

Evaluating hospitalized children for preseptal cellulitis: A single-center experience and current literature review

 Berker Okay,¹  Ceren Dogan Kalinbacoglu,¹  Gulsen Akkoc,²  Halil Ugur Hatipoglu,¹
 Omer Dogan,³  Kamil Sahin,¹  Derya Buyukkayhan⁴

¹Department of Pediatrics, University of Health Sciences, Haseki Training and Research Hospital, Istanbul, Turkiye

²Department of Pediatric Infectious Diseases, Marmara University Pendik Training and Research Hospital, Istanbul, Turkiye

³Department of Cardiology, Istinye State Hospital, Istanbul, Turkiye

⁴Department of Neonatology, University of Health Sciences, Haseki Training and Research Hospital, Istanbul, Turkiye

ABSTRACT

OBJECTIVE: Preseptal cellulitis is an infection of the palpebrae and the periorbital superficial tissue and is more common in children than adults. This study aims to evaluate the demographic and clinical characteristics of children hospitalized for preseptal cellulitis and the factors affecting these characteristics.

METHODS: In this retrospective, single-center study, 101 children hospitalized for preseptal cellulitis between March 2019 and March 2022 were included. The patients were divided into 2 groups as under five years old and over five years old.

RESULTS: 56 patients (55.4%) were male and the median age was 56 (24–89) months. All patients had eye swelling. Periorbital erythema was seen in 81 (80.1%), conjunctivitis in 39 (38.6%), eye discharge in 30 (29.7%) patients. The most common treatment was ampicillin-sulbactam+clindamycin (77.2%). Mean treatment duration was 8.42±2.89 days, clinical improvement was 5.01±2.20 days. Patients with leukocytosis had longer duration of treatment compared to patients without leukocytosis (9.3±3.1 vs. 7.8±2.5 days, p=0.009). While the lymphocyte level was higher in patients under 5 years of age compared to patients over 5 years of age (p<0.001); neutrophil (p<0.001), hemoglobin (p=0.002) and NLR (p<0.001) levels were low. The duration of clinical improvement was short in patients under 5 years of age (4.4±1.6 vs. 5.6±2.5 days, p=0.005).

CONCLUSION: The most common finding in patients with preseptal cellulitis was swelling in the eye. The presence of leukocytosis in patients may be used to predict the duration of treatment. Age was an important factor in predicting the duration of clinical improvement in patients.

Keywords: Children; eye; preseptal cellulitis.

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Preseptal cellulitis is an infection of the anterior portion of the eyelid, not involving the orbit or other ocular structures. It rarely causes serious complications. Therefore, it requires rapid diagnosis and treatment. Preseptal cellulitis is common in childhood and often

develops after trauma and sinusitis [1, 2]. Patients usually present with ocular pain, eyelid swelling, and erythema. Orbital cellulitis may present with additional ocular symptoms, such as proptosis, eye pain, decreased vision, and limited extraocular motility [2, 3].

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Correspondence: Berker OKAY, MD. Saglik Bilimleri Universitesi, Haseki Egitim ve Arastirma Hastanesi, Cocuk Sagligi ve Hastaliklari Klinigi, Istanbul, Turkiye.

Tel: +90 212 453 20 00 e-mail: drberkerokay@gmail.com

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Preseptal and orbital cellulitis are two infections surrounding the orbital septum with very different potential outcomes. Diagnosis is based on clinical examination and computed tomography (CT) imaging of the orbit and sinuses. A history of sinusitis, insect bites, or local facial or eyelid trauma supports the diagnosis. Preseptal cellulitis is much more common than orbital cellulitis, and both are more common in children than adults [3, 4]. Preseptal cellulitis is most commonly caused by bacteria such as *Staphylococcus aureus* and *Streptococcus*, and it resolves after 5–7 days with appropriate antibiotic therapy [5, 6]. In this study, we evaluated the demographic and clinical characteristics of children hospitalized for preseptal cellulitis and the factors affecting them.

