Original Article

Leucocyte Volume, Conductivity, and Scatter at Presentation in COVID-19 Patients

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Received: 26-Oct-2022;
Revision: 05-Apr-2023;
Accepted: 03-May-2023;
Published: 14-Jul-2023

Abstract

Background: In COVID-19 patients, besides changes in leucocyte count, morphological abnormalities of circulating blood cells have been reported. **Aim:** This study aims to investigate the relationship between the morphological and functional properties of leucocytes and the severity of the disease in COVID-19 patients. **Materials and Methods:** Blood samples were collected from COVID-19 patients (n = 130) at the time of admission. The patients were stratified according to the comorbidity, age, LDH, lymhocyte count score as mild, moderate, and severe. Complete blood count and the cell population data were analyzed by the Volume, conductivity, scatter (VCS) technology on Beckman Coulter LH-780 hematology analyzer. Kruskal–Wal`lis test was used to assess the differences between the groups with subsequent Bonferroni correction. **Results:** Neutrophil count was increased, and lymphocyte count was decreased in severe patients compared to mild patients. The increase in the percent of neutrophils and the neutrophil/lymphocyte ratio in the severe patient group was significant in comparison to both the moderate and the mild group. The dispersion of the neutrophil volume and conductivity showed significant changes depending on the severity of the disease. The lymphocyte volume, lymphocyte-volume-SD and lymphocyte-conductivity as well as the monocyte-volume and monocyte-volume-SD were significantly increased in severe patients in comparison to mild patients. The increase of lymphocyte and monocyte volume in severe patients was also significant in comparison to moderate patients. **Conclusions:** COVID-19 infection leads to important changes in cell population data of leucocytes. The volumetric changes in lymphocytes and monocytes are related to the severity of the disease.

Keywords: *Cell population data, Covid-19, leukocytes, lymphocytes, monocytes, neutrophils, volume conductivity scatter parameters*

Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is still an ongoing pandemic. The clinical spectrum ranges from mild flu-like symptoms to severe and progressive pneumonia leading to acute respiratory distress and multi-organ failure.[1] COVID-19 has been reported to give rise to alterations in complete blood count (CBC), prominently variable leucocyte count accompanied with neutrophilia, lymphopenia, and thrombocytopenia indicating worse prognosis in COVID-19 positive patients.[2-5] The guideline reported by the International Federation of Clinical Chemistry IFCC puts forward that lymphopenia has become a hallmark of SARS-CoV-2 infection, and it is also associated with disease

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_737_22

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How to cite this article: Örmen M, Doruk ÖG, Gözgöz H, Kutlu A, Nurcan G, Sevinç C, *et al.* Leucocyte volume, conductivity, and scatter at presentation in COVID-19 patients. Niger J Clin Pract 2023;26:771-8.

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severity.[5] Considering the frequent combination of lymphopenia with neutrophilia, an increased neutrophil-to-lymphocyte ratio has been suggested as a prognostic marker.[3,6-7] Furthermore, absolute lymphocyte count, as well as neutrophil to lymphocyte ratio, has been included in various clinical prognostic scores in COVID-19 patients.[8,9]

In addition, morphological anomalies of circulating blood cells observed on the peripheral blood smear in COVID-19 patients have been reported by several authors.[3,5,10-12] Gérard *et al*.[11] have found that 5%–10% of CBC from COVID-19 patients were flagged by the blood cell counters (MO flag for the Beckman-Coulter DxH 800 and Blasts/AbnLymphs for the Sysmex × 10) and required peripheral blood film assessment. It has been shown that atypical lymphocyte morphology is common in COVID-19, and atypical plasmacytoid lymphocytes are highly associated with the disease**.** A pronounced granulocytic reaction with immaturity, dysmorphism, and apoptotic-degenerative morphology has been described in the early phase of symptom aggravation, usually coinciding with hospital admission.[12]

The novel hematology analyzers report data which reflect the morphological and functional properties of leukocytes, generally referred to as cell population data (CPD) which has become an integral part of CBC, and thus, it can be obtained rapidly and freely. Over the last few years, the CPD have been thoroughly investigated for their possible clinical applications.[13] The most frequent use of this data has been done for the diagnosis of sepsis.[14-17] Volumetric changes in neutrophils, monocytes, and lymphocytes have been described in sepsis and bacteremic patients, as an early manifestation of immune cell responses to severe infections.[18,19] Changes in neutrophil volume, conductivity, and scatter have been particularly stressed as a screening tool in neonatal sepsis.[20-23] The leukocyte CPD data have been shown to be useful also for the prediction of sepsis in special patient groups[24-28] as well as in the differential diagnosis of acute febrile illness.[29-32]

There is also a growing number of publications related to the diagnostic and prognostic value of CPD in COVID-19.[3,4,33-37] In this study, it was aimed to investigate the relationship between CPD parameters and the severity of the disease in COVID-19 patients. The cellular morphological and functional characteristics of neutrophils (NE), lymphocytes (LY), and monocytes (MO) were evaluated in patients stratified according to the severity of the disease.

