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

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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 COVID-19 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,
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


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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:

TABLES:

Table 1: Comparison of variables between the groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Frequency</th>
<th>Percentage (%)</th>
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<tr>
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<td></td>
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<td>Non-severe</td>
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<tr>
<td></td>
<td>Female</td>
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<tr>
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<tr>
<td></td>
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<tr>
<td>Non-severe</td>
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</tr>
<tr>
<td></td>
<td>No</td>
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</tr>
<tr>
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<tr>
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<tr>
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<tr>
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<tr>
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</tr>
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</table>

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

<table>
<thead>
<tr>
<th>Test result variables</th>
<th>Area</th>
<th>Std. Error</th>
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<th>Asymptotic 95% Confidence Interval</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower bound</td>
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<td>0.794</td>
<td>0.052</td>
<td>0.000</td>
<td>0.692</td>
</tr>
<tr>
<td>d-NLR</td>
<td>0.842</td>
<td>0.046</td>
<td>0.000</td>
<td>0.752</td>
</tr>
<tr>
<td>LMR</td>
<td>0.317</td>
<td>0.064</td>
<td>0.006</td>
<td>0.192</td>
</tr>
<tr>
<td>PLR</td>
<td>0.630</td>
<td>0.067</td>
<td>0.052</td>
<td>0.497</td>
</tr>
</tbody>
</table>
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