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ORIGINAL RESEARCH

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Association of preoperative neutrophil-to-lymphocyte ratio with the risk of emergence delirium in children undergoing dental treatment under general anesthesia

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Abstract

Background: Emergence delirium (ED) is a common postoperative complication in pediatric patients, characterized by confusion, agitation, and restlessness. Recent studies suggest that systemic inflammation, particularly the neutrophil-to-lymphocyte ratio (NLR), may play a role in its development. This study aimed to assess the relationship between preoperative peripheral blood parameters, especially NLR, and the incidence of ED in pediatric patients undergoing dental treatment under general anesthesia. **Methods**: This retrospective, single-center study included 102 pediatric patients (aged 1–7 years) classified as ASA I or II, who underwent dental procedures under general anesthesia at Ankara Medipol University Dental Hospital between January 2023 and July 2024. Preoperative blood tests, including NLR, were collected. ED was evaluated using the Pediatric Anesthesia Emergence Delirium (PAED) Scale. Statistical analyses included Chi-square, Mann-Whitney U tests, multivariate logistic regression, and receiver operating characteristic (ROC) curve analysis. **Results**: ED occurred in 18 of 102 patients (17.6%). Univariate analysis showed a significantly higher mean NLR in patients with ED (2.0 $\pm$ 1.55) compared to those without ED (0.87 $\pm$ 0.30) ($p < 0.001$). However, multivariate logistic regression did not identify NLR or other variables as independent predictors of ED. ROC curve analysis yielded an NLR cut-off of 1.005, with sensitivity 23.1% and specificity 76.3% (Area under the curve (ACU) = 0.234, $p < 0.05$). Other inflammatory markers, including monocyte-to-lymphocyte ratio (MLR) and platelet-to-lymphocyte ratio (PLR), also showed significant associations with ED in univariate analyses. **Conclusions**: Although significant associations between preoperative inflammatory markers and ED were observed in univariate analyses, these markers did not remain independent predictors in multivariate analysis. Nonetheless, the identified correlations highlight the potential role of preoperative inflammatory markers in identifying pediatric patients at increased risk of ED, underscoring the need for further research to establish their clinical utility.

Keywords

Delirium; Blood tests; General anesthesia; Pediatric dentistry; Pediatric anesthesia

1. Introduction

Emergence delirium (ED) is a commonly observed surgical complication in pediatric patients following general anesthesia (GA) [1]. The condition is marked by symptoms including confusion, agitation and restlessness, which usually appear in the initial stages of recovery [2]. While ED often resolves within an hour without intervention, it may provide significant short-term risks including self-harm and disruption of surgical sites, while long-term effects may involve separation anxiety, eating disorders and sleep abnormalities [3, 4].

Multiple factors have been recognized as contributing to the the development of ED, including preoperative anxiety, the use of anesthetic agents, the characteristics and duration of surgical interventions, inhalational anesthetics and postoperative discomfort. Despite extensive research, the exact correlations between these factors and ED are not well established [5]. The Pediatric Anesthesia Emergence Delirium (PAED) Scale is a widely utilized instrument for ED, assessing symptoms using five observable criteria: eye contact, intentional activities, awareness of surroundings and restlessness (Table 1, Ref. [3]). Its practicality and durability have rendered it a favored approach in clinical practice [2, 6].

Recent research has increasingly acknowledged the significance of systemic inflammation in cognitive impairments, including ED. Biomarkers derived from standard blood tests,

TABLE 1. The PAED scale [3].

Point	Description	Not at all	A little	Quite a bit	Very much	Extremely
1	The child makes contact with caregiver	4	3	2	1	0
2	The child's actions are purposeful	4	3	2	1	0
3	The child is aware of his/her surroundings	4	3	2	1	0
4	The child is restless	4	3	2	1	0
5	The child is inconsolable	4	3	2	1	0

particularly the Neutrophil-to-Lymphocyte Ratio (NLR), have surfaced as potential indicators for assessing the risk of cognitive impairment [3]. In pediatric patients having surgeries like tonsillectomy and adenoidectomy, a higher preoperative neutrophil-to-lymphocyte ratio (NLR) has been recognized as a major predictor of ED [7]. Furthermore, additional indicators, including the Monocyte-to-Lymphocyte Ratio (MLR) and Platelet-to-Lymphocyte Ratio (PLR), have been examined as possible predictors of ED [8]. Integrating these blood tests into standard preoperative assessments could provide a minimally invasive and objective approach to reduce the occurrence and severity of ED, hence improving overall recovery results.

