

## ORIGINAL ARTICLE

**Evaluation of Neutrophil Percentage to Albumin Ratio as Predictor of Mortality in Patients with Covid-19**HASEEB U REHMAN<sup>1</sup>, RIZWANA SALIK NUKRICH<sup>1</sup>, MUHAMMAD AZHAR AHMED<sup>2</sup>, SYED MUHAMMAD UMAIR DILAWAR<sup>3</sup>, ELISHA SHALIM<sup>4</sup><sup>1</sup>Consultant Pulmonologist, Sindh Infectious Disease Hospital and Research Center Karachi<sup>2</sup>Senior Registrar Pulmonology, Ojha Institute of Chest Diseases Dow University of Health Sciences Karachi<sup>3</sup>Consultant Pulmonologist, Shaheed Mohtarma Benazir Bhutto Institute of Trauma Karachi<sup>4</sup>Clinical Research Associate, Sindh Infectious Disease Hospital and Research CenterCorresponding author: Haseeb U Rehman, Email: [haseebsoomro87@yahoo.com](mailto:haseebsoomro87@yahoo.com)**ABSTRACT****Background:** Inflammatory acute respiratory syndrome (SARS) is caused by the COV-2 virus. Neutrophils have been implicated in the pathophysiology of the COVID-19 pandemic since its inception, particularly in individuals with advanced disease. This is confirmed by a large number of studies.**Methods:** The study included 200 patients, of whom 100 were in the critical group (group 1) and 100 were in the non-critical group (group 2). White blood cell (WBC) percentage, neutrophil count, albumin, and demographic information were recorded. Neutrophil percentage x 100 /Albumin (g/dl) was used to construct the neutrophil count to albumin ratio (NPAR). To determine whether the measure may be utilized as a predictor for mortality, the NPAR is then compared between groups 1 and 2, as well as between discharge and mortality groups.**Results:** Age and gender had no statistically significant differences in either group. There were no significant variations in the median (IQR) values of neutrophil count (89 vs 91.25), WBC (15.65 vs 14.9), and NPAR (41.3 vs 43.7) between the two groups. Significant differences in albumin (3.330.521 vs. 3.10.51) were identified between the critical and non-critical groups.**Conclusion:** According to our research, the COVID-19 patients' NPAR is a poor predictor of mortality. More study is still required to verify and elucidate the clinical implications of these findings.**Keywords:** Covid-19, Albumin, Neutrophil, Mortality, SARS**INTRODUCTION**

SARS CoV-2, often referred to as coronavirus infections in 2019 (COVID-19), causes severe acute respiratory syndrome. It is a member of the coronavirus family. An acute inflammatory respiratory infection known as SARS COV-2 [1-4].

The most common and cost-effective method for evaluating whether there is any inflammation is to count peripheral leukocytes, particularly neutrophils. Blood cells called neutrophils mediate acute inflammation, and a high neutrophil count indicates a persistent infection [5].

Acute infections cause albumin levels to drop because it is a negative acute phase reactant (6). Low albumin levels are associated with higher mortality risks in hospitalized patients. Low albumin levels have been linked to poor outcomes and mortality, according to numerous studies. [6]

Acute kidney damage, rectal cancer, septic shock, and cardiogenic shock are among the recent studies that have indicated the two combination marker neutrophil-albumin ratio (NPAR) might be utilized as a prognostic inflammatory predictor for death in hospitalized patients [7, 9, 10]. According to a different study, NPAR can be used to predict the prognosis of COVID-19 patients who are hospitalized. According to the study, patients with high NPAR readings have a higher probability of dying than those with low NPAR values. [11].

This study seeks to investigate the relationship between NPAR values at admission for COVID-19-positive critical and non-critical patients and mortality.

The NPAR will be determined using neutrophil\*100/albumin (g/dl) as a percentage.

**MATERIAL AND METHODS****Study design:** The Sindh Infectious Disease Hospital and Research Center in Karachi, Pakistan, served as the study's location. It is a unique facility just for COVID-19 patients. The goal of this retrospective observational study is to examine the potential for using albumin and the neutrophil/albumin ratio as indicators of mortality in COVID-19 patients in both critical and non-critical settings. The patients with confirmed COVID-19 who spent more than one day in the hospital between January 2022 and March 2022 make up the study population.

According to a simplified proportion calculation, a sample size of 199 was computed, with a 95% confidence range and a 5% margin of error.

