



SPECTRUM OF HAEMATOLOGICAL ABNORMALITIES IN COVID-19 PATIENTS: A 1-YEAR STUDY IN A TERTIARY CARE CENTRE IN NORTH EAST INDIA.

Pathology

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) is a novel infectious disease caused by SARS-CoV-2 which was first recognized in Wuhan, China, in December 2019. Patient of COVID-19 presents with wide range of hemostatic abnormalities. The aim of this study is to evaluate the pattern of the hematological parameters in COVID-19 patients. **Method:** A cross-sectional study was conducted in Department of Pathology, RIMS, Imphal from May 2020 to May 2021. Total of 594 COVID-19 positive cases were included, data collected in IBM SPSS Statistics 21 was statistically analysed. **Results:** Among the 594 patients, 366 (61.6%) were male, 228 (38.4%) female with an age range of 1 to 90 years (Mean $\pm$ SE, 44.21 $\pm$ 18.52). COVID -19 was most common in the age group of 21-30 years and 31-40 years. Low hemoglobin was seen in 191 cases (32.2%), lymphopenia in 217 cases (36.5%), leukocytosis in 163 cases (27.4%) and thrombocytopenia in 160 cases (26.9%). **Conclusion:** Lymphopenia, neutrophilic leukocytosis, decreased hemoglobin and thrombocytopenia were common findings in Covid-19 patients with a male predominance.

KEYWORDS

Coronavirus disease (COVID-19); Lymphopenia; Leucocytosis; Thrombocytopenia

INTRODUCTION

In late December 2019, an outbreak of a mysterious pneumonia characterised by fever, dry cough, and fatigue and occasional gastrointestinal symptoms happened in a seafood wholesale wet market, the Huanan Seafood Wholesale Market, in Wuhan, Hubei, China.¹ However, in the following month (January) thousands of people in China, including many provinces (such as Hubei, Zhejiang, Guangdong, Henan, Hunan, etc) and cities (Beijing and Shanghai) were attacked by the rampant spreading of the disease. Eventually, the disease travelled to other countries and quickly established itself as a global pandemic till date. The exact mode of transmission of the disease is not 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-based and contact based.² The Covid -19 pandemic has heavily affected the global population. As of 10 December 2021, 4:48 pm CET, there have been 267,865,289 confirmed cases of Covid -19 including 5,285,888 deaths, reported to WHO.^{3,4} Further, in India, a total of 34,697,860 confirmed cases of Covid -19 and a total of 475,636 deaths has been reported as of December 13, GMT, 2021.⁵ On the regional front, Manipur recorded a total of 108545 confirmed cases of Covid -19 and a total of 1716 deaths as of 13 December, 2021.⁷

Coronavirus is an enveloped, positive single strand RNA virus. It belongs to the Orthocoronavirinae subfamily, as the name, with the characteristic "crown-like" "spikes on their surfaces." Covid -19 is a systemic infection with cardiovascular, pulmonary, gastrointestinal, neurological and haematological manifestations.^{8,10} Covid -19 have been found to affect the haematological system in a varied manner according to various studies conducted in this area. A study conducted by Zhang W et al¹¹ showed, an increase in lymphocytes in 18.75% of the patients. Another study done to investigate the level of WBC among hospital admitted patients with COVID -19 and showed that leukopenia developed in 20% of patients.¹² A more recent study in Hanchuan City People's Hospital showed decreased WBC count among the vast majority (99%) of COVID -19 infected patients.¹³ Low platelets level (thrombocytopenia) was noted among COVID-19 patients on admission and ICU patients in 552 hospitals in 30 different provinces of China.¹⁴ In Beijing, 72.5% of COVID -19 patients developed thrombocytopenia among 13 patients from three hospitals, however, the reduction on platelet count did not reach to the level at

which bleeding happens.¹⁵ On the other hand, no significant changes in platelets level between patients with ARDS and patients without ARDS was reported in a study conducted by Wu et al.¹⁶ Other common alterations in haematological parameters in patients with COVID -19 are included prolonged activated partial thromboplastin time (APTT) as well as elevated D - dimer levels. Such coagulation parameters were markedly higher among COVID -19 patients compared with healthy controls individuals.¹⁷ Several studies have reported abnormality in D - dimer levels.^{18,19} Additionally, the complications and severity of the disease among patients with community acquired pneumonia was significantly associated with D - dimer elevated levels.²⁰ Thus, higher D- dimer level is associated with patients who require ICU treatment and more severe cases.¹⁹ Considering the high infectivity and increase mortality rates of patients infected with COVID -19, early diagnosis and appropriate treatment of patients likely to develop serious disease is of utmost importance in the present scenario. Real time polymerase chain reaction (RT -PCR) is considered the gold standard for the detection of COVID -19, but is not without any limitations. Limited testing capacity, high false -negativity, the need for qualified personnel, high cost, and delays in obtaining results make it difficult for mass screening in a situation where the virus is rapidly spreading.²¹

Complete blood counts (CBC) are easily performed and inexpensive. Included in the CBC are values such as white blood count, Neutrophil, Lymphocyte and Platelet count (PLT), Mean platelet volume and certain ratios of these values. These can be used as inflammatory markers. Regulated by mast cell, epithelial cells and macrophages, Neutrophil also take part in inflammatory processes. The role of lymphocytes in both inflammation and infection is evident.

