(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 4, Issue 6, Page No: 311-317
November-December 2021

IJMSCR

Admission Hemogram Panel in Diagnosing and Predicting the Severity of COVID-19 Patients in a Tertiary Care Hospital in Kerala

Bhagya Lakxmi C[1]*, Vasant P K[2], M Gopalakrishna Pillai[3]
[1]Resident, [2]Professor, [3]Head of the Department,
Department of General Medicine,
[1]AIMS, Amrita Vishwa Vidyapeetham, Kochi, Kerala, India
[2,3]AIMS, Kochi, Kerala, India

***Corresponding Author:**
Bhagya Lakxmi C
Resident, Department of General Medicine, AIMS, Amrita Vishwa Vidyapeetham, Kochi, Kerala, India

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Background: COVID-19 being a pandemic, differentiating severe from non-severe cases and predicting the disease progression by better use of the commonly available laboratory parameters would help reduce the mortality, morbidity, healthcare expenditure. At present, there is no single marker that can convincingly predict the severity of COVID in an individual. Several studies have demonstrated the usefulness of individual hemogram parameters in the prediction and risk stratification of COVID-19 infections, however there is a lack of consistency of data across these studies and there are no studies done hitherto in the south Indian population. Our study was done with the primary objective to analyze the effectiveness of admission hemogram parameters as a panel in differentiating severe from non-severe cases and in predicting the disease progression and with the secondary objective to look for the cut-off point of the variables to differentiate these groups.

Materials And Methods: It is a single-centre prospective observational study. Independent sample t-test, Mann Whitney, Chi-square and ROC analysis were done using IBM SPSS software.

Results: The mean age of subjects in the severe group was 63.5±14.55 and in the non-severe group was 48.6±16.61 ($p < 0.001$). NLR, d-NLR, LMR, PLR, RDW and LCR in the severe group were 14.35±13.86, 6.3±4.84, 6.03±20.17, 263.98±246.27, 15.39 ±4.26 and 388.75±2074.63 and in the non-severe group were 3.5±2.92, 2.2±1.59, 3.15±1.76, 148.98±78.45, 13.88±1.77 and 636.04±1846.14 respectively, which were all statistically significant.

Conclusion: We conclude by saying that severity of COVID-19 and the probability of ICU admission can be better predicted by using admission hemogram panel than individual hemogram parameters

Keywords: COVID-19, NLR,PLR,RDW,LCR

Introduction

Coronaviruses are enveloped RNA viruses belonging to the Orthocorona-viridae sub-family [1]. It was in December 2019 that the first COVID-19 case was reported in Wuhan, China. COVID-19 eventually turned out to be a pandemic and more than 236,599,025 confirmed cases of COVID- 19, including 4,831,486 deaths were reported to the WHO [2] as of 10th October 2021 of which 80% were categorized as mild/moderate cases while the severe and critically ill patients contributed to 15% and 5% respectively; most of them needing in-patient care of which around 20% needed intensive care [3,4]. The mortality rate of ICU patients comes close to 61.5% [5].

Elderly age, diabetes mellitus, systemic hypertension, ischemic heart disease, obesity and immunosuppressed states are risk factors for developing severe COVID-19 infection. Present assessment and prediction of the progression of COVID-19 are based on clinical examination and serial monitoring of inflammatory markers such as erythrocyte sedimentation rate (ESR), serum ferritin, lactate dehydrogenase, C-reactive protein (CRP), interleukin-1B (IL-1B), IL-6, IL-12, interferon (IFN), monocyte chemoattractant protein (MCP) and serum IFN-γ-induced protein 10 (IP-10) all of which are linked to the severity of COVID19 infection, pulmonary inflammation and lung damage [6,7,8].

Unfortunately, most of these investigations are not available to the majority of the population especially in the developing countries and there is no single marker that can convincingly predict the severity of COVID in an individual, emphasizing the importance of the need for a one time, low cost, universally available, easy to perform laboratory test with a low turn around time that would reduce the morbidity, mortality and global healthcare expenditure as a result of early prediction of disease severity and progression.

