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Original Article

Investigating the Diagnostic Significance of Neutrophil Percentage to Albumin Ratio (NPAR) in Patients with Infectious Meningitis

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ABSTRACT

Background: Meningitis, characterized by inflammation of the meninges, typically presents with fever, headache, and neck rigidity. Despite the availability of numerous diagnostic techniques, determining the etiology of infectious meningitis remains challenging, often leading to diagnostic delays and increased mortality. The neutrophil percentage-to-albumin ratio (NPAR) is a novel biomarker for systemic infection and inflammation.

Objective: To assess the neutrophil-to-albumin ratio in cases of infectious meningitis.

Methods: Following REC approval (05/01/REC-206-2020), this cross-sectional study included 78 patients with clinical findings consistent with meningitis. Data on age, gender, fever, headache, neck rigidity, and Glasgow Coma Scale (GCS) were collected. NPAR was calculated by dividing the neutrophil percentage by serum albumin levels. Statistical analysis was performed using SPSS 22.0 for T-test (two-tailed) and Pearson Correlation. Results were presented as mean±SD (95% CI) with a significance level of $p<0.05$.

Results: The mean age of patients was 27 years. The mean GCS score was 11±1.59, serum albumin levels were 3.44±0.5 mg/dl, neutrophil percentage was 75.6±7.2%, and the neutrophil-to-albumin ratio (NPAR) was 0.22±0.03. Common symptoms such as fever, neck rigidity, and headache were present in all cases, while seizures were observed in 36 cases.

Conclusion: The study indicated a significant correlation between elevated NPAR levels and cases of infectious meningitis, suggesting NPAR as a potential diagnostic marker.

Keywords: Diagnostics, Infection, Inflammation, Meningitis, NPAR.

INTRODUCTION

Meningitis, an inflammatory condition involving the brain meninges and spinal cord, remains a significant cause of mortality. The common etiological agents of meningitis include viruses, bacteria, and fungi, with incidence and frequency varying by geographic region and over time. Bacterial meningitis is frequently caused by a group of pathogens such as Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae, Streptococcus agalactiae, Escherichia coli, and Listeria monocytogenes. The classic presentation of the disease includes symptoms such as fever, neck stiffness, headache, anorexia, vomiting, lethargy, and neuropsychological impairment, which affect up to 50% of survivors (1). Complications of meningitis include significant disabilities such as vision problems, deafness, seizures, and brain damage (2, 3).

While adults are less commonly affected, symptoms in children, immunocompromised individuals, the elderly, and those with chronic conditions are often less specific. The nonspecific nature of symptoms can delay the initiation of appropriate antimicrobial therapy. Thus, there is a critical need for effective, objective, and rapid diagnostic tools to accurately identify the disease etiology. Diagnostic laboratories play a crucial role in predicting and identifying the causative agents of meningitis (4). Various factors increase the risk of meningitis, including an individual's vaccination status, immunocompromised state, parameningeal infection,

developmental and anatomical defects in the brain and spinal cord, as well as acquired skill defects and medical device implantation (5).

The pathogenesis of meningitis follows a typical pattern involving the colonization of the nasopharynx, mucosal invasion, bloodstream invasion, and subsequent central nervous system (CNS) involvement. Listeria monocytogenes, for instance, can also spread through the gastrointestinal and genitourinary tracts, posing unique diagnostic and therapeutic challenges. This Gram-positive bacterium thrives in diverse environments, including soil, water, and food products. Ingestion of contaminated food, particularly unpasteurized dairy products, raw vegetables, and processed meats, can lead to gastrointestinal infection and subsequent dissemination to the CNS (6, 7).

Listeria monocytogenes can traverse the intestinal barrier, enter the bloodstream, and directly access the CNS via hematogenous dissemination, crossing the blood-brain barrier and evading host defense mechanisms. This unique pathogenesis, combined with the bacterium's affinity for specific CNS cell types, triggers a robust inflammatory response, leading to meningitis symptoms such as fever, headache, neck stiffness, and altered mental status (8, 9, 10). In rare cases, the disease may be acquired directly through the cribriform plate, enabling direct invasion of the CNS. In immunocompetent individuals, mucosal immunity typically eliminates bacterial colonization, with neutrophils being the earliest leukocyte subtype to initiate the inflammatory response and migrate to the CNS (11, 12).

