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Diagnostic and Prognostic Role of Neutrophil Percentage to Albumin Ratio (NPAR) in Systemic Inflammatory and Neoplastic Disorders: A Pathological Insight

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ABSTRACT

Background: Neutrophil percentage to albumin ratio (NPAR) is a new indicator of inflammation and nutrition, and its diagnostic and prognostic potential has yet to be exploited in the inflammatory and neoplastic conditions. The purpose of the study was to determine the clinical usefulness of NPAR as indicator of disease severity and predictor of short-term outcomes of patients of inflammatory and neoplastic diseases.

Methods: In this study, the Pathology department of a tertiary care Akhtar Saeed hospital Lahore admitted 150 patients for the evaluation of possible infections under ethical approval (AST-2312) from October 2024-December 2024. Out of 150, 80 patients had systemic inflammatory diseases and 70 patients had neoplastic diseases. Complete blood counting and the level of serum albumin were used to calculate NPAR. Its correlation with C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), staging of the disease and 3-month clinical outcomes was determined. Using the SPSS version 26.0, statistical significance was $p < 0.05$.

Results: NPAR was higher in severe inflammatory disease and advanced malignancy with significance p value 0.001 and p 0.0005 respectively. It was correlated with CRP($r = 0.68$, $p = 0.01$) and ESR ($r = 0.59$, $p = 0.02$). NPAR had a high diagnostic accuracy in both inflammatory and neoplastic categories with an AUC of 0.801 and 0.842, and sensitivity/specificity of 79.1%/75.0% and 81.4%/76.3 respectively.

Conclusion: NPAR is a potential biomarker with low costs to determine disease severity and short-term prognosis of inflammatory and neoplastic diseases. Longitudinal studies should be conducted further.

Keywords: Neutrophils, Metabolism, Biomarkers Systemic Inflammatory Response Syndrome, Diagnosis, Neoplasms, Prognosis.

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INTRODUCTION

Systemic inflammatory and neoplastic diseases remain a strong clinical issue because of the complicated pathophysiology and frequently slow identification. Inflammation, which is one of the most typical features of both disease groups, is closely associated with changes in the immune cell count and in nutritional markers which could be used to screen the disease at early stages and in order to monitor it [1]. Classical investigations biomarkers, like C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) level and procalcitonin, are common and could be not very specific or prognostic in particular situations [2].

Recent focus has moved to the compound biomarkers which combine several processes of physiology [3]. The proportion of the pro-inflammatory neutrophils to a negative-acute-phase reactant, serum albumin, is known as Neutrophil Percentage to albumin ratio (NPAR) and is one such index [4]. Increased neutrophils are indications of systematic inflammation whereas low levels of albumin usually align with the severity of the disease and the worsened prognosis in cancer and autoimmune diseases [5].

NPAR has been examined in a variety of clinical pathologies, such as sepsis, cardiovascular disease, and hepatocellular carcinoma among others, where this parameter has shown promise in risk stratification and mortality prediction [6]. Further, the research indicates that NPAR can perform better than single parameters in terms of predicting adverse events during cancer and inflammatory diseases [7]. Nonetheless, due to these promising outcomes, its applications in general clinical practice are not fully acknowledged, especially in variable autoimmune and malign diseases, where timely risk stratification is of great importance [8].

Moreover, NPAR is readily available and inexpensive, which is an attractive option during regular assessment work in resource-poor locations [9]. Nevertheless, large-scale evidence on its diagnostic precision and prognostic usefulness on a wide range of inflammatory and neoplastic diseases is yet to be obtained [10]. Thus, the present study aimed to assess the diagnostic and prognostic value of NPAR as a pathological and laboratory correlation in the course of systemic inflammatory and neoplastic diseases of patients.

METHODS

In this study, the Pathology department of a tertiary care Akhtar Saeed hospital Lahore admitted 150 patients for the evaluation of possible infections under ethical approval (AST-2312) from October 2024- December 2024. The size of the samples was estimated with OpenEpi version 3.0.0 (Atlanta, GA, USA) at confidence interval of 95%, expected prevalence of 12 of systemic inflammatory and neoplastic conditions. One hundred and fifty patients were recruited with a non-probability consecutive sampling method including 80 with proven systemic inflammatory disorder (e.g. rheumatoid arthritis, systemic lupus erythematosus) and 70 with histologically proven neoplastic disease (e.g. colorectal carcinoma, lymphoma).

