ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 09 | September - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

PROGNOSTIC ROLE OF NLR AND RBS LEVELS IN DIABETIC PATIENTS WITH SEVERE COVID-19 DISEASE

Endocrinology

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ABSTRACT

Objective-This retrospective study was done to assess the role of NLR (Neutrophil to lymphocyte ratio) and RBS (RANDOM BLOOD SUGAR) levels at the time of admission as prognostic markers and correlate them with clinical outcome.

Materials and methods: A total of 100 diabetic patients with severe COVID-19 Disease, requiring ICU admission were studied at SRN Hospital, Prayagraj. Blood samples were sent for various inflammatory markers along with random blood glucose levels. Patients were divided as survivors and non- survivors.

Results: The mean NLR was higher in the group of patients who did not survive (11.35±8.09) than in the patients who survived (7.79±5.27). Mean RBS (in mg/dL) in the survivor group and the non-survivor group at the time of admission was 232.19±133.75 and 333.41±130.81 respectively. The NLR, RBS, CRP cutoff were identified as >7.247, >254.6 mg/dL,>12.86 mg/L respectively to predict mortality using the ROC curve (p value <0.05).

Conclusion:NLR and RBS at the time of admission can be easily used as surrogate markers for predictors of mortality. Screening and intensive glucose control is strictly recommended for all diabetic patients.

KEYWORDS

Covid-19, NLR, Diabetes, RBS, Mortality, Inflammatory markers

1. INTRODUCTION

COVID-19 is a rapidly spreading disease which mainly involves the respiratory tract. The WHO declared it as a major pandemic in the month of March 2020.[1] Currently, the disease has affected nearly 31 million of the population and is responsible for the death of 4.1 million people.[2]

After causing two major waves in India, it has been observed that diabetes which affects nearly 65 million of the Indian population, is also a major risk factor of mortality in COVID-19.[3]

Such patients are far more likely to develop serious complications ranging from need of ICU, longer hospital stay, need of mechanical ventilation and death due to hypoxemic respiratory failure.[4]

Poorly controlled diabetes mellitus is a major risk factor for infection as hyperglycemia effectively impairs the immune response and causes delayed healing of various infections, including various skin and mucosal infections as well.[5] Hence, the effects could have easily been anticipated.

Inflammation plays a key role in the pathogenesis of COVID-19 and COVID-19 is a classical example of inflammation and dysregulated immune response resulting in compromise of the host.[6]

Various inflammatory markers are therefore used to assess the prognosis of patients in COVID-19. One such inflammatory marker is neutrophil lymphocyte ratio. Neutrophil to Lymphocyte ratio has been widely studied in sepsis and has been found to be an effective marker of systemic inflammation.[7]

This study was planned to evaluate the role of neutrophil lymphocyte ratio in diabetic patients affected with severe COVID-19 disease.

2. MATERIALS AND METHODS

This study was conducted in Swaroop Rani Hospital, MLN Medical College, Prayagraj, Uttar Pradesh which is a tertiary care centre for COVID 19. It was a retrospective observational study. The biochemical parameters of diabetic patients presenting to this centre between 1 April 2021 to 21 May 2021 were recorded.

A total of 100 patients admitted in COVID ICU SRN hospital were taken in this study. Patients were diagnosed to have COVID 19 by RT-PCR at Department of Microbiology MLN medical college, Prayagraj.

2.1 INCLUSION CRITERIA

Only those patients were included in the study who had diabetes (either known or newly diagnosed) and required admission to COVID ICU owing to development of severe symptoms of the disease (defined as SpO2 of <90% on room air or RR >30/min).

2.2 EXCLUSION CRITERIA

Patients with mild or moderate COVID-19 symptoms were not included in the study. Patients of leukemia, or any other malignancy were also excluded.

2.3 BIOCHEMICAL PARAMETERS

The routine biochemical investigations were sent at the time of admission of all the patients, which included CBC(Complete blood count), Liver and kidney function tests, Random Blood Sugar and various inflammatory markers such as C- Reactive Protein, D Dimer. Neutrophil to lymphocyte ratio was calculated at day 1 of admission and was compared among both the groups. The outcome was defined as survival or mortality during the hospital stay. The biochemical parameters were compared among survivors and non-survivors.

2.4 STATISTICAL ANALYSIS

Baseline characteristics were compared among survivors and non-survivors. Continous variables were expressed as mean ± standard deviation and correlation was compared using Student's t test and Mann-Whitney U test. The associations between inflammatory markers and clinical outcomes were analysed using multivariate binary regression analysis adjusted for age and sex. Receiver operating characteristic (ROC) curves were drawn to assess the accuracy of various indicators in predicting prognosis of COVID-19. Data analyses were performed using SPSS 23 and P values<0.05 were considered statistically significant.

Table 1: Comparison of characteristics among survivors and non survivors.

