Original Article

Study of Laboratory Parameters in COVID-19 Patients at a Tertiary Care Teaching Hospital in Uttar Pradesh

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Abstract

Introduction: COVID-19 infection has been affecting vast population all over the world since 2019. It is very important to make optimum use of routine laboratory parameters in evaluating severity of COVID-19 disease. This will help the clinicians to improve allocation of technical human resources to patients who require it the most. During the path of the COVID-19 disease, inflammatory indices such as lactate dehydrogenase (LDH), C-reactive protein (CRP), interleukin-6 (IL-6), biomarkers like serum procalcitonin (PCT), and ferritin and indices of coagulation profile like D-Dimer, PT levels, and hematological parameters like total leukocyte count, platelets carry prognostic value. The objective of the study is to estimate the utility of various laboratory Biochemical and Hematological parameters in COVID-19 disease. **Materials and Methods:** The present study is a retrospective cross-sectional observational study conducted in tertiary care rural teaching hospital. The study was conducted from September 1, 2020, to January 31, 2021. The study was carried out on the patients who were hospitalized in Isolation Ward and COVID ICU in our L3 COVID hospital. All patients with positive SARS-CoV-2 nucleic acid test results were included in the study. A sample size of 310 patients was taken. The basic demographic details were collected from the admission records. The confirmatory test for SARS-CoV-2 was done using the WHO-approved kits based on real-time reverse transcription polymerase chain reaction for which suspected cases underwent nasopharyngeal/oropharyngeal swab testing. The levels of CRP, IL-6, PCT, ferritin LDH, D-dimer, complete blood counts, PT were based on standardized methods obtained using various biochemical and hematological laboratory analyzers. Data of investigation reports were gathered from electronic patient record system. Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows (version 25.0). **Results:** Our study clearly shows that levels of IL-6, D Dimer, PT, and LDH are quite significantly raised in majority of patients while PCT and ferritin being somewhat nonspecific show an increase but not to that significant numbers. The hematological parameters show levels which indicate mild anemia, leukocytosis, neutrophilia , lymphopenia, and thrombocytopenia in patients infected with COVID-19 disease. **Conclusion:** COVID-19 is an unexplored, new entity with a sudden worldwide onset. The medical fraternity is yet to conquer and analyse this novel virus.

Keywords: COVID-19 disease, laboratory, parameters

Introduction

COVID-19 infection has been affecting vast population all over the world since 2019. COVID-19-infected patients show spectrum of clinical symptoms, i.e., fever, cough, muscle aches, breathlessness. In worst case scenario cytokine storm, acute respiratory distress syndrome-like conditions can lead to mortality.[1,2] It is very important to make optimum use of laboratory tests in evaluating gravity of COVID-19 illness. This shall help the clinicians to improve allocation of technical human resources to patients who require it the most. Majorly published literature emphasizes on clinical spectrum of this disease but the literature which discusses laboratory parameters is restricted.[3] During the path of the COVID-19 disease, inflammatory indices such as lactate dehydrogenase (LDH), C-reactive protein (CRP), IL-6, biomarkers like serum procalcitonin (PCT) and ferritin, and Indices of Coagulation profile such as D-Dimer, PT levels, and hematological parameters like total leukocyte count, platelets carry prognostic value.[4] The objective of our study is to assess laboratory parameters of 310 patients confirmed

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with SARS-CoV-2 infection admitted in tertiary care teaching hospital. The institution is authorized L3 COVID facility and is fully equipped center with dedicated Isolation ward and intensive care units for treatment of COVID-positive patients.

Objective

The objective of the study is to estimate the utility of various laboratory Biochemical and hematological parameters in COVID-19 disease.

Materials and Methods

Study design

The present study is a retrospective cross-sectional observational study conducted in a tertiary care rural teaching hospital.

Study setting

The study was carried out on blood samples of patients who were hospitalized in Isolation Ward and COVID ICU in our L3 COVID hospital. All patients with positive SARS-CoV-2 nucleic acid test results were included in the study. The study was conducted from September 1, 2020, to January 31, 2021.

