



HAEMATOLOGICAL PARAMETERS IN COVID-19 PATIENTS: OUR EXPERIENCE IN A TERTIARY CARE HOSPITAL IN THE NORTH EAST INDIA

Pathology

Junu Devi*

Associate Professor Department of Pathology, Gauhati Medical College, Guwahati, Assam, India. *Corresponding Author

Nilay Talukdar

PGT, Department of Pathology, Gauhati Medical College, Guwahati, Assam, India.

ABSTRACT

BACKGROUND: Covid-19 is a disease caused by Severe Acute Respiratory Distress syndrome Coronavirus 2 (SARS-CoV-2). Various changes occur in different haematological parameters in Covid-19 patients. Objective of the study is to evaluate the changes in primary haematological parameters and their significance in different groups of Covid-19 patients. **METHODS:** Laboratory data of randomly selected 100 laboratory confirmed SARS-CoV-2 positive patients (Covid 19) in a tertiary care centre (Gauhati Medical College Hospital) were retrospectively collected. Demographic data and laboratory test results of the patients were analysed. **RESULTS:** Covid 19 is more common in above 50 years of age. It slightly more common in males. Leukocytosis, lymphopenia ($P < 0.008$), thrombocytopenia, decreased haemoglobin levels ($P < 0.01$), decrease red blood cell count ($P < 0.0001$) were most commonly seen in above 50 age group ($P < 0.05$). Monocytosis ($P < 0.006$) was seen in below 50 years age groups. **CONCLUSION:** Covid-19 is more common in above 50 years age group. Changes in haematological parameters are good index and can be useful as indicators of disease progression and also helpful in disease prevention.

KEYWORDS

Covid-19, SARS-CoV-2, Haematology, Parameter

INTRODUCTION:

Severe Acute Respiratory Syndrome Corona virus 2 (SARS-CoV2) is a member of the subgenus *Sarbecovirus* of the genus *Betacoronavirus* in the family Coronaviridae.¹ It was first described in December 2019 when an out-break of unexplained pneumonia caused by SARS-CoV-2 occurred in Wuhan China.² The infection caused by SARS-CoV-2 had become major global health concern and World Health Organization (WHO) declared Pandemic status. SARS-CoV2 infected people of almost all countries worldwide.¹ This newly identified corona virus was described as novel corona virus by WHO and disease caused by it named as corona virus disease 2019 (Covid-19).³ Fever, dry cough and fatigue are the main manifestations of the disease. Patients with mild symptoms recover in 7-10 days. Severely infected patients often have dyspnoea or hypoxemia one week after the onset of symptoms. In some cases they can immediately progress to acute respiratory distress syndrome (ARDS), septic shock, metabolic acidosis, coagulation dysfunctions and multiple organ failure.⁴

Haematological parameters are important to correlate the signs and symptoms of Covid-19 patients which provide clues to aid diagnosis. Many cases of SARS CoV2 infection are associated with alteration of CBC (Complete Blood Counts) most commonly leukopenia. The extent of deviation from normal CBC appeared to correlate with severity of the disease. Severe cases were found to have higher leukocyte counts than the non-severe cases.⁵

There are four severity levels of Covid-19 based on the clinical manifestations- mild, moderate, sever and critical disease.⁶ Although many studies have described clinical, radiological and few laboratory test associated with Covid-19 there are only few studies on haematological parameter assessment specifically CBC analysis.

Purpose of the present study is to see the effect of Covid-19 on primary haematological parameters -WBC, RBC, Platelets and Haemoglobin(Hb),RBC indices, Neutrophil lymphocyte ratio(NLR) according to different age groups.

Materials And Methods : It is an observational study done in a tertiary care teaching hospital in the North East India. Randomly selected hundred patients during the period from July 2020 to October 2020, were analysed. Patients with positive SARS-COV2 RNA detected in nasal swab specimen by RTPCR were eligible. According to various literatures elderly people are at a higher risk of COVID-19 infection due their decreased immunity and body reserves, as well as multiple associated comorbidities like diabetes, hypertension, chronic kidney disease and chronic obstructive pulmonary disease. Comorbidities are more common above 50 years of age. Therefore, we divided the patients into two group according to age - below 50 years and above 50 years of age. Those patients in 0- 50 years are categorize as low risk(LR) group and those above 51- 80 years or above are

categorize as high risk group (HR).

