# Cell Population Data Analysis for Early Diagnosis and Prognosis of COVID-19: A Case-Control Study

**Running title:** Cell population data analysis

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## Abstract

**Background:** Several hematological indicators have been linked to the intensity and course of COVID-19 infection, including platelets, total white blood cell count, lymphocytes, neutrophils (as well as the neutrophil-lymphocyte and platelet-lymphocyte ratios), and hemoglobin. The purpose of this study was to assess the utility of cell population data (CPD) of lymphocytes and monocytes parameters in the early diagnosis of SARS-CoV-2 infection.

**Methods:** The baseline complete blood count examination for 222 patients with proven Coronavirus Disease of 2019 (COVID-19) (case group) and 161 patients with negative for COVID-19 investigations (control group). Lymphocyte and monocyte CPD were calculated in both the groups. The independent t-test was used to compare the mean values between the two groups receiver operating characteristic analysis was performed to evaluate the discriminating capacity of the individual parameters.

**Results:** The analysis revealed that Standard Deviations of Monocyte Volume (SDMV) and Lymphocyte Conductivity (SDLC) showed highest significance in predicting SARS-CoV-2 infection. SDMV had a sensitivity of 93.7% and SDLC had a sensitivity of 80.6% at cut-off values of 22.25 and 10.9, respectively. In the case group, 49 of the 222 patients were treated in the intensive care unit showed higher SDMV when compared with the remaining 173 patients who were asymptomatic or mildly symptomatic (P-value <0.03).

**Conclusion:** Our study demonstrates that SDMV and SDLC can serve as reliable and cost-effective markers for early prediction of SARS-CoV-2 infection. Furthermore, SDMV shows potential as a prognostic biomarker. These findings highlight the potential utility of CPD parameters in COVID-19 diagnosis and prognosis.

**Keywords:** COVID-19, Early diagnosis, Monocyte, Lymphocyte, Prognosis.

## Introduction

Most patients with Coronavirus Disease of 2019 (COVID-19) infection are asymptomatic or have mild symptoms. Only 14% develop severe infection requiring intensive care admission (1). Identification of asymptomatic and mildly symptomatic individuals is essential for isolation in order to control the spread of infection. In a hospital setting, clinicians face a major hurdle in identifying those infected with COVID-19 amongst patients with varied clinical disorders seeking medical attention.

The gold-standard investigation for diagnosing SARS-CoV-2 infection is Reverse Transcription Polymerase Chain Reaction (RT-PCR). However, it has its own de-merits such as high cost, need for technical expertise and unavailability in many resources' poor settings. Therefore, there is increasing interest amongst researchers to find an alternative, less expensive, quicker, and reliable methods for detection of this viral infection. In this regard, the analysis of cell population data (CPD) parameters, based on their demonstrated utility in other infections, offers a promising avenue for the early detection of SARS-CoV-2 infection.

The Beckman Coulter LH 780, a fully automated hematology analyzer generates cell CPD based on Volume (V), Conductivity (C), and Scatter(S) principle to provide us the white blood cell (WBC) differential counts of complete blood counts. The cell's volume (V) is obtained by voltage impedance, conductivity (C) is by radiofrequency which provides information about the internal structure, and the information about cytoplasmic granularity and nuclear complexity is given by laser light scatter (S). The Beckman Coulter LH-780 analyzer has a separate screen that gives statistical information on each WBC population (mean and standard deviation [SD]) of their VCS parameters.

There are published papers regarding the utility of the CPD parameters in early detection of sepsis, viral fevers, leukemia, and lymphomas (2-12). To the best of our knowledge, there are only three studies available in the literature which has investigated the utility of CPD parameters in COVID-19 infection (13-17). These studies (13-17) have shown encouraging results of utilizing CPD parameters in terms of their ability to predict infection. However, a comprehensive analysis of these parameters and their association with different disease severities is still lacking. This study aimed to analyze the utility of lymphocyte and monocyte CPD data in the early prediction of COVID-19 infection. The VCS parameters of lymphocytes and monocytes were compared between COVID-19-infected patients and patients who were negative for the COVID-19 pathogen. Similarly, the VCS parameters were analyzed as prognostic markers among COVID-19 patients requiring intensive care treatment.