Despite various diagnostic techniques available for infectious meningitis, determining its precise etiology remains challenging. This study aimed to assess the diagnostic significance of the neutrophil percentage to albumin ratio (NPAR) in patients with infectious meningitis.

This study aimed to assess the neutrophil to albumin ratio in cases of infectious meningitis.

METHODS

Following the approval from the Research Ethics Committee (REC approval number 05/01/REC-206-2020), a cross-sectional study was conducted at the Department of Neurosurgery and Diagnostic and Research Laboratory of Liaquat University Hospital in Hyderabad. The study utilized a random non-probability sampling technique and included a sample size of 78 participants with a three-month follow-up period from October to December 2023. The inclusion criteria encompassed patients presenting with meningitis symptoms such as fever, nausea, vomiting, and neck stiffness. Exclusion criteria were set to omit subjects with conditions like purpura, recent neurosurgery, immunosuppression, and those currently on other bacterial antibiotics.

Peripheral blood samples (5ml each) were collected from the participants at the time of admission, following the signing of informed consent forms. The samples were collected in EDTA tubes to ensure proper preservation for subsequent analysis. Statistical analysis was performed using SPSS version 22.0. The data were analyzed using T-tests and Pearson correlation, with a significance level set at a p-value of less than 0.05.

The study protocol received prior approval from the Research Ethics Committee (REC approval number 05/01/REC-206-2023). It is noteworthy that this research did not involve any human or animal-based pathology lab work.

RESULTS

Table 1 Descriptive Statistics of Quantitative Variables

Statistics of Quantitative Variables				
	Minimum	Maximum	Mean	Std. Deviation
AGE	20	38	27.50	5.488
GCS	9	14	11.64	1.598
serum Albumin (m/dl)	2.60	4.10	3.4414	.54706
Neutrophil	50.00%	90.20%	75.5857%	13.87648%
NEUTROPHIL to ALBUMIN ratio	.18	.29	.2236	.03201

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This table provides the minimum, maximum, mean, and standard deviation for the age of patients, Glasgow Coma Scale (GCS) scores, serum albumin levels (measured in mg/dl), neutrophil percentages, and the neutrophil-to-albumin ratio (NAR). These metrics offer insights into the variability and central tendency of each variable within the dataset.

Table 2 Frequency Counts for Symptoms Presence (n=68)

Counts for Symptoms Presence (n=68)			
S.no	Symptoms	Present	Absent
	Fever	42	0
	Neck Rigidity	42	0
	Headache	42	0
	Seizures	36	6

The table lists the frequency counts for the presence and absence of key symptoms among patients fever, neck rigidity, headache, and seizures. This frequency distribution highlights the commonality of symptoms in the studied patient population.