Additionally, Thrombocytes also have importance in the regulation of various inflammatory processes while these parameters can be used as inflammatory markers by themselves, their ratios to one another may also be indicators of early inflammation.^{22,23} Circulating leucocytes respond to stress by increasing neutrophils and reducing lymphocytes; the ratio of these two parameters is also used as inflammatory marker.²⁴ Thus, abnormal haematological values in patients with COVID -19 may aid in early risk stratification and prognostication of these patients, ultimately leading to earlier interventions and ideally more favourable outcomes.²⁵

The present study aims at bringing forward the significance of the changes in haematological abnormalities in COVID -19 patients by using a simple and inexpensive test like a complete blood count (CBC). By monitoring parameters such as haemoglobin, absolute lymphocyte, neutrophilic count, platelet count, and total white blood cell (WBC) this study will try to show the common haematological abnormalities in COVID -19 patients which might help in the early diagnosis and better management of these patients.

METHODS

A cross sectional retrospective study spanning 1 year from May 2020 to May 2021 was conducted in the Department of Pathology, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur. All patients who tested positive for COVID-19 by RT-PCR and admitted in RIMS hospital during the study period were included in the study. Patient with known case of chronic diseases like chronic kidney disease, heart disease, liver disease and haematological disorders and patient undergoing immunosuppressive therapy were excluded from the study. All together 594 samples were studied. Venous blood was collected in an EDTA vacutainer tube from each patient by experienced medical professional. The samples were processed in Mindray BC-5150 5-part automated haematological analyser. Haemoglobin (Hb), total WBC count, absolute count of neutrophils, lymphocytes, monocytes and eosinophils along with platelet count were determined. Quality of test results were maintained by running commercially prepared three levels quality control reagents (low, normal and high) before running the patient's sample. Standard operational procedures (SOP) were strictly followed during the sample analysis. The reagents and samples were regularly checked.

Diagnostic criteria for Anemia : Male: Hb < 130 g/L, Female: Hb < 120 g/L, Leukopenia: WBC < 4 × 10⁹/L, Leukocytosis : WBC > 10 × 10⁹/L, Lymphopenia: ALC < 1 × 10⁹/L, Thrombocytopenia: platelet count < 150 × 10⁹/L.

Data collected was entered and analysed using IBM SPSS Statistics 21 for Windows. Descriptive statistics like mean, standard deviation, percentage and proportion were used.

Ethical approval was obtained from the Research Ethics Board, RIMS, Imphal. Consent was obtained from each patient before the procedure. Data collected were kept secured.

RESULTS

All together 594 samples were analysed, majority of the cases were male comprising 366 (61.6%) and 228 (38.4%) females with an age range from 1 to 90 years (Mean±SE, 44.21±18.52) Most of the cases were in the age group of 21-30 years and 31-40 years with 117 (19.7%) cases in each. Figure 1 shows the distribution of cases according to age groups.

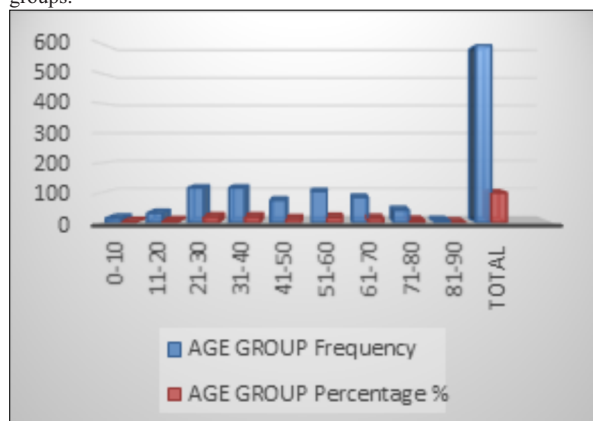


Figure 1: Bar graph showing the age-wise distribution of COVID-19 positive patients. (n=594)

Haemoglobin was decreased in 191 cases (32.2%) which was mostly seen in the 51-60 and 61-70 age groups with 43 and 33 cases each. (Table 1)

Leukocytosis was seen in 163 cases (27.4%) which was mostly seen in the 51-60 and 61-70 age groups with 43 and 40 cases each. Most of the cases with high TLC showed neutrophilic predominance which was

also seen in the 51-60 and 61-70 age group with 56 and 52 cases each. (Table 2)

Table 1: Table Showing Frequencies Of Hb Concentration Among COVID-19 Positive Patients

Haemoglobin	Frequency	Percent %
Increased	18	3
Decreased	191	32.2
Normal	385	64.8
Total	594	100

Table 2: Table Showing Frequencies Of WBC Count Among COVID-19 Positive Patients.