## Methods

This prospective, observational, case-control study was conducted from August 2020 to October 2020 after obtaining ethical clearance from the Institutional Ethics Committee (20/171). In this study, 400 adult (age>18 years of both gender) patients-222 patients (case group) with positive RT-PCR (TRUPCR SARS-CoV-2 kit, 3B Black Bio-Biotech, Bhopal, India) and 178 patients (control group) with negative RT-PCR were included. The TRUPCR kit has sensitivity of 73% and specificity of 100% (18).

The case group (n=222) were patients who came with the symptoms of COVID-19 and on further testing by HRCT showed features of COVID-19 and/or RT-PCR were found to be positive for the same. The control group included patients with respiratory complaints suspicious of SARS-CoV-2 infection who subsequently tested negative as well as asymptomatic patients in whom RT-PCR testing was performed as a part of work-up for a planned invasive procedure. Out of 178 control patients, 17 had

laboratory proven other viral / bacterial infections and hence were excluded from the control group. After exclusion 161 patients with negative RT-PCR were included in the control group.

Whole blood venous samples were collected in K2 EDTA for baseline complete blood count examination for all the patients. The blood sample was analyzed on the Beckman Coulter LH-780 haematology analyzer (Beckman Coulter, Brea, CA) within 4 hours of collection. In addition, CPD of lymphocytes and monocytes were documented which is provided by the haematology analyser as mean and standard deviation values. The VCS parameters were recorded by a Pathologist from the Coulter screen without knowing the COVID-19 infection status of the patient's sample. The demographic information such as age and gender was also noted. Approval for this study was obtained from the Institutional Human Ethics Committee (ref no: 20/171) and complies with all regulations.

**Statistical analysis:**

The data were expressed in mean ± standard deviation. The independent t-test was used to compare the mean values between the two groups. All analyses including receiver operating characteristics were performed with IBM, SPSS software, version 23.0 (SPSS, Chicago, IL). A P value of less than 0.05 was considered significant.

## Result

### Population characteristics

There were 146 males and 76 females in the case group (n=222) and 90 males and 71 females in the control group (n=161). The mean age in the case group was 51.4 ± 17.1 years and in the control, group was 46.3 ± 19 years.

### Clinical characteristics

The symptoms in the case group ranged from fever (84%), myalgia (58%), dry cough (62%), dyspnea (45%), diarrhea (27%), and anosmia (16%). CT chest in 75% (168 out of 222 cases) showed patchy ground glass opacity, suggestive of atypical viral pneumonia. Out of the 222 COVID-positive cases, 49 cases were managed in the intensive care unit (ICU).

### Leucocytes and VCS parameters for early prediction of SARS-CoV-2 infection

The baseline WBC total count and absolute differential counts of the leucocytes were compared between the case and control (Table 1). On comparison, it showed a significant decrease in the absolute counts of the monocyte, eosinophil, and basophil populations in COVID-19 positive patients in comparison with the control. There were no significant differences in total leukocyte count and absolute counts of neutrophil and lymphocyte observed between the cases and controls. Thus, considerable eosinopenia and monocytopenia have been observed in the WBC parameters in COVID-19 cases. Though there had been a substantial decrease in the absolute lymphocyte count in COVID-19 patients, the variation was not statistically significant.

