Preseptal and Orbital Cellulitis: Thirteen Years of Experience and a Novel Scoring System (SNIPPED Score) for Differentiation

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Research Article

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Abstract
We aimed to evaluate clinical and laboratory characteristics of children with preseptal cellulitis (PC) or orbital cellulitis (OC) and to determine whether easily-accessible parameters could be used to predict OC. The data of children diagnosed with PC or OC between January 2008 and December 2020 were evaluated. Patients aged between 1 month and 18 years who were treated with intravenous antibiotics were included. Logistic regression analysis was performed to identify possible parameters in differentiating between PC and OC. A beta coefficient-based method was used to derive the scoring system. A total of 375 patients (202 [53.9%] boys), of whom 35 (9.3%) had OC, were evaluated. Median age was 44 (min-max: 1-192) months. Compared to those with PC, patients with OC were older (p = 0.001), had fever and upper respiratory tract infection (URTI) symptoms more frequently, and demonstrated prolonged symptom and hospitalization times (p≤0.001 for all). Significant differences between groups were observed for numerous parameters; however, logistic regression analysis revealed only five parameters independently associated with OC. The SNIPPED score variables and weights were as follows: sinusitis (2 points), neutrophil-to-lymphocyte ratio > 6.78 (3 points), platelet count > 420.5 x10³/mm³ (2 points), proptosis (4 points) and duration of symptoms ≥ 4 days (4 points). A cut-off of ≥ 7 points for OC diagnosis was found to have 91.4% sensitivity, 96.2% specificity, 71.1% PPV, 99.1% NPV and 95.7% accuracy.

Conclusion: In addition to showing previously known properties of OC versus PC, our study demonstrated that easily-accessible parameters could be used for the identification of OC.

What Is Known
- Orbital infections are common in the pediatric age group. Although preseptal cellulitis (PC) is benign, orbital cellulitis (OC) may cause complications which may be serious and fatal.
- The definite diagnosis of OC is via imaging which may neither be readily available nor easy to access in resource limited settings.

What is New
- A novel SNIPPED score [sinusitis (2 points), neutrophil-to-lymphocyte ratio >6.78 (3 points), platelet count >420.5 x10³/mm³ (2 points), proptosis (4 points) and duration of symptoms ≥4 days (4 points)] may be used to identify OC in pediatric patients.
- ≥ 7 points from the SNIPPED score was found to have 91.4% sensitivity, 96.2% specificity, 71.1% PPV, 99.1% NPV and 95.7% accuracy to distinguish OC from PC.

Introduction
Orbital infections may be seen in all age groups, but greater frequency is observed in the pediatric population [1]. In cases where the infection penetrates the orbital septum (which forms a barrier between preseptal and post-septal spaces) the condition is called orbital cellulitis (OC). Orbital infections may occur due to spread from the sinuses and by organisms that originate in the upper respiratory tract or skin. Other inciting factors include insect bites, odontogenic infections and trauma [2]. Although preseptal cellulitis (PC) is relatively benign, OC may cause complications including loss of visual acuity, cavernous sinus thrombosis, meningitis, intracranial abscess and septic embolus, if not managed early [3]. Differentiation between PC and OC may be difficult clinically, and there are no laboratory parameters that can directly aid in the discrimination of these two situations.

The aim of this study was to evaluate demographic, clinical and laboratory features, imaging studies, treatment modalities and outcomes of children with orbital infections. Also, we aimed to identify any laboratory parameters that could help differentiate OC from PC, and whether a scoring system could be devised with these parameters.