Materials and Methods

Study population and design

This study includes all the adult individuals (≥18 years old) admitted to the pandemic outpatient clinic of Izmir Dokuz Eylul University Medical Faculty Hospital between March 10th, 2020 and June 1st 2020 and tested (+) for SARS-CoV-2 by real-time reverse transcriptase-polymerase chain reaction from a nasopharyngeal swab of the patient (n = 130). Patients whose history included any type of hematologic disorder were excluded. The donors admitted to Blood Bank and confirmed as being (−) for COVID-19 constituted the age and sex-matched control group (n = 153).

In order to evaluate the severity of the disease, the CALL (comorbidity, age, LDH, lymhocyte count) score was used. If the score is <6, the patients are classified as mild, if 6–9 as moderate and >9 as severe. CALL score was calculated for each patient at the time of admission, and the patients were stratified according to their scores as mild (n = 50), moderate (n = 45), and severe (n = 35).[38]

Laboratory analyses

Blood samples were collected at the time of admission in BD vacutainer tubes (BD Vacutainer Systems, Franklin Lakes, NJ) containing K_2EDTA. Analyses were performed within 4 h after collection on Beckman Coulter LH-780 (Beckman Coulter Inc., Miami, FL) hematology analyzer. Direct current impedance measures cell volume, accurate size of all cell types, and the degree of cell size variation are reported; radio frequency opacity characterizes conductivity, a measurement of the internal composition and nuclear volume of each cell; laser beam measures light scatter, related to cell surface topography, cytoplasmic granularity, and nuclear structure.[13] For each leukocyte subpopulation, mean and standard deviation of the mean are calculated for Volume, conductivity, scatter (VCS) parameters reported in arbitrary units of light scattering. Currently, these morphometric parameters are for research use only; their clinical utility has not been established.

Statistical analysis

Data were presented as median (25–75 percentile) for continuous variables and frequency (number and percentage; %) for categorical variables. For all statistical analyses and tests, SPSS was used (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). Groups were tested for normality using the Shapiro–Wilk test, and p value < 0.05 was considered as a non-normal distribution. Nonparametric Kruskal–Wallis test was used to assess the difference between the

groups, and subsequently, post hoc analysis was also done with Bonferroni correction to assess pairwise comparisons.

Ethical approval

The study was approved by the local Ethics Committee (22.06.2020/14-03) as well as the Scientific Research Platform of Turkish Ministry of Health (2020-06-10T23-11-17).

Results

The characteristics of the patient group including demographics, clinical symptoms, and signs at admission and comorbidities obtained from the patients' electronic medical records are shown in Table 1.

The CBC and CPD data of the patient and the healthy control group are presented in Tables 2 and 3, respectively.

Table 1: Demographic, clinical data of the patients (*n*=130) at presentation

	n	%
Gender, (f/m)	75/55	58/42
Age mean±SD years (min–max)	59.7±21.97 (21–97)	
Comorbidity (−)/(+)	60/70	46/54
Comorbidity (−)/(1)/>1)	60/40/30	46/31/23
Hypertension	48	37
Diabetes mellitus	12	9
Neoplasia	12	9
Cardiovascular disease/Congestive Heart failure	9/7	7/5
Chronic obstructive pulmonary disease	6	5
Chronic kidney disease	4	3
Clinical signs at presentation		
Cough	55	42
Fatigue	54	42
Dyspnea	37	28
Fever	33	25
Myalgia	24	18

Table 2: Leukocytes count, absolute and relative neutrophil, lymphocyte, and monocyte counts in COVID-19 patients at presentation versus the controls