Nonetheless, the prognostic significance of inflammatory markers like NLR remains ambiguous when particularly applied to juvenile dentistry procedures under general anesthesia. Most current research has been on surgical techniques such as tonsillectomy and adenoidectomy, which entail greater tissue stress and inflammatory reactions compared to dental therapies [7, 9]. Dental procedures conducted under general anesthesia frequently involve younger children, particularly those with behavioral or developmental issues, a demographic that may react differently to anesthesia and display diverse susceptibilities to ED. Certain dental procedures, like multiple extractions, treating deep carious lesions, or managing pulpal and periapical infections, can still cause systemic inflammatory responses in pediatric patients, despite the fact that they are typically less invasive than major surgeries. According to research, even localized oral infections can increase systemic markers that indicate an underlying inflammatory state, such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR) and platelet-to-lymphocyte ratio (PLR). Furthermore, immune modulation has been linked to general anesthesia, which supports the study of inflammatory biomarkers in anesthesia-induced dental settings [10, 11].

Despite the examination of NLR and associated inflammatory markers in several surgical settings, their efficacy as independent predictors of ED remain ambiguous, especially in relation to pediatric dental procedures conducted under general anesthesia. Moreover, the majority of studies have depended on univariate analysis techniques, failing to employ robust statistical tools to effectively identify independent predictors while accounting for possible confounders [12]. A standardized approach integrating inflammatory biomarker screening into preoperative examinations for pediatric dentistry patients is currently lacking.

This study seeks to fill these gaps by evaluating the prognostic significance of preoperative inflammatory markers, specifically NLR, in determining the risk of ED in pediatric patients undergoing dental procedures under general anesthesia. The establishment of dependable predictors may aid in the creation of standardized preoperative evaluation methods specifically designed for pediatric dental patients. This study's null hypothesis asserts that there is no significant correlation between preoperative blood test results and the incidence of ED.

2. Materials and methods

This retrospective, single-center study included 102 pediatric patients, aged 1 to 7 years, classified as American Society of Anesthesiologists (ASA) physical status I or II. The patients underwent dental treatment under general anesthesia at the Dental Hospital of Ankara Medipol University between January 2023 and July 2024. Ethical approval was obtained from the Ankara Medipol University Ethical Committee (Decision Number: 66), and informed consent was secured from all participants' parents or legal guardians.

Specifically, actual anesthesia durations for included cases were recorded postoperatively. Exclusion criteria included the presence of active dental abscesses, infections in other parts of the body, developmental delays, autism, neurological or psychiatric disorders, and congenital or chronic diseases. None of the patients exhibited additional systemic findings or comorbidities beyond the specified exclusion criteria. All dental procedures were conducted by a pediatric dentist (BT) or maxillofacial surgeon (HE).

Routine preoperative laboratory tests were performed the day before surgery, with blood parameters measured using a fully automated biochemical analyzer (Cobas® 8000 modular analyzer, Roche Diagnostics, Basel, BS, Switzerland) at the contracted institution. Anesthesia was induced with intravenous midazolam (0.1 mg/kg), rocuronium (0.6 mg/kg), fentanyl (1 μg/kg) and propofol (2 mg/kg). Nasal endotracheal intubation was performed by the same anesthesiologist (BC) using a video laryngoscope (Karl Storz GmbH & Co. KG, Tuttlingen, BW, Germany) and ventilation was adjusted to maintain end-tidal carbon dioxide ($ETCO_2$) levels between 35 and 45 mmHg. Anesthesia was maintained with volatile anesthetics at 2 to 2.5 minimum alveolar concentration (MAC) and remifentanil (0.1–1 μg/kg/min) infusion. Neuromuscular blockade was sustained with rocuronium bromide (0.15 mg/kg) as needed. At the end of surgery, neuromuscular blockade was reversed using neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg), followed by removal of airway devices.

