Research article

Hematological profile of COVID-19 patients in Ramanagar district, Karnataka- A cross sectional study

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ABSTRACT

Introduction and Aim: Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which rapidly evolved into a pandemic infecting humans all over the world. Whether hematologic and immunologic responses play a crucial role in progression of COVID-19 is still not clear. Increasing scientific evidence has shown that abnormalities in routine hematological tests, have the potential to diagnose SARS-CoV-2 infection in an economical way. Major laboratory changes indicating systemic inflammation and multi-organ impairment including hematopoietic system leading to lymphocytopenia, neutrophilia, eosinopenia, mild thrombocytopenia and ratios derived from these hematological parameters indicated severe disease and/or fatal outcomes. The aim was to study the hematological profile of Covid-19 patients admitted at a tertiary care hospital at Ramanagar district.

Materials and Methods: This retrospective study included 260 confirmed cases of Covid-19 diagnosed at a tertiary health care centre. Demographic, clinical, laboratory, treatment, and outcome data were extracted from the institutional electronic medical records after obtaining permission from the concerned authorities. From CBC test results obtained neutrophil lymphocyte ratio was derived.

Results: The present study revealed that majority of Covid positive patients presented with lymphopenia. While a significant association was observed between N/L ratio and disease severity, no significant association was seen between platelet count and severity of the disease.

Conclusion: Since the results of the present study features lymphopenia among large proportion of patients and elevated N/L ratio among critically ill patients these markers could be utilized as useful prognostic indicators during the initial assessment of disease severity and thus appropriate management can be planned for such patients before the condition of the patient deteriorates.

Keywords: Hematological profile; COVID-19; lymphopenia; N/L ratio.

INTRODUCTION

Millions of people worldwide were affected by Coronavirus disease 2019 (COVID-19). The disease is caused by Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a positive-strand RNA virus belonging to *Coronaviridae* family with similarities in genomic structure of about 80% with SARS-CoV, whose symptoms bear a resemblance to community-acquired pneumonia (1,2). It has rapidly evolved from an epidemic outbreak into pandemic infecting humans all over the world. Many cases of pneumonia of unknown cause were reported in city of Wuhan since early December 2019 that swiftly spotted much attention. A new strain of coronavirus was identified in early January 2020, using next-generation sequencing from an infected patient, and was explicitly named as SARS-CoV- 2 by the Chinese Center for Disease Control and Prevention (CCDCP; 3). However, the World Health Organization (WHO) termed the new virus 2019 as novel coronavirus (2019-nCoV) on 12 January 2020 and then officially named this infectious disease as coronavirus disease 2019 (COVID-19) on 12th February 2020. On 11th March 2020, COVID-19 was declared as a pandemic by WHO (4).

Studies related to SARS-CoV and MERS-CoV infections have established the relationship between abnormalities of laboratory indices including leukocytes, lymphocytes, and eosinophil counts (5). Whether hematologic and immunologic responses play a crucial role in progression of coronavirus disease 2019 (COVID-19) is still not clear. Markedly shrunken spleen with reduced lymphocyte and macrophage proliferation was seen in autopsy of patients who died due to COVID-19 (1).

Lymphocyte's role in both inflammation and infections has been apparent. In recent studies, prognostic indicators in COVID-19-positive patients included circulating biomarkers representing

