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ORIGINAL ARTICLE

Association of preoperative neutrophil–lymphocyte ratios with the emergence delirium in pediatric patients after tonsillectomy and adenoidectomy: an observational prospective study

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Abstract

Purpose The study aimed to investigate potential risk factors for emergence delirium (ED) in pediatric patients after tonsillectomy and adenoidectomy (T&A).

Methods This prospective, single-center observational study enrolled children aged 3–7 years who underwent T&A under general anesthesia. ED was assessed according to DSM-IV or V criteria. Receiver operating characteristic curve analysis was performed to evaluate the predicative and cut-off values of risk factors, including age, preoperative anxiety level, postoperative pain and neutrophil–lymphocyte ratio (NLR) for ED. Univariate and multivariate logistic regression analyses were performed to investigate risk factors for ED.

Results 94 pediatric patients who underwent T&A were enrolled and 19 developed ED (an incidence of 25.3%). Receiver operating characteristic analysis indicated that preoperative NLR was a significant predictor of ED with a cut-off value of 0.8719 and an area under the curve (AUC) of 0.671 (95% confidence interval (CI) 0.546–0.796, $P=0.022$). Preoperative NLR (<0.8719) and postoperative pain were independent risk factors associated with ED (odds ratio: 0.168, 95% CI 0.033–0.858, $P=0.032$; odds ratio: 7.298, 95% CI 1.563–34.083, $P=0.011$) according to multivariate logistic regression analysis.

Conclusions Preoperative NLR level and postoperative pain were independent risk factors for ED in pediatric patients undergoing T&A.

Keywords Children · Emergence delirium · Risk factor

Introduction

Emergence delirium (ED) is a well-known early postoperative disturbance in children's awareness of and attention to their environment with disorientation and perceptual alterations after general anesthesia [1]. This is especially prevalent in pediatric patients receiving tonsillectomy and adenoidectomy (T&A), with an incidence ranging from 13 to 26% [2, 3]. Although ED typically resolves within 1 h without any severe complications, delirious children are at greater risk of negative postoperative behavioral changes [4, 5]. Self-harm, aggravation of surgical incisions, and removal of IV lines may occur in the short term, while maladaptive behavioral changes, such as separation anxiety, eating disorders, and sleep disturbances may occur in the long term [6]. Many factors can affect ED, including preoperative anxiety, use of preanesthetic medication, type of surgery, use of inhaled anesthetics, and postoperative pain [2]. Specific correlations among these factors have not been determined.

Peripheral blood cell parameters can be used as circulating biomarkers for systemic inflammation and they have been investigated in numerous diseases, including cardiovascular diseases and cancers [7, 8]. In adult orthopedic surgery patients who experience delirium, high values for the NLR, monocyte–lymphocyte ratio (MLR), and the systemic immune-inflammation index (SII) are related to cognitive decline. Furthermore, preoperative SII is an independent risk factor for postoperative delirium in elderly patients [9] and preoperative red cell distribution

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width predicts postoperative delirium after coronary artery bypass grafting [10]. Higher NLR, mean platelet volume, and platelet distribution width are associated with postoperative delirium in patients undergoing esophagectomy [11]. Peripheral blood cell parameters of patients with tonsillitis were higher than those in healthy individuals [12]. Red blood cell distribution width (RDW) is a biomarker that can indicate chronic infection in patients with tonsillitis and can, therefore, inform the clinical decision to perform surgery [13]. The NLR can be used in chronic tonsillitis patients as an effective auxiliary method to determine the necessity and timing of tonsillectomy and to plan postoperative follow-up [14]. However, few studies have addressed the association between peripheral blood cell parameters and pediatric ED.

This study investigated potential risk factors for ED in pediatric patients receiving T&A and whether blood cell parameters can predict ED.

Methods

This prospective, single-center, observational study was approved by the Medical Scientific Research Ethics Review Committee of Ningxia Medical University General Hospital (KYLL-2022-1266). Informed consent was obtained from the parents or legal guardians of the patients at outpatient clinics or during preoperative visits. The study was conducted in a tertiary university hospital between December 2022 and June 2023 and adhered to Good Clinical Practice guidelines and the principles of the Declaration of Helsinki.