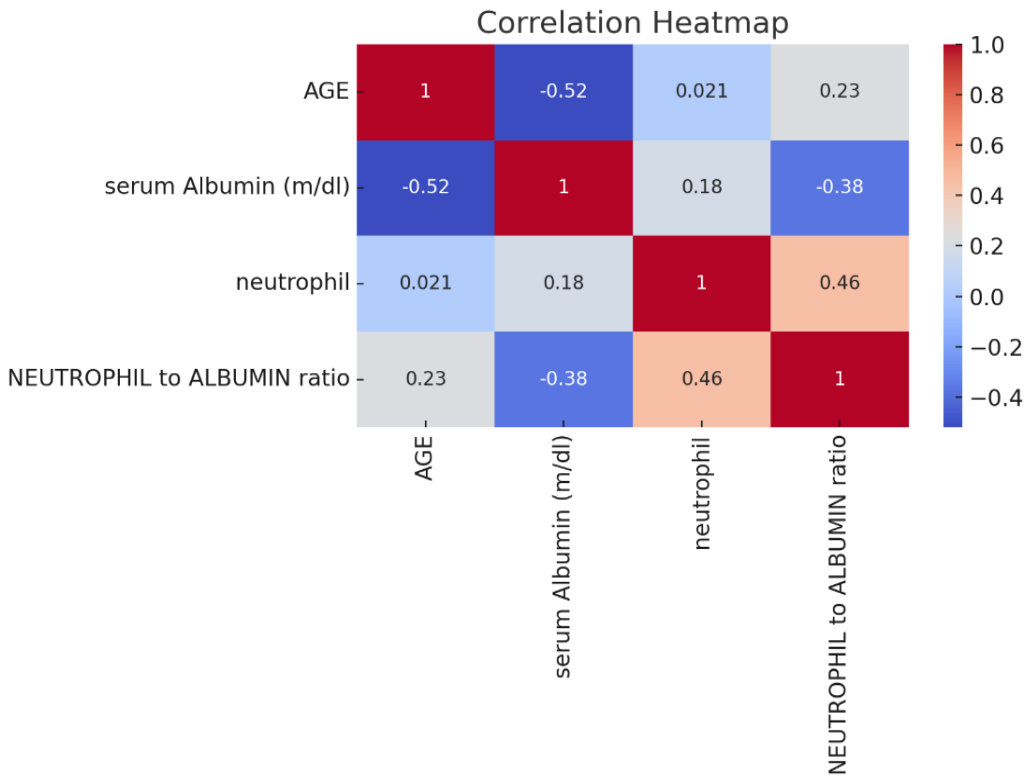

Figure 1 Correlation Heatmap of Quantitative Variables

The heatmap visualizes the Pearson correlation coefficients among quantitative variables, providing a color-coded representation of the strength and direction of correlations. It aids in quickly identifying significant positive or negative relationships among variables.

Table 3 Correlation Analysis Among Quantitative Variables

Analysis Among Quantitative Variables						
		AGE	GCS	serum Albumin (m/dl)	neutrophil	NEUTROPHIL to ALBUMIN ratio
AGE	Pearson Correlation	1	.180	-.426	-.245	-.099
	Sig. (2-tailed)		.539	.129	.399	.738
	N	14	14	14	14	14
GCS	Pearson Correlation	.180	1	-.338	-.556*	-.018
	Sig. (2-tailed)	.539		.237	.039	.951
	N	14	14	14	14	14
serum Albumin (m/dl)	Pearson Correlation	-.426	-.338	1	.442	-.208
	Sig. (2-tailed)	.129	.237		.113	.475
	N	14	14	14	14	14
Neutrophil	Pearson Correlation	-.245	-.556*	.442	1	.197
	Sig. (2-tailed)	.399	.039	.113		.500
	N	14	14	14	14	14
NEUTROPHIL to ALBUMIN ratio	Pearson Correlation	-.099	-.018	-.208	.197	1
	Sig. (2-tailed)	.738	.951	.475	.500	
	N	14	14	14	14	14
*. Correlation is significant at the 0.05 level (2-tailed).						

This table presents the Pearson correlation coefficients among age, GCS scores, serum albumin levels, neutrophil percentages, and the neutrophil-to-albumin ratio. It includes significance levels (Sig. 2-tailed) to indicate the strength and significance of each correlation. A significant correlation is marked with an asterisk (*) at the 0.05 level (2-tailed).

Table 4 T-Test Results for Key Parameters

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Parameter	Mean	S.D ±	T-Value	P-Value
Age	27.50	5.488	18.750	0.00001
GCS	11.64	1.598	27.254	0.00001
Albumin	3.4414	.54706	23.538	0.00001

