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Exploring the Correlation between Neutrophil Count and Ischemic Stroke in Patients at Bolan Medical College Hospital, Quetta.

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ABSTRACT

Background:

Ischemic stroke is considered to be one of the greatest causes of morbidity and mortality in the world. New data indicate that neutrophil counts increase could be a contributor to the pathophysiology and severity of acute ischemic stroke.

Materials & Methods:

The study was a cross-sectional correlational study conducted at a 6 month period (01 May 2025 to 30 October 2025) in the department of Neurology Medicine, Bolan Medical Complex Hospital, Quetta, Balochistan among 38 patients diagnosed with acute ischemic stroke and confirmed by neuroimaging. The extent of stroke was identified through the assistance of the National Institutes of Health Stroke Scale (NIHSS) and the functional outcome at discharge was assessed through the assistance of the Modified Rankin Scale (mRS). The data were analyzed using SPSS 24 and correlation model and regression model with statistical significance of $p = 0.05$.

Results:

The average age was 58.2 years of age with 60.5 percent of them being males. The neutrophil count was higher with the severity of stroke (mild: 5.8 ± 1.2 x 10 9/L; moderate: 7.6 ± 1.5 x 10^9/L; severe: 9.1 ± 1.7 x 10 9/L; $p = 0.002$). The number of neutrophils had a positive correlation with NIHSS ($r = 0.56$, $p = 0.001$) and mRS ($r = 0.48$, $p = 0.003$). After adjusting for confounders, the association remained significant ($\beta = 0.39$, $p = 0.012$).

Conclusions:

Higher neutrophil count within 24 hours of stroke onset independently predicts greater stroke severity and poorer short-term functional outcome.

Keywords: Adult; Inflammation; Ischemic Stroke; Leukocytes; Prognosis; Stroke Severity Index

INTRODUCTION

Ischemic stroke is one of the leading causes of long-term disability and death globally which reduces cerebral blood flow suddenly causing neuronal loss, followed by neurological deficits. [1] Stroke imposes an ever-increasing global burden, especially in lower-middle-income countries like Pakistan where restricted availability of specialized stroke care and advanced neuroimaging often limits early diagnosis and management. [2]

After the ischemic incident an inflammatory response develops, in which different immune cells become activated and migrate into the tissue of the ischemic brain. Of which neutrophils have been identified as important mediators of early injury and later repair. [3] They represent one of the early wave of immune cells invading into the ischemic area that secrete proteolytic enzymes, reactive oxygen species (ROS), neutrophil extracellular traps (NETs) which potentiate neuronal damage and compromise blood–brain barrier integrity. [4]

Further, greater neutrophil counts have been observed to associate with larger infarct volumes, higher rates of cerebral edema and poor functional outcomes post-ischemic stroke. [5] High neutrophil-to-lymphocyte ratio (NLR), an integrated indicator of systemic inflammation, has been associated with early neurological deterioration and poor recovery following recanalization therapy. Furthermore, elevated pre-thrombolysis neutrophil level is a predictor of poor clinical prognosis suggesting that systemic inflammation prior to the treatment may contribute to stroke development and response to therapy. [6] These data indicate that peripheral leukocyte dynamics may serve as biological evidence for predicting cerebral ischemic injury and prognostication in acute stroke care.

The pathophysiological mechanism of the detrimental effect of neutrophil in IS has been clarified along with a gradual increase in findings from recent years. Neutrophil extracellular traps (NETs) – lattice-like structures consisting of chromatin and antimicrobial proteins – have been

reported to be prominent mediators of post-stroke inflammation and thrombosis. [7-8] NETs not only exacerbate neuronal damage, but also induces microvascular obstruction and thus worsens the ischemic injury[9]. Apart from their action on tissue damage, neutrophils may also be a reflection of the global inflammation that occurs in stroke patients. In patients receiving reperfusion therapy, subjects with higher neutrophils are reported to develop more severe cerebral-edema and poorer functional recovery. In the same vein, a study by Jickling et al. demonstrated that increased neutrophil counts were associated with poorer clinical outcomes after endovascular management, further supporting the prognostic value of these markers. [8-10]