Patients And Methods
This retrospective study was conducted by evaluating the data of pediatric patients diagnosed with PC or OC between January 2008 and December 2020 at the Pediatric Infectious Diseases Department of our hospital. A medical database search was made with the following ICD-10 (International Classification of Diseases-10) codes: inflammation of the eyelids (H01), disorders of eyelids (H02.8, H02.9), ocular involvement in infectious diseases (H03.1), and orbital disorders including cellulitis and abscess (H05). Patients aged between 1 month and 18 years who were admitted to the hospital and treated with intravenous (IV) antibiotics were included in the study. Patients who were admitted with symptoms similar to PC with different final diagnosis and patients followed with outpatient oral antibiotic therapy were excluded. The demographic characteristics of patients, symptoms at admission, duration of oral antibiotic therapy before admission, affected eye (unilateral/bilateral and right/left), the duration of symptoms and treatment, the type (preseptal/orbital) and etiological cause (trauma, insect bite, sinusitis, conjunctivitis, odontogenic infections, dacryocystitis) of orbital infection were recorded from patient history and medical files. Laboratory parameters including complete blood count (white blood cell count [WBC], absolute neutrophil count [ANC], absolute lymphocyte count [ALC], and platelet count, mean platelet volume [MPV]), acute phase reactants [C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)], and culture results (blood, cerebrospinal fluid, and conjunctival swab cultures) were also recorded. Hematological indices, such as neutrophil-to-lymphocyte ratio (NLR), MPV-to-lymphocyte ratio (MPVLR), platelet-to-lymphocyte ratio (PLR), were calculated. Finally, indications and findings of imaging studies [orbital computerized tomography (CT), orbital magnetic resonance imaging (MRI)] and whether surgical intervention was performed were recorded from the electronic medical database.

The clinical diagnosis of PC was made according to physical examination findings when there was just eyelid edema with warmth and tenderness without restriction of ocular movements, proptosis or loss of vision. If there were findings of proptosis, limitations in ocular motility with or without additional signs (such as conjunctival inflammation with chemosis, orbital pain, loss of vision and afferent pupillary defect), OC was diagnosed in a preliminary fashion and...
was confirmed according to radiological evidence showing involvement of the orbital soft tissue posterior to the orbital septum [4]. Blood culture had been obtained from all patients. Lumbar puncture (LP) had been performed in infants who had signs of systemic infection and when meningitis could not be excluded.

Ophthalmology and otolaryngology consultations were requested when needed. Imaging studies had been ordered when there was a suspicion of OC or when patients had proptosis, ophthalmoplegia or when physicians had been unable to open patients’ eyelids due to extreme eyelid edema (preventing evaluation of ocular movements). If patients needed orbital surgery, they were referred to an ophthalmology department. Beta-lactam/beta-lactamase inhibitors had been commenced empirically in all patients, but treatments were adjusted or changed with respect to culture, antibiotic sensitivity and imaging results. When clinical and laboratory improvement had been achieved, patients were discharged for outpatient follow-up by switching to alternant oral antibiotic therapy. Total duration of treatment (IV plus oral) was at least 10 days in PC and 14 to 21 days in OC.

**Statistical Methods**

The statistical analyses of this study were performed via the SPSS software (version 22.0) for the Windows operating system. Normality of distribution in continuous variables was assessed with Q-Q plots and the Shapiro-Wilk test. Given the presence of normal distribution, comparisons between groups were performed with the Student’s *t* test; whereas, the Mann-Whitney *U* test was used to compare variables without normal distribution. The distributions of categorical data in the two groups were compared with Chi-squared tests. Multivariate regression via the backward conditional method was performed to determine factors that were independently effective on OC diagnosis. All parameters that demonstrated significant difference between patients with PC and OC in univariate analysis were included in the model, as well as parameters that were known risk factors of OC (ophthalmoplegia and proptosis). Receiver operating characteristic (ROC) analyses were performed at two stages: the first was to identify cut-off values for continuous variables showing significance in multivariable analysis (for categorical transformation), the second was to identify cut-off values for the scoring system (detailed below). Any *p* value lower or equal to 0.05 was accepted to demonstrate statistical significance.

**Deriving The Scoring System**

As described above, we identified factors that were independently associated with OC diagnosis by performing logistic regression. ROC curves were created for parameters that were found to be significant in multivariable logistic regression and cut-off values were identified with the Youden *J* method. Next, in order to be able to derive a score system based on categorical factors, we dichotomized continuous variables with cut-off values obtained from initial ROC analyses. A second logistic regression analysis for OC diagnosis was conducted via the enter method with the dichotomous variables identified in the previous step. Weights were assigned to each significant parameter by rounding the beta coefficients of regression analysis (not odds ratio) to the nearest integer [5]. Finally, scores were calculated for each patient, ROC analysis was performed, and two relevant cut-off points for the score were identified. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated.

**Results**

There were a total of 375 patients of whom 202 (53.9%) were boys. Thirty-five (9.3%) children had OC and 340 (90.7 %) had PC. Overall median age was 44 (min-max: 1–192) months. Median age of patients with OC was higher than the patients with PC (*p*<0.001).

