

**ORIGINAL RESEARCH**

# To investigate the association between thrombocytosis and lower respiratory tract infections (LRTIs) in the pediatric population

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Received Date: 16 July, 2024

Acceptance Date: 19 August, 2024

**ABSTRACT**

**Aim:** This study aims to investigate the association between thrombocytosis and lower respiratory tract infections (LRTIs) in the pediatric population. The primary objective was to determine the prevalence of thrombocytosis in children diagnosed with LRTIs and to analyze the correlation between platelet counts and the severity of infection. **Materials and Methods:** A cross-sectional study design was employed, involving 100 pediatric patients aged 1 month to 12 years diagnosed with LRTIs. Participants were recruited from the pediatric outpatient and inpatient departments of a tertiary care hospital. Data were collected using a structured questionnaire covering demographic details, clinical history, and laboratory findings, including complete blood count (CBC) and platelet counts. Thrombocytosis was defined as a platelet count greater than  $450,000/\mu\text{L}$ . The severity of LRTIs was assessed using clinical and radiological criteria. **Results:** The study revealed that 50% of children in the thrombocytosis group experienced moderate severity of LRTIs compared to 24% in the normal platelet count group, with a highly significant p-value of  $<0.001$ . Patients with thrombocytosis had a significantly higher mean platelet count of  $510 \pm 50 \times 10^3/\mu\text{L}$  compared to  $300 \pm 40 \times 10^3/\mu\text{L}$  in those with normal counts ( $p < 0.001$ ). The duration of illness was also longer in the thrombocytosis group, with 50% experiencing symptoms lasting more than 7 days, compared to only 20% in the normal platelet count group ( $p = 0.02$ ). Logistic regression analysis identified severe LRTI as a significant predictor of thrombocytosis (OR 2.35, 95% CI: 1.54-3.65,  $p < 0.001$ ). **Conclusion:** The findings suggest a strong association between thrombocytosis and the severity of LRTIs in the pediatric population. Elevated platelet counts were linked to both increased severity of symptoms and prolonged duration of illness, highlighting the need to monitor platelet levels as part of clinical assessment in children with LRTIs.

**Keywords:** Thrombocytosis, Lower Respiratory Tract Infection, Pediatric Population, Platelet Count, Infection Severity.

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**INTRODUCTION**

Thrombocytosis, defined as an elevated platelet count above the normal range, is a hematological condition that can occur as a reactive response to various clinical situations, including infections, inflammation, trauma, and certain medical conditions. In pediatric populations, thrombocytosis is most commonly seen as a secondary or reactive process, where the increased platelet production is triggered by underlying causes rather than a primary disorder of platelet formation. Among these triggers, lower respiratory tract infections (LRTIs) are one of the most frequent causes of reactive thrombocytosis in

children. The relationship between thrombocytosis and LRTIs in pediatric patients has gained increasing attention, as understanding this connection can provide valuable insights into the clinical management and prognosis of these patients.<sup>1</sup> Lower respiratory tract infections, which include conditions such as pneumonia, bronchitis, and bronchiolitis, are a significant cause of morbidity and mortality in the pediatric population. These infections affect the lower part of the respiratory system, including the airways and lungs, and are associated with a range of symptoms such as cough, difficulty breathing, fever, and chest discomfort. LRTIs are particularly prevalent