Determination of sample size

A sample size of 310 patients was calculated by taking prevalence as 50% and standard error as 5.67%. Then, by using formula for sample size calculation we calculated sample size and result came out to be 311 which was rounded off and taken as 310.

Ethical approval

Objective of the study were explained to the institutional ethical committee and ethical approval was taken (SIMS/2020/08/523).

Informed consent

A written informed consent in bilingual language, i.e., English/Hindi was obtained from each patient or their guardian.

Method of data collection

Using the hospital admission records, salient demographic details were gathered. The confirmatory test for SARS-CoV-2 was done using WHO-approved kits based on real-time reverse transcription-polymerase chain reaction for which suspected cases underwent nasopharyngeal/oropharyngeal swab testing.[5-7] All patients were subjected to detailed clinical evaluation, routine hematological and biochemical investigations, electrocardiogram and chest X-ray at the time of admission. Other investigations such as ultrasound abdomen, echocardiogram, and high-resolution computed tomography scan were done if indicated clinically. CRP testing was done using slide method based on principle of agglutination. Values of IL-6, PCT, and ferritin were obtained using CLIA method on Beckman Biochemistry Analyzer.[8] Value of LDH was obtained using IFCC method on BS200 mindray Biochemistry Analyzer.[8] Value of D-Dimer was obtained using CLIA method on Mini Vidas Biochemistry Analyzer.[8]. Values of Complete Blood Counts were obtained from Sysmex 5Part Cell Counter (XS-800i) instrument. The Value of PT was obtained using Hemostasis Analyzer (Hemostat XF-10).[8] Data of investigation reports were gathered from electronic patient record system.

Statistical analysis

Statistical analysis was performed utilizing the Statistical Package for the Social Sciences (SPSS) for Windows (version 25.0). Microsoft Excel Sheet (version 13.0) was used to enter the collected data which was imported to SPSS (version 25.0) (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp) and the whole statistical analysis was done using this software. A $P < 0.05$ was considered statistically significant. All the highly significant values were rounded off as <0.001.

Observations

Table 1 and Figure 1 show out of 310 patients enrolled in the study 69.4% of them were males and 30.6% of them were females.

Table 2 and Figure 2 show out of 310 patients enrolled in the study, maximum patients infected with COVID-19 belonged to age group of 50–70 years.

Figure 3 depicts levels of IL-6 in 310 covid patients . 235 patients showed higher than normal values of IL 6 (>6.40) while 75 patients showed a normal value of IL-6.

Figure 4 depicts Procalcitonin levels in 310 covid patients, 112 patients showed higher than normal values of Procalcitonin (>0.25) while 198 patients showed a normal value of Procalcitonin.

Figure 5 shows serum ferritin levels of 310 covid patients, 133 patients showed values higher than 300ng/mL while 175 patients had a normal value of Serum ferritin and 2 patients showed a value of less than 10ng/ml.

Figure 6 Bar chart shows D Dimer levels of 310 covid patients, 235 patients showed higher than normal values of D Dimer (>0.50) while 75 patients had a normal value.

Figure 7 Bar chart shows LDH levels in 310 COVID patients, 213 patients showed higher than normal values of LDH (>214) while 97 patients had a normal value.

Table 1: Details of study group on the basis of gender demographics ($n=310$)

	Frequency (%)
Female	95 (30.6)
Male	215 (69.4)

Table 2: Details of study group on the basis of age demographics ($n=310$)

Age groups	Number of patients
<30	19
30-50	82
50-70	133
>70	76

Table 3: Detailed statistical analysis of laboratory investigations (n=310)

