

Evaluation and Medical Management of the Pediatric Patient With Orbital Cellulitis/Abscess: A Systematic Review

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BACKGROUND AND OBJECTIVES: Pediatric orbital cellulitis/abscess (OCA) can lead to vision loss, intracranial extension of infection, or cavernous thrombosis if not treated promptly. No widely recognized guidelines exist for the medical management of OCA. The objective of this review was to summarize existing evidence regarding the role of inflammatory markers in distinguishing disease severity and need for surgery; the role of imaging in OCA evaluation; and the microbiology of OCA over the past 2 decades.

METHODS: This review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Searches were performed in MEDLINE (Ovid), Web of Science Core Collection, Scopus, CINAHL (EBSCO), and Cochrane Central Register of Controlled Trials (CENTRAL), most recently on February 9, 2021.

RESULTS: A total of 63 studies were included. Most were

descriptive and assessed to have poor quality with high risk of bias. The existing publications evaluating inflammatory markers in the diagnosis of OCA have inconsistent results. Computed tomography imaging remains the modality of choice for evaluating orbital infection. The most common organisms recovered from intraoperative cultures are *Streptococcus* species (*Streptococcus anginosus* group, group A *Streptococcus*, and pneumococcus) and *Staphylococcus aureus*. Methicillin-resistant *S aureus* in culture-positive cases had a median prevalence of 3% (interquartile range, 0%-13%).

CONCLUSION: This systematic review summarizes existing literature concerning inflammatory markers, imaging, and microbiology for OCA evaluation and management. High-quality evidence is still needed to define the optimal medical management of OCA. *Journal of Hospital Medicine* 2021;16:680-687. © 2021 Society of Hospital Medicine

Orbital cellulitis/abscess (OCA) is a potential complication of sinusitis. If not treated promptly, it can result in vision loss, intracranial infection, or cavernous sinus thrombosis.^{1,2} In 1970, Chandler et al³ classified orbital complications of acute sinusitis into five groups: inflammatory edema (group 1); orbital cellulitis (group 2); subperiosteal abscess (SPA) (group 3); orbital abscess (group 4); and cavernous sinus thrombosis (group 5). Group 1, or preseptal cellulitis, is significantly different from groups 2, 3, and 4, collectively referred to as OCA, which affect the actual orbital content.

Children with OCA are generally hospitalized so they can be treated with intravenous antibiotics. While orbital abscesses (group 4) are typically treated surgically, successful medical management has been reported for cases of orbital cellulitis

and SPA (groups 2 and 3).^{4,5} No widely accepted guidelines exist for the evaluation and medical management of OCA, resulting in significant variation in care.⁶ The purpose of this systematic review is to summarize existing evidence guiding the medical management of OCA regarding laboratory testing, imaging, and microbiology. This review does not address surgical considerations.

METHODS

The review protocol has been registered in the PROSPERO International Prospective Register of Systematic Reviews (crd.york.ac.uk/prosperto/index.asp; identifier: CRD42020158463), and the review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.⁷

Search Strategy

A systematic search of the literature was designed and conducted by a medical librarian (ES), with input from the research team (AB, SM). The search strategy included Medical Subject Headings (MeSH) terms and keywords related to orbital or subperiosteal cellulitis/abscess and children; see Appendix Table 1 for the complete search strategy. Searches were conducted in

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MEDLINE (Ovid), Web of Science Core Collection, Scopus, CINAHL (EBSCO), and Cochrane Central Register of Controlled Trials (CENTRAL) using advanced search techniques relative to each database. Searches were last conducted on February 9, 2021.

Eligibility Criteria

The study designs (retrospective and prospective) included in the search were limited to randomized clinical trials, cohort studies, case-control studies, and case series with participants <18 years of age. Case reports describing fewer than 5 patients and literature reviews were excluded. Studies including a combination of adult and pediatric patients were included if pediatric outcomes were reported separately. Only studies available in English were included.

