



ORIGINAL RESEARCH PAPER

Haematology

ROUTINE HEMATOLOGICAL FINDINGS IN PATIENTS WITH COVID-19 AT A TERTIARY CARE HOSPITAL, MIZORAM

KEY WORDS: Hematological parameters, Covid 19, disease's severity, Mizoram.

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ABSTRACT

Background: The pandemic coronavirus disease 19 (COVID-19) infection remains the leading cause of death globally. Early detection of severe infections and complications is the dire challenges to improve care and reduce mortality. Routine blood test is simple, easily accessible and assessing haematological parameters for prediction and triaging of COVID-19 disease severity with risk stratification will have a great prognostic significance in patient outcome. Therefore, this study aims to evaluate the hematological parameters and their predictive value for assessing disease severity in confirmed COVID-19 patients. **Methods:** A hospital based retrospective cross-sectional study was conducted in the Department of Pathology, Zoram Medical College & associated State Referral Hospital, Falkawn, Mizoram a comprehensive dedicated Covid Hospital in the state of Mizoram, India on confirmed 500 Covid 19 patients admitted between August 2021 and October 2021. Data was recruited after taking approval from the Institutional Ethics Committee. Hematological parameters were compared between mild, moderate and severe disease. Quantitative variables were analyzed by mean where as Categorical variable gender was presented in form of frequency. Continuous variables were analyzed by using non parametric, Kruskal Wallis test while categorical variables were analyzed by chi-square test. Data was analyzed in SPSS version 29. P-value equal or less than 0.05 was considered significant. **Result:** Out of 500 patients 169 (33.8%) were categorized as mild, 185 (37%) moderate and 146 (29.8%) severe. Analysis shows that the variables under study: Age, Hemoglobin (Hb), Total Leukocyte Count (TLC), Erythrocyte Sedimentation Rate (ESR), Neutrophil-to-lymphocyte ratio (NLR), Platelet-to-lymphocyte count ration (PLR), Platelet Count (PLT), Absolute Neutrophil Count (ANC) and Absolute Lymphocyte Count (ALC) shows significant difference among mild, moderate and severe patients having p values less than critical value ($\alpha = 0.05$). **Conclusion:** This study demonstrated that haematological parameters from a simple routine blood test shows significant differences in mild, moderate and severe Covid 19 patients and can serve as a useful predictors of severity in COVID-19 patients with increase of total leucocyte count and other markers ESR, NLR and PLR co-relating with severe disease.

INTRODUCTION:

On the 30th January 2020, WHO declared the novel Coronavirus outbreak a public health emergency of international concern (PHEIC). And the new virus was named "COVID-19" on 11th February 2020 and was declared as a pandemic on the 11th March 2020 by WHO[1]. Since then, several variants have emerge due to mutation of the virus leading to multiple waves of the pandemic creating significant health, economic, social and scientific burden[2]. Despite the fact that all countries take significant diagnostic, therapeutic, and preventive steps at varying levels, SARS-COV-2 infection remains the leading cause of death globally[3]. Better insights in the pathogenesis of the disease has lead to evolving treatment modalities for the novel Coronavirus infection.

Since the declaration of COVID-19 pandemic until October 31, 2021, India has reported over 4.5 lakhs of death because of COVID-19[4]. Mizoram, a small state in the north-eastern part of India with a population of 13.32 lakhs (2021 census) recorded the first case of Covid 19 on March 24, 2020[5]. The

first registered death because of COVID-19 in the state was on October 28, 2020 at Zoram Medical College (ZMC), and from the first recorded death on October 28, 2020 till October 31, 2021, the mortality related to COVID-19 as recorded by the state government was 432 and out of these deaths, 324 occurred during their stay at ZMC[6].

COVID-19 is a systemic infection with symptoms in the cardiovascular, pulmonary, gastrointestinal, neurological, and hematological systems[7,8]. Clinical laboratory has played a crucial role in management of the disease[9]. Studies have shown that blood parameters are essential for early prediction in assessing severity and evaluating prognosis[10]. While these parameters may be used as inflammatory markers by themselves, their ratios to one another may also be indicators of early inflammation [11,12]. Many studies revealed that when the condition of COVID-19 infections worsens, numerous hematological abnormalities can be noticed, many of which are warning signs for very bad clinical outcomes[13,14,15]. The current study was conducted to examine and determining the role of routine hematological

parameters in predicting severity of COVID-19 infection and outcome.