Symptoms were similar in the PC and OC groups, except for fever and upper respiratory tract infection (URTI) symptoms which were significantly more common in the OC group (*p*<0.001 for both). Demographic, clinical, laboratory findings, indications and results of imaging studies, and antimicrobial treatment of patients are depicted in Table 1.
|                           | Overall patients  | Preseptal group (n = 340) | Orbital/postseptal group (n = 35) | P      |
|---------------------------|-------------------|---------------------------|-------------------------------|--------|
| Age, median, months       | 44 (1-192)        | 38 (1-192)                | 84 (12–168)                   | <0.001 |
| Gender, boys, n (%)       | 202 (53.9%)       | 184 (54.1%)               | 18 (51.4%)                    | 0.761  |
| Male:female ratio         | 1.16:1            | 1.17:1                    | 1.05:1                        |        |
| Bilaterally effected eye, n (%) | 17 (4.5%)       | 17 (5%)                   | 0                             | 0.176  |
| Right eye, n (%)          | 191 (51%)         | 169 (49.7%)               | 22 (62.9%)                    | 0.235  |
| Symptoms                  |                   |                           |                               |        |
| Fever                     | 156 (41.6%)       | 128 (37.6%)               | 28 (80%)                      | <0.001 |
| Periorbital edema         | 375 (100%)        | 340 (100%)                | 35 (100%)                     | 0.577  |
| Hyperemia                 | 352 (93.9%)       | 318 (93.5%)               | 34 (97.1%)                    | 0.396  |
| Conjunctivitis            | 107 (28.5%)       | 97 (28.5%)                | 10 (28.6%)                    | 0.996  |
| Eye discharge             | 137 (36.5%)       | 116 (34.1%)               | 11 (31.4%)                    | 0.746  |
| URTI symptoms             | 99 (26.4%)        | 81 (23.8%)                | 18 (51.4%)                    | <0.001 |
| Duration of symptoms, days | 3 (1–15)         | 3 (1–15)                  | 5 (2–15)                      | <0.001 |
| Duration of hospitalization, days | 4 (1–21)   | 4 (1–14)                 | 8 (1–21)                      | <0.001 |
| Laboratory evaluations    |                   |                           |                               |        |
| WBC (x10^3/mm^3)          | 11.6 (4.3–40)     | 11.3 (4.3–40)             | 18.9 (6.3–28.9)               | <0.001 |
| ANC (x10^3/mm^3)          | 6.12 (0.3–34.9)   | 5.9 (0.3–34.9)            | 16 (2.1–24)                   | <0.001 |
| ALC (x10^3/mm^3)          | 3.46 (0.53–13.6)  | 3.6 (0.53–13.6)           | 1.8 (0.6–8.16)                | <0.001 |
| Platelet count (x10^3/mm^3) | 342 (125–885)    | 339 (125–885)            | 422 (224–789)                 | 0.001  |
| MPV (FL)                  | 7.9 (5.5–11)      | 8 (5.5–11)                | 7.5 (6.2–10.3)                | 0.004  |
| CRP (mg/dL)               | 16 (1-450)        | 13 (1-368)                | 143 (10–450)                  | <0.001 |
| ESR (mm/hour)             | 28 (2-160)        | 25 (2–95)                 | 76 (14–160)                   | <0.001 |
| NLR                       | 1.75 (0.07–26.6)  | 1.62 (0.07–14.5)          | 11 (1-26.67)                  | <0.001 |
| PLR                       | 104 (15.3-581.1)  | 96.9 (15.3-581.1)         | 257 (55.2–540)                | <0.001 |
| MPVLR                     | 2.33 (0.49–17.74) | 2.19 (0.49–17.7)          | 4.1 (0.96–17.1)               | <0.001 |
| Imaging and reasons       |                   |                           |                               |        |
| CT                        | 57 (15.2%)        | 24 (7%)                   | 33 (94.2%)                    | <0.001 |
| MRI                       | 6 (1.6%)          | 1 (0.2%)                  | 5 (14.2%)                     | <0.001 |
| Proptosis                 | 21 (5.6%)         | 7 (2%)                    | 14 (40%)                      | <0.001 |
| Ophthalmoplegia           | 5 (1.3%)          | 0                         | 5 (14.2%)                     | <0.001 |
| Unable to evaluate the eye movements | 37 (9.8%) | 15 (4.4%) | 22 (62.8%) | <0.001 |
| Trauma                    | 2 (0.5%)          | 2 (0.5%)                  | 0                             | 0.221  |
| Treatment                 |                   |                           |                               |        |
| B lactam / b lactamase inhibitors | 306 (81.6%) | 300 (88.2%) | 6 (17.1%) | <0.001 |
| Clindamycin               | 55 (14.6%)        | 20 (5.8%)                 | 35 (100%)                     | <0.001 |
| 3rd generation cephalosporins | 72 (19.2%) | 43 (12.6%) | 29 (82.8%) | <0.001 |

