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Neutrophil–Lymphocyte Ratio as a Predictor of Delirium Tremens in Alcohol Withdrawal: A Retrospective Study

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ABSTRACT

Background: Delirium tremens is the most severe presentation of alcohol withdrawal and is associated with significant medical complications. Simple inflammatory markers obtained from routine blood counts could support early risk stratification.
Objectives: To estimate the frequency of delirium tremens among inpatients admitted with alcohol withdrawal and to evaluate the neutrophil–lymphocyte ratio (NLR) as a predictor of delirium tremens.
Methods: A retrospective record review was conducted among adult inpatients treated for alcohol withdrawal in a tertiary care teaching hospital. Sociodemographic variables, alcohol-use history, clinical course, and admission laboratory parameters were extracted from case records. NLR was calculated using neutrophil and lymphocyte percentages from the complete blood count. Patients were grouped into delirium tremens (DT) and no-DT categories. Group comparisons were performed using appropriate non-parametric tests, and receiver operating characteristic analysis was applied to determine the optimal NLR cut-off.
Results: Among 135 patients, 17 developed DT during admission. Median NLR was markedly higher in the DT group compared with the no-DT group. An NLR cut-off of ≥4.28 demonstrated good discrimination for DT with high specificity and an excellent negative predictive value. In regression analysis, increasing NLR remained independently associated with DT.
Conclusion: Elevated NLR at admission was associated with subsequent development of delirium tremens in alcohol withdrawal. NLR is an inexpensive, rapidly available marker that can complement clinical monitoring to identify patients who need closer observation and early escalation of care.

Keywords*: Alcohol withdrawal; Delirium tremens; Neutrophil–lymphocyte ratio; Inflammation; Predictive marker.*

INTRODUCTION

Alcohol use disorder remains a major contributor to morbidity, premature mortality, and health-care utilisation across the world. Abrupt cessation or marked reduction in heavy and prolonged alcohol intake can precipitate alcohol withdrawal syndrome, a clinical state characterised by autonomic hyperactivity, tremor, insomnia, agitation, and perceptual disturbances [1,2]. Although many patients experience mild-to-moderate symptoms, a clinically important subgroup progresses to complicated withdrawal in the form of withdrawal seizures or delirium tremens. Delirium tremens represents the most severe and life-threatening manifestation, typically occurring 48–96 hours after the last drink, and is characterised by fluctuating consciousness, disorientation, severe agitation, hallucinations, and marked autonomic instability [1,3,5]. Even in contemporary clinical settings, delirium tremens is associated with prolonged hospitalisation, need for intensive monitoring, and risk of complications such as aspiration, arrhythmias, and metabolic derangements [1,3].

Early identification of patients at high risk for delirium tremens is therefore essential. Standard bedside assessment tools and clinical judgement remain the cornerstone of care; however, risk stratification based solely on symptoms can be challenging when patients present late, provide unreliable histories, or have comorbid medical illness [3,4]. Laboratory parameters that are inexpensive, objective, and routinely obtained at admission could strengthen triage decisions and guide the intensity of monitoring. Inflammation and neuroimmune activation are increasingly recognised as contributors to delirium pathophysiology, and systemic inflammatory markers have shown associations with delirium in diverse clinical populations [8,11,12].

The neutrophil–lymphocyte ratio, derived from the differential leukocyte count, reflects the balance between innate and adaptive immune responses. It has been proposed as a rapid index of physiological stress and systemic inflammation and has been explored as a prognostic marker in several medical conditions [9,10]. Recent studies have also reported higher NLR values among patients who develop delirium, including hospitalised older adults and patients with acute neurological illness [11-13]. In the context of alcohol withdrawal, a retrospective study reported that elevated NLR within 24 hours of admission predicted delirium tremens with clinically useful discrimination [14].

Indian data on affordable biomarkers for predicting delirium tremens remain limited, despite the clinical importance of timely recognition in high-volume inpatient services. Against this background, the present study was undertaken in a tertiary care teaching hospital to examine the role of admission NLR in predicting delirium tremens. The objectives of the study were (i) to describe the sociodemographic and alcohol-use profile of inpatients with alcohol withdrawal, (ii) to estimate the frequency of delirium tremens during admission, and (iii) to evaluate the predictive performance of NLR for delirium tremens.

MATERIALS AND METHODS

Study design and setting: This hospital-based retrospective observational study was conducted in the Department of Psychiatry, Government Hospital for Mental Care, Andhra Medical College, Visakhapatnam, India. Case records of inpatients managed for alcohol withdrawal were reviewed after obtaining institutional ethics committee approval. Data were collected using de-identified codes, and the extracted dataset was stored in password-protected files accessible only to the study team.

