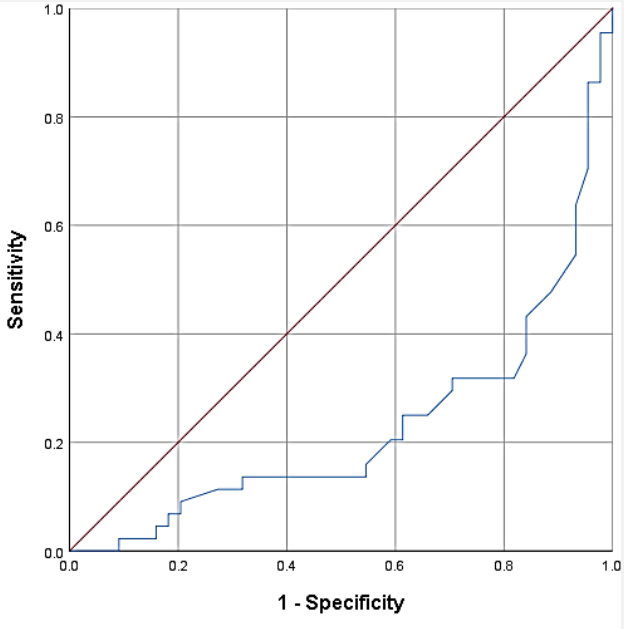

Figure 1: ROC of RDW values for proposing the outcome morbidity in HIV patients.

Discussion

The study first approached RDW values in patients with viral infections in eastern Sudan in our district. According to our research, 39% of patients with viral infections had increased RDW levels. In comparison to patients with normal values, those with elevated RDW, and consequently more pronounced anisocytosis, had a higher risk of morbidity. These results are consistent with previous studies [11-13].

RDW rises as people become older, especially in women [14]. This is most likely caused by aging's simultaneous development of diminished RBC deformability. Similarly, RDW is recognized as a significant risk factor in diagnosing and looking at patients with viral diseases [11-13]. While the exact process is still unknown, a combination of validated viral indicators and RDW can aid in the earlier detection of patients with a viral infection, allowing for more targeted and appropriate care.

In our study, patients with viral diseases had a similar prevalence of greater RDW with older age and male sex. Additionally, anemia was more prevalent in patients with higher RDW [15,16], findings consistent with past research and typical of groups with pre-existing medical problems [17-19].

The specific process via which RDW elevation occurs is uncertain in COVID-19 patients. Prior research revealed a relationship between enhanced RDW and heightened inflammatory oxidative stress indicators and poor iron metabolism, which would eventually encourage RBC apoptosis and variation in morphology [17,18]. Patients with COVID-19 are found to have a substantial inflammatory reaction that may result in multiorgan failure. The elevated COVID-19 RDW is probably because of this inflammatory reaction [20].

Elevated RDW has been linked in multiple studies to severe COVID-19 and a higher chance of death. RDW was substantially correlated with 30-day mortality in COVID-19 patients admitted to critical care units, according to a Spanish observational study. COVID-19-related mortality was predicted with 80% sensitivity and 59% specificity using an RDW cut-off value of 13.5% [21]. Therefore, For COVID-19 patients, RDW can be a useful sign for determining the severity and course of the illness.

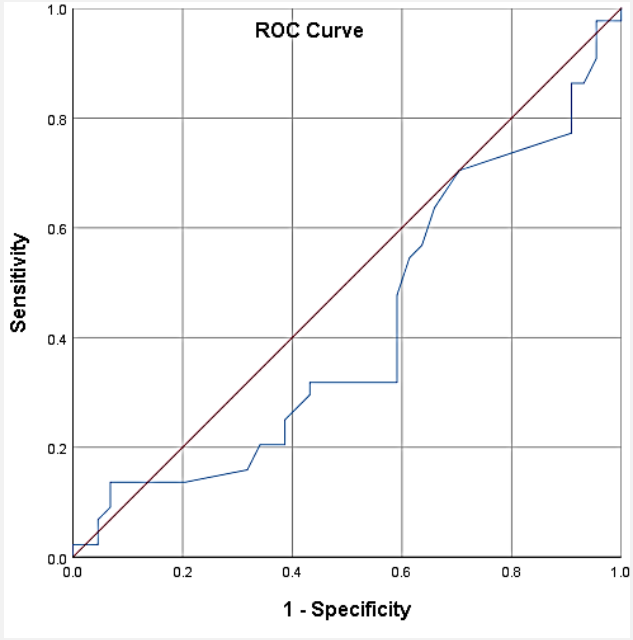

Figure 2: ROC of RDW values for predicting the outcome morbidity in COVID-19 patients.