Participants

Children aged 3–7 years with an American Society of Anesthesiologists (ASA) physical status of I or II and who were scheduled for elective T&A surgery requiring general anesthesia were included. Participants were excluded if they had any of the following: ongoing adenoid and tonsil inflammation, infection in other parts of the body, developmental delays, autism, neurological or psychiatric diseases associated with symptoms of agitation, anxiety, attention deficit, or sleep disturbances, a recent history (within a month) of receiving general anesthesia or surgery, congenital or other genetic conditions that could potentially influence brain development, acute diseases such as severe vomiting and diarrhea occurring in the week before surgery, congenital or chronic diseases such as congenital heart disease, kidney system disease, and blood system disease, or autoimmune or immune deficiency disease.

Anesthesia

On the day before surgery, potential participants were identified from the elective surgery list by a member of the research team. Written informed consent was obtained from the children's parents or guardians. All children were required to fast for 8 h for solids and 2 h for clear liquids prior to surgery.

Anesthesia management is implemented by a single designated anesthesiologist based on a unified intravenous anesthesia plan. Each child, who had received no medication, was under parental surveillance in the preoperative waiting area, and their the modified Yale Preoperative Anxiety Scale (mYPAS) score was measured to assess preoperative anxiety levels [15].

On arrival at the operating theater, standard monitoring was applied, including non-invasive arterial blood pressure measurement, pulse oximetry, electrocardiography, and Bispectral index (BIS) monitoring. Intravenous access was established in the right upper extremity, and muscle relaxation was observed in the left extremity. Anesthesia was induced using intravenous midazolam at 0.1 mg/kg, sufentanil at 0.03 μg/kg, rocuronium at 0.6 mg/kg, and propofol at 2 mg/kg. A tracheal tube was inserted for airway control and end-tidal carbon dioxide ($ETCO_2$) concentrations were maintained at 35–45 mmHg during surgery using a volume-controlled ventilator. Anesthesia was maintained using propofol at 4–6 mg/kg/h and remifentanil at 0.1–0.2 μg/kg/min to maintain BIS values between 40 and 60. If the BIS value changed or heart rate and blood pressure fluctuated (an increase of 20% compared with the baseline) during the operation, fentanyl at 0.15–0.7 μg/kg was added as required. The train of four (TOF) stimulation during the operation was maintained at 0–1, and 0.15 mg/kg of rocuronium bromide was added as required. At the end of the operation, if TOF T2 occurred and the patients' oral secretions were completely cleared, neostigmine 0.05 mg/kg and atropine 0.02 mg/kg were given. External stimuli were minimized after pharyngeal and tracheal suction. The anesthesiologists then removed the airway devices and closely monitored the patients until they regained hemodynamic stability and consciousness. Subsequently, the patients were transferred to the post-anesthesia care unit (PACU).

When the patients arrived in the PACU, their ED and pain scores were measured by a well-trained researcher every 10 min until discharge. Finally, the patient was judged to have postoperative pain and emergence delirium based on the maximum value of the evaluation results. Pediatric Assessment of Emergence Delirium (PAED) was conducted to assess the severity of ED [16]. The PAED scale is an observational measure of five aspects of child behavior (caregiver eye contact, purposeful movement, evidence of awareness of surroundings, restlessness, and inconsolability). Ratings are summed to produce a total score ranging from 0 to 20; larger scores indicate greater severity. Pain was measured using Face, Legs, Activity, Cry, and Consolability (FLACC) scores [18]. For a PAED score > 12, and a FLACC score > 4, fentanyl at 0.5 μg/kg was administered and repeated if the ED or pain did not subside within 10 min after the previous administration. Patients were discharged when they returned to an alert and calm state and had a modified Aldrete score ≥ 9 [19].

Laboratory tests

On the morning before surgery, 2–3 ml of fasting venous blood were collected from all patients and centrifuged at 1000 rpm for 10 min (centrifuge radius, 12 cm) for 2 h. Serum supernatant was collected and stored at − 80.0 °C. A fully automatic biochemical analyzer was used to measure the levels of whole blood cell parameters, and the average value of three tests was used as the final result.

