|| ISSN(online): 2589-8698 || ISSN(print): 2589-868X ||
International Journal of Medical and Biomedical Studies
Available Online at www.ijmbs.info
NLM (National Library of Medicine ID: 101738825)
Index Copernicus Value 2019: 79.34
Original Research Article
Volume 5, Issue 8; August: 2021; Page No. 188-198

# NEUTROPHIL-LYMPHOCYTIC RATIO (NLR) OR ALBUMIN-GLOBULIN RATIO (AGR) WHICH ONE IS A BETTER PREDICTOR MARKER IN ASSESSMENT OF SEVERITY OF COVID-19 INFECTION

**Dr. Parul Barya**[1] (JR-3rd Year)**, Dr. Sanjeev Narang**[2] (Professor & Head)**, Dr. V. K. Jain**[3] (Professor) **& Dr. Romi Shrivastava**[4] (Associate Professor)
**Dept. of Pathology, Index Medical College Hospital Research Centre, Indore**[1,2,3&4]

**Article Info:** Received 16 June 2021; Accepted 06 August 2021
**DOI:** https://doi.org/10.32553/ijmbs.v5i8.2109
**Corresponding author:** Dr. Sanjeev Narang
**Conflict of interest:** No conflict of interest.

**Abstract**
The current study retrospectively enrolled, 75 confirmed COVID-19 patients who were hospitalized in a tertiary care hospital from December 2020 to February 2021. The diagnosis was confirmed by RT-PCR from nasopharyngeal swab.
Demographic data and laboratory values were collected from medical records and patient file. The following variables were recorded for each COVID-19 patient: age, sex, chest CT severity scores of lung involvement at admission, history of Comorbidities like diabetes mellitus, hypertension were noted and laboratory findings like Absolute neutrophils count, Absolute lymphocytes count recorded from Complete blood count of patient and Serum albumin, globulin level recorded from Liver function test of patient.
This study proves that N-L ratio is more accurate predictor of severity of SARS-COVID-19 infection than A-G ratio with more sensitivity, specificity, positive and negative predictive value and can be used as a severity marker in places where medical resources is limited. However, a larger study with more subjects requires for exact correlation.
**Keywords:** NLR, AGR, Severity & COVID-19.

## Introduction

Since December 2019, cases of disease related severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), now known as COVID-19 (coronavirus disease 2019), have rapidly spread world-wide in short period of time. The World Health Organization (WHO) has officially recognised COVID-19 as a pandemic and countries worldwide are now facing huge challenges trying to prevent its further spread as well as treating the growing number of COVID-19 patients. In fact, although the majority of cases are usually self-limiting with mild symptoms such as low-grade fever and cough, the disease can be fatal [6].

There is an increased urgent need to detect new biomarkers in order to identify cases of COVID-19 that will evolve unfavourably in adults and children. These biomarkers must be easy to measure and accessible to most hospitals that manage COVID-19 cases. The proposed ratios (albumin to globulin and Neutrophil-Lymphocytic Ratio) seem to be more accurate than each value separately and could be included in the initial assessment of patients that have tested PCR positive for SARS-CoV-2, in order to identify those who are at risk of developing ARDS. In addition, they can be measured during hospital or ICU admissions to evaluate the course of the illness

In a recent meta-analysis, increased CRP, lymphopenia, and increased LDH were significantly associated with the severity of the disease (1). The levels of certain laboratory values that proved to be elevated in cytokine storm (ferritin, procalcitonin, and troponin) may not be available at most hospital laboratories or are mainly used for research purposes (IL-6) (2, 3). On the other hand, complete blood count, albumin, and globulin are readily available, shortly after admittance, and are often part of an admission workup, in general hospitals and particularly in intensive care units (ICU).

Albumin and globulin are two important components of serum proteins and have been proven to be involved in systemic inflammation. A low serum albumin reflects a poor nutritional status, liver and kidney dysfunction, and has been shown to be an independent predictor of poor survival in critically ill patients. Decreased albumin at admission has been an independent risk factor associated with unimprovement during follow-up in COVID-19 patients (4). On the other hand, an increased globulin level may reflect a chronic inflammatory response. Thus, the additive effect of both albumin and globulin would not only be a prognostic factor for potential COVID-19 complications during the course of the illness, but also an initial risk index of SARS-CoV-2 positive individuals. Wu et al. showed recently that the level of albumin is significantly lower [30.40 g/L (27.15–33.35) vs. 33.70 g/L (30.95–36.30), $p < 0.001$] and the globulin level higher [31.60 g/L (29.35–35.05) vs. 30.00 g/L (28.25–32.55), $p = 0.004$] in COVID-19 patients with ARDS comparative with those without ARDS (5).

The NLR in the peripheral blood is related to the systemic inflammatory state and disease activity and shows prognostic value in cardiovascular diseases, autoimmune diseases, malignant tumours and infectious diseases [7-10].

For patients with COVID-19, in addition to severe lung lesions, prominent derangement of the lymph haematopoietic system has been noted [11]. An elevated NLR may reflect the severity of COVID-19 and the immune status of the patients.