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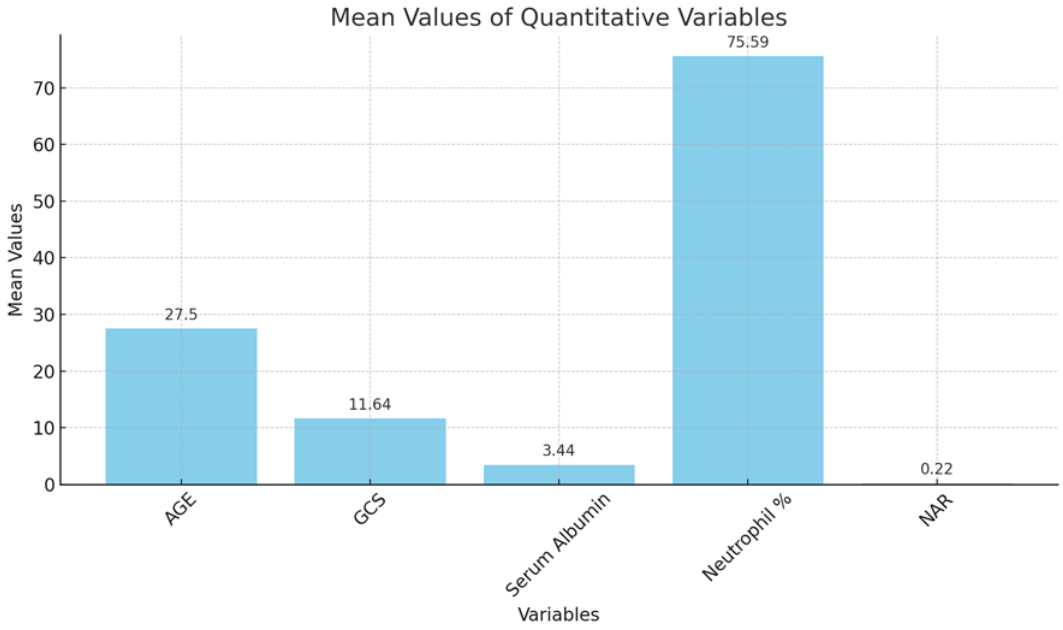
Table 4 T-Test Results for Key Parameters				
Neutrophil	75.5857%	13.87648%	20.381	0.00001
NAR	.2236	.03201	26.132237	0.00001

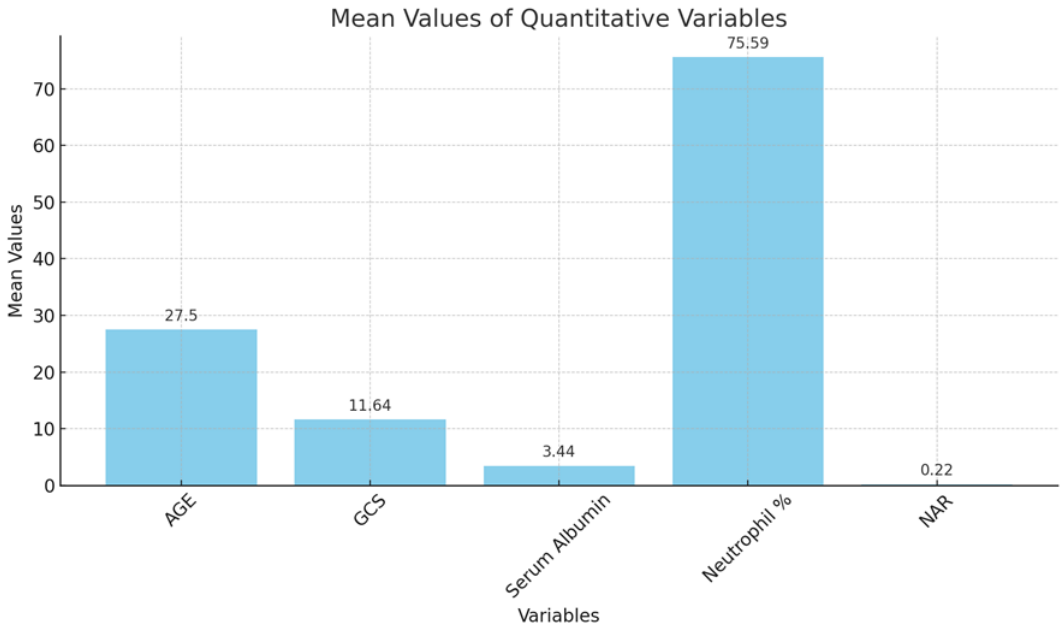
This table shows the T-test analysis results, including mean values, standard deviations (S.D ±), T-values, and P-values for age, GCS scores, albumin levels, neutrophil percentages, and the neutrophil-to-albumin ratio. The analysis tests the mean of each variable against a hypothesized population mean, with P-values indicating the significance of the results.

