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A Comparative Study in Hematological Parameters between First Wave Vs Second wave in ICU and non-ICU COVID-19 Patients in India

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Authors' contributions

This work was carried out in collaboration among all authors. Author EY, who did immense help in collecting data and has access to all data in this study. Author MV for accuracy of the data analysis. Author SS contributed for the research, experimental design and critical revision of the manuscript. All authors have reviewed and approved the final version.

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ABSTRACT

Aim: This study aims to determine similarities and differences in haematological parameters between the patients from two waves of severe acute respiratory syndrome coronavirus-2 infection at the time of hospital admission and identify risk biomarkers of COVID19 severity.
Study Design: A retrospective study.
Place of Study: The study was carried out in Saveetha Medical College and Hospital, Tamil Nadu, India.
Methodology: A total of 300 patients with COVID-19 infection, consisting of 150 patients from the first wave (April to June 2020) and 150 patients from the second wave (March to May, 20) were considered for this study. The hematological parameters of the patients were examined. Of the sample population from the first wave, 131 were admitted to the non-intensive care unit, and 19 were admitted to the intensive care unit (ICU). Of the sample population selected from the second wave, 101 were admitted to the non-intensive care unit and 49 were admitted to the intensive care

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unit. Statistical analysis of the data for both waves was carried out, and relevant findings were presented.

Results: Haematological parameters data were compared between the COVID19 positive patients admitted to ICU and non- ICU across both infection waves. On gender distribution, males were more than females in both waves. Degree of freedom analyses revealed an association of hematological parameters with the subsequent illness progression and severity in both the waves.

Conclusion: Our study showed that the severity of the disease was more in the second wave, especially among ICU patients than in the first wave. The majority of the infected patients were males in both waves. However, the presence of comorbidities, immune response, the severity of the infection, and other risk factors determines the progression of the disease.

Keywords: COVID-19 first wave; second wave; hematological parameters; neutrophilia; lymphopenia; neutrophil- lymphocytes ratio.

1. INTRODUCTION

COVID-19 is caused by the virus SARS-CoV-2 and was declared a global pandemic by the World Health Organization. It was first recognized in Wuhan city, China, in December 2019 [1]. In India , approximately 31,998,158 got infected, and 428,715 died due to COVID19 infection till August 10, 2021. Genetic sequencing of the virus suggests that it is a beta coronavirus closely linked to the SARS virus. The exact mode of transmission of the disease is not well known, and while the current information is limited, it supports person-to-person transmission. The most possible routes of transmission are thought to be droplet and contact-based [1,2]. The clinic pathological spectrum of SARS-CoV-2 infection is broad ranging from asymptomatic infection to fatal condition. Patients with mainly an upper respiratory tract infection are over 90% more likely to have more severe conditions and death, usually in older adults and people with certain pre-existing medical conditions [3]. Some common clinical manifestations in patients suffering from critical COVID-19 disease includes pneumonia, respiratory failure, acute respiratory distress syndrome (ARDS), venous thrombosis, lung thromboembolism, lung fibrosis, septic shock, systemic inflammatory response, renal damage, cardiovascular damage, blood vessel damage, and multiple organ failure [4]. Early detection of patients prevents the development of critical illness and optimizes the use of hospital resources [5]. COVID‑19 diseases are closely associated with haematological parameter changes in the complete blood picture. Haematological parameters have an important role in the early detection of the disease, considering the information they provide to clinicians regarding the inflammatory process [6]. This information includes hemoglobin, red blood cells indices, Total Leukocyte counts, Differential leukocyte counts, Platelet counts, neutrophil-lymphocyte ratio, and platelet- lymphocytes ratio to determine the severity of the infection [6]. Countries like India have faced a two-wave pattern in reported cases of COVID-19. In India, the first period of the pandemic was between the end of January to November of 2020, corresponding to the entire first wave, and the second period, was between February to June of 2021, corresponding to part of the second wave. Alterations in various haematological parameters between both waves have been recently documented in the world literature on SARS-Cov-2 infection. Hence, this study is an attempt to evaluate the similarities and differences of haematological parameters in COVID-19 patients in the Indian population in a single tertiary care centre.