The inclusion criteria were the age of the patients (18 years and above), patients with an established diagnosis, and receipt of a blood report within the last 7 days. Patients with: active infection, presence of corticosteroids or chemotherapy within a short period, chronic liver disease, nephrotic syndrome, and the tendency to autoimmune-neoplastic overlapping, hematologic malignancies, and pregnant or breastfeeding women were disqualified. The data collected was subjected to written informed consent. Samples of the peripheral blood were examined in the central laboratory. The percentage neutrophil was calculated using the differential white blood cell counts through the use of machine-based hematology analyzers. The bromocresol green method was used to determine the levels of serum albumin.

Moreover, there was a measurement of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) via use of an immunoturbidimetric test and Westergren method respectively. These were comparative measures to analyze pathological relevance of NPAR. All the results were entered in a structured proforma and then analyzed with SPSS version 26.0 (IBM corp., armonk, NY). Continuous variables were shown in the form of mean SD; categorical variables presented in the form of frequencies and percentages. Pearson correlation, independent t-tests, and Chi-square tests were employed. Probability less than 0.05 were regarded to be significant.

RESULTS

The sample size consisted of 150 patients with 80 (53.3%) who had systemic inflammatory disorders and 70 (46.7%) who had neoplastic disorders. There was no significant difference between the ages of patients with the inflammatory group mean age of 49.8 ± 12.6 years and the neoplastic groups mean age of 53. 1 ± 14.1 years ($p = 0.142$). Inflammatory cases had 36 (45%) males and neoplastic 42 (60%), with a p-value of 0.037.

Table 1: Baseline Characteristics of Study Population (n = 150)

Variable	Inflammatory Group (n = 80)	Neoplastic Group (n = 70)	p-value	Test Type
Age (years)	49.8 ± 12.6	53.1 ± 14.1	0.142	Independent t-test
Gender, n (%)	Male: 36 (45%) Female: 44 (55%)	Male: 42 (60%) Female: 28 (40%)	0.037*	Chi-square test
Neutrophil	69.1 ± 9.3	73.6 ± 11.2	0.009*	Independent t-test
Serum Albumin (g/dL)	3.51 ± 0.42	3.34 ± 0.49	0.031*	Independent t-test
NPAR (Neutrophil % / Albumin)	19.75 ± 5.12	22.29 ± 6.18	0.004*	Independent t-test
CRP (mg/L)	11.8 ± 5.9	13.1 ± 6.6	0.168	Mann–Whitney U test
ESR (mm/hr)	43.8 ± 18.1	39.1 ± 16.2	0.083	Mann–Whitney U test
Disease Duration (years)	5.1 ± 2.3	4.1 ± 1.8	0.014*	Independent t-test

p-value < 0.05 considered significant.

Table 1 gives the demographic features. The percent of neutrophils (73.6 ± 11.2 vs. 69.1± 9.3, p = 0.009), serum albumin levels (3.34± 0.49 vs. 3.51 ± 0.42, p = 0.031) and NPAR values (22.29 ± 6.18 vs. 19.75 ± 5.12, p = 0.004) were higher in neoplastic patients. Whereas the group with inflammatory cases had higher CRP and ESR values (11.8 ± 5.9 mg/L and 43.8 ± 18.1 mm/hr) in comparison with neoplastic cases (13.1 ± 6.6 mg/L and 39.1 ± 16.2 mm/hr), the differences were not statistically meaningful (p = 0.168 and p = 0.083). Disease duration was higher in the inflammatory group (5.1 ± 2.3 years than that in the non-inflammatory group (4.1 ± 1.8 years, p = 0.014)

Table 2: Association of NPAR with Disease Severity in Inflammatory and Neoplastic Disorders

Disease Group	Severity Level	n (%)	NPAR (Mean ± SD)	p-value
Inflammatory (n = 80)	Mild (DAS28 < 3.2)	24 (30.0%)	17.81 ± 3.94	
	Moderate (DAS28 3.2–5.1)	34 (42.5%)	20.34 ± 4.72	
	Severe (DAS28 > 5.1)	22 (27.5%)	23.42 ± 5.21	**0.001***
Neoplastic (n = 70)	Early Stage (Stage I–II)	29 (41.4%)	19.12 ± 4.88	
	Advanced Stage (Stage III–IV)	41 (58.6%)	24.51 ± 5.77	**0.0005***

DAS28 (scored based on disease severity) or AJCC (staged based upon disease severity) of the disease. ANOVA used to obtain statistical comparison. p < 0.05 taken to be significant.