WBC	Frequency	Percent %
Leucocytosis	163	27.4
Leukopenia	34	5.7
Normal	397	66.8
Total	594	100

Lymphopenia was seen in 217 cases (36.4%) %, mostly in the 51-60 and 61-70 age groups with 57 and 43 cases each. (Table 3).

Table 3: Table Showing Frequencies Of Absolute Lymphocyte Count Among COVID-19 Positive Patients

LYMPHOCYTES	Frequency	Percent%
Lymphocytosis	24	4
Lymphopenia	217	36.5
Normal	353	59.4
Total	594	100

Thrombocytopenia was seen in 160 cases (26.9%), mostly in the 51-60 and 41-50 age group with 30 and 29 cases each. (Table 4).

Table 4: Table Showing Frequencies Of Platelet Count Among COVID-19 Positive Patients

PLATELET	Frequency	Percent
Thrombocytosis	21	3.5
Thrombocytopenia	160	26.9
Normal	413	69.5
Total	594	100

Most of the cases showed normal eosinophil and monocyte count with 546 (91.9%) and 528(88.9%) each.

DISCUSSION

In the present study majority of the patients were male with 366 (61.6%) cases which was similar to the other studies done by Huang et al, Guan W et al, Wu et al, Chen et al, Wang D et al, Yang X et al, Zhou et al, Liu Y et al, Anurag et al and Agrawal et al where male predominance was 58.1%, 58.1%, 72%, 68%, 58.1%, 54.3%, 67%, 58.8% and 75.4% respectively. 1,14,16,18,19,27,28,29,30,31 However , in the study done by Fan et al, there was equal sex distribution of Covid-19 positive cases .34 Our age range of 1 to 90 years, mean age of 44.21±18.52 was also similar to these studies. 1,14,16,18,19,27,28,29,30,31 Haemoglobin was decreased in 191 cases (32.2%) in our study , mostly seen in the 51-60 and 61-70 age groups which was also similar to the studies of Chen et al and Qian GQ et al where it was decreased in 51% and 36.3% of the cases respectively.18,33 In the study by Fan et al hemoglobin was decreased in the severe patients admitted in the ICU.32 However , in the study done by Wang Z et al, most of the patients had normal hemoglobin level.34.

In our study, leukocytosis was seen in 163 cases (27.4%) in which most of the cases showed neutrophilic predominance. These findings were also similar to the study by Chen et al and Wu et al where 38% and 34.5% of the cases showed neutrophilia respectively.18,35 In the studies by Wang D et al and Qian et al neutrophilic leucocytosis was seen in the more severe cases admitted in the ICU.19,36 However in the studies done by Huang et al, Fan et al, Wan et al, Xu et al, Zhang et al and Zhou et al, leukopenia was seen in 25%, 29.2%, 20.7, 21%, 19.6% and 17% respectively.1,32,37,38,39,40.

Lymphopenia was seen in 217(36.4%) of our cases and it is the most common finding in many studies done on Covid-19 patients. In the study done by Huang et al, Chen et al, Wang D et al, Fan et al, Qian et al, Wang Z et al, Wan et al, Zhang et al, Zhou et al, Yang et al and Zachariah et al lymphopenia was seen in 63%, 35%, 64%, 36.9%,

30.7%, 42%, 50.4%, 75.4%, 40%, 85% and 72% respectively. 1, 18, 19, 32, 33, 34, 37, 39, 40, 41, 42 Significant higher neutrophil to lymphocyte ratio, low monocyte and low eosinophil count was observed among the severe cases in the study done by Qin et al.36.

In the present study thrombocytopenia was seen in 160 cases (26.9%), mostly seen in the 41-50 and 51-60 age group, similarly thrombocytopenia was seen in the studies done by Guan et al, Chen et al, Fan et al, Qian et al, Wu et al, Wan et al and Zhou et al with 36.2%, 12%, 20%, 10.9%, 18.8%, 17% and 7% respectively. 14, 18, 32, 33, 35, 37, 40. Normal platelet count was seen in the studies done by Wang Z et al and Yang X et al. 34, 41.

CONCLUSION

From this study we can conclude that lymphopenia, thrombocytopenia, neutrophilic leucocytosis and decreased haemoglobin are common haematological abnormalities seen in COVID-19 patients, especially in the older adults age groups of 51-60 and 61-70. There was no significant changes in other haematological parameters. Therefore, monitoring and evaluation of these haematological parameters may be utilized as useful prognostic factor for early prediction of disease severity and appropriate management of the patients.

Conflict Of Interest

There are no conflicts of interest.

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