Many retrospective and prospective studies correlated NLR with severity of COVID-19 infection and defined a cut-off value of NLR for prognosis. One prospective study validates the findings through a large sample of 352 patients and extends the role of NLR in predicting disease deterioration and serious clinical outcomes, such as shock. Furthermore, this study identified an NLR cut-off value of 2.6937, above which most patients' (≥ 82.0%) condition worsened and serious clinical outcomes occurred; patients with an NLR about this cut-off (NLR ≥ 2.6937) were included in the high-risk group, and the negative predictive value (the possibility of ruling out the outcomes) of a ratio below the cut-off value was ≥95.7%. [12]

As both AGR and NLR are proven proinflammatory marker in various infections and inflammatory diseases. Both as individual parameter as well as their ratio has been proven tool in recent pandemic of CORONA virus infection. Various studies showed the correlation of AG-ratio and NL-ratio with severity and prognosis of patient with corona virus infection. As mechanism of change in their value as inflammatory marker is different, depending upon involvement of organ by pathogen. So, there would be a fair possibility that one of the markers would be better than other. None of the study in present literature compared both marker as which one is more specific and sensitive as a prognostic or severity index marker for corona virus infected patients.

**Material and Methods**

The current study retrospectively enrolled,75 confirmed COVID-19 patients who were hospitalized in a tertiary care hospital from December 2020 to February 2021. The diagnosis was confirmed by RT-PCR from nasopharyngeal swab.

Demographic data and laboratory values were collected from medical records and patient file. The following variables were recorded for each COVID-19 patient: age, sex, chest CT severity scores of lung involvement at admission, history of Comorbidities like diabetes mellitus, hypertension were noted and laboratory findings like Absolute neutrophils count, Absolute lymphocytes count recorded from Complete blood count of patient and Serum albumin, globulin level recorded from Liver function test of patient.

Severity of the patient was defined from percentage of involvement of lung in HRCT chest and categorised in three groups mild, moderate and severe according to CT severity index and percentage of Oxygen saturation at the time of admission.
Cut-off for Neutrophil to lymphocytes ratio was defined as 4, and patient with NLR >4 would be considered as significant of severity.
Cut-off for Albumin to Globulin ratio was defined as 1, and value less than 1 would be considered as significant of severity.

CT severity index would be scored as 0-25, according to percentage and number lobe involvement. Score 1-7/25 would be considered as mild, 8-17/25 would be considered as moderate and more than 18 would be considered as severe lung involvement.

Oxygen saturation at room air less than 90% at the time of admission would be considered as significant of severity.

**Statical analysis**

The data was analysed using online statistical software like GraphPad, Epi Info, etc. The descriptive statistics was presented in the form of numbers and percentages. Comparison between two groups was done using Unpaired 't' test and between more than two groups was done using one-way ANOVA test. Correlation between two parametric variables was done using Pearson Coefficient of correlation. ROC curve was drawn between NLR and CT scan grading; and AGR and CT scan grading and cut-off of NLR and AGR were generated. Based on these cut-offs the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of NLR(cut-off) and AGR(cut-off) was calculated against the CT scan severity grading. A p value of < 0.05 was taken as statistically significant.

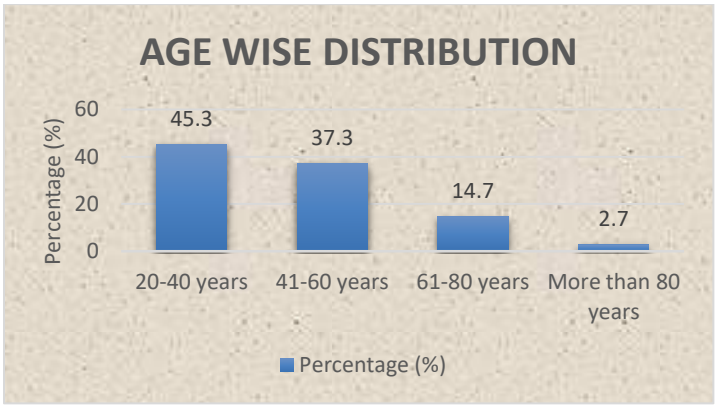
**Results**

**Data analysis and interpretation**

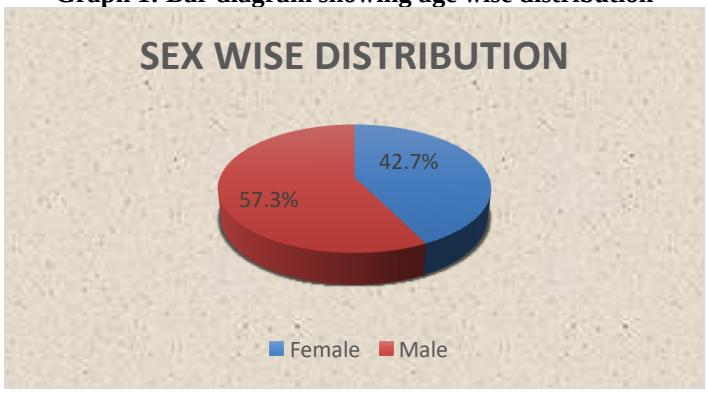
**Table 1: Distribution of patients according to demographics**

| Demographic Variables | Number | Percentage |
|---|---|---|
| **Age:** | | |
| • 20-40 years | 34 | 45.3 |
| • 41-60 years | 28 | 37.3 |
| • 61-80 years | 11 | 14.7 |
| • More than 80 years | 2 | 2.7 |
| **Sex:** | | |
| • Female | 32 | 42.7 |
| • Male | 43 | 57.3 |
| Total | 75 | 100.0 |