Study participants and eligibility criteria: Adult inpatients (≥18 years) admitted with alcohol withdrawal syndrome were eligible. Diagnosis of alcohol use disorder and withdrawal states was based on treating-psychiatrist documentation in the medical record using standard diagnostic criteria [6]. Delirium tremens was defined as an acute fluctuating disturbance in attention and awareness with disorientation and perceptual disturbances during withdrawal, requiring inpatient management, as recorded by the clinician [1,5]. Records with adequate clinical notes and baseline laboratory investigations were included. Patients with concurrent chronic liver disease, renal failure, heart disease, known diabetes mellitus, active tuberculosis, or acute severe infections were excluded to minimise confounding influences on inflammatory indices.

Data collection and variables: A structured proforma was used to extract sociodemographic details (age, sex, marital status, residence, socioeconomic status, and occupation) and alcohol-use variables (age at initiation, years since initiation, years since daily use, and average daily intake in units). For alcohol intake, one unit was considered equivalent to approximately 10 g of ethanol based on standard clinical documentation. The clinical outcome of interest was development of delirium tremens during the index admission, as documented in the case record. Baseline laboratory parameters were obtained from admission investigations and included haemoglobin, total white blood cell count, platelet count, serum transaminases (SGOT, SGPT), random blood sugar, and differential counts of neutrophils and lymphocytes.

Computation of neutrophil–lymphocyte ratio: NLR was calculated by dividing the neutrophil percentage by the lymphocyte percentage from the differential leukocyte count, as described in prior literature [9]. NLR was available for 134 of 135 patients, and analyses involving NLR used complete-case data.

Statistical analysis: Data were analysed using statistical software (SPSS). Continuous variables were summarised as median with interquartile range (IQR) and categorical variables as frequency with percentage. Normality was assessed using the Shapiro–Wilk test, and non-normally distributed variables were compared using the Mann–Whitney U test. Receiver operating characteristic (ROC) curve analysis was used to evaluate the discriminative ability of NLR and to determine the optimal cut-off value using the Youden index. Univariable logistic regression estimated odds ratios for DT, and a multivariable model examined the independent association between NLR and DT after adjusting for clinically relevant covariates (age, total WBC, and SGOT). A two-sided p value < 0.05 was considered statistically significant.

Ethical Approval

Case records of inpatients managed for alcohol withdrawal were reviewed only after obtaining approval from the Institutional Ethics Committee(220/IECAMC/SEP2025), Andhra Medical College, Visakhapatnam, Department of Psychiatry, Government Hospital for Mental Care, Visakhapatnam, Andhra Pradesh, India. Data were collected using de-

identified participant codes, and no personal identifiers were extracted. The dataset was stored in password-protected files and access was restricted exclusively to the study team to ensure confidentiality and data security.

RESULTS

A total of 135 inpatients with alcohol withdrawal were included in the analysis. The majority were aged 30–49 years, and most participants were male, married, and from urban areas (Table 1). Most participants belonged to lower or upper-lower socioeconomic strata, with labourers forming the largest occupational group.

Table 1. Sociodemographic profile of the study participants (N = 135)

Variable	Category	n (%)
Age group (years)	18–29	22 (16.3)
	30–39	47 (34.8)
	40–49	48 (35.6)
	50–59	16 (11.9)
	≥60	2 (1.5)
Sex	Male	127 (94.1)
	Female	6 (4.4)
	Missing	2 (1.5)
Marital status	Married	119 (88.1)
	Unmarried	16 (11.9)
Religion	Hindu	127 (94.1)
	Christian	6 (4.4)
	Muslim	2 (1.5)
Residential area	Urban	85 (63.0)
	Rural	50 (37.0)
Socioeconomic status	Lower (L)	87 (64.4)
	Upper lower (UL)	34 (25.2)
	Lower middle (LM)	10 (7.4)
	Missing	4 (3.0)
Occupation	Labor	56 (41.5)
	Driver	13 (9.6)
	Security	9 (6.7)
	Business	7 (5.2)
	Painter	6 (4.4)
	Others	41 (30.4)
	Missing	3 (2.2)

The overall median duration since alcohol initiation was 13 years (IQR: 9–20), and the median duration of daily alcohol use was 6 years (IQR: 4–10). The median daily alcohol intake was 7.0 units/day (IQR: 3.6–10.0). Delirium tremens developed in 17 patients (12.6%) during admission (Table 2).