MATERIALS AND METHOD

Study Design

This was a hospital based retrospective cross-sectional study,conducted in the Department of Pathology, Zoram Medical College& associated State Referral Hospital, Falkawn,Mizoram a comprehensive dedicated Covid Hospital in the state of Mizoram, India.

Sampling Size And Procedure

Data was recruited after taking approval from the Institutional Ethics Committee. Data of three months was collected from August 2021 to October 2021. Total of confirmed 500 Covid-19 positive patients, both genders between 17 and 75-year age were included. Patients with known cytopenias due to disease other than covid, chronic liver disease and known hematological diseases were excluded. Peripheral blood samples were collected in an EDTA vial on the first day of hospital admission and sent to laboratory for analysis. Complete blood cell counts and white blood cell (WBC) differentiation were performed on Sysmex 100. The presence of erythroblasts, immature granulocytes (IG) and deranged profiles were evaluated microscopically. ESR was performed manually and calculation of NLR and PLR was done manually.

Operational Definition

Case definition for COVID-19 and categorization of patients into mild,moderate and severe was done according to the clinical severity as laid down by the government of India, Clinical management Protocol for COVID-19 (in adults), version 6, 24.05.21. Mild disease was defined as symptoms of fever, sore throat, cough, nasal congestion, malaise, headache without shortness of breath or hypoxia (normal saturation). Moderate disease was defined as patients with pneumonia with presence of clinical features of dyspnea and or hypoxia, fever, cough, oxygen saturation≤93% on room air and respiratory rate ≥ 24 per minute and not requiring critical during their illness. All patients requiring critical care during illness with no known co-morbidities influencing hematological parameters were taken as severe disease.

Statistics And Data Analysis

Descriptive analysis was performed on all the variables. Hematological parameters were compared between mild, moderate and severe disease. Quantitative variables hemoglobin (Hb), erythrocyte sedimentation rate (ESR), total leukocyte count (TLC), absolute lymphocyte count (ALC), absolute neutrophil count (ANC), neutrophil to lymphocyte ratio (NLR),Platelet-to-lymphocyte count ration (PLR),Platelet Count (PLT) (in lakhs), Absolute Neutrophil Count (ANC) and Absolute Lymphocyte Count (ALC) were analyzed by meanwhereas Categorical variable gender was presented in form of frequency. Continuous variables were analyzed by using non parametric, Kruskal Wallis test while categorical variables were analyzed by chi-square test. Data was analyzed in SPSS version 29. P-value equal or less than 0.05 was considered significant. The study included 500 patients out of which 169 (33.8%) were categorized as mild, 185 (37%) moderate and 146 (29.8%) severe.

RESULTS:

The haematological parameters and data records of the study population comprising of 500 patients were reviewed and categorized. Majority (26%) of the COVID-19 were in the age group ≥ 65 years and above, 55.6% were females, 44.4% were males (Table 1a). The mean values of various variables considered in the study against disease severity of mild, moderate and severe is shown in Table 1b.

Table 1a: Gender Distribution With Respect To Disease Severity.

Gender	Levels			Total	Total in percentage (%)
	Mild	Moderate	Severe		
Female	105	96	56	257	55.6%
Male	64	89	90	243	44.4%
Total	169	185	146	500	100%

Table 1b. Mean values of variables against disease severity

Variables	Units	Disease Severity		
		Mild	Moderate	Severe
Age	In years	40.54	54.58	57.36
Hemoglobin (Hb)	(g/dL)	13.14	12.49	12.53
Total Leukocyte Count (TLC)	X10 ³ /μL	6142.26	7957.46	12509.07
Absolute Neutrophil Count (ANC)	X10 ³ /μL	3701.20	5553.01	10633.32
Absolute Lymphocyte Count (ALC)	X10 ³ /μL	1882.90	1818.42	1291.35
Neutrophil-to-lymphocyte ratio (NLR)		2.39	3.84	12.17
Platelet Count (PLT) (in lakhs)	X10 ³ /μL	2.53	2.31	2.34
Platelet-to-lymphocyte count ratio (PLR)		149.79	167.87	255.66
Erythrocyte Sedimentation Rate (ESR) r)	(mm/h	50.42	56.83	67.98

