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ORIGINAL RESEARCH

Hematological and Coagulation parameter analysis in COVID 19 positive patients – A Retrospective Study

[1]Dr. Lekha M.B., [2]Dr. Supritha Rajesh, [3]Dr. Nikil Sanaba Paramesh, [4]Dr. Manjunatha Y.A.

[1]Associate Professor, [2]3rd year Postgraduate, [4]Professor & HOD, Department of Pathology, Dr. B.R. Ambedkar Medical College and Hospital, Bangalore, Karnataka, India
[3]Associate professor, Department of Orthopaedics, Dr. B.R. Ambedkar Medical College and Hospital, Bangalore, Karnataka, India

Corresponding Author
Dr. Lekha M.B.
Associate professor, Department of Pathology, Dr. B.R. Ambedkar Medical College and Hospital, Bangalore, Karnataka, India

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Abstract

Introduction: Coronavirus disease (COVID)-19 affects multi-organ system and is associated with changes in the hematological parameters.

Objective: To explore hematological and coagulation parameters in Reverse transcription polymerase chain reaction (RT-PCR) confirmed COVID-19 positive patients.

Methods: This retrospective single center study included laboratory records of 300 patients diagnosed with COVID-19 using RT-PCR test and having complete records of hematology and coagulation parameter analysis during August to November 2020. Demographics and hematological data including age, sex, hemoglobin count, total leucocyte count, neutrophil count, absolute neutrophil count (ANC), lymphocyte count, absolute lymphocyte count (ALC), platelet count, D-Dimer, serum ferritin, C reactive protein and lactose dehydrogenase levels were recorded. Descriptive statistics were performed.

Results: The Mean ± SD age of patients was 51.1±15.6. Majority (n=121, 40.3%) of patients were middle aged (31-50 years) and males (n=205, 68.3%). Overall, Mean ± SD of hemoglobin count was 12.4±2.2g/dL. Mean ± SD total leucocyte count, ANC, ALC and platelet count were 11047.2±5638.4/mm^3, 8885.8±5613.4/mm^3, 1517.7±805.4/mm^3 and 1.7±1.0lakh/mm^3, respectively. The Mean ± SD of D-dimer, C-reactive protein, ferritin and Lactose dehydrogenase were 21.3±192.1ng/mL, 36.1±41.8mg/L, 485.2±452.2ng/mL and 707.4±488.9U/L, respectively. Significant deviation from normal range was observed ($p<0.05$). While, hemoglobin count (41.9%) and lymphocyte count (65.8%), platelet count (51.2%), ANC(44.6%) and ALC (74.1%) decreased more often, increased total count (49.0%), neutrophil count (66.1%), D-Dimer (70.2%), C reactive protein (77.6%), ferritin (54.7%) and lactose dehydrogenase (79.7%) were noted. Age and sex was significantly associated with changes in hemoglobin, neutrophil, lymphocyte, ALC and D-Dimer counts ($p<0.05$).

Conclusion: COVID-19 is associated with altered hematological and coagulation parameters suggesting the importance of Laboratory investigations at the initial stage of disease.

Keywords: COVID-19, C reactive protein, D-Dimer, hematology, neutrophil

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Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) causing coronavirus disease 2019 (COVID 19) has rapidly evolved from its first outbreak in Wuhan, China into a pandemic with over 548 million infections and more than 6 million deaths to date.[1] Although initially the virus was implicated as a respiratory pathogen, several researches have indicated its pathogenicity across multiple systems including cardiovascular, gastrointestinal, neurological, hematopoietic and immunological systems.[2,3] Severe and critical result in complications including septic shock, heart failure, disseminated intravascular coagulation, ischemic limbs, stroke and venous thromboembolism.[4] Based on clinical presentation, respiratory function tests and radiographic findings patients are categorized as mild, moderate and severe disease.[5] Further, evidence of changes in the laboratory parameters including hematological and biochemical parameters are found to be beneficial in grading severity of COVID-19.[6]

Viral induced variation in the peripheral blood count are well established in other common viral infections. Similarly, previous reports indicate abnormal changes in the hematological parameters in COVID-19 patients including those in early phases of infection.[6-8] Further, COVID-19 disease is also related to major hypercoagulability. Increased levels of C reactive protein D dimer, ferritin and lactose dehydrogenase have been reported.[9-12] These risk predictors will not only help in risk stratification, but also help strategize treatment plan to decrease the incidence of mortality. Therefore, a complete diagnostic workup and careful evaluation of laboratory indices at the initial phases of infection ensures timely intervention. The present retrospective study was thus planned with an aim to explore hematological and coagulation parameters and evaluate the incidence of change in the hematological and coagulation parameters in Reverse transcription polymerase chain reaction (RT-PCR) confirmed COVID-19 positive patients. We further evaluated the effect of age and sex on the hematological changes.

