

Age-Related Clinical Characteristics and Treatment Patterns in Hospitalized Orbital Cellulitis: A Real-World Federated Database Study

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Abstract

Orbital cellulitis is an uncommon but potentially severe infection that can lead to vision-threatening complications and mortality. Differences in clinical characteristics and management between pediatric and adult patients remain incompletely characterized at the population level. This study evaluated demographic features, associated risk factors, and treatment patterns of orbital cellulitis using a large real-world database.

A retrospective cohort study was conducted using the TriNetX US Collaborative Network. Hospitalized patients diagnosed with orbital cellulitis (ICD-10-CM code H05.01) were stratified into pediatric (≤ 18 years) and adult (> 18 years) cohorts. Demographics, body mass index (BMI), antecedent upper respiratory infections, chronic sinusitis, comorbid diabetes mellitus (DM) or neoplasms, laboratory parameters, antibiotic regimens, and ocular adnexal surgery were analyzed.

A bimodal age distribution was observed (mean age 12 vs 54 years). Pediatric patients more frequently had antecedent upper respiratory infections and sinusitis and were commonly treated with lincomycin. Adults showed higher BMI, greater prevalence of DM and neoplasms, and more frequent use of broad-spectrum antimicrobial therapy and ocular adnexal surgery.

These findings highlight distinct clinical profiles between pediatric and adult orbital cellulitis and support age-specific management strategies.

Introduction

Orbital cellulitis is an uncommon but potentially vision- and life-threatening infection if not diagnosed and treated promptly. In terms of epidemiology, its incidence¹ differs significantly between pediatric and adult populations, with reported rates of 1.6 per 100,000 in children and 0.1 per 100,000 in adults. This suggests a greater prevalence in the pediatric population.

In children, orbital cellulitis typically follows an upper respiratory tract infection and is often caused by gram-positive organisms such as *Staphylococcus* and *Streptococcus* species. These cases usually respond well to single-agent antibiotic therapy due to the anatomical characteristics of incompletely developed paranasal sinuses.

In contrast, adult cases frequently involve preceding sinusitis, dental infections, or intraocular foreign bodies, and are commonly polymicrobial. The causative organisms often include gram-positive, gram-negative, and anaerobic bacteria, likely due to the fully developed and enclosed paranasal sinus anatomy in adults. These presentations typically necessitate the use of broad-spectrum intravenous antibiotics, such as third-generation cephalosporins in combination with aminoglycosides or quinolones, administered for at least two weeks. Furthermore, surgical intervention, particularly drainage of a subperiosteal orbital abscess, is more commonly required in adults to prevent complications such as intracranial extension and potential neurological sequelae.

The complications^{2,3} of orbital cellulitis can be severe. In the pre-antibiotic era, vision loss occurred in up to 20% of cases. With the advent of empirical antibiotic therapies, such complications have become rare. However, the overall landscape of disease burden has shifted in recent decades, with chronic conditions such as diabetes mellitus, malignancies, and autoimmune diseases becoming more prominent. Simultaneously, the global prevalence of overweight and obesity has increased, particularly in developed countries. These trends may influence both the risk of infection and the clinical course of orbital cellulitis.

Given these evolving patterns, key research questions arise: Have the risk factors for orbital cellulitis changed over time? What are the current demographic characteristics of affected patients? If these questions can be answered, we may further reduce the ophthalmic and systemic complications associated with this condition.

To address these questions, we utilized the TriNetX US Collaborative Network^a a federated real-world database based in the United States that aggregates de-identified clinical data from over 124 million patients across more than 71 healthcare organizations. This resource includes patient demographics, diagnoses, medications, laboratory results, and body mass index (BMI), among other data.

Materials and Methods

This study used a retrospective observational approach, drawing on extensive electronic medical records available through the TriNetX US Collaborative Network. This database offers a wide range of patient information including diagnoses, medical procedures, prescriptions, laboratory results, and genetic profiles. For this study, the network provided data from approximately 124 million patients across 71 healthcare organizations during the research timeframe, with the bulk of the data coming from institutions in the United States. The index date was defined as the first inpatient encounter with an ICD-10-CM diagnosis code for orbital cellulitis during the study period. Each patient was included once. Comorbidities were assessed during the pre-index lookback period, laboratory values were selected from the index encounter using the value closest to diagnosis, and medications/procedures were captured during the index hospitalization.

