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Original Research Article

A Study to Compare the Mean Value of Various Hematological Parameters from the COVID-19 Patients (Survivors and Non-Survivors) to Assess Their Role in Prognostication and Prediction of Mortality

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Abstract

Aim: The aim of the present study was to compare the mean value of hematological parameters from the COVID-19 patients (survivors and non-survivors), in order to assess their role in prognostication and prediction of mortality.

Methods: The Retrospective cross-sectional study was conducted at department of Pathology. On the basis of the disease outcome, these 500 patients were then divided into two principal groups, group 1, and group 2. Group 1 had 50 non survivors and group 2 had the rest 450 survivors of COVID-19 infection.

Results: The mean age of patients in RTPCR positive COVID-19 cases was 53 years. Most patients were in 4th-6th decade, followed by those in 7th decade and more. Mortality was comparatively higher in patients with age more than 60 years with statistically significant p value of 0.007. Male predominance was seen with 232 males of 350 COVID-19 patients, and this was also observed in both the groups (non survivors and survivors). Normal range of hemoglobin (Hb), total leucocyte count (TLC), neutrophil percent (N%), absolute neutrophil count (ANC), lymphocyte percent (L%), absolute lymphocyte count (ALC), eosinophil percent (E%), absolute eosinophil count (AEC) and platelet count as per our laboratory cut offs. We chose the variables with more than 0.6 area under receiver operating characteristic curve. Thus, TLC, neutrophil percent, ANC, NLR, MLR, PLR and SII were found to have AUC of 0.652 (p=0.007), 0.786 (p=0.000), 0.718 (p =0.000), 0.786 (p=0.000), 0.654 (p=0.000), 0.684 (p=0.000) and 0.738 (p=0.000) respectively.

Conclusion: Elevated TLC, neutrophil percent, ANC, NLR, MLR, PLR and SII at admission are useful in prognostication and prediction of mortality in COVID-19 patients.

Keywords: Hematology parameters, COVID-19, NLR, SII, neutrophil count, eosinophil

Introduction

The novel corona viral infection resulting in severe acute respiratory syndrome (SARS) in humans has been declared a global pandemic by the World Health Organisation (WHO) and has affected more than one million people worldwide since its initial outbreak in Wuhan, China in December 2019. [1] The global pandemic caused by severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) infection in humans has resulted in increased morbidity and mortality worldwide. It continues to be a great challenge to the healthcare system in many countries even today. Coronavirus disease 2019 (COVID-19) was first isolated from the respiratory airway epithelial cells of humans and was named SARS-CoV-2. [2] The SARS-CoV-2 is a single-stranded positive-sense ribonucleic acid (RNA) virus that spreads by droplet infection and affects humans by attaching to angiotensin converting enzyme-2 (ACE-2) receptor in the airway epithelial cells leading to lung parenchymal involvement. [3]

While most patients develop an uncomplicated illness, approximately 1% to 4% develop severe lung involvement with a progressive reduction in oxygen saturation requiring admissions to the ICU. [4] The ACE-2 receptors are also distributed in the heart, kidneys, liver, intestine, vascular endothelium, cerebral cortex, and hematopoietic cells. Hence SARS-CoV-2 infection will manifest as

a systemic disease with the involvement of multiple organ systems including gastrointestinal, neurological, immunological, cardiovascular, and hematopoietic systems. [3]

Several studies have found a wide range of hematopoietic abnormalities in SARS-CoV-2 infection which are directly related to the disease progression, clinical severity, and mortality among the affected individuals. [3] Cytokine storm is characterized by increased levels of cytokines including tumor necrosis factor-alpha (TNF-α), interleukin (IL)-6, etc. in the plasma and is associated with worsening of the COVID-19 patient's clinical condition. These inflammatory cytokines also affect the hematological system causing abnormalities of complete blood count (CBC) parameters, peripheral smear, coagulation studies, etc. [5]

Autopsies done in Europe revealed the pathology of respiratory failure and ARDS in COVID-19 disease. Extrapulmonary manifestations involving heart, lung, kidneys and bone marrow were found. Micro vascular injury and thrombosis were detected in pulmonary vessels. [6] Electron microscopy and molecular diagnosis helped in better understanding of the pathology predominantly occurring in the respiratory tract. [7] Endothelial inflammation, diffuse alveolar damage are associated with hyperreactivity and hyperinflammation of cellular immune system leading to severe hypoxia and acute respiratory distress syndrome. [8]

The aim of the present study was to compare the mean value of hematological parameters from the COVID-19 patients (survivors and non-survivors), in order to assess their role in prognostication and prediction of mortality. This study was approved by ethical committee of the institute.

Materials and Methods

The Retrospective cross-sectional study was conducted at department of Pathology, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India. On the basis of the disease outcome, these 500 patients were then divided into two principal groups, group 1, and group 2. Group 1 had 50 non survivors and group 2 had the rest 450 survivors of COVID-19 infection.