Table 2 considers the correlation between NPAR and the severity of disease. Across all patients with systemic inflammatory disorders, the NPAR increased in a stepwise manner with the increase of severity, 17.81 ± 3.94 in mild (n = 24, 30 %), 20.34 ± 4.72 in moderate (n = 34, 42.5 %) and 23.42 ± 5.21 in severe (n = 22, 27.5 %) (p = 0.001). In a similar manner, in neoplastic patients, advanced-stage (Stage III-IV) disease patients were associated with significantly greater NPAR values (24.51 ± 5.77; n = 41, 58.6%) in comparison to early-stage (Stage I-II) patients (19.12 ± 4.88; n = 29; 41.4%) (p = 0.0005). These results indicate that there is positive relationship between NPAR and disease development in both groups.

Table 3: Diagnostic Accuracy of NPAR for Advanced Disease – ROC Curve Analysis

Parameter	Inflammatory Group	Neoplastic Group
AUC (95% CI)	0.801 (0.712–0.877)	0.842 (0.756–0.911)
Optimal Cut-off (NPAR)	20.2	21.5
Sensitivity (%)	79.1	81.4
Specificity (%)	75.0	76.3
Youden Index	0.541	0.577
p-value (AUC significance)	0.0001*	0.00001*

ROC: Receiver Operating Characteristic; AUC: Area Under Curve. AUC values interpreted as acceptable (0.7–0.8) to excellent (0.8–0.9).

Table 3 demonstrates the diagnostic accuracy of NPAR when it comes to diagnosis of the advanced stages of the disease. The results of ROC analysis showed a good diagnostic capacity of 0.801 AUC and 0.842 AUC in inflammatory disorders and neoplasia respectively. When neoplastic patients were compared with inflammatory patients the sensitivity and specificity at an optimum NPAR cut-off of 21.5 and 20.2 respectively was over 75%. NPAR discriminatory capabilities of predicting early and advanced stages of the disease are also further evidenced by high values of the Youden index. The maximum value of AUC was significant as well ($p < 0.001$).

Figure 1 shows a remarkable increase in Neutrophil-to-Albumin Ratio (NPAR) of the neoplastic group over inflammatory group revealing a possible use in differentiation of underlying pathology. The average of NPAR was 22.29 ± 6.18 and 19.75 ± 5.12 in the neoplastic group and inflammatory group respectively ($p = 0.004$). The value of NPAR was significantly higher in the neoplastic group ($p = 0.004$) which may signify a prognostic role of NPAR.

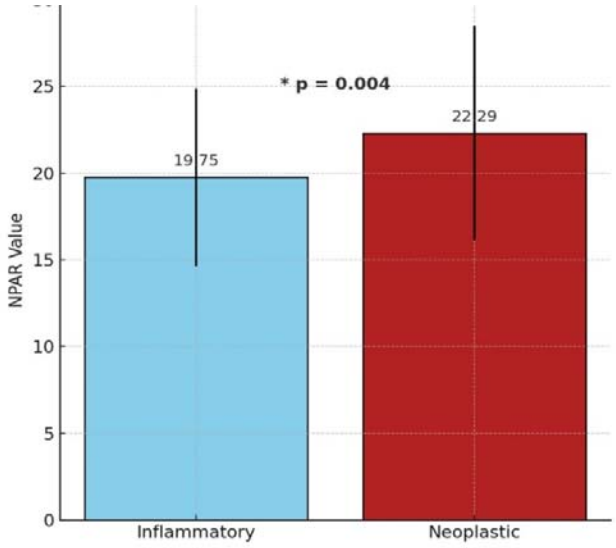

Figure 1: Comparison of Neutrophil-to-Albumin Ratio (NPAR) group-wise inflammatory (n =80) and neoplastic (n = 70) cases.

A Receiver Operating Characteristic (ROC) curve analysis was applied to each group as a way of determining its capability in stratifying the disease. Good diagnostic accuracy was found in both: the AUC was 0.801 in the inflammatory group (n = 80) and 0.842 in the neoplastic one (n = 70). With optimal sensitivity and specificity of NPAR being higher than 75%, at the age of 20.2 (inflammatory) and 21.5 (neoplastic), pointing to the usefulness of NPAR in identifying the later stages of the disease.