Parameter	COVID 19 group (*n*=130)		Control Group (*n*=153)	
	Median	(25–75 IQR)	Median	(25–75 IQR)
WBC (×10^9/L)	6.40*	(4.98–8.43)	7.31	(6.51–8.44)
NE (×10^9/L)	4.10	(2.70–5.63)	4.02	(3.53–4.95)
NE (%)	64.30*	(56.35–74.85)	56.90	(51.95–61.70)
LY (×10^9/L)	1.35*	(1.00–1.73)	2.27	(1.93–2.67)
LY (%)	24.65*	(14.53–32.38)	32.3	(27.37–36.06)
MO (×10^9/L)	0.50*	(0.40–0.70)	0.62	(0.43–0.79)
MO (%)	8.90	(6.83–10.93)	10.09	(5.24–10.46)
NE/LY ratio	2.56*	(1.74–5.33)	1.79	(1.47–2.27)

WBC, White blood cells; NE, neutrophils; LY, lymphocytes; MO, monocytes; IQR, interquartile range. *Significant at p<0.05

The CBC and CPD data of the patients stratified according to their CALL scores are presented in Tables 4 and 5, respectively.

The neutrophil count was increased and the lymphocyte count was decreased significantly in the severe disease group in comparison to the mild disease group (p = 0.027 and p = 0.005, respectively). The increase in the percent of neutrophils and the neutrophil/lymphocyte ratio observed in the severe patient group was significant in comparison to both the moderate (p = 0.005 and p = 0.008, respectively) and the mild (p < 0.001 and p < 0.001, respectively) groups. Although the absolute monocyte count showed no significant difference between the groups, the percentage of monocytes were significantly increased (p = 0.027) in the moderate group and decreased (p = 0.031) in the severe group in comparison to the mild patients [Table 4].

Considering the VCS parameters, NE-volume-SD and NE-conductivity-SD were significantly increased in severe patients in comparison to mild patients (p = 0.004 and P < 0.001 respectively), the increase in NE-conductivity-SD was significant also for moderate patients in comparison to mild patients (p = 0.022). The LY-volume, LY-volume-SD, LY-conductivity, and LY-conductivity-SD were significantly increased in severe patients in comparison to the mild patients (p = 0.001, P = 0.019, p = 0.017, p = 0.020, respectively), and the increase of LY-volume in the severe group was also significant in comparison to the moderate patients (p = 0.029). The MO-volume and MO-volume-SD were significantly increased in severe patients in comparison to mild patients (p < 0.001 and p = 0.009, respectively), and the increase of MO-volume in severe patients was also significant in comparison to the moderate patients (p = 0.027). The MO-conductivity-SD in the moderate group was found to be increased in comparison to the mild group (p = 0.007); no significant difference was observed for the severe patient group [Table 5].

Discussion

CBC is the first line laboratory test applied in symptomatic COVID-19 infection. The CBC analysis conducted in this study clearly reflects that decreased percentage and absolute count of lymphocytes are the most prominent findings in severe infection. The ongoing research has suggested that SARS-CoV-2 exhausts and eliminates natural killer cells and T cells, leading to lymphopenia.[4] This has been further explained by the reduction in the absolute number of CD4+ and CD8+ T lymphocytes, which display markers related to activation or exhaustion/ senescence, due to the altered expression of master

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Table 3: Cell population data in COVID-19 patients at presentation versus the controls

Parameter	COVID 19 group (*n*=130)		Control group (*n*=153)	
	Median	(25–75 IQR)	Median	(25–75 IQR)
NE-volume	141.45*	(137.98–148.10)	136.10	(133.07–138.81)
NE-volume-SD	20.53*	(19.13–22.55)	18.92	(18.21–19.60)
NE-conductivity	146.30	(140.50–151.60)	145.66	(142.28–148.47)
NE-conductivity-SD	5.84	(5.33–6.57)	6.39	(5.92–6.83)
NE-scatter	146.60*	(141.88–150.70)	119.23	(116.47–122.14)
NE-scatter-SD	11.01*	(10.15–12.74)	12.25	(11.36–13.88)
LY-volume	83.80*	(80.65–87.68)	84.64	(82.37–86.59)
LY-volume-SD	14.38*	(13.54–15.85)	13.15	(12.61–13.90)
LY-conductivity	116.90*	(111.48–119.75)	47.22	(44.79–49.35)
LY-conductivity-SD	9.19*	(8.07–11.17)	10.53	(9.94–12.0)
LY-scatter	71.50*	(68.15–78.05)	112.00	(108.70–114.84)
LY-scatter-SD	16.44*	(15.10–17.91)	14.03	(13.40–15.25)
MO-volume	169.10*	(161.73–176.43)	157.88	(155.05–160.19)
MO-volume-SD	21.25*	(18.93–23.26)	16.41	(15.66–17.33)
MO- conductivity	125.10*	(119.18–128.70)	120.65	(118.22–123.78)
MO-conductivity-SD	4.52	(4.11–5.15)	4.92	(4.70–5.25)
MO-scatter	92.90*	(90.15–96.15)	70.52	(68.16–72.61)
MO-scatter-SD	10.11	(9.37–10.85)	10.10	(9.53–11.14)