Study endpoints

The occurrence of ED measured according to age-appropriate validated scales were the primary outcome measure. The secondary outcomes were the preoperative mYPAS score [20], the Induction Checklist Compliance (ICC) score [20], the FLACC score, the total consumption of analgesics, sedatives and muscle relaxant, the duration of surgery and anesthesia, extubation time (from the cessation of anesthetics to the removal of airway devices), eye-opening time (from the cessation of anesthetics to eye opening or hand squeezing on verbal command), emergence time (from the cessation of anesthetics to the discharge from the operating theatre), and the length of stay in the PACU.

Sample size calculation

Sample size was calculated according to the sample size estimation formula, $n = \mu_\alpha^2 \times p \times (1\text{-}p)/\delta^2$, where p is the overall proportion and δ is the tolerance. Based on a 26% incidence of ED after pediatric otolaryngology surgery, $p = 0.26$, type I error $\alpha = 0.05$ (equivalent to $\mu_\alpha = 1.96$), and artificially adjusted $\delta = 0.1$. Therefore, $n = (1.96)^2 \times (0.26) \times (1\text{–}0.26)/(0.1)^2 = 74$, representing a dropout rate of 20%, and a final sample size of 89.

Statistical analysis

The software of SPSS 26.0 (SPSS Inc., Armonk, NY, USA) and GraphPad Prism 9.0 (GraphPad Inc., California, USA) were used for data analysis. Categorical and continuous data were expressed as a number (with a percentage, *n*%) and mean levels (with standard deviation) as appropriate. We estimated a sample size of at least 89 patients would be required to provide a 5% significance level and 80% power. Ninety-four patients were enrolled in the final analysis, which fully meets the statistical requirements. The chi-squared test, Fisher's exact test, the Mann–Whitney *U*-test and Student's *t*-test were used for statistical analysis as appropriate. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predicative and cut-off values of risk factors for ED. To investigate risk factors for ED, univariate and multivariate logistic regression analyses were performed. Bilateral $p < 0.05$ was considered statistically significant.

Results

During the study period, 109 patients were initially enrolled and 15 were excluded according to the exclusion criteria. 94 patients were included in the final analysis and 19 of them experienced ED (an incidence of 25.3%; Fig. 1).

The mean age of the cohort was 5.2 years and the majority (62 of 94, 66.0%) were male. Most of the enrolled patients underwent adenoidectomy, and approximately half received T&A. The average age of the patients who experienced ED was 4.65 years, which was younger than the average age of 5.39 years of the patients without ED ($P = 0.04$). The average height of ED patients was also lower than that of non-ED patients ($P = 0.042$). Patients with a higher mYPAS score ($P = 0.019$) were more likely to develop ED. Furthermore, postoperative pain was significantly associated with ED development ($P = 0.002$). No intragroup differences were observed between ED and non-ED groups with respect to gender, the education level of patients and parents, body mass index, ICC score, pathological stage, type of surgery, main anesthetic agent, length of stay, and duration of operation or anesthesia ($P > 0.05$, Table 1).

As shown in Table 2, the white blood cell, neutrophil count, monocyte count, platelet, hematocrit, mean platelet volume, red blood cell,, neutrophil–monocyte ratio, platelet–monocyte ratio, platelet–neutrophil ratio, platelet–lymphocyte ratio, platelet–white blood cell ratio, RDW, SII values were similar between ED and non-ED