Material and methods

This retrospective single center study was conducted in the Department of Pathology, Dr. B.R. Ambedkar Medical College, Bengaluru from August 2020 to November 2020. The study protocol was approved by the institutional ethics committee prior to study initiation. All patients diagnosed with COVID-19 based on the WHO interim guidance [13] with positive SARS-CoV-2 RNA in the swab specimens of throat, having records of hematology and coagulation parameter analysis results were included in the study. Suspected COVID-19 patients with negative RT-PCR test and those with incomplete lab records were excluded from the analysis. We also included one case of fracture shaft of femur with a positive RT-PCR test that developed fat embolism with deranged hematological parameters and elevated D-dimer levels. Patient records were retrieved from hospital database.

Details on patients demographics including age and sex, hematological parameters including hemoglobin count, total leucocyte count, neutrophil count, absolute neutrophil count (ANC), lymphocyte count, absolute lymphocyte count (ALC), platelet count and coagulation parameters including D-Dimer, serum ferritin, C reactive protein and lactose dehydrogenase levels were recorded. Laboratory variables were further categorized as normal range, decreased and increased. Hemoglobin count (12-18g/dL), total leucocyte counts (4000-11000/mm^3), neutrophil count (40-75%), absolute neutrophil count (ANC; 1500-8000/mm^3), lymphocyte count (20-40%), absolute lymphocyte count (ALC; 1500-6000/mm^3), platelet count (1.5-4lakh/mm^3), D-dimer (0.4ng/dL), serum ferritin (1-3ng/mL), C reactive protein (0-6mg/L), Lactose dehydrogenase (140-214U/L) were considered as cut off normal ranges. The values beyond these ranges were categorized as increased and decreased. Neutrophil to lymphocyte ratio (NLR) was calculated and 3.13 was considered the cut off value.

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Continuous variables were summarized as mean, standard deviations and median values. Categorical variables were presented as frequency and percentages. Mean of hematological variables were compared with normal values using one sample t test with confidence level set at 95% and alpha of 0.05. The association of age and sex on hematological changes were assessed using chi square test or fisher exact test. P value of less than 0.05 was considered statistically significant. All statistical analysis was performed using SPSS version 22.

Results

The present study consisted of 300 patients with diverse age range of 10 to 95 years. The Mean±standard deviation (SD) age of patients was 51.1±15.6. Majority (n=121, 40.3%) of patients were middle aged (31-50 years). Approximately two third of the study population comprised of males (n=205, 68.3%)(**Table 1**).

Variable		**N=300**
Age, years	Mean±SD	51.1±15.6
	Median (min, max)	50.0(10.0, 95.0)
Age distribution, years, n(%)	<=30	31(10.3)
	31-50	121(40.3)
	51-70	115(38.3)
	>70	33(11.0)
Sex, n(%)	Male	205(68.3)
	Female	95(31.7)

Table 1: Baseline demographics of study population

(Table 2)summarizes the descriptive statistics of hematological parameters. In our study the hemoglobin count of patients ranged from 5.3-17.4g/dL with median of 12.75g/dL and mean±SD of 12.4±2.2g/dL. The mean difference from normal range was statistically significant (p=0.001). Mean±SD total leucocyte count and platelet count were 11047.2±5638.4/mm^3 and 1.7±1.0lakh/mm^3, respectively. Mean±SD of neutrophil count and ANC were 77.3±13.9% and 8885.8±5613.4/mm^3, respectively, which were higher than the normal range (p=0.000 and p=0.007, respectively). The mean±SD of lymphocyte (17.3±11.7%) and ALC (1517.7±805.4/mm^3) were significantly lower than the normal range (p=0.000, both). The mean±SD NLR was 3.8±6.6 was higher than the normal range, but the difference was non-significant (p=0.077).

