DOI: 10.7860/JCDR/2022/56018.16794

Original Article

Pathology Section

Comparative Assessment of WBC Scattergram, Histogram and Platelet Indices in COVID-19 and Non COVID-19 Patients: A Cross-sectional Study

NIKHIL[1], SUBHASHISH DAS[2], RAJU KALYANI[3]

ABSTRACT

Introduction: Coronavirus Disease-2019 (COVID-19) is an extremely transmissible infectious disease. Detection of coronavirus by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) requires expert skills and moreover, it is not widely available in all the laboratories.

Aim: To evaluate Red Blood Cell (RBC), platelet histogram and White Blood Cell (WBC) scattergram graphic patterns and interpretation of corresponding parameters along with peripheral smear in 500 COVID-19 RT-PCR positive study cases (COVID-19) and to compare them with normal study controls (non COVID-19).

Materials and Methods: This was a laboratory-based cross-sectional observational study, conducted at a fully accredited National Accreditation Board for testing and calibration Laboratories's (NABL) Central Diagnostic Research Laboratory, RL Jalappa Hospital Tamaka, Kolar, Karnataka, India from September 2020 to April 2021. RBC, platelet histogram, WBC scattergram graphic patterns with corresponding parameters were noted in RT-PCR COVID-19 positive patients and compared with controls using (Automated Haematology Analyser XN11500). Cases were further subcategorised into moderate and severe categories. For statistical analysis, Chi-square test or Fisher's-Exact test, Independent t-test was used for assessing qualitative and quantitative data, respectively. Mean and standard deviation were depicted in box plots. Receiver Operating Characteristic (ROC) curve was used for predicting severity. A p-value <0.05 was considered statistically significant.

Results: Among 500 subjects, males were 359 and females 141 with the mean age 50.5 years. Present study showed a characteristic finding of "sandglass" effect in WBC scattergram which is described as discontinuous cluster of plasmacytoid lymphocytes. RBC histogram and parameters did not show any significant changes. In severe COVID-19 cases, among WBC, parameters most common finding was neutrophilia. Platelet Lymphocyte Ratio (PLR), Platelet Monocyte Ratio (PMR), Platelet Neutrophil Ratio (PNR) were statistically significant in severe COVID-19 cases (p-value <0.001) corresponding ROC curve for WBC and platelet showed WBC count and PLR as the significant parameter in severe COVID-19 positive cases.

Conclusion: Current study reported a specific and unique sandglass effect in WBC scattergram in severe COVID-19 subjects which can help the physicians for predicting the severity of disease and to prevent further progression of disease.

Keywords: Coronavirus disease 2019, Haematological indices, Red blood cell, White blood cell

INTRODUCTION

The adverse effects of Coronavirus Disease-2019 (COVID-19) pandemic have been more pronounced in the developing countries with poor socio-economic conditions with no universal health coverage facilities. Although molecular diagnostic methods such as RT-PCR is considered as a hallmark for the final diagnosis of COVID-19 infections, better diagnostic method which is more economical, readily accessible to the general population and can be easily performed in the laboratory without requirement of specially skilled manpower. Hence, authors undertook the present study based on WBC scattergram, histogram along with platelet indices in COVID-19 infected cases. Histogram, although a neglected part of automated hemogram, when interpreted scientifically can provide valuable clinical information both for diagnostic as well as for prognostic purposes [1]. To the best of our knowledge, there is paucity of studies on the role of histogram evaluation and its clinicopathological correlation in COVID-19 infections. One study is done by Foldes D et al., [2] regarding the same concept. The present study is one such effort in that direction, so as to evaluate if routine and cost effective investigations like Complete Blood Count (CBC) and its associated histogram could lead to a better and judicious allocation of financial and human resources for combating COVID-19 infections, particularly in a resource constraint set-up like the present study.

The objectives of the study, were to evaluate the graphic patterns of histogram, WBC scattergram, platelet indices in COVID-19 positive patients and further comparatively assess the difference of graphic patterns and platelet indices between moderate and severe COVID-19 cases and compare them with controls.

MATERIALS AND METHODS

This was a laboratory-based cross-sectional observational study, conducted at a fully accredited National Accreditation Board for testing and calibration Laboratories's (NABL), Central Diagnostic Research Laboratory, RL Jalappa Hospital Tamaka, Kolar, Karnataka, India from September 2020 to April 2021. The study was approved by Institutional Ethical Committee IEC No. SDUMC/KLR/IEC/60/2021-22) and written informed consent was obtained from all the study participants.