2. MATERIALS AND METHODS

A retrospective study was carried out in line with research regulations, including the approval of the Ethical Committee. A total of 300 patients with COVID-19 infection from both 1st and 2nd waves were taken for this study. The diagnosis was confirmed by detecting SARS-CoV-2 RNA in oro-nasopharyngeal swab samples and Radiological images findings. Haematological parameters of 150 patients affected in the first wave, out of which 131 patients were admitted in non-intensive care units and 19 patients were admitted in intensive care units during the period of April to June 2020. 150 patients were affected in the second wave, out of which 101 patients were admitted in non-intensive care units and 49 patients were admitted in intensive care units during the period of March to May 2021. Analysis of haematological parameters was done by Sysmex Automated Haematology Analyser XN-

1000 at the department of Haematology, Saveetha Medical College and Hospital, India

3. RESULTS

Of the 150 cases admitted during the first wave, there were more males (69%) than females (31%) with a male to female ratio of 2.1:1. Among the 150 cases admitted in the second wave, there were more males (69%) than females (31%) with a male to female ratio of 1.7:1. The gender distribution among the admitted cases in both waves showed a male predominance (Table 1) (Fig. 1). The most common changes seen in both waves include Anaemia, Leukopenia, Leukocytosis, Neutrophilia, lymphopenia, thrombocytopenia and a few cases of thrombocytosis. Furthermore, the need for intensive care unit admission, length of hospitalization and oxygen demand at the time of hospital admission for the patients were more in the second wave than in the first infection wave.

Table1. Gender distribution comparison of 1st and 2nd wave

Parameters	COVID-19 patients in the 1st wave	COVID-19 patients in the 2nd wave
Total no. of cases	150	150
Sex	Male - 103 Female - 47	Male - 95 Female - 55

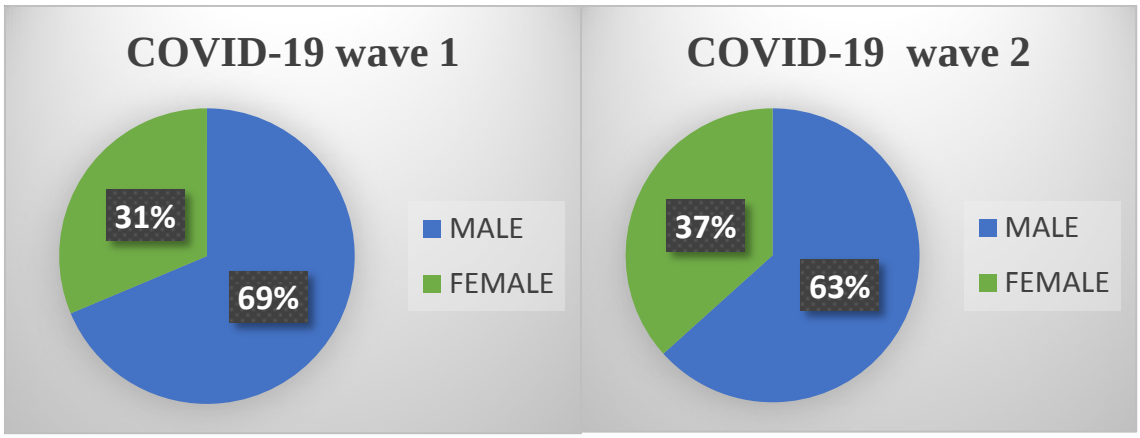

Fig. 1. Gender distribution showing male predominance in both waves

Table 2. Hematological parameters-comparison between 1st and 2nd wave in COVID19 patients admitted in the intensive care unit