**Ethics committee Approval:** The Dow University of Health Sciences Institutional Review Board (IRB-2161/DUHS/EXEMPTION/2021/857) has approved this study.**Statistical Analysis:** Data analysis was carried out using SPSS. The normal distribution of the data was determined using the Shapiro-Wilk test. The median and interquartile range were used to represent continuous variables. The frequency and percentages in the tables were used to interpret the category variables. The Mann-Whitney test compares data that are not normally distributed. The categorical data were analyzed using the Fischer test. Logistic regression was employed to ascertain whether the predictor variables significantly predicted the mortality. The albumin and NPAR values are examined using Receiver Operating Properties (ROC) curve analysis to forecast mortality. The sensitivity and specificity will be determined if there are substantial limit values. A two-tailed p-value of >0.05 is regarded as significant.**RESULTS**

This retrospective analysis includes data from 200 patients in total. Following that, the information is divided into two distinct groups: group 1 (critical COVID-19 patient) and group 2. (non-critical COVID-19 patients). In terms of gender, there was no difference between the two groups, which were both gender homogeneous. Group 1's median age ranged from 53.5 to 70, whereas group 2's was 67. (57.50-73.75). With a p value of 0.037, the age difference between groups 1 and 2 was statistically significant. The detailed demographic shown in table 1.

Table 2 shows the WBC, albumin, neutrophil, and NPAR values for both groups. WBC was 15.65 (10.375-20.325), neutrophils were 89 (84.25-91) and albumin was 3.33±0.521 in group 1. In group 1, discharge was 21 (21%), and mortality was 79 (79%). In group 2, the median (IQR) neutrophil count was 91.5(85.25-93.75), the albumin count was 3.1±0.51, and the median (IQR) WBC count was 14.9(10.375-20.325). In group the mortality was 37 (37%) and the discharge was 63 (63%). Albumin was found significant between the groups (group 1; 3.33±0.521, group 2; 3.1±0.51, p-value= 0.023). Mortality also been found to be

significant between the groups with p-value=<0.0001. In mortality group the NPAR median (IQR) was 43.76 (27.44 - 60.14) and in the discharge group the median was 41.96 (25.77 - 56.10). when compared the mortality and discharged NPAR there found to be no significant difference between them as shown in fig (1). When compared to NPAR of group 1 with group 2, there was no significant change between the both groups. Analysis was carried out. The NPAR, WBC, Albumin, and Absolute Neutrophil Count were among the parameters. According to the results of the logistic regression, the NPAR was not a reliable indicator of patient mortality in the COVID-19 cohort. As stated in table 2, WBC (p-value=0.008) and Absolute neutrophil count (p-value=0.02) were determined to be significant. RTo establish the cut off values for NPAR, WBC, and Absolute Neutrophil Count, ROC analysis was used. Table 3 shows the NPAR under the curve value (AUC 0.529, CI=0.448-0.609). It is discovered that the sensitivity is 50% and the specificity is 46.4% at the cutoff of 43.71

Table 1: Demographics and Clinical Characteristics

Parameters	Critical (n=100)	Non-critical (n=100)	p-Value
Age	63(52.5-70)	67(57.50-73.75)	0.037
Gender Male / Female	51.04% / 48.96%	56.25% / 43.37%	0.0836
Comorbidity	82 (82%)	83 (83%)	0.878
Diabetes Mellitus	44 (44%)	39(39%)	0.473
Hypertension	57 (57%)	57 (57%)	1
Asthma	8 (8%)	0	0.004
Ischemic Heart Disease	14 (14%)	17 (17%)	0.696
Chronic Kidney Disease	3 (3%)	10 (10%)	0.045

Table 2: Comparison Of Clinical And Laboratory Results

Parameters	Critical (n=100)	Non-Critical (n=100)	p-Value
NPAR	41.3(26.66-54.43)	43.7(27.5-65.03)	0.304
Albumin	3.33±0.521	3.1±0.51	0.023
Neutrophil	89(84.25-91)	91.5(85.25-93.75)	0.025
ANC	1.35x10 <sup>4</sup> (8.77x10 <sup>3</sup> -1.83x10 <sup>4</sup> )	1.35x10 <sup>4</sup> (9.003x10 <sup>3</sup> )	0.817
WBC	15.65(10.375-20.325)	14.9(10.375-20.325)	0.993
Outcomes			
Discharge	21	63	<0.0001
Death	79	37	

