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Red cell distribution width, platelet distribution width, and plateletcrit as indicators of prognosis in COVID-19 patients - A single-center study

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ABSTRACT

Background: COVID-19 is still present in the world, though the extent varies by region and country. According to the World Health Organization, there have been over 617 million confirmed cases of COVID-19 and over 13 million deaths worldwide since the pandemic began on March 10, 2023. **Aims and Objectives:** This is a study conducted with the aim of providing biomarkers to predict COVID-19 disease progression and mortality based on red cell indices and platelet indices which are commonly measured as part of a complete blood count (CBC). **Materials and Methods:** A prospective study was conducted during the peak of the second wave of COVID-19 from March 2021 to June 2021. The study included 540 patients who were admitted to the Government General Hospital, Nizamabad, and had tested positive for COVID-19 by RT-PCR. Red Blood Cell (RBC), Hematocrit (HCT), Red cell indices like Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Red Cell Distribution width (RDW) and Platelet indices like Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Plateletcrit (PCT), Platelet–Large Cell Ratio were taken from CBC analyzer Sysmex XN-1000 and analyzed statistically. The patients were then followed up for a period of 14 days to track their outcomes. **Results:** In the data, majority were male n = 334 (62%) and n = 280 (38%) were female. 70.37% (n = 380) were survivors and 29.63% (n = 160) were non-survivors. Red blood cell, red cell indices such as RDW-CV and RDW-SD, and platelet indices such as PCT and PDW were significantly higher in non-survivors compared to survivors with $P < 0.05$. **Conclusion:** Non-survivors had significantly higher levels of RDW-CV, RDW-SD, PCT, and PDW compared to survivors. These parameters in combination can be useful for predicting COVID-19 mortality at early stage in forthcoming waves.

Key words: COVID-19; Red blood cells; Red cell distribution width; Platelet distribution width; Plateletcrit

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INTRODUCTION

COVID-19 was caused by SARS-CoV-2, first appeared in Wuhan, China, in December 2019 and quickly spread throughout the world, resulting in a pandemic. When an infected person talks, coughs, or sneezes, the virus spreads primarily through respiratory droplets. COVID-19 symptoms can range from mild to severe and include fever, cough, fatigue, body aches, loss of smell or taste, and difficulty breathing. While some people may experience only mild symptoms or none at all, others may experience severe illnesses such as pneumonia, acute respiratory distress syndrome, and organ failure.[1] Public health measures such as vaccination, mask use, physical separation, and hand hygiene are recommended to help prevent the spread of COVID-19. COVID-19 had infected and killed millions of people around the world.[2]

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A complete blood count (CBC) is a common laboratory test that determines the composition of blood components such as red blood cells (RBCs), white blood cells (WBCs), and platelets. CBCs can be useful in the management of COVID-19 patients by evaluating the changes in WBC count, platelet count, and hemoglobin (HB) levels over time which can aid in monitoring the severity of COVID-19.[3] CBC can assess treatment response by monitoring changes in WBC count and is also used to evaluate the efficacy of COVID-19 treatments such as antiviral medications. By evaluating platelet count and HB levels, it can also help identify potential COVID-19 complications such as blood clotting disorders or anemia. Overall, CBC can be a useful tool in the management of COVID-19 patients, helping health-care providers to make informed decisions regarding diagnosis, treatment, and monitoring of the disease.[4]

A fully automated hematology analyzer called the Sysmex XN-1000 is used in clinical laboratories to examine blood samples. It performs a CBC and differential WBC count using a combination of technologies, including optical and impedance measurements.[5] With a throughput of up to 100 samples per hour, the XN-1000 is designed to provide accurate and reliable results. It can also be linked to a laboratory information system to help with data management and result reporting. It is frequently used in conjunction with other laboratory instruments and tests to aid in the diagnosis and monitoring of a variety of conditions such as anemia, infections, and leukemia.[6]

Red cell indices and platelet indices are laboratory measurements that provide information on the size, shape, and content of RBCs and platelets, respectively. These indices can be useful in the evaluation of COVID-19 patients, as they may provide insights into the physiological changes associated with the disease. Various studies have reported abnormalities in red cell indices, such as decreased mean corpuscular volume (MCV) and increased red cell distribution width (RDW), and also abnormalities in platelet indices, such as decreased mean platelet volume (MPV) and increased platelet distribution width (PDW), in COVID-19 patients.[7] These changes in red cell and platelet indices may be indicative of underlying inflammation or other physiological changes associated with COVID-19 infection. Overall, they can be useful in the evaluation and management of COVID-19 patients, providing additional information to help health-care providers make informed decisions regarding diagnosis, treatment, and monitoring of the disease.[8]