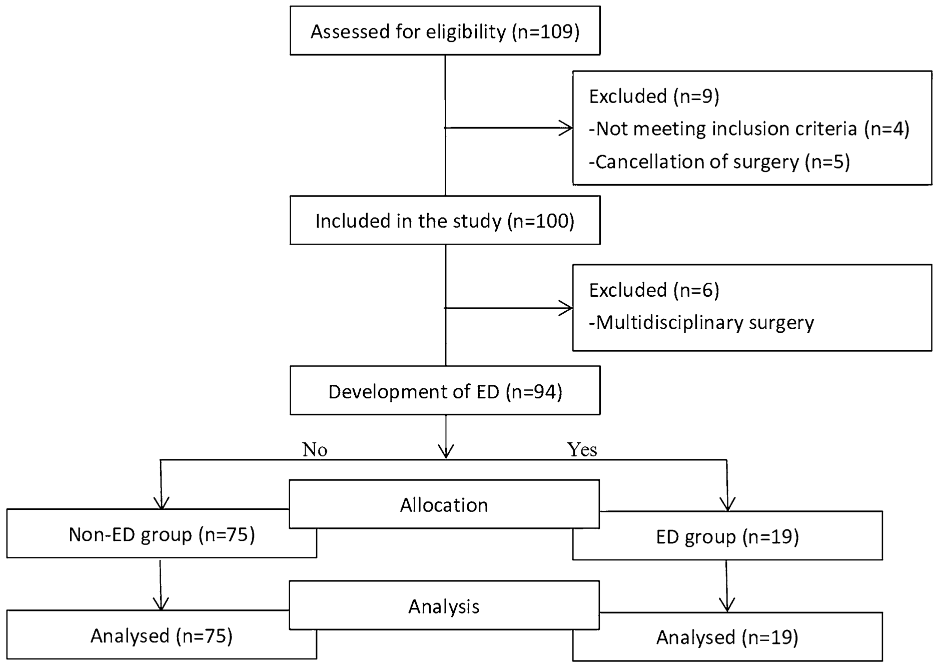

Fig. 1 Flow diagram of patient assessment. ED, emergence delirium

groups ($P > 0.05$). The patients who developed ED showed a significantly higher lymphocyte count (LYM#) compared with those without ED ($P = 0.035$). Moreover, significantly lower NLR ($P = 0.022$) and MLR ($P = 0.031$) values were observed in the ED group than in the non-ED group (Table 2).

To investigate the predictive value of risk factors for ED, ROC curve analyses were performed. NLR was a significant predictor for ED with a cut-off value of 0.8719, an area under the curve (AUC) of 0.671, a sensitivity of 54.7%, and a specificity of 84.2% (95% CI 0.546–0.796, $P < 0.05$). MLR and LYM# were also predictors for ED. MLR had a cut-off value of 0.1014, an AUC of 0.66, a sensitivity of 88%, and a specificity of 52.6% (95% CI 0.502–0.818, $P < 0.05$). LYM# had a cut-off value of 3.775, an AUC of 0.658, a sensitivity of 57.9%, a specificity of 73.3% (95% CI 0.515–0.801, $P < 0.05$). The cut-off values of other risk factors (MYPAs, age and height) are presented in Fig. 2.

To investigate potential risk factors for ED, univariate and multivariate logistic regression analyses were performed. In univariate logistic regression analysis, age (< 4.87 years), height (< 1.07 m), LYM# (> 3.775×10^9/L), NLR (< 0.8719) MLR (< 0.1014) and postoperative pain (yes vs. no) were potential risk factors. However, multivariate logistic regression revealed that just preoperative NLR (< 0.8719) and postoperative pain were independent risk factors associated with ED (odds ratio: 0.168, 95% CI 0.033–0.858, $P = 0.032$; odds ratio: 7.298, 95% CI 1.563–34.083, $P = 0.011$, Table 3).

Discussion

In this study, we found that preoperative NLR level and postoperative pain were independent risk factors for ED in pediatric patients undergoing T&A. To our knowledge, this is the first description of a close association between preoperative peripheral blood cell parameters and postoperative cognitive change in pediatric patients after T&A.