Several studies have demonstrated the usefulness of individual hemogram parameters in the prediction and risk stratification of COVID-19 infections. Neutrophil-to-Lymphocyte Ratio (NLR) and derived-NLR (d-NLR) have been proven to be a simple and reliable measure of systemic inflammation [9]. Platelet-to-Lymphocyte Ratio (PLR) was shown to be a negative prognostic factor for inflammatory illnesses when it is increased as a result of an increase in platelet count and a reduction in lymphocyte count. Higher levels appear to be linked to more severe types of the disease and more hospitalizations in critical care. Despite numerous potential advantages, there is currently no cut-off point at which a severe type of the disease may be detected [10]. Similarly, Lymphocyte-to-Monocyte Ratio (LMR) has been attributed to the severity of COVID-19 infection and Lymphocyte-to-C-reactive protein Ratio (LCR) was observed to be able to distinguish COVID-19 infected patients of different severity (mild/moderate, severe and critically ill) and was superior to NLR in this regard [11]. Increased mortality risk was seen in patients with elevated RDW at the time of hospital admission [12].

India being a lower-middle-income as per the world bank data and that there is a lack of consistency of data across these studies and also that there are no such studies done hitherto in the south Indian population this study was done with the primary objective to analyze the effectiveness of admission hemogram parameters as a panel in differentiating severe from non-severe cases and in predicting the disease progression and with the secondary objective to look for the cut-off point of the variables to differentiate severe from non-severe COVID-19 infections.

Materials And Methods: Our study is a single-centre prospective observational study. The sample size was deduced based on the result of Area under the curve of PLR (0.784) in identifying patients with severe or non-severe cases, observed in an earlier publication [13] and with 80% power and 95% confidence. COVID-19 antigen or RT-PCR positive patients for whom baseline NLR, d-NLR, LMR, PLR, RDW and LCR could be derived and who gave a written consent were included. Patients who were not willing to take part in the study were excluded.

Statistical Tool:

Statistical analysis was performed using IBM SPSS version 20.0 software (SPSS inc, Chicago, USA). Categorical variables were expressed using frequency and percentage. Numerical variables were represented using mean and standard deviation.

Statistical Details:

Independent sample t-test and Mann Whitney test was used to test the statistical significance of the difference in the mean of continuous variable between the severe and non-severe group for normal data and skewed data respectively.

To find the ideal cut off value of NLR, d-NLR, LMR, PLR, RDW and LCR variables for the prediction of patients with severe or non-severe cases of COVID-19, ROC curve analysis was used.

To test the statistical significance of the association of categorical variables between severe and non-severe groups, a chi-square test was used.

To test the most significant predictors of Severity of Covid 19 patients multivariable logistic regression was applied. Diagnostic measures such as sensitivity,

Volume 4, Issue 6; November-December 2021; Page No 311-317

specificity, predictive value of positive & negative and accuracy were computed.

Results:

Our total study population was 80, out of which 40 had severe and 40 had non-severe COVID. The mean age of subjects in the severe group was 63.5±14.55 and in the non-severe group was 61.7±16.61 which is comparable. Females were higher in the severe group, 19(47.5%) than the non-severe group, 8(20%) which is statistically significant, p=0.009.

Subjects with diabetes were 19(47.5%) in the severe and 11(27.5%) in the non-severe groups which was not statistically significant (p=0.065) while those with systemic hypertension were 16(40%) and 8 (80%) in the severe and non-severe groups respectively and it was statistically borderline significant, p=0.051. 20(50%) and 8(20%) in the severe group and 2(5%) each in the non-severe group had renal dysfunction and chronic liver disease respectively. Renal dysfunction was statistically significant (p=<0.001) while the chronic liver disease was not (p=0.091). Subjects with coronary artery disease were higher in the severe group, 11(27.5%) than the non-severe group, 2(5%) and were statistically significant, p=0.015.

NLR in the severe group was 14.35±13.86 and in the non-severe group was 3.5±2.92 which is statistically significant, p <0.001. d-NLR in the severe group was 6.3±4.84 and in the non-severe group was 2.2±1.59 which is statistically significant, p <0.001. LMR in the severe group was 6.03±20.17 and in the non-severe group was 3.15±1.76 which is statistically significant, p <0.007. PLR in the severe group was 263.98±246.27 and in the non-severe group was 148.98±78.45 which is statistically significant, p <0.048. RDW in the severe group was 15.39 ±4.26 and in the non- severe group was 13.88±1.77 which is statistically significant, p <0.033. LCR in the severe group was 388.75±2074.63 in the severe group and 636.04±1846.14 in the non-severe group which was statistically significant (p<0.001).