Various studies are available regarding WBC count, neutrophils, lymphocytes, and platelets individually or in ratios such as NLR, LMR, PLR . Very limited research is available regarding Red cell Indices and Platelet indices that played prominent role in Covid-19 diagnosis and mortality prediction. Fully automated multichannel instruments can measure approximately 8–20 components in full blood count. These instruments have a high precision level in cell counting and cell sizing techniques which are superior to manual techniques. Results are generally accurate if they are carefully calibrated and if their operation is ensured by quality control procedures.[9]

In this study we tried to identify the parameters that may be useful to diagnose and predict mortality of COVID-19 at an early stage based on RBC count, hematocrit (HCT), RBC indices such as MCV, mean corpuscular HB (MCH), MCHC, RDW and platelet indices such as PCT, MPV, PDW, PLCR obtained from automated CBC analyzer Sysmex Xn-1000.

Aims and objectives

The present study was done to provide parameters that helps in early diagnosis and prediction of Covid-19 mortality based on red cell indices and platelet indices.

MATERIALS AND METHODS

A prospective study was done at the Department of Pathology, Government Medical College and General Hospital, Nizamabad, for a period of 4 months, i.e., during the period March 2021–June 2021. A total of 540 RTPCR-positive patients were included in the study.

Ethical committee clearance has been take for study

Inclusion criteria

COVID-19 patients with positive RTPCR were included in the study

Exclusion criteria

Pregnant women and age group <10 years were excluded from the study.

Data collection

CBC was done by using a fully automated analyzer SYSMEX XN-1000 (Figure 1), and red cell indices such as MCV, MCH, MCHC, RDW-CV, and RDW-SD and platelet indices such as PDW, MPV, PCT, PLCR, and PLCC were taken and entered into MS Excel Sheet timely and analyzed.

Data regarding HB, RBC, WBC, platelets, HCT, MCV, MCH, MCHC, RDW CV, RDW SD, PDW, MPV, PCT, and PLCR were taken from 540 COVID-19-positive patients and compared between survivors and non-survivors using statistical methods.

Statistical analysis was done using IBM Statistical Package for Social version 22.0. The mean±standard deviation of HCT, MCV, MCH, MCHC, RDW-CV, RDW-SD, MPV, PDW, PCT, PLCR, and PLCC of COVID-19-affected

patients were taken and mean values were compared between survivors and non-survivors using Student's independent t-test.

RESULTS

Total 540 RTPCR positive patients were included in the study. Out of them males were n=334(62%) and females were n=206 (38%). 70.37% (n=380) were survivors and 29.63% (n=160) were non-survivors. Majority were male.

Table 1 shows the The mean±standard deviation of WBC (cells/cumm) in survivors and non-survivors was 10134.7±8273.8 and 100029.2±4887.9, respectively, with P=0.92. The mean±standard deviation of RBC (millions/cumm) in survivors and non-survivors was 4.8±2.8 and 4.3±1.09, respectively, with P=0.03. The mean±standard deviation of HB (g/dL) in survivors and non-survivors was 12.7±2.4 and 12.3±3.08, respectively, with P=0.35.

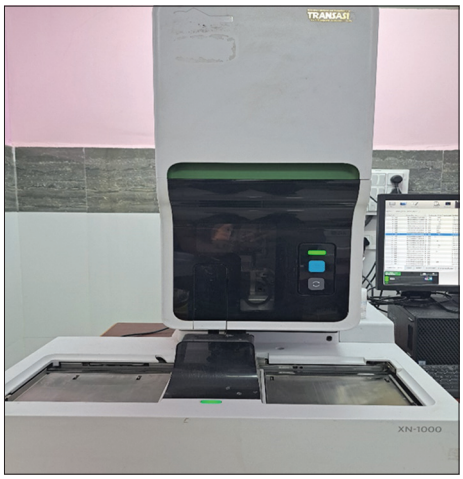

Figure 1: SYSMEX XN-1000

The mean±standard deviation of MCV (fl) in survivors and non-survivors was 85.1±8.6 and 84.6±9.7, respectively, with P=0.73. The mean±standard deviation of MCH (pg/dL) in survivors and non-survivors was 27.9±2.8 and 27.2±4.6, respectively, with P=0.24. The mean±standard deviation of MCHC (g/dL) in survivors and non-survivors was 42.1±49.8 and 31.7±2.5, respectively, with P=0.10. The mean±standard deviation of RDW-CV (%) in survivors and non-survivors was 13.6±1.2 and 14.8±1.9, respectively, with P=0.00. The mean±standard deviation of RDW-SD (fl) in survivors and non-survivors was 45.1±11.7 and 48.0±7.4, respectively, with P=0.04.

