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Original Research Paper

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NEUTROPHIL TO ALBUMIN RATIO AS A PROGNOSTIC MARKER OF DISEASE SEVERITY IN COVID 19 INFECTION AND ITS RELATION TO NEUTROPHIL LYMPHOCYTE RATIO

Dr Kavya	2rd Year Resident General Medicine
Dr Vidyasagar Cr	Professor And Hou General Medicine
Dr Jithendra Chaitanya	Senior Resident Dept Of General Medicine
Dr Pujitha.s.n	Senior Resident Dept Of General Medicine
Dr.manohar Gowda	2rd Year Resident General Medicine

ABSTRACT

Introduction: Covid-19 is an acute inflammatory respiratory disease that has been affecting the world for a while now. Severity of the disease can be assessed by various prognostic markers like leucocyte count, neutrophil count, lymphocyte count etc.

Aim & objective:

1. To estimate Neutrophil Albumin Ratio (NAR) in Covid 19 positive patients within 24 hours of admission
2. To compare NAR (Neutrophil Albumin Ratio) and NLR (Neutrophil Lymphocyte Ratio) as prognostic markers of disease severity in COVID 19 infection.

Methodology: Present study was a retrospective Observational study carried out on 250 RTPCR confirmed Covid 19 positive patients admitted in department of General Medicine at RLJH Hospital. Complete blood count, neutrophil count, lymphocyte count and serum albumin were recorded. NAR and NLR was correlated with 3 categories of patients based on the severity of the disease. The outcome of each patient (Recovery/Death) was correlated with the NAR and NLR. **Results & discussion:** Severity of the disease was significantly associated with Total leucocyte Count ($P<0.001$), Neutrophil count and Lymphocyte count. ($p<0.001$) and Serum Albumin. There was a statistically significant difference found between NAR and severity and NLR and severity. NAR is better predictor of mortality than NLR. NAR is a better prognostic marker of severity of disease in Covid 19 with higher specificity.

KEYWORDS : NAR , Disease severity, COVID-19 infection , coronavirus , prognostic marker

INTRODUCTION:

The World Health Organization (WHO) has recently declared Covid19 a public health emergency of international concern.[1] The current Covid-19 case statistics in India are 3lakh new infections along with 290 lakh recoveries and 63 lakh deaths. [3] Extensive lung damage in Covid 19 patients appears to be associated with initial high viral load, neutrophil infiltration in the lungs with elevated cytokines with a decrease of peripheral T lymphocytes.[4]

Neutrophil count mark an early inflammatory response and was demonstrated as an important marker for systemic infection. Albumin is a negative acute phase reactant and decreases in acute infection. Hence the prognostic relevance of Neutrophil Albumin Ratio(NAR) in Covid 19 and categorization of patients is essential.

Neutrophils cause endothelial injury and necro-inflammation via complement activation and promote venous thrombosis during Covid 19.[5] Albumin downregulates the expression of ACE 2 receptors. Low serum albumin levels were associated with increased risk of mortality.[6]

Covid 19 involving the circulatory, nervous and renal systems was observed.[7]

Present study was conducted to see NAR as prognostic marker in Covid 19 infection and comparing NAR with MLR as markers of severity in COVID 19 infection.

AIM & OBJECTIVES:

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2. To compare NAR (Neutrophil Albumin Ratio) and NLR (Neutrophil Lymphocyte Ratio) as prognostic markers of disease severity in COVID 19 infection.

MATERIAL & METHODS:

Present study was a retrospective Observational study carried out at at R L Jalappa hospital, Kolar. Study population was 250 RTPCR confirmed Covid 19 positive patients admitted in department of General Medicine at RLJH Hospital. Study period was JULY 2021-SEPTEMBER 2021. Source of data was medical records of study population at hospital.

Inclusion Criteria:

1. RTPCR confirmed Covid 19 Positive patients for nasal and oropharyngeal swab
2. Age more than 18 years

Exclusion Criteria:

1. pregnant patients
2. Patients with Malignancy

Study was approved by ethical committee of the institute. Data was collected from the hospital records. Data collected was sociodemographic data, clinical history and clinical course of the patients. Reports of investigations were recorded. Complete blood count and serum Albumin were collected within 24 hours of admission.