The incidence of ED in this prospective observational study was 25.3%, which was consistent with the ED incidence range of 13% to 26% in children undergoing otolaryngological procedures [3]. Numerous factors can contribute to ED, such as rapid return to consciousness in an unfamiliar environment, agitation during anesthetic induction, preoperative anxiety, use of preanesthetic medication, type of surgery, use of inhaled anesthetics, postoperative pain, and preschool age [2]. Univariate logistic regression showed preschool age, height and postoperative pain to be associated with ED, which is consistent with previous findings that indicate ED to be more frequent in younger children [21]. The higher frequency of ED in preschool children can be explained by exacerbated emotional lability when faced with a stressful situation in a strange environment. At this age, areas of the hippocampus are still physiologically immature and favor cerebral instability [22]. An explanation for shorter children being more prone to ED is that younger children tend to be shorter. High scores for preoperative anxiety are predictive of adverse neurological events following anesthesia, such as agitation

Table 1 Patient characteristics

	Non-ED group ($n=75$)	ED group ($n=19$)	*P* value
Age (year), mean ± SD	5.39 ± 1.4	4.65 ± 1.24	0.040*
Sex, *n* (%)			0.419
Male	48 (64)	14 (73.68)	
Female	27 (36)	5 (26.32)	
Height (m), mean ± SD	1.15 ± 0.12	1.09 ± 0.1	0.042*
Weight (kg), mean ± SD	21.8 ± 7.15	19.37 ± 6.88	0.186
BMI (kg/m^2), mean ± SD	16.14 ± 2.78	15.26 ± 5.2	0.312
Only child, *n* (%)	48 (64)	10 (52.63)	0.363
Receive preschool education, *n* (%)	45 (60)	10 (52.63)	0.560
Current residence, *n* (%)			0.884
Urban areas	46 (61.33)	12 (63.16)	
Rural areas	29 (38.67)	7 (36.84)	
Mother's education is bachelor's degree or above, *n* (%)	55 (73.33)	17 (89.47)	0.138
Father's education is bachelor's degree or above, *n* (%)	63 (84)	18 (94.74)	0.226
Chronic tonsillitis, *n* (%)	44 (58.67)	11 (57.89)	0.951
Chronic rhinitis, *n* (%)	63 (84)	16 (84.21)	0.982
OSAHS, *n* (%)	22 (29.33)	8 (42.11)	0.286
Grading of tonsil hypertrophy, *n* (%)			0.918
I	14 (18.67)	4 (21.05)	
II	15 (20)	4 (21.05)	
III	20 (26.67)	6 (31.58)	
IV	26 (34.67)	5 (26.32)	
Degree of adenoid blockage, mean ± SD	0.69 ± 0.17	0.69 ± 0.18	0.981
Disease duration (year), mean ± SD	1.46 ± 1.14	1.26 ± 0.78	0.478
ASA physical status, *n* (%)			0.848
I	22 (29.33)	6 (31.58)	
II	53 (70.67)	13 (68.42)	
Premature birth, *n* (%)	12 (16)	4 (21.05)	0.601
Caesarean section, *n* (%)	44 (58.67)	10 (52.63)	0.635
mYPAS score, mean ± SD	42.2 ± 17.14	53.05 ± 20.03	0.019*
ICC score, mean ± SD	3.09 ± 3.63	4.32 ± 4.07	0.204
Postoperative pain, *n* (%)	29 (38.67)	15 (78.95)	0.002*
Total length of stay (day), mean ± SD	3.31 ± 2.27	3.47 ± 2.7	0.783
Postoperative length of stay (day), mean ± SD	1.99 ± 1.4	2.21 ± 1.81	0.560
Type of surgery, *n* (%)			0.640
Adenoidectomy	35 (46.67)	11 (57.89)	
Tonsillectomy	7 (9.33)	1 (5.26)	
T&A	33 (44)	7 (36.84)	
Midazolam (mg), median (IQR)	1 (1.1)	1 (1.1)	0.380
Propofol (mg), median (IQR)	100 (71.125)	80 (60.120)	0.624
Rocuronium (mg), median (IQR)	10 (10.12)	10 (8.12)	0.331
Sufentanil (ug), median (IQR)	7.5 (5.10)	7.5 (5.10)	0.891
Remifentanil (ug), mean ± SD	274.07 ± 143.73	270.75 ± 152.63	0.929
Intraoperative hypotension, *n* (%)	20 (26.67)	5 (26.32)	0.975
Intraoperative hypertension, *n* (%)	3 (4)	3 (15.79)	0.060
Duration of anesthesia (min), mean ± SD	49.03 ± 19.21	50.05 ± 21.36	0.839
Duration of surgery (min), mean ± SD	38.63 ± 15.57	37 ± 24	0.719
Emergence time (min), median (IQR)	18 (14.24)	17 (13.24)	0.527
Eye opening time (min), median (IQR)	12 (8.19)	13 (7.18)	0.562
Extubation time (min), median (IQR)	4 (2.6)	4 (1.6)	0.846