NE, neutrophils; LY, lymphocytes; MO, monocytes; SD, standard deviation; IQR, interquartile range. *Significant at $p<0.05$

Table 4: Leukocytes count, absolute and relative neutrophil, lymphocyte, and monocyte counts in COVID-19 patients at presentation, partitioned according to Call Score

Parameter	Mild group (*n*=50)		Moderate group (*n*=45)		Severe group (*n*=35)	
	Median	(25–75 IQR)	Median	(25–75 IQR)	Median	(25–75 IQR)
WBC ($\times10^9$/L)	5.85	(4.95–7.12)	6.70	(4.65–9.10)	7.52	(5.20–9.70)
NE ($\times10^9$/L)	3.65	(2.50–5.10)	3.80	(2.80–6.10)	5.20*	(3.00–7.20)
NE (%)	61.50	(54.48–66.98)	64.30	(55.55–75.05)	73.60*,†	(63.90–82.20)
LY ($\times10^9$/L)	1.50	(1.20–2.10)	1.50	(1.05–1.70)	1.20*	(0.70–1.40)
LY (%)	28.10	(20.88–35.20)	25.40‡	(14.55–32.85)	14.60*	(12.30–25.20)
MO ($\times10^9$/L)	0.50	(0.40–0.73)	0.60	(0.40–0.75)	0.40	(0.30–0.70)
MO (%)	9.30	(7.38–11.23)	9.80‡	(7.30–11.15)	7.60*	(4.10–9.70)
NE/LY ratio	2.14	(1.55–3.33)	2.52	(1.71–5.13)	5.15*,†	(2.54–6.63)

WBC, White blood cells; NE, neutrophils; LY, lymphocytes; MO, monocytes; IQR, interquartile range. *Significantly different from the mild group, $p<0.05$. †Significantly different from the moderate group, $P<0.05$. ‡Significantly different from the mild group, $p<0.05$

regulators and several chemokine receptors that lead to the exhaustion of these cells.[4] Lymphopenia is also accepted as a useful predictor for prognosis and is incorporated into the CALL score, which was used to stratify patients according to the severity of the disease in this study.

Additionally, the elevated NE/LY ratio is widely accepted as a key hematological finding, which is related to the poor clinical outcomes as well.[4,5] In this study, it was noticed that, while the percentage and absolute number of lymphocytes clearly discriminated the mild disease from the severe disease, the NE/LY ratio enabled the distinction between mild and severe disease as well as moderate and severe disease.

Alterations in the absolute number of monocytes have also been reported, and it has been suggested that the lower absolute counts of total monocytes generally observed in patients with COVID-19 are associated with extravasation and migration of monocytes to the affected tissues.[34] Intra-alveolar mononuclear cell (macrophages, lymphocytes, neutrophils) infiltrates have been described as one of the main pathological findings in autopsy and animal models and suggested to be responsible for fueling inflammation.[34,39] The significantly low monocyte count in COVID-19 patients, which is even more prominent in severe patients, may be considered the phenotypical sign of these pathological mechanisms.

The immunological and inflammatory responses to COVID-19 infection give rise to changes in the morphological characteristics of circulating blood cells in addition to their absolute and relative counts. In this study, the CPD of circulating blood cells in COVID-19 has been examined in relation to the severity of the

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Table 5: Cell population data in COVID-19 patients partitioned according to call score