Outcome Measures

The outcome measures were determined a priori based on three clinical questions:

- Q1. What is the role of inflammatory markers—white blood cell (WBC) count, C-reactive protein (CRP), and fever—in distinguishing between the following: preseptal cellulitis (group 1) and OCA (groups 2, 3, and 4); orbital cellulitis (group 2) and abscess (groups 3 and 4); and patients who do and do not require surgery?
- Q2. What is the role of imaging in the evaluation of OCA?
- Q3. What is the microbiology of OCA over the past 2 decades? What is the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA)?

Screening

Two review authors (AB, SM) performed both the title/abstract and full-text screen, independently applying the eligibility criteria. Disagreements were discussed, and conflicts were resolved with input from a third reviewer author (ES). Duplications were removed. When two studies had overlapping patient data, the study with fewer data points was excluded.

Data Extraction and Synthesis

All studies included after the full-text screen were divided based on the clinical question they answered (Q1, Q2, Q3 above). Some studies reported outcomes pertinent to more than one question. Two review authors were assigned to each clinical question. They independently reviewed each article and extracted the pertinent data into question-specific extraction sheets. Articles assigned to Q2 were reviewed by two pediatric neuroradiologists. For each study, the following details were extracted: authors, location, year, study type, study period, population, and number and ages of participants. Details that were question-specific included: (Q1) values and/or percentages for inflammatory markers; (Q2) reasons for imaging or type of imaging; and (Q3) participants managed surgically and culture results. The data were then synthesized in table and/or narrative format. For Q3, the organisms identified from intraoperative and blood cultures in each study were mathematically combined. When possible, prevalence

was calculated using the number of patients with at least one pathogen recovered as the denominator. If this number was not available, the number of patients who underwent surgery was used as the denominator.

Quality Assessment

No randomized controlled trials were identified. More than 90% of the studies identified and included were retrospective descriptive studies. By the nature of the case series design, the study quality was felt to be poor, with high risk of bias. The Joanna Briggs Institute Critical Appraisal tools for systematic reviews were used to appraise each individual study included (Appendix Table 2).⁸ The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) criteria were used in rating the quality of evidence for each question.⁹

RESULTS

A summary of the search strategy and study selection is provided in the Figure (PRISMA flow diagram). The initial search identified 3007 studies. After duplicates were removed and general eligibility criteria applied, 94 articles remained. Question-specific eligibility criteria, discussed in the following sections, were then applied, resulting in 63 articles included in the review.

Q1: Are Inflammatory Markers, Including Fever, WBC, and CRP, Useful in Distinguishing Preseptal Cellulitis (group 1) From OCA (Groups 2, 3, and 4); Orbital Cellulitis (group 2) From Abscess (Groups 3 and 4); or Identifying Patients Who Require Surgical Intervention?

Fever and elevation of the WBC count and CRP have been used to assess the severity of certain pediatric infections^{10,11} and therefore may be helpful in distinguishing severity of illness in OCA. Studies included in this section provided numerical values for at least one of the following: WBC count, CRP, or percentage of patients with fever for at least one type of orbital infection. Included studies had at least five patients per group.

Thirty-three articles were screened for the inflammatory marker section. Thirteen were excluded for the following reasons: no numbers reported for inflammatory markers ($n = 6$); group 1 and groups 2, 3, and 4 results combined ($n = 6$); fewer than five patients with orbital cellulitis included ($n = 1$). Twenty studies were included: 18 case series and 2 retrospective cohorts. Appendix Table 3 summarizes the data from studies included. Based on GRADE criteria, the body of evidence included in this section is of low quality.⁹

Distinguishing Between Preseptal and OCA

Eleven studies were included in this section (Table 1). WBC count was significantly higher in patients with groups 2, 3, and 4 than group 1 in two studies (Devrim et al,¹² $P < .01$; Santos et al,¹³ $P = .025$). CRP was significantly higher in patients with groups 2, 3, and 4 than group 1 in four studies (Öcal Demir et al,¹⁴ $P = .02$; Devrim et al,¹² $P < .01$; Ohana-Sarna-Cahan et al,¹⁸ $P < .001$; Santos et al,¹³ $P < .001$). Patients with groups 2, 3, and