Patients without haematological data are excluded from the study. Blood samples collected from Covid 19 patients were analysed for Complete blood count. Peripheral smears were prepared and stained with Leishman stain and correlated with findings of auto-analyzer results and cells were studied to see any morphological changes. Statistical analysis was done in excel sheet and $P < 0.05$ was taken as statistically significant.

Results and Observations: Primary haematological parameters of 100 patients were analysed.

Table: 1 Distribution of Covid 19 patients according to age and gender

Age group	Male	Female	Total
0-10	00	00	00 %
11-20	04	02	06 %
21-30	13	06	19 %
31-40	07	02	09 %
41-50	06	02	08 %
51-60	12	11	23 %
61-70	16	14	30 %
71-80 or >80	03	02	05 %
Total	61	39	100%

It has been noted that there are 42 cases in 0-50 years age range (low risk) and 58 cases in 51-80 or more than 80 years age range (high risk). Numbers of patients in high risk group is more than low risk group. M:F = 1.5 ($P = 0.5$).

Table:2 Distribution of Covid-19 patients according to religion

Religion	HR group N=58	LR group N=42	Total	P value
Hindu	31	28	59 %	P=0.39 chi square value =1.84
Muslim	18	10	28 %	
Christian	09	04	13 %	
Others	00	00	00 %	
Total	58	42	100 %	

Though maximum numbers of cases are seen in the Hindu community than other religions but it has no statistical significance ($P = 0.39$).

Table:3 Distribution of numbers of patients in High Risk (HR) & Low Risk (LR) group according to Haemoglobin (Hb) levels

Haemoglobin level	HR group n=58	LR group n=42	P value
Normal (13-15g/dl)	17	22	0.0196
Decreased (< 13g/dl)	41	20	Chi square value=5.4501

It has been noted that maximum numbers of Covid 19 patients in high risk group showed lower level of haemoglobin than low risk group which is statistically significant ($P=0.0196$)

TABLE 4: Distribution of total count of different cell lines in high risk (HR) and low risk(LR) groups of covid-19 patients

CELLS RANGE	HR GROUP N=58	LR GROUP N=42	P VALUE
WBC			
NORMAL (4.00-11.00 X $10^3/\mu\text{L}$)	50 (86.2%)	38 (90.4%)	$P = 0.81$
INCREASED ($> 11.00 \times 10^3/\mu\text{L}$)	06 (10.34%)	03 (7.14%)	
DECREASED ($< 4.00 \times 10^3/\mu\text{L}$)	02 (3.4%)	01 (2.3%)	
RBC			
NORMAL (4.5- 5.5X $10^6/\mu\text{L}$)	09 (15.5%)	28 (66.66%)	$P < 0.001$
INCREASED ($> 5.5 \times 10^6/\mu\text{L}$)	00 (00%)	02 (4.7%)	
DECREASED ($< 4.4 \times 10^6/\mu\text{L}$)	49 (84.4%)	12 (28.57%)	
PLATELETS			
NORMAL (150.400.00 $10^3/\mu\text{L}$)	47 (81.0%)	34 (80.95%)	$P = 0.32$
INCREASED ($> 400.00 \times 10^3/\mu\text{L}$)	01 (1.72%)	03 (7.14%)	
DECREASED ($< 150.00 \times 10^3/\mu\text{L}$)	10 (17.24%)	05 (11.90%)	

WBC SERIES – Differences in HR and LR groups are statistically not significant. Leukocytosis is slightly more common in HR group

RBC SERIES – Difference in HR and LR group are statistically significant. Maximum numbers of patients in HR group are anaemic

PLATELETS- Difference in HR and LR group are statistically not significant. Thrombocytopenia is slightly more common in HR group

TABLE 5: Distribution of white blood cells in High Risk (HR) and Low Risk (LR) groups