Table 2 depicts the VCS parameters of the white blood cell population - it is observed that the Mean Lymphocyte Volume (MLV), Mean Lymphocyte Scatter (MLS) and Mean Monocyte Scatter (MMS) are significantly decreased in COVID-19 cases when compared to the controls. The standard deviation values of Lymphocyte Volume (SDLV), Lymphocyte Conductivity (SDLC), Lymphocyte Scatter (SDLS), Monocyte Volume (SDMV) and Monocyte Conductivity (SDMC) were increased only in the COVID-19 patient population. The other VCS parameters such as Mean values of Lymphocyte Conductivity (MLC), Monocyte Volume (MMV), Monocyte Conductivity (MMC) and Standard deviation of Monocyte Scatter (SDMS) showed no significant difference between the two groups.

The sensitivity and specificity of the VCS parameters were calculated at a desirable cut-off value for using them as early predictors of SARS-CoV-2 infection. The ROC curve of SDMV (Figure 1) shows AUC of 0.71. SDMV demonstrated a sensitivity of 93.7% and specificity of 67% at a cut-off value 22.25. Among the lymphocyte VCS parameters, SDLC (Figure 2) at a cut-off value 10.9 (AUC – 0.63) demonstrated a sensitivity of 80.6% and specificity of 60%.
The sensitivity and specificity of SDMV and SDLC were compared with the gold - standard RT-PCR for detection of COVID-19 (Table 3).
49 of the 222 COVID-19 cases needed ICU management. The efficacy of SDMV and SDLC to predict the need for intensive care management among the patients was examined because it was discovered that these parameters were significantly raised in COVID-19 instances. The COVID-19 patients receiving treatment in the intensive care unit were compared to the other patients in the case group based on their SDMV and SDLC scores (Table 4). It's interesting to note that we also discovered a significant rise in SDMV in COVID-19 patients receiving ICU care.

**Discussion**

In practice, it is necessary to have trustworthy and easily available COVID-19 biomarkers in order to determine whether to immediately segregate a patient and start targeted treatments while awaiting confirmation test results. The WBC and CPD values that are readily available were shown in this study to be useful as predictive and diagnostic indicators at the beginning of COVID-19.
The average ages of patients in both groups were 51.4 ± 17.1 and 46.3 ± 19 years, respectively. In every category, there were a greater proportion of men than women. These results also agreed with other earlier research that found a larger percentage of individuals over fifty years of age and a majority of men (19, 20).
In recently published studies, the role of lymphocytes and monocytes in the immune mechanisms against SARS-CoV-2 viral infection has been established (18-20). In our study, we found a significant decrease in monocytes and eosinophils as reported in the literature (21-24). There were no significant changes in the absolute neutrophil and lymphocyte counts in contrast to the studies in the literature where neutrophilia and lymphopenia were observed [22,24]. The decrease in monocyte and eosinophil counts can probably be attributed to increased apoptosis, which occurs during the pro-inflammatory cytokine storm in COVID-19 (24-27). Sehanobish. E et al. have noted this, stating that eosinopenia might be used as an early diagnostic technique for COVID-19 patients (28). The present study did not find decreased WBC, neutrophil, or lymphocyte numbers in COVID-19 patients, as other studies reported (21-25).
The Beckman Coulter analyzer utilizes cellular population data as a parameter for differential determination. They correlate to a morphological examination of leukocyte subtypes and several types of research studies have shown that a diagnosis of bacterial, viral, or parasite illnesses may benefit from their investigation (13-17).
Of the lymphocyte CPD, SDLV, SDLC and SDLS were significantly increased. This can be attributed to the presence of reactive lymphocytes and size variation observed in them. MLV, MLS were significantly decreased. This is due to the decrease in laser light scatter observed in reactive lymphocytes. In our study, SDLC had sensitivity of 80.6% and specificity of 60% at a cut off value 10.9. This finding was not reported in other similar studies in literature (12-16).
Size variation in monocyte was observed as increase in SDMV. Similar finding has been reported in the literature (12-17). In our study SDMV had 93.7% sensitivity and 67% specificity at a cut off value 22.25, which was comparable to other studies (Table