Sample size calculation: Sample size was estimated using 95% confidence interval and an absolute error of 10%, comes to 500. Formula used for estimating sample size was as follows-

$$n=\frac{Z^2_{1-\alpha/2}\, p(1-p)}{d^2}$$

d=absolute precision 0.03, $\alpha/2$=desired confidence interval 95%, p=expected proportion=0.6, Z^2=level of confidence according to the standard normal distribution (for a level of confidence of 95%, Z=1.96).

p=estimated proportion of the population that presents the characteristic (when unknown p=0.5).

d=tolerated margin of error (the real proportion within 10%).

Utilising the above values, sample size was estimated to be around

When p=1/2 (0.5)

$n=(z)^2/4d^2$

To calculate with a 95% level of confidence and a margin of error of 10%, $n=(1.96)^2/4(0.05)^2=500.13$

Inclusion criteria: All healthy adult subjects without any clinical symptoms were taken as study controls. Study controls were all the above age of 18 years, who tested negative for COVID-19 by RT-PCR without any clinical symptoms consistent with COVID-19 and all subjects above 18 years of age who tested positive on RT-PCR were considered as COVID-19 positive cases and categorised into mild, moderate and severe. Similar to study done by Osman J et al., mild categories data was not collected as these patients had undergone uneventful recoveries [3]. As per Zhou F et al., protocol, 500 cases were further categorised into moderate (n=266) and severe (234).

- Moderate category subjects included who clinically presented with fever, sore throat, cough but not fulfilling the criteria of severe disease.
- Severe COVID-19 subjects included patients with respiratory rate of more than 30 times/min, oxygen saturation ≤90% in resting state or in respiratory failure in need of mechanical ventilation or in state of shock [4].

Exclusion criteria: Subjects with history of cardiovascular disease, haematological and thromboembolic disorders, history of any trauma and surgery in past six months, bedridden patients and pregnant females, patients on anticoagulants (as anticoagulants can alter the CBC parameters) were excluded from the study.

Study Procedure

Socio-demographic data of the all the study participants was collected from hospital records. Standard protocols were followed for collection of venous samples in EDTA (Ethylenediamine-Tetraacetic Acid) vial for estimation of CBC. While collecting blood samples, COVID-19 safety protocols were followed including utilisation of Personal Protective Equipment (PPE). Following parameters were evaluated which included CBC, RBC and platelet histogram, WDF (WBC differential fluorescence scattergram along with peripheral smear. All these parameters were analysed on five part fully Automated Haematologyanalyser (Sysmex XN 11500) which was daily calibrated as per NABL quality control standards. Various ratios were calculated from the haematological parameters. The RBC parameters evaluated along with RBC histogram included Haemoglobin (Hb), RBC count (Red blood cell count), PCV (Packed Cell Volume), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC) and RDW (Red cell Distribution Width). WBC parameters evaluated with WBC scattergram included WBC count, neutrophils, lymphocytes, eosinophil's, basophils and monocytes. Platelet parameters evaluated with platelet histogram included platelet count, MPV (Mean Platelet Volume), Platelet Distribution Width (PDW), Platelet Large Cell Ratio (P-LCR), Plateletcrit (PCT). Ratios derived from these parameters mainly platelet indices PLR (Platelet-Lymphocyte Ratio), PMR (Platelet Monocyte Ratio), PNR (Platelet Neutrophil Ratio) were evaluated in both cases and controls.

STATISTICAL ANALYSIS

Data collected were entered into Microsoft excel data sheet and was analysed using Statistical Package for Social Sciences software (SPSS) version 22.0 (IBM SPSS Statistics, Somers NY, USA). Categorical data was represented in the form of frequencies and proportions. Chi-square test or Fisher's-Exact test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation demonstrated in the box plots. Independent t-test was used as test of significance to identify the mean difference between two quantitative variables. ROC curve was used to analyse the efficiency of various parameter in predicting severity. A test that predicts an outcome no better than chance has an area under the ROC curve of 0.5. An area under the ROC curve above 0.8 indicated fairly good prediction. For graphical representation of data, Microsoft excel and Microsoft word was used to obtain various types of graphs. A p-value (probability that the result is true) of 0.05 was considered as statistically significant.

RESULTS

Demographic parameters of COVID-19 subjects: A total of 500 COVID-19 positive patients were included for the study, while 500 patients served as controls. On basis of disease severity, subjects were divided into moderate (n=266) and severe (n=234) categories and the mean age of the patients was 50.5 years with more cases observed in males (n=359) as compared to females (n=141) with p-value of 0.725 which was not substantially significant. No significant difference was found between gender and severity [Table/Fig-1]. In present study, maximum distribution of COVID-19 positive cases in the age group between 41-60 years was 236 (47.2%) followed by 61-80 years 120 (24%) followed by 21-40 years 110 (22%), 81-100 years 22 (4.4%) and ≤20 years 12 (2.4%) [Table/Fig-2]. In moderate COVID-19 cases, out of 236 patients, 124 (52.5)% of the patients were in the age group of 41-60 years. Out of 120, 70 (58.3%) patients were in the age group of 61-80 years. Out of 110 patients, 72 (65.4%) patients were in the age group of 21-40 years.