	N	**Mean**	**Standard deviation**	**Median**	**Min**	**Max**	**P value**
Hemoglobin, mg/dL	298	12.4	2.2	12.75	5.3	17.4	0.001
Total leucocyte count, cells/mm^3	298	11047.2	5638.4	10940.0	2480.0	58830.0	0.000
Neutrophil count, %	298	77.3	13.9	81.0	32.1	94.7	0.000
Absolute neutrophil count, cells/mm^3	293	8885.8	5613.4	2271.0	959.0	54711.0	0.007
Lymphocyte count , %	298	17.3	11.7	14.65	1.9	58.5	0.000
Absolute lymphocyte count, cells/mm^3	294	1517.7	805.4	599.49	240.0	6764.98	0.706
Plateletcount, cells/mm3	295	1.7	1.0	1.45	0.3	6.98	0.000
Neutrophil lymphocyte ratio	293	3.8	6.6	4.9	0.1	49.6	0.077

Table 2: Descriptive statistics of hematological parameters

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(Table 3) summarizes the descriptive analysis of coagulation parameters. While the median D dimer was 0.6ng/mL, mean±SD was high 21.3±192.1ng/mL without significant deviation from normal range (p=0.061). The mean±SD C-reactive protein, ferritin and Lactose dehydrogenase were 36.1±41.8mg/L, 485.2±452.2ng/mL and 707.4±488.9U/L, respectively. The mean differences were significantly higher than normal range (p=0.000, for all)

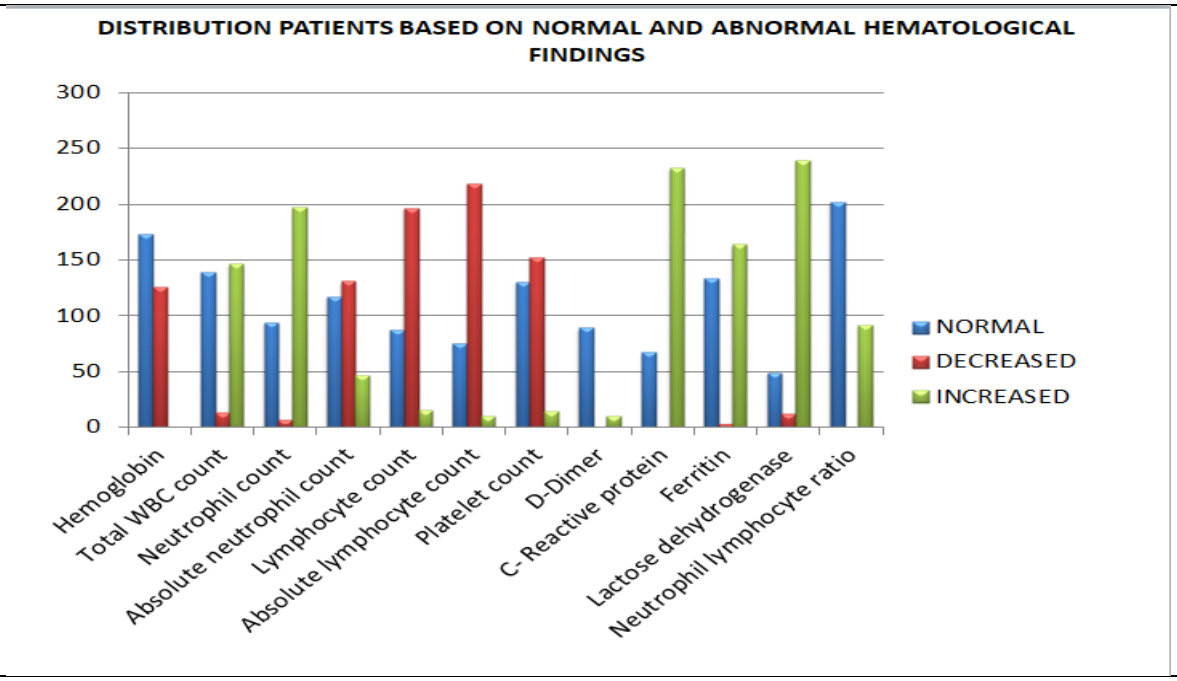
	N	Mean	Standard deviation	Median	Min	Max	P value
D-Dimer, ng/mL	299	21.3	192.1	0.619	0.1	2990.17	0.061
C-reactive protein, mg/L	299	36.1	41.8	18.4	0.5	170.70	0.000
Ferritin, ng/mL	298	485.2	452.2	341.5	7.1	2528.2	0.000
Lactose dehydrogenase U/L	299	707.4	488.9	640.4	35.3	2710.6	0.000

Table 3: Descriptive analysis of coagulation parameters

The distribution of patients based on normal and abnormal hematological and coagulation parameter findings are summarized in (**Table 4) (Graph 1)**.