Graphs for Tables

Graph 1: Descriptive Statistics of Quantitative Variables



Graph 2: Descriptive Statistics of Quantitative Variables



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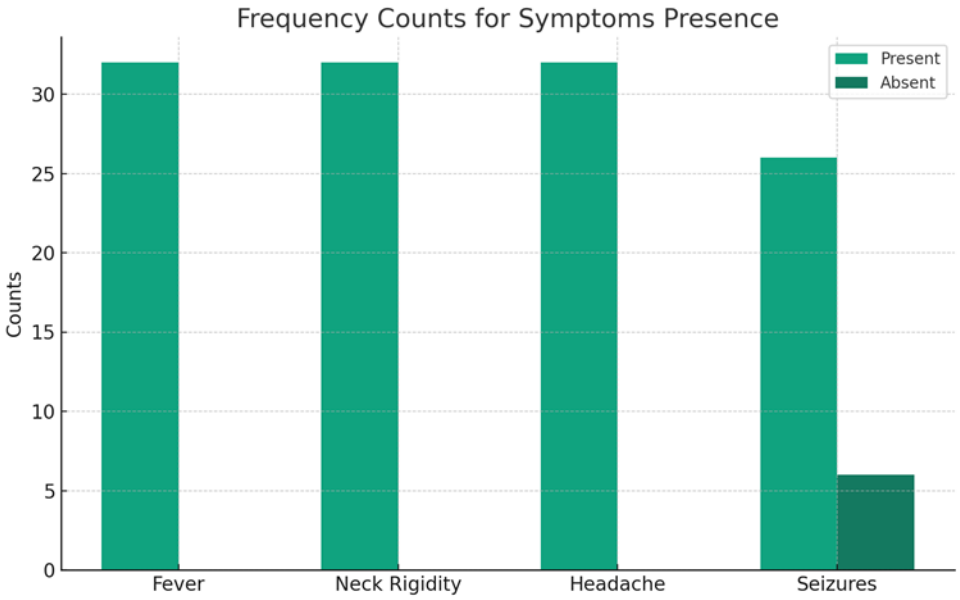
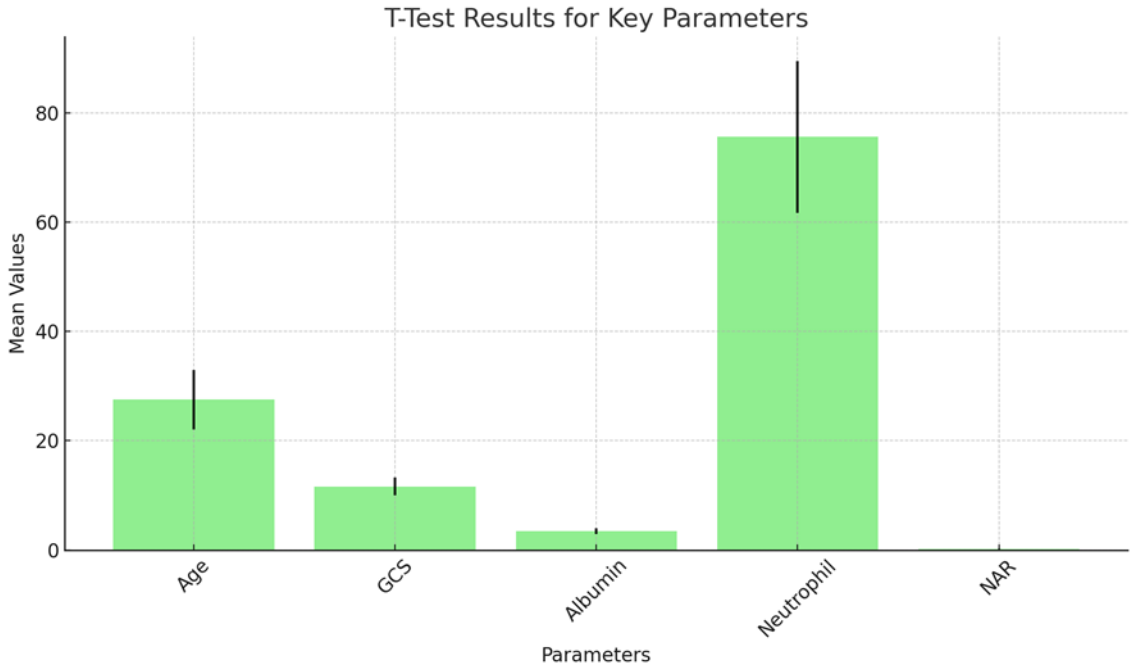
Graph 3: Frequency Counts for Symptoms Presence