Parameters	COVID-19 patients in the intensive care unit during the first wave (Mean ± SD)	COVID-19 patients in the intensive care unit during the-second wave (Mean ± SD)	P- value
Haemoglobin (g/dl)	11.83 ± 2.2 Minimum- 8.3 Maximum- 16.5	11.94 ± 2.3 Minimum- 6.6 Maximum- 15.7	0.87
RBC (x 10^6/ µl)	4.27 ± 0.5 Minimum- 3.4 Maximum- 5.3	4.35 ± 0.8 Minimum- 2.2 Maximum- 5.4	0.06
Haematocrit (%)	36.4 ± 6.3 Minimum- 26.8 Maximum- 49.1	39.27 ± 8.1 Minimum- 20.6 Maximum- 66.8	0.18
MCV (fL)	85.4 ± 9.1 Minimum- 62.9 Maximum-95.9	88.6 ± 7.5 Minimum- 66.1 Maximum- 102.3	0.14

Parameters	COVID-19 patients in the intensive care unit during the first wave (Mean ± SD)	COVID-19 patients in the intensive care unit during the second wave (Mean ± SD)	P- value
MCH (pg)	27.25 ± 3.4 Minimum- 19.6 Maximum- 31.3	27.40 ± 2.8 Minimum- 18.0 Maximum- 35.0	0.85
MCHC (g/dl)	31.86 ± 1.3 Minimum- 29.1 Maximum- 33.6	30.73 ± 1.8 Minimum- 27.0 Maximum- 34.7	0.02
RBC distribution width(%)	14.95 ± 1.6 Minimum- 12.3 Maximum- 19.4	15.01 ± 2.0 Minimum- 12.3 Maximum- 19.4	0.90
WBC (x 10^3/µl)	12.7 ± 5.6 Minimum- 5.58 Maximum- 28.02	18.1 ± 11.8 Minimum- 3.52 Maximum- 59.37	0.06
Neutrophil count (%)	84.4 ± 6.8 Minimum- 61.4 Maximum- 91.0	90.3 ± 7.0 Minimum- 64.7 Maximum- 97.4	0.003
Lymphocyte count (%)	10.9 ± 5.2 Minimum- 4.9 Maximum- 25.8	6.6 ± 1.2 Minimum- 1.2 Maximum- 31.0	0.01
Eosinophil count (%)	0.5 ± 1.5 Minimum- 0 Maximum- 5.6	0.3 ± 0.9 Minimum- 0 Maximum- 5.8	0.40
Monocyte count (%)	3.8 ± 1.7 Minimum- 0 Maximum- 7.1	2.5 ± 1.3 Minimum- 0.6 Maximum- 6.2	0.001
Basophil count (%)	0.1 ± 0.07 Minimum- 0.1 Maximum- 0.4	0.1 ± 0.13 Minimum- 0 Maximum- 0.6	0.70
Absolute Neutrophil count	10,918 ± 5155 Minimum- 3426 Maximum- 24,601	16,923 ± 11,517 Minimum- 2478 Maximum- 56,579	0.03
Absolute Lymphocyte count	1255 ± 427 Minimum- 591 Maximum- 2297	778 ± 414 Minimum- 145 Maximum- 2648	0.001
Absolute Eosinophil count	46 ± 125 Minimum- 0 Maximum- 456	27 ± 77 Minimum- 0 Maximum- 459	0.45
Absolute Monocyte count	489 ± 415 Minimum- 0 Maximum- 1837	438 ± 372 Minimum- 40.9 Maximum- 1781	0.63
Absolute Basophil count	18 ± 11 Minimum- 1 Maximum- 56	23 ± 24 Minimum- 0 Maximum- 118	0.44
Platelet count (x 10^3/ µl)	3.01 ± 1.4 Minimum- 0.93 Maximum- 6.06	1.77 ± 1.1 Minimum- 0.21 Maximum- 5.41	0.001
Neutrophil lymphocyte ratio	9.32 ± 4.08 Minimum- 2.38 Maximum- 17.92	27.13 ± 22.15 Minimum- 2.08 Maximum- 80.91	0.001
Lymphocyte monocyte ratio	2.69 ± 1.2 Minimum- 0 Maximum- 4.7	3.3 ± 3.7 Minimum- 0.3 Maximum- 21.0	0.45