Variable	Normal	Decreased count	Increased count
	N (%)	N (%)	N (%)
Hemoglobin	173(58.1)	125(41.9)	-
Total WBC count	139(46.6)	13(4.4)	146(49.0)
Neutrophil count	94(31.5)	7(2.3)	197(66.1)
Absolute neutrophil count	117(39.8)	131(44.6)	46(15.6)
Lymphocyte count	87(29.2)	196(65.8)	15(5.0)
Absolute lymphocyte count	75(25.5)	218(74.1)	1(0.3)
Platelet count	130(43.9)	152(51.4)	14(4.7)
D-Dimer	89(29.8)	-	210(70.2)
C- Reactive protein	67(22.4)		232(77.6)
Ferritin	133(44.3)	3(1.0)	164 (54.7)
Lactose dehydrogenase	49(16.3)	12(4.0)	239(79.7)
Neutrophil lymphocyte ratio	202(68.9)	-	91(31.1%)

Table 4: Distribution patients based on normal and abnormal hematological findings



Graph 1

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In our study 125(41.9%) patients had hemoglobin count <12g/dL. Total leucocyte count was increased and decreased in 146(49.0%) and 13(4.4%) patients, respectively. While 197(66.1%) patients had increased neutrophil count, 196(65.8%) patients had decreased lymphocyte counts. ANC and ALC were decreased in 33(44.6%) and 218(74.1%) patients, respectively. More than half of patients had decreased platelet counts (n=152, 51.2%). Increase in D-Dimer, C reactive protein, ferritin and lactose dehydrogenase were seen in 210(70.2%), 232(77.6%), 164 (54.7%) and 239(79.7%) patients, respectively.

Association of age on the hematological and coagulation parameters are shown in (**Table 5)**.

Variable	values	<=30	31-50	51-70	>70	Total	P value
Hemoglobin	12-18g/dL	26	86	52	9	173	0.000
	<12g/dL	5	35	61	24	125	
Total leucocyte count	4000-11000/mm^3	16	54	56	12	139	0.589
	<4000/mm^3	3	5	3	2	13	
	>11000/mm^3	12	60	56	18	146	
Neutrophil count	40-75%	17	40	29	8	94	0.017
	<40%	2	2	3	0	7	
	>75%	12	77	83	25	197	
Absolute neutrophil count	1500-8000/mm^3	18	49	37	12	117	0.135
	<1500/mm^3	8	48	58	17	131	
	>8000/mm^3	5	21	17	3	46	
Lymphocyte count	20-40%	17	39	26	5	87	0.001
	<20%	10	75	84	27	196	
	>40%	4	5	5	1	15	
Absolute lymphocyte count	1500-6000/mm^3	16	34	23	2	75	0.000
	<1500/mm^3	14	84	89	31	218	
	>6000/mm^3	1	0	0	0	1	
	<1.5lakh/mm^3	10	60	64	18	152	
	>4lakh/mm^3	3	7	2	2	14	
D-Dimer	0.4ng/dL	17	77	87	29	210	0.007
	>0.4ng/dL	14	43	28	4	89	
C-Reactive protein	0-6mg/L	25	91	90	26	232	0.871
	>6mg/L	6	30	24	7	67	
Ferritin	1-3ng/mL	17	52	45	19	133	0.148
	<1ng/mL	0	3	0	0	3	
	>3ng/mL	14	66	70	14	164	
Lactose dehydrogenase	140-214U/L	6	18	21	4	49	0.237
	<140U/L	0	4	4	4	12	
	>214U/L	25	99	90	25	239	
	≤3.13	25	76	80	21	202	0.307
Neutrophil lymphocyte ratio	>3.13	6	41	32	12	91	

Table 5: Association of age on hematological and coagulation parameters

Compared to other age groups, incidence of decreased hemoglobin was higher in age group 51-70 years (p=0.000). Age was significantly associated with changes in hematological parameters such as neutrophil count (p=0.017), lymphocyte count (p=0.001), ALC (p=0.000). Coagulation parameter D-Dimer was lower in age group 31-50 years (p=0.007). Association of sex on the hematological and coagulation parameters are shown in **(Table 6)**. Incidence of

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decreased hemoglobin counts (p=0.000) and increased D-dimer counts (p=0.016) were higher in males than females. No significant association was noted between sex and other hematological or coagulation factors (p<0.05).