MATERIALS AND METHODS

Study Design

This retrospective single-center study included 101 children hospitalized for preseptal cellulitis between March 2019 and 2022. It excluded patients aged >18 years or with comorbid diseases, outpatient treatment, and unclear differential diagnoses (Fig. 1). All patients' clinical variables and laboratory test panels during hospitalization were obtained from medical records. Data on demographics (e.g., age and sex), medical treatment, hospitalization, treatment duration, clinical recovery duration, and the presence of predisposing factors were also obtained from medical records. The patients were divided by age into two groups: \leq five and >five years.

The period before the age of five is infancy and preschool, and this distinction was made due to etiological differences. Normal age-based levels were used for hemoglobin, leukocytosis, and leukopenia in laboratory results [7]. This study complied with the Declaration of Helsinki. The study protocol was approved by the Haseki Training and Research Hospital Ethics Committee and the Ministry of Health (approval no: 85-2022; date: May 11, 2022).

Management and Treatment

The preseptal cellulitis diagnosis was made according to the patients' clinical, laboratory, and radiological features. A pediatrician and an ophthalmologist diagnosed patients who did not undergo CT. Some of the patients received oral antibiotics after discharge. Treatment was determined according to the patient's general condition, symptom severity, laboratory results at hospitalization and follow-up,

Highlight key points

- Incompletely treated sinusitis and buccal infections are the most common causes of preseptal cellulitis.
- Age is a factor affecting the clinical healing process in patients with preseptal cellulitis.
- Initial leukocyte values can be used to determine the duration of treatment.
- Complications can be prevented with early diagnosis, correct and adequate treatment.

treatment response, and time to duration of clinical improvement. An infectious disease specialist and pediatrician determined all patients' treatment regimens. Teicoplanin treatment was added to patients who did not clinically improve after 48 hours of treatment. Clinical improvement was defined as regression of the patient's erythema and ocular findings, improvement in their general condition, and improvement in laboratory values (acute phase reactants such as white blood cells and C-reactive protein). All patients were followed up by at least three doctors, one infectious diseases specialist, and two pediatricians.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences 22.0 for Windows (IBM Corp, Armonk, NY, USA). The Kolmogorov–Smirnov test was used to assess the normality of the data. Normally distributed continuous variables are expressed as the mean \pm standard deviation and were compared between groups using Student's *t*-test. Nonnormally distributed variables are expressed as the median (25th–75th percentiles) and were compared between groups using the Mann–Whitney *U* test. Categorical variables are expressed as percentages and were compared between groups using the Chi-square test. All results with a two-sided *p*-value of <0.05 were considered statistically significant.

RESULTS

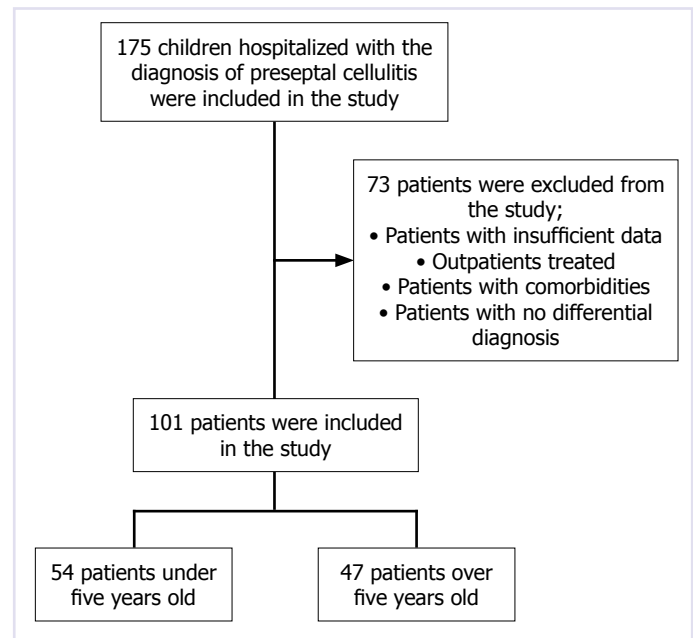
Demographics and Clinical and Laboratory Findings of Preseptal Cellulitis Cases