Patients with severe disease had the highest mean age of 57.36 years, followed by patients with moderate severity (54.58 years) and patients with mild severity were found to have lowest mean age (40.54 years). The hemoglobin (Hb) level for patients with mild cases was found to be highest with mean Hb level 13.14 g/dL. There was less difference between moderate and severe groups for this measurement (12.53 and 12.10 g/dL respectively). Total Leukocyte Count (TLC) increased from mild, moderate to severe with a mean of 6142.26 cell/mm3, 7957,46 cells/mm3 and 12509.07 cells/mm3respectively. The mean Erythrocyte Sedimentation Rate (ESR) also increased from mild, moderate to severe patients and found to be 50.42 , 56.83, 67.98 mm/hr respectively. It was also found that Neutrophil-to-lymphocyte ratio (NLR) and Platelet-to-lymphocyte (PLR) ratio increased from mild, moderate to severe patients. Platelet Count (PLT) mean was found to be lowest in moderate severity patients with mean 2.31 and the highest in mild patients with mean 2.53. Absolute Neutrophil Count (ANC) mean also increased from mild, moderate to severe patients with mean values 3701.20, 5553.01 and 10633.32 /L respectively. Absolute Lymphocyte Count (ALC) mean decreased from severe, moderate to mild severity with mean 1291.35, 1818.42 and 1882.90 /L respectively. The significant differences among mild, moderate and severe patients with respect to variables under study is given as below (Table 2).

Table 2a: Kruskal-Wallis Test for finding significance among Mild, Moderate and Severe.

Variables	Test statistic s	Df	Asymptomatic significance (2-sides)
Age	65.146	2	<.001*
Hemoglobin	8.866	2	0.012
Total Leukocyte Count (TLC)	53.649	2	<.001
Absolute Neutrophil Count (ANC)	92.166	2	<.001
Absolute Lymphocyte Count (ALC)	66.449	2	<.001
Neutrophil-Lymphocyte Ratio (NLR)	144.862	2	<.001
Platelet Count	7.837	2	0.02

Platelet-Lymphocyte Ratio (PLR)	26.631	2	<.001
Erythrocyte Sedimentation Rate (ESR)	31.446	2	<.001

Table 2b. Kruskal-Wallis Test for finding significance between Mild, Moderate and Severe disease severity.

Variables	Mild Vs Moderate		Mild Vs Severe		Moderate Vs Severe	
	Test statistics	Asymptomatic significance (2-sides)	Test statistics	Asymptomatic significance (2-sides)	Test statistics	Asymptomatic significance (2-sides)
Age	-105.827	<.001	-115.164	<.001*	-9.337	0.559
Hemoglobin	40.836	0.008	39.895	0.014*	-0.941	0.953
Total Leukocyte Count (TLC)	53.649	0.012	-116.989	<.001*	-78.455	<.001*
Absolute Neutrophil Count (ANC)	-66.184	<.001	-156.531	<.001*	-90.346	<.001*
Absolute Lymphocyte Count (ALC)	42.809	0.005	131.245	<.001*	88.436	<.001*
Neutrophil-Lymphocyte Ratio (NLR)	-83.695	<.001	-196.281	<.001*	-112.586	<.001*
Platelet Count	26.293	0.084	44.557	0.006*	18.264	0.245
Platelet-Lymphocyte Ratio (PLR)	-12.017	0.434	-78.769	<.001*	-66.752	<.001*
Erythrocyte Sedimentation Rate (ESR)	-38.491	0.009	-87.244	<.001*	-48.753	0.001*

Analysis shows that for variables under study: Age, Hemoglobin (Hb), Total Leukocyte Count (TLC), Erythrocyte Sedimentation Rate (ESR), Neutrophil-to-lymphocyte ratio (NLR), Platelet-to-lymphocyte count ration (PLR), Platelet Count (PLT), Absolute Neutrophil Count (ANC) and Absolute Lymphocyte Count (ALC) it was found that there was significant difference among mild, moderate and severe patients. All variables were having p values less than critical value (= 0.05) . This showed that at least two out of three disease severity (mild, moderate and severe) have differences amongst them when compared against the variables studied at 95% Confidence Level, (Table 2a).

Further analysis is done comparing the variables to find significance between disease severity. It is carried out in three analysis. First analysis is significant analysis between Mild and Moderate, second analysis for Mild and Severe and lastly for Moderate and Severe cases, (Table 2b) .

Comparison between mild and moderate disease severity showed a statistically significant difference in all variables except for platelet count and platelet to lymphocyte ratio. The mean Platelet count was lower in moderate cases as compared to mild cases, however not statistically significant, $p=0.084$. Platelet to lymphocyte ratio was higher in moderate cases, however the difference was not statistically significant, $p=0.434$. Upon comparison between mild and severe cases, the differences for all variables were statistically significant.

Comparison between moderate and severe cases showed a statistically significant difference in most of the variables except for age, hemoglobin level and platelet count. The mean age was higher in severe cases however not statistically significant, $p=0.559$. Mean hemoglobin level and platelet

count was lower in moderate as compared to severe cases, however not statistically significant, $p=0.953$ and 0.245 respectively.