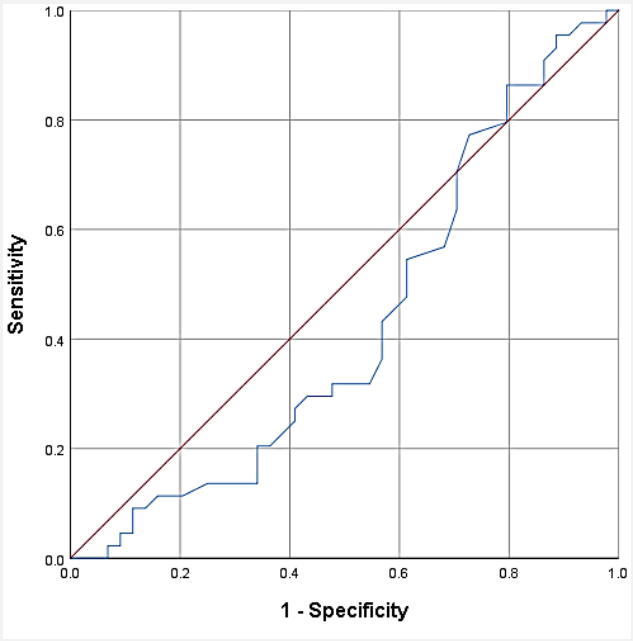

Figure 3: ROC of RDW values for anticipating the outcome morbidity in HBV patients.

The current study showed that 18 HBV patients with higher RDW values exhibited noticeable liver impairment. A study found that elevated RDW levels were significantly increased in patients with HBV-related hepatitis and could reflect disease severity [13]. A persistent case of hepatitis B is also associated with increased RDW. Research has demonstrated that in patients with chronic hepatitis B, a rise in RDW is correlated with viral load. Thus, RDW can distinguish between current and dormant infections of cirrhosis linked to HBV [21].

Elevated RDW values can aid as an independent predictor of morbidity in patients with HBV infection, which is the most important finding from our research.

We found in this study that RDW is a useful tool for predicting the morbidity of HBV-positive patients, despite its relatively poor prediction power (AUC=0.427, cut-off 13.7%, P<0.236). We, therefore, hypothesize that this variation is a significant element influencing the course of the disease and may serve as a powerful marker for those infected with HBV.

Even though the precise pathophysiological procedure underlying the connection between RDW, HIV infection, and associated morbidity is undetermined, any systemic factor that affects red cell homeostasis, such as inflammation or oxidative stress, may be involved [22]. The inflammatory condition caused by HIV replication along with the disease itself may help to explain the causality between an elevated RDW and HIV reported in the medical literature [23,24].

The current study found that RDW/HIV had a greater predictive power (AUC=0.222, cut-off 14.8%, P<0.000) and may be utilized to anticipate the morbidity of HIV-infected patients. This study offers information on the potential significance of RDW in HIV-positive Sudanese patients, emphasizing its link to inadequate disease control.

This study has limitations, and much more exploration is required to fully understand the implications of elevated RDW levels in HIV, COVID-19, and HBV infections. Future studies must increase the sample size and define the important RDW cut-off value by multi-centered research. Additionally, there are differences in the RDW measuring techniques, and the definition criteria have not been standardized. Furthermore, it would be beneficial to ascertain the reference ranges of RDW for various diseases and ethnic groups. Studying whether RDW may be utilized as an ongoing marker of changes in viral diseases is also crucial and fascinating.

Conclusion

In summary, RDW is an emerging prognostic indicator for viral infections, including COVID-19, HBV, and HIV. Monitoring RDW levels can provide valuable insights into disease severity and morbidity risk prediction.

Funding: Nil.

Competing of interests: None declared.

References

1. Bloom DE, Cadarette D. Infectious Disease Threats in the Twenty-First Century: Strengthening the Global Response. Front Immunol. 2019; 10: 549. doi: 10.3389/fimmu.2019.00549.

2. Owoicho O, Olwal CO, Quaye O. Potential of laser-induced fluorescence-light detection and ranging for future stand-off virus surveillance. Microb Biotechnol. 2021; 14(1): 126-135. doi: 10.1111/1751-7915.13698.

3. Samson Adewoyin A, Adeyemi O, Omolola Davies N, Abiola Ogbenna A. Erythrocyte Morphology and Its Disorders. Erythrocyte. Intech Open. 2019. http://dx.doi.org/10.5772/intechopen.86112.

4. Asmamaw M, Sime T, Kene K, Fekadie Baye M, Teshome M, Zawdie B. Evaluation of Red Blood Cell Parameters as a Biomarker for Long-Term Glycemic Control Monitoring Among Type 2 Diabetic Patients in Southwest Ethiopia: A Cross-Sectional Study. Diabetes Metab Syndr Obes. 2021; 14: 4993-5000. doi: 10.2147/DMSO.S348907.

5. Dugdale AE, Badrick T. Red blood cell distribution width (RDW)-a mechanism for normal variation and changes in pathological states. J Lab Precis Med. 2018; 3: 73. doi: 10.21037/jlpm.2018.08.03.