5) (13,15). The specificity percentage observed in our study and in previously published studies is low (13,15,16). This could be because our control group was made up of patients with other underlying illnesses, and these parameters can also be altered in other illnesses (2-4). Recent reports indicate the mechanism of infection with SARS-CoV-2 can explain the dysregulated expression of cytokines, primarily IL-6 and IL-10, erroneous increase of pathological monocytes and increase of genes involved in their cell death pathway, which explain the CPD changes observed at disease onset in severe as compared to mild forms of COVID-19 (29,30). Hence, we observe that SDMV in COVID-19 patients. The current study suggests the use of baseline WBC counts and VCS characteristics, which can enhance diagnostic characterization and help distinguish between severe and non-severe presentations. Our findings highlight the necessity of additional work to create precise admission algorithms based on the VCS parameters of WBCs in order to better support COVID-19 patients. This study had some limitations. One of the limitations of this study is that the control population included patients without a diagnosis of COVID. Some of these patients could have had other viral diseases which could alter the cell population data. Another limitation is the small number of cases studied.

**Author Contributions**

Drs PKR and PMS supervised the study, collected data and wrote the manuscript. Dr PNK supervised the project and revised the manuscript. Dr KS analyzed data, statistical analysis, and wrote the manuscript. The manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work, if that information is not provided in another form.

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Not applicable.

**Conflicts of interest**

Not applicable.

**Ethical statement**

Approval from the Institute Ethical Committee was obtained for the study (20/171).

**Data availability statement**

The data that support the findings of this study are not publicly available due to ethical and confidentiality restrictions but may be available from the corresponding author upon reasonable request and subject to institutional approval.

**References**

1. Zhu Z, Cai T, Fan L, et al. Clinical value of immune-inflammatory parameters to assess the severity of coronavirus disease 2019. Int J Infect Dis. 2020;95:332-9.

2. Zhu Y, Cao X, Tao G, Xie W, Hu Z, Xu D. The lymph index: a potential hematological parameter for viral infection. Int J Infect Dis. 2013;17(7):e490-e493.
3. Shrivastava V, Ahmad S, Mittal G, Gupta V, Shirazi N, Kalra V. Evaluation of haematological and volume, conductivity and scatter parameters of leucocytes for aetiological diagnosis of undifferentiated fevers. Trans R Soc Trop Med Hyg. ]2017;111(12):546-554.
4. Choccalingam C. Volume, conductance, and scatter parameters of neoplastic and nonneoplastic lymphocytes using Coulter LH780. J Lab Physicians. 2018;10(1):85-88.
5. Zeng X, Xing H, Wei Y, et al. Monocyte volumetric parameters and lymph index are increased in SARS-CoV-2 infection.Int J Lab Hematol. 2020;42(6):e266-e269.
6. Arora, P., Gupta, P. K., Lingaiah, R., & Mukhopadhyay, A. K. (2019). Volume, conductivity, and scatter parameters of leukocytes as early markers of sepsis and treatment response. Journal of Laboratory Physicians, 11(1),29-33. https://doi.org/10.4103/JLP.JLP_102_18.
7. Zhou N, Liu L, Li D, Zeng Q, Song X. VCS parameters of neutrophils, monocytes and lymphocytes may indicate local bacterial infection in cancer patients who accepted cytotoxic chemotherapeutics. Eur J Clin Microbiol Infect Dis. 2016;35(1):41-48. doi:10.1007/s10096-015-2499-2
8. Nesargi, P., Niranjan, H.S., Bandiya, P. et al. Neutrophil Volume, conductivity and scatter (VCS) as a screening tool in neonatal sepsis. Sci Rep **10**, 4457 (2020). https://doi.org/10.1038/s41598-020-61434-z
9. Chaves F, Tierno B, Xu D. Quantitative determination of neutrophil VCS parameters by the Coulter automated hematology analyzer: new and reliable indicators for acute bacterial infection. American journal of clinical pathology. 2005 Sep 1;124(3):440-4.
10. Kannan A, Selvam P. The potential of using VCS parameters of neutrophils and monocytes as an early diagnostic tool in acute bacterial infections. Nat J Lab Med. 2017;6:2-38.
11. RAI S, SINGH S, PHILIPOSE CS, MENDONCA BS, BASAVARAJU VK. Utility of DxH 800 VCS Parameters and Lymph Index in Predicting Dengue. Journal of Clinical & Diagnostic Research. 2019 Aug 1;13(8).
12. Rajeswaran PK, Kumar PN, Shanmugam K. The Application of Automated Cell Population Data for Early Diagnosis of Dengue Fever. International Journal of Advanced Medical and Health Research. 2023 Jan 1;10(1):27-31.
13. Ognibene A, Lorubbio M, Magliocca P, et al. Elevated monocyte distribution width in COVID-19 patients: The contribution of the novel sepsis indicator. Clin Chim Acta. 2020;509:22-24.
14. Naoum FA, Ruiz ALZ, Martin FHO, Brito THG, Hassem V, Oliveira MGL. Diagnostic and prognostic utility of WBC counts and cell population data in patients with COVID-19. Int J Lab Hematol. 2021;43 Suppl 1(Suppl 1):124-128. doi:10.1111/ijlh.13395
15. Zeng X, Xing H, Wei Y, et al. Monocyte volumetric parameters and lymph index are increased in SARS-CoV-2 infection. Int J Lab Hematol. 2020;42(6):e266-e269. doi:10.1111/ijlh.13323
16. Vasse M, Ballester MC, Ayaka D, et al. Interest of the cellular population data analysis as an aid in the early diagnosis of SARS-CoV-2 infection.Int J Lab Hematol. 2020;00:1-7.