inflammation and the immune system dysfunction. Additionally, studies suggested that various inflammatory processes were regulated by thrombocytes and indicators of early inflammation included inflammatory biomarkers and their ratios (6, 7). Since, hematological parameters play a significant role in early diagnosis of the disease, due to the information they provide to physicians, their use in terms of diagnosis of Covid 19 has not been much investigated. In this current scenario of inextinguishable jeopardy, the major concern would stress on identification of effective diagnostic and prognostic biomarkers for the diagnosis and progression that indicate towards clinical worsening and mortality. Also increasing scientific evidence has proved the role of routine laboratory tests, particularly hematological tests in the diagnosis of SARS-CoV-2 infection. These parameters may assist in the prognosis of the disease and in the optimization of clinical monitoring which would be of more help in a rural setup where sophisticated investigations may not be available. Experience gained from previous SARS patients, caused by SARS-CoV-1 was known to cause thrombocytopenia by direct viral infection of bone marrow haematopoietic stem cells, auto-antibodies and immune complex formation, disseminated intravascular coagulopathy (DIC) and platelet consumption in lung epithelium (1). Also, there is scientific evidence suggesting relationship between major laboratory changes, systemic inflammation and multi organ impairment including hematopoietic system of which lymphocytopenia, neutrophilia, eosinopenia, mild thrombocytopenia being most common and ratios derived from these haematological parameters indicated severe disease and/or fatal outcomes (8). Thus the present study aims to search for routine hematological variables that may aid in the clinical diagnosis of suspected patients with SARS-CoV-2 infection or that can prognosticate the severity of the disease.

MATERIALS AND METHODS

This retrospective study included 260 diagnosed cases of Covid-19 diagnosed as per Ministry of Health and Family Welfare protocol and guidelines from Government of Karnataka (9, 10) admitted at a tertiary health care centre. Those admitted were categorized into mild, moderate and severe based on respiratory rate and SPO_2 levels. Baseline characteristics, clinical, laboratory, treatment, and outcome data was obtained from the Institutional electronic medical records after obtaining permission from the concerned authorities. Only RT-PCR and CBC test results obtained initially was used in the present study. From the values obtained Neutrophil Lymphocyte ratio (N/L) was derived. For studying the relationship between N/L ratio and severity of the disease, the patients were classified into two groups as those with N/L ratio<4 and N/L ratio >4 as previously described based on the findings of Patrice Forget (11).

Statistical analysis

The demographic and hematological parameters were expressed as mean ± standard deviation. To determine the normal distribution Kolmogorov–Smirnov test was used. For testing the association between severity of the disease and hematological parameters like N/L ratio and platelet counts, Pearson Chi square and Fisher exact test was used.

RESULTS

Among 260 confirmed cases of Covid-19, 63.6% were males and 36.4 % were females and the average age was 43.62. Vital haematological parameters included Hemoglobin (Hb) percentage, packed cell volume (PCV), Red Blood Cell (RBC) count, Mean Corpuscular volume (MCV), Hemoglobin concentration (MCH) and Mean corpuscular hemoglobin concentration (MCHC).

Out of the total cases, 20% of them had haemoglobin levels < 12 g%, Packed cell volume< 36%, 8% had RBC count<3.8million cells/cubic mm, 37.5% had MCV of <93fl, 20% of them had MCH <27pg and only 0.7 % of them had MCHC value of 31.5g/dl though their average values were 13.75, 41.48, 4.79, 84.12, 29.02 and 36.08 respectively (Table 1).

Table 1: Red blood cell parameters

Parameters	Minimum	Maximum	Mean±SD
Hemoglobin (g %)	6.3	18.8	13.75±2.17
Packed cell volume (%)	19.1	55.4	41.48±24.08
RBC(million/mm^3)	2.2	6.66	4.79±0.70
MCV(femto litre)	53.7	108.7	84.12±7.45
MCH (pg)	14.5	34.8	29.02±20.03
MCHC(g/dl)	27	36.6	36.04±21.98

SD = Standard Deviation

Laboratory data related to Leucocyte count revealed 9% of individuals featuring Neutrophil count of <40 (Neutropenia), 69% of individuals with Lymphocyte count <20 (Lymphopenia) and 3% of individuals with eosinophil count <1 (Eosinopenia) with their average values recorded as 62.86, 29.72 and 3.37 respectively (Table 2).