Laboratory investigation	Mean±SD	95% CI	Median	Range	Minimum value	Maximum value	*P*
IL-6	40.70±119.09	51.513260	6.79	135.48	1.12	1356.60	<0.001
Procalcitonin	0.46±2.57	0.7277502	0.21	38.59	0.01	38.6	0.148
Ferritin	343.22±312.05	176.910	245.80	1447	5	1452	0.019
D-Dimer	1.66±1.92	0.045	0.90	8.8	0.2	9	<0.001
LDH	360.67±283.83	85.127079	258.20	2591.7	78.7	2670.4	<0.001
Hemoglobin	12.12±4.43	0.14614	12.00	11	5.00	16	0.001
TLC	10,192±5090.31	1238.249	9350.00	31900	1500	33400	0.006
Neutrophil (%)	77.33±10.27	3.957	78.50	78	18	96	<0.001
Lymphocyte (%)	17.93±9.41	0.532	16.00	73	03	76	<0.001
Platelets	2.12±1.06	0.02568	1.95	5.80	0.10	5.90	<0.001
PT	14.64±2.27	1.4827	13.90	11.3	10.3	21.6	<0.001

SD: Standard deviation, CI: Confidence interval, IL-6: Interleukin-6, LDH: Lactate dehydrogenase, PT: Prothrombin time, TLC: Total leukocyte count

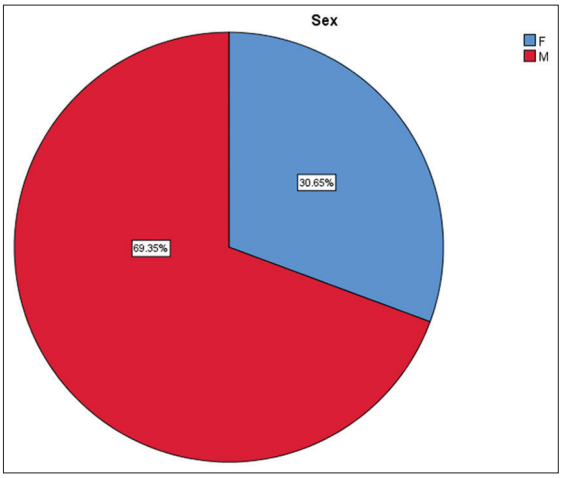

Figure 1: Pie chart showing sex distribution of 310 COVID patients

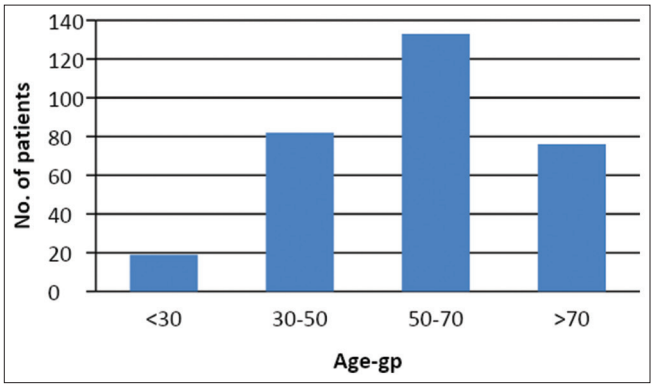

Figure 2: Bar diagram showing age distribution of 310 COVID patients

Table 3 illustrates the detailed statistical analysis of five Laboratory Investigations, i.e., IL-6, PCT, Ferritin, D Dimer, and LDH among the patients of COVID-19 (n = 310) considered in our study.

Table 4 shows out of 310 patients enrolled in the study, 41.6% were positive for CRP and 58.4% were negative for CRP.

IL-6 of 310 patients was found to be in a range from 1.12 to 1356.6 with a mean value of 40.7 pg/ml. 75.8% patients showed higher than normal values of IL 6 while 24.19% patients had a normal value of IL-6 [Table 5].

PCT of 310 patients was found to be in a range from 0.01 to 38.6 with a mean value of 0.46 ng/ml. 36.12% patients showed higher than normal values while 63.87% patients had a normal value [Table 6].

Serum ferritin of 310 patients was found to be in a range from 5 to 1452 ng/mL with a mean value of 343.22 ng/ml. 42.91% patients showed values higher than 300 ng/mL while 57.09% patients had a normal value [Table 7].