The above table shows the demographic variables of the study patients.
34 (45.3%) patients were in the age group 20-40 years, 28 (37.3%) patients were in the age group 41-60 years, 11 (14.7%) patients were in the age group 61-80 years and 2 (2.7%) patients were in the age group more than 80 years.
The mean age of the patients was 47.51 ± 16.13 years with a range from 20 years to 90 years.
There were 32 (42.7%) females and 43 (57.3%) males in the present study with a male: female ratio of 1.34 : 1. There was a male preponderance in the study.




**Graph 1: Bar diagram showing age wise distribution**

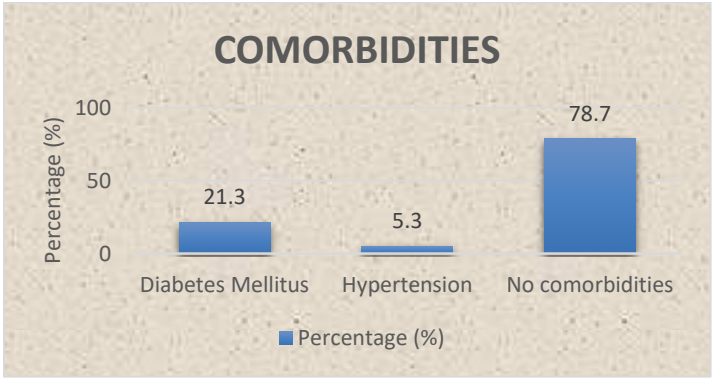



**Graph 2: Pie diagram showing sex wise distribution**

**Table 2: Distribution according to comorbidities**

| Comorbidities | Number | Percentage |
|---|---|---|
| Diabetes Mellitus | 16 | 21.3 |
| Hypertension | 4 | 5.3 |
| No comorbidities | 59 | 78.7 |

In the present study, 16 (21.3%) patients were having diabetes mellitus and 4 (5.3%) patients were having hypertension. Rest of the patients i.e. 59 (78.7%) were not having any other comorbidities.

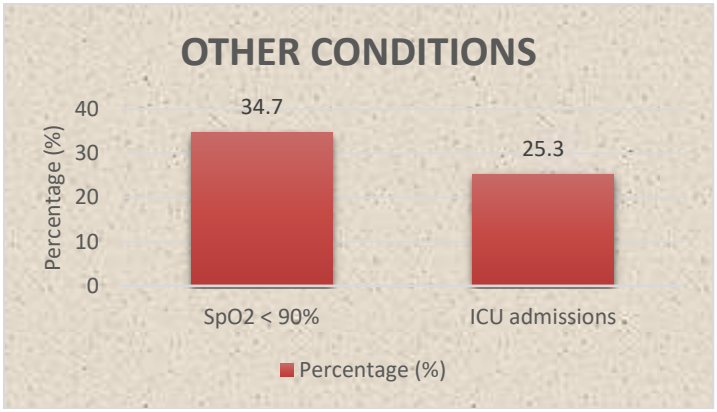



**Graph 3: Bar diagram showing comorbidities**

**Table 3: Distribution according to other conditions**

| Other conditions | Number | Percentage |
|---|---|---|
| SpO2 < 90% | 26 | 34.7 |
| ICU admissions | 19 | 25.3 |

In the present study, 26 (34.7%) patients had SpO2 < 90%, while 19 (25.3%) patients required ICU admissions.

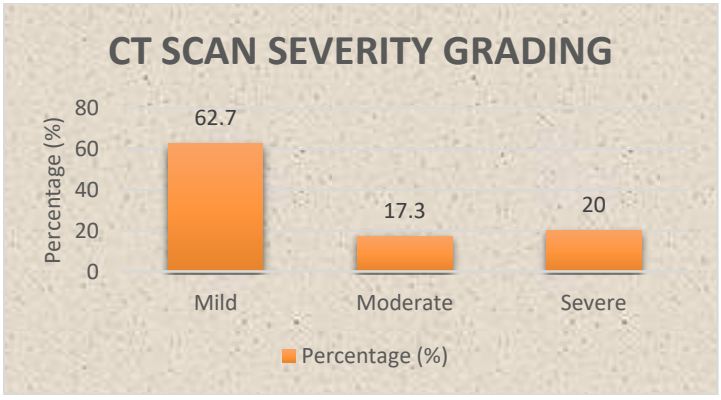



**Graph 4: Bar diagram showing other conditions**

**Table 4: CT scan severity grading**

| CT Scan Severity Grading | | Number | Percentage |
|---|---|---|---|
| Mild | (<=7 / 25) | 47 | 62.7 |
| Moderate | (8-17 / 25) | 13 | 17.3 |
| Severe | (>18 / 25) | 15 | 20.0 |
| Total | | 75 | 100.0 |

According to CT scan severity grading, 47 (62.7%) patients had mild severity grade, 13 (17.3%) patients had moderate severity grade and 15 (20.0%) patients had severe grade.