17. Vasse M, Sukhachev D, Ballester MC, Delcominette F, Mellot F, Habarou F, Védrenne A, Jolly E, Sukhacheva E, Farfour E, Pascreau T. Prognostic value of cellular population data in patients with COVID-19. Informatics in medicine unlocked. 2023 Jan 1;38:101207.
18. Singh J, Yadav AK, Pakhare A, Kulkarni P, Lokhande L, Soni P, Dadheech M, Gupta P, Masarkar N, Maurya AK, Nema S, Biswas D, Singh S. Comparative analysis of the diagnostic performance of five commercial COVID-19 qRT PCR kits used in India. Sci Rep. 2021 Nov 10;11(1):22013. doi: 10.1038/s41598-021-00852-z. PMID: 34759300; PMCID: PMC8580981.
19. Richardson, S.; Hirsch, J.S.; Narasimhan, M.; Crawford, J.M.; McGinn, T.; Davidson, K.W.; The Northwell COVID-19 Research Consortium. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA 2020, 323, 2052–2059.
20. Kala M, Ahmad S, Dhebane M, Das K, Raturi M, Tyagi M, Kusum A. A Cross-Sectional Comparative Characterization of Hematological Changes in Patients with COVID-19 Infection, Non-COVID Influenza-like Illnesses and Healthy Controls. Viruses. 2023; 15(1):134. https://doi.org/10.3390/v15010134
21. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, et al. Hematological findings and complications of COVID-19. Am J Hematol. 2020;95(7):834-847.
22. Sun S, Cai X, Wang H, et al. Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China. Clin Chim Acta. 2020;507:174-180.
23. Violetis OA, Chasouraki AM, Giannou AM, Baraboutis IG. COVID-19 Infection and Haematological Involvement: a Review of Epidemiology, Pathophysiology and Prognosis of Full Blood Count Findings [published online ahead of print, 2020 Jun 29]. SN Compr Clin Med. 2020;1-5.
24. Li Q, Ding X, Xia G, et al. Eosinopenia and elevated C-reactive protein facilitate triage of COVID-19 patients in fever clinic: A retrospective case-control study. EClinicalMedicine. 2020;23:100375. Published 2020 May 3.
25. Xia Z. Eosinopenia as an early diagnostic marker of COVID-19 at the time of the epidemic. E Clinical Medicine. 2020;23:100398. Published 2020 Jun 18.
26. Soni M. Evaluation of eosinopenia as a diagnostic and prognostic indicator in COVID-19 infection. Int J Lab Hematol.2020; 00:1-5.
27. Mardani R, Ahmadi Vasmehjani A, Zali F, et al. Laboratory Parameters in Detection of COVID-19 Patients with Positive RT-PCR; a Diagnostic Accuracy Study. Arch AcadEmerg Med. 2020;8(1):e43. Published 2020 Apr 4.
28. Sehanobish E, Barbi M, Fong V, Kravitz M, Sanchez Tejera D, Asad M, Matsumura C, Ferastraoaru D, O'Neill M, Karagic M, Akbar N. COVID-19-induced anosmia and ageusia are associated with younger age and lower blood eosinophil counts. American Journal of Rhinology & Allergy. 2021 Nov;35(6):830-9.
29. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. Critical reviews in clinical laboratory sciences. 2020 Aug 17;57(6):389-99.
30. Yan Q, Li P, Ye X, Huang X, Mo X, Wang Q, Zhang Y, Luo K, Chen Z, Luo J, Niu X. Longitudinal peripheral blood transcriptional analysis of COVID-19 patients captures disease progression and reveals potential biomarkers. MedRxiv. 2020 May 8:2020-05.

