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Spectrum Of Changes In Various Hematological Parameters In Covid-19 Patients – A Tertiary Centre Study

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Abstract

Aims and Objectives: To analyse the spectrum of changes in various haematological parameters in Covid 19 infected patients.

Materials and Methods: This is a retrospective, observational study conducted on 100 patients with laboratory confirmed covid 19 status. Data was collected from patients admitted in Covid-19 ward and ICU between October 1st 2021 to December 31st 2021. Basic demographic data was collected from Laboratory Information System(LIS) of our hospital . Whole blood EDTA sample sent from Covid-19 ward and ICU were processed in Beckman coulter DXH 520 hematology analyser for complete blood counts. Statistical analysis of the data was done and presented.

Results: A total of 100 patients were included in the study; showed varied hematological parameters. Demographic data revealed age ranging from 10 – 80 years of age. Males constituted 58 cases (58%) and females 42 cases (42%) with a male to female ratio of 1.3:1. Complete Blood Count (CBC) showed Hemoglobin (Hb) concentration ranged from 8.5 -19 g/dL and median value was 12.5gm/dL. RDW ranged from 12.6 – 20.1 with 38 cases showing > 15. Leucocytosis was observed in 39 (39%) cases with neutrophilic predominance. High ANC values seen in 44 (44%) cases. High ALC 17 seen in (17%) cases. Thrombocytopenia (<150000) seen in 80 (80%) cases. Increased NLR (>4.0) was seen in 41 cases.

Conclusion: Baseline alterations in CBC parameters with demographic data in the present study along with the articles reviewed from various countries can be used for risk stratification and timely treatment of Covid-19 infected patients.

Keywords: Covid-19, Hematology, Neutrophil to Lymphocyte ratio, Thrombocytopenia

Introduction

The novel corona virus, also known as COVID-19 and SARS-COV-2, was first reported in Wuhan, China, in December 2019 and is a highly contagious single stranded RNA virus. It has raised a global concern by rampantly spreading over 110 countries affecting over 118,000 cases in a short span of less than 4 months. Hence, World Health Organization (WHO) declared COVID-19 a pandemic on March 11. [1]By December 2022, there were 644,611,867 confirmed cases of COVID-19, including 6,631,588 deaths (2.2% mortality), reported by the World Health Organization (WHO).[2]

Clinically, COVID-19 presents with a wide range of signs and symptoms with primarily manifesting as a respiratory infection and later involving multiple systems. Symptoms are of wide variety; ranging from flu like symptoms to breathlessness, persistent dry

cough, loss of taste, loss of smell and other gastrointestinal symptoms. Common fatal complications including pneumonia, ARDS, metabolic acidosis, venous and arterial thrombotic complications, septic shock, and death. [3]Nearly 20% of patients with COVID-19 become critically ill, with a high mortality ranging from 8.1% to 33%.[4]With access to and appropriate use of existing and developing life-saving tools, COVID-19 can become a manageable disease with significantly reduced morbidity and mortality.

Although molecular identification of the virus by RT-PCR polymerase chain reaction (PCR) is the recommended method in diagnosing COVID-19 infection by WHO; radiological, biochemical biomarkers, and hematological studies are substantially important in risk stratification, patient follow-up, and outcome prediction.[5]

Complete blood count is the most easily available and the most common laboratory test performed and many of the hematological indices are varied in Covid-19 infected patients as revealed by the articles published by various countries.

Neutrophil Lymphocyte ratio (NLR) and PLR reflects the balance of the body's innate (neutrophil) and adaptive (lymphocyte) immune response. It is one of the important prognostic markers of systemic inflammatory response in critically ill patients along with other biochemical markers like d-Dimer, C-Reactive Protein, ferritin, IL-6 and pro-calcitonin.[6]

Lymphopenia is typically observed in positive Covid-19 patients and is considered as a cardinal laboratory finding, mostly associated with thrombocytopenia.[7] In addition to the above changes, presence of atypical lymphocytes, inclusion bodies, vacuolization, and blast-like lymphocytes (activated lymphocytes) on microscopy are also observed in COVID-19 patients.[8]

Hence, in the current COVID-19 scenario, it would be of utmost importance to explore if the most routine and cost-effective tests like CBC could serve as an aid in determining patient's clinical status or predicting severity of the disease leading to a better and judicious management of patient with early and timely clinical intervention.