Parameter	Mild group (*n*=50)		Moderate group (*n*=45)		Severe group (*n*=35)	
	Median	(25–75 IQR)	Median	(25–75 IQR)	Median	(25–75 IQR)
NE-volume	141.05	(137.68–145.43)	141.20	(137.90–147.30)	143.60	(138.00–154.30)
NE-volume-SD	19.69	(18.89–20.99)	20.77	(18.88–23.46)	22.13*	(20.07–23.03)
NE-conductivity	144.25	(139.23–150.03)	146.40	(141.90–151.55)	148.40	(140.50–153.80)
NE-conductivity-SD	5.48	(5.06–6.05)	5.84‡	(5.38–6.74)	6.24*	(5.75–6.94)
NE-scatter	146.75	(143.25–150.55)	146.10	(141.05–150.30)	146.60	(139.50–152.30)
NE-scatter-SD	10.92	(9.95–12.74)	11.04	(10.28–12.65)	10.79	(10.06–12.87)
LY-volume	82.65	(79.68–86.03)	83.40	(80.45–86.45)	87.40*,†	(83.50–91.20)
LY-volume-SD	14.05	(13.31–15.01)	14.33	(13.48–15.94)	14.94*	(14.02–16.52)
LY-conductivity	114.45	(107.88–118.53)	117.60	(112.20–119.90)	118.30*	(114.80–123.40)
LY-conductivity-SD	8.59	(7.52–10.31)	9.42	(8.03–11.34)	10.13*	(8.46–12.37)
LY-scatter	71.00	(67.68–76.10)	71.50	(66.45–79.20)	72.80	(68.30–80.50)
LY-scatter-SD	16.09	(15.07–17.68)	16.72	(15.45–17.85)	16.44	(15.07–19.81)
MO-volume	164.20	(160.98–171.48)	168.00	(161.60–175.95)	175.80*,†	(166.30–183.70)
MO-volume-SD	19.98	(17.48–22.39)	21.92	(19.70–23.22)	22.06*	(19.83–25.38)
MO-conductivity	124.75	(118.13–128.23)	125.30	(118.95–128.90)	126.10	(119.80–128.70)
MO-conductivity-SD	4.31	(3.92–4.87)	4.87‡	(4.29–5.37)	4.62	(4.17–5.51)
MO-scatter	92.45	(90.38–96.15)	92.80	(89.65–96.05)	94.00	(89.50–99.30)
MO-scatter-SD	10.34	(9.61–10.96)	10.04	(9.28–10.90)	9.96	(9.00–10.58)

NE, neutrophils; LY, lymphocytes; MO, monocytes; SD, standard deviation; IQR, interquartile range. *Significantly different from the mild group, $p<0.05$. †Significantly different from the moderate group, $p<0.05$. ‡Significantly different from the mild group, 0.05

disease, which was evaluated according to the CALL score. The CALL score was chosen since it has proved to have a high negative predictive value and also allowed reliable identification of patients at low risk, which makes it suitable for outpatient management.[8] The CPD was analyzed using the VCS technology of Beckmann–Coulter automatic hematology analyzer. Considering that there is a limited number of studies on COVID-19 using the same technology, the results were also compared to the studies using the Sysmex XN hematology analyzers, which differentiate the cells according to the intensity of forward scatter (FSC) light indicating the volume, side scatter light providing information about internal cell structure and granularity, and fluorescence light indicating the amount of DNA and RNA in the cell.[34]

Neutrophils

Activation of neutrophils is considered an important feature of COVID-19. The increase in the volume of neutrophils, as well as monocytes and lymphocytes previously described in sepsis and bacteremic patients, may point out that volumetric changes are an early manifestation of immune cell responses to severe infections.[18] Our findings indicate that NE-volume was increased in COVID-19 patients, yet no significant difference was detected due to the severity of the disease. It should be noted that there are controversial findings regarding the change in the volume of neutrophils in COVID-19.[4,34-36] It has been reported that in patients with active COVID-19, the NE-FSC value indicating the NE-volume was lower than healthy controls and there were no differences between patients with active COVID-19 and convalescents.[4] It was also observed that NE-FSC was lower than in the control; in addition, it decreased with the severity of the disease.[34] On the other hand, a study conducted in an emergency department reported that patients with severe and fatal disease presented with increased volume of neutrophils.[35]

The prominent increase observed in NE-scatter as a surrogate of granularity and vacuoles provides further support to the activation of neutrophils in COVID-19 patients. It should be noted that no significant difference was observed related to disease severity. The inflammatory process is characterized by an accelerated exchange of the pool of circulating neutrophils, and this is associated with the appearance of immature and band neutrophils, which have less ability to light scattering.[4] Thus, the activation of neutrophils begins at the onset of the disease and there are ongoing changes in the neutrophil population during the course of the disease.