CELLS	HR GROUP N=58	LR GROUP N=42	P VALUE
Polymorphs(Absolute)			
Normal (1.50-7.00x $10^3/\mu\text{L}$)	41 (70.6%)	33 (78.5%)	$P = 0.67$
Increased ($> 7.00 \times 10^3/\mu\text{L}$)	15 (27.5%)	08 (19.0%)	
Decreased ($< 1.50 \times 10^3/\mu\text{L}$)	02 (3.4%)	01 (2.3%)	
Lymphocytes (Absolute)			
Normal (1.00 - 3.70x $10^3/\mu\text{L}$)	23 (39.65%)	33 (78.5%)	$P < 0.0003$ CHI SQUARE VALUE = 18.08
Increased ($> 3.70 \times 10^3/\mu\text{L}$)	05 (8.6%)	03 (7.14%)	
Decreased ($< 1.00 \times 10^3/\mu\text{L}$)	30 (51.7%)	06 (14.2%)	
Monocytes (Absolute)			
Normal (0.05-0.70x $10^3/\mu\text{L}$)	32 (55.0%)	10 (23.8%)	$P < 0.006$ CHI SQUARE VALUE = 10.0079
Increased ($> 0.70 \times 10^3/\mu\text{L}$)	25 (43.1%)	30 (71.4%)	
Decreased ($< 0.05 \times 10^3/\mu\text{L}$)	01 (1.7%)	02 (4.7%)	
Eosinophils (Absolute)			
Normal (0.05- 0.45x $10^3/\mu\text{L}$)	50 (86.2%)	37 (88.09%)	$P = 0.44$
Increased ($> 0.45 \times 10^3/\mu\text{L}$)	06 (10.3%)	02 (4.7%)	
Decreased ($< 0.05 \times 10^3/\mu\text{L}$)	02 (3.4%)	03 (7.1%)	
Neutrophil Lymphocyte Ratio (NLR)			
Normal (1-3)	21 (36.2%)	29 (69.0%)	$P < 0.008$ Chi square Value = 7.8147
Increased			
Mild (4-8)	25 (43.1%)	11 (26.1%)	
Moderate (9-18)	05 (8.6%)	01 (2.4%)	
Severe (> 18)	07 (12.0%)	01 (2.4%)	

Lymphopenia is more common in HR group (51.7%) than LR group (14.2%) which is statistically significant ($P < 0.0003$).

Monocytosis is more common in LR group (71.4%) than HR group (43.1%) which is statistically significant ($P < 0.006$)

NLR – numbers of patients showing higher value of NLR is more in

high risk group than low risk group ($P < 0.008$)

TABLE 6: Distribution of values of RBC indices in HR and LR group

RBC INDICES	HR GROUP (n=58)	LR GROUP (n=42)	P VALUE
MCV			$P = 0.2363$
NORMAL (76-98 fl)	42 (72.4%)	28 (66.6%)	
INCREASED (> 98 fl)	00 (00%)	02 (4.7%)	
DECREASED (< 76 fl)	16 (27.5%)	12 (28.5%)	
MCH			$P < 0.0321$ CHI SQUARE VALUE=6.8786
NORMAL (27-32 pg)	33 (56.8%)	31 (73.8%)	
INCREASED (> 32 pg)	02 (3.4%)	04 (9.5%)	
DECREASED (< 27 pg)	23 (39.6%)	07 (16.6%)	
MCHC			$P = 0.1778$
NORMAL (32-36%)	32 (55.1%)	29 (69.0%)	
INCREASED ($> 36\%$)	01 (1.7%)	02 (4.7%)	
DECREASED ($< 32\%$)	25 (43.1%)	11 (26.1%)	

The difference of MCH values in HR and LR group are statistically significant

DISCUSSION :