Variable	values	Male	Female	Total	P value
Hemoglobin	12-18g/dL	138	35	173	0.000
	<12g/dL	67	58	125	
Total WBC count	4000-11000/mm^3	93	46	139	0.160
	<4000/mm^3	12	1	13	
	>11000/mm^3	98	48	146	
Neutrophil count	40-75%	65	29	94	0.944
	<40%	5	2	7	
	>75%	133	64	197	
Absolute neutrophil count	1500-8000/mm^3	80	37	117	0.797
	<1500/mm^3	87	44	131	
	>8000/mm^3	33	12	46	
Lymphocyte count	20-40%	60	27	87	0.976
	<20%	133	63	196	
	>40%	10	5	15	
Absolute lymphocyte count	1500-6000/mm^3	50	25	75	0.324
	<1500/mm^3	150	68	218	
	>6000/mm^3	0	1	1	
Platelet count	1.5-4lakh/mm^3	90	40	130	0.652
	<1.5lakh/mm^3	104	48	152	
	>4lakh/mm^3	8	6	14	
D-Dimer	0.4ng/dL	69	20	89	0.016
	>0.4ng/dL	135	75	210	
C-Reactive protein	0-6mg/L	40	27	67	0.062
	>6mg/L	164	68	232	
Ferritin	1-3ng/mL	88	45	133	0.410
	<1ng/mL	3	0	3	
	>3ng/mL	114	50	164	
Lactose dehydrogenase	140-214U/L	35	14	49	0.753
	<140U/L	9	3	12	
	>214U/L	161	78	239	
Neutrophil lymphocyte ratio	≤3.13	136	66	202	0.609
	>3.13	64	27	91	

Table 6: Association of sex on hematological and coagulation parameters

Discussion

This retrospective study illustrates the higher incidence of changes in hematological and coagulation parameters in COVID-19 positive patients. Although study population consisted of diverse population with varying age range from 10 to 95 years majority of patients were middle aged which is consistent with the other COVID-19 study reports across the world.[14-15] Our study population comprised of males predominantly (68%) which is consistent with a study by Taj et al.[16]. Previous studies suggest that severity of COVID-19 infection is higher in males than females supports the higher male frequency in our study.[17]

Across studies, various hematological factors are being considered as a predictor of severity

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and outcome of COVID-1 infection.[6,8,15] In our study there was significant difference of mean values of various hematological parameters including total leucocyte count and platelet count, neutrophil count, ANC lymphocyte and ALC than normal range. These results were further substantiated by higher incidence of decreased hemoglobin (41.9%), platelet counts (51.2%), ANC (44.6%), lymphocyte count (65.8%) ALC (74.1%) and increased levels of total leucocyte count (49.0%). These findings are consistent with report by Taj et al[16] and Keshi et al[15] who observed leukocytosis and neutrophilia related to the increased inflammatory response to the COVID-19 infection.

Decreased platelet count is one of the characteristics of COVID-19 infection. In our study, decreased platelet counts were observed in 51% patients which is much higher than 20% reported by Fan et al [10].On the other hand, the incidence of decreased leucocyte count were much lower (4.4% vs. 19%).

NLR is an inflammatory marker used to predict the prognosis of various diseases including cancer, cardiovascular diseases, infections and sepsis.[14] It is positively related to severity of disease, higher levels indicate poor prognosis.[18,19] Previous studies have demonstrated elevated neutrophil to lymphocyte ratio as independent predictor of disease severity and mortality in COVID-19 patients.[20,21] Based on results by Liu et al,[22] 3.13 was considered the cut off value for NLR. Approximately 30% of patients had increased NLR ratio and the difference of mean NLR with normal value was not significant. This may indicate that the COVID-19 infection was non severe among patients in our study population.

D-dimer level is one of the component of coagulation profile used as a screening test for abnormal clotting. Previous studies have reported significant positive correlation between D-Dimer and COVID-19 severity.[23] Respiratory infections resulting in diffuse alveolar damage and pulmonary embolism lead to increased D-Dimer levels.[24] As COVID-19 is predominantly a respiratory disease, increased D Dimer levels are expected. In our study, although increased D-Dimer levels were seen in 77.6% of patients, with a median of 0.6ng/mL and mean±SD of 21.3±192.1ng/mL, however, no significant without significant deviation from normal range indicating non-severity of infection in our study population.