This retrospective study was exempted from requiring informed consent as it analyzed pre-existing, de-identified data without any intervention or direct interaction with individuals. Data anonymization adhered to the HIPAA Privacy Rule de-identification criteria specified in section § 164.514(a). The study was conducted in accordance with the ethical standards of the Declaration of Helsinki (revised 2013) and was approved by the Institutional Review Board of Taipei Medical University (N202504104).

Results

As shown in Table 1, a total of 23,169 hospitalized patients with orbital cellulitis were identified in the TriNetX Research Database. The overall mean age was 45 ± 25 years. Among them, 4,941 patients were

in the pediatric group (≤ 18 years), and 18,228 were in the adult group (> 18 years).

Table 1
Demographics of orbital cellulitis inpatients (N = 23,169)

Characteristic	Adult (> 18 y, n = 18,228)	Pediatric (≤ 18 y, n = 4,941)
Number of patients	18,228	4,941
Gender ratio (M/F)	47/51	62/38
Mean age (years $\pm$ SD)	54.3 $\pm$ 21.0	11.7 $\pm$ 4.29
Ethnicity - White (%)	63	53
Ethnicity - Black or African American (%)	18	23
Ethnicity - Other (%)	3	9
Ethnicity - Asian (%)	4	4
Notes: Values are presented as mean $\pm$ SD or percentage, unless otherwise indicated.		

There was a male predominance in the pediatric group (M/F: 62/38), while the adult group showed a slight female predominance (M/F: 47/51). Age distribution revealed a bimodal pattern, with a more prominent peak in the pediatric population (mean age 11.7 $\pm$ 4.29 years) and a second peak in middle-aged adults (mean age 54.3 $\pm$ 21 years).

In terms of ethnicity, the majority of patients in both groups were White—63% in the adult group and 53% in the pediatric group. The pediatric group had a higher percentage of Black or African American (23% vs. 18%) and Other races (9% vs. 3%), while Asian representation was consistent across both groups (4%). Table 2 presents the baseline comparison statistics between adult and pediatric groups, including clinical association factors (such as diabetes, neoplasm, overweight), treatments (antibiotic regimens and ocular adnexal surgery), and relevant laboratory values (including blood glucose and CRP).

Table 2
Comparison of clinical characteristics, risk factors, laboratory findings, and treatments
between pediatric and adult orbital cellulitis inpatients

Variable	Pediatric Group	Adult Group	p-value
BMI (mean $\pm$ SD)	20.5 $\pm$ 6.29	28.8 $\pm$ 7.79	< 0.0001
Overweight (%)	9	32	< 0.0001
Acute URI (%)	68	48	< 0.0001
Chronic sinusitis (%)	45	31	< 0.0001
Diabetes mellitus (%)	1	25	< 0.0001
Neoplasm (%)	8	39	< 0.0001
Blood glucose (mg/dL)	100 $\pm$ 23.7	115 $\pm$ 50.4	< 0.0001
HbA1c (%)	5.65 $\pm$ 1.38	6.39 $\pm$ 1.88	< 0.0001
C-reactive protein (mg/L)	35.4 $\pm$ 42.1	40.1 $\pm$ 60.7	< 0.0001
Lincomycin (%)	46	39	< 0.0001
3rd generation cephalosporin (%)	57	60	< 0.0001
Quinolone (%)	23	46	< 0.0001
Aminoglycoside (%)	18	31	< 0.0001
Erythromycin (%)	28	49	< 0.0001
Tetracycline (%)	3	33	< 0.0001
Sulfonamide (%)	16	34	< 0.0001
Antifungal (%)	16	33	< 0.0001
Antiviral (%)	13	26	< 0.0001
Ocular adnexal surgery (%)	8	12	< 0.0001
Notes: Values are presented as mean $\pm$ SD or percentage. URI = upper respiratory infection.			