*All values are given as median (minimum-maximum)

WBC: White blood cell count, ANC: Absolute neutrophil count, ALC: Absolute lymphocyte count, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, CT: Computed tomography, MPV: Mean platelet volume, MPVLR: MPV-to-lymphocyte ratio, MRI: Magnetic resonance imaging, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, URTI: Upper respiratory tract infection
Overall patients \( (n = 375) \)  | Preseptal group \( (n = 340) \)  | Orbital/postseptal group \( (n = 35) \)  | \( P \)  
---|---|---|---
Glycopeptid  | 8 (2.1%)  | 3 (0.8%)  | 5 (14.2%)  | \( \leq 0.001 \)  
Acyclovir  | 36 (9.6%)  | 36 (10.5%)  | 0  | \( 0.043 \)  

*All values are given as median (minimum-maximum).

WBC: White blood cell count, ANC: Absolute neutrophil count, ALC: Absolute lymphocyte count, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, CT: Computed tomography, MPV: Mean platelet volume, MPVLR: MPV-to-lymphocyte ratio, MRI: Magnetic resonance imaging, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, URTI: Upper respiratory tract infection

Etiology was identified in 312 (83.2%) patients (Table 2). Overall, the most common etiology was odontogenic infection \( (n = 71, 22.7\%) \), which was not identified in the OC group \( p = 0.003 \).

| Etiology / predisposing factors identified \( (n = 312) \)  | Preseptal group \( (n = 288) \)  | Orbital group \( (n = 24) \)  | \( p \)  
---|---|---|---
Odontogenic infections  | 71 (22.7\%)  | 71  | 0  | \( 0.003 \)  
Conjunctivitis  | 64 (20.5\%)  | 64  | 0  | 0.100  
Sinusitis  | 46 (14.7\%)  | 26  | 20  | \( \leq 0.001 \)  
Maxillary  | 10  | 5  | 5  |  
Pansinusitis  | 8  | 2  | 6  | 0.533  
Maxillary and ethmoid sinusitis  | 9  | 2  | 7  |  
Ethmoid sinusitis  | 2  | 0  | 2  |  
Herpes virus infections  | 35 (11.2\%)  | 35  | 0  | \( 0.046 \)  
Dacryocystitis  | 30 (9.6\%)  | 30  | 0  | 0.067  
Nasolacrimal duct obstruction  | 12/30  | 12  | 0  |  
Insect bite  | 24 (7.6\%)  | 24  | 0  | 0.104  
Trauma  | 14 (4.4 \%)  | 14  | 0  | 0.221  
Hordeolum  | 10 (3.2\%)  | 10  | 0  | 0.304  
Occult bacteremia  | 8 (2.5\%)  | 8  | 0  | 0.359  
Otitis media  | 7 (2.2\%)  | 6  | 1  | 0.649  
Idiopathic orbital inflammation  | 3 (0.9\%)  | 0  | 3  | \( \leq 0.001 \)  

Blood culture positivity was not detected in any of the patients. Lumbar puncture and cerebrospinal fluid (CSF) culture was performed in 37 (9.9\%) patients. No microorganism was detected in any of the CSF cultures. The median age of patients who underwent LP was lower than those who did not \( [3\text{ months (min-max: 1–15 months)} \text{ vs. 50 months (min-max: 1-192 months)}, \text{ p}[.001] \]. Conjunctival culture was performed in only 75 (20\%) patients and 40 (53.3\%) of the cultures had no growth. \textit{Staphylococcus} spp. were the most commonly identified \( (n = 18, 24\%) \) organisms in conjunctival cultures (four methicillin-resistant \textit{S. aureus}, 12 methicillin-susceptible \textit{S. aureus}, and two coagulase negative \textit{Staphylococci}). \textit{Streptococcus} spp. growth was present in eight \( (10.6\%) \) conjunctival cultures (three with \textit{S. anginosus} group, two with group A \textit{Streptococcus}, and three with \textit{S. viridans}). Other microorganisms detected in conjunctival cultures were \textit{Streptococcus pneumonia} in five, \textit{Haemophilus influenza} in three and \textit{Candida glabrata} in one. One conjunctival swab polymerase chain reaction test revealed \textit{Adenovirus}. 