NAR and NLR were estimated and the patients were classified into 3 categories mild, moderate and severe at the time of presentation based on clinical guidelines.

1. MILD - Upper respiratory tract symptoms, fever without breathlessness spo2 >94%@Room air; Respiratory rate < 24cpm
2. MODERATE - breathlessness with spo2 <94%@Room air; Respiratory rate ≥24cpm
3. SEVERE - breathlessnesss spo2 <90%@room air; Respiratory rate ≥30cpm

NAR and NLR was correlated with these 3 categories of patients based on the severity of the disease. The outcome of each patient (Recovery/Death) was correlated with the NAR and NLR.

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data.

Continuous data was represented as mean and standard deviation. ANOVA was used as test of significance to identify the mean difference between more than two quantitative variables

Receiver operating characteristic (ROC) and optimal cut-off points were chosen for the calculation of sensitivity, specificity, positive and negative predictive values. A test that predicts an outcome no better than chance has an area under the ROC curve of 0.5. An area under the ROC curve above 0.8 indicated fairly good prediction.

RESULTS:

- Table 1 shows distribution of study subjects according to sex and severity. Out of total 250 patients 87 were females and 163 were male. There was no statistically significant difference found between sex and severity (p= 0.904).

Table 1:- Distribution of subjects according to sex and severity

	SEVERITY			Total
	Mild	Moderate	Severe	
Female	36	18	33	87
	41.4%	20.7%	37.9%	100.0%
Male	72	31	60	163
	44.2%	19.0%	36.8%	100.0%
Total	108	49	93	250
	43.2%	19.6%	37.2%	100.0%

- Statistically significant difference was found between age and severity of patients with covid 19 infection. (P<0.001)
- Severity of the disease was significantly associated with Total leucocyte Count (P<0.001). Similarly, Neutrophil count and Lymphocyte count were significantly associated with severity of the infection. (p<0.001) There was a statistically significant difference found between Serum Albumin and severity.

Table 2:- Comparison of age, TLC, Neutrophil, Lymphocytes, Serum Albumin according to severity.

	SEVERITY						P-value
	Mild		Moderate		Severe		
	Mean	SD	Mean	SD	Mean	SD	
AGE	46.42	15.21	49.35	13.55	57.60	12.23	<0.001
TLC	9.68	5.01	11.09	6.66	13.59	6.35	<0.001
Neutrophil	77.783	9.88	77.17	12.13	86.57	8.58	<0.001
Lymphocytes	17.830	8.43	15.95	8.50	10.31	5.43	<0.001
Serum Albumin	3.36	.24	3.28	.34	2.77	.59	<0.001

- Mean NAR increases as the severity of the disease increases. There was a statistically significant difference found between NAR and severity. There was a statistically significant difference found between NLR and severity. (table 3)

Table 3:- Comparison of NAR, NLR according to severity.

	SEVERITY						P value
	Mild		Moderate		Severe		
	Mean	SD	Mean	SD	Mean	SD	
NAR	23.01	3.74	23.80	5.10	33.23	10.79	<0.001
NLR	6.72	8.78	8.21	10.68	12.26	11.17	<0.001

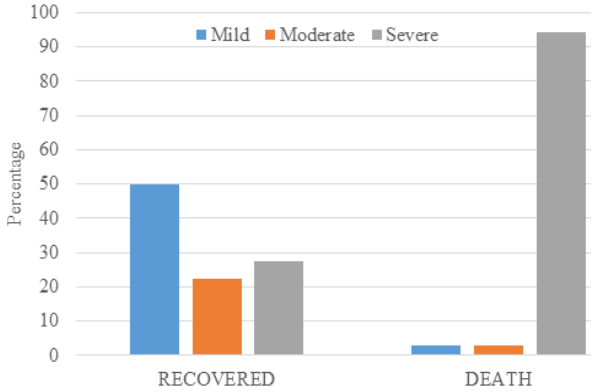

Figure 1:- Graph showing Distribution of subjects according to Mortality and severity.