The area under the curve (AUC) of NLR, d-NLR, LMR, PLR, RDW and LCR were 0.794, 0.842, 0.317, 0.630, 0.639 and 0.255 respectively.

Discussion:

In our study, most of the subjects were elderly and the ages between the two groups were comparable. Females, diabetics, hypertensives, CLD, chronic kidney disease (CKD) and CAD were higher in the severe group than the non-severe group reinforcing the fact that the risk of developing a severe disease is higher in patients with co-morbidities despite subjects from both groups having similar ages.

NLR, derived from neutrophil and lymphocyte counts is used to assess the severity of bacterial infections [14]. Several studies have shown that NLR can be used in predicting the severity of COVID-19 [15,16,17]. However, it is still not clear if NLR can be used in differentiating severe cases from non-severe cases.

Sun et al. showed that the NLR was not useful in differentiating these two groups, but in Wang et al's study, NLR could actually differentiate the two. This discrepancy could be due to the sample size being small, particularly in the severe group (n=10) [14,16]. As silent hypoxia is associated with mortality risk, early discrimination of severe patients from non-severe patients can aid in early optimal treatment initiation [18,19]. According to Bal et al LCR alone could differentiate severe from non-severe disease, while NLR could not, however, NLR could reasonably differentiate severe from critically ill patients [11].

In our study, comparison of baseline NLR, d-NLR, PLR, RDW and LCR between the severe and non-severe groups were statistically significant. In order to look at the predictive potential, we analyzed the ROC presented in Fig. 1 and calculated the optimal cut-off values. Cut offs of LMR, PLR, RDW and LCR could not be used as a predictive biomarkers because their AUC were less than 0.70. The optimal cut-off values for NLR and d-NLR were 24.26 and 20.05 respectively. The highest specificity and sensitivity were 0.75 and 0.80, 0.72 and 0.77 for NLR and d-NLR respectively.

Thus using the hemogram parameters as a panel would increase the probability of predicting the course and severity of COVID on the day of admission itself. The limitation of our study is that the laboratory tests were done only at the time of admission and serial labs were not taken into account and that this was a single-centre study. Further studies may be needed to provide evidence for

Volume 4, Issue 6; November-December 2021; Page No 311-317

correlating laboratory parameters with disease progression and treatment response.

Conclusion:

We conclude by saying that using hemogram parameters as a panel can be used to differentiate patients with severe from non-severe COVID-19 infection on day of admission and baseline NLR and d-NLR in particular can help in predicting the severity of COVID-19 infections.

Acknowledgements:

I thank my family, my colleagues, faculties of Department of General Medicine, AIMS, Amrita Vishwa Vidyapeetham for helping me do this.

References:

1. Richman DD, Whitley RJ, Hayden FG, eds. Clinical virology, 4th edn. Washington: ASM Press, 2016.
2. World Health Organization. Coronavirus disease 2019 (COVID-19): situation report, 114. 2020.
3. Sun P, Qie S, Liu Z, Ren J, Li K, Xi J. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: a single arm meta-analysis. J Med Virol. 2020;92(6):612–7.
4. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. Travel Med Infect Dis. 2020;34:101623.
5. Yang X, Yu Y, Xu J, Shu H, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Resp Med. 2020;8(5):475–81.
6. Wong CK, Lam CWK, Wu AKL, et al. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. Clin Exp Immunol 2004; 136: 95–103.
7. Zenga F, Huang Y, Guo Y, Yina M, Chena X, Xiao L, et al. Association of inflammatory markers with the severity of COVID-19: A meta-analysis. International Journal of Infectious Diseases 96 (2020) 467–474. pmid:32425643.
8. Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR, and PLR in COVID-19 patients. Int Immunopharmacol. 2020; 84:1 06504. pmid:32304994.
9. Sengul EA, Artunay O, Kockar A, Afacan C, Rasier R, Gun P, et al. Correlation of neutrophil/lymphocyte and platelet/ lymphocyte ratio with visual acuity and macular thickness in age-related macular degeneration. Int J Ophthalmol. 2017; 10 (5). pmid:28546933.
10. Man MA, Rajnoveanu RM, Motoc NS, Bondor CI, Chis AF, Lesan A, Puiu R, Lucaciu SR, Dantes E, Gergely-Domokos B, Fira-Mladinescu O. Neutrophil-to-lymphocyte ratio, platelets-to- lymphocyte ratio, and eosinophils correlation with high-resolution computer tomography severity score in COVID-19 patients. Plos one. 2021 Jun 28;16(6):e0252599.
11. Bal T, Dogan S, Cabalak M, Dirican E. Lymphocyte-to-C-reactive protein ratio may serve as an effective biomarker to determine COVID-19 disease severity. Turkish Journal of Biochemistry. 2021 Feb 1;46(1):21-6.
12. Foy BH, Carlson JCT, Reinertsen E, et al. Association of Red Blood Cell Distribution Width With Mortality Risk in Hospitalized Adults With SARS-CoV-2 Infection. JAMA Netw Open. 2020;3(9):e2022058.
13. Henry BM, Benoit JL, Benoit S, Pulvino C, Berger BA, Olivera MH, Crutchfield CA, Lippi G. Red blood cell distribution width (RDW) Predicts COVID-19 severity: a prospective, observational study from the cincinnati SARS-CoV-2 emergency department cohort. Diagnostics. 2020 Sep;10(9):618.
14. Naess A, Nilssen SS, Mo R. Role of neutrophil to lymphocyte and monocyte to lymphocyte ratios in the diagnosis of bacterial infection in patients with fever. Infection 2017;45:299–307.
15. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. J Am Med Assoc 2020;323:1061–9.
16. Sun S, Cai X, Wang H, He G, Lin Y, Lu B, et al. Abnormalities of peripheral blood system in

patients with COVID-19 in Wenzhou, China. Clin Chim Acta 2020;507:174–80.

17. Fu J, Kong J, Wang W, Wu M, Yao L, Wang Z, et al. The clinical implication of dynamic neutrophil to lymphocyte ratio and D-dimer in COVID-19: a retrospective study in Suzhou China. Thromb Res 2020;192:3–8.
18. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. Signal Transduct Target Ther 2020;5:33.
19. Teo J. Early detection of silent hypoxia in COVID-19 pneumonia using smartphone pulse oximetry. J Med Syst 2020;44:134

TABLES:

Table 1: Comparison of variables between the groups

Group		Frequency	Percentage (%)
Sex			
Severe	Male	32	80
	Female	8	20
Non-severe	Male	21	52.5
	Female	19	47.5
Diabetes Mellitus			
Severe	Yes	19	47.5
	No	21	52.5
Non-severe	Yes	11	27.5
	No	29	72.5
Systemic Hypertension			
Severe	Yes	16	40
	No	24	60
Non-severe	Yes	8	20
	No	32	80
Renal dysfunction			
Severe	Yes	20	50
	No	20	50
Non-severe	Yes	2	5
	No	38	95
Chronic Liver Disease			
Severe	Yes	8	20
	No	32	80

Volume 4, Issue 6; November-December 2021; Page No 311-317

Non-severe	Yes	2	5
	No	38	95
Coronary Artery Disease			
Severe	Yes	11	27.5
	No	29	72.5
Non-severe	Yes	2	5
	No	38	95

Table 2: Comparison of variables between the groups

Variable	Group	n	mean	SD	median (IQR)	p-value
NLR	Severe	40	14.35	13.86	10 (4.25, 17.75)	<0.001
	Non-severe	40	3.5	2.92	2 (2, 3)	
d-NLR	Severe	40	6.3	4.84	5.50 (2, 8.75)	<0.001
	Non-severe	40	2.2	1.59	2 (1, 2)	
LMR	Severe	40	6.03	20.17	2 (1, 2.75)	0.007
	Non-severe	40	3.15	1.76	3 (2, 4)	
PLR	Severe	40	263.98	246.27	170 (115.50, 325.5)	0.048
	Non-severe	40	148.98	78.45	128.5 (96.25, 182.25)	
RDW	Severe	36	15.39	4.26	14 (13, 16)	0.033
	Non-severe	40	13.88	1.77	13.5 (13, 14)	
LCR	Severe	40	388.75	2074.63	15.63 (7.86, 48.2)	<0.001
	Non-severe	38	636.04	1846.14	108.38 (27.22, 343.42)	