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Three hundred and twenty-eight (87.5%) patients underwent ophthalmology consultation and 46 (12.3%) underwent otorhinolaryngology consultation. Sixty (16%) had undergone orbital imaging (54 had orbital CT and six had orbital MRI). The indications for imaging studies were: inability to evaluate eye movements in 37 (61.6%) patients, proptosis in 21 (35%), ophthalmoplegia in four (6.6%), and history of trauma in five (8%). Thirteen patients (7 boys, 6 girls) with OC were diagnosed as having subperiosteal/orbital abscess with orbital imaging studies and ten of them needed surgical intervention. Mean abscess diameter was 20.3 ± 13.6 millimeters. Median age of the patients with subperiosteal abscess was 120 (min-max: 36–156) months and other characteristics are detailed in Table 3.
| Patient | Age (months) | Sex | Symptoms | Duration of symptoms (days) | Previous oral antibiotic therapy (days) | Predisposing factor | Treatment | Method of cranial imaging | Reason for cranial imaging | Findings on cranial imaging | Sur |
|---------|--------------|-----|----------|---------------------------|-----------------------------------------|---------------------|------------|--------------------------|--------------------------------|----------------------------|-----|
| 1       | 36           | F   | Periorbital edema and hyperemia, eye discharge | 7                          | None                                   | Not identified      | Ceftriaxone + clindamycin | CT          | Unable to open eyelids and inability to evaluate the eye movements | Contrast-enhancing subperiosteal abscess (7 mm) | No   |
| 2       | 36           | M   | Periorbital edema and hyperemia, eye discharge | 5                          | None                                   | Maxillary and ethmoid sinusitis | Ceftriaxone + clindamycin | CT          | Unable to open eyelids and inability to evaluate the eye movements | Peripherally contrast-enhancing abscess located at the lateral of the right orbit (6 mm) | No   |
| 3       | 52           | F   | Periorbital edema and hyperemia | 5                          | None                                   | Not identified      | Ceftriaxone + clindamycin | CT          | Proptosis | 10 mm contrast-enhancing subperiosteal abscess | Yes |
| 4       | 60           | M   | Fever, periorbital edema and hyperemia, eye discharge | 7                          | 5                                      | Maxillary sinusitis | Ceftriaxone + clindamycin | CT          | Proptosis and inability to evaluate the eye movements because of extreme edema | 35 mm contrast-enhancing subperiosteal abscess located at the medial of the right orbit | Yes |
| 5       | 70           | M   | Fever, URTI symptoms, vomiting, periorbital edema and hyperemia | 3                          | None                                   | Ethmoid sinusitis | Ceftriaxone + clindamycin | CT          | Proptosis | 16 mm contrast-enhancing subperiosteal abscess near ethmoid sinus wall | Yes |
| 6       | 76           | M   | Fever, periorbital edema and hyperemia | 7                          | 3                                      | Not identified      | Ceftriaxone + clindamycin | MRI         | Ophthalmoplegia (restricted eye movements upwards) | 26 mm contrast-enhancing abscess displacing the superior rectus muscle | Yes |
| 7       | 120          | F   | Fever, periorbital edema and hyperemia, eye discharge, URTI symptoms | 8                          | 5                                      | Pan sinusitis       | Ceftriaxone + clindamycin + vancomycin | CT          | Proptosis and inability to evaluate the eye movements because of extreme edema | 50 mm contrast-enhancing subperiosteal abscess in the medial wall of right orbit | Yes |
| 8       | 128          | F   | Fever, URTI symptoms, periorbital edema and hyperemia | 4                          | None                                   | Pan sinusitis       | Ceftriaxone + clindamycin | CT          | Proptosis | 12 mm contrast-enhancing abscess in the left orbit | Yes |
| 9       | 132          | F   | Periorbital edema and hyperemia | 4                          | None                                   | Pan sinusitis       | Ceftriaxone + clindamycin | CT          | Unable to open eyelids and inability to evaluate the eye movements | 40 mm contrast-enhancing subperiosteal abscess in the right orbit | Yes |