Aims And Objectives:

To analyse the spectrum of changes in various haematological parameters in Covid 19 infected patients

Materials And Methods:

The current study is a retrospective study from October 2021 to December 2021 for a period of 3 months. 100 patients with confirmed COVID-19 infection admitted to BGS Global Institute of Medical Sciences are included in our study. A confirmed case of Covid-19 was defined by a positive result on a reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay of a specimen collected from nasopharynx. The blood samples were collected at the time of admission, in EDTA anticoagulant vacutainer. The samples were processed in Beckman Coulter DXH 520 5-part hematology analyzer. Hemoglobin (Hb), Hematocrit (HCT), Red blood cell count (RBC), Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), Red cell distribution width (RDW), WBC, Neutrophils (absolute neutrophil count), lymphocytes (absolute lymphocyte count), Platelet count, MPV. The demographic details and patient reports were accessed through the hospital data management system.

Descriptive statistics were used to summarize the data; results are reported as ranges or/and median as appropriate. Categorical variables were summarized as counts and percentages.

Results:

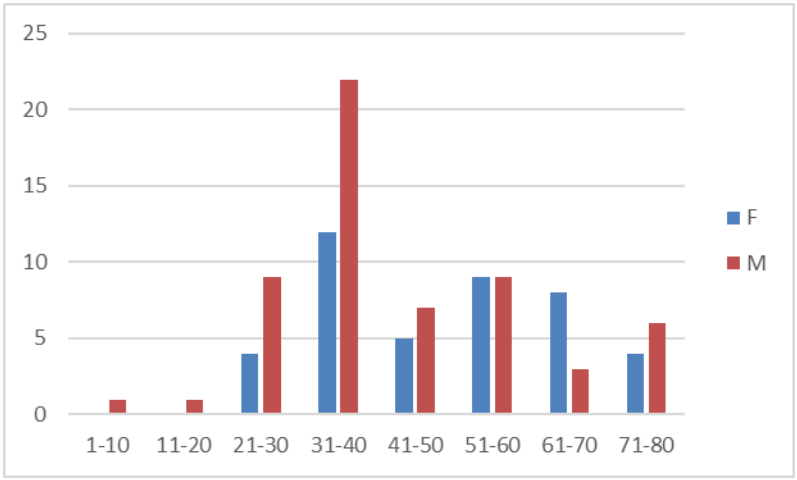
Out of 100 patients, **Age** ranged from 10-80 years of age in the current study. Males constituted 58 cases (58%) and females 42 cases (42%) with a male to female ratio of 1.3:1. Peak distribution of cases was seen in the age ranging from 31-40 years.

Volume 6, Issue 1; January-February 2023; Page No 612-618

Table 1 : Age and sex distribution of Covid-19 patients.

Age in years	Female	Male	Total	% of Grand Total
1-10	0	1	1	1%
11-20	0	1	1	1%
21-30	4	9	13	13%
31-40	12	22	34	34%
41-50	5	7	12	12%
51-60	9	9	18	18%
61-70	8	3	11	11%
71-80	4	6	10	10%
Total	**42**	**58**	**100**	**100**

Figure 1 : Bar chart showing age and sex distribution of Covid-19 patients



Hemoglobin concentration (Hb) ranged from 8.5 -19 g/dL and median value was 12.5gm/dL (mean 12.46); Reduced Hb was noted in 25 patients (25%) of which 14 females and 11 males were noted.

HCT concentration: 74 % of the patients had normal values; Higher HCT (>50) was noted in 3% of the cases; whereas lower value (<35) was noted in 23% of the cases.

RBC ranged from 2.8 – 6.9 with a mean of 4.39 (median 4.3). Normal RBC values was observed in 81 (81%) cases; RBC value was reduced (< 3.8) in 18 cases (18%) Increased in one case who was a female.

MCV ranged from 63 –114fL; less than 80 seen in 42 (42%) cases, more than 100 was seen in 3 (3%) cases. Rest of the 56 cases had normal values.

MCH ranged from 20.2 – 37pg; less than 27 seen in 21 (21%) cases; more than 31 seen in 7 (7%) cases. Rest 62 cases (62%) had normal MCH values.

MCHC ranged from 24 – 34g/dL; less than 32g/dL was seen in 63 (63%) cases; 37 cases (37%)had normal values.

RDW ranged from 12.6 – 20.1. 38 cases showed > 15 indicating moderate to severe anisopoikilocytosis.