D Dimer of 310 patients was found to be in a range from 0.2 to 9 ng/mL with a mean value of 1.66 ng/ml. 75.81% patients showed higher than normal values of D Dimer while 24.19% patients had a normal value [Table 8].

LDH of 310 patients was found to be in a range from 78.70 to 2670.4 U/L and showed a mean value of 360 U/L. 68.71% patients showed higher than normal values of LDH while 31.29% patients had a normal value [Table 9].

Hemoglobin of 310 patients was found to be in a range from 5 to 16 g/dl with a mean value of 12.1 g/dl. 67.75% patients showed lower than normal values while 32.25% patients had a normal value [Table 10].

Total leukocyte count of 310 patients was found to be in a range from 1500 to 33,400/cumm with a mean value of 10,192/cumm. 36.77% patients showed higher than normal values of 11,000/cumm while 57.41% patients had a normal value [Table 10].

Neutrophil percentage in differential leukocyte count (DLC) of 310 patients was found to be in a range from 18 to 96% with a mean value of 77.33%. 65.48% patients showed higher than normal values while 34.19% patients had a normal value [Table 10].

Lymphocyte percentage in DLC of 310 patients was found to be in a range from 3% to 76% with a mean value of 17.93%. 61.93% patients showed lower than normal values while 35.48% patients had a normal value [Table 10].

Table 4: Laboratory analysis of C-reactive protein qualitative test done in COVID-19 patients (*n*=310)

	Frequency (%)
Negative	181 (58.4)
Positive	129 (41.6)
Total	310 (100.0)

Table 5: Serum concentration of interleukin-6 in 310 subjects (normal value - <6.4 pg/ml)

Total patients	Increased (>6.4)	Normal (<6.4)
310	235 (75.80%)	75 (24.19%)

Table 6: Procalcitonin levels in 310 patients (normal value <0.25 ng/mL)

Total patients	>0.25	Normal
310	112 (36.12%)	198 (63.87%)

Table 7: Ferritin levels in 310 patients (normal value 10-300 ng/mL)

Total patients	>300	<10	Normal
310	133 (42.90%)	2 (0.6 (0.64%)	175 (56.45%)

Table 8: D Dimer levels in 310 patients (normal value <0.4 ng/mL)

Total patients	>0.4	Normal
310	235 (75.80%)	75 (24.19%)
310	235	75

Table 9: Lactate dehydrogenase levels in 310 patients (normal value <140-214 U/L)

Total patients	>214	Normal
310	213 (68.70%)	97 (31.29%)

Table 10: Hemoglobin levels in 310 patients (normal value <13.5 g/dl)

Total patients	<13.5	Normal
310	210 (67.75%)	100 (32.25%)

Table 11: Total leukocyte count levels in 310 patients (normal value 4000-11,000/cumm)

Total patients	>11,000	<4000	Normal
310	114 (36.77%)	18 (5.80%)	178 (57.41%)

Platelet of 310 patients was found to be in a range from 0.10 to 5.90 × 10^9/L with a mean value of 2.12 × 10^9/L. 28.70% patients showed lower than normal values of platelets while 68.70% patients had a normal value [Table 10].