CT: Computed tomography, F: Female, M: Male, MRI: Magnetic resonance imaging, URTI: Upper respiratory tract infection
| Patient | Age (months) | Sex | Symptoms | Duration of symptoms (days) | Previous oral antibiotic therapy (days) | Predisposing factor | Treatment | Method of cranial imaging | Reason for cranial imaging | Findings on cranial imaging | Sur |
|---------|--------------|-----|----------|-----------------------------|------------------------------------------|--------------------|------------|--------------------------|----------------------------|--------------------------------|-----|
| 10      | 144          | M   | Fever, periorbital edema and hyperemia, eye discharge | 5                           | None                                      | Maxillary and ethmoid sinusitis        | Ceftriaxone + clindamycin | CT                       | Proptosis and inability to evaluate the eye movements because of extreme edema | 40 contrast-enhancing orbital abscess in the lateral wall of left orbit | Yes |
| 11      | 144          | M   | Fever, periorbital edema and hyperemia, eye discharge, URTI symptoms | 8                           | 7                                        | Maxillary sinusitis                    | Ceftriaxone + clindamycin | CT                       | Proptosis                    | 15 orbital abscess in the lateral wall of right orbit | Yes |
| 12      | 156          | M   | Fever, periorbital edema and hyperemia, eye discharge | 9                           | 7                                        | Maxillary sinusitis                    | Ceftriaxone + clindamycin | CT                       | Inability to evaluate the eye movements because of extreme edema | 10 mm contrast enhancing lateral wall abscess of orbit | No  |
| 13      | 156          | F   | Fever, periorbital edema and hyperemia | 3                           | None                                      | Pan sinusitis                          | Ceftriaxone + clindamycin | MRI                      | Proptosis                    | 16 mm subperiosteal abscess between frontal bone and the orbit | Yes |

CT: Computed tomography, F: Female, M: Male, MRI: Magnetic resonance imaging, URTI: Upper respiratory tract infection

Multivariate logistic regression was performed with OC diagnosis as the dependent variable. The results showed that having sinusitis, NLR, symptom duration, platelet count, and proptosis were independently associated with OC diagnosis (Table 4).

**Table 4.** Factors independently associated with OC diagnosis, multivariable logistic regression

| Parameters | Initial backward conditional regression | Second regression |
|------------|----------------------------------------|-------------------|
|            | β coef | Standard Error | p    | Exp(β) | 95.0% Confidence Interval for Exp (β) | β coef |
| Sinusitis  | 2.183  | 0.876          | 0.013| 8.870  | 1.592 | 49.423 | 2.347 |
| NLR        | 0.385  | 0.097          | <0.001| 1.469  | 1.214 | 1.778 | 3.290 |
| Platelet count | 0.009  | 0.003          | <0.001| 1.009  | 1.002 | 1.016 | 2.375 |
| Proptosis  | 4.574  | 1.132          | <0.001| 96.923 | 10.549 | 890.524 | 4.378 |
| Duration of symptoms (days) | 0.662  | 0.167          | <0.001| 1.938  | 1.396 | 2.690 | 4.032 |
| Dependent Variable: OC diagnosis | Backward conditional method. Nagelkerke R²=0.790 | 'Enter' method |

NLR: Neutrophil-to-lymphocyte ratio, OC: Orbital cellulitis

Following the identification of these five variables, we derived the OC risk score system (SNIPPED standing for: Sinusitis, NLR, Platelet count, Proptosis, Duration of symptoms) according to beta coefficients (Table 5). Two threshold values were identified from the score: one with respect to the Youden $J$ index of the ROC analysis ($\geq 7$ points) and the other according to the score at which specificity first reached 100% ($\geq 12$ points). With a cut-off value of $\geq 7$, the SNIPPED score had sensitivity, specificity, PPV, NPV, and accuracy values of 91.4%, 96.2%, 71.1%, 99.1%, and 95.7, respectively.