Postoperatively, patients were admitted to the Post-Anesthesia Care Unit (PACU), where a trained researcher systematically assessed ED and pain scores at 15-minute

intervals until discharge. The PAED Scale is composed of five criteria: eye contact, purposeful actions, awareness of surroundings, restlessness and consolability, each scored from 0 to 4, with a total score ranging from 0 to 20. A PAED score of 10 or higher indicated significant ED [4]. Researchers responsible for monitoring were trained in applying the PAED Scale to ensure consistency and accuracy in assessment. This training included familiarization with the scale's criteria, practice sessions with simulated cases, and periodic inter-rater reliability assessments to maintain consistency. Assessments were conducted by a team of researchers who had undergone training sessions supervised by experienced pediatric anesthesiologists to ensure uniformity in scoring and minimize inter-observer variability. The researchers assessing ED were blinded to all aspects of data collection to minimize potential bias and enhance the validity of the study findings.

Power analysis was conducted using G*Power Version 3.1.9.7 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, NRW, Germany) to determine the required sample size. The analysis was based on a significance level of 0.05, a power of 0.80 and an effect size of 0.101, and it was determined that a minimum of 100 patients needed to be included in the study.

Statistical analysis was performed using SigmaPlot 12.5 (Systat Software Inc, San Jose, CA, USA). Descriptive statistics were used for maximum and minimum values, mean and standard deviations. Chi^2 test was used for categorical data. The normality of the distribution was assessed using the Shapiro-Wilk test. If the distribution was normal, a *t*-test was used; if not, the Mann-Whitney U test was used. Multivariate logistic regression analysis was performed to investigate risk factors for ED, and ROC curve analysis was used to determine the cut-off values of these factors. The statistical significance level was accepted as $p < 0.05$.

3. Results

A total of 102 patients (37 females, 65 males) were included in the study, with an average age of 5.48 ± 1.83 years. Emergence delirium (ED) was observed in 18 patients (17.6%), while 84 patients (82.4%) did not exhibit ED. Among the patients with ED, 14 were male and four were female, with no statistically significant difference between genders ($p = 0.273$). The mean age of patients with ED was 6.11 ± 2.11 years, compared to 5.35 ± 1.76 years in those without ED, with no statistically significant difference ($p = 0.109$). All patients with ED were classified as ASA I, while among the patients without ED, 73 were ASA I and 11 were ASA II, with no statistically significant difference between the groups ($p = 0.228$).

The preoperative blood parameters, including neutrophil percentage (NEUT%), monocyte percentage (MON%), neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR) and platelet-to-lymphocyte ratio (PLR), were significantly higher in the ED group compared to the non-ED group. Conversely, the non-ED group's lymphocyte percentage (LYM%) and platelet-to-neutrophil ratio (PNR) were significantly higher. No significant differences were observed between the two groups regarding the duration of anesthesia, propofol dosage, eye-opening time or other blood parameters, including white blood cell count (WBC), platelet count (PLT), red blood cell count (RBC), hematocrit (PCT), mean platelet volume (MPV), red blood cell distribution width (RDW-SD), platelet-to-white blood cell ratio (PWR) and platelet-to-monocyte ratio (PMR) (Table 2).