CHARACTERISTICS	SURVIVORS (MEAN± STANDARD DEVIATION)	NON-SURVIVORS (MEAN± STANDARD DEVIATION)	p VALUE
AGE	60.48±11.08	62.24±13.54	
MALE SEX	28 (56%)	30 (60%)	
TLC	11670±6288.05	12066±6229.74	0.7524
NLR	7.79±5.27	11.35±8.09	0.0106
D DIMER	2.76±2.76	4.53±3.94	0.0107
CRP	21.71±32.74	53.65±39.84	<0.0001
RBS	232.19±133.75	333.41±130.81	0.0002

Table 2: Multivariate Binary Logistic Regression to study the association of Mortality with various parameters

Variable	Coefficient	Std. Error	Odds ratio	95% CI	P
D-DIMER	0.12439	0.072724	1.1325	0.9820 to 1.3060	0.0872
CRP	0.022010	0.0070382	1.0223	1.0082 to 1.0365	0.0018
NLR	0.096211	0.044181	1.1010	1.0097 to 1.2006	0.0294
RBS	0.0055579	0.0019159	1.0056	1.0018 to 1.0094	0.0037

Table 3:ROC Curves Of Neutrophil Lymphocyte Ratio (NLR), CRP (C- Reactive Protein), RBS Levels At The Time Of Admission In Association With Mortality

	NLR	CRP	RBS
Area under the ROC curve (AUC)	0.676	0.769	0.730
Standard Error [a]	0.0541	0.0486	0.0526
95% Confidence interval [b]	0.575 to 0.766	0.674 to 0.848	0.632 to 0.814
z statistic	3.245	5.534	4.369
Significance level P (Area=0.5)	0.0012	<0.0001	<0.0001
Associated criterion	>7.25	>12.86	>254.6
Sensitivity	74.00	84.00	78.00

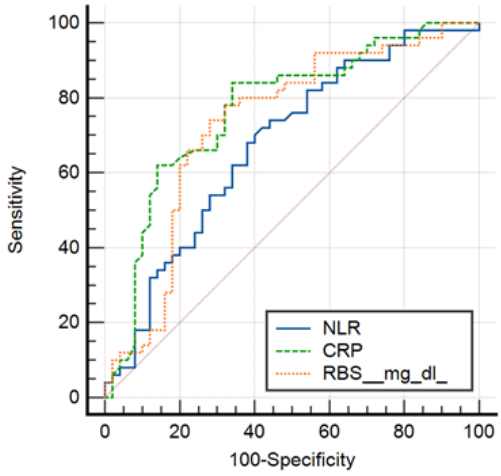

Figure 1: ROC curves of neutrophil lymphocyte ratio (NLR), CRP, RBS levels at the time of admission in association with mortality

RESULTS

A total of 100 diabetic patients were included in the study. Patients were divided into two groups- survivors and non survivors, each having 50 patients. Both groups were matched in terms of age and sex. The mean NLR was higher in the non-survivor group (11.35±8.09) than the survivor group (7.79±5.27) (p value- 0.0106).

Mean RBS at the time of admission was 232.19±133.75 in the survivor group and was significantly lower than the mean of the non- survivor group, being 333.41±130.81 (p value 0.0002).

The multivariate logistic regression models, adjusted for age and sex concluded that patients who had a higher NLR, RBS and even CRP at the time of admission had increased chances of mortality .

ROC curves were plotted to predict the mortality on the basis of NLR, RBS, CRP which identified the cut-off to be >7.247, >254.6 mg/dL, >12.86 mg/L respectively (p value <0.05).

DISCUSSION

A total of 100 patients diagnosed with severe COVID-19 and who were diabetics were included in the study. The value of NLR >7.25 was taken as cut-off to predict mortality as determined by the ROC curve. Liu G et al [8] did a similar study on 134 type 2 diabetics with COVID-19 in Renmin Hospital of Wuhan. ROC curve results displayed that higher NLR predicted severity of disease with AUC of 0.730 which was statistically significant, (P value of 0.002, 95% CI- 0.607-0.854). They concluded that COVID-19 diabetes patients with higher NLR had an increased severity of the disease and a longer duration of hospital stay.

Another retrospective study was done by Liu Y et al[9], who analysed 245 patients of COVID-19 admitted to the Zhongnan Hospital of Wuhan University from January 1 to February 29 . They concluded that for each unit increase in NLR, there was a 8% higher risk of mortality (OR = 1.08; 95% CI, 1.01 to 1.14; P = 0.0147). Liu J et al[10] did a prospective study on 61 patients infected with COVID-19 and concluded that when age ≥ 49.5 years old and NLR ≥ 3.3, 46.1% of the COVID-19 patients with mild disease will become severe, and the mean time is 6.3 days.

Cai Y et al[11] conducted a study on 941 hospitalised patients to assess the correlation of fasting blood glucose levels with mortality. FBG ≥7.0 mmol/L was found to be a independent risk factor for the mortality of COVID-19 regardless of the presence or not of a history of diabetes (hazard ratio, 2.20 [95% CI, 1.21-4.03]; P = 0.010). Yang P et al[12] did a study on 263 patients of COVID-19 and found that the patients with a fasting plasma glucose level of ≥11.1 mmol/L (200 mg/dL) had an increased risk of mortality. (HR, 2.09; 95% CI, 1.21-3.64).

CONCLUSION

The study aimed to assess the role of NLR and RBS levels at the time of admission in diabetic patients predict mortality, which are both widely available and cost effective parameters. Both NLR and RBS levels easily predict mortality. The study concludes that intensive glycemic control should be a target of all diabetics. As diabetes is a major co-morbidity responsible for increased mortality in COVID-19, diabetic patients should be effectively screened and get vaccinated as soon as possible.

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