In our study, NE-volume-SD and NE-conductivity-SD showed significant differences depending on the severity of the disease. Another study has also found significant differences in the neutrophil compartment when analyzing the width of dispersion with respect to granularity, activity, and cell volume defined as NE-WX, NE-WY, and NE-WZ, respectively. As compared to patients with mild course, severely ill patients displayed increases in the width of dispersion of activity

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and cell volume as surrogates for increased cellular heterogeneity, immaturity, and dysregulation in severe COVID-19.[40] Using proteomic profiling and a machine learning prediction algorithm, it has been determined that there are numerous proteins that constitute a neutrophil signature as the most direct evidence that neutrophil activation is a hallmark of severe disease.[41] These findings also point out to the key role of neutrophils in the pathogenesis of COVID-19.

Lymphocytes

Significant changes were observed in the VCS parameters of lymphocytes in COVID-19 patients. The dispersion of lymphocyte volume, LY-volume-SD, was found to be significantly higher in the COVID 19 group in comparison to the healthy controls. The lymphocyte volume as well as the LY-volume-SD was observed to be significantly increasing parallel to the increase in disease severity. In addition, the change in LY-conductivity showed a similar pattern. These findings may be related to the previously reported increases observed in certain subpopulations of lymphocytes. Reactive lymphocytes, antibody-synthesizing lymphocytes, and high fluorescence lymphocyte cells detected by Sysmex XN or XE series automated cytometry were reported to be higher as compared with controls.[34,42] Martens *et al*.[34] also stated that these subsets constituted an even higher proportion of total lymphocytes in patients with cytokine storm syndrome. Examination of peripheral blood film has also revealed the presence of highly pleomorphic atypical lymphocyte population, plasmacytoid lymphocytes illustrated to be highly associated with SARS-COV-2.[10,11]

An interesting finding of this study is that LY-conductivity was significantly higher in COVID-19 patients than in healthy controls, and this increase continued depending on the severity of the disease. There are very few reports about the conductivity of lymphocytes; one study reported a slight but significant increase in severe patients, while another one reported that LY-conductivity showed a significant decrease in COVID-19 patients in comparison to healthy controls.[35,36]

Monocytes

In viral infections, monocytes are considered the first responders in a proportional magnitude that matches to the intensity of microbial exposure.[19] Our findings reveal that MO-volume and MO-volume SDare prominently increased in response to COVID-19 infection and also to the severity of the disease. These findings related to monocytes' size are parallel to previously reported research conducted with Beckman DxH hemocytometers.[33,35,37,43,44] It has been demonstrated that MO-volume-SD is a parameter that can separate COVID-19-positive patients vs COVID-19-negative patients, with a sensitivity of 91.6% and specificity of 63%.[33] While one study reported patients hospitalized in high-intensity care units showed significantly elevated monocyte distribution width (MDW) with respect to middle or low symptomatic ones and the use of this parameter was suggested as a prognostic marker.[43] Another study has revealed that MDW has a strong correlation with poor prognosis of COVID-19.[44]

In addition, changes in granularity and cell membrane permeability, possibly reflecting the activated state of the monocytes, have been reported.[34] This is in agreement with the significantly elevated levels of MO-conductivity and MO-scatter observed in our study of COVID-19 patients. Unlike the volumetric changes, the increase in these parameters was not found to be associated with disease severity.

Previous studies suggested that circulating monocytes and tissue macrophages participate in all stages of COVID-19.[45] Monocytes infected with SARS-CoV-2 were shown to sustain viral genome replication, express higher levels of pro-inflammatory cytokines, and may undergo cell death.[46] Thus, blood monocytes seem to reflect the impact of infection on the host.[45] Marked anisocytosis, cytoplasmic vacuolization, and paucity of granules have been observed in the peripheral blood film of the patients.[47] It has been proposed that monocytes in COVID-19 patients have increased lipid droplet accumulation, which have important functions in the modulation of inflammatory mediator production.[46] These metabolic alterations are expected to lead to changes in the morphological features of monocytes. Increased MO-conductivity and MO-scatter levels in COVID-19 patients are comparable with these studies.

In conclusion, important variations have been observed in CPD in COVID-19 patients. The volumetric changes of lymphocytes and monocytes are particularly noticeable in severe patients, pointing to the possible importance of LY-volume and MO-volume as prognostic markers.

Limitations and further studies

One limitation of this study is that CPD levels obtained by different hematology analyzers are not standardized; therefore, it is hard to compare the results of different studies performed with different analyzers.

It is known that automated hematology parameters, CPD as well as CBC, may be dynamic during the course of the disease. Therefore, longitudinal monitoring of COVID-19 patients will be helpful to better elucidate the effect of SARS-CoV-2 on WBC morphology changes that are reflected by CPD.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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