Increased levels of serum ferritin, Lactose dehydrogenase and C-reactive protein were considered predictors of acute respiratory distress syndrome, higher troponin-T levels, myocardial injury, hospitalization with intensive care and mortality[25,26] Similar to reports by Taj et al,[16] in our study, increased levels of C reactive protein was seen in 70.2% of patients with an overall mean±SD of 36.1±41.8mg/L. The frequency was lesser than 41.6% reported by Puri et al [27].

Ferritin is an iron-storing protein primarily involved in acute phase reactions. Elevated levels of serum ferritin are seen during viral infections due to inflammation.[28] Previous studies have reported positive association of serum ferritin with COVID-19 severity. In our study 77.6% patients reported elevated serum ferritin levels and the overall mean±SD was 485.2±452.2ng/mL significantly higher than the normal range. These findings are consistent with reports by Zhou et al[4] and Puri et al.[27]

The enzyme lactose dehydrogenase is activated secondary to tissue damage and it precipitates inflammatory reaction. In COVID-19, in the presence of tissue damage, lactose dehydrogenase activates inflammatory response and results in hypoxia, necrosis and cell death.[28,29] Hence, elevated levels of the enzyme are common in COVID-19 disease. In our study, the overall mean±SD of lactose dehydrogenase (707.4±488.9U/L) was significantly higher than normal levels. Frequency of patients with elevated lactose dehydrogenase levels were 79.7%, which was in accordance to reports by Puri et al[27] Zhou et al.[4]

It is well known that older age and males are at higher risk of COVID-19 infection[30] In view of this, we further assessed the effect of demographics on hematological and/or coagulation parameters in COVID-19 positive patients. Compared to other age groups, incidence of

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decreased hemoglobin was higher in age group 51-70 years (p=0.000). Age was significantly associated with changes in hematological parameters such as neutrophil count (p=0.017), lymphocyte count (p=0.001), ALC (p=0.000). Coagulation parameter D-Dimer was lower in age group 31-50 years (p=0.007). Association of sex on the hematological and coagulation parameters are shown in Table 6. Incidence of decreased hemoglobin counts (p=0.000) and increased D-dimer counts (p=0.016) were higher in males than females. No significant association was noted between sex and other hematological or coagulation factors ($p<0.05$).

In our study apart form age and sex other baseline clinical characteristics including status of comorbidities, underlying medications were not recorded. Secondly, disease severity on admission/consultation was not recorded which may influence hematological changes and disease prognosis. While we recorded the commonly used hematological and coagulation parameters associated with COVID-19, specific coagulation related parameters like fibrinogen and von-willebrand factor antigen were not recorded which could have shed more light into the COVID-19 infection related changes. Although 300 patients is an adequate sample size for a single center study, we further recommend multicenter studies having larger samples including patients with different regions, ethnicities and cultural background, with and without comorbidities to further substantiate the demographic relationship with hematological changes.

Conclusion

COVID-19 results in significant changes in hematological and/or coagulation parameters including decreased hemoglobin, lymphocytes, platelets, ANC and ALC and increased leucocytes, neutrophils, D-Dimer, C reactive protein, serum ferritin and lactose dehydrogenase. Moreover, these changes were influenced by demographics factors. These findings highlight the importance of Laboratory investigations at the initial stage of COVID-19 disease.

References

1. World Health Organization. WHO Coronavirus (COVID-19) Dashoard. Last updated 23 June 2022. Available from: https://covid19.who.int/. Last accessed 25 June 2022.
2. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ; HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020 Mar 28;395(10229):1033-1034.
3. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020 Apr;18(4):844-847.
4. Zhou F, Yu T, Du R et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective Cohort study. Lancet 2020; 395:1054-62.
5. Liao D, Zhou F, Luo L, Xu M et al. Haematological characteristics and risk factors in the classification and prognosis evaluation of COVID-19: a retrospective cohort study. Lancet Haematol 2020 July 20; 7: 671-78.
6. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associatedwith poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020; 18: 844- 47.
7. Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol. 2020 Jun;7(6):e438-e440.
8. Fei Y, Tang N, Liu H, Cao W. Coagulation Dysfunction. Arch Pathol Lab Med. 2020 Oct 1;144(10):1223-1229.
9. Guevara-Noriega KA, Lucar-Lopez GA, Nuñez G, Rivera-Aguasvivas L, Chauhan I.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 02, 2023

