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A study on comparison of severity markers in first wave and second wave of COVID-19 in tertiary care centre: Our experience

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Abstract---Background: Haematological parameters have an important role in the early detection of the COVID19 disease. This study is aimed to study the hematological severity markers of COVID19 infected patients in first wave versus second wave in a tertiary care centre. Methods: This is a retrospective study done in government medical college/government general hospital, Suryapet. We collected the information regarding patient's data from hospital records who were admitted in the hospital during first wave in September 2020 and

compared it with the patients admitted in the second wave in May 2021. Results: In our study, a total of 341 patients with COVID19 infection admitted in our hospital were included. 136patients were admitted in first wave and 205 patients were admitted in the second wave. Out of 136 patients in first wave, 95 were admitted in non-ICU ward and 41 were included in ICU ward. We found that there is increased Absolute Neutrophil count, decreased Absolute Lymphocyte count and Platelet counts in second wave ICU patients. Conclusion: We conclude that based on the haematological parameters disease severity was more pronounced in second wave, especially ICU patients than first wave.

Keywords---COVID-19, absolute lymphocyte count, neutrophilia, first wave, second wave.

Introduction

The first case of the coronavirus disease-19 (COVID-19) pandemic was documented in the city of Wuhan, Hubei province, China in December 2019 [1]. Although more than half of cases of COVID-19 remain asymptomatic, other individuals experience symptoms ranging from influenza-like episodes (fever, cough, myalgia, etc.) to pneumonia, and occasionally respiratory distress along with thromboembolic complications (severe COVID-19)2. Several new kinds of covid variants emerge due to mutations leading to multiple waves or spikes of the pandemic. 3 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. Haematological parameters have an important role in the early detection of the disease, considering the information they provide to clinicians regarding the inflammatory process [4]. This study is aimed to study the hematological severity markers of COVID19 infected patients in first wave versus second wave in a tertiary care centre.

Materials and Methods

This is a retrospective study done in government medical college/government general hospital, Suryapet. We collected the information regarding patient's data from hospital records who were admitted in the hospital during first wave in September 2020 and compared it with the patients admitted in the second wave in May 2021. Hematological Parameters like haemoglobin, total leucocyte count, absolute neutrophil count, absolute lymphocyte count and platelet counts were compared. Statistical analysis was done by IBM SPSS software trial/student version 21. Results were expressed in numbers, frequencies, means and standard deviations. A P - value less than 0.05 was considered significant.

Results

In our study, a total of 341 patients with COVID19 infection admitted in our hospital were included. 136patients were admitted in first wave and 205 patients

were admitted in the second wave. Out of 136 patients in first wave, 95 were admitted in non-ICU ward and 41 were included in ICU ward. In the second wave, out of 205 patients 74 were admitted in ICU ward and 131 patients were admitted in non-ICU ward. According to age in first wave, mean age of patients admitted in ICU is 58.3years and non-ICU is 49.9years. Mean age of patients admitted in ICU in second wave is 51.3years and in non-ICU ward is 48.6years. There is statistical significant difference in age of ICU patients among both waves(p=0.007). According to gender, among 136 patients in first wave 87(63.9%) patients are males and 49(36%) patients are females. In second wave 205 patients, 149(72.6%) patients are males and 56(27.3%) patients are females. Equal gender distribution was observed, difference between these groups is not significant (p=0.08)

Table 1
Comparison of variables in ICU patients

Variables	First wave		Second wave		P- Value
	Mean	SD	Mean	SD	
Age	58.3	11.6	51.3	14	0.007
Haemoglobin	12.2	2.6	13.4	2.5	0.01
Total leucocyte count	10.7	5.5	12.2	6.3	0.2
Absolute Neutrophil count	9.1	5.0	11.2	5.4	0.04
Absolute Lymphocyte count	1.1	0.6	0.8	0.3	0.0005
Platelet count	280.7	181.0	217.9	98.2	0.01

Table 1 shows the comparison of haematological parameters in ICU patients in first wave and second wave. Mean Hemoglobin was lower (12.2) in first wave ICU patients compared to Second wave(13.4), difference between the means are statistically significant(p=0.01). Mean Total leucocyte count was low(10.7) in first wave compared with Second wave(12.2), difference between the means is not significant(p=0.2). Absolute Neutrophil count was high (11.2) in second wave ICU patients when compared with the first wave (9.1), difference between the means is statistically significant(p=0.04). Absolute Lymphocyte count was low (0.8) in second wave compared with First wave, but the difference between the means is statistically significant(p=0.0005). Mean Platelet count was low (217.9) in second wave ICU patients compared with the first wave (280.7), difference between means is statistically significant(p=0.01)