MATERIALS AND METHODS

The present study was planned as a cross-sectional correlational research study carried out to determine the association between neutrophil count with ischemic stroke severity and outcomes in patients admitted in Department of Neurology Medicine, Bolan Medical Complex Hospital, Quetta, Baluchistan. The duration of study was of six months from 01 May2025–30 October 2025 after completion of permissions from IRC of College of Physicians and Surgeons Pakistan (ERC No.Estt: /BMCH/DA-I/2025/484) and Ethical review board of Bolan Medical Complex. The research protocol was ethically approved by an independent regional ethics committee in accordance with the ethical standards laid down in the Declaration of Helsinki (2013). All patients or legal guardians gave their written consent before entering the study, after having received information about the objectives and procedures associated with participation in this study (including likely benefits and risks involved). The study was conducted in strict confidence, and all identifying information was coded to ensure patient confidentiality.

The research used a non-probability consecutive sampling method that included all eligible patients which met the inclusion criteria during the study period. Very clear selection criteria were set out to reduce the risk of confounding factors. Adults aged 18 to 65 years who had acute ischemic stroke (confirmed by CT or MR imaging), neutrophil count measured in the first 24 hours after symptom onset, and provision of informed consent by the patient or a legal representative were eligible to participate. Patients with hemorrhagic stroke or transient ischemic attack (TIA) were excluded, because these diseases have different pathophysiological mechanisms and inflammatory patterns than those of IS that may confound the relationship between neutrophil count and clinical outcome. Patients with active systemic infections, autoimmune and inflammatory diseases, or hematological diseases were also excluded as these disorders directly affected leukocyte and neutrophil counts independently of the study. Patients receiving corticosteroid or immunosuppressive treatment were also excluded, because those treatments change systemic inflammatory responses and might influence the neutrophil counts. Furthermore, the list did not recruit patients with missing data either prospectively or retrospectively to maintain data quality and promote accuracy in statistical analysis.

The sample size was estimated using WHO sample size calculator for correlation studies, according to previous literature that has reported r = 0.483 between neutrophil count and ischemic stroke outcomes[9]. At a = 0.05 and power (1 − β) of 80%, the sample size necessary for testing was estimated as being minimum n = 32 patients. This target sample size was increased by 20% in order to adjust for any possible dropouts, missing data and non-responses, resulting in a target of n = 38 subjects.

Records of all admitted patients diagnosed with acute ischemic stroke were prospectively collected on a pre-designed proforma working at Bolan Medical Complex. Following ethical clearance and obtaining informed consent from patients, structured interviews conducted by trained medical professionals were used to collect the demographic data such as age, sex, the area of residence. Specific details including the time of stroke onset, presenting symptoms, past medical history (including hypertension, diabetes mellitus, ischemic heart disease and atrial fibrillation), and medication were collected by standard questionnaire. All patients were exposed to the National Institutes of Health Stroke Scale (NIHSS) for neurologic evaluation on admission for assessment of stroke severity. Functional status at the time of discharge, was evaluated by Modified Rankin Scale (mRS), a quantitative measurement of post-stroke disability. Review of neuroimaging reports was performed to ensure existence, site and size of infarction.

Neutrophil count (cells/μL), total white blood cell count, and lymphocyte count derived from routine CBC were collected from the hospital records within 24hr of symptom onset. Neutrophil count (using an order of magnitude) was the primary independent variable, and stroke severity (NIHSS scores) and functional outcome (mRS scores) were key dependent variables. All data collected was entered into an electronic database to avoid loss or distortion, double-checked for consistency and was kept under limited assessment for confidentiality. Verification of data entered was checked by the principal investigator for quality control. Statistical analysis was conducted with the aid of SPSS (version 24.0; IBM Corp., Armonk, NY, USA). We summarized the demographical, clinical and laboratory features of patients using descriptive statistics. The mean ±

standard deviation (SD) for normally distributed data and the median with interquartile range (IQR) were used to represent continuous variables that were normally or non-normally distributed. Frequency and percentage for categorical variables were presented.