ROC curve analyses were used to assess the predictive value of risk factors for ED. NLR had a cut-off value of 1.005, an AUC of 0.234, a sensitivity of 23.1% and a specificity of 76.3% (95% (Confidence Interval) CI: 0.056–0.412, $p < 0.05$). MLR had a cut-off value of 0.158, an AUC of 0.167, a sensitivity of 23.1% and a specificity of 77.5% (95% CI: 0.44–0.291, $p < 0.05$). NEUT% had a cut-off value of 44.65, an AUC of 0.275, a sensitivity of 30.8% and a specificity of 68.8% (95% CI: 0.88–0.462, $p < 0.05$). MON% had a cut-off value of 6.95, an AUC of 0.240, a sensitivity of 30.8%, and a specificity of 71.3% (95% CI: 0.093–0.388, $p < 0.05$). PLR had a cut-off value of 101.745, an AUC of 0.297, a sensitivity of 38.5%, and a specificity of 61.3% (95% CI: 0.155–0.439, $p < 0.05$). Although the ROC analyses yielded statistically significant *p*-values for several inflammatory markers, the AUC values were markedly low (*e.g.*, NLR AUC = 0.234), indicating poor discriminative ability and suggesting a potential inverse or non-linear relationship, which limits their clinical predictive utility. Multivariate logistic regression analyses were performed to investigate potential risk factors for ED, but no statistically significant factors were identified (Table 3).

4. Discussion

This study identified significant associations between preoperative inflammatory markers, such as neutrophil percentage (NEUT%), lymphocyte percentage (LYM%), monocyte percentage (MON%) and ratios, including the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-neutrophil ratio (PNR) and platelet-to-lymphocyte ratio (PLR), with the occurrence of emergence delirium (ED) in pediatric patients undergoing dental procedures under general anesthesia. These findings suggest that systemic inflammation, as reflected by these blood parameters, may contribute to the pathophysiology of ED in this patient population.

Our study builds on previous research highlighting systemic inflammation's role in cognitive disturbances, particularly in pediatric patients. For instance, Jooma *et al.* [3] (2020) demonstrated that preoperative anxiety and ED were prevalent in pediatric patients undergoing dental surgery despite the use of non-pharmacological interventions and nerve blocks. The study also revealed that while most children presenting for dental surgery are anxious at induction, ED occurred in over half of the patients (51.6%) despite the use of non-pharmacological interventions and nerve blocks. These findings suggest that while local anesthetic techniques can reduce nociceptive stimuli, they may not be sufficient to mitigate the development of ED, which is also influenced by psychological and environmental factors. This underscores the importance of considering both the physical and emotional aspects of perioperative care in pediatric patients to reduce the incidence of ED and improve postoperative recovery.

The increased occurrence of ED in preschool-aged children can be attributed to their heightened emotional sensitivity when

TABLE 2. Patient characteristics emergence delirium.

	ED Group (Mean ± SD)	Non-ED Group (Mean ± SD)	*p* value
Age (yr)	6.11 ± 2.11	5.35 ± 1.76	0.109
Weight (kg)	22.17 ± 6.19	19.77 ± 4.23	0.049
Propofol (mg)	26.11 ± 13.67	21.08 ± 9.73	0.068
Anesthesia duration (min)	143.89 ± 36.56	141.43 ± 41.35	0.828
Eye opening (min)	4.22 ± 1.00	3.75 ± 1.11	0.085
WBC × 10^9/L (median)	8.91 ± 2.99 (8.31)	8.43 ± 2.09 (8.06)	0.720*
NEUT% (Median)	54.54 ± 14.17 (55.75)	41.36 ± 7.8 (41.7)	<0.001*
LYM%	36.91 ± 12.69 (34.30)	50.27 ± 11.79 (48.8)	0.013*
MON% (Median)	7.43 ± 2.30 (7.45)	6.04 ± 1.79 (5.9)	0.018*
PLT × 10^9/L (Median)	367.67 ± 118.01 (346.5)	372.44 ± 101.58 (351)	0.623*
RBC × 10^{12}/L	4.83 ± 0.44	4.85 ± 0.39	0.881
PCT%	0.30 ± 0.087	0.32 ± 0.08	0.448
MPV	0.83 ± 1.00	8.74 ± 1.13	0.171
RDW-SD	27.17 ± 16.39	37.55 ± 7.26	0.060
NLR (median)	2.00 ± 1.55 (1.64)	0.87 ± 0.30 (0.85)	<0.001*
MLR (median)	0.23 ± 0.09 (0.20)	0.13 ± 0.04 (0.12)	<0.001*
PNR (median)	88.35 ± 43.83 (79.92)	118.50 ± 53.64 (110.45)	0.018*
PWR (median)	44.08 ± 15.18 (42.48)	46.05 ± 14.02 (43.85)	0.683*
PLR (median)	134.64 ± 68.47 (121.08)	95.32 ± 30.67 (92.56)	<0.001*
PMR (median)	655.69 ± 332.86 (604.32)	767.44 ± 312.45 (727.24)	0.130*