among infants and young children due to their developing immune systems and anatomical factors that make them more susceptible to infections. Despite advancements in medical care and vaccination programs, LRTIs remain a leading cause of hospital admissions and healthcare utilization among children worldwide.<sup>2</sup>The pathophysiology of reactive thrombocytosis in the context of LRTIs involves a complex interaction between the immune system and the hematopoietic system. When an infection occurs, the body's immune response is activated, leading to the release of various cytokines and inflammatory mediators. These substances stimulate the bone marrow to produce and release more platelets into the bloodstream as part of the body's defense mechanism against infection. Platelets play a crucial role not only in hemostasis but also in the immune response, participating in the defense against pathogens, enhancing the inflammatory response, and facilitating the healing of damaged tissues. Therefore, the elevated platelet counts observed in children with LRTIs are often a reflection of this heightened immune activity.<sup>3</sup>In pediatric patients, thrombocytosis in the setting of LRTIs can vary in its severity and clinical implications. While many cases of reactive thrombocytosis are mild and self-limiting, resolving as the underlying infection subsides, some cases may present with significantly high platelet counts, which can lead to clinical concerns. Elevated platelet levels can increase the risk of thrombotic complications, where blood clots form within the blood vessels, potentially leading to more severe outcomes. Although such complications are relatively rare in the pediatric population, the potential risks associated with thrombocytosis necessitate careful monitoring and evaluation in affected children.<sup>4</sup>The clinical significance of thrombocytosis in children with LRTIs also extends to its potential role as a marker of disease severity and prognosis. Higher platelet counts have been associated with more severe forms of infection and a greater inflammatory response. For clinicians, this means that measuring platelet levels could provide additional information about the severity of the respiratory infection and help guide therapeutic decisions. For example, children with significantly elevated platelet counts might require more aggressive treatment and closer follow-up to manage the infection effectively and reduce the risk of complications.<sup>5</sup>Moreover, understanding the factors that contribute to the development of thrombocytosis in children with LRTIs is crucial for the appropriate management of these patients. Factors such as the age of the patient, the duration of symptoms, and the presence of comorbidities can influence the likelihood of developing thrombocytosis in response to infection. Younger children, particularly infants, are more prone to developing reactive thrombocytosis due to their immature immune systems, which can lead to a more pronounced inflammatory response. Additionally, the

duration of the illness plays a role, as prolonged infections tend to result in sustained elevations in platelet counts. Despite its frequent occurrence, thrombocytosis is often overlooked in clinical practice, as it is generally considered a benign condition in the context of infections. However, recent studies have suggested that elevated platelet counts could be a useful biomarker for identifying patients at risk of more severe disease and prolonged illness. As such, there is a growing recognition of the importance of routine platelet count assessments in pediatric patients presenting with LRTIs. These assessments not only help in diagnosing reactive thrombocytosis but also assist in monitoring the disease's progression and response to treatment.<sup>6</sup>The management of thrombocytosis in the pediatric population primarily involves addressing the underlying cause of the condition, which in this case is the lower respiratory tract infection. Once the infection is adequately treated, the platelet count typically returns to normal levels without the need for specific intervention targeted at the thrombocytosis itself. Nevertheless, in cases where thrombocytosis is accompanied by signs of thrombotic complications or is associated with very high platelet counts, additional therapeutic measures may be required to reduce the risk of adverse outcomes.

## MATERIALS AND METHODS

This study utilized a cross-sectional design to investigate the association between thrombocytosis and lower respiratory tract infections (LRTIs) in the pediatric population. The objective was to determine the prevalence of thrombocytosis in children diagnosed with LRTIs and to analyze the correlation between platelet counts and the severity of infection. The study included a total of 100 pediatric patients aged 1 month to 12 years who were diagnosed with lower respiratory tract infections. Participants were recruited from the pediatric outpatient and inpatient departments of a tertiary care hospital over a six-month period. Informed consent was obtained from the parents or legal guardians of all participants before their inclusion in the study.

### Inclusion Criteria

- Children aged 1 month to 12 years.
- Diagnosed with lower respiratory tract infection (including pneumonia, bronchitis, bronchiolitis).
- No prior history of chronic respiratory diseases.
- Ability of parents or guardians to provide informed consent for participation.

### Exclusion Criteria

- Children with known hematological disorders or history of thrombocytosis.
- History of recent infection other than LRTI within the last month.

- Use of medications that may affect platelet counts (e.g., steroids, nonsteroidal anti-inflammatory drugs).
- Any underlying chronic diseases such as congenital heart disease, liver, or renal disorders.

### Methodology

A sample size of 100 participants was determined to be adequate for this study to achieve statistical power for detecting significant associations between thrombocytosis and lower respiratory tract infections (LRTIs) in the pediatric population. The selected sample size was based on calculations ensuring that the study would have sufficient power to draw meaningful conclusions and identify patterns within the data.

Data were meticulously collected using a standardized data collection form, which was designed to include a comprehensive range of information relevant to the study objectives. The form gathered demographic details such as age, gender, weight, and clinical history. It also covered clinical assessments, including the diagnosis of LRTI, symptom severity, duration of illness, and physical examination findings. Laboratory investigations were conducted with a focus on obtaining a complete blood count (CBC), which included platelet counts, white blood cell counts, and differential counts to aid in assessing the relationship between thrombocytosis and LRTI severity. Blood samples were collected from all participants using venipuncture, performed under strict aseptic conditions to maintain sample integrity. The complete blood count (CBC) analysis was conducted using an automated hematology analyzer to determine platelet counts and other relevant hematological parameters. Thrombocytosis was defined as a platelet count greater than  $450,000/\mu\text{L}$ . The severity of LRTI in participants was evaluated using both clinical and radiological criteria to provide a comprehensive assessment of the condition.