31. Lapić I, Brenčić T, Rogić D, et al. Cell population data: Could a routine hematology analyzer aid in the differential diagnosis of COVID-19? [published online ahead of print, 2020 Oct 20]. Int J Lab Hematol. 2020;10.1111/ijlh.13368.

**Table 1.** Comparison of total leucocyte and differential leucocyte counts between case and control groups

| Parameter $\times 10^3/\mu l$ | Case (n=222) | Control (n=161) | P-Value |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | |
| Total leukocyte count | 8.7±6.7 | 10±6.4 | 0.05 |
| Absolute neutrophil count | 6.3±5.8 | 7.1±5 | 0.17 |
| Absolute lymphocyte count | 1.6±3 | 2±4.4 | 0.35 |
| Absolute monocyte count | 0.5±0.3 | 0.6±0.4 | 0.02* |
| Absolute eosinophil count | 0.09±0.2 | 0.18±0.2 | 0.00* |
| Absolute basophil count | 0.008±0.03 | 0.02±0.06 | 0.00* |

**Table 2.** Comparison of VCS parameters of lymphocytes and monocytes between case and control groups

| Parameter | Case (n=222) | Control (n=161) | P-Value | Cut off | AUC | 95% CI | Sensitivity % | Specificity % |
|---|---|---|---|---|---|---|---|---|
| | Mean ± SD | Mean ± SD | | | | | | |
| MLV | 82.2 ±5.5 | 84.3±6.2 | 0.00* | 81.95 | 0.38 | 0.326-0.440 | 49.5 | 28 |
| SDLV | 16.1±2.1 | 15.5±2.7 | 0.02* | 15.03 | 0.607 | 0.548-0.665 | 69.4 | 52 |
| MLC | 116.6±6.9 | 117.1±3.5 | 0.39 | 115.5 | 0.394 | 0.337-0.451 | 49.5 | 31 |
| SDLC | 13.8±4 | 12.2±2.8 | 0.00* | 10.9 | 0.634 | 0.577-0.690 | 80.6 | 60 |
| MLS | 67.3±7.6 | 70.6±8.1 | 0.00* | 68.85 | 0.373 | 0.316-0.430 | 59 | 40 |
| SDLS | 19.3±3.7 | 18.2±3.3 | 0.03* | 16.94 | 0.609 | 0.551-0.666 | 79.3 | 40.4 |
| MMV | 172.3±9.8 | 169.5±10.3 | 0.06 | 167.85 | 0.601 | 0.543-0.658 | 66.7 | 50 |
| SDMV | 24.3±1.3 | 20.7±4.3 | 0.00* | 22.25 | 0.716 | 0.599-0.738 | 93.7 | 67 |
| MMC | 123.9±3.7 | 124.3±4 | 0.33 | 123.95 | 0.450 | 0.392-0.508 | 50 | 42.5 |
| SDMC | 5.4±1.2 | 5.1±1.1 | 0.01* | 4.81 | 0.604 | 0.546-0.662 | 70 | 46.9 |
| MMS | 88.7±5.8 | 91.8±5.1 | 0.00* | 90.85 | 0.346 | 0.291-0.401 | 39.2 | 40 |
| SDMS | 9.99±1.68 | 9.89±1.60 | 0.68 | 10.02 | 0.515 | 0.457-0.573 | 50.5 | 51 |