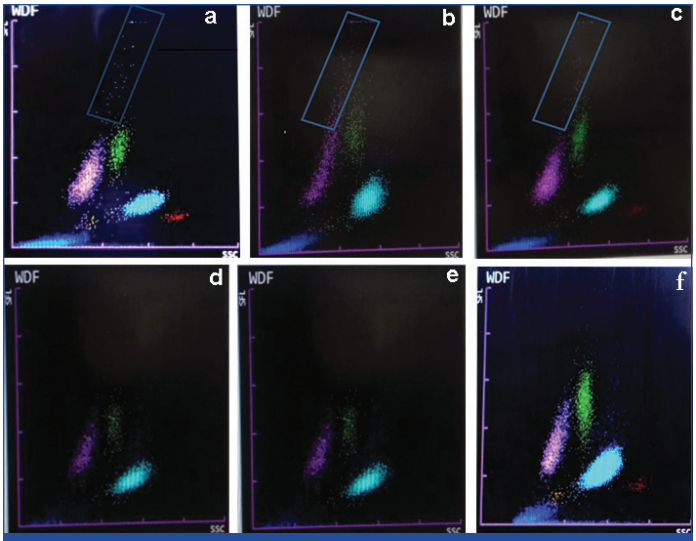
Gender	Moderate n (%)	Severe n (%)
Female	77 (54.6)	64 (45.4)
Male	189 (52.6)	170 (47.3)

[Table/Fig-1]: Distribution of subjects according to gender and severity. p-value=0.725, not significant

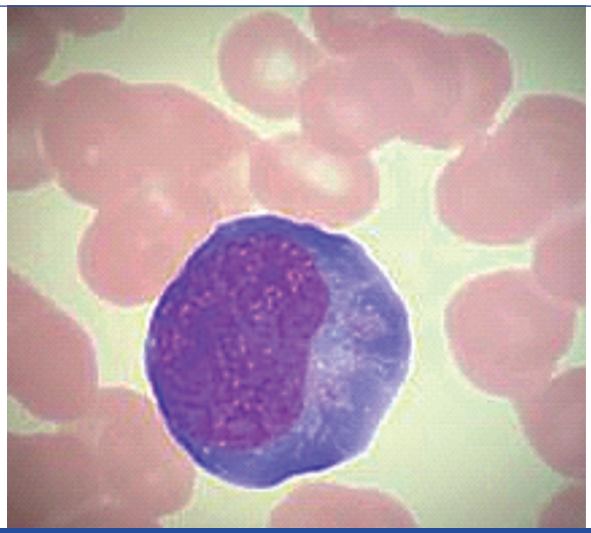
Age (in years)	n (%)	Moderate COVID-19 cases n (%)	Severe COVID-19 cases n (%)
≤20	12 (2.4)	-	12
21-40	110 (22)	72 (65.4)	38 (34.5)
41-60	236 (47.2)	124 (52.5)	112 (47.4)
61-80	120 (24)	70 (58.3)	50 (41.6)
81-100	22 (4.4)	-	22
Total	500 (100)	266	234

[Table/Fig-2]: Distribution of COVID-19 positive patients according to age group.

WBC differential fluorescence scattergram: One of the most significant finding of the present study was the observation regarding "sandglass" effect which is described as discontinuous cluster of plasmacytoid lymphocytes represented by more than four dots in upper graduated column of scattergram depicted in [Table/Fig-3a-3e] which is considered as a feature of COVID-19 infection, as no other viral infective causes are known to demonstrate such kind of features in the scattergram. In current study, 68.3% (160/234) of the severe COVID-19 patients showed similar pattern of "sandglass effect" in WBC scattergram. Age and sex matched controls did not demonstrate sandglass effect as depicted in [Table/Fig-3f]. Lymphocyte with eccentric round nucleus and basophilic cytoplasm with perinuclear hof can be appreciated in [Table/Fig-4].



[Table/Fig-3]: WDF scattergram in a COVID-19 infected patient demonstrates. Sandglass effect: cluster of lymphocytes >4 dots with plasmacytoid lymphocytes on the smear. i) Severe cases- a,b,c; ii) Moderate cases- d,e; iii) Normal cases-f Normal WDF scattergram pattern in controls (non infected patient).