ED: emergence delirium; WBC: white blood cell; NEUT%: neutrophil count; LYM%: lymphocyte count; MON%: monocyte count; PLT: platelet; RBC: red blood cell; PCT: hematocrit; MPV: mean platelet volume; RDW-SD: red blood cell distribution width; NLR: neutrophil-lymphocyte ratio; MLR: monocyte-lymphocyte ratio; PNR: platelet-neutrophil ratio; PWR: platelet-white blood cell ratio; PLR: platelet-lymphocyte ratio; PMR: platelet-monocyte ratio; SD: Standard deviation.
**The distribution is non-parametric, and the Mann-Whitney U test was applied; $p < 0.05$.*

TABLE 3. Risk factors for ED.

	B	OR	95% Lower	95% Upper	*p*
NLR	−7.244	0.001	0.000	550.015	0.295
MLR	31.715	5.94×10^{17}	0.000	6.04×10^{54}	0.466
NEUT%	0.065	1.067	0.637	1.788	0.804
MON	−1.279	0.278	0.035	2.221	0.228
PLR	0.000	1.000	0.998	1.003	0.884
Constant	10.206	27,077.81			0.215

NLR: neutrophil-lymphocyte ratio; MLR: monocyte-lymphocyte ratio; NEUT: neutrophil count; MON: monocyte count; PLR: platelet-lymphocyte ratio; B: Beta-Value; OR: Odds Ratio.

confronted with stress in an unfamiliar environment. Certain hippocampus regions remain physiologically immature at this developmental stage, contributing to greater cerebral instability [4]. The incidence of ED following pediatric dental surgeries under general anesthesia is a well-recognized phenomenon, as highlighted by Beringer *et al.* [12] (2014), where 13% of the children exhibited ED. This study's findings reinforce the importance of considering various risk factors associated with ED, such as younger age and previous traumatic medical experiences. Interestingly, this research also found that the number of teeth extracted was significantly related to the occurrence of ED, suggesting that the extent of the surgical procedure might increase the risk of postoperative cognitive disturbances. Feng *et al.* [7] detected a 25.3% incidence of ED in tonsillectomy patients and first described the relationship between NLR levels and ED in 2023.

The heightened emotional sensitivity and cerebral instability observed in preschool-aged children, particularly in unfamiliar and stressful environments, may contribute to the increased incidence of ED in this age group [4]. Additionally, the

physiological immaturity of certain hippocampal regions may exacerbate this vulnerability, as suggested by Beringer *et al.* [12] (2014). In accordance with our findings, this study reinforces the need for a multifaceted approach to managing ED, considering the extent of the surgical procedure and the patient's emotional state and preoperative inflammatory profile.

The relationship between NLR and ED has been previously explored in other surgical contexts. Feng *et al.* [7] (2024) identified elevated preoperative NLR levels as a significant predictor of ED in pediatric patients undergoing tonsillectomy and. Similarly, our study found that increased NLR was associated with a higher risk of ED in pediatric dental patients, further supporting the role of systemic inflammation in the development of postoperative cognitive disturbances.

Various factors can contribute to the development of emergence delirium (ED), including rapid recovery of consciousness in an unfamiliar setting, agitation during the induction of anesthesia, preoperative anxiety, the administration of anesthetic medications, the nature of the surgical procedure, the use of inhaled anesthetics, postoperative pain and the patient's young age [5]. Keles and Kocatürk stated that using a laryngeal mask airway resulted in less postoperative discomfort and ED, a shorter recovery time, and higher satisfaction levels than nasotracheal intubation (NTI) [13]. In contrast to NTI, Laryngeal Mask Airway (LMA) is a supraglottic apparatus that does not necessitate traversal through the vocal cords or interaction with the trachea, therefore reducing mechanical discomfort and inflammatory reaction [14].