DISCUSSION

Results of the study illustrates routine hematological findings and their co-relation with disease severity in patients with COVID- 19. The findings of our study were in line with only minor differences from other previous studies and research. Our result is supported by a previous study conducted in Wuhan and Ethiopia, which stated that increase of age could increase the severity of COVID-19[12,16,17]. This might be due to the fact that as age increases, the risk of acquiring chronic medical conditions increases, similar to previous viral infections such as influenza A [18]. The F:M ratio is higher with 55.6% female out of 500 patients which contradicts Guan et al, Li et al and Xu et al.. where the male percentage was higher in their studies[19,20,21]. While no significant difference was observed by Usul E et al regarding hemoglobin, higher levels were seen in COVID-19 positive male patients and is possible that these results are also affected by other reasons, such as the presence of comorbidities or anemia, and habits such as cigarette smoking[22], with mild patients having highest mean hemoglobin (13.1g/dL) in our findings.

According to several studies, patients with severe outcomes from COVID-19 have a consistently increased WBC count [23,24,25]. The findings of our study were in agreement with the results of several studies conducted by Henry et al. [26], Penaloza et al. [27], and Sukrisman et al. [28] which concluded elevated TLC, ANC and significantly lower ALC in severe and critical Covid patients are associated with a poor prognosis [29]. Although ESR was shown to be significantly increased in groups with COVID-19 severe pneumonia in our study, Kurt C et al concluded it was not prognostic and had less benefit for diagnosis and is beneficial to follow up along with other parameters[30]. Several studies revealed that there was an insignificant difference in platelet counts between severe and non-severe covid patients. However, Qu et al. showed that among 30 hospitalized patients with COVID-19, those presenting with a peak in the platelet count during the disease course had worse outcomes and other studies reported that a lower platelet count had been observed in patients with more severe COVID-19 [31,32]. Inversely, our studies reported Platelet Count (PLT) mean was lowest in moderate severity patients with mean 2.31lakhs/cumm and the highest in mild patients with mean 2.53 lakhs/cumm, however the differences were not statistically significant ($p>0.05$).

PLR is an indicator of inflammation, considered central to the pathogenesis of COVID-19. Dysfunctional immune response with progressive inflammation has been associated with severe COVID-19 disease and poor outcomes. According to Simon et al., Sarkar et al meta analysis, PLR has no role in predicting markers of severity but does predict mortality in COVID-19 patients [33,34] . However, in our study Platelet-to-lymphocyte count ratio (PLR) mean increase from mild, moderate to severe patients which indicates as a prediction severity marker. NLR of peripheral blood has been used to distinguish between different types of infections [35]. Our analysis shows significance differences and increase from mild, moderate and severe case which is in concordance as Covid 19 severity predictor with many studies carried out in Wuhan[13]. Moreover, several studies indicated that NLR and PLR had significantly higher values in severe COVID-19 patients and confirmed that they have a predictive role [36]. Systemic inflammation index (SII: (neutrophils x platelets)/lymphocytes) which can be calculated from haematological parameters though not included in this study, has also been shown to have a superior predictive capacity for adverse outcomes in patients with COVID-19 (37).

Limitations

This study is retrospective, the data may be incomplete or inconsistent, making it difficult to collect essential clinical and behavioural variables that could potentially limit the study's findings. Since the sample size of the study was small and confined to one hospital, it may reduce the generalizability of the findings. Furthermore, because the design is cross-sectional, it does not show changes in patients' dynamic hematological profiles or the precise associations between hematological changes and disease severity.

CONCLUSION

Routine blood examination is an affordable, easily accessible test even in remote areas with almost no risk and minimal discomfort. In our single-centered preliminary study, we demonstrated that parameters from a simple routine hematological workup has significant differences in mild, moderate and severe Covid 19 patients and can serve as a useful predictors of severity in COVID-19 patients. Coronavirus disease 2019 has prominent manifestations in the hematopoietic system and common haematological abnormalities have been identified in COVID-19 patients. Finally, an increase of total leucocyte count and other markers ESR, NLR and PLR seem to correlate with severe disease. This review has emphasized the importance of laboratory information in the management of COVID-19, further studies are worth describing the association between the dynamic haematological responses, SII and the progression and outcome of the disease. e disease.

Competing Interests: None declared

Ethics Committee Approval: Our study was supported with the approval of the Institutional Ethics Committee, Zoram Medical College

Informed Consent: Informed consent was obtained from the patients included in the study.

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