Hundred patients were analysed in the present study and of the patients maximum numbers of patients (30%) were in the 61-70 years age group. Minimum numbers of cases (06%) seen in 11-20 years age group in both male and female. In the present study cases were divided into two groups according to age, below 50 years (low risk group) and above 50 years (high risk group). Of the patients, 61% were male and 39% female. M:F ratio is 1.6 which is statistically not significant ($P = 0.5$). Wang et al found 51.1% male and 48.9% female.⁴ There was no significant difference in gender composition between the two groups of patients ($P > 0.05$). In the present study occurrence of Covid 19 in males is slightly higher than females. According to few other studies also males are slightly more commonly affected by Covid 19 than females. Moreover, males develop more severe form and more likely to die from the disease compared to females. According to literatures this observation may be because of high comorbidities and higher likelihood of behavioural risk as well as increased angiotensin converting enzyme 2 (ACE2) levels in males.

Out of hundred patients most were of Hindu (59%) while the minority were of Muslims (28%) or Christians (13%) which is statistically not significant ($P = 0.39$).

Out of 58 HR cases 17 (29.3%) had normal levels of haemoglobin (Hb) and 41 (70.6%) had decreased level of haemoglobin. In LR group out of 42 cases 22 (52.3%) had normal haemoglobin and 20 (47.6%) cases had decreased haemoglobin levels. Maximum numbers of anaemic patients are in high risk group ($P < 0.0196$). Lippi G et al reported haemoglobin value was significantly lower in Covid-19 patients with severe disease than in those with milder form.⁷ Changzheng Wang et al also reported that levels of haemoglobin was significantly lower with severe disease than those in non-severe group ($P < 0.05$).⁴ Haemoglobin was below normal range in 51% of 99 patients SARS- Cov-2 infection reported by Jin Yin-Tan Hospital.⁸ In one study Hb% was low in severe group than non-severe group ($P < 0.001$).⁹ Zhou et al also reported Hb% was low in severe cases than non-severe cases ($P = 0.002$).¹⁰ It may be because of inflammatory response in Covid-19 may interfere with erythropoiesis and give rise to decreased Hb% level. Low Hb% may be an indicator of disease progression.¹¹ Therefore HR group (> 50 years) with low HB% are vulnerable for disease progression. Another study reported HB%, RBC, HCT parameters in the severe group were significantly lower than those in non severe group ($P < 0.05$).⁴ Lippi and Mattiuzzi in their four meta analysis studies reported that patients with severe symptoms exhibited lower HB level compare to those with mild symptoms.⁷ In the present study 84% of patients in HR group and 28.5% patients of LR group had decrease RBC counts which was highly significant ($P < 0.0001$). Among the RBC indices (MCV, MCH, MCHC) MCH was significantly lower ($P < 0.03$) in patients of above 50 years age group than the patients younger than 50 years. Therefore, in the present study it has been noted that numbers of anaemic patient in high risk group are more than low risk group

In the present study we found maximum numbers of cases both in HR (86.2%) and LR (90.4%) group had normal leukocytic count. One

study reported normal WBC counts in 68% of patients.¹² Leukocytosis was noted in 10.34% cases of HR group and 7.14% cases of LR group in the present study. Leukopenia was noted in 3.4% HR patient and 2.3% LR patients. Both leukocytosis and leukopenia were more common in HR patients which does not have any statistical significance ($P=0.81$). Artur et al reported 45.0% of patients had normal range ($4.00-11.00 \times 10^3/\text{U/L}$) of leukocytes, 30.0% had elevated WBC counts ($>11.00 \times 10^3/\text{U/L}$).¹ Rise and fall of WBC counts appeared to correlate with disease severity and age of the patients. In the present study, HR patients had more neutrophil counts (27.5%) than LR patients (19.0%) ($P=0.67$). Severely ill patients had more neutrophil counts than non-severe group.⁵ Higher neutrophil counts were detected in ARDS patients.¹³ Non survivor patients developed more higher neutrophil counts and more severe lymphopenia.¹⁴