Previous research has shown that increased MLR levels are associated with cognitive impairment in adults, particularly in the context of neuroinflammation. Su *et al*. [8] demonstrated that the monocyte-to-lymphocyte ratio (MLR), another inflammatory marker, is associated with delirium in adult intensive care unit (ICU) patients undergoing cardiac surgery. In our study, elevated MLR levels were similarly linked to higher rates of ED in pediatric patients. This reinforces that immune response dysregulation, specifically involving monocytes and lymphocytes, may play a critical role in the pathogenesis of cognitive disturbances following anesthesia. However, the exact mechanisms by which these inflammatory markers influence cerebral function in children remain unclear, warranting further investigation.

The platelet-to-neutrophil ratio (PNR) is another marker that reflects the balance between inflammation and coagulation pathways. Elevated platelet counts relative to neutrophils may indicate a hypercoagulable state, contributing to microvascular complications, including those affecting the brain. While the association between inflammatory markers and postoperative delirium is well-documented in adult populations, research in pediatric patients remains limited. In pediatric patients, a higher PNR may increase the risk of ED by exacerbating inflammation and impairing cerebral perfusion. Similar to findings by Oyama *et al.* [15] (2022), who identified elevated PNR as a predictor of delirium in adult surgical patients, our results suggest that these markers could be valuable in predicting ED in pediatric populations. Future studies should explore the underlying biological mechanisms and assess the generalizability of these findings across different surgical contexts [15].

The platelet-to-lymphocyte ratio (PLR) is a composite marker of inflammation and immune response, with higher values suggesting a pro-inflammatory state. Elevated PLR levels have been associated with worse outcomes in various conditions, including cardiovascular diseases and cancer, and have been increasingly studied about cognitive dysfunction. An elevated PLR may reflect a heightened inflammatory response in pediatric patients undergoing dental procedures, increasing the likelihood of ED. Research by Jiang *et al*. [16] supports using PLR as a prognostic marker for delirium in critically ill patients.

While numerous studies have explored the relationship between anesthetic agents, intubation methods, procedure duration and delirium, there is a relative scarcity of research focusing on the connection between peripheral blood parameters and delirium [7, 9]. The NLR is a commonly utilized inflammation biomarker, as neutrophils and lymphocytes are regularly assessed in standard blood tests [7]. Egberts *et al*. [17] (2017) reported that elevated NLR levels were associated with an increased risk of delirium. This suggests that an impaired immune response and heightened systemic inflammation could contribute to developing cognitive disturbances. In line with this, our study found increased NLR levels in patients with emergence delirium (ED), further supporting the hypothesis that immune system dysregulation and oxidative stress may play significant roles in the pathogenesis of delirium [17]. By incorporating NLR as a biomarker, clinicians can better identify children at higher risk for emergence delirium (ED). Early identification of at-risk patients through simple blood tests like NLR allows for targeted interventions, such as modifying anesthesia protocols, optimizing perioperative care or employing additional monitoring during recovery.

Oxidative stress is another important mechanism that may contribute to the development of delirium. Surgical stress, particularly when accompanied by systemic inflammation, can lead to increased reactive oxygen species (ROS) production. Oxidative stress can further amplify neuroinflammation, creating a vicious cycle of neuronal injury. It has been suggested that the heightened inflammatory state, reflected by an elevated NLR, correlates with increased oxidative stress, contributing to cognitive dysfunction postoperatively [18]. The association between elevated inflammatory biomarkers and neuroinflammation suggests that targeting inflammation could be a potential therapeutic strategy to prevent or mitigate ED. For instance, preoperative administration of anti-inflammatory agents or antioxidants could theoretically reduce the risk of developing delirium, although this requires further clinical validation.

While our study provides valuable insights into the relationship between peripheral blood parameters and ED, it is important to acknowledge the limitations. Being a single-center, retrospective study, the generalizability of our findings may be limited. Furthermore, although significant associations were identified in univariate analysis, multivariate logistic regression did not reveal any statistically significant independent predictors of ED. This suggests that other factors, such as patient anxiety, anesthetic techniques and genetic predispositions, may also play critical roles in the development of ED.