Table 3: Area under curves (AUC) of NLR, d-NLR, LMR, PLR and RDW

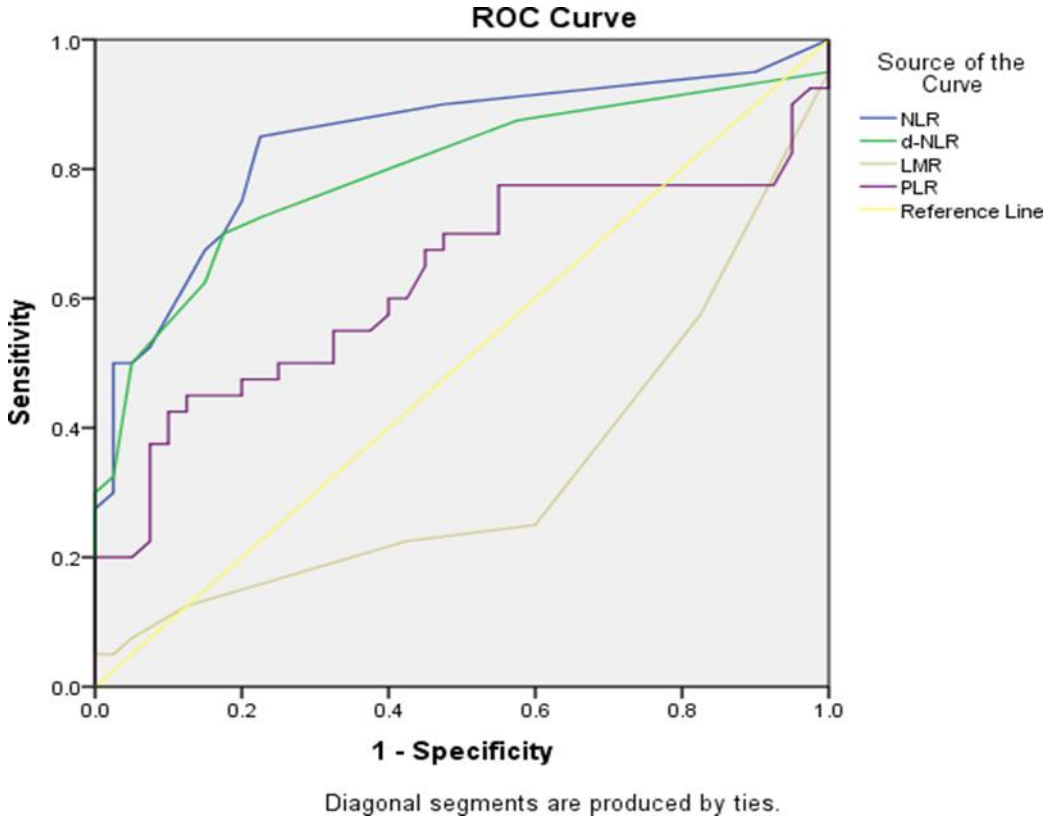
Test result variables	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower bound	Upper bound
NLR	0.794	0.052	0.000	0.692	0.897
d-NLR	0.842	0.046	0.000	0.752	0.933
LMR	0.317	0.064	0.006	0.192	0.442
PLR	0.630	0.067	0.052	0.497	0.762

Volume 4, Issue 6; November-December 2021; Page No 311-317

RDW	0.639	0.064	0.037	0.514	0.764
LCR	0.255	0.057	0.000	0.143	0.367

FIGURES:

Figure 1: ROC curve to differentiate severe from non-severe COVID-19 cases



NLR – Neutrophil Lymphocyte Ratio, d-NLR – derived Neutrophil Lymphocyte Ratio, LMR – Lymphocyte Monocyte Ratio, PLR – Platelet Lymphocyte Ratio

Volume 4, Issue 6; November-December 2021; Page No 311-317