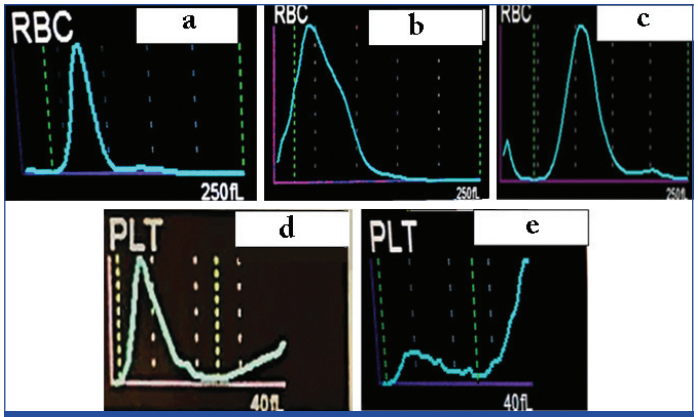
[Table/Fig-4]: Stained image showing plasmacytoid lymphocyte (X1000, H&E stain).

RBC histogram: RBC histogram represented a Gaussian or bell-shaped distribution in 95% of cases [Table/Fig-5a] with 3% of cases showed microcytic RBC's [Table/Fig-5b] with curve deviated towards left and 2% of cases showed macrocytic RBC's [Table/Fig-5c] with curve deviated towards the right in COVID-19 positive cases as reflected in the histogram.

Platelet histogram: The normal platelet histogram curve starts and ends at the baseline and should lay between upper Platelet Discriminator (PU) and lower Platelet Discriminator (PL) [Table/Fig-5d]. In the present study, thrombocytopenia curve in platelet histogram was observed in 210 cases (42% of cases) [Table/Fig-5e].

Haematological parameters of COVID-19 patients versus controls: Leucocytosis, neutrophilia, lymphopenia were characteristic findings noted in COVID-19 patients. On comparing COVID-19 patients (n=500) with controls (n=500), there was no substantial significant difference found in the RBC parameters and for WBC parameters statistical significant difference was found for WBC count, neutrophils, lymphocytes, eosinophil's, monocytes (p-value <0.001) and for platelet parameters PLR, PMR and PNR were found to substantially significant between the two categories (p-value <0.001) [Table/Fig-6].

Hematologic parameters of COVID-19 patients based on severity of disease: The COVID-19 patients were further classified into moderate and severe, statistically significant differences were observed in WBC count, neutrophils, lymphocytes, eosinophil's, PLR, PMR, PNR. The ratios PLR, PMR and PNR were found to



[Table/Fig-5]: a) RBC Histogram in COVID-19 positive patients. No Flags were observed in RBC histogram in both moderate and severe cases for COVID-19 positive patients; b) RBC histogram scattergram representing microcytic RBC's and; c) Representing macrocytic RBC's in severe COVID-19 positive patients; d) Platelet histogram: Normal platelet histogram graphic pattern; e) Platelet histogram showing thrombocytopenia with a LD flag in severe COVID-19 cases. Thrombocytopenia was noted more in severe COVID-19 cases as reflected in [Table/Fig-6] also.

be increasing uniformly from moderate to severe categories [Table/Fig-6]. Box plots demonstrating differences in platelet indices profile between moderate and severe categories of COVID-19 are depicted in [Table/Fig-7].

The ROC curve for WBC parameters showed that neutrophils as depicted in [Table/Fig-8a] can be considered as crucial factor with Area Under Curve [Table/Fig-8c] (AUC: 0.967) to differentiate between moderate and severe cases. ROC curve for platelet parameters as depicted in [Table/Fig-8b]. PLR (AUC: 0.746) can be considered as a factor for distinguishing moderate and severe cases [Table/Fig-8d].