Pearson`s correlation coefficient and Spearman's rank correlation were used to evaluate normally and non-normally distributed data, respectively in order to test the primary hypothesis that there are relationships between neutrophil count with NIHSS score and mRS score. The direction and strength of association were interpreted as per the usual statistical conventions. Neutrophil counts for various categories of stroke severity and outcomes were compared at the group level using Analysis of Variance (ANOVA) or Kruskal–Wallis test as appropriate. Multivariable linear and logistic regression models were fitted to adjusting for potential confounding (age, sex, hypertension and diabetes mellitus). The results were expressed in terms of odds ratios (ORs) with 95% confidence intervals (CIs). A p-value <0.05 was regarded as statistically significant.

RESULTS

The study was conducted on 38 patients who were diagnosed with acute ischemic stroke in Bolan Medical Complex Hospital, Quetta. The average age of the study population was 58.2 ±10.4 years, ranging between 34-72 years. The number of males (23) 60.5% and females (15) 39.5% was respectively, with male-to-female ratio of 1.5:1. The most common of the comorbid conditions was hypertension (63.2%), then diabetes mellitus (31.6%), and ischemic heart disease (21.1%). The average time interval between the beginning of the symptoms and the admission to the hospital was 6.3 + 3.2 hours. **Table 1** shows the detailed demographic and clinical characteristics.

The average total white blood cell (WBC) count of the participants was 10.4 ± 2.6 x10 9/L, the average neutrophil count was 7.5 ± 2.1 x10 9/L and the average lymphocyte count was 1.9 ± 0.8 x10 9/L. With stratification based on the stroke severity, a gradual buildup of neutrophil was apparent in the mild and severe stroke groups. The neutrophil count of mild stroke patients (NIHSS 05) was 5.8 1.2 ×109/L, moderate stroke (NIHSS 615) was 7.6 1.5 ×109/L and severe stroke (NIHSS 16) was 9.1 1.7 ×109/L. This tendency was statistically significant (p=0.002) which is presented in **Table 2.**

The correlation analysis also showed the count of neutrophils had significant positive correlation with stroke severity (NIHSS score) and functional outcome (mRS score). The correlation coefficient of neutrophil count vs. NIHSS was r = 0.56 (p = 0.001), and neutrophil count vs. mRS was r = 0.48 (p = 0.003), which showed that more neutrophil levels were linked with more neurological impairment and poorer short-term outcomes **Table 3**.

The correlation between neutrophil count and NIHSS, following the multivariate regression analysis that controlling the potential effects of the confounders, including their ages, gender, hypertension, and diabetes mellitus, also demonstrated a statistically significant association between neutrophil count and the severity of the stroke (adjusted β = 0.39, p = 0.012).

Table 1. Baseline Demographic and Clinical Characteristics of Study Population (n = 38)

Variable	Mean ± SD / n (%)
Age (years)	58.2 ± 10.4
Male	23 (60.5%)
Female	15 (39.5%)
Hypertension	24 (63.2%)
Diabetes mellitus	12 (31.6%)
Ischemic heart disease	8 (21.1%)
Atrial fibrillation	4 (10.5%)
Time from onset to admission (hours)	6.3 ± 3.2
Total WBC count ($\times 10^9$/L)	10.4 ± 2.6
Neutrophil count ($\times 10^9$/L)	7.5 ± 2.1
Lymphocyte count ($\times 10^9$/L)	1.9 ± 0.8

Table 2. Comparison of Mean Neutrophil Count Across Stroke Severity Groups (Based on NIHSS Score)

Stroke Severity	N (%)	Mean Neutrophil Count ($\times 10^9$/L) ± SD
Mild (NIHSS ≤ 5)	12 (31.6%)	5.8 ± 1.2
Moderate (NIHSS 6–15)	17 (44.7%)	7.6 ± 1.5
Severe (NIHSS ≥ 16)	9 (23.7%)	9.1 ± 1.7
p-value (ANOVA)	0.002	

Table 3. Correlation between Neutrophil Count and Stroke Severity / Outcome

Variable	Correlation Coefficient (r)	p-value
Neutrophil count vs NIHSS score	0.56	0.001
Neutrophil count vs mRS score	0.48	0.003

DISCUSSION

The objective of this study was to evaluate the relation of neutrophil count with ischemic stroke severity in patients presenting at Bolan Medical Complex Hospital, Quetta. Their findings showed a positive correlation with increased neutrophil counts and stroke severity based on the NIHSS as well as poor short-term functional outcome according to mRS. These results indicate that an increase in neutrophils early on is a simple, convenient and cost-effective biomarker for prognostic evaluation in (Acute Ischemic Stroke) AIS.