As summarized in Table 2, significant differences were observed between pediatric and adult orbital cellulitis inpatients. Adults had a higher mean BMI (28.8 $\pm$ 7.79 vs. 20.5 $\pm$ 6.29) and a greater prevalence of overweight (32% vs. 9%; both p < 0.0001), whereas pediatric cases were more often associated with acute upper respiratory tract infections (68% vs. 48%) and chronic sinusitis (45% vs. 31%; both p < 0.0001). In contrast, diabetes mellitus (25% vs. 1%) and neoplasms (39% vs. 8%) were strongly linked to adult patients (p < 0.0001). Laboratory analyses revealed higher blood glucose (115 $\pm$ 50.4 vs. 100 $\pm$ 23.7 mg/dL) and HbA1c (6.39 $\pm$ 1.88 vs. 5.65 $\pm$ 1.38) in adults, consistent with greater glycemic dysregulation,

as well as elevated CRP levels (40.1 ± 60.7 vs. 35.4 ± 42.1 ; $p < 0.0001$), reflecting a heightened inflammatory response.

In terms of antibiotic therapy, pediatric patients were more frequently treated with lincomycin (46% vs. 39%), whereas adults were significantly more likely to receive broader-spectrum or combination regimens, including quinolones (46% vs. 23%), third-generation cephalosporins (60% vs. 57%), erythromycin (49% vs. 28%), aminoglycosides (31% vs. 18%), tetracyclines (33% vs. 3%), sulfonamides (34% vs. 16%), as well as antifungal (33% vs. 16%) and antiviral agents (26% vs. 13%) (all $p < 0.0001$). These findings highlight more complex and aggressive antimicrobial strategies in adult patients. Additionally, ocular adnexal surgery was performed more often in the adult group (12% vs. 8%; $p < 0.0001$).

Discussions

Although prior population-based studies have reported a higher incidence of orbital cellulitis in children^{5,6}, adults comprised the majority of hospitalized orbital cellulitis cases identified in this TriNetX cohort. Therefore, our findings should be interpreted as age-specific differences among hospitalized cases rather than population-level incidence estimates.

Although rare, orbital cellulitis is a high-stakes clinical condition that can result in vision-threatening and even life-threatening complications if not recognized and treated in a timely manner. In pediatric patients, the disease is often preceded by upper respiratory tract infections (URIs), especially in those under 12 years old. Viral URIs can lead to inflammation and obstruction of the paranasal sinuses, particularly the ethmoid sinus, which is anatomically closest to the orbit. Due to the absence of lymphatics in the sinuses, local immune defense relies on phagocytes such as macrophages, and thus the area is vulnerable to secondary bacterial or even fungal infections.

In children, the immune system is still developing, which may increase susceptibility to orbital cellulitis. However, the pathogens are often limited to gram-positive bacteria (e.g., *Staphylococcus* and *Streptococcus* spp.)^{7,8}, and these cases typically respond well to single-agent antibiotics, such as lincomycin, as observed in this study.

In contrast, adult patients often experience polymicrobial infections due to the fully developed and enclosed paranasal sinus anatomy, which facilitates infections involving gram-positive, gram-negative, and anaerobic bacteria. Therefore, adults frequently require broad-spectrum antibiotic coverage, such as vancomycin, third-generation cephalosporins, quinolones, aminoglycosides, or metronidazole. A study from Boston Children's Hospital⁹ reported a 60.9% use of vancomycin, even though methicillin-resistant *Staphylococcus aureus* (MRSA) was isolated in only 5% of cultures. In our study, vancomycin use was 51%, closely mirroring those findings.

The greater complexity of antimicrobial regimens in adults—evidenced by higher use of quinolones, cephalosporins, erythromycin, tetracycline, sulfonamides, antivirals, and antifungals—reflects the

diversity of causative organisms and anatomical considerations. In some cases, both pediatric and adult patients may develop a subperiosteal abscess, necessitating surgical drainage to prevent spread to the intraconal space, cavernous sinus, or intracranial compartment. Surgical indications include abscess volume > 1 cm³ or diameter > 2 cm, or involvement of surgically inaccessible areas^{9,10,11}. Our findings—12% of adult patients underwent ocular adnexal surgery versus 8% in children—are in line with these clinical patterns.