**Graph 5: Bar diagram showing CT scan severity grading**

**Table 5: Comparison of mean NLR in relation to various parameters**

| | | No. | NLR [Mean±SD] | 't' value | P value |
|---|---|---|---|---|---|
| Age¶ | 20-40 years | 34 | 3.07 ± 4.47 | F value = 4.600 | 0.005* |
| | 41-60 years | 28 | 8.21 ± 7.41 | | |
| | 61-80 years | 11 | 9.23 ± 8.70 | | |
| | >80 years | 2 | 9.90 ± 7.21 | | |
| Sex§ | Female | 32 | 4.53 ± 4.39 | -1.689, df=73 | 0.096, NS |
| | Male | 43 | 7.22 ± 8.15 | | |
| Diabetes Mellitus§ | No | 59 | 4.45 ± 5.89 | -4.370, df=73 | 0.001* |
| | Yes | 16 | 12.07 ± 7.21 | | |
| Hyper-tension§ | No | 71 | 5.87 ± 6.92 | -1.104, | 0.273, NS |

| | | | | | |
|---|---|---|---|---|---|
| | Yes | 4 | 9.78 ± 5.97 | df=73 | |
| SpO2 <90%§ | No | 49 | 2.17 ± 1.73 | -10.740, df=73 | 0.001* |
| | Yes | 26 | 13.44 ± 6.99 | | |
| ICU Admission§ | No | 56 | 3.88 ± 5.52 | -5.615, df=73 | 0.001* |
| | Yes | 19 | 12.54 ± 6.61 | | |
| CT Severity Grade¶ | Mild | 47 | 2.15 ± 2.14 | F value = 68.367 | 0.001* |
| | Moderate | 13 | 8.77 ± 3.61 | | |
| | Severe | 15 | 16.04 ± 7.78 | | |

***§ - Unpaired 't' test applied.***
***¶ - One-Way ANOVA test applied.***
***A p value of < 0.05 was taken as statistically significant.***

The above table shows the comparison of mean NLR in relation to various parameters.

**Age:** The mean NLR in age group 20-40 years was 3.07 ± 4.47, in the age group 41-60 years it was 8.21 ± 7.41, in the age group 61-80 years it was 9.23 ± 8.70 and in the age group more than 80 years it was 9.90 ± 7.21. The F value obtained was 4.600 and p value was =0.005 which is statistically significant, showing a significantly varying mean NLR in relation to various age groups. The mean NLR was lowest in the age group 20-40 years and it was highest in the patients of age more than 80 years.

**Sex:** The mean NLR in the females was 4.53 ± 4.39 and in males it was 7.22 ± 8.15. The difference was found to be statistically not significant (p=0.096), showing a comparable mean NLR value between the females and males.

**Diabetes Mellitus:** The mean NLR in the patients with diabetes mellitus was 12.07 ± 7.21, while in non-diabetics it was 4.45 ± 5.89. The difference was found to be statistically significant (p=0.001), showing a significantly high mean NLR in diabetic patients.

**Hypertension:** The mean NLR in the patients with hypertension was 9.78 ± 5.97 and in patients without hypertension was 5.87 ± 6.92. The difference was found to be statistically not significant (p=0.273), showing a comparable mean NLR between the hypertensives and the non-hypertensives.

**$SpO_2$< 90%:** The mean NLR in the patients with $SpO_2$< 90% was 13.44 ± 6.99, while in patients with SpO2 more than 90% was 2.17 ± 1.73. The difference was found to be statistically significant (p=0.001), showing a significantly higher mean NLR in patients with $SpO_2$< 90%.

**ICU admission:** The mean NLR in the patients who required ICU admission was 12.54 ± 6.61 and in patients who did not require ICU admission was 3.88 ± 5.52. The difference was found to be statistically significant (p=0.001), showing a significantly higher mean NLR in patients who required ICU admission.

**CT Severity Score:** The mean NLR in mild grade was 2.15 ± 2.14, in the moderate grade it was 8.77 ± 3.61 and in the severe grade it was 16.04 ± 7.78. The F value obtained was 68.367 and the P value was 0.001, which is highly significant. This shows that there is a variation in the mean NLR among the CT severity grades. The mean NLR was lowest in the mild group and it was highest in the severe grade. With the increase in CT severity grade, the mean NLR also showed an increase.