It is striking that mean neutrophil numbers rise incrementally from the mild to the severe stroke group (5.8 ± 1.2, 7.6 ± 1.5 and 9.1 ± 1.7 $\times 10^9$/L, respectively; p =0.002), indicating a straightforward dose–response relationship between systemic inflammation activation and stroke severity. This is in line with recent findings that focus on the predictive role of inflammatory cell ratios in cerebrovascular diseases. In a 2024 meta-analysis, higher NLR was significantly associated with adverse outcomes and increased death in acute ischemic stroke patients further confirming the role of neutrophilic inflammation as a driver of neuronal injury. [11] In analogous fashion, a separate 2023 analysis highlighted the role of neutrophil extracellular traps (NETs) in exacerbating ischemic injury thereby indicating that NET-targeting may benefit post-ischemic prognosis. [12]

The findings of the present study are consistent with previous investigations that showed a correlation between increased leukocytes and neutrophils with severe neurological impairment. [13] Similar results were also demonstrated in another 2022 study, high pre-treatment neutrophil level being related to poor outcome in patient after endovascular thrombectomy, again supporting that association between systemic inflammation and clinical decline. [14] Neutrophil function attenuation reduces stroke infarct volume and improves outcomes, as demonstrated in experimental studies. For example, all-trans retinoic acid treatment has been shown to provide protection against acute ischemic injury by modulating neutrophil activation via the STAT1 signaling pathway. [15] This indicates that the deleterious effect of neutrophils is not a consequence only, but likely also an antecedent process in stroke.

The average total WBC was 10.4 ± 2.6 $\times 10^9$/L and predominated by neutrophils, similar to findings in previous studies. [16] Zhang et al. showed that elevated neutrophil counts were independent risk factors for first-ever stroke in hypertensive individuals, highlighting the potential prognostic importance of neutrophilic inflammation before clinical stroke. [17] Taken together, these findings suggest a broad pathophysiological continuum in which chronic inflammation primes people for cerebrovascular events whereas acute neutrophil activation contributes to worsening of ischemic injury.

In addition, the existence of activated microglia in that early stage of ischemia depletion has been demonstrated to be neuroprotective indicating intricate relationship between innate immune cells at the level of the neurovascular unit[19]. Similarly, reports from investigations of MS and ischemic stroke have uncovered shared neutrophil-driven inflammatory programs and peripheral effectors[18].

A multivariate analysis in this study also showed that this relationship between neutrophil count and stroke severity remained significant following adjustments for age, sex and vascular co-morbidities (β = 0.39, p = 0.012). This suggests the relationship of neutrophil elevation to neurologic impairment is not confounded by classical risk factors (i.e., hypertension and diabetes mellitus). [19-20]

This study had a number of limitations that need to be taken into account when interpreting results. First, the small sample size restricted to one tertiary care center may hinder generalization to larger populations. Second, despite use of stringent inclusion and exclusion criteria to reduce confounding, unmeasured factors including infection status, effects of any medication or inflammatory comorbidities could have affected the neutrophil counts. Third, the degree of neutrophil levels was measured at only 1 time point (between onset and up to 24 hours after stroke) whereas serial measurements may have identified more clearly temporal trends in neutrophils that could relate to outcomes.

CONCLUSION

The current study showed that increased neutrophil count at the 24-hour post-acute ischemic stroke is strongly associated with higher baseline neurological deficit and poor short-term functional

outcome. Due to its simplicity, accessibility and low cost nature, neutrophil count may be used as a convenient biomarker assisting prompt risk stratification and prognostic evaluation in ischemic stroke patient population even at primary care level or resource constrained facility. Additional large multicenter studies are needed to confirm these findings and investigate targeted anti-inflammatory approaches for prevention of stroke- related neuronal injury.

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