ED emergence delirium, *M* male, *ASA* American Society of Anesthesiologists, *BMI* body mass index, *OSAHS* obstructive sleep apnea–hypopnea syndrome, *mYPAS* Modified Yale Preoperative Anxiety Scale, *ICC* Induction Checklist Compliance, *A&T* Adenoidectomy and Tonsillectomy

*$P < 0.05$

Table 2 Laboratory tests associated with ED

	Non-ED ($n=75$)	ED ($n=19$)	*P* value
WBC ($\times 10^9$/L), median (IQR)	7.13 (6.16, 8.53)	7.71 (6.49, 8.83)	0.337
NEUT# ($\times 10^9$/L), median (IQR)	2.80 (2.11, 3.75)	2.56 (1.95, 2.89)	0.311
LYM# ($\times 10^9$/L), median (IQR)	3.34 (2.85, 4.03)	3.90 (3.17, 4.68)	0.035*
MXD# ($\times 10^9$/L), median (IQR)	0.49 (0.39, 0.60)	0.42 (0.37, 0.59)	0.264
PLT ($\times 10^9$/L), median (IQR)	327 (292, 384)	347 (312, 390)	0.386
RBC ($\times 10^{12}$/L), mean ± SD	4.76 ± 0.33	4.81 ± 0.46	0.609
PCT (%), median (IQR)	0.31 (0.28, 0.35)	0.32 (0.30, 0.36)	0.294
MPV (fL), median (IQR)	9.2 (8.8, 9.7)	9.4 (8.9, 10.0)	0.974
SD (fL), mean ± SD	37.61 ± 2.19	37.14 ± 2.27	0.408
NLR, median (IQR)	0.88 (0.60, 1.13)	0.68 (0.55, 0.85)	0.022*
NMR, median (IQR)	5.85 (4.59, 7.73)	5.29 (4.67, 6.10)	0.489
MLR, median (IQR)	0.15 (0.12, 0.18)	0.10 (0.09, 0.17)	0.031*
PNR, mean ± SD	122.06 ± 50.24	139.92 ± 45.22	0.162
PWR, median (IQR)	45.1 (39.18, 55.96)	49.79 (39.27, 56.40)	0.825
PLR, median (IQR)	100.95 (81.73, 121.09)	96.25 (68.29, 108.78)	0.294
PMR, median (IQR)	630.19 (567.35, 883.33)	866.67 (590.48, 937.84)	0.155
SII, median (IQR)	285.08 (188.34, 434.79)	241.49 (187.37, 274.59)	0.121

ED emergence delirium, *WBC* white blood cell, *NEUT#* neutrophil count, *LYM#* lymphocyte count, *MXD#* monocyte count, *PLT* platelet, *PCT* hematocrit, *MPV* mean platelet volume, *RBC* red blood cell, *SD* red blood cell distribution width, *NLR* neutrophil–lymphocyte ratio, *NMR* neutrophil–monocyte ratio, *PMR* platelet–monocyte ratio, *MLR* monocyte–lymphocyte ratio, *PNR* platelet–neutrophil ratio, PLR platelet–lymphocyte ratio, *SII* platelet × neutrophil/lymphocyte, *PWR* platelet–white blood cell ratio

$^*p < 0.05$

upon awakening and behavioral changes. Examination of a cohort of 791 children showed that the risk for agitation upon awakening increases by 10% for each 10-point increase in preoperative anxiety evaluation score [23]. However, our study results showed that there was no statistical significance between anxiety level and postoperative ED, which may be related to the use of benzodiazepines in all children after entering the operating room.