**Table 5.** A novel scoring system (SNIPPED score) for predicting orbital cellulitis in pediatric patients
A predisposing factor was sinusitis. The orbital surgery rate in the current study was 28.5% in the OC group and 2.6% overall. In a study which evaluated 175 patients with orbital infections, 54 (25%) children had orbital cultures performed and the most common pathogen was S. aureus. In a 10-year report including 94 patients (67 PC and 27 OC), the most common pathogen was S. aureus. All patients in our study group who needed surgery were above 3 years old and the most identified pathogens were S. anginosus group (15%), while S. aureus was identified in 9% of all patients. In our study, only three of the cultures yielded S. aureus. Orbital abscess development is associated with various parameters, including sinusitis, NLR, platelet count, proptosis, and duration of symptoms. Among laboratory parameters, regression analysis only revealed that NLR and platelet count were associated with OC. Although inflammatory parameters are elevated in both PC and OC, the absolute levels of acute phase reactants may be helpful in clinical practice. For instance, higher CRP levels were reported to be associated with post-septal disease in a recent study. NLR is a parameter which is studied in bacterial infections such as neonatal sepsis, urinary tract infection and community acquired pneumonia. A recent study which included 243 children with orbital infections, of whom 51 (20.6%) had OC, found that an NLR value of > 3.14 could differentiate OC from PC with a sensitivity of 75.5% and a specificity of 77.4%. Our threshold of NLR (> 6.78) in OC patients seems a bit higher compared to the previous study; but these differences may be due to the well-known variations (based on measurement and devices) in NLR values.

Conjunctival cultures are frequently sterile in children with orbital infections. However, the most commonly identified organisms include Streptococcus spp., Staphylococcus spp., respiratory gram-negative organisms, and anaerobes. In our study, the most common was Staphylococcus spp. (24%). Similarly, in a 10-year report including 94 patients (67 PC and 27 OC), the most common pathogen was S. aureus (local abscess, eye swab, and blood cultures) in both adult and pediatric patients. The authors also noted that S. aureus and S. pyogenes were the only agents identified in pediatric cases, while S. viridans, Pseudomonas spp., Escherichia coli, H. influenzae, Fusobacterium spp., Peptostreptococcus spp. demonstrated growth in the cultures of the adult group. A recent study that evaluated 213 pediatric cases with orbital infections reported that orbital cultures were performed in 54 (25%) children and the most common pathogen was S. aureus. In a previous research including 94 children with OC (in which a pathogen was recovered in 31% of patients), the most commonly identified pathogen was S. anginosus group (15%), while S. aureus was identified in 9% of all patients. In our study, only three of the cultures yielded S. anginosus group. Therefore, empirical treatment should cover all these pathogens in children with orbital infections.

There are a few systematic reviews that focus on the management of pediatric patients with periorbital cellulitis. In children with PC, IV antibiotics should be considered for infants and those with signs of serious systemic infection. Because the meninges are susceptible to inoculation in the infant age group, LP should be performed unless the clinical picture precludes meningitis. In our study group, LP was performed in 9.9% of patients, but meningitis was not diagnosed in any subjects.

OC is treated with the administration of IV antibiotics after the patient is hospitalized. If the patient fails to respond to antibiotic treatment within 24 to 48 hours, it is reasonable to perform CT to look for an orbital abscess and/or plan for surgery. Orbital abscess development is associated with various factors, such as being older than 3 years old, having peripheral blood neutrophil count greater than 10,000/mm³, presence of periorbital edema and having received treatment with antibiotics previously. All patients in our study group who needed surgery were above 3 years old and the most identified predisposing factor was sinusitis. The orbital surgery rate in the current study was 28.5% in the OC group and 2.6% overall. In a study which evaluated 175 patients with orbital infections, 54 (25%) children had orbital cultures performed and the most common pathogen was S. aureus. In a 10-year report including 94 patients (67 PC and 27 OC), the most common pathogen was S. aureus. All patients in our study group who needed surgery were above 3 years old and the most identified predisposing factor was sinusitis. The orbital surgery rate in the current study was 28.5% in the OC group and 2.6% overall. In a study which evaluated 175 patients with orbital infections, 54 (25%) children had orbital cultures performed and the most common pathogen was S. aureus. In a 10-year report including 94 patients (67 PC and 27 OC), the most common pathogen was S. aureus. All patients in our study group who needed surgery were above 3 years old and the most identified predisposing factor was sinusitis. The orbital surgery rate in the current study was 28.5% in the OC group and 2.6% overall. In a study which evaluated 175 patients with orbital infections, 54 (25%) children had orbital cultures performed and the most common pathogen was S. aureus. In a 10-year report including 94 patients (67 PC and 27 OC), the most common pathogen was S. aureus. All patients in our study group who needed surgery were above 3 years old and the most identified predisposing factor was sinusitis. The orbital surgery rate in the current study was 28.5% in the OC group and 2.6% overall.
pediatric cases (36 had OC), 27 patients had subperiosteal abscess and surgery was needed in 31 (1.7%) of all patients [10]. Another study found the rates of surgical intervention as follows: 29% overall (n = 93), 48.7% in the 39 patients with OC and 14.8% in the 54 patients with PC. The higher rates of surgery may be related to the inclusion of adult patients in this study [11]. It was stated that the proportion of patients requiring surgery increased with age in a study which evaluated 40 children treated for subperiosteal abscess [23]. It may be feasible to suggest that older children and those with sinusitis may benefit from being monitored more carefully about the development of subperiosteal abscess. In our study, surgical intervention was required in all but three of the patients with subperiosteal abscesses. In these three patients, abscess diameter was small, fever and other symptoms resolved quickly, response was well to antibiotic treatment, and close monitoring was performed. Ultimately, control imaging studies were normal. Patients who underwent surgery did not attend follow-up visits which presents one of the limitations of this study.