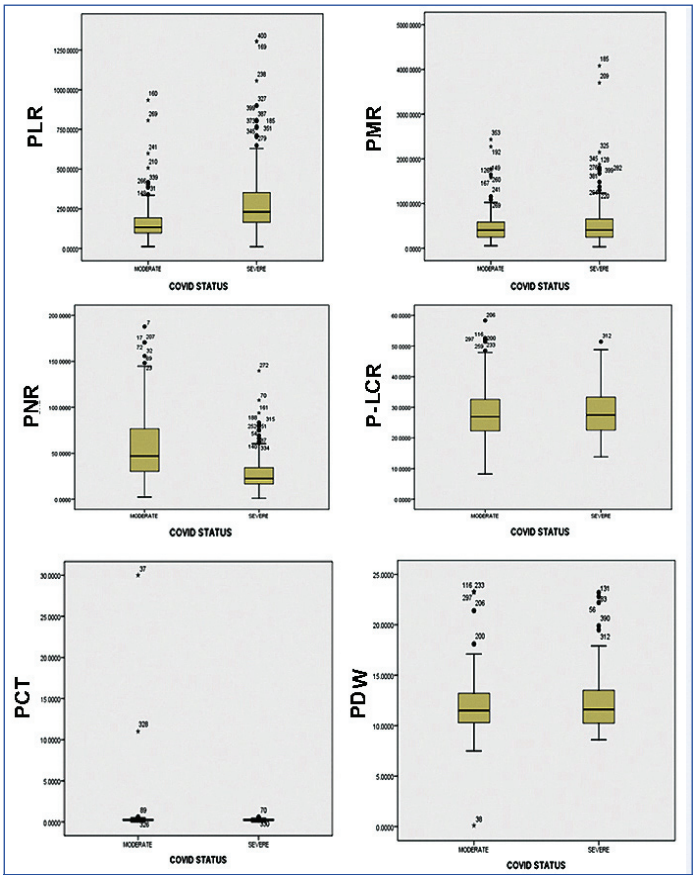
DISCUSSION

Male preponderance was seen in present study. Possible mechanisms for higher proportion of males being affected have been proposed, one is elevated expression of ACE-2 receptors (Angiotensin-Converting Enzyme-2 receptors) in males in comparison to females. Other is sex-based immunological differences driven by gender hormone and X chromosome. Major factor considered is lifestyle habits as high levels of smoking and drinking habits among males as compared to females. Irresponsible attitude of men towards basic preventive measures such as regular hand washing, use of sanitisers, wearing of face mask and lack of proper compliance regarding the need to strictly follow home isolation [5].

The present study is the first Indian study catering, providing important insights into scattergram and histogram patterns induced by COVID-19 from the Indian perspective. The current study reported a specific "sandglass" effect on the WBC scattergram of COVID-19 positive patients. No mention of such observation of sandglass effect in COVID-19 has been documented in any of the Asian/or Southeast-Asian studies as per authors' review of literature. In sandglass pattern, plasmacytoid lymphocytes are represented by more than four dots in upper graduated column of scattergram [6,7]. This pattern was observed in severe COVID-19 cases corresponding to which plasmacytoid lymphocytes are reflected in the peripheral blood smears. Plasmacytoid lymphocytes are absent in healthy subjects and plasmacytoid lymphocytes have been reported in COVID-19 patients as demonstrated by the study done by Foldes D et al., [2] Further immunological exploration is needed to validate these findings. Although WDF scattergram did not show sandglass effect in controls whereas plasmacytoid lymphocytes were noted in controls. Present study demonstrates that WDF scattergram can be an effective screening method to detect severity in COVID-19 patients before higher level investigations are ordered as reflected in results of the current study, where 68.3% of severe COVID-19 positive cases demonstrated

Parameters	Moderate		Severe		Controls		p-value
	Mean	SD	Mean	SD	Mean	SD	
Age (in years)	46	18	55	15	58	16	0.212
PDW (%)	11.9603	2.6827	12.2513	2.6627	12.9603	2.8827	0.272
MPV (fL)	10.4621	1.1384	10.5178	1.0298	11.4621	1.3384	0.606
P-LCR (%)	28.0726	8.2944	28.6843	7.9623	29.0726	8.3944	0.448
PCT (%)	0.4360	2.1365	0.2467	0.0956	0.4760	3.1365	0.222
PLR	159.16	113.79	288.91	207.27	161.1637	123.7943	<0.001
PMR	468.9	352.9102	541.78	513.13	488.9	362.8	<0.001
PNR	56.5070	37.5945	28.3071	20.34	61.42	38.156	<0.001
Platelet count (×10^9/L)	244	100	239	103	248	100	0.650
WBC count (µL)	8231.7	3707.1	15297.4	11405.5	8156.6	3247.8	<0.001
Neutrophils (%)	63	15	86	8	63	15	<0.001
Lymphocytes (%)	26	12	9	6	26	12	<0.001
Eosinophils (%)	1	3	0	2	1	3	<0.001
Monocytes (%)	9	4	5	3	9	4	0.265
Basophils (%)	0	0	0	0	0	1	0.288
Haemoglobin (g/dL)	13.0840	2.1944	12.9068	2.5370	13.891	2.124	0.449
RBC count (millions/mm^3)	4.5966	0.7003	4.5604	0.8546	5.1966	0.7141	0.638
PCV (%)	38.1137	5.8128	37.5581	7.0074	39.227	5.8927	0.381
MCV (fL)	83.2005	7.2541	82.8215	7.9162	84.1596	7.4519	0.613
MCH (pg)	28.5658	3.2982	28.4246	3.2765	29.3567	3.4962	0.665
MCHC (g/dL)	34.2758	1.8541	34.2890	1.7790	34.3751	1.8941	0.942
RDW (%)	13.8205	2.2942	14.4790	5.2249	13.8304	2.3142	0.092