Table 3. Hematological parameters comparison between 1st and 2nd wave in COVID19 patients admitted in non-intensive care units

Parameters	COVID-19 patients in non- ICU in the first wave (Mean ± SD)	COVID-19 patients in non-ICU in the second wave (Mean ± SD)	P- value
Haemoglobin (g/dl)	13.0 ± 2.0 Minimum- 4.2 Maximum- 17.2	12.5 ± 2.1 Minimum- 5.4 Maximum- 16.1	0.05
RBC (x 10^6/ µl)	4.5 ± 0.7 Minimum- 1.3 Maximum- 6.8	4.5 ± 1.1 Minimum- 1.6 Maximum- 13.7	0.93
Haematocrit (%)	39.6 ± 9.6 Minimum- 4.8 Maximum- 91.3	39.6 ± 8.0 Minimum- 20.6 Maximum- 94.5	1.00
MCV (fL)	87.2 ± 6.2 Minimum- 67.4 Maximum- 114	87.0 ± 9.8 Minimum- 30.8 Maximum- 107.8	0.82
MCH (pg)	28.5 ± 3.1 Minimum- 13.3 Maximum- 39.7	28.0 ± 3.6 Minimum- 14.3 Maximum- 40.4	0.26
MCHC (g/dl)	32.8 ± 1.4 Minimum- 28.0 Maximum- 36.4	31.7 ± 2.0 Minimum- 24.4 Maximum- 41.7	0.001
RBC distribution width(%)	13.6 ± 2.0 Minimum- 2.8 Maximum- 25.5	15.4 ± 11.1 Minimum- 11.5 Maximum- 123.0	0.07
WBC (x 10^3/µl)	6.78 ± 2.4 Minimum- 1.54 Maximum- 14.8	7.4 ± 4.3 Minimum- 2.03 Maximum- 31.26	0.17
Neutrophil count (%)	62.5 ± 12.7 Minimum- 34.7 Maximum- 91.5	71.8 ± 14.0 Minimum- 36.2 Maximum- 95.7	0.001
Lymphocyte count (%)	29.4 ± 11.2 Minimum- 5.7 Maximum- 56.5	22.2 ± 12.0 Minimum- 1.8 Maximum- 52.4	0.001
Eosinophil count (%)	1.5 ± 2.1 Minimum- 0 Maximum- 12.1	0.7 ± 1.4 Minimum- 0 Maximum- 9.7	0.001
Monocyte count (%)	5.6 ± 2.2 Minimum- 1.1 Maximum- 13.1	4.9 ± 2.5 Minimum- 0.3 Maximum- 13.3	0.002
Basophil count (%)	0.3 ± 0.3 Minimum- 0 Maximum- 2.0	0.1 ± 0.1 Minimum- 0 Maximum- 0.7	0.001
Absolute Neutrophil count	4308 ± 2025 Minimum- 900 Maximum- 11,471	5628 ± 4112 Minimum- 1129 Maximum- 28,978	0.002
Absolute Lymphocyte count	1916 ± 948 Minimum- 449 Maximum- 5717	1369 ± 680 Minimum- 183 Maximum- 3513	0.001
Absolute Eosinophil count	126 ± 219 Minimum- 0	46 ± 83 Minimum- 0	0.001