Participant's inclusion and exclusion criteria: 500 real time reverse transcription polymerase chain reaction (RTPCR) positive COVID-19 hospitalized patients of age more than 12 years and of both genders were included in the study.

Exclusion Criteria for the Study Were:

a) Patients who were admitted for COVID-19 treatment but were of age 12 years or below.

b) RTPCR positive cases who got referred elsewhere within 24 hours of admission

c) As well as SARS-CoV-2 RTPCR negative cases.

Methodology for sample collection and reporting: Universal precautions and WHO guidelines for sample collection of COVID-19 cases was followed.[9] For SARS-COV-2 RTPCR, nasopharyngeal/ oropharyngeal swabs were collected by trained paramedical staff and RTPCR was carried out in molecular laboratory department of the institute. Whole blood samples of the studied population (500 patients) were collected for analysis in Ethylene-di-amine tetra-acetic acid (EDTA) vacutainers by trained nursing staff/ paramedical staff and were analyzed on SYSMEX XN- 550L six-part hematology analyzer in pathology department of the hospital.

Data Collection: Demographic data, hematology parameters of these patients on admission as well as their final outcome were extracted from the Hospital management and Laboratory information system. The data collected was then transferred to Microsoft excel sheet. NLR, MLR, PLR and SII was calculated and entered in the data sheet. NLR was calculated by dividing absolute neutrophil count by absolute lymphocyte count. Similarly, MLR was obtained by dividing absolute monocyte count by absolute lymphocyte count. PLR was also achieved by dividing platelet count by absolute lymphocyte count. SII was calculated as= (absolute neutrophil count x platelet count)/absolute lymphocyte count.

Statistical Analysis

SPSS 21.0 version statistical software was used for analysis. Continuous variables were presented as mean ± standard deviation (SD). Categorical variables were expressed as frequencies and percentages. Chi square test was used to calculate difference between qualitative variables. t-test was used to measure differences in means of different parameters. p-value less than 0.05 was considered as statistically significant. Receiver-operating characteristic (ROC) curve for sensitivity, specificity values was analyzed for predicting mortality among groups.

Results

Table 1: Comparison of mean values of hematological parameters according to outcome (non survivors and survivors) in COVID -19 patients

Variables	All cases (N=500)	Non survivors, Group 1 (n=50)	Survivors, Group 2 (n=450)	*p*- value
Demographic Parameters				
Age (years)				
>12-30	90	0	90	0.007
31-60	252	22	230	
> 60	158	28	140	
Gender				
Males	325	35	399	0.525
Females	175	15	160	
Hematological Parameters*				
Hemoglobin	12.88 ± 2.48	12.54 ± 2.88	12.95 ± 2.08	0.314
RDW – SD	42.98 ± 6.74	44.06 ±7.93	44.86 ± 6.65	0.384
TLC	8632 ± 5870	11834 ± 7564	8358 ± 5632	0.001
Neutrophil percent	71.75 ± 15.45	86.82 ±7.53	71.52 ±15.42	0.000
ANC	6572 ± 4884	10972 ± 7312	6190 ±4434	0.000
Lymphocyte percent	21.76 ± 15.05	9.35 ± 6.08	22.88 ± 15.12	0.000
ALC	1656 ± 3384	1284 ± 1796	1695 ± 3485	0.512
Eosinophil percent	0.61 ± 1.22	0.06 ± 0.16	0.64 ± 1.26	0.014
AEC	38.50 ± 82.36	3.79 ±10.81	41.52 ± 85.15	0.020
Platelet count	2.42 ± 0.95	2.68 ± 1.26	2.40 ± 0. 92	0.128
NLR	7.21 ± 8.41	15.03 ± 13.00	6.53 ± 7.54	0.000
MLR	0.34 ± 0.34	0.51 ±0.44	0.32 ± 0.33	0.005
PLR	242.86 ± 229.89	412.50 ± 463.06	228.11 ± 191.56	0.000
SII	1831.784 ± 2442.506	3978.772 ± 3660.671	1645.090 ± 2218.565	0.000

The mean age of patients in RTPCR positive COVID-19 cases was 53 years. Most patients were in 4th-6th decade, followed by those in 7th decade and more. Mortality was comparatively higher in patients with age more than 60 years with statistically significant p value of 0.007. Male predominance was seen with 232 males of 350 COVID-19 patients, and this was also observed in both the groups (non survivors and survivors). Normal range of hemoglobin (Hb), total leucocyte count (TLC), neutrophil percent (N%), absolute neutrophil count (ANC), lymphocyte percent (L%), absolute lymphocyte count (ALC), eosinophil percent (E%), absolute eosinophil count (AEC) and platelet count as per our laboratory cut offs.