The clinical and demographic characteristics of the 101 children hospitalized for preseptal cellulitis are shown in Table 1. Fifty-six were male (55.4%). The median age of all 101 patients was 56 (24–89) months. Median age did not differ significantly between male (52 [25–94] months) and female (58 [24–86] months) patients (*p*=0.920). All patients included in this study had eye-

TABLE 1. Demographic and clinical data of the study population

Variables	Total (n=101)
Boy, (%)	55.4
Age (months), (25 th –75 th percentile)	56 (24–89)
Patients under five years old, (%)	53.5
Complaints and clinical findings, (%)	
Eyelid swelling	100
Eyelid erythema	80.2
Purulent discharge	20.7
Fever	11.9
Conjunctival erythema	38.6
Eye involvement	
Right eye	42.6
Left eye	49.5
Bilateral	7.9
Predisposing factors, (%)	
Sinusitis	18.8
Buccal infection	16.8
Insect bite	12.8
Herpes infection	8.9
Trauma	6.9
Complicated upper respiratory tract infection	4
Foreign body infections	3
Seasonal distribution (%)	
Spring	44.5
Summer	16.8
Autumn	10.8
Winter	27.7
Laboratory findings	
Hemoglobin (g/dl)	12.6±1.6
WBC (/mm ³)	12113±4900
Neutrophil (/mm ³)	6938 (4230–8400)
Lymphocyte (/mm ³)	3850 (2570–4420)
NLR	1.65 (0.98–2.98)
Platelet (/mm ³)	333131±96884
CRP (g/L)	20.9 (1.1–22.8)
Treatment, (%)	
Ampicillin-sulbactam + clindamycin	77.2
Ampicillin-sulbactam + acyclovir	4.9
Ampicillin-sulbactam + teicoplanin	8.9
Ceftriaxone	8.9
Sequential oral therapy, (%)	69.3
Treatment durations (days)	8.4±2.89
Clinical improvement (days)	5.01±2.20

WBC: White blood cell; NLR: Neutrophil lymphocyte ratio; CRP: C-Reactive protein. Values are given as mean±standard deviation or median (25th–75th percentile).

**FIGURE 1.** Flowchart of the study.

lid swelling. Eyelid erythema was present in 81 (80.2%) patients, conjunctival erythema in 39 (38.6%), purulent discharge in 30 (29.7%), and fever in 12 (11.9%). The right eye was involved in 43 patients (42.6%), the left eye in 50 (49.5%), and both eyes in eight (7.9%). There was no significant relationship between the frequencies of clinical findings and sex ($p=0.510$).

The predisposing factors were sinusitis in 19 patients (18.8%), buccal infection in 17 (16.8%), insect bite in 13 (12.8%), herpes infection in nine (8.9%), trauma in seven (6.9%), upper respiratory tract infection in four (4%), and foreign body in three (3%). Since this was a retrospective study, no predisposing factor could be determined for other patients. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction was negative for all patients between March 11, 2020, and March 1, 2022. Preseptal cellulitis was most common in spring (44.5%), followed by winter (27.7%), summer (16.8%), and autumn (10.8%).

An orbital CT was performed for 85 patients (84.2%) to confirm the diagnosis and exclude orbital cellulitis. All CT images were compatible with preseptal cellulitis. Periocular thickening was seen in 67 patients (78.8%), edema in 32 (37.6%), and increased density in 27 (31.7%).