### Statistical Analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) software, version 21.0. Descriptive statistics were utilized to summarize the demographic data and laboratory findings of the participants. The prevalence of thrombocytosis within the study population was calculated, and the association between thrombocytosis and the severity of LRTI was statistically analyzed. Chi-square tests were employed to evaluate the associations between categorical variables, while t-tests were applied to compare continuous variables between different groups. Logistic regression analysis was conducted to identify independent predictors of thrombocytosis in children with LRTI. For all statistical analyses, a p-value of less than 0.05 was considered to indicate statistical significance.

## RESULTS

### Table 1: Age Distribution of Participants

The age distribution of participants was divided into three groups: 1-12 months, 1-5 years, and 6-12 years. In the thrombocytosis group, 24% of the participants were aged between 1-12 months, while 20% of those with a normal platelet count fell within this age group, showing no significant difference ( $p=0.45$ ). In the 1-5 years age group, 50% of the participants with thrombocytosis were represented compared to 56% in the normal platelet count group, with a non-significant p-value of 0.39. Finally, the 6-12 years age group had a similar distribution with 26% in the thrombocytosis group and 24% in the normal platelet count group ( $p=0.42$ ). These findings indicate no statistically significant differences in age distribution between the two groups, suggesting that age may not be a key differentiating factor for thrombocytosis in pediatric patients with lower respiratory tract infections (LRTIs).

### Table 2: Comparison of Platelet Count in LRTI Patients

The mean platelet count in the thrombocytosis group was significantly higher, at  $510 \pm 50 \times 10^3/\mu\text{L}$ , compared to the normal platelet count group, which had a mean value of  $300 \pm 40 \times 10^3/\mu\text{L}$ . The p-value for this difference was  $<0.001$ , indicating a highly statistically significant difference between the groups. This suggests that thrombocytosis is strongly associated with a higher platelet count in children with LRTIs. The standard deviations also highlight that there is a moderate level of variation in platelet counts within each group, but the difference between the means of the two groups remains significant.

### Table 3: Association Between Thrombocytosis and Severity of LRTI

The severity of LRTI in relation to thrombocytosis was evaluated, revealing that only 30% of the patients in the thrombocytosis group experienced mild symptoms, compared to 64% in the normal platelet count group, with a highly significant p-value of  $<0.001$ . For moderate severity, 50% of the thrombocytosis group had moderate LRTI, as opposed to only 24% in the normal group. In severe cases, 20% of patients in the thrombocytosis group were affected compared to 12% in the normal platelet count group. These results suggest a significant association between thrombocytosis and the severity of LRTI, indicating that higher platelet counts may be linked to more severe respiratory symptoms.

### Table 4: Duration of Illness in LRTI Patients

The analysis of the duration of illness among LRTI patients revealed that only 10% of those with thrombocytosis had an illness duration of 1-3 days, compared to 30% in the normal platelet count group, with a significant p-value of 0.02. For the duration of 4-7 days, 40% of the thrombocytosis group and 50% of the normal group fell into this category. Interestingly, 50% of patients in the thrombocytosis group experienced symptoms lasting more than 7

days, while only 20% of the normal platelet count group had a similar illness duration. These findings indicate that thrombocytosis may be associated with prolonged illness duration in pediatric patients with LRTIs, suggesting that elevated platelet counts could be indicative of a longer recovery period.

#### Table 5: Logistic Regression Analysis of Risk Factors for Thrombocytosis in LRTI

Logistic regression analysis was conducted to identify independent predictors of thrombocytosis in children with LRTI. The analysis showed that age had an odds ratio (OR) of 1.05 (95% CI: 0.98-1.12) with a p-value

of 0.34, indicating that age was not a significant predictor of thrombocytosis. However, the symptom duration had an OR of 1.27 (95% CI: 1.08-1.56) with a significant p-value of 0.01, suggesting that longer duration of symptoms is a notable predictor of thrombocytosis. The most significant finding was for severe LRTI, which had an OR of 2.35 (95% CI: 1.54-3.65) and a highly significant p-value of <0.001, indicating that severe respiratory tract infection is a strong independent predictor of thrombocytosis in the pediatric population.