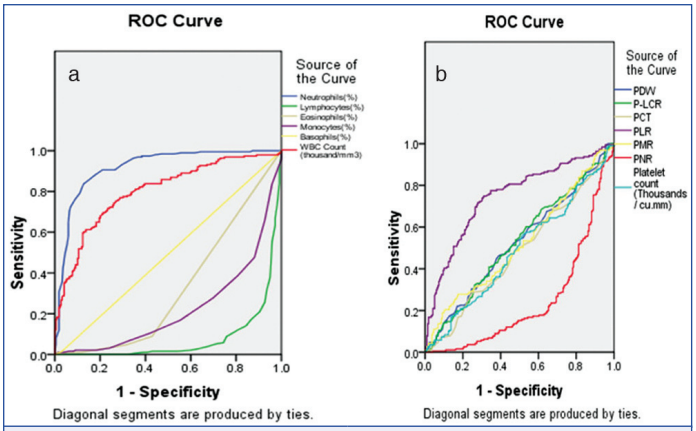
[Table/Fig-6]: Comparison of various parameters based on severity according to Fisher's-Exact test.
p-value <0.05 was considered as statistically significant
PLR: Platelet lymphocyte ratio; PMR: Platelet monocyte ratio; PNR: Platelet neutrophil ratio; MPV: Mean platelet volume; PDW: Platelet distribution width; P-LCR: Platelet large cell ratio; PCT: Plateletcrit; RBC count: Red blood cell count; PCV: Packed cell volume; MCV: Mean corpuscular volume; MCH: Mean corpuscular haemoglobin; MCHC: Mean corpuscular haemoglobin concentration and RDW: Red cell distribution width



[Table/Fig-7]: Comparison of Platelet indices between moderate and severe cases through box plots. Box plots demonstrates as the severity increases from moderate to severe cases, the mean is increased as demonstrated in the four platelet parameters.
PLR: Platelet lymphocyte ratio; P-LCR: Platelet lymphocyte ratio; PCT: Plateletcrit; PDW: Platelet distribution width

sandglass effect and it is a simple, economical and non invasive diagnostic method. In COVID-19 associated lymphopenia, WDF scattergram analysis appears to be more accurate than peripheral blood smear and demonstration of plasmacytoid lymphocytes can be a useful alternative for haematology centres where WDF scattergram is not available [8,9]. "Sandglass effect " on WDF can acts as a reliable tool in assisting physicians to pilot the medical management of suspected symptomatic COVID-19 subjects at the time of admission. WDF is of great diagnostic help particularly in a rural and resource constraint set-up centre as ours where capital intensive and radiological interventions are not readily available and most of the patients belong to poor socio-economic background having variable non specific clinical presentation [3].

The RBC Histogram, Normal RBC Histogram has two discriminators RBC Lower discriminator (RL) and RBC upper discriminator (RU). RL discriminator fluctuates between 25 and 75 fL. RU discriminator fluctuates between 200 and 250 fL [10]. In the present study, RBC histogram and platelet histogram did not show major variations in graphic patterns when both cases and controls were assessed. COVID-19 is a multisystemic organ disease caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) [11]. It is considered to be more contagious than previous SARS-CoV that occurred in 2003 and or MERS-CoV (Middle-East Respiratory Syndrome Coronavirus) that occurred in 2012 [12-14]. SARS-CoV-2 essentially affects the lung, leading to Acute Respiratory Distress Syndrome (ARDS). The possible pathogenic mechanism considered is the virus attaches to the ACE-2 receptors and enters into alveolar epithelial cells stimulating a cytokine storm resulting in inflammatory response and ultimately resulting in damage to the tissues [15]. These cytokines can induce significant alterations in the haematopoietic cells, mainly neutrophils and lymphocytes. WBC count and neutrophil counts were significantly higher in COVID-19 patients, especially in severe COVID-19 positive patients. Result of



c) Area under the curve	
Test result variable (s)	**Area**
Neutrophils (%)	0.917
Lymphocytes (%)	0.078
Eosinophils (%)	0.325
Monocytes (%)	0.222
Basophils (%)	0.492
WBC count (thousand/mm^3)	0.800

d) Area under the curve	
Test result variable (s)	**Area**
PDW	0.524
P-LCR	0.528
PCT	0.483
PLR	0.746
PMR	0.522
PNR	0.242
Platelet count (thousands/mm^3)	0.488

[Table/Fig-8]: a) ROC curve for WBC, neutrophils, eosinophils, monocytes basophils in predicting severity; b) ROC curve for platelet parameters in predicting severity; c) Area under curve for WBC parameters in predicting severity; d) Area under curve for platelet parameters in predicting severity.
PDW: Platelet distribution width; P-LCR: Platelet lymphocyte ratio; PCT: Plateletcrit; PLR: Platelet lymphocyte ratio; PMR: Platelet monocyte ratio; PLR: Platelet neutrophil ratio

present study were similar to the study done by Chen N et al., [16], Ding X et al., [17].