Overall, there were no notable changes in RBC parameters apart from Hb and HCT which could be due to pre-existing anemia.

Volume 6, Issue 1; January-February 2023; Page No 612-618

Table 2 : Calculation of haematological parameters of Covid-19 patients.

Parameters	Mean	Median	Range
HB	12.46	12.25	8.5-19.1
RBC	4.39	4.3	2.8-6.9
RDW	14.71	14.4	12.6-20.1
WBC	9936	8525	2000-29400
Neutrophil	72.46	73	35-95
ANC	7581	6245	927-27930
Lymphocyte	22.13	20.5	4-58
ALC	1901.3	1551	214-8372
Eosinophil	1.5	1	0-5
Platelets	127479	112500	32520-394000
NLR	5.45	3.41	0.6-23.75

Total WBC count:

Ranged from 2000-29,400 ; mean of 9936 and median of 8525

Normal (4000-11000) WBC count seen in 40(40%) cases; High WBC count(>11000) seen in 39 (39%) cases. All these cases with high TLC showed neutrophilic predominance.

Low WBC count (< 4000) observed in 21 (21%) cases

The differential count in patients with leucopenia showed lymphocytic predominance in 2 (2%) cases while neutrophilic predominance in 19 (19%) cases.

Absolute Neutrophil Count ranged from 927-27930 with a mean of 7581 and median of 6245.

Normal ANC value (2000 – 7000) was seen in 47 (47%) cases.

Low ANC value observed in 9 (9%) cases.

High ANC values seen in 44 (44%) cases. 14 Females and 30 males were noted.

Of the 44 cases, 38 cases (86%) showed leucocytosis and 6 (13%) had normal TLC.

Absolute Lymphocyte Count ranged from 214 – 8372 with a mean of 1901 and median of 1551.

ALC values were normal in 56 (56%) cases.

Low ALC observed in 27 (27%) cases of which 15cases were males and 12 were females.

High ALC 17 (17%) cases.

Neutrophil Lymphocyte Ratio ranged from 0.6 – 23.75; with a mean of 5.45 and median of 3.41.

Out of 100 cases, normal values (0.7-4.0) seen in 58 (58%) cases

Reduced NLR (<0.7) was seen in 1 case;

Increased NLR (>4.0) was seen in 41 cases.

Females were 16 and males were 25 cases.

Platelet count:

Platelet count ranged from 32520 – 394000 with mean of 127479 and a median of 1,12,500.

Thrombocytopenia(<150000) seen in 80 (80%) cases.

Thrombocytosis (> 350000) seen in 3 (3%) cases.

Rest 17 cases (17%) had normal platelet count.

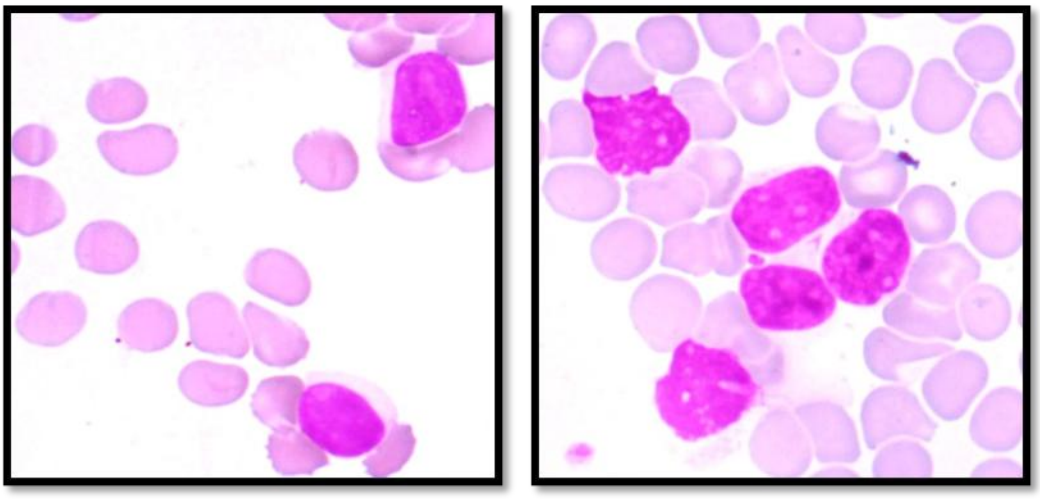
Platelet Lymphocyte Ratio ranged from 8 -869.