Table 2. Alcohol-use characteristics and delirium tremens (DT) status (N = 135)

Variable	Overall Median (IQR)	No DT Median (IQR)	DT Median (IQR)	p value
Years since alcohol initiation (years)	13 (9–20)	14 (9–20)	12 (9–16)	0.865
Years since daily alcohol use (years)	6 (4–10)	6 (4–10)	6 (4–9)	0.559
Daily alcohol consumption (units/day)	7.0 (3.6–10.0)	7.0 (3.6–10.0)	7.0 (6.0–8.0)	0.817
Development of DT	17 (12.6%)	118 (87.4%)	17 (12.6%)	—

On laboratory comparison, the DT group had significantly lower platelet counts and a distinct differential count pattern, characterised by higher neutrophil percentages and lower lymphocyte percentages (Table 3). Consequently, NLR was substantially higher in the DT group (median 4.9; IQR: 3.8–6.9) compared with the no-DT group (median 2.8; IQR: 2.2–3.9), and this difference was statistically significant (p = 0.001).

Table 3. Laboratory profile and NLR comparison between DT and No-DT groups

Parameter	No DT Median (IQR)	DT Median (IQR)	p value
Haemoglobin (g/dL)	13.6 (12.6–14.7)	13.4 (12.4–15.0)	0.897
Total WBC (/µL)	6800 (5500–8600)	6900 (5500–9200)	0.518
Platelet count (lakh/µL)	2.1 (1.6–2.5)	1.7 (0.9–2.5)	0.048

SGOT (U/L)	46 (28–80)	55 (32–78)	0.722
SGPT (U/L)	42 (27–62)	55 (36–84)	0.172
Random blood sugar (mg/dL)	98 (84–118)	112 (102–116)	0.054
Neutrophils (%)	71 (65–75)	77 (70–83)	0.018
Lymphocytes (%)	24 (19–29)	16 (12–20)	0.001
Neutrophil–lymphocyte ratio (NLR)*	2.8 (2.2–3.9)	4.9 (3.8–6.9)	0.001

*NLR was available for 134/135 patients.

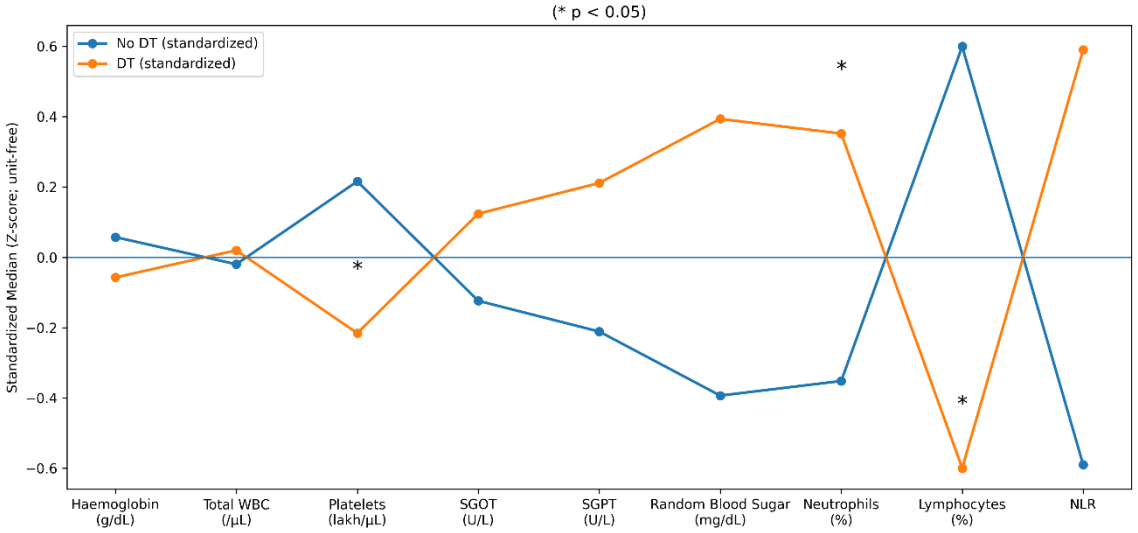

Figure 1: Laboratory profile and NLR comparison between DT and No-DT groups

ROC analysis demonstrated that NLR showed good discrimination for delirium tremens, with an area under the curve of 0.74 (95% CI: 0.57–0.89). An optimal cut-off of NLR ≥ 4.28 provided a sensitivity of 64.7% and specificity of 82.1%, with a negative predictive value of 94.1% (Table 4). Patients with NLR ≥ 4.28 had higher odds of DT in unadjusted analysis, and NLR remained independently associated with DT on adjusted analysis.