The findings for male being more affected were identical to study done by Ozcelik N et al., showing higher proportion of males being affected as compared to females [18]. The probable reason for increased WBC count and neutrophil can be prolonged hypoxia in COVID-19 positive subjects stimulating release of granulocytes from bone marrow as a compensatory mechanism [19]. Similar findings were seen in ROC curve for WBC parameters which showed that neutrophils can be considered as vital factor to differentiate between moderate and severe cases. Lymphopenia was observed in the current study. Plausible mechanisms to explain lymphopenia, one is that virus results in lymphocyte death by targeting lymphocytes which express the ACE-2 receptor and other potential mechanism to be considered are cytokines {tumour especially Interleukin-6 (IL-6)}, which is a key interleukin released in COVID-19 disease can induce deficiency of lymphocytes [20]. Study done by Guan WJ et al., [15] showed lymphopenia in 82.1% patients. In lung infection caused by virus, eosinophils have a tendency to get assembled in infected tissues to resist the virus infection, therefore eosinopenia is noted [21].

Platelet count serve as a sensitive indicator for severity of disease. In present study, the difference between platelet counts between cases and controls were not statistically significant. Changes in platelet count might be due to viral invasion of haematopoietic cells or invasion of bone marrow stromal cells [22,23]. Normally the platelet curve is left skewed, however, in case of thrombocytosis, curve is elevated and in case of thrombocytopenia, the curve is depressed from the normal. In case of multipeak platelet anisocytosis, multiple peaks are observed with PL and PU flags, PL flag appears, when lower discriminator exceeds by >10% and PU flag appears, when upper discriminator exceeds by >40% [24]. In the present study, platelet indices such as PLR,PMR,PNR were statistically significant. PLR, PMR were higher in severe cases and PNR was on lower side in severe cases and were utilised as biomarker for evaluation of the severity of infection. The results of current study were consistent with study done by Qu R et al., [25] and stated that PLR can be a novel marker for monitoring severity of disease in COVID-19 subjects. Similar findings noted in ROC curve for platelet parameters PLR (AUC: 0.746) can be considered as a factor for distinguishing moderate and severe cases.

Limitation(s)

Reported associations between haematological parameters, scattergram and histogram patterns and severity of disease cannot be concluded, as it is a unicentric study. Large multicentre studies are required to overcome these limitations and further substantiate findings of the current study.

CONCLUSION(S)

The most common haematological findings noted in COVID-19 patients in present study were leucocytosis, neutrophilia, lymphopenia, eosinopenia. PLR, PMR, PNR platelet indices can be considered as biomarkers for predicting severity in COVID-19 subjects. ROC curve depicted neutrophils and PLR can act as an important parameter to distinguish severe from moderate disease. A specific and unique pattern "sandglass effect" in severe COVID-19 subjects was reported. Current study provides vital insights regarding this topic, which can help the physicians for predicting the severity of disease and clinicians can take efficacious treatment measures well in advance and prevent further progression of disease.

Declaration: The study has been presented in 62nd Annual Conference of Indian Society of Haematology and Blood Transfusion (ISHBT).

REFERENCES

[1] Thomas ETA, Bhagya S, Majeed A. Clinical utility of blood cell histogram interpretation. J Clin Diagn Res. 2017;11(9):OE01-04. Doi: 10.7860/JCDR/2017/28508.10620.
[2] Foldes D, Hinton R, Arami S, Bain BJ. Plasmacytoid lymphocytes in SARS-CoV-2 infection (COVID-19). Am J Hematol. 2020;95(7):861-62. Doi: 10.1002/ajh.25834.
[3] Osman J, Lambert J, Templé M, Devaux F, Favre R, Flaujac C, et al. Rapid screening of COVID-19 patients using white blood cell scattergrams, a study on 381 patients. Br J Haematol. 2020;190(5):718-22. Doi: 10.1111/bjh.16943.
[4] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet. 2020;395(10229):1054-62. Doi: 10.1016/S0140-6736(20)30566-3.
[5] Bwire GM. Coronavirus: Why men are more vulnerable to Covid-19 than women? SN Compr Clin Med. 2020;2(7):874-76. Doi: 10.1007/s42399-020-00341-w.
[6] van Mirre E, Vrielink GJ, Tjon-a-Tsoi N, Hendriks H, de Kieviet W, ten Boekel E. Sensitivity and specificity of the high fluorescent lymphocyte count-gate on the Sysmex XE-5000 hematology analyzer for detection of peripheral plasma cells. Clin Chem Lab Med. 2011;49(4):685-88. Doi: 10.1515/CCLM.2011.100.
[7] Linssen J, Jennissen V, Hildmann J, Reisinger E, Schindler J, Malchau G. Identification and quantification of high fluorescence stained lymphocytes as antibody synthesizing/secreting cells using the automated routine hematology analyzer XE-2100. Cytometry B Clin Cytom. 2007;72(3):157-66. Doi: 10.1002/cyto.b.20150.
[8] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020;395(10223):507-13. Doi: 10.1016/S0140-6736(20)30211-7.
[9] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. Doi: 10.1016/S0140-6736(20)30183-5.
[10] Sinha R, Dhotre S, Goswami HM. Interpretation of RBC histograms and their correlation with peripheral smear findings in patients of anemialnt. J Contemp Med. 2020;6:62-66.
[11] Pujani M, Raychaudhuri S, Verma N, Kaur H, Agarwal S, Singh M, et al. Association of hematologic biomarkers and their combinations with disease severity and mortality in COVID-19- An Indian perspective. Am J Blood Res. 2021;11(2):180-90.