Parameters	COVID-19 patients in non- ICU in the first wave (Mean ± SD)	COVID-19 patients in non-ICU in the second wave (Mean ± SD)	P- value
Absolute Monocyte count	Maximum- 1637 368 ± 152 Minimum- 39	Maximum- 428 340 ± 220 Minimum- 22	0.26
Absolute Basophil count	Maximum- 767 22 ± 23 Minimum- 0	Maximum- 1250 13 ± 13 Minimum- 0	0.001
Platelet count (x 10^3/ µl)	Maximum- 183 2.25 ± 0.8 Minimum- 0.14	Maximum- 58 2.05 ± 0.8 Minimum- 0.41	0.06
Neutrophil lymphocyte ratio	Maximum- 4.70 2.8 ± 2.2 Minimum- 0.6	Maximum- 4.71 5.6 ± 6.8 Minimum- 0.7	0.001
Lymphocyte monocyte ratio	Maximum- 16.0 5.8 ± 2.9 Minimum- 1.5	Maximum- 53.1 5.6 ± 5.5 Minimum- 0.7	0.74
	Maximum- 19.1	Maximum- 46.8	

Hb concentration changes in both waves in the ICU: Among the 19 cases of ICU admitted in the first wave, 5 cases were anemic and 14 cases were normal. Among the 49 cases in the second wave, 13 cases were anaemic. Hence ,anaemia was observed among the ICU cases of both waves of covid-19. The Minimum haemoglobin observed in the first wave was 8.3 g% and the second wave showed a minimum of 6.6g% .

WBC changes in both waves in the ICU: In the first wave, no one was leukopenia, 7 cases had a normal WBC count, and 12 cases had leucocytosis.In the second wave, 14 cases had normal WBC count, 2 cases had leukopenia, and 33 cases had leukocytosis. The minimum WBC count observed was 5580 cells/cu.mm and the maximum WBC count was 28000cells/cumm in the first wave, whereas in the second wave, the minimum WBC count observed was 3520 cells/cu.mm and the maximum WBC count was 59370 cells/cumm.

Platelet changes among both waves in the ICU: In the first wave, 12 cases had normal platelet count, 4 cases had low platelet count and 3 cases had thrombocytosis. In the second wave, 22 cases had normal platelet count, 25 cases had low platelet count and 2 cases—had thrombocytosis. The minimum platelet count observed was 93000 cells/cu.mm and the maximum platelet count was 6.06 lakhs/cumm in the first wave while in the second wave the minimum platelet count observed was 21000 cells/cu.mm and the maximum platelet count was 5.41lakhs/cumm.

NLR changes among both the waves in ICU: The minimum NLR observed was 2.38 and the maximum was 17.92 in the first wave, while in the second wave, the minimum NLR observed was 2.08 and the maximum was 80.91 .

Hb concentration changes among both the waves in non-ICU: Among the 131 cases of non-ICU admitted in the first covid ,16 cases were anemic and 115 cases were normal. Among 101 cases in the second wave 18 cases were anaemic and the remaining were normal. Hence, anemia was observed among the non-ICU cases of both waves of covid-19 .The Minimum haemoglobin observed in the first wave was 4.2 g% and while the minimum for the second wave was 5.4g%.

WBC changes among both the waves in non-ICU: In the first wave, 13 cases had neutropenia, 110 cases had normal WBC count and 8 cases had leukocytosis .In the second wave, 19 cases had leukopenia , 69 cases–had normal counts, and 13 cases had leukocytosis. The minimum WBC count observed was 5580 cells/cu.mm and the maximum WBC count was 28000cells/cumm in the first wave while in the second wave, the minimum WBC count observed was 3520 cells/cu.mm and the maximum WBC count was 59370 cells/cumm .