Table 4. Predictive performance of NLR for delirium tremens (DT)

Measure	Result
ROC AUC (95% CI)	0.74 (0.57–0.89)
Optimal NLR cut-off	≥ 4.28
Sensitivity	64.7%
Specificity	82.1%
Positive predictive value (PPV)	34.4%
Negative predictive value (NPV)	94.1%
Unadjusted odds ratio (NLR ≥ 4.28)	8.38 (95% CI: 2.79–25.21)
Adjusted odds ratio per 1-unit rise in NLR†	1.19 (95% CI: 1.04–1.37), p = 0.014

DISCUSSION

In this retrospective cohort of inpatients admitted with alcohol withdrawal, delirium tremens occurred in 12.6% of patients. This frequency aligns with the recognised spectrum of complicated withdrawal described in clinical reviews and practice guidelines, where DT is less common than uncomplicated withdrawal but carries disproportionate risk and resource needs [1,3]. Given the clinical consequences of DT, the search for pragmatic and low-cost predictors is clinically relevant in high-burden inpatient settings.

The principal finding of the study was that admission neutrophil–lymphocyte ratio was significantly higher among patients who subsequently developed delirium tremens. The difference was driven by a combination of higher neutrophil percentages and lower lymphocyte percentages in the DT group, reflecting an amplified stress-inflammatory response. NLR is widely viewed as an integrated marker of systemic inflammation and neuroendocrine stress, and its utility has been demonstrated across heterogeneous conditions [9,10]. Alcohol withdrawal is associated with sympathetic overactivity, sleep disruption, dehydration, and metabolic stress, all of which can influence immune-cell trafficking and cytokine signalling, plausibly elevating NLR in those progressing to severe withdrawal states [1,2].

Our findings are consistent with earlier work examining NLR in delirium. In a landmark review, delirium has been conceptualised as a final common pathway of acute brain dysfunction that is frequently triggered by systemic inflammation and physiological stress [8]. Elevated NLR has been associated with incident delirium among hospitalised

older adults and has been reported in acute neurological illness cohorts, supporting inflammatory imbalance as a measurable correlate of delirium susceptibility [11-13]. Most importantly, Yıldırım and colleagues reported that NLR measured within 24 hours of admission predicted delirium tremens in patients with alcohol withdrawal syndrome, highlighting NLR as a potentially useful bedside biomarker in addiction settings [14]. Although optimal cut-off values vary across populations due to differences in baseline inflammation, comorbidity profiles, and sampling times, the direction and clinical implication of association remain consistent.

From a clinical standpoint, the predictive metrics observed in this study suggest practical value. The cut-off of NLR ≥ 4.28 achieved high specificity and an excellent negative predictive value, indicating that a low NLR can help identify patients at lower risk of DT who can be managed with standard monitoring protocols. Conversely, an elevated NLR should be interpreted as a warning signal prompting closer observation, early correction of physiological derangements, and proactive optimisation of withdrawal management strategies recommended in evidence-based guidelines [3,4]. Lower platelet counts in the DT group also merit attention, as thrombocytopenia is common in heavy alcohol use and can reflect hepatic dysfunction, nutritional deficiency, or bone marrow suppression, indicating more advanced systemic involvement.

Overall, the results reinforce the concept that a simple ratio derived from routine complete blood counts can add incremental information to clinical assessment. Future prospective studies incorporating symptom severity scores such as CIWA-Ar and serial NLR measurements could further refine cut-offs and improve bedside risk models for delirium tremens [7].

Limitations

This study was based on retrospective record review from a single tertiary centre, which restricts generalisability. Delirium tremens status depended on clinical documentation, and variability in charting influences misclassification. NLR was derived from a single admission sample, and serial inflammatory measurements were not available. Residual confounding from unrecorded infections, nutritional status, and hepatic dysfunction could not be fully controlled despite exclusion criteria.

CONCLUSION

Delirium tremens developed in 12.6% of inpatients admitted with alcohol withdrawal, highlighting a clinically relevant burden in tertiary-care detoxification settings. On admission, DT cases demonstrated a distinct inflammatory profile with higher neutrophil proportions, lower lymphocyte proportions, and significantly increased neutrophil–lymphocyte ratio, indicating heightened systemic stress response. The NLR threshold of ≥4.28 provided meaningful risk stratification with high specificity and an excellent negative predictive value, suggesting strong utility for ruling out DT in low-risk patients. Given its low cost, immediate availability from routine haemograms, and ease of calculation, NLR can be integrated into early assessment protocols to guide closer surveillance, prompt escalation, and more targeted allocation of inpatient monitoring resources.

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