Graph 4: T-Test Results for Key Parameters



DISCUSSION

Meningitis, an inflammation affecting the meninges of the brain, typically presents with fever, headache, and nuchal rigidity. This syndrome bears significant global mortality and morbidity. Despite the availability of active antibacterial agents, meningitis remains fatal in many cases. The diagnosis is commonly made through cerebrospinal fluid examination (13, 14). However, the determination of infectious meningitis remains challenging, often leading to diagnostic delays. Infection-induced inflammation significantly contributes to elevated neutrophil percentages and decreased albumin concentrations, thereby altering NAR values (15).

The study's mean age was 27 years with a standard deviation of 5.488, ranging from 20 to 38 years. This contrasts with findings by Kittipat et al., who reported the most common age group as 49 years, predominantly involving men (10). Similarly, Lene Fogt et al. and Diederik van et al. noted higher incidence rates among young children (<5 years), teenagers, young adults (16–21 years), and

the elderly population (>65 years) (16). Another study highlighted that while meningitis can affect individuals of any age, infants are at higher risk, particularly those between 15 and 20 years, with males being more commonly affected (17).

In the present study, 32 cases exhibited symptoms such as fever, neck rigidity, and headache, with seizures observed in 26 cases. Maria et al. also identified fever, headache, nausea, and vomiting as typical signs of meningitis (18). Yun Feng Shi et al. found that affected individuals aged 30–60 years presented with high fever, headache, chills, malaise, and myalgia, with severe headache being a prominent finding (17, 18). The mean Glasgow Coma Scale value was 11, with a standard deviation of 1.59 (19).

Peripheral blood leukocyte analysis, particularly the neutrophil percentage, is widely used to evaluate infection and inflammation. Albumin is known for its antioxidative, anti-inflammatory, and osmoregulatory properties (17). The mean serum albumin value in this study was 3.4414 mg/dl, and the neutrophil percentage was 75.5857% (20, 21). The Neutrophil to Albumin Ratio (NPAR) has been studied as an independent prognostic marker in patients with encephalitis, malignancy, and other diseases (22). In this study, 36 cases of infective meningitis were evaluated for NPAR, with the best cut-off value for predicting infective meningitis being 0.25 and a mean NPAR value of 0.2236 (range 0.18 to 0.29) (23).

The study's limitations include its single-center design and limited sample size, restricting the generalizability of the results to medically managed infective meningitis cases. Additionally, only the predictive value of NPAR on admission was investigated, leaving the dynamic alteration of NPAR over time unexplored. Future studies should focus on the informative value of the NPAR trajectory over time to better predict infective meningitis (24).

Despite these limitations, the study contributes valuable insights into the diagnostic significance of NPAR in patients with infectious meningitis. The findings suggest that NPAR can serve as a useful diagnostic marker, potentially aiding in the timely identification and management of the disease. However, further research with larger, multi-center studies is necessary to validate these findings and explore the dynamic changes in NPAR over time.

CONCLUSION

The findings of this study suggest that elevated Neutrophil Percentage to Albumin Ratio (NPAR) is associated with infectious meningitis, highlighting its potential as a diagnostic marker. However, to validate these results and ensure their clinical applicability, further research is necessary. Conducting multicenter studies with larger and more diverse patient populations will enhance the generalizability and reliability of these findings. Such studies will provide deeper insights into the diagnostic and prognostic value of NPAR and help identify any confounding factors across different demographics. Future research should also explore the underlying mechanisms linking NPAR to meningitis pathophysiology, offering a better understanding of the inflammatory processes involved and potentially guiding improved clinical decision-making and patient management strategies.

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