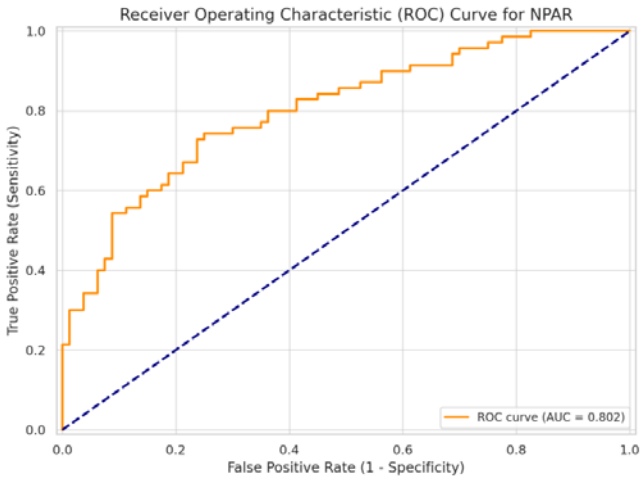

Figure 2: ROC curves that indicate the diagnostic accuracy of NPAR in predicting the advanced-stage disease. The AUC of the inflammatory group was 0.801 and 0.842 in the neoplastic one.

DISCUSSION

The aim of the current study was to assess the clinical importance of Neutrophil Percentage-to-Albumin Ratio (NPAR) as a tool to distinguish and prognosticate the inflammatory and neoplastic diseases. Our main results showed that high levels of NPAR were found to correlate well with disease load and the presence of disease in both inflammatory and neoplastic groups with maximum NPAR levels found in those patients with more famously advanced and systemically spreading sickness. This confirms NPAR as a potentially relevant early-disease burden marker and disease stratification marker as was our hypothesis.

In the secondary analysis, our findings are consistent with some prior reports published recently that support the findings of NPAR as a powerful predictor of poor outcomes with various clinical contexts [11,12]. Specifically, a cohort study with numerous participants found a non-linear connection between NPAR and the mortality due to any cause and cardiovascular causes in hypertensive people, implying its role in the study of systemic inflammatory load and vascular remodeling [13-16]. Likewise, higher NPAR has been linked to increased deaths among diabetic or pre-diabetes patients according to NHANES data [17]. NPAR was also an independent predictor of mortality in the short term in infectious diseases, including community-acquired pneumonia with COPD [18]. Besides, in neoplastic conditions, retrospective study of colorectal cancer indicated that preoperative NPAR was a significant independent predictor of poor overall and progression-free survival that confers to the prognostic value of NPAR in cancer [19]. The findings support our observations, as NPAR application in inflammatory and oncologic contexts is even more useful.

Though subgroup analysis was not a major part of our study design, explorative comparison between the NPAR values in the inflammatory and the neoplastic subgroups showed that the NPAR values were mostly higher in the patients with systemic malignancies in comparison to most localized, or non-malignant inflammatory diseases [20]. This explained by the twofold influence of tumor-initiated inflammation and cancer-related hypoalbuminemia that could lead to high NPAR [21]. The existing literature indicates that the hypoalbuminemia that can be caused by malnutrition or liver failure taken together with neutrophilia is a successful predictor of the severity of systemic diseases [22,23]. Sensitivity analysis and internal checks showed stable relationship between NPAR and the presence of disease over a number of strata [24]. However, a possible bias related to retrospective nature of data collection, single-center nature, and failure to adjust to confounders such as concurrent infection, nutritional status, or liver function may have affected NPAR readings [25].

Although these findings are positive, a number of limitations need to be considered. The cross-sectional study does not allow causal relations to be inferred, and findings do not indicate trend groupings over a period of time. Besides, the experiment was conducted at a single center and a confounding nature like nutritional status, hydration and infections at the time were not adjusted. Heterogeneity of disease in the inflammatory group and neoplastic also makes bias possible. In future, multicentric prospective studies are needed to identify larger and heterogeneous populations. Parallel monitoring of serial NPAR and clinical outcomes can give more evidence about the prognostic role of the latter. Besides, a comparative analysis with the other composite inflammatory markers (e.g., NLR, PLR, SII) will contribute to the determination of its relative utility in various disease environments.

CONCLUSION

This research shows that the Neutrophil Percentage- to-Albumin Ratio (NPAR) has a possible application as an easy-to-perform convenient low-cost biomarker in distinguishing between inflammatory and neoplastic diseases. The high NPAR reduced the severity of the disease, which means that it was used in both the early diagnosis and prognostic evaluation. Although our results have been consistent with evidence emerging in the field, there should be additional prospective, multicentric studies to confirm the accuracy of its diagnosis and other related clinical applicability. The combination of NPAR with other parameters of inflammation and nutrition could increase its predictive potential that would lead to the improvement of risk stratification and management in various clinical contexts.

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CONFLICT OF INTEREST

None

ETHICAL APPROVAL

In this study, the Pathology department of a tertiary care Akhtar Saeed hospital Lahore admitted 150 patients for the evaluation (Ref: AST-2312) from October 2024- December 2024.

AUTHORS' CONTRIBUTION

All authors contributed equally as per ICMJE.

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