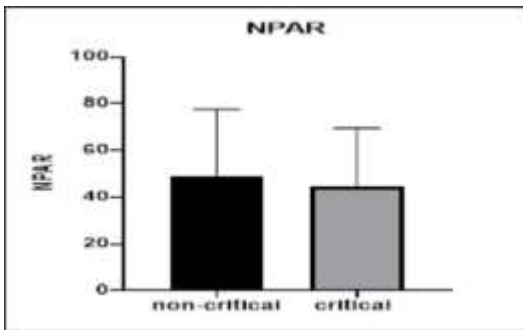


Figure 1: The Results Of "Neutrophil Count To Albumin Ratio" Were Schematized According To Whether The Disease Was Critical Or Not

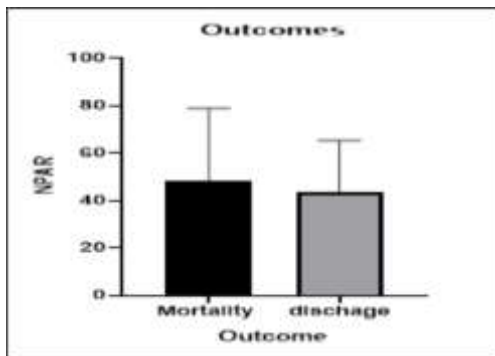


Figure 2: The Results Of "Neutrophil Count To Albumin Ratio" Were Schematized According To Discharge And Mortality.

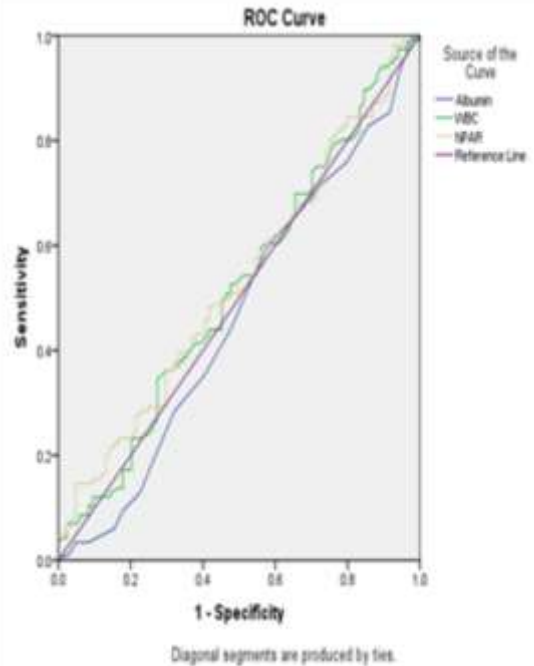


Figure 3: NAR: Neutrophil Count to Albumin Ratio; WBC: White Blood Cell; ANC: Absolute Neutrophil Count

Table 3: Area Under the Curve

Test Result Variable(s)	Area	Std. Error <sup>a</sup>	Asymptotic Sig. <sup>b</sup>	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Albumin	.466	.042	.412	.384	.548
WBC	.518	.042	.662	.437	.600
NPAR	.529	.041	.486	.448	.609

The test result variable(s): Albumin, WBC, NPAR has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption  
 b. Null hypothesis: true area = 0.5

## DISCUSSION

The results of the logistic regression analysis revealed that NPAR was not significantly associated with the ability to predict mortality, and the ROC curve analysis failed with an AUC value of 0.52, demonstrating the inadequacy of NPAR as a method for predicting mortality in COVID-19 patients.

WBC and absolute neutrophil count were shown to be important indicators of death in COVID-19 patients. As evidenced by the research, neutrophils play a crucial role in the immune system. Neutrophils secrete cytokines and chemokines. Chemokines and cytokines are then released, stimulating angiogenesis, cytotogenesis, and antiviral defense, which can assist control the immunological response. [12]. A cytokine-chemokine storm produced on by elevated peripheral blood neutrophil levels during some viral illnesses can result in lung injury and acute respiratory distress syndrome. [13]. The WBC count at admission in COVID-19 can also be connected to mortality. [14]. In the logistic regression analysis, we also discovered a significant difference between the WBC counts of the death group and the discharge group. According to NPAR literature, a cutoff value above 201.5 will have a sensitivity of 71.1% and a specificity of 71.7%, making it a significant predictor parameter for death. [12]. In our investigation, we found that the majority of patients had similar amounts of albumin, WBC, neutrophils, and NPAR. The lack of a statistically significant finding may be attributable to population differences among nations or to the fact that the

majority of patients in the mortality (84.3%) and discharge (79.8%) groups had comorbid conditions.

Our study's finding suggest that the NPAR is a poor predictor of mortality in COVID-19 patients. To confirm and further explain the clinical importance of these findings, more investigation is still required.

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