With respect to risk factors, our study confirmed several well-established associations. Pediatric patients demonstrated higher rates of preceding upper respiratory tract infections (68% vs. 48%) and chronic paranasal sinusitis (45% vs. 31%), whereas diabetes mellitus (25% vs. 1%) and neoplasms (39% vs. 8%) were predominantly associated with adult patients (all $p < 0.0001$). These findings align with the distinct pathophysiological mechanisms underlying orbital cellulitis in different age groups.

An emerging and noteworthy insight from our study was the significant association of overweight (BMI > 27) with orbital cellulitis, particularly in adults (32% vs. 9%). This may reflect the rising global prevalence of overweight and obesity over the past three decades⁴, especially in developed nations. Overweight status is associated with a proinflammatory state and is a well-known risk factor for type 2 diabetes mellitus (T2DM) via insulin resistance. Therefore, even patients without established diabetes but with prediabetic profiles (as seen in our adult group with a mean blood glucose of 115 ± 50.4 mg/dL) may be at increased risk for orbital cellulitis.

From a clinical standpoint, overweight may be the only identifiable risk factor in otherwise healthy-appearing young or middle-aged adults. Addressing overweight and associated metabolic dysfunctions may reduce the risk of orbital cellulitis and its recurrence, thereby lowering the burden of disease.

Strengths and Limitations

This study has several strengths and limitations. As a retrospective observational cohort study, the findings are inherently subject to potential confounding and bias. Moreover, the TriNetX is EMR-based, which raises the possibility of coding inaccuracies. Despite these limitations, the large sample size—with data from over 124 million patients across more than 60 healthcare organizations—provides substantial statistical power and enhances the generalizability and clinical relevance of our findings when interpreted appropriately.

Conclusions

Using the TriNetX US Collaborative Network, we found that orbital cellulitis is more prevalent in pediatric patients (mean age 12 years, male predominance), whereas adults (mean age 54 years) more often had complex comorbidities, received broader antibiotic regimens, and underwent ocular adnexal surgery at higher rates. These findings suggest that management should be tailored to age and etiology, combining appropriate parenteral antibiotics with surgical intervention when indicated, while also addressing

modifiable risk factors such as overweight and prediabetes to reduce disease burden and preserve visual and systemic health.

Declarations

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Author contributions: The authors confirm their contribution to the paper as follows. CAH was responsible for the study conception, design, reviewing and editing. THC and ZU helped acquired the tables, figures and did the literature review. JCY and MHS helped with data interpretation and manuscript editing. All authors have contributed to the manuscript and approved the submitted version.

Data availability statement:

The data supporting this study were obtained from the TriNetX Research Network, a federated, de-identified electronic health record database. Individual-level patient data cannot be shared publicly due to privacy regulations and data use agreements. Researchers with institutional access to TriNetX may reproduce the analyses and obtain aggregated results following the platform's policies. Requests for access should be directed to TriNetX (<https://www.trinetx.com>) and are subject to approval under their standard data use agreements.

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Clinical trial number: not applicable.

Human Ethics and Consent to Participate declarations: Ethics approval was obtained from the Institutional Review Board of Taipei Medical University. Informed consent was waived because this study used pre-existing, de-identified data.