**Table 6: Comparison of mean AGR in relation to various parameters**

| | | **No.** | **AGR [Mean±SD]** | **'t' value** | **P value** |
|---|---|---|---|---|---|
| Age¶ | 20-40 years | 34 | 1.39 ± 0.36 | F value = 4.603 | 0.005* |
| | 41-60 years | 28 | 1.05 ± 0.32 | | |
| | 61-80 years | 11 | 1.25 ± 0.40 | | |
| | >80 years | 2 | 1.15 ± 0.71 | | |
| Sex§ | Female | 32 | 1.19 ± 0.36 | -0.880, df=73 | 0.382, NS |
| | Male | 43 | 1.27 ± 0.41 | | |
| Diabetes Mellitus§ | No | 59 | 1.31 ± 0.38 | 3.713, df=73 | 0.001* |
| | Yes | 16 | 0.94 ± 0.28 | | |
| Hyper-tension§ | No | 71 | 1.25 ± 0.39 | 1.547, df=73 | 0.126, NS |
| | Yes | 4 | 0.95 ± 0.32 | | |
| SpO2 <90%§ | No | 49 | 1.42 ± 0.29 | 7.184, df=73 | 0.001* |
| | Yes | 26 | 0.89 ± 0.30 | | |
| ICU Admission§ | No | 56 | 1.34 ± 0.33 | 4.417, df=73 | 0.001* |
| | Yes | 19 | 0.93 ± 0.38 | | |
| CT Severity | Mild | 47 | 1.43 ± 0.28 | F value = | 0.001* |

| | | | | | |
|---|---|---|---|---|---|
| Grade¶ | Moderate | 13 | 0.91 ± 0.35 | 28.855 | |
| | Severe | 15 | 0.89 ± 0.28 | | |

***§ - Unpaired 't' test applied.***
***¶ - One-Way ANOVA test applied.***
***A p value of < 0.05 was taken as statistically significant.***

The above table shows the comparison of mean AGR in relation to various parameters.

**Age:** The mean AGR in age group 20-40 years was 1.39 ± 0.36, in the age group 41-60 years it was 1.05 ± 0.32, in the age group 61-80 years it was 1.25 ± 0.40 and in the age group more than 80 years it was 1.15 ± 0.71. The F value obtained was 4.603 and p value was =0.005 which is statistically significant, showing a significantly varying mean AGR in relation to various age groups. The mean AGR was lowest in the age group 41-60 years and it was highest in the patients of age between 20-40 years.

**Sex:** The mean AGR in the females was 1.19 ± 0.36 and in males it was 1.27 ± 0.41. The difference was found to be statistically not significant (p=0.382), showing a comparable mean AGR value between the females and males.

**Diabetes Mellitus:** The mean AGR in the patients with diabetes mellitus was 0.94 ± 0.28, while in non-diabetics it was 1.31 ± 0.38. The difference was found to be statistically significant (p=0.001), showing a significantly low mean AGR in diabetic patients.

**Hypertension:** The mean AGR in the patients with hypertension was 0.95 ± 0.32 and in patients without hypertension was 1.25 ± 0.39. The difference was found to be statistically not significant (p=0.126), showing a comparable mean AGR between the hypertensives and the non-hypertensives.

**$SpO_2$< 90%:** The mean AGR in the patients with $SpO_2$< 90% was 0.89 ± 0.30, while in patients with SpO2 more than 90% was 1.42 ± 0.29. The difference was found to be statistically significant (p=0.001), showing a significantly lower mean AGR in patients with $SpO_2$< 90%.

**ICU admission:** The mean AGR in the patients who required ICU admission was 0.93 ± 0.38 and in patients who did not require ICU admission was 1.34 ± 0.33. The difference was found to be statistically significant (p=0.001), showing a significantly lower mean AGR in patients who required ICU admission.

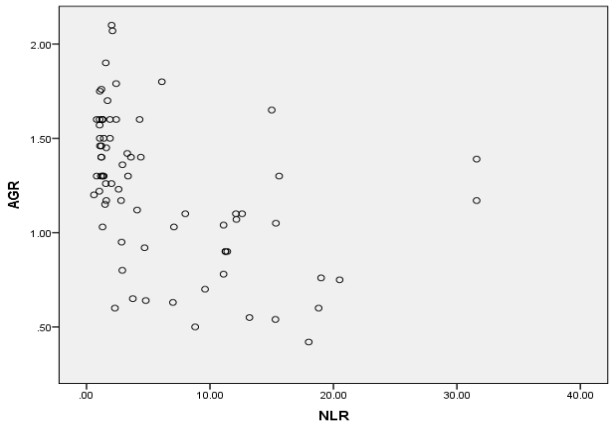
**CT Severity Score:** The mean AGR in mild grade was 1.43 ± 0.28, in the moderate grade it was 0.91 ± 0.35 and in the severe grade it was 0.89 ± 0.28. The F value obtained was 28.855 and the P value was 0.001, which is highly significant. This shows that there is a variation in the mean AGR among the CT severity grades. The mean AGR was highest in the mild group and it was lowest in the severe grade. With the increase in CT severity grade, the mean AGR shows a significant decrease.