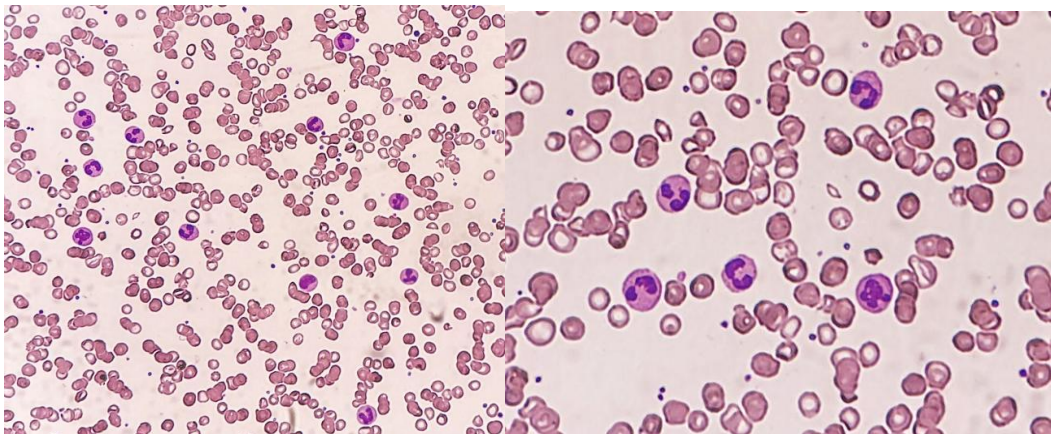

Fig. 2a & b. Peripheral blood smear of COVID-19 patient showing microcytic hypochromic red blood cells and increased neutrophils

Platelet changes among both the waves in non- ICU: In the first wave, 20 cases had low platelet count,110 cases had normal counts, and 1 case had thrombocytosis. In the second wave, 27 cases had low platelet count, 74 cases had normal counts, and 1 case had thrombocytosis. The minimum platelet count observed was 14,000 cells/cu.mm and the maximum count was 4.7 lakhs/cumm in the first wave while in the second wave, the minimum platelet count observed was 41,000 cells/cu. mm and the maximum—count was 4.7 lakhs/cumm.

NLR changes among both the waves in non-ICU: The minimum NLR observed was 0.6 and the maximum NLR was 16.0 in the first wave while in the second wave the minimum NLR observed was 0.7 and the maximum NLR was 53.1.

4. DISCUSSION

The present study showed that most of the haematological parameters behaved similarly across both 1st and 2nd waves of COVID19 infection with regard to disease severity, however, remarkable differences were found in Hemoglobin concentration, and in the differential counts of Neutrophils, Lymphocytes, and Monocytes. Statistically significant differences were also seen in the absolute counts of Neutrophils and Lymphocytes, Platelet count, and the Neutrophil Lymphocyte ratio (NLR) in critically ill patients admitted to the ICU. Whereas in non- ICU patients, Hemoglobin concentration, Mean corpuscular hemoglobin concentration, Red cells distribution width, Leukocyte counts, Neutrophil counts, lymphocytes counts, eosinophils count monocytes counts, Absolute neutrophil counts, Absolute lymphocyte counts, Absolute eosinophils counts, Absolute basophil counts , platelet counts and Neutrophil lymphocyte ratio (NLR) showed significant differences between both waves. On combined analysis of both ICU and non-ICU patients showed a decrease in haemoglobin concentration and MCHC in the second wave rather than the first wave. Neutrophilia and Lymphopenia were observed in second wave patients but not in first wave patients. There was an increase in NLR in both the waves but more severe in second wave patients. Here, by using a single tertiary care centre study and keeping several variables identical, we found that a predictive model developed with data from the first wave of infection could be validated in a second wave, but some risk biomarkers lost their independent significance. Our study, from—a multivariate analysis, could be affected by a series of confounding and collider biases. Therefore, it should be considered as a descriptive analysis that cannot be interpreted in causal terms, but that suggests candidate predictors of poor prognosis at the time of hospital admission. Blood cell interactions are essential in the pathogenesis of inflammation, immune responses, hemostasis, and oncogenesis [7]. Several observational studies have suggested that the NLR, lymphocyte proportion, and the platelet-to-lymphocyte ratio (PLR) are inflammatory markers of immune-mediated, metabolic, prothrombotic, neoplastic diseases, and are widely investigated as useful predictors for prognosis in various diseases caused by infection. Researches done recently on COVID-19 indicated that severe patients tended to have higher NLR [8].