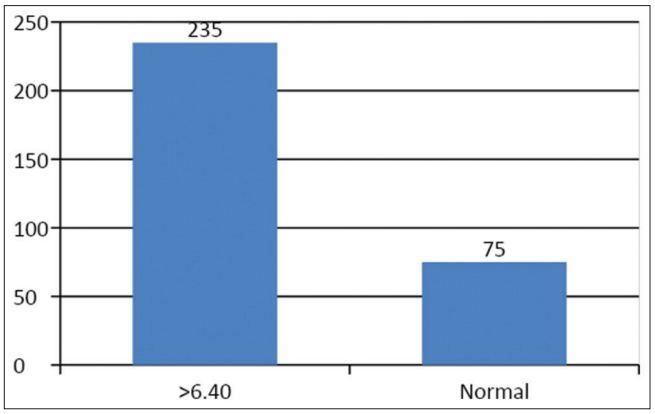

Figure 3: Bar chart showing levels of interleukin-6 in 310 COVID patients

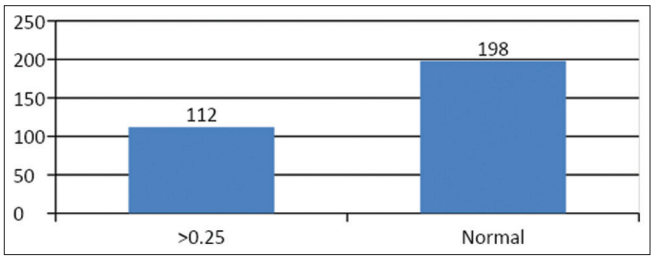

Figure 4: Bar chart showing procalcitonin levels in 310 COVID patients

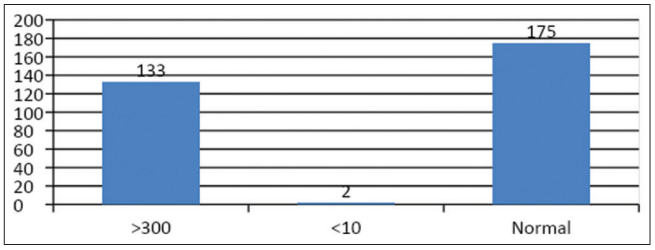

Figure 5: Bar chart showing serum ferritin levels of 310 COVID patients

Prothrombin time (PT) of 310 patients was found to be in a range from 10.3 to 21.6 s with a mean value of 14.64 s. 46.45% patients showed higher than normal values of while 53.555% patients had a normal value [Table 10].

Table 11 shows Total Leukocyte Count levels in 310 patients(Normal value 4000-11000/cumm), 114 patients (36.77%) showed higher than normal values of TLC (greater than 11,000/cumm) while 178 patients (57.41%) showed a normal value of TLC and 18 patients (5.80%) showed TLC lower than normal value. (less than 4000/cumm).

Table 12 depicts percentage of Neutrophils in differential leukocyte counts in 310 patients (normal value of Neutrophils - 40%-75%), 203 patients (65.48 %) showed higher than normal values (greater than 75%) while 106 patients (34.19%) showed a normal percentage of Neutrophils and 1 patient (0.32 %) showed percentage of Neutrophil to be lower than normal value. (less than 40%).

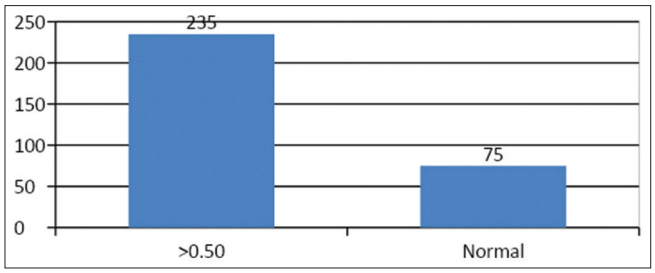

Figure 6: Bar chart showing D Dimer levels of 310 COVID patients

Table 12: Neutrophil in differential leukocyte count levels in 310 patients (normal value 40%-75%)

Total patient	>75	<40	Normal
310	203 (65.48%)	1 (0.32%)	106 (34.19%)

Table 13: Lymphocyte in differential leukocyte count levels in 310 patients (normal value 20%-40%)

Total patients	>40	<20	Normal
310	8 (2.58%)	192 (61.93%)	110 (35.48%)

Table 14: Platelet levels in 310 patients (normal value 150-400×10⁹/L)

Total patients	>4.5	<1.5	Normal
310	8 (2.58%)	89 (28.70%)	213 (68.70%)

Table 15: Prothrombin time levels in 310 patients (normal value 12-14 s)

Total patients	>14	Normal
310	144 (46.45%)	166 (53.55%)

Table 13 depicts percentage of Lymphocytes in differential leukocyte counts in 310 patients (normal value of Lymphocytes - 20%-40%), 8 patients (2.58 %) showed higher than normal values (greater than 40%) while 110 patients (35.48%) showed a normal percentage of Lymphocytes and 192 patients (61.93 %) showed percentage of Lymphocytes to be lower than normal value. (less than 20%).