**Table 7: Correlation between NLR and AGR**

| Correlation | 'r' value | P value |
|---|---|---|
| NLR to AGR | -0.449 | 0.001 |

***Pearson coefficient of correlation applied. P value =0.001, Highly significant***

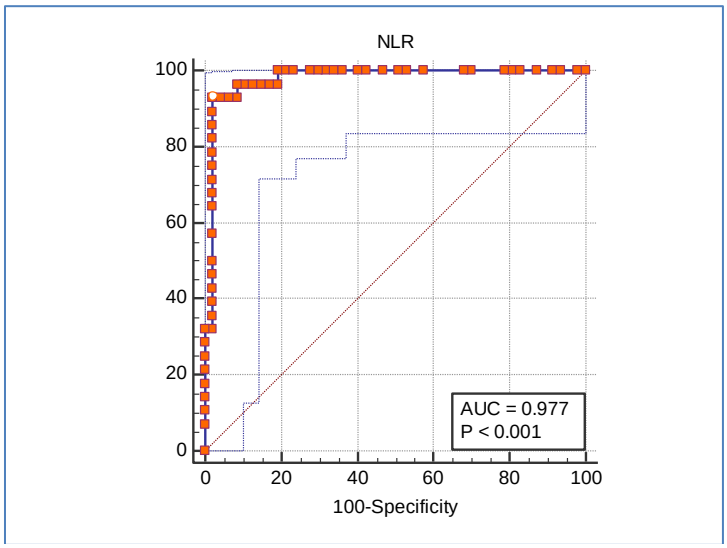
In the present study, the correlation between NLR and AGR was found to be negative, fair and statistically significant (p=0.001), showing that as the NLR ratio is increasing the AGR ratio is decreasing and this correlation is statistically significant.




**Graph 6: Scatter plot showing correlation between NLR and AGR**

## ROC CURVE ANALYSIS

**Table 8: ROC curve of NLR in relation to CT scan severity**




| | |
|---|---|
| Variable | NLR |
| Classification variable | CTGrade2 |

| | |
|---|---|
| Sample size | 75 |
| Positive group [a] | 28(37.33%) |
| Negative group [b] | 47(62.67%) |

[a]CTGrade2 = 1
[b]CTGrade2 = 0

| | |
|---|---|
| Disease prevalence (%) | unknown |

**Area under the ROC curve (AUC)**

| | |
|---|---|
| Area under the ROC curve (AUC) | 0.977 |
| Standard Error[a] | 0.0161 |
| 95% Confidence interval[b] | 0.913 to 0.998 |
| z statistic | 29.554 |
| Significance level P (Area=0.5) | <0.0001 |

[a] DeLong et al., 1988
[b] Binomial exact

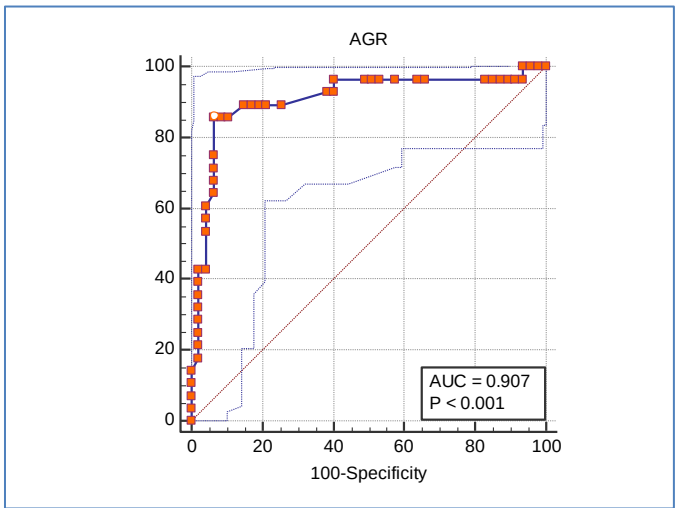
**Youden index**

| | |
|---|---|
| Youden index J | 0.9073 |
| Associated criterion | >4.4 |
| Sensitivity | 92.86 |
| Specificity | 97.87 |

The above table shows the ROC curve of NLR in relation to CT scan severity.
The CT scan severity of moderate and severe were combined and called positive and mild severity was called as negative. There were 28 (37.33%) positive cases and 47 (62.67%) negative cases.
The ROC curve of NLR was drawn against the CT scan severity grading.
The area under the curve was found to be 0.977, which is 'excellent'. The associated criterion obtained was >4.4 (cut-off). This shows that for an NLR more than 4.4, the patient can be labelled as having severity score severe and for an NLR less than 4.4, the patient can be labelled as having severity score mild.

At this cut-off the sensitivity of NLR in the diagnosis of severity of the disease is 92.86% and the specificity is 97.87%. Both sensitivity and specificity are very high and NLR can be independently used for the diagnosis of severity of covid-19 patients.