**Abbreviations:** VCS, Volume, Conductivity and Scatter; MLV, Mean Lymphocyte Volume; SDLV, Standard Deviation of Lymphocyte Volume; MLC, Mean Lymphocyte Conductivity; SDLC, Standard Deviation of Lymphocyte Conductivity; MLS, Mean Lymphocyte Scatter; SDLS, Standard Deviation of Lymphocyte Scatter; MMV, Mean Monocyte Volume; SDMV, Standard Deviation of Monocyte Volume; MMC, Mean Monocyte Conductivity; SDMC, Standard Deviation of Monocyte Conductivity; MMS, Mean Monocyte Scatter; SDMS, Standard Deviation of Monocyte Scatter.

**Table 3.** Comparison of the sensitivity and specificity of SDMV and SDLC with the gold-standard RT-PCR

| Parameter/Test method | Sensitivity (%) | Specificity (%) | 95% CI |
|---|---|---|---|
| SDMV | 93.7 | 67 | 0.599-0.738 |
| SDLC | 80.6 | 60 | 0.577-0.690 |
| RT-PCR [18] | 73 | 100 | 0.528–0.829 |

**Table 4.** Comparison of SDMV and SDLC values between the COVID-19 patients treated in the intensive care unit with others in the case group

| Parameter | Hospitalised COVID-19 patients treated in the Intensive Care Unit (Mean ±SD) (n= 49) | Non-ICU hospitalised COVID-19 patients (Mean ±SD) (n= 173) | P-Value |
|---|---|---|---|
| SDMV | 25 ± 1.2 | 22 ± 1.8 | 0.03* |
| SDLC | 15.4 ± 0.8 | 14.8 ± 1.1 | 0.60 |

Abbreviations: SDMV, Standard Deviation of Monocyte Volume; SDLC, Standard Deviation of Lymphocyte Conductivity.

**Table 5.** Comparison of SDMV in the present study with the other studies

| Study | Cut-Off value | Sensitivity | Specificity | AUC | Sample size of COVID-19 positive cases |
|---|---|---|---|---|---|
| Present study | > 22.25 | 93.7% | 67% | 0.71 | 222 |
| A.Ognibene et al[13] | > 20 | 98% | 65% | 0.91 | 41 |
| X. Zeng et al [15] | > 20.11 | 82.26% | 72.58% | 0.85 | 93 |