Table 2
Comparison of variables in non-ICU patients

Variables	First wave		Second wave		P- Value
	Mean	SD	Mean	SD	
Age	49.9	14.4	48.6	13.4	0.4
Haemoglobin	13.2	1.9	12.8	2	0.1
Total leucocyte count	9.9	4.7	10.2	4.7	0.6
Absolute Neutrophil count	7.4	4.2	9.1	6.4	0.04
Absolute Lymphocyte count	1.8	0.7	1.4	1	0.001
Platelet count	277	130	262.2	125.5	0.3

Table 2 shows the comparison of haematological parameters in Non ICU patients in first wave and second wave. Mean Hemoglobin was lower (12.8) in second wave non-ICU patients compared to Second wave (13.2), difference between the means are not statistically significant (p=0.1). Mean Total leucocyte count was low (9.9) in first wave compared with Second wave (10.2), difference between the means is not significant(p=0.6). Absolute Neutrophil count was high (9.1) in second wave non-ICU patients when compared with the first wave (7.4), difference between the means is statistically significant(p=0.04). Absolute Lymphocyte count was low (1.4) in second wave compared with First wave, but the difference between the means is statistically significant(p=0.001). Mean Platelet count was low (262.2) in second wave ICU patients compared with the first wave (277), difference between means is not statistically significant(p=0.3)

Discussion

COVID-19 is an enveloped single – stranded RNA virus which binds to an intrinsic membrane protein with enzymatic activity called ACE-2 receptors, which activates the renin angiotensin – aldosterone system.These ACE-2 receptors are expressed on endothelial cells, pulmonary alveolar cells, heart, kidney cells. These receptors shows 10 fold more affinity for SARS-Cov -2 virus than the SARS- Cov-1. [5,6,7] . COVID-19 is primarily manifested as a respiratory tract infection, emerging data indicates that it should be regarded as a systemic disease involving multiple systems including cardiovascular, respiratory, gastrointestinal, neurological, hematopoietic and immune system. 8-10. First case of COVID-19 in India was registered in January 2020 [11], it took more than a year to complete the first wave of COVID19 infection in India. During the prolonged first wave, India registered a less number of confirmed daily cases when compared with many other countries; this scenario started changing from March 2021, with the rapid rise of COVID-19-positive cases throughout the country. A comparison of COVID-19 positive cases between India and the rest of the world, as represented in the repository 'ourworldindata', showed that the first wave in India started in March 2020, achieved a peak in September 2020 with more than 90,000 confirmed cases/day, and gradually decreased in intensity with 10,000 confirmed cases/day in February 2021. Except for few countries including India, most of the other countries witnessed the first wave of COVID-19 before August 2020 while the second wave started appearing in August–September 2020 [12] followed by the third wave in March 2021 [13]. A comparative analysis of the number of COVID-19-positive patients in India with respect to other continents showed that India was behind or missed one wave that raised from September 2020 to February 2021. India witnessed Second wave of COVID19 in February to June of 2021.

In our study we found that older age group were admitted in ICU than non-ICU. This is in comparison with Fan et al. [20] study, in which median age of ICU patients was 54 years old while the median age of nonICU patients was 42 years old (P = 0.02) and Wang DW [19] et al. study, in which median age of ICU patients was 66 years and non-ICU patients was 51 years (P < 0.001). In both waves, Males were more commonly affected than females. In comparison of ICU patients haemoglobin, Absolute Neutrophil Count, Absolute Lymphocyte count and Platelet count showed statistically significant difference in both waves. In Non-ICU patients, Absolute Neutrophil Count and Absolute Lymphocyte count showed

Statistical significance. Neutrophilia and Lymphopenia are observed in both waves, both severity is more in second wave ICU patients. Thus the data from the first wave proved accurately in the second wave of COVID19, except few variables. There may be bias in our study, this could help in accessing the prognosis of patient at the time of hospital admission.

In our study, we found that haemoglobin showed statistically significant difference in ICU patients of first and second waves(p=0.001). In Non –ICU patients, there was no statistical significance between both waves(p=0.1). In Huang CL et al. Study [14] with 41 patients of COVID-19 pneumonia showed that the haemoglobin level of severe patients was lower, although the difference was not marked (122.0 g/l (111.0 - 128.0) vs 130.5 g/l (120.0 - 140.0), P = 0.20). In Guan WJ et al. [15] study, the haemoglobin level of 128.0 g/L (111.8 - 141.0) in severe group was lower than that of 135.0 g/L (120.0 - 148.0) in non-severe group (P < 0.001). The low incidence of anaemia in COVID-19 may relate to the long-life span of erythrocyte and the compensatory proliferation of erythrocyte induced by pneumonia associated hypoxia [16]. Hemoglobin acts as a carrier for oxygen to various organs in the circulatory system of our body. When the concentration of hemoglobin is low in our circulation, the transport of oxygen to several organs in the body will be disrupted, 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 virushemoglobin interactions will cause the virus to attack the heme on the 1-beta chain of hemoglobin and cause hemolysis [17]