**Table 9: ROC curve of AGR in relation to CT scan severity**




| | |
|---|---|
| Variable | AGR |
| Classification variable | CTGrade2 |

| | |
|---|---|
| Sample size | 75 |
| Positive group [a] | 28(37.33%) |
| Negative group [b] | 47(62.67%) |

[a]CTGrade2 = 1
[b]CTGrade2 = 0

| | |
|---|---|
| Disease prevalence (%) | Unknown |

**Area under the ROC curve (AUC)**

| | |
|---|---|
| Area under the ROC curve (AUC) | 0.907 |
| Standard Error[a] | 0.0415 |
| 95% Confidence interval[b] | 0.818 to 0.962 |
| z statistic | 9.821 |
| Significance level P (Area=0.5) | <0.0001 |

[a] DeLong et al., 1988
[b] Binomial exact

**Youden index**

| | |
|---|---|
| Youden index J | 0.7933 |
| Associated criterion | ≤1.1 |
| Sensitivity | 85.71 |
| Specificity | 93.62 |

The above table shows the ROC curve of AGR in relation to CT scan severity.
The CT scan severity of moderate and severe were combined and called positive and mild severity was called as negative. There were 28 (37.33%) positive cases and 47 (62.67%) negative cases.
The ROC curve of AGR was drawn against the CT scan severity grading.
The area under the curve was found to be 0.907, which is 'excellent'. The associated criterion obtained was ≤1.1 (cut-off). This shows that for an AGR less than or equal to 1.1, the patient can be labelled as having severity score severe and for an AGR more than 1.1, the patient can be labelled as having severity score mild.

At this cut-off the sensitivity of AGR in the diagnosis of severity of the disease is 85.71% and the specificity is 93.62%. Both sensitivity and specificity are very high and AGR can be independently used for the diagnosis of severity of covid-19 patients.

**SENSITIVITY, SPECIFICITY, POSITIVE PREDICTIVE VALUE, NEGATIVE PREDICTIVE VALUE AND DIAGNOSTIC ACCURACY**

**Table 10: Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of NLR (cut-off) against CT scan severity**

| | | CT Scan grading | | Total |
|---|---|---|---|---|
| | | Negative | Positive | |
| **NLR (cut-off)** | Negative | 46 | 2 | 48 |
| | Positive | 1 | 26 | 27 |
| | Total | 47 | 28 | 75 |

The above table shows the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of NLR (cut-off) against CT scan severity.
Here, NLR(cut-off) has been taken as >4.4.
CT scan grading (<=7, Mild) has been considered as Negative and grading (>7, Moderate + Severe) has been considered as severe. The analysis of NLR has been done against this CT scan severity grading.

Sensitivity= 92.86%
Specificity= 97.87%
Positive predictive value= 96.30%
Negative predictive value= 95.83%
Diagnostic accuracy= 96.00%

**Table 11: Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of AGR (cut-off) against CT scan severity**

| | | CT Scan grading | | Total |
|---|---|---|---|---|
| | | Negative | Positive | |
| **AGR (cut-off)** | Negative | 44 | 4 | 48 |
| | Positive | 3 | 24 | 27 |
| | Total | 47 | 28 | 75 |

The above table shows the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of AGR (cut-off) against CT scan severity.
Here, AGR(cut-off) has been taken as $\leq$1.1.
CT scan grading (<=7, Mild) has been considered as Negative and grading (>7, Moderate + Severe) has been considered as severe. The analysis of AGR has been done against this CT scan severity grading.
Sensitivity= 85.71%
Specificity= 93.62%
Positive predictive value= 88.89%
Negative predictive value= 91.67%
Diagnostic accuracy= 90.67%

**Discussion**

The current difficulty in COVID-19 pandemic management is the shortage of medical resources, especially critical care resources in developing as well as developed countries. Early identification critical illness and risk stratification management will help alleviate insufficient medical resources and might reduce mortality.

The COVID-19 pneumonia is not severe in the early stage, but the critical patients deteriorated on 7–14 days of illness course and entered a state of severe pneumonia and acute respiratory failure. The critically ill or death of patients with COVID-19 infection were mostly of an old age and associated with comorbidities. In the study diabetes significantly associated with raised NLR and low AGR in severe COVID-19 infection.

In the study, the data of 75 patients with RT-PCR proven COVID-19 were analysed, the baseline characteristics of patient with laboratory reports compared with imaging features were demonstrated.

The CT scan severity of moderate and severe were combined and called positive and mild severity was called as negative. The ROC curve of NLR was drawn against the CT scan severity grading.

The area under the curve was found to be 0.977, which is 'excellent'. The associated criterion obtained was >4.4 (cut-off). This shows that for an NLR more than 4.4, the patient can be labelled as severe and vice versa.

At this cut-off the sensitivity of NLR in the diagnosis of severity of the disease is 92.86% and the specificity is 97.87%. Both sensitivity and specificity are very high and NLR can be independently used for the diagnosis of severity of covid-19 patients.

A recent study by Qin et al. showed a significantly higher NLR in patients with severe forms of COVID-19 in a cohort of 452 hospitalised patients [13]. Another study by Arturo Ciccullo from Italy also showed that a higher NLR at hospital admission was associated with a more severe outcome in 74 patients: in particular, a NLR of >4 was a predictor of admission to the ICU. Patients with severe disease presented a significantly higher NLR at admission compared with patients with a milder form of COVID-19.