[12] Wang C, Deng R, Gou L, Fu Z, Zhang X, Shao F, et al. Preliminary study to identify severe from moderate cases of COVID-19 using combined hematology parameters. Ann Transl Med. 2020;8(9):593-98. Doi: 10.21037/atm-20-3391.
[13] Gates B. Responding to Covid-19 - A once-in-a-century pandemic? N Engl J Med. 2020;382(18):1677-79. Doi: 10.1056/NEJMp2003762.
[14] Pullano G, Pinotti F, Valdano E, Boëlle PY, Poletto C, Colizza V. Novel coronavirus (2019-nCoV) early-stage importation risk to Europe, January 2020. Euro Surveill. 2020;25(4):2000057. Doi: 10.2807/1560-7917.ES.2020.25.4.2000057.
[15] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. China medical treatment expert group for COVID-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708-20.
[16] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020;395(10223):507-13. Doi: 10.1016/S0140-6736(20)30211-7.
[17] Ding X, Yu Y, Lu B, Huo J, Chen M, Kang Y, et al. Dynamic profile and clinical implications of hematological parameters in hospitalized patients with coronavirus disease 2019. Clin Chem Lab Med. 2020;58(8):1365-71. Doi: 10.1515/cclm-2020-0411.
[18] Ozcelik N, Ozyurt S, Yilmaz Kara B, Gumus A, Sahin U. The value of the platelet count and platelet indices in differentiation of COVID-19 and influenza pneumonia. J Med Virol. 2021;93(4):2221-26. Doi: 10.1002/jmv.26645.
[19] Li X, Wang L, Yan S, Yang F, Xiang L, Zhu J, et al. Clinical characteristics of 25 death cases with COVID-19: A retrospective review of medical records in a single medical center, Wuhan, China. Int J Infect Dis. 2020;94:128-32.
[20] Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, et al. Lymphopenia predicts disease severity of COVID-19: A descriptive and predictive study. Signal Transduct Target Ther. 2020;5(1):33. Doi: 10.1038/s41392-020-0148-4.
[21] Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020;75(7):1730-1741. Doi: 10.1111/all.14238.
[22] Liu Y, Sun W, Guo Y, Chen L, Zhang L, Zhao S, et al. Association between platelet parameters and mortality in coronavirus disease 2019: Retrospective cohort study. Platelets. 2020;31(4):490-96. Doi: 10.1080/09537104.2020.1754383.
[23] Yang X, Yang Q, Wang Y, Wu Y, Xu J, Yu Y, et al. Thrombocytopenia and its association with mortality in patients with COVID-19. J Thromb Haemost. 2020;18(6):1469-72. Doi: 10.1111/jth.14848.
[24] Doig K, Butina M. A Methodical approach to interpreting the platelet parameters of the complete blood count. Clinical Lab Sci. 2017;30(3)194-201. Doi: https://Doi.org/10.29074/ascls.30.3.194.
[25] Qu R, Ling Y, Zhang YH, Wei LY, Chen X, Li XM, et al. Platelet-to-lymphocyte ratio is associated with prognosis in patients with coronavirus disease-19. J Med Virol. 2020;92(9):1533-41. Doi: 10.1002/jmv.25767.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate, Department of Pathology, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research (SDUAHER), Kolar, Karnataka, India.
2. Professor, Department of Pathology, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research (SDUAHER), Kolar, Karnataka, India.
3. Professor, Department of Pathology, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research (SDUAHER), Kolar, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Subhashish Das,
Professor, Department of Pathology, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research (SDUAHER), Kolar, Karnataka, India.
E-mail: daspathology@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 10, 2022
- Manual Googling: Apr 21, 2022
- iThenticate Software: Jun 14, 2022 (16%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 04, 2022**
Date of Peer Review: **Apr 04, 2022**
Date of Acceptance: **May 31, 2022**
Date of Publishing: **Aug 01, 2022**