Seventy patients (69.3%) were treated orally after discharge. The average treatment duration of the patients was 8.4 ± 2.8 days, and their time to clinical improvement

TABLE 2. Demographic and clinical data of patients according to age groups

Variables	Under five years old (n=54)	Above five years old (n=47)	p
Boy, (%)	55.5	55.3	0.920
Complaints and clinical findings, (%)			
Eyelid erythema	81.5	78.7	0.762
Purulent discharge	35.1	23.4	0.200
Fever	13	10.6	0.710
Conjunctival erythema	44.4	31.9	0.200
Eye involvement			
Right eye	55.5	27.6	0.004
Left eye	33.3	68	<0.001
Bilateral	11.1	4.2	0.200
Predisposing factors, (%)			
Sinusitis	11.1	27.6	0.002
Buccal infection	13	21.2	0.270
Insect bite	11.1	14.9	0.420
Herpes infection	3.7	14.9	0.050
Trauma	5.5	8.5	0.340
Seasonal distribution, (%)			
Spring	38.9	51	0.220
Summer	16.7	17	0.960
Autumn	16.7	4.2	0.045
Winter	27.8	27.6	0.980
CT findings, (%)			
Thickness increase	66.7	65.9	0.940
Edema	25.9	38	0.190
Density increase	20.3	34	0.120
Laboratory findings			
Hemoglobin (g/dl)	12.17±1.30	13.12±1.75	0.002
WBC (/mm ³)	12536±4912	11606±4891	0.350
Neutrophil (/mm ³)	5675 (4032–6830)	7310 (4705–9605)	<0.001
Lymphocyte (/mm ³)	3945 (3252–5737)	2650 (2020–3280)	<0.001
NLR	1.26 (0.80–1.73)	2.54 (1.73–4.01)	<0.001
Platelet (/mm ³)	330648±108349	336111±82153	0.780
CRP (g/L)	5.35 (1.33–16.38)	9.4 (1.1–27.4)	0.500
Leukocytosis, (%)	31.5	48.9	0.080
Treatment, n (%)			
Sequential oral therapy, (%)	68.5	70.2	0.850
Treatment durations (days)	7.93±2.63	8.98±3.11	0.070
Clinical improvement (days)	4.43±1.60	5.68±2.58	0.005

CT: Computed Tomography; WBC: White blood cell; NLR: Neutrophil lymphocyte ratio; CRP: C-Reactive protein. Values are given as mean±standard deviation or median (25th–75th percentile).

was 5.0±2.2 days. There were no significant correlations between the time to clinical improvement and parameters other than age.

No patients developed orbital cellulitis or other complications.

Age-Based Comparisons of Demographics, Clinical and Laboratory Findings, and Treatment

The patients were divided by age into two groups: <five (n=54) and >five (n=47) years (Table 2). The sex ratio did not differ significantly between age groups (p=0.050).

Right eye involvement was higher in patients aged \leq five years ($p=0.004$), and left eye involvement was higher in patients aged $>$ five years ($p<0.001$). Predisposing factors did not differ significantly between groups. When laboratory parameters were compared between groups, patients aged \leq five years had higher lymphocyte levels ($p<0.001$) but lower neutrophil levels ($p<0.001$), hemoglobin levels ($p=0.002$), and neutrophil-lymphocyte ratios ($p<0.001$).

Total treatment times were nonsignificantly longer for patients aged $>$ five years ($p=0.068$). The time to clinical improvement was shorter in patients aged \leq five than $>$ five years (4.4 ± 1.6 vs. 5.6 ± 2.5 days, $p=0.005$).

Evaluation of Factors Affecting the Duration of Treatment

Treatment durations were longer in patients with than without leukocytosis (9.3 ± 3.1 vs. 7.8 ± 2.5 days, $p=0.009$). However, no significant relationships existed between demographic and clinical characteristics and total treatment time except for age and leukocytosis.

DISCUSSION

This study evaluated the demographic and clinical characteristics of children hospitalized for preseptal cellulitis and the factors affecting them. Its main results were: (i) eye swelling and redness were the most common complaints in patients with preseptal cellulitis, with ampicillin-sulbactam + clindamycin therapy sufficient to treat most cases; (ii) the time to clinical improvement was shorter in patients aged \leq five than $>$ five years.