6. Zhang Z, Chew GM, Shikuma CM, Gangcuangco LMA, Souza SA, et al. Red blood cell distribution width as an easily measurable biomarker of persistent inflammation and T cell dysregulation in antiretrovirally treated HIV-infected adults. HIV Clinical Trials. 2018; 19(5): 172-176. https://doi.org/10.1080/15284336.2018.1514821

7. Karampitsakos T, Akinosoglou K, Papaioannou O, Panou V, Koromilias A, et al. Increased Red Cell Distribution Width Is Associated With Disease Severity in Hospitalized Adults With SARS-CoV-2 Infection: An Observational Multicentric Study. Front Med (Lausanne). 2020; 7: 616292. doi: 10.3389/fmed.2020.616292.

8. Guray Y, Ipek EG, Guray U, Demirkan B, Kafes H, et al. Red cell distribution width predicts mortality in infective endocarditis. Arch Cardiovasc Dis. 2014; 107(5): 299-307. doi: 10.1016/j.acvd.2014.04.008.

9. Bohn MK, Lippi G, Horvath A, Sethi S, Koch D, et al. Molecular, serological, and biochemical diagnosis and monitoring of COVID-19: IFCC taskforce evaluation of the latest evidence. Clin Chem Lab Med. 2020; 58(7): 1037-1052. doi: 10.1515/cclm-2020-0722.

10. Cappellini MD, Motta I. Anemia in Clinical Practice-Definition and Classification: Does Hemoglobin Change With Aging? Semin Hematol. 2015; 52(4): 261-9. doi: 10.1053/j.seminhematol.2015.07.006.

11. Gallego ML, Pérez-Hernández IA, Palacios R, Ruiz-Morales J, Nuño E, et al. Red cell distribution width in patients with HIV infection. Open Journal of Internal Medicine. 2012; 2: 7-10. doi: 10.4236/ojim.2012.21002.

12. Wang C, Zhang H, Cao X, Deng R, Ye Y, et al. Red cell distribution width (RDW): A prognostic indicator of severe COVID-19. Ann Transl Med. 2020; 8(19): 1230. doi: 10.21037/atm-20-6090.

13. Zhu M, Han M, Xiao X, Lu S, Guan Z, et al. Dynamic Differences Of Red Cell Distribution Width Levels Contribute To The Differential Diagnosis Of Hepatitis B Virus-related Chronic Liver Diseases: A Case-control Study. Int J Med Sci. 2019; 16(5): 720-728. doi: 10.7150/ijms.31826.

14. Yoon HE, Kim SJ, Hwang HS, Chung S, Yang CW, et al. Progressive rise in red blood cell distribution width predicts mortality and cardiovascular events in end-stage renal disease patients. PLoS One. 2015; 10(5): e0126272. doi: 10.1371/journal.pone.0126272.

15. Tonelli M, Sacks F, Arnold M, Moye L, Davis B, et al. For the Cholesterol and Recurrent Events (CARE) Trial Investigators. Relation between Red Blood Cell Distribution Width and Cardiovascular Event Rate in People with Coronary Disease. Circulation. 2008; 117(2): 163-168. doi: 10.1161/CIRCULATIONAHA.107.727545.

16. Seo SG, Lee MY, Park SH, Han JM, Lee KB, et al. The association between red cell distribution width and incident hypertension in Korean adults. Hypertens Res. 2020; 43(1): 55-61. doi: 10.1038/s41440-019-0334-3.

17. Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: A simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci. 2015; 52(2): 86-105. doi: 10.3109/10408363.2014.992064.

18. Lippi G, Mattiuzzi C, Cervellin G. Learning more and spending less with neglected laboratory parameters: the paradigmatic case of red blood cell distribution width. Acta Biomed. 2016; 87(3): 323-328.

19. Lippi G, Salvagno GL, Guidi GC. Red blood cell distribution width is significantly associated with aging and gender. Clin Chem Lab Med. 2014; 52(9): e197-9. doi: 10.1515/cclm-2014-0353.

20. Chai X, Hu L, Zhang Y, et al. Specific ACE2 Expression in Cholangiocytes May Cause Liver Damage After 2019-nCoV Infection. bioRxiv. 2020. DOI: 10.1101/2020.02.03.931766.

21. Henry BM, Benoit JL, Benoit S, Pulvino C, Berger BA, 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). 2020; 10(9): 618. doi: 10.3390/diagnostics10090618.

22. Patel KV, Ferrucci L, Ershler WB, Longo DL, Guralnik JM. Red blood cell distribution width and the risk of death in middle-aged and older adults. Arch Intern Med. 2009; 169(5): 515-23. doi: 10.1001/archinternmed.2009.11.

23. Lippi G, Turcato G, Cervellin G, Sanchis-Gomar F. Red blood cell distribution width in heart failure: A narrative review. World J Cardiol. 2018; 10(2): 6-14. doi: 10.4330/wjc.v10.i2.6.

24. Al-Kindi SG, Zidar DA, McComsey GA, Longenecker CT. Association of Anisocytosis with Markers of Immune Activation and Exhaustion in Treated HIV. Pathog Immun. 2017; 2(1): 138-150. doi: 10.20411/pai.v2i1.199.