Our pooled analysis showed a significant association of decreased hemoglobin and RBC indices. ~~On~~ Peripheral blood smear examination of some patients showed microcytic hypochromic red blood cells in both waves but more in ICU patients (Fig. 2 a&b). Based on a meta-analysis, anemia seems to be associated with an enhanced risk of severe COVID-19 infection. The possible pathophysiological link between anemia and severe COVID-19 may be multifactorial [9-12]. In the circulation system, hemoglobin acts as a carrier for oxygen to target organs in the body. When the concentration of hemoglobin in the circulation is low, the transport of oxygen to several organs in the body will be disrupted, therefore causing hypoxia that will eventually result in multiple organ dysfunction, especially the respiratory system. SARS-CoV-2 can interact with hemoglobin on the erythrocyte through ACE2, CD147, and CD26 receptors. Both virus-hemoglobin interactions will cause the virus to attack the heme on the 1-beta chain of hemoglobin and cause hemolysis [13]. Other recent studies suggest SARS-CoV-2 may mimic the action of hepcidin which increases circulating and tissue ferritin while inducing serum iron deficiency and lack of hemoglobin, by consequence. The resulting hyperferritinemia will give rise to ferroptosis, with high oxidative stress and lipoperoxidation that can precipitate the inflammatory/immune over-response 'cytokine storm', and cause a severe outcome of the disease.A study by Agrawal A et al. found hemoglobin concentration was 13.85g/dl & 13.12g/dl in asymptomatic and symptomatic patients, respectively. Patients with decreased RBC indices should be advised to take extra precautions to minimize risk exposure [14].

A high white blood cell count is common in critically ill patients because damaged cells induce innate inflammation in the pulmonary parenchyma, which is largely mediated by pro-inflammatory macrophages and granulocytes [15]. Increased neutrophil differential and absolute counts have also been reported as a feature of COVID-19, with neutrophil activation being a prominent feature of blood transcriptomes in severe cases. Further analysis of granulocytes reveals alteration in gene expression in these cells, as opposed to a mere change in number in the circulation. Some markers of immature neutrophil are also upregulated in severe vs mild COVID-19 patients. In addition, plasma levels of LCN2, RETN and HGF produced by neutrophils, were recently proposed as predictors of clinical severity in critically ill patient.The median absolute neutrophil count in a study by Huang et al.11 was 5.0 x109/L, 5.0 x109/L in Wang et al.12, 4.47 x109/L in Wu et al.13, 2.7 x109/L in Young et al.14 and 2.6 x109/L in a study by Fan et al. Chen et al.22 study represented a median absolute neutrophil count of 5.0 x109/L and 38 cases (38%) showed neutrophilia. In this study, we found that lymphopenia was a predictor of the clinical severity and slow recovery of patients with COVID-19 disease. It was associated with inflammatory markers, grades of pneumonia severity and prolonged hospitalization. Normalization of lymphocyte count denotes recovery of COVID-19. SARS-CoV directly infects primary T cells and induces massive apoptosis leading to lymphopenia, while aborting the viral expansion in these cells. Coronavirus, also infects and destroys lymphocytes, which facilitate viral replication and persistence. Many previous studies, showed that the pathogenesis of COVID-19 have been linked to the virus's ability to infect T cells through the angiotensin-converting enzyme 2 receptors and cluster of differentiation, CD147-spike proteins [10].The final results were decreased levels of CD3+, CD4+, CD8+ T lymphocytes, and increased regulatory T cells. The elevation of pro-inflammatory cytokines with T cell lymphopenia predisposes to cytokine storm, thus resulting in more lymphocytic apoptosis and multi-organ failure in COVID-19 patients [11]. This mechanism is due to the activation of caspase-1 as an effector element of inflammasome promoting IL-1β production and inducing pyroptosis of lymphocytes. It was reported that SARS-CoV-related Viro-porin 3a activates the NLRP3 inflammasome and induces the secretion of IL-1β, which indicates that the SARS-CoV infection can cause cell pyroptosis [12]. The Viro-porin 3a has also been identified on the genome of SARS-CoV-2, which indicates that SARS-CoV-2 may cause NLRP3 inflammasome activation. SARS-CoV-2 can induce pyroptosis, particularly in lymphocytes, by induction of NLRP3 inflammasome. Elevated serum levels of IL-1β in COVID-19 patients also indicate the occurrence of pyroptosis, because IL-1β release is a downstream process of lymphocytes pyroptosis [13,14].