Table 2: ROC curve analysis for SARS-CoV-2 patients

Markers	AUC	Cut off	Sensitivity	Specificity	95% CI	*p* value
TLC*	0.652	≥ 8115.00	60%	62%	0.542-0.767	0.007
Neutrophil percent†	0.786	≥ 84.25	70%	72%	0.714-0.855	0.000
ANC‡	0.718	≥ 7131.98	63%	69%	0.616- 0.819	0.000
NLR	0.786	≥ 8.57	70%	73%	0.713- 0.853	0.000
MLR	0.654	≥ 0.27	63%	58%	0.566-0.751	0.000
PLR	0.684	≥ 231.75	70%	65%	0.57- 0.792	0.000
SII	0.738	≥ 2050.076	63%	75%	0.643-0.831	0.000

We chose the variables with more than 0.6 area under receiver operating characteristic curve. Thus, TLC, neutrophil percent, ANC, NLR, MLR, PLR and SII were found to have AUC of 0.652 (p=0.007), 0.786 (p=0.000), 0.718 (p =0.000), 0.786 (p=0.000), 0.654 (p=0.000), 0.684 (p=0.000) and 0.738 (p=0.000) respectively.

Discussion

First reports of outbreak of cases of pneumonia in December 2019 came from Wuhan (People's Republic of China). [10] The causative agent is a novel Corona virus, named as severe acute respiratory syndrome Corona virus 2 (SARS –CoV-2). Infection caused by this virus was termed Corona virus disease- 2019 (COVID-19). [11] With global spread of this infection, World Health Organization (WHO) declared it as a pandemic on 11th March 202. [12] As of 30th June 2021, there have been 3,03,16,897 confirmed COVID-19 cases and 3,97,637 deaths related to it in India. [13]

The mean age of patients in RTPCR positive COVID-19 cases was 53 years. Most patients were

in 4th-6th decade, followed by those in 7th decade and more. Mortality was comparatively higher in patients with age more than 60 years with statistically significant p value of 0.007. According to studies till date, raised NLR constitutes the most significant hematological alteration in COVID-19 cases and NLR, neutrophilia, lymphopenia, and leucocytosis correlate with disease severity. [14-17] Male predominance was seen with 232 males of 350 COVID-19 patients, and this was also observed in both the groups (non survivors and survivors). Normal range of hemoglobin (Hb), total leucocyte count (TLC), neutrophil percent (N%), absolute neutrophil count (ANC), lymphocyte percent (L%), absolute lymphocyte count (ALC), eosinophil percent (E%), absolute eosinophil count (AEC) and platelet count as per our laboratory cut offs. NalbantAhmet concluded from his study that NLR is significantly elevated in COVID-19 patients and observed that cut off value of NLR of ≥2.4 increases the likelihood of COVID-19 infection by 20.5 times. [18] Similarly, other studies have observed that elevated NLR was an independent prognostic marker in COVID-19 patients. [19]

We chose the variables with more than 0.6 area under receiver operating characteristic curve. Thus, TLC, neutrophil percent, ANC, NLR, MLR, PLR and SII were found to have AUC of 0.652 (p=0.007), 0.786 (p=0.000), 0.718 (p =0.000), 0.786 (p=0.000), 0.654 (p=0.000), 0.684 (p=0.000) and 0.738 (p=0.000) respectively. Normal to mild thrombocytopenia has been observed in few studies on COVID-19. In some studies, platelet count was found to be significantly reduced in severe cases. [20] This might be due to sepsis induced disseminated intravascular coagulopathy and/ or direct platelet- viral interaction. [21] Even though platelet count was not statistically significant between fatal (group 1) and non-fatal positive cases (group 2), the PLR was significantly higher in group 1 and had a cut off value of 231.75 (sensitivity 70% and specificity of 65%) for prediction of mortality in RTPCR positive COVID-19 patients. A study by RongQu highlighted that increase in PLR during treatment was associated with longer hospital stay. Their study recommended prompt intervention to prevent further deterioration when the PLR is > 126.7. [22]

The other hematological parameters of statistical significance were percentage of eosinophils in the differential count and absolute eosinophil count (AEC) at admission of COVID-19 cases. Eosinophils are increased in CBC in patients with parasitic infections and allergies. Role of eosinophils in peripheral blood has been analyzed in few studies on COVID-19 patients including fatal cases and all of them have documented severe eosinopenia at admission and its role as indicator of poor outcome.[24-27] It has been stated in these studies that cause of this eosinopenia can be multifactorial, as a result of decreased eosinophil synthesis in bone marrow to increased eosinophil apoptosis due to type 1 interferons.

Conclusion

Elevated TLC, neutrophil percent, ANC, NLR, MLR, PLR and SII at admission are useful in prognostication and prediction of mortality in COVID-19 patients.

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