If preseptal cellulitis is not treated in time, it can rapidly progress and cause complications such as orbital cellulitis, vision loss, subperiosteal abscess, orbital abscess, and cavernous sinus thrombosis. Its most common causes are sinusitis, local trauma, insect bites, tooth abscesses, and middle ear infections [8, 9]. In our study, the most common causes were buccal and sinus infections and insect bites. Our study's low frequency of insect bites is likely because younger children may not have noticed them.

Preseptal cellulitis is frequently observed in boys and those aged \leq five years. It is frequently observed in this age group due to their lack of hygiene and sensitivity to infection [10–12]. It often develops due to sinusitis, insect bites, and foreign bodies. Therefore, unilateral involvement is often seen. Diseases such as angioedema and nephrotic syndrome should be considered in the differential diagnosis of bilateral involvement [11–13]. In

our study, male patients aged \leq five years were also frequent. Bilateral involvement was observed only in 7.9%.

Patients with preseptal cellulitis commonly have infection findings, such as swelling of the eyes, erythema, and purulent discharge. This condition arises due to the causes and inflammation associated with preseptal cellulitis [10, 14]. Preseptal cellulitis incidence increases in spring due to increased insect bites and conjunctivitis [6, 14, 15]. In our study, eyelid swelling (100%) and erythema (80.2%) were the most common findings. In addition, it was observed frequently in winter and spring, possibly due to climatic conditions and the coronavirus disease 2019 (COVID-19) pandemic. Comprehensive prospective studies on this subject are needed.

Adding teicoplanin or clindamycin to ampicillin-sulbactam or ceftriaxone is recommended for treatment. The duration of antibiotic therapy is as important as the antibiotics [10, 11]. Treatment for 5–7 days is sufficient, but if cellulitis symptoms persist, it should be extended until erythema and swelling subside [16, 17]. Many studies reported intravenous treatment durations of 4–6 days and positive results with outpatient intravenous treatment [14, 17–19]. We added teicoplanin to patients showing no clinical improvement after 48 hours of treatment and acyclovir to patients with the herpes virus. In our study, the total treatment duration was 8.42 ± 2.89 days, and the time to clinical improvement was 5.01 ± 2.20 days, longer than in other studies. It is believed that the patients' low socioeconomic level and poor personal hygiene affect this situation. In our study, the time to clinical improvement was longer in patients aged $>$ five than \leq five years (4.4 ± 1.6 vs. 5.6 ± 2.5 days, $p=0.005$). Since sinusitis is high as a predisposing factor in this age group, it may have affected the time to clinical recovery.

While lymphocytosis develops in infections in children aged \leq five years, neutrophil levels increase after age five [20, 21]. Therefore, lymphocyte and neutrophil levels differed between age groups. The frequencies of physiological anemia and anemia are higher in children aged \leq five years compared to other age groups [21–23]. We found low hemoglobin levels in this age group. In addition, we found longer treatment durations for patients with leukocytosis. However, no significant relationship was found between leukocytosis and the time to clinical improvement. While the time to clinical improvement does not change, treatment prolongation can be explained by the serious approach to these patients since pediatricians in our clinic want to provide in-hospital intravenous treatment until leukocytosis is resolved.

In our study, no complications developed in patients treated for preseptal cellulitis. Their early diagnosis and adequate treatment prevented complications.

Limitations

Since most preseptal cellulitis patients were treated as outpatients with oral antibiotic therapy, the relatively small number of patients treated with hospitalization is a limitation of our study. Another limitation is its retrospective and single-center design. In addition, its lack of a control group can be considered a limitation.

Conclusions

The most common finding in the patients was swelling in the eye. Age was important in determining the patients' time to clinical improvement. The presence of leukocytosis in patients could be used to predict treatment duration. Inadequate treatment of preseptal cellulitis may lead to serious complications. Early diagnosis and adequate treatment with antibiotics are required to prevent complications.

Ethics Committee Approval: The Haseki Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 11.05.2022, number: 85-2022).

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