The strength of this study is the large number of cases included over a 13-year period. Another strength is that, to our knowledge, this study is the first pediatric research that has found a novel scoring system to distinguish OC from PC. Previous studies show that imaging is required to differentiate between PC and OC; however, imaging is expensive and, more importantly, may not be available in resource-limited settings. The value of this scoring system comes from the fact that it drives its results from readily available and/or cheaply measured parameters. Although the ≥ 7-point cut-off has very good accuracy for the diagnosis of OC, the second cut-off point (≥ 12) was identified to describe a value that could be used for definite OC diagnosis in settings where imaging is not readily-available. In addition, this threshold can be used to quickly identify the severity of a patient when clinical suspicion is insufficient or imaging may be delayed.

There are some limitations to discuss. First, this is a retrospective study and carries all limitations associated with this design (ascertainment bias, selection bias). Second, although the number of patients included is respectable, all data is from only one tertiary center; thus, it may be feasible to perform prospective multicenter studies to better evaluate and confirm this scoring system by performing stratification based on various patient-related characteristics, including sex, age, race, and factors affecting the parameters used for scoring. Finally, it must be noted that we include a temporal parameter (duration of symptoms) in the scoring system. It is evident that judging the utility of this variable in patients who apply before 4 days of symptoms will require further studies. In relation, physicians must be aware of the fact that they must repeat score calculation daily until the 4th day when symptoms continue. However, to conclude, we believe that this score may be helpful to distinguish between PC and OC, since the early and promptly diagnosis and treatment of OC may prevent complications.

**List Of Abbreviations**

- **ALC**: Absolute lymphocyte count
- **ANC**: Absolute neutrophil count
- **CRP**: C-reactive protein
- **CSF**: Cerebrospinal fluid
- **CT**: Computerized tomography
- **ESR**: Erythrocyte sedimentation rate
- **ICD-10**: International Classification of Diseases-10
- **IV**: Intravenous
- **LP**: Lumbar puncture
- **MPV**: Mean platelet volume
- **MPVLR**: MPV-to-lymphocyte ratio
- **MRI**: Magnetic resonance imaging
- **NLR**: Neutrophil-to-lymphocyte ratio
- **NPV**: Negative predictive value
- **OC**: Orbital cellulitis
- **PC**: Preseptal cellulitis
- **PLR**: Platelet-to-lymphocyte ratio
- **PPV**: Positive predictive value
- **ROC**: Receiver operating characteristic
- **SNIPPED**: Sinusitis, neutrophil-to-lymphocyte ratio, platelet count, proptosis, duration of symptoms
URTI: Upper respiratory tract infection

WBC: White blood cell count

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Authors’ Contributions

Study conception and design: RY, FNO, MP, GT; Literature review: RY, SO, ZSS, AYS, RGC, Acquisition of data: All authors; Analysis and interpretation of data: RY; Drafting of manuscript: RY, GT; Critical revision for important intellectual content: GT, MP, FNO; Final approval of the version to be published: All authors

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