In our study, we found that there was increase in white blood cell count in second wave ICU patients when compared with the first wave but the difference between the means is not statistically significant. (p=0.2) similar to Fan et al. [20] study (P = 0.87). 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 proinflammatory macrophages and granulocytes [18]. In our study, Absolute Neutrophil Count was increased in both waves showing statistically significant differences between the means of ICU and Non-ICU patients (p=0.04 & p=0.04). In Huang CL et al. [14] showed that median absolute neutrophil count (ANC) in ICU cases was 10.6 (5.0 - 11.8) x 109 /L, much higher than the 4.4 (2.0 x 6.1) x 109 /L in Non-ICU cases (P = 0.00069). In Wang DW [19] et al. study, median ANC of ICU and Non-ICU patients was 4.6 (2.6 - 7.) x 109 /L and 2.7 (1.9 - 3.9) x 109 /L, respectively. In Fan et al. study,[20] study of 69 confirmed cases of SARS– COV-2 infection from Singapore showed that ICU patients tend to develop neutrophilia with a median peak absolute neutrophil count of 11.6 x 109 /L, compared to 3.5 x 109 /L in the Non-ICU group.

We found that Lymphopenia was more pronounced in second wave ICU patients indicating severe dysfunctional inappropriate immune system during COVID19 progression, showing statistical significant difference with the first wave(p=0.0005). In Guan et al. [15] study, severe cases presented with lymphocytopenia more frequently (96.1 %, 147/153) vs non severe cases (80.4 %, 584/726); P < 0.001. Huang et al. [14] study showed that 85 % (11/13) of patients needing ICU care presented with low lymphocyte count vs. 54 % (15/28) of patients that did not need ICU care (P = 0.045). Wang DW et al. [19] study

found that ICU cases presented with lower lymphocyte count (median: 0.8, IQR: 0.5 - 0.9) vs. non-ICU cases (median: 0.9, IQR: 0.6 - 1.2) ; P = 0.03. Lymphocytes and their subsets play an important role in regulating immune homeostasis and inflammatory response in our body. The adaptive immune response to viral infections is exerted through the effector function of cytotoxic T lymphocyte (CTL)[21] response which specifically recognize and kill virus infected cells. Lymphocytes express the corona virus receptor ACE2 on their surface;[22] thus SARS–COV-2 may directly infect lymphocytes and ultimately lead to lysis.

The cytokine storm which is characterized by markedly increased levels of interleukins (mostly IL - 6, IL - 2, IL - 7, granulocyte colony stimulating factor, interferon - γ inducible protein 10, MCP - 1, MIP1 - a) and tumour necrosis factor (TNF) - alpha may also promote lymphocyte apoptosis. [23-25] Substantial cytokine activation may also be associated with atrophy of lymphoid organs, including the spleen, and further impairs lymphocyte turnover. [26] Jiang et al. [27] evaluated lymphocyte subsets in 103 patients, which revealed that CD3+, CD4+, and CD8+T cells and NK cells were significantly decreased in COVID-19 patients with a more severe decrease in CD8+T cells compared with CD4+T cells. Liu et al. [28] also found that the higher the RNA load in the nasopharynx, the lower the CD4+ and CD8+T lymphocyte count and these changes were closely related to the severity of COVID – 19.

In our study, we found that mean platelet count was lower in second wave ICU patients when compared with first wave showing statistical significant differene(p=0.01). In Non-ICU groups, platelet counts were almost similar with P=0.3. Thrombocytopenia cases were observed in second wave ICU patients. In Wang DW et al. [19] study, no significant difference (P = 0.78) was noted in platelet count between ICU cases (median: 142; IQR: 119 - 202) vs Non-ICU cases (median: 165; IQR: 125 - 188). In Huang et al. Study [14], 8 % (1/13) of patients needing ICU care presented with low platelet count vs 4 % (1/27) of patients that did not need ICU care (P = 0.45). Several mechanisms by which COVID-19 causes thrombocytopenia has been proposed which include - 1) Reduction in platelet production by direct viral infection of bone marrow cells by the virus, destruction of bone marrow progenitor cells by cytokine storm, and indirect effect of lung injury, 2) increased platelet destruction by autoantibodies and immune complex 3) platelet aggregation in the lungs, resulting in microthrombi and platelet comsumption.[26]. The limitations of the study is single centered study with limited number of patients, did not include other haematological parameters like Eosinophil count, Monocyte counts. As it is a retrospective study, there could be unintentional patient selection bias and complete information was not available for all the patients.

Conclusion

We conclude that Males were commonly involved in both the waves. Hematological parameters behaved similarly in both waves, but severity of the disease was more pronounced in second wave ICU patients with Neutrophilia, Lymhopenia and reduction in platelet counts. This has led to increased hospital stay, demand for oxygen in second wave. Presence of comorbidities, immune response and severity of disease will determine the progression of disease. Large

scale studies involving multiple tertiary care centres are required for further analysis.

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