17 (17%) cases has high PLR with value > 172; of which highest PLR was seen in 1 male with value of 869.

Microscopy of peripheral blood smear showed presence of lymphopenia with reactive lymphocytes predominantly of monocytoid type (Figure 2).

Volume 6, Issue 1; January-February 2023; Page No 612-618

Figure 2: Peripheral blood smears (a, b) showing reactive (activated) lymphocytes on Covid-19 patients. (Leishman stain, 100X oil immersion)



Discussion:

In the presence of a rapidly emerging novel corona virus infection, identification of hematological parameters could help predict disease severity and prognosis thus guiding clinical care.

In our study, we observed that more men (58%) were affected compared to the women (42%). MERS-CoV and SARS-CoV have also been found to infect more males than females.[9,10,11] The reduced susceptibility of females to viral infections could be attributed to the protection from X-chromosome and sex hormones, which play an important role in innate and adaptive immunity. Additionally, about half of patients infected by 2019-nCoV had chronic underlying diseases, mainly cardiovascular, cerebrovascular, renal, hepatic diseases and Diabetes; this is similar to MERS-CoV.[10]

In the present study, low hemoglobin was observed in 25% of the patients. These results are consistent with the findings of Anegundi R et al.[7] Proposed mechanisms for reduced haemoglobin: a) SARSCoV-2 damages RBC membranes due to presence of angiotensin and ACE2-interacting proteins on the surface of RBCs b) direct attack of heme by virus c) dysregulated iron metabolism and d) auto-immune haemolytic anaemia within a timeframe of the cytokine storm.[12]

ALC was low in significant number of cases (27%) in the study. This result suggests that 2019-nCoV might mainly act on lymphocytes, especially T lymphocytes, as does SARS-CoV. Virus particles spread through the respiratory mucosa and infect other cells, induce a cytokine storm in the body, generate a series of immune responses, and cause changes in peripheral white blood cells and immune cells such as lymphocytes. Some patients progressed rapidly with ARDS and septic shock, which was eventually followed by multiple organ failure. Therefore, early identification and timely treatment of critical cases is of crucial importance.[13] Some studies suggest that a substantial decrease in the total number of lymphocytes indicates that corona virus consumes many immune cells and inhibits the body's cellular immune function. Damage to T lymphocytes might be an important factor leading to exacerbations of patients. Affinity for the virus for lymphocytic ACE receptors may attribute to its direct cytopathic effect. The low absolute value of lymphocytes could be used as a reference index in the diagnosis of new corona virus infections in the clinic.[14]

High NLR is indicative of patient's response to inflammatory insult, with neutrophils rising in response to stress, which, when overwhelming, induces lymphocyte apoptosis.[15,16] Neutrophils here seems act to as a double-edged sword. There is hypothesis that Neutrophil Extracellular Traps (NETs) released by neutrophils contribute to organ damage and death in COVID–19 patients. Also that development of Acute Respiratory Distress Syndrome (ARDS), thick mucus secretions in the airways and the development of blood clots, were

Volume 6, Issue 1; January-February 2023; Page No 612-618

similar to the symptoms of diseases already known to the researchers as being caused by NETs.[17]

Fox et al, Yao et al have documented neutrophil in the pulmonary capillaries of the three autopsy samples of COVID–19 patients further supports the theory that neutrophils may be responsible for mortality in the severe coronavirus cases.[18,19] Taken together, the high ANC with associated lymphocytopenia and hence a high NLR, seems to be an affirmation of dysregulated immune system which identify patients who have lesser physiological reserve to compete the inflammatory insult.

SARS-CoV-2 inhibits bone marrow hematopoiesis through specific receptors causing lymphopenia and thrombocytopenia.[8] Platelet production is also impaired due to direct viral insult to the bone marrow and impaired fragmentation of megakaryocytes due to COVID-19 induced damage to the lung and pulmonary capillary bed. However, data on thrombocytopenia is variable in various studies. Singh et al showed that incidence of thrombocytopenia as high as 57% amongst non-survivors.[8] In our study, severe thrombocytopenia (< 50,000) was seen in 4% of the cases. This was similar to the study by Patel et al.[9]

In this study, majority of the cases of thrombocytopenia showed high MPV ranging from 9.5 - 12.5% indicating the increased destruction of platelet and henceforth early release of young giant platelets.