Table 14 shows Platelet levels in 310 patients(Normal value 150-400×109 /L), 8 patients (2.58%) showed higher than normal values of Platelet count (greater than 4.5 Lakh ie > 450×109 /L) while 213 patients (68.70%) showed a normal value of Platelet and 89 patients (28.70%) showed Platelet lower than normal value. (less than 1.5 Lakh ie < 150×109 /L).

Table 15 shows Prothrombin time levels in 310 patients (normal value 12-14 seconds), 144 patients (46.45%) showed higher than normal values of Prothrombin time (greater than 14 seconds) while 166 patients (53.55%) showed a normal value of Prothrombin Time.

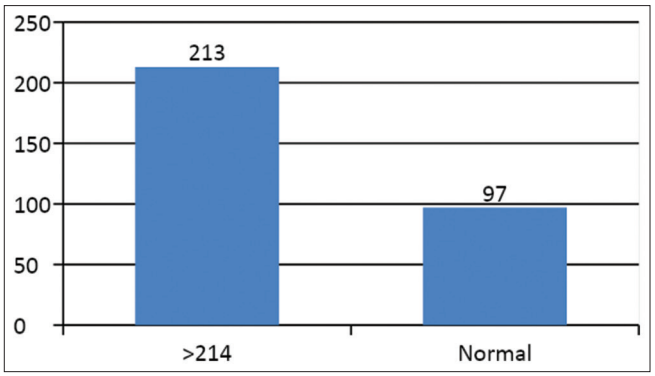

Figure 7: Bar chart showing LDH levels in 310 COVID patients

Discussion

Any kind of infection or injury brings about inflammatory and immune response which results in release of important mediators like interleukin-6 (IL-6). It has been seen that IL-6 level rises excessively in severe COVID-19 infection as a result of amplified dysfunctional host immune response. Higher levels of IL-6 indicate a progressive inflammatory response which might lead to respiratory failure and such patients require ICU care in the form of intubation or mechanical ventilation and are cause of mortality as a result of COVID infection.[9]

In our study, 75.8% patients showed higher than normal values of IL 6 while 24.19% patients had a normal value of IL-6, signifying the importance of IL-6 in inflammation associated with COVID infection. The $P < 0.001$ shows the statistical significance of the same. Similar findings were observed by Chen *et al*.[10] where 52% of patients showed increased IL-6 levels at the time of admission.

PCT is a hormone which is an amino acid glycoprotein precursor of calcitonin. PCT is released from parenchymal tissue in patients suffering from bacterial infection, and hence, PCT levels are increased in infections. The normal PCT is below 0.05 ng/mL in healthy individuals.[11] In our study, 36.12% patients showed higher than normal values while 63.87% patients had a normal value. PCT shows higher levels when COVID is associated with bacterial infections and hence only 36.12% patients show higher values. The *P* value is, however, <0.148 making it an insignificant entity. Guan *et al*.[12] showed elevated PCT in 5.5% cases.

In our study, out of 310 patients enrolled in the study, 41.6% were positive for CRP. Studies by Henry *et al*.[13] and Tan *et al*.[14] also showed that CRP levels were positive in patients infected with COVID.

Elevated D-dimer occurs in patients because of abnormal coagulation function. It has been documented in many studies that level of D dimer is strikingly raised in patients who have been suffering from serious COVID infection. It can be said that in patients affected gravely by COVID infection, the level of D-dimer would be amplified and hence there is a definitive

association between COVID infection and D-dimer levels. It has also been noted that distressingly ill patients with COVID infection present with diffuse alveolar damage and pulmonary embolism in the lungs which can result in strikingly raised D-dimer level.[15]

In our study, 75.81% patients showed higher than normal values of D Dimer while 24.19% patients had a normal value. Similar findings were observed in study by Han *et al*.[16] where D-dimer was markedly higher among COVID patients.