The univariate logistic regression of risk factors for ED showed that decreased NLR and MLR and lymphocytosis were associated with ED, which was different to the findings in adults. In adults, elderly delirium patients showed significantly higher levels of NLR and MLR before orthopedic surgery compared with non-delirium patients. Cognitive impairment in Alzheimer's disease, human immunodeficiency virus infection, stroke, and dementia are associated with immunosuppression, which is characterized by a decreased population and/or dysfunction of lymphocytes [24–26]. In preoperative children with elevated leukocytes, asymptomatic leukocytosis can indicate infection, which may lead to postoperative pneumonia, sepsis, systemic inflammatory response syndrome and other poor prognoses. Therefore an increased white blood cell count before surgery can be used as an independent risk factor for postoperative complications. For patients whose white blood cell count exceeds the critical value before surgery, vigilance should be increased, and antibiotics should be administered orally or intravenously; the surgery should be delayed if necessary [27, 28]. In contrast to the pathogen killing actions of neutrophils, lymphocytes have an anti-inflammatory function and protect endothelial cells. All the children we included had a history of preoperative antibiotic treatment within two weeks, therefore, the NLR and MLR of children undergoing T&A may show a decrease before surgery, while lymphocyte numbers may show an increase [29].

Our multivariate logistic regression analysis indicated postoperative pain as an independent risk factor for ED in pediatric patients after T&A, which is consistent with previous findings. Postoperative pain refers to a sore throat, which is often severe [17]. Considering the long half-life of fentanyl and the adverse reactions of opioids such as dizziness, nausea, vomiting, all children with postoperative pain are in the PACU administered analgesics only once. Pediatric guidelines for postoperative delirium based on evidence-based medicine and expert consensus state that age-specific assessment tools should be used for pain assessment. The reasons for the association between ED and postoperative pain, as well as the pathophysiology of ED, remain to be elucidated. A possible explanation is that any condition capable of interfering with brain activity may make the brain vulnerable, and favor the emergence of neurological manifestations after surgery [18]. However, in patients undergoing general anesthesia under caudal block for analgesia, a high incidence of ED upon awakening was observed, indicating that even

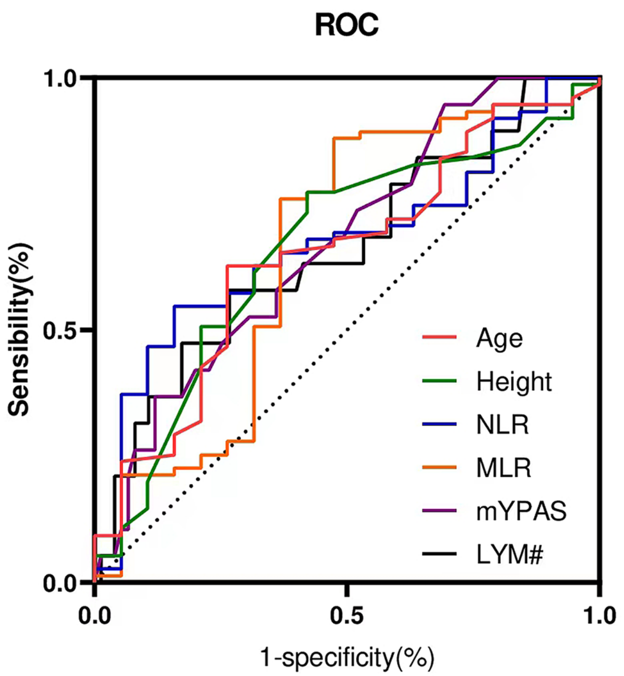

Fig. 2 Predictive value of risk factors for ED; ROC curve analysis. Age, AUC = 0.648 (0.514–0.783), $P < 0.05$, Cut-off = 4.87, Sensitivity = 62.7%, Specificity = 73.7%; Height, AUC = 0.66 (0.522–0.798), $P < 0.05$, Cut-off = 1.07, Sensitivity = 77.3%, Specificity = 57.9%; NLR, AUC = 0.671 (0.546–0.796), $P < 0.05$, Cut-off = 0.8719, Sensitivity = 54.7%, Specificity = 84.2%; MLR, AUC = 0.66 (0.502–0.818), $P < 0.05$, Cut-off = 0.1014, Sensitivity = 88%, Specificity = 52.6%; MYPAs, AUC = 0.672 (0.543–0.800), $P < 0.05$, Cut-off = 32.45, Sensitivity = 94.7%, Specificity = 30.7%; LYM#, AUC = 0.658 (0.515–0.801), $P < 0.05$, Cut-off = 3.775, Sensitivity = 57.9%, Specificity = 73.3%

when postoperative pain is efficiently treated or absent, ED may occur [30].