Coagulation Panel in Patients with SARS-CoV2 Infection (COVID-19). Ann Clin Lab Sci. 2020 May;50(3):295-298.
10. Fan BE, Chong VCL, Chan SSW, Lim GH, Lim KGE, Tan GB, et al. Hematologic parameters in patients with COVID-19 infection. Am J Hematol. 2020 Jun;95(6):E131-E134.
11. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr 30;382(18):1708-1720.
12. Huang X, Wei F, Yang Z, Li M, Liu L, Chen K. Lactose Dehydrogenase in Patients with Severe COVID-19: A Meta-Analysis of Retrospective Study. Prehosp Disaster Med. 2020 Aug;35(4):462-463.
13. World Health Organization. Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases, 19 March 2020. Available from: https://www.who.int/publications/i/item/10665-331501 Last accessed: 25 June 2022
14. Asghar MS, Khan NA, Haider Kazmi SJ, Ahmed A, Hassan M, Jawed R, et al. Hematological parameters predicting severity and mortality in COVID-19 patients of Pakistan: a retrospective comparative analysis. J Community Hosp Intern Med Perspect. 2020 Oct 29;10(6):514-520.
15. Keski H. Hematological and Inflammatory Parameters to Predict the Prognosis in COVID-19. Indian J Hematol Blood Transfus. 2021 Oct;37(4):534-542.
16. Taj S, Kashif A, Arzinda Fatima S, Imran S, Lone A, Ahmed Q. Role of hematological parameters in the stratification of COVID-19 disease severity. Ann Med Surg (Lond). 2021 Feb;62:68-72.
17. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, Liu S, Yang JK. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. Front Public Health. 2020 Apr 29;8:152.
18. Yamanaka T, Matsumoto S, Teramukai S, et al. The baseline ratio of neutrophils to lymphocytes is associated with patient prognosis in advanced gastric cancer. Oncology. 2007;73:215–220.
19. Rangel FAL. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C reactive protein in patients with severe coronavirus disease 2019 (COVID-19): A meta- analysis. J Med Virol. 2020 Oct;92(10):1733-1734.
20. Liao D, Zhou F, Luo L, Xu M, Wang H, Xia J, et al. Haematological characteristics and risk factors in the classification and prognosis evaluation of COVID-19: a retrospective cohort study. Lancet Haematol. 2020 Sep;7(9):e671-e678.
21. Gaffoor N, Archana Shetty, Muralidhar A, Minal J, Nikhil PV, Edupuganti HS.White Blood Cells in COVID-19: A Study on Viral Induced Cytopathic Changes in the Peripheral Smear J Clin of Diagn Res.2022; 16(3):EC08-EC11
22. Liu J, Liu Y, Xiang P, Pu L, Xiong H, Li C, et al. Neutrophil-to- lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage. J Transl Med. 2020 May 20;18(1):206.
23. Bansal A, Singh AD, Jain V, Aggarwal M, Gupta S, Padappayil RP, et al. The association of D-dimers with mortality, intensive care unit admission or acute respiratory distress syndrome in patients hospitalized with coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. Heart Lung. 2021 Jan-Feb;50(1):9-12
24. Snijders D, Schoorl M, Schoorl M, Bartels PC, van der Werf TS, Boersma WG. Ddimer levels in assessing severity and clinical outcome in patients with community‐acquired pneumonia. A secondary analysis of a randomised clinical trial. Eur J Intern Med 2012;23:436‐41.
25. Chen W, Zheng KI, Liu S, Yan Z, Xu C, Qiao Z. Plasma CRP level is positively

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 02, 2023

associated with the severity of COVID-19. Ann Clin Microbiol Antimicrob. 2020 May 15;19(1):18.

26. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. Am J Hematol. 2020 Jul;95(7):834-847.
27. Puri SS, Singhal P, Singhal S. Study of laboratory parameters in COVID‑19 patients at a tertiary care teaching hospital in Uttar Pradesh. Acta Med Int 2021;8:100‑6.
28. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. 2020 Jul 1;180(7):934-943.
29. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus‑infected pneumonia in Wuhan, China. JAMA 2020;323:1061‑9\
30. Farshbafnadi M, Kamali Zonouzi S, Sabahi M, Dolatshahi M, Aarabi MH. Aging & COVID-19 susceptibility, disease severity, and clinical outcomes: The role of entangled risk factors. Exp Gerontol. 2021 Oct 15;154:111507.