In the present study majority of patients in HR group found to have lymphopenia (51.7%) than LR group (14.2%) ($P<0.0003$). Lui et al reported majority of patients had lymphocytes counts below $1 \times 10^3/\text{U/L}$.¹⁵ Another study reported lymphocytopenia in 42.0% of patients most of them exhibited only mild to moderate clinical symptoms. A higher proportion of patients with severe symptoms (61.1%) being diagnosed with leukopenia.¹⁶ One study reported 9% cases with decreased levels of WBC and lymphopenia in 35% cases.⁸ In another study lymphopenia was noted in 98% of patients.¹⁷ Huang CL reported leukopenia in 25% patients and lymphopenia in 63% patients.⁵

Monocytosis was seen in 43.1% of HR patients and 71.4% LR patients. According to literature monocytosis is the sign of recovery. Singh et al reported that the appearance of increased monocytes in a blood smear may indicate an improvement in the patients clinical condition.¹⁸ In the present study due to good immune response in younger age group (LR) recovery rate was more which correlate with high monocytes counts ($P<0.006$).

Eosinophil count was high in 10.3% patients of HR and 4.7% LR patients. 3.4% in HR and 7.1% in LR patients had low eosinophils counts. Rest of the patients had normal eosinophil counts ($P=0.44$)

The neutrophil lymphocyte ratio (NLR) is an easily measurable and inexpensive marker of systemic inflammation. The neutrophil lymphocyte ratio (NLR) has been shown to serve as a useful reliable indicator of severe illness. Severely ill Covid-19 patients show higher NLR when compared with non-severe cases.¹¹ Patients with chronic diseases may progress from mild symptoms to severe disease, NLR should be monitored starting from hospitalization, because high NLR potentiates the symptoms severity.¹⁹ In the present study it was found that more numbers of patient with higher value of NLR were seen in above 50 years age group than below 50 years age group ($P<0.008$). Another study reported that the population of age >50 years patients with higher NLR were prone to develop severe illness than those with low NLR value and below 50 years of age.¹¹ Findings are almost similar to our study.

In the present study 17.2% patients in HR group and 11.9% patients of LR group developed thrombocytopenia ($P=0.32$). Lippi et al.¹⁴ suggested that a low platelet count is associated with severe form of the disease, according to different studies low platelet count may be due to decrease production, increase destruction and increased consumption of platelet. However, the exact cause of thrombocytopenia and the role of platelets in Covid-19 is not established. Further research is recommended on this topic to know the exact cause. Another study reported severe cases (57%) exhibited more thrombocytopenia than non-severe cases (31.6%) ($P<0.001$).

Most of the patients of our study had increased ESR levels. Zhang et al reported that ESR has been proven to be a powerful parameter for predicting the severity of Covid-19.²⁰

In the present study it has been observed that leukocytosis, lymphopenia, thrombocytopenia, decreased haemoglobin and increased NLR are more common in patients who are more than 50 years of age (HR). However monocytosis is more common in patients less than 50 years of age (LR) which indicate recovery state. From these observations it has been noted that patients with >50 years of age are at more risk to disease progression. Other studies have also shown that leukocytosis, lymphopenia, thrombocytopenia, decreased haemoglobin levels, increased NLR are common in severe group (most

patients are in elderly age group) than non-severe group (most are below fifty years of age). So whenever any one of these findings is seen in any patient irrespective of age group proper care should be taken so that disease cannot progress to severe stage.

CONCLUSION:

Covid-19 is an infectious viral disease caused by SARS-COV-2. Patients with >50 years of age with haematological abnormalities are more vulnerable to disease progression than patients younger than 50 years of age which is supported by our findings. However more studies with larger numbers of data are recommended for more accurate results.

REFERENCES:

- Artur Slomka, Mariusz Kowalewski, Ewa Zekanowska. Corona virus disease 2019 (COVID-19): A short review on haematological manifestations. *Pathogens* 2020;9,493;
- Danying Liao et al. Haematological characteristics and risk factors in the classification and prognosis evaluation of Covid 19 : A retrospective cohort study. *Lancet Haematol* 2020. Published online July 10, 2020. [https://doi.org/10.1016/S2352-3026\(20\)30217-9](https://doi.org/10.1016/S2352-3026(20)30217-9)
- Jiang S, Shi Z, Shu Y, Song J, Gao GF, Tan W, Guo D. A distinct name is needed for the new coronavirus. *Lancet* 2020;395,949.
- Changzheng Wang et al. Preliminary study to identify sever form moderate cases of COVID-19 using combined haematology parameters. *Annals of Translational Medicine* 2020; 8(9):593.
- Huang C; Wang Y; Li X, Ren L, Zhao J; Hu Y, Zhang L, Fan G, Xu J, Gu X et al. Clinical features of patients infected with 2019 Novel Coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
- Danying Liao et al. Haematological characteristics and risk factors in the classification and prognosis evaluation of COVID-19: a retrospective cohort study. *www.thelancet.com/haematology*. Published online July 10, 2020. [https://doi.org/10.1016/S2352-3026\(20\)30217-9](https://doi.org/10.1016/S2352-3026(20)30217-9)
- Lippi G, Mattiuzzi C. Haemoglobin value may be decreased in patients with severe Coronavirus disease 2019. *Haematol. Transfus. Cell Ther.* 2020;42,116-117
- Chen NS, Zhou M, Ding X, Qu JM, Gong FY, Han Y, Qin Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 395(10223):507-513.
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX et al. (2020) Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* <https://doi.org/10.1056/NEJMoa2002032>. [Online ahead of print]
- Zhou YG, Fu BQ, Zheng XH, Wang DS, Zhao CC, Qi YJ et al (2020). Aberrant pathogenic GM-CSF+ T cells and inflammatory CD14+ CD16+ monocytes in severe pulmonary syndrome patients of a new coronavirus. *bioRxiv*. <https://doi.org/10.1101/2020.02.12.945576>
- Xiaoqing Liu, Run Zhang, Guangsheng. Haematological findings in coronavirus disease 2019: indication of progression of disease. *Annals of hematology* (2020) 99:1421-1428
- Xu, X.W, Wu, X.X, Jiang X.G, Xu, K.J, Ying, L.J, Ma, CL, Li SB, Wang, H.Y, Zhang, S, Chen H.N, et al. Clinical findings in a group of patients infected with the 2019 Novel Coronavirus (SARS-COV-2) outside of Wuhan, China: Retrospective case series. *BMJ* 2020,368,m606.
- Wu CM, Chen XY, Cai YP, Xia JA, Zhou X, Xu S, et al (2020). Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med*. <https://doi.org/10.1001/jamainternmed.2020.0994> [online ahead of print]
- Wang DW, Hu B, Hu C, Zhu FF, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z (2020). Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus infected pneumonia in Wuhan, China. *JAMA* 323(11):1061-1069
- Liu, K, Fang, YY, Deng, Y, Liu, W, Wang, MF, Ma, JP, Xiao, W, Wang, Y.N, Zhong, M.H, Li, CH et al. Clinical characteristics of Novel coronavirus cases in tertiary Hospital in Hubei Province. *Chin. Med. J(Eng)* 2020,133,1025-1031
- Guan, W.J, Ni, Z.Y, Hu, Y, Liang, W.H, Ou, C.Q, He, J.X, Liu, L, Shan, H, Lei, C.L, Hui, D.S.C et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N. Eng. J. Med.* 2020,382, 1708-1720
- Wong RS, Wu A, To KF, Lee N, Lam CW, Wong CK et al (2003). Haematological manifestation in patients with severe acute respiratory syndrome: retrospective analysis. *BMJ* 326(7403):1358-1362
- Singh A, Sood N, Narang V, Gopal A. Morphology of COVID-19- affected cells in peripheral blood film. *BMJ case Rep.* 2020, 13, e236117
- Gustavo D. Pimentel, Maria C.M. Dela Vega, Alessandro Laviano. High neutrophil to lymphocyte ratio as a prognostic marker in COVID-19 patients. *Clinical Nutrition* 2020; vol 40; P 101-102.
- Zhang H, Wang H, Fu Z, Luo M, Zhang Z, Zhang K, He Y, Wan D, Zhang L, Wang J, et al. Potential factors for prediction of disease severity of COVID-19 patients. *MedRxiv* 2020.