NLR and PLR, both derived inflammatory indices, have an advantage of being relatively stable compared to individual blood cell parameters. PLR indicates the degree of cytokine storm and may serve as a novel marker for monitoring disease progression in Covid-19 patients.[12]

Most common peripheral blood smear finding is presence of lymphopenia with reactive lymphocytes, of which a subset appeared monocytoid or lympho-plasmacytoid type with vacuolar changes in the cytoplasm.[12] (Figure 2)

Limitations:

The study has a limitation that no asymptomatic carrier was included. We could not analyse and study the prognosis of the included cases. Severity of the patients was assumed based on admission to ICU, and not correlated clinically.

Conclusion:

Based on the demographic studies and routine haematological data, our study suggests that in adults, TLC, ANC, ALC, NLR and meticulous examination of peripheral smear can be used as a screening tool to identify patients requiring intensive care and thus enable the clinician for risk stratification and guide intervention.

References:

1. Al-Saadi EAKD, Abdulnabi MA. Hematological changes associated with COVID-19 infection. J Clin Lab Anal. 2022 Jan;36(1):e24064.
2. WHO Coronavirus Disease (COVID–19) Dashboard. Available from:https://covid19.who.int/
3. Smeeta Gajendra. Spectrum of hematological changes in COVID-19. Review article. Am J Blood Res 2022;12(1):43-53.
4. Liao D, Zhou F, Luo L, Xu M, Wang H, 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.
5. WHO policy brief: Covid-19 testing. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Policy_Brief-Testing-2022.1
6. Yan X, Li F, Wang X, Yan J, Zhu F, Tang S, et al. Neutrophil to lymphocyte ratio as prognostic and predictive factor in patients with coronavirus disease 2019: A retrospective cross-sectional study. J Med Virol. 2020;Nov:92(11):2573-2581.
7. Anegundi R, Rajeshwari T, CA Arathi, M Raghavendra. Impact of covid-19 on hematological parameters-a single centre study, International journal of scientific Research. 2020;Dec: 9(12).
8. Singh A, Verma S P, Kushwaha R, et al. (March 25, 2022) Hematological Changes in the Second Wave of SARS-CoV-2 in North India. Cureus 14(3): e23495.
9. Patel KV, Parmar AR, Sharma BS, Thacker M, Patel N, Patel B. A study of hematological parameters in patients with COVID-19 infection

Volume 6, Issue 1; January-February 2023; Page No 612-618

at a tertiary care centre. J Pathol Nep 2021;11:1852- 1858.
10. Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. Int J Infect Dis 2016; 49: 129–33.
11. Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection. J Immunol 2017; 198:4046–53.
12. Pujani M, Raychaudhuri S, Verma N, Kaur H, et al. Association of Hematologic biomarkers and their combinations with disease severity and mortality in COVID-19- an Indian perspective. Am J Blood Res. 2021 Apr 15;11(2):180-190.
13. Chen N, Zhou M, Dong X, Qu J, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020 Feb 15;395(10223):507-513.
14. Liu WJ, Zhao M, Liu K, Xu K, et al. T-cell immunity of SARS-CoV: Implications for vaccine development against MERS-CoV. Antiviral Res. 2017 Jan;137:82-92.
15. O'Mahony JB, Palder SB, Wood JJ, McIrvine A, Rodrick ML, Demling RH, et al. Depression ofcellular immunity after multiple trauma in the absence of sepsis. J Trauma. 1984Oct;24(10):869–75.
16. Dahn MS, Whitcomb MP, Lange MP, Jacobs LA. Altered T-lymphocyte subsets in severesepsis. Am Surg. 1988 Jul;54(7):450–5.
17. Barnes BJ, Adrover JM, Baxter-Stoltzfus A, Borczuk A, Cools-Lartigue J, Crawford JM, et al.Targeting potential drivers of COVID–19: Neutrophil extracellular traps. J Exp Med. 2020.Jun;217(6).
18. Fox SE, Akmatbekov A, Harbert JL, Li G, Quincy Brown J, Vander Heide RS. Pulmonary and cardiac pathology in African American patients with COVID-19: an autopsy series from New Orleans. Lancet Respir Med. 2020 Jul;8(7):681-686.
19. Yao XH, Li TY, He ZC, Ping YF, et al. [A pathological report of three COVID-19 cases by minimal invasive autopsies]. Zhonghua Bing Li Xue Za Zhi. 2020 May 8;49(5):411-417.

Volume 6, Issue 1; January-February 2023; Page No 612-618