Table 2: White blood cell parameters

Parameters	Minimum	Maximum	Mean±SD
WBC count (cells/mm^3)	2600	16770	7610±4284
Neutrophils	32	95	62.86±13.7
Lymphocyte	6	60	29.72±13.34
Eosinophils	0	9	3.37±1.76

SD =Standard deviation

Table 3: Cross tab of N/L ratio and severity of disease

		Parameters	Mild	Moderate	Severe	Total
N/L ratio category	*1	Count	52.0	16.0	15.0	210.0
		Expected count	48.2	19.6	22.9	210.0
		% within severity	88.1	66.7	53.6	81.7
	#2	Count	7.0	8.0	13.0	47.0
		Expected count	10.8	4.4	5.1	47.0
		% within severity	11.9	33.3	46.4	18.3

N/L Ratio <4, N/L Ratio>4

Table 4: Test of association between N/L ratio and severity of the disease

Parameters	Value	df	Asymp.Sig. (2-sided)	Exact Sig. (2-sided)
Chi-square test	22.82	3	0.00	0.00
Likelihood ratio	19.42	3	0.00	0.00
Fisher's Exact Test	19.77			0.00
No of valid Cases	257			

Table 5: Cross tab of platelet count and severity of disease

		Parameters	Mild	Moderate	Severe	Total
Platelet count category	*1	Count	28.0	12.0	17.0	69.0
		Expected count	31.8	13.1	15.3	69.0
		% within severity	48.3	50.0	60.7	54.8
	#2	Count	30.0	12.0	11.0	57.0
		Expected count	26.2	10.9	12.7	57.0
		% within severity	51.7	50.0	39.3	45.2

*Platelet count <1.5, # Platelet count >1.5

Table 6: Test of association between N/L ratio and severity of the disease

Parameters	Value	df	Asymp.Sig. (2-sided)	Exact Sig. (2- sided)
Pearson Chi-Square	4.250	3	0.236	0.243
Likelihood Ratio	4.406	3	0.221	0.227
Fisher's Exact test	4.196		…	0.245
No. of valid cases	126			

Relationship between disease severity and N/L Ratio revealed a significant association with the severity of the disease. However there was no significant association between platelet count and severity of the disease (Tables 3-6).

DISCUSSION

Since high infectivity and mortality rates are seen among patients suffering from COVID-19, until now, many articles related to the clinical features and laboratory data of COVID-19 patients have been discussed (11-13), in which most of the laboratory findings featured significant differences in the hematological parameters between severe and mildly infected patients during admission. The role of laboratory parameters in assessing the disease severity of COVID-19 were also published in several articles (14-16). The current study attempted to display the values of routine hematological tests and its association with the disease severity.

The mean hemoglobin in our study was found to be within normal range. A few studies have shown relatively higher Hemoglobin content in Covid positive patients. Probable explanation would be presence of comorbidities, cigarette smoking and gender in the study group. Stringent large scale studies accounting for the above mentioned factors can shed more light on this parameter variation (7).

The present study revealed that majority of them presented with lymphopenia which is quite similar to the studies of Zaboli *et al* (17) and Zhao *et al* (18). Since neutrophils on the other hand are the cell lines of defence and are increased as a part of the cytokine surge in COVID patients, combining both, the neutrophil to lymphocyte ratio (NLR) has been used as a parameter to differentiate the type of infection. NLR is significantly more in patients with fever due to bacterial infections than those with fever due to a viral etiology. In Covid the same has been used for grading the severity. The present study revealed a significant association between N/L ratio and disease severity quite consistent to the findings of Acar *et al*(19) and Wig *et al*(20) whose findings concluded that NLR at the initial admission has high predictive value for progressive disease worsening and adverse clinical outcome. However there was no significant association between platelet count and severity of the disease, which was similar to the study of Taj *et al* (21) who stressed the importance of NLR at the initial admission in the prognosis of disease besides other haematological parameters.

Limitations of current study

The study included a relatively small sample size. Hematological parameters obtained at the time of admission is only studied. Serial counts have not been accessed. Further studies shall include the dynamic hematological profile in assessing the prognosis and initiating appropriate interventions.

CONCLUSION

The results of the present study features lymphopenia among large proportion of patients and elevated NL ratio among critically ill patients. Thus these markers may be utilized as useful prognostic indicators during the initial assessment of disease severity and thus appropriate management can be planned for such

patients before the condition of the patient deteriorates in resource limited settings.

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CONFLICT OF INTEREST

None

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