Children with chronic tonsillitis have an impaired immune profile because of continuous inflammatory stimulation by pathogens that leads to increased concentrations of pro-inflammatory cytokines compared with healthy individuals [31]. Accumulating evidence shows that the innate immune system is involved in the peripheral inflammatory response to trauma and circulating pro-inflammatory cytokines can enter the central nervous system through disruption to the blood–brain barrier resulting in neuroinflammation. An immature blood–brain barrier and inflammation of the central nervous system are therefore possible reasons for ED in preschool children [32, 33]. Neutrophils and lymphocytes are white blood cells. These cells play important roles in mediating the peripheral and central inflammatory response and are involved in regulating the inflammation that results in cognitive dysfunction [24, 34]. NLR is widely used peripheral blood biomarkers of inflammation because neutrophils and lymphocytes are routinely measured in standard blood examinations [31]. In the present study, preoperative NLR significantly lower in delirium children before T&A, suggesting innate immune activation and potential neuroinflammation played an important role in pediatric patients before T&A. According to our results, decreased preoperative NLR is an independent risk factor of ED in preschool children after T&A. Hence, as one of the most common and routine tests in clinical practice, complete blood cell tests should be highly valued in identifying children at high risk for delirium.

This study has some limitations. Firstly, our study is a small-sample, single-center, prospective study and only patients who had received T&A were included. Secondly, we only recorded the NLR once at admission. The association between ED and dynamic changes in blood indices after surgery requires further study. Thirdly, our study did not include a control patient group and we did not determine NLR values in patients before they became ill. Therefore, their normal ranges were not known and it was unclear whether the NLR values of the non-ED group were normal or high. Lastly, to determine whether the risk

Table 3 Risk factors associated with ED; univariate and multivariate logistic regression analyses

	Univariate		Multivariate	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age (< 4.87 years vs ≥ 4.87 years)	0.213 (0.069–0.654)	0.007*	0.793 (0.163–3.868)	0.774
Height (< 1.07 m vs ≥ 1.07 m)	0.213 (0.074–0.615)	0.004*	0.288 (0.060–1.397)	0.122
MYPAs (> 32.45 vs ≤ 32.45)	7.962 (1.002–63.26)	0.050		
Postoperative pain (yes vs. no)	5.948 (1.797–19.687)	0.004*	7.298 (1.563–34.083)	0.011*
LYM# ($> 3.775 \times 10^9$/L vs $\leq 3.775 \times 10^9$/L)	3.781 (1.33–10.748)	0.013*	1.228 (0.270–5.592)	0.791
NLR (< 0.8719 vs ≥ 0.8719)	0.155 (0.042–0.579)	0.006*	0.168 (0.033–0.858)	0.032*
MLR (< 0.1014 vs ≥ 0.1014)	0.123 (0.039–0.383)	0.000*	0.206 (0.043–0.997)	0.050

ED emergence delirium, *mYPAS* Modified Yale Preoperative Anxiety Scale, *LYM#* lymphocyte count, *NLR* neutrophil–lymphocyte ratio, *MLR* monocyte–lymphocyte ratio

[*] $P < 0.05$

factors identified here have high predictive power, large multi-center clinical cohorts and observational studies are needed.

Conclusions

In conclusion, we found that age, postoperative pain, MLR level, NLR level and lymphocytosis were related to ED in pediatric patients after T&A. Preoperative NLR and postoperative pain are independent risk factors for ED in pediatric patients with T&A, especially large-scale clinical studies are needed to explore these findings further.

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Data availability All data analyzed during this study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors have no conflicts of interest to declare that are relevant to the content of this article.

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