In the study by Guan et al. there were 914 patients out of 1099 with lymphopenia on admission while 370 cases (33.7%) had leukopenia [15]. Wu et al.13 showed an association between lymphopenia and the

development of acute respiratory distress syndrome (ARDS). A study done by Agrawal A et al in India highlighted a comparison of hematological parameters among asymptomatic and symptomatic COVID-19 patients. They had 9 out of 17 cases (52.94%) that were symptomatic and 10 out of 85 cases (11.76%) of asymptomatic patients with lymphopenia. A total of 19 out of 102 (18.63%) patients showed lymphopenia [16].

In our study, haematological biomarker of increased neutrophil-to-lymphocyte ratio at admission was found to be an independent risk factor for severe disease and mortality in COVID-19 patients .Neutrophil-to-lymphocyte ratio is stress and immune parameter. In COVID-19, the elevated neutrophils indicate the degree of the inflammatory response, and the decreased lymphocytes indicate the degree of immune imbalance. These associations are amplified by the concept of NLR [16,17]. The normal values of NLR in adults ranges from 1 to 2.3. The cut-off value of NLR could predict poor COVID-19 infection and it varies widely [18]. Liu et al. studied 115 COVID-19 infected patients and found the risk of developing severe disease is >50% in those with age ≥ 50 and NLR ≥ 3,13 at the time of first admission [18]. The study with 161 COVID-19 patients done by Wang et al found that NLR was statistically significantly higher in those who had severe infection than those who had more moderate infection. Lagadinou et al. Stated in their study with 64 adult patients in Greece that neutrophil lymphocyte ratio could predict the severity of SARS-cov2 infection. The presence of dyspnea, increased NLR were determined as independent risk factors for ICU admission, and NLR > 5.3 were found as optimal cut-off values for predicting admission to ICU [19].Several cohort studies on similar population found a statistically significant strong association of in-hospital mortality with neutrophil-lymphocyte ratio > 3.1. Due to some lack of a single universal definition for severe COVID-19 infection and the variable outcome measures used in different studies could explain this wide range and variances. However, there is an idea about the value of elevated neutrophil lymphocyte ratio in predicting severe COVID infection.

5. CONCLUSIONS

We concluded, that most of the hematological parameters analyzed behaved similarly in the two waves of COVID19 depending on the different disease stage of patients at the time of hospitalization. However, simple univariate analysis conducted in both waves revealed that hematological parameters such as anemia, neutrophilia, lymphopenia, monocytosis and increased NLR were associated with poor prognosis in patients admitted to the intensive care unit in the second compared to the first wave of covid-19. Other hematological parameters did not show any significant changes. Also, increased hospital stay, demand for oxygen, intensive care unit necessity and increased mortality rate were higher in COVID 19 second wave in India.

According to our knowledge many people died and children became orphaned during this COVID-19 pandemic in India. So an absolute there is a need psychological and financial support for the people who lost their loved ones.

6. LIMITATIONS OF THE STUDY

There were some limitations in our study. Firstly, this was a retrospective study, therefore, complete information was not available for all the patients. Secondly, our study was based on a data from a single tertiary care centre in Tamil Nadu; largescale studies involving other Tertiary hospitals are required.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

ETHICAL APPROVAL

This study was approved by the Ethics Committee of Saveetha Medical and Hospital.

CONSENT

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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