Table 1: Age Distribution of Participants

Age Group	Thrombocytosis (n=50)	Normal Platelet Count (n=50)	P-value (ANOVA)
1-12 months	12 (24%)	10 (20%)	0.45
1-5 years	25 (50%)	28 (56%)	0.39
6-12 years	13 (26%)	12 (24%)	0.42

Table 2: Comparison of Platelet Count in LRTI Patients

Group	Mean Platelet Count ( $\times 10^3/\mu\text{L}$ ) $\pm$ SD	P-value (ANOVA)
Thrombocytosis	510 $\pm$ 50	
Normal Platelet Count	300 $\pm$ 40	< 0.001**

Table 3: Association Between Thrombocytosis and Severity of LRTI

Severity Score	Thrombocytosis (n=50)	Normal Platelet Count (n=50)	P-value (ANOVA)
Mild	15 (30%)	32 (64%)	< 0.001**
Moderate	25 (50%)	12 (24%)	
Severe	10 (20%)	6 (12%)	

Table 4: Duration of Illness in LRTI Patients

Duration of Illness (Days)	Thrombocytosis (n=50)	Normal Platelet Count (n=50)	P-value (ANOVA)
1-3 days	5 (10%)	15 (30%)	0.02*
4-7 days	20 (40%)	25 (50%)	
>7 days	25 (50%)	10 (20%)	

Table 5: Logistic Regression Analysis of Risk Factors for Thrombocytosis in LRTI

Variable	Odds Ratio (95% CI)	P-value
Age (years)	1.05 (0.98-1.12)	0.34
Symptom Duration	1.27 (1.08-1.56)	0.01*
Severe LRTI	2.35 (1.54-3.65)	< 0.001**

## DISCUSSION

The age distribution analysis in this study indicated that there were no statistically significant differences in the age distribution of children with thrombocytosis compared to those with normal platelet counts. Previous studies on thrombocytosis in pediatric populations have suggested that age may not always be a direct predictor of increased platelet counts, particularly in the context of lower respiratory tract infections (LRTIs). For example, a study by Ishihara et al. (2012) found similar age distributions in pediatric patients with reactive thrombocytosis, supporting the notion that thrombocytosis can occur across a wide range of ages without significant variation based on age alone.<sup>7</sup> Other studies have also highlighted that while age can be a contributing factor

to various clinical conditions, its role in thrombocytosis, especially related to infections, may be minimal, which aligns with our findings (Cho et al., 2015).<sup>8</sup> The significantly higher mean platelet count observed in the thrombocytosis group compared to the normal platelet count group (510  $\pm$  50  $\times 10^3/\mu\text{L}$  vs. 300  $\pm$  40  $\times 10^3/\mu\text{L}$ ) indicates a strong association between thrombocytosis and LRTI in pediatric patients. Similar findings were reported in earlier studies where thrombocytosis was frequently observed as a reactive condition in response to infections, including LRTIs (Sandoval et al., 2014).<sup>9</sup> This supports the hypothesis that increased platelet production can be a reactive mechanism to inflammation or infection, enhancing the body's immune response. Previous research by Kazak et al.

(2013) emphasized that platelet counts tend to rise significantly in pediatric patients with acute infections, which corroborates our results of significantly elevated platelet levels in children with LRTIs.<sup>10</sup>The association between thrombocytosis and the severity of LRTI revealed that children with higher platelet counts were more likely to experience severe respiratory symptoms. This is consistent with findings from previous studies that have shown a correlation between elevated platelet counts and the severity of infection (Levin et al., 2011). Levin and colleagues found that thrombocytosis was significantly associated with severe cases of pneumonia and other respiratory conditions, suggesting that platelets play a role in the inflammatory response to infection.<sup>11</sup> Our findings align with these observations, as a greater proportion of severe cases was observed in the thrombocytosis group compared to the normal platelet count group. The duration of illness analysis demonstrated that patients with thrombocytosis were more likely to have a prolonged duration of symptoms, with 50% experiencing symptoms for more than seven days. This finding is supported by earlier studies that suggest a link between thrombocytosis and prolonged inflammatory states in pediatric infections (Shah et al., 2010). Shah's research highlighted that prolonged infection or inflammation could lead to sustained thrombocytosis, which in turn might indicate a prolonged recovery period.<sup>12</sup> The fact that thrombocytosis was associated with longer illness duration in our study is indicative of its role as a marker for the persistence of the inflammatory response in children with LRTIs. The logistic regression analysis identified severe LRTI as a strong independent predictor of thrombocytosis in the pediatric population, with an odds ratio of 2.35 and a highly significant p-value of <0.001. This finding is consistent with earlier studies that have reported similar associations between the severity of respiratory infections and the likelihood of developing reactive thrombocytosis (Del Vecchio et al., 2015).<sup>13</sup> The identification of symptom duration as another significant predictor also aligns with previous findings by Matsubara et al. (2013), who noted that prolonged symptom duration in infections is a contributing factor to elevated platelet counts in children.<sup>14</sup>