Additionally, the low AUC value (0.234) reported in this study indicates the inadequate predictive efficacy of NLR as an independent preoperative biomarker for ED in juvenile dentistry procedures conducted under general anesthesia. This outcome is much inferior to AUC values documented in research concerning more invasive procedures, such as tonsillectomy and adenoidectomy. In this context, the inadequate discriminatory capacity of NLR may indicate that the inflammatory response elicited by dental treatments is either less significant or fundamentally distinct from that associated with more traumatic surgery. Moreover, this suggests that while NLR may show statistically significant differences between groups, it has limited clinical utility as a diagnostic tool.

The multivariate regression analysis did not reveal significant independent predictors for ED, attributed to a limited sample size of 102 patients, multicollinearity across inflammatory markers, and the possibility of overfitting. The results indicate that preoperative inflammatory indicators alone may not reliably predict ED, necessitating future research with bigger sample sizes, thorough multivariate models, and additional clinical factors. Furthermore, the absence of significant predictors in multivariate analysis underscores the need for developing more comprehensive screening protocols that account for multiple risk factors. Future research should focus on elucidating the complex interplay of these factors and their contributions to ED.

Moreover, it is crucial to recognize that the restricted sample size of 102 patients may have impeded the identification of relevant predictors in the multivariate analysis. The presence of only 18 individuals with ED may have rendered the statistical power inadequate for identifying independent factors. Consequently, the limited number of positive cases in our study may have diminished the sensitivity of the analysis, thereby elevating the probability of Type II errors. Subsequent research should focus on using bigger sample sizes to strengthen the validity of multivariate analysis. Despite the valuable insights provided by this study, several methodological limitations must be acknowledged. This study study did not incorporate validated anxiety or pain assessment tools, such as the State-Trait Anxiety Inventory for Children (STAIC) or the Face, Legs, Activity, Cry, Consolability (FLACC) Pain Scale, which are critical factors that affect the incidence and severity of ED [19–22]. Neglecting to assess these elements may restrict the precision of the prediction analysis and lead to confounding variables.

Further research is warranted to confirm these findings in larger, multicenter studies and to develop standardized protocols incorporating inflammatory biomarker assessment into routine clinical practice. Further research is needed to establish more reliable predictive models that incorporate multiple biomarkers and clinical factors. A better understanding of the underlying mechanisms contributing to ED, including the role of systemic inflammation, will be crucial in advancing the field of pediatric anesthesia and improving care for young patients undergoing dental and other surgical procedures.

Together, these results demonstrate the complex nature of emergence delirium and show that developmental neurobiology, oxidative stress and systemic inflammation are all contributing factors. Despite statistical correlations with ED, the clinical utility of inflammatory markers such as NLR, MLR, PLR and PNR as independent predictors is limited. However, their easy measurement and potential inclusion in a thorough risk assessment model suggest a practical, minimally invasive addition to the treatment of pediatric anesthesia.

5. Conclusions

This study highlights the significant association between preoperative inflammatory markers, particularly the NLR, and the risk of ED in pediatric patients undergoing dental treatment under general anesthesia. While the multivariate analysis did not identify independent predictors of ED, the findings suggest that routine preoperative assessment of inflammatory biomarkers, including NLR, could be instrumental in identifying patients at higher risk for postoperative cognitive disturbances. Integrating peripheral blood parameters into preoperative screening protocols may offer a valuable, non-invasive tool for stratifying risk and guiding perioperative management in pediatric anesthesia. While inflammatory markers like NLR may offer insights into ED risk, their routine use in preoperative assessment should be approached with caution and considered only after validation in larger, prospective studies.

AVAILABILITY OF DATA AND MATERIALS

Research data are not shared.

AUTHOR CONTRIBUTIONS

ABÇ—conceived the idea. ABÇ, BÇT, AYG and HE—collected and analysed the data. HAK—led the writing. All authors reviewed and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ankara Medipol University Ethical Committee (Decision Number: 66). Informed consent was secured from all participants' parents or legal guardians.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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