The mean±standard deviation of platelets (lakhs/cumm) in survivors and non-survivors was 2.7±2.3 and 2.6±1.3, respectively, with P=0.90. The mean±standard deviation of PCT (%) in survivors and non-survivors was 0.24±0.13 and 0.3±0.3, respectively, with P=0.01. The mean±standard deviation of MPV (fl) in survivors and non-survivors was 9.7±1.5 and 11.5±10.9, respectively, with P=0.01. The mean±standard deviation of PDW (fl) in survivors and non-survivors was 13.6±4.1 and 16.5±8.2, respectively, with P=0.00. The mean±standard deviation of PLCR (%) in survivors and non-survivors was 24.8±8.4 and 26.3±8.4, respectively, with P=0.26.

The mean values of WBC, HB, MCV, MCH, and MCHC of non-survivors and survivors were in the normal range and no statistically significant difference was observed. MPV and PLCR were high in non-survivors compared to survivors, but no statistically significant difference was observed. RBC, RDW-CV, RDW-SD, PCT, and PDW mean

Table 1: WBC, RBC, HB, RBC indices, and platelet indices between survivors and non-survivors

Parameters	Survivors (n=380)		Non-survivors (n=160)		P-value (t-test)
	Mean±standard deviation	Standard error	Mean±standard deviation	Standard error	
WBC (cells/cumm)	10134.7±8273.8	862.6	100029.2±4887.9	620.7	0.92
RBC (millions/cumm)	4.8±2.8	0.3	4.3±1.09	0.14	0.03
HB (g/dL)	12.7±2.4	0.24	12.3±3.08	0.4	0.35
Red cell indices					
MCV (fl)	85.1±8.6	0.9	84.6±9.7	1.2	0.73
MCH (pg)	27.9±2.8	0.3	27.2±4.6	0.6	0.24
MCHC (g/dL)	42.1±49.8	5.2	31.7±2.5	0.3	0.10
RDW-CV (%)	13.6±1.2	0.1	14.8±1.9	0.2	0.00
RDW-SD (fl)	45.1±11.7	1.2	48.0±7.4	0.9	0.04
Platelet indices					
Platelets (lakhs/cumm)	2.7±2.3	0.2	2.6±1.3	0.2	0.90
PCT (%)	0.24±0.13	0.01	0.3±0.3	0.04	0.01
MPV (fl)	9.7±1.5	0.1	11.5±10.9	1.4	0.11
PDW (fl)	13.6±4.1	0.4	16.5±8.2	1.04	0.00
PLCR (%)	24.8±8.4	0.8	26.3±8.4	1.06	0.26

WBC: White blood cell, RBC: Red Blood Cell, HB: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, PCT: Plateletcrit, MPV: Mean platelet volume, PDW: Platelet distribution width, PLCR: Platelet–large cell ratio. (P<0.05 considered statistically significant)

values were significantly high (P<0.05) in non-survivors when compared to survivors.

DISCUSSION

Complete blood picture (CBP) is a basic screening test done for every patient in all medical institutions, and it is also easily accessible and affordable to the community. Because of high automation technology, CBP became the first choice in early screening, diagnosis, monitoring, and follow-up of patients with any illness.[10]

RBC

COVID-19-affected organs include the liver, kidneys, lungs, heart, and heart and blood vessels. RBCs, which are in charge of transferring oxygen from the lungs to the body's tissues, may be impacted by COVID-19 as a result.[10,11]

COVID-19 patients may have lower levels of HB, the protein that carries oxygen in RBCs, and a higher prevalence of anemia, a condition marked by low levels of either RBCs or HB.[11] In the study that was published in the *Journal of Medical Virology in* 2021, COVID-19 patients who needed to be admitted to the intensive care unit (ICU) had a higher rate of anemia than those who did not.[12] Our study showed non-significance of HB between survivors and non-survivors. However, RBC significantly reduced in non-survivors compared to survivors. More investigation is required to ascertain the precise mechanisms by which COVID-19 affects RBCs, as well as the magnitude of this impact and its clinical relevance.