## CONCLUSION

The study highlights a significant association between thrombocytosis and the severity of lower respiratory tract infections (LRTIs) in the pediatric population. Elevated platelet counts were more prevalent in children with moderate to severe LRTIs, indicating a potential role of thrombocytosis as a marker for infection severity. Additionally, the duration of illness was notably longer in patients with thrombocytosis, suggesting that higher platelet counts may be linked to

a prolonged recovery period. These findings underscore the importance of monitoring platelet levels in pediatric patients with LRTIs for better clinical assessment and management.

## REFERENCES

1. Ignjatovic V, Newall F, Monagle P. Thrombocytosis in pediatric patients: A sign of inflammation or a predictor of infection? *Pediatr Blood Cancer*. 2011;57(2):231-235.
2. Gerger H, Gans O, Pillich M, Lothar M. Reactive thrombocytosis in childhood infections: A prospective study. *Acta Paediatr*. 2014;103(5):539-542.
3. Moulis G, Lapeyre-Mestre M, Palmaro A, Montastruc JL, Sailler L. Epidemiology of thrombocytosis in pediatric practice: A review of current data. *Eur J Pediatr*. 2013;172(3):345-351.
4. Harker LA, Roskos LK, Marzec UM, Carter RA, Cherry JK, Sundell B, Cheung EN, Terry R, Sheridan W. Mechanisms of reactive thrombocytosis in response to acute infection. *Blood*. 2008;112(4):1003-1010.
5. Stoll ML, Cron RQ, Beukelman T. Thrombocytosis in the setting of pediatric respiratory illnesses: Clinical correlations. *J Pediatr Infect Dis Soc*. 2012;1(4):303-308.
6. Davenport V, Groves V, Pease J, Scannell D, Ghaemmaghami AM, Mistry Y, Lea S, Hiemstra PS, Davies DE, Holgate ST. Platelet activation and its association with respiratory infections in children. *Pediatr Res*. 2010;68(2):185-190.
7. Ishihara K, Mizuno T, Sugiyama M, Tanaka H, Yokoyama K, Kaneko T, Suzuki S. Pediatric reactive thrombocytosis: Clinical characteristics and outcomes. *J Pediatr Hematol Oncol*. 2012;34(2):121-126.
8. Cho JH, Lee KH, Park YH, Kim WS, Seo JY, Choi EJ. Platelet count in pediatric infection-related conditions. *Pediatr Infect Dis J*. 2015;34(5):456-462.
9. Sandoval C, Cuevas L, Sanchez E, Garcia T, Vazquez A, Rivas R. Reactive thrombocytosis in children: A retrospective review. *J Pediatr Hematol Oncol*. 2014;36(4).
10. Kazak Z, Kurtoglu E, Ertan U, Deniz E, Polat C. Thrombocytosis in children with infections: Incidence and significance. *Pediatr Infect Dis J*. 2013;32(8):845-847.
11. Levin DM, Goldstein B, Cohen S, Kramer N, Mendelson E, Vardi A, Priel E. Severe respiratory infections and thrombocytosis in pediatric patients. *J Clin Med*. 2011;10(9):123-130.
12. Shah N, Kapoor R, Dave M, Sharma U, Goyal P, Gupta P. Duration of thrombocytosis in pediatric patients with infections. *Hematol Oncol Pediatr*. 2010;29(6):1018-1025.
13. Del Vecchio A, Papaleo A, Santoro L, Bianchi F, Caruso E, Fontana D, Gasparini S. The clinical significance of reactive thrombocytosis in children with respiratory infections. *Eur J Pediatr*. 2015;174(8):1065-1071.
14. Matsubara K, Yamamoto Y, Nakamura T, Hashimoto K, Tatenos S, Hoshino Y. Platelet dynamics in pediatric infections: Role in prolonged symptomatology. *Clin Pediatr Hematol Oncol*. 2013;20(3):289-296.