The *P* value shows significant value of <0.001. Ferritin, an iron-storing protein is an acute phase reactant. Its levels show a marked increase during viral infections thus acting as a marker of viral replication. Its levels are raised gravely in COVID-19 because of excessive inflammation. It has been documented in many studies that the level of ferritin is nearly linked to patients who have been suffering from serious COVID infection and the chances of recovery are low and chances of morbidity are high in such patients.[17] In our study, 42.91% patients showed values higher than 300 ng/mL while 57.09% patients had a normal value. *P* = 0.019 shows that ferritin is a significant parameter in the course of COVID-19 disease. Similarly, findings were observed in study by Zhou *et al*.[18]

LDH is an enzyme which is produced as a result of tissue damage and is responsible for precipitating inflammatory reaction in retaliation to tissue damage in COVID infection and further instigates hypoxia, necrosis, and cell death.[19] In our study, 68.71% patients showed higher than normal values of LDH while 31.29% patients had a normal value. The *P* value came out to be highly significant, i.e., <0.001. Similarly, findings were observed in study by Zhou *et al*.[18]

In our study, 67.75% of the COVID-19 patients showed decrease in hemoglobin in the form of mild anemia. *P* = 0.001 further shows the statistical significance of the same. This could be as a result of release of inflammatory factors which can cause damage to RBCs, reduced erythropoiesis which finally leads to anemia.[20] Similar findings were observed in study by Blomme *et al*.[21]

In our study, it was noted that out of the patients who were ill with COVID, 36.77% showed increase in total leukocyte count. *P* value is, however, 0.006 making it an insignificant entity. Leukocytosis could be result of superimposed bacterial infections in COVID patients which causes increase in leukocytes level.[10,20] Total leukocyte level was also seen significantly higher by Bloome *et al*.[21] and Henry *et al*.[13]

Neutrophilia was observed in 65.48% patients in the present study and *P* value came out to be highly significant, i.e., <0.001. Neutrophilia as a result of superimposed bacterial infection is decisive in determining outcome of COVID-19 disease.[10,20] Similar findings were observed in study by Qian *et al*.[22] and Mo *et al*.[23]

Lymphocytes play an important role in protecting body against any kind of viral attack. In our study, lymphocytopenia was observed in 61.93% patients and *P* value came out to be highly significant, i.e., <0.001. Similar findings were observed in study by Guan *et al*.[12] and Wang *et al*.[24]

Thrombocytopenia is a complication seen in critically ill COVID patients who further have associated risk of developing DIC which can result in multiorgan failure.[25] In our study, thrombocytopenia was observed in 28.70% patients and the *P* value came out to be highly significant, i.e., <0.001. Similar findings were observed in study by Henry *et al*.[13] and Luipi *et al*.[26]

Henry *et al*.[13] noted that in patients affected gravely by COVID infection, leukocytosis, lymphopenia, and thrombocytopenia would be seen in complete blood count and there is a definitive association between COVID infection and levels of these hematological parameters. Similar findings were observed in our study.

It has been documented by various studies that COVID-19 infection induces defects in Hemostasis. Study by Tang *et al*.[27] concluded finding of higher levels PT in infected cases. Similar findings were noted in the present study where PT was increased in 46.45% patients and *P* value came out to be highly significant, i.e., <0.001.

Conclusion

COVID-19 is an unexplored, new entity with a sudden worldwide onset. The medical fraternity is yet to conquer and analyze this novel virus. Our study clearly shows that values of IL-6, D Dimer, PT, and LDH are quite significantly raised in majority of patients while PCT and ferritin being somewhat nonspecific show an increase but not to that significant numbers. The hematological parameters show levels which indicate mild anemia, leukocytosis, neutrophilia lymphopenia, and thrombocytopenia in patients infected with COVID-19 disease.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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