Figure 2 shows Comparsion of ROC curve of NAR and NLR in predicting mortality. NAR has Area under curve of 0.786 (95% CI 0.730 to 0.835). NLR has area under curve of 0.709 (95% CI 0.649 to 0.76). NAR has better Area under the curve (AUC) than NLR. So, NAR is better predictor of mortality than NLR.

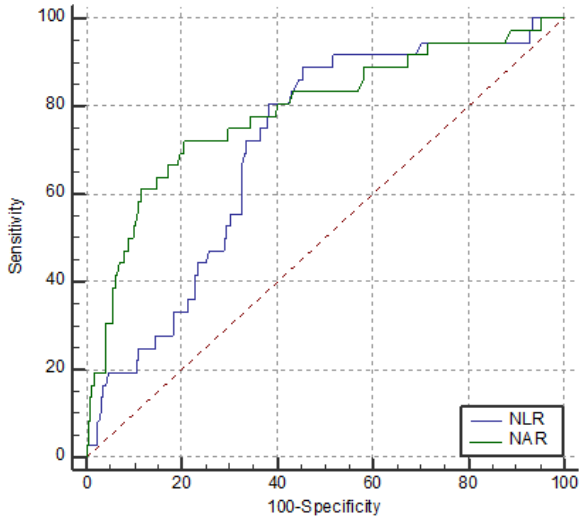

Figure 2:- Comparsion of ROC curve of NAR and NLR in predicting mortality.

	AUC	SE	95% CI
NLR	0.709	0.0426	0.649 to 0.765
NAR	0.786	0.0461	2.730 to 0.835

Table 4 shows Sensitivity of NAR (72.22%) was lower than sensitivity of NLR (88.89%). NAR (79.44%) has higher specificity than NLR (54.67%) so NAR is a better prognostic marker of severity of disease in Covid 19 infection

Table 4: Comparison of NAR and NLR as prognostic test for severity of covid infection

	Cut off value	Sensitivity	Specificity	PPV	NPV
NAR	>28.38	72.22%	79.44%	37.1%	94.4%
NLR	>5.72	88.89%	54.67%	24.8%	96.7%

DISCUSSION:

In our study, 65.2% patients were male and 34.8% patients were female. There was no statistically significant difference found between sex and severity (p= 0.904). Statistically significant difference was found between age and severity of patients with Covid 19 infection. (P<0.001)

In our study, Severity of the disease was significantly associated with Total leucocyte Count (P<0.001), Neutrophil count and Lymphocyte count. (p<0.001)

Neutrophils release chemokines and cytokines which stimulates cytogenesis, angiogenesis, antiviral defense and play an important role in immune response. [8]

Mean serum albumin in patients with mild disease was 3.36± 0.24, in patients with moderate disease was 3.28 ± 0.34 and 2.77± 0.59 in patients with severe disease. There was a statistically significant difference found between Serum Albumin and severity.

In COVID 19 infection, neutrophils increased leading to cytokine storm and ultimately lung injury with acute respiratory distress syndrome. [9]

Albumin is a negative acute-phase reactant and decreases in acute infection. Low albumin levels are associated with increased mortality and poor prognosis. 6. Similar to our study, Aziz et al and Mardani R et al found significantly lower albumin level in severe patients. [10,11]

There was a statistically significant difference found between NAR and severity. Mean NLR in patients with mild disease was 6.72±8.78 while it was increased to 12.26 ± 11.17 in patients with severe disease.

In our study, NAR has better Area under the curve (AUC) than NLR. So, NAR is better predictor of mortality than NLR. NAR is a better prognostic marker of severity of disease in Covid 19 infection with

higher specificity.

Similar to our study, previous studies found that neutrophil count, Neutrophil to lymphocyte ratio and Neutrophil to albumin ratio were important prognostic markers of severity in COVID 19 infection. [9,12-14]

CONCLUSION:

Neutrophil Albumin Ratio is more specific, better marker of severity of disease than Neutrophil lymphocyte ratio.

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