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Figures

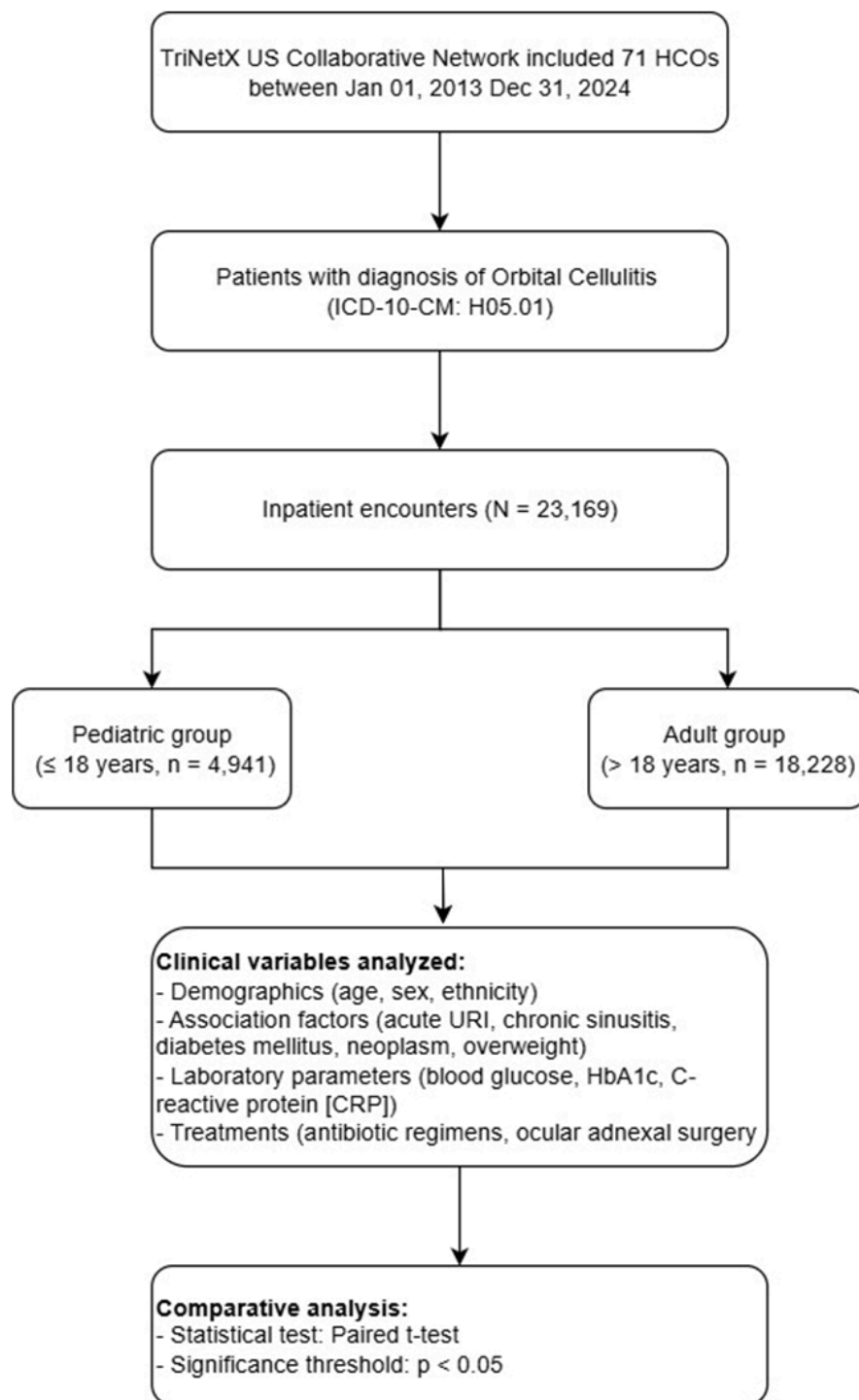


Figure 1

Flowchart of patient inclusion and analytic workflow for the comparison of clinical characteristics, association factors, laboratory findings, and treatment patterns between pediatric and adult inpatients with orbital cellulitis. As shown in Figure 1, hospitalized patients with a diagnosis of orbital cellulitis were identified using the ICD-10-CM code H05.01, and only inpatient encounters were included. The cohort was stratified into pediatric (≤18 years) and adult (>18 years) groups. Demographic variables

(age, sex), association factors (acute upper respiratory tract infection, chronic sinusitis, diabetes mellitus, neoplasms, and overweight status defined as BMI >27), laboratory parameters (blood glucose, HbA1c, and C-reactive protein), and treatment characteristics (antibiotic prescriptions and ocular adnexal surgery) were analyzed. Comparisons between pediatric and adult groups were performed using paired t-tests, with statistical significance defined as $p < 0.05$.