RDW

It is a quantitative measurement of cell volume variation which is derived by pulse height analysis and equivalent to degree of anisocytosis analyzed microscopically. It may be expressed in terms of CV in percentage or standard deviation (SD) in femtoliters (fl). RDW-SD is the calculated width 20% height level of red cell size distribution histogram in fl(Femtolitres). RDW CV is calculated by standard deviation of the mean cell size by the MCV of the red cells and multiplying by 100 to convert to a percentage. RDW-CV in general plays a significant role in differentiating iron deficiency anemia (RDW increased) and megaloblastic anemia (RDW increased) and is usually normal in thalassemia trait and other causes of macrocytosis.[13]

There is evidence which suggests that RDW in COVID-19 patients may serve as a useful marker for disease severity. Higher RDW levels have been linked to worse outcomes, such as a higher risk of mortality and more severe disease, according to studies. In COVID-19 patients, RDW may also be a helpful marker for tracking disease development. It is crucial to remember that RDW is a non-specific marker and that it can be elevated in a wide range of diseases, including anemia, inflammation, and infection. It should therefore be used in conjunction with other clinical and laboratory markers to aid in the diagnosis and treatment of COVID-19 patients.[14] Our study showed significantly high RDWCV and RDWSD in non-survivors compared to survivors with P=0.00 and 0.04, respectively.

PDW

A measure of the variation in platelet size in a blood sample is called PDW. Several studies have looked at the relationship between PDW and COVID-19. PDW levels are higher in COVID-19 patients, especially in those with more severe diseases.[15] They were found to be significantly higher in COVID-19 patients who needed admission to the ICU compared to those who did not in a study that was published in the *Journal of Medical Virology* in 2021.[12] PDW, on the other hand, is a non-specific marker that can be influenced by a variety of factors, including inflammation and other underlying medical conditions. Our study showed significantly high values in non-survivors compared to survivors with P=0.00.

PCT

A measurement of the volume occupied by platelets in a specific volume of blood is called PCT. A few studies have looked at platelet parameters, including PCT, in COVID-19 patients, despite the paucity of research on the relationship between PCT and COVID-19 in particular.[16] Patients with COVID-19 who needed to be admitted to the ICU had PCT levels that were significantly lower than those of patients who did not.[12] However, a study published in the *Journal of Clinical Medicine* in 2020 found that PCT levels were not significantly different between COVID-19 patients and healthy controls.[17] Our study showed significantly low PCT values in non-survivors compared to survivors with P=0.01. It is critical to remember that PCT, like PDW, is a non-specific marker that is susceptible to a variety of influences.

Parameters such as RBC, RDW, PDW, and PCT in combination may be used to predict prognosis in COVID-19 patients at early stage with high accuracy. However, red cell and platelet indices obtained from automated hematology analyzers do not provide a complete picture of the disease. Other factors, such as imaging studies, clinical symptoms, and laboratory tests for inflammatory markers, may be needed to fully assess disease severity. No significant change was observed in parameters such as HCT, MCV, MCH, MCHC, MPV, PLCR, and PLCC of COVID-19-affected survivors and non-survivors.

Limitations of the study

As it is a single-center study with a small sample size, our study may have limited generalizability to other populations. Additionally, the lack of data at intervals for patients limited the accuracy and completeness of our findings. Large-scale

studies with more diverse patient populations and more frequent data collection may be needed to further validate our findings and to better understand the role of RBC and platelet parameters in COVID-19.

CONCLUSION

Automated hematology analyzers can be a valuable tool in the management of COVID-19 patients, providing rapid and accurate analysis of CBC and differential parameters. RBCs, red cell indices such as RDW-CV and RDW-SD, and platelet indices such as PCT and PDW parameters obtained from them may be useful in the early diagnosis and prediction of COVID-19 mortality at an early stage in forthcoming waves.

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Authors' Contributions:
KUD- Literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation, and submission of article; **RNC-** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **ML-** Design of study, statistical analysis, and interpretation; **MIL-** Review manuscript; **FB-** Review manuscript; **SV-** Literature survey and preparation of figures, coordination, and manuscript revision.

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