The ROC curve of AGR was found to be 0.907, which is 'excellent'. The associated criterion obtained was ≤1.1 (cut-off). This shows that for an AGR less than or equal to 1.1, the patient can be labelled as having severity score severe and vice versa.

At this cut-off the sensitivity of AGR in the diagnosis of severity of the disease is 85.71% and the specificity is 93.62%. Both sensitivity and specificity are very high and AGR can also be independently used for the diagnosis of severity of covid-19 patients.

A study by Ruili LI from Beijing also correlated various laboratory parameters including AGR and compared with CT severity index and found significant correlation of change in AGR with CT severity[15].

This study tries to find out that which one is more accurate predictor marker of severity of COVID- 19 infection and result showed that NLR as compared to AGR is better predictor marker in terms of sensitivity (92.86 vs.85.71), specificity (97.87 vs. 93.62), positive predictive value (96.3 vs. 88.9) and negative predictive value (95.83 vs. 91.67). Even Diagnostic accuracy of NLR is significantly higher (96 vs 90.67) for predicting severity in moderate to severely infected COVID-19 patients.

## Conclusion

This study proves that N-L ratio is more accurate predictor of severity of SARS-COVID-19 infection than A-G ratio with more sensitivity, specificity, positive and negative predictive value and can be used as a severity marker in places where medical resources is limited. However, a larger study with more subjects requires for exact correlation.

## References

1. Zhang Z-L, Hou Y-L, Li D-T, Li F-Z. Laboratory findings of COVID-19: a systematic review and meta-analysis. Scand J Clin Lab Invest. (2020) 80:441– 7. doi: 10.1080/00365513.2020.1768587
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. (2020) 395:497–506. doi: 10.1016/S0140-6736(20)30183-5
3. Coomes EA, Haghbayan H. Interleukin-6 in COVID-19: a systematic review and meta-analysis. medRxiv [Preprint]. (2020). doi: 10.1101/2020.03. 30.20048058
4. Zhang J, Wang X, Jia X, Li J, Hu K, Chen G, et al. Risk factors for disease severity, unimprovement, and mortality of COVID-19 patients in Wuhan, China. Clin Microbiol Infect. (2020) 26:767–72. doi: 10.1016/j.cmi.2020.04.012
5. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. (2020) 180:934–43. doi: 10.1001/jamainternmed.2020.0994
6. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020;395:1054–1062. doi: 10.1016/S0140-6736(20)30566-3. Errata in: Lancet 2020;395:1038; Lancet 2020;395: 1038. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
7. Huguet E, Maccallini G, Pardini P, et al. Reference values for neutrophil to lymphocyte ratio (NLR), a biomarker of cardiovascular risk, according to age and sex in a Latin American population. Curr Probl Cardiol. 2019;100422. [PubMed]
8. Wang X, Qiu L, Li Z, Wang XY, Yi H. Understanding the multifaceted role of neutrophils in Cancer and autoimmune diseases. *Front Immunol.* 2018;**9**:2456. doi: 10.3389/ fimmu. 2018.02456. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
9. Mei Z, Shi B, Wang J, et al. Prognostic role of pretreatment blood neutrophil-to-lymphocyte ratio in advanced cancer survivors: a systematic review and meta-analysis of 66 cohort studies. *Cancer Treat Rev.* 2017;**58**:1–13. doi: 10.1016/j.ctrv.2017. 05.005 [PubMed] [CrossRef] [Google Scholar]
10. Russell CD, Parajuli A, Gale HJ, et al. The utility of peripheral blood leucocyte ratios as biomarkers in infectious diseases: a systematic review and meta-analysis. *J Inf Secur.* 2019;**78**(5):339–348. [PMC free article] [PubMed] [Google Scholar]
11. Yao XH, Li TY, He ZC, et al. A pathological report of three COVID-19 cases by minimally invasive

autopsies. *Zhonghua Bing Li Xue Za Zhi.* 2020;**49**(0):E9. [PubMed] [Google Scholar

12. Predictive value of the neutrophil to lymphocyte ratio for disease deterioration and serious adverse outcomes in patients with COVID-19: a prospective cohort study Zhi-Yong Zeng,[1] Shao-Dan Feng,[2] Gong-Ping Chen,[3] and Jiang-Nan Wu[4;]BMC Infect Dis. 2021; 21: 80.
13. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. *Clin Infect Dis.* 2020 Mar 12 doi: 10.1093/cid/ciaa248. [Epub ahead of print] [PMC free article] [PubMed] [CrossRef] [Google Scholar]
14. Arturo Ciccullo et al. Neutrophil-to-lymphocyte ratio and clinical outcome in COVID-19: a report from the Italian front lineInt J Antimicrob Agents. 2020 Aug; 56(2)10.1016/j.ijantimicag.2020. 106017[PMC free article] [PubMed] [CrossRef] [Google Scholar]
15. Li, R., Liu, G., Huang, X. *et al.* Dynamic changes in clinical and CT characteristics of COVID-19 cases with different exposure histories: a retrospective study. *BMC Infect Dis* 20, 567 (2020). https://doi.org/10.1186/s12879-020-05306-x