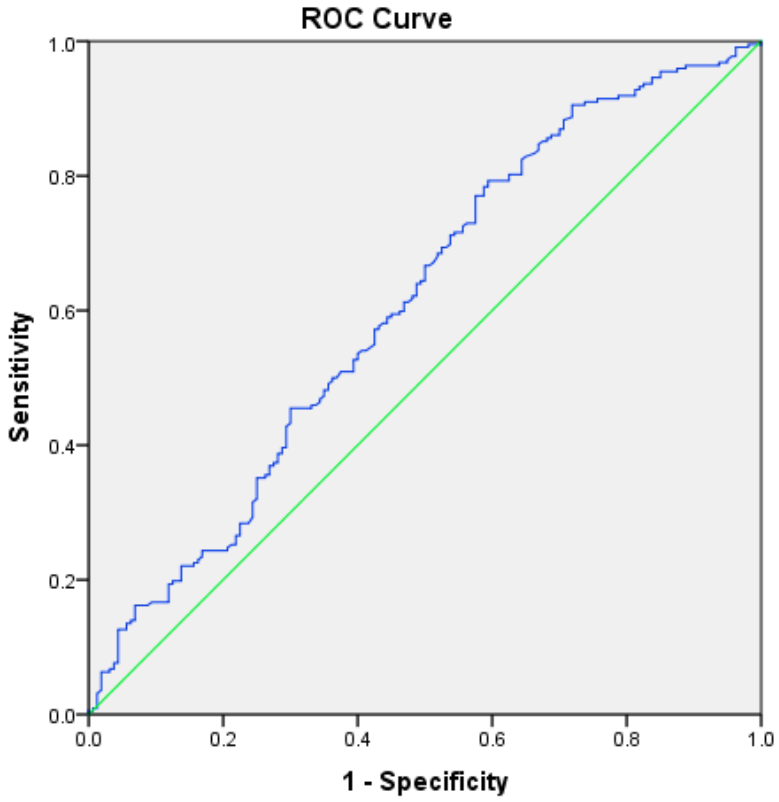


**Figure 1.** ROC curve analysis for SDMV performance in differentiating COVID-19 patients from other patients. SDMV has a sensitivity of 93.7% and specificity of 67% at a cut-off value of 22.35.

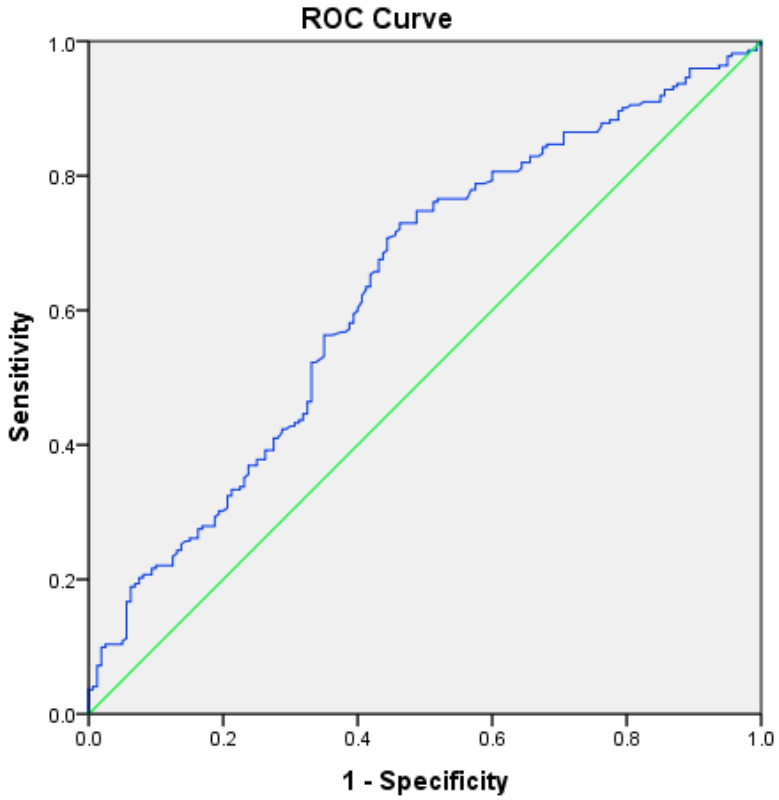


**Figure 2.** ROC curve analysis for SDLC performance in differentiating COVID-19 patients from other patients. At a cut-off value 10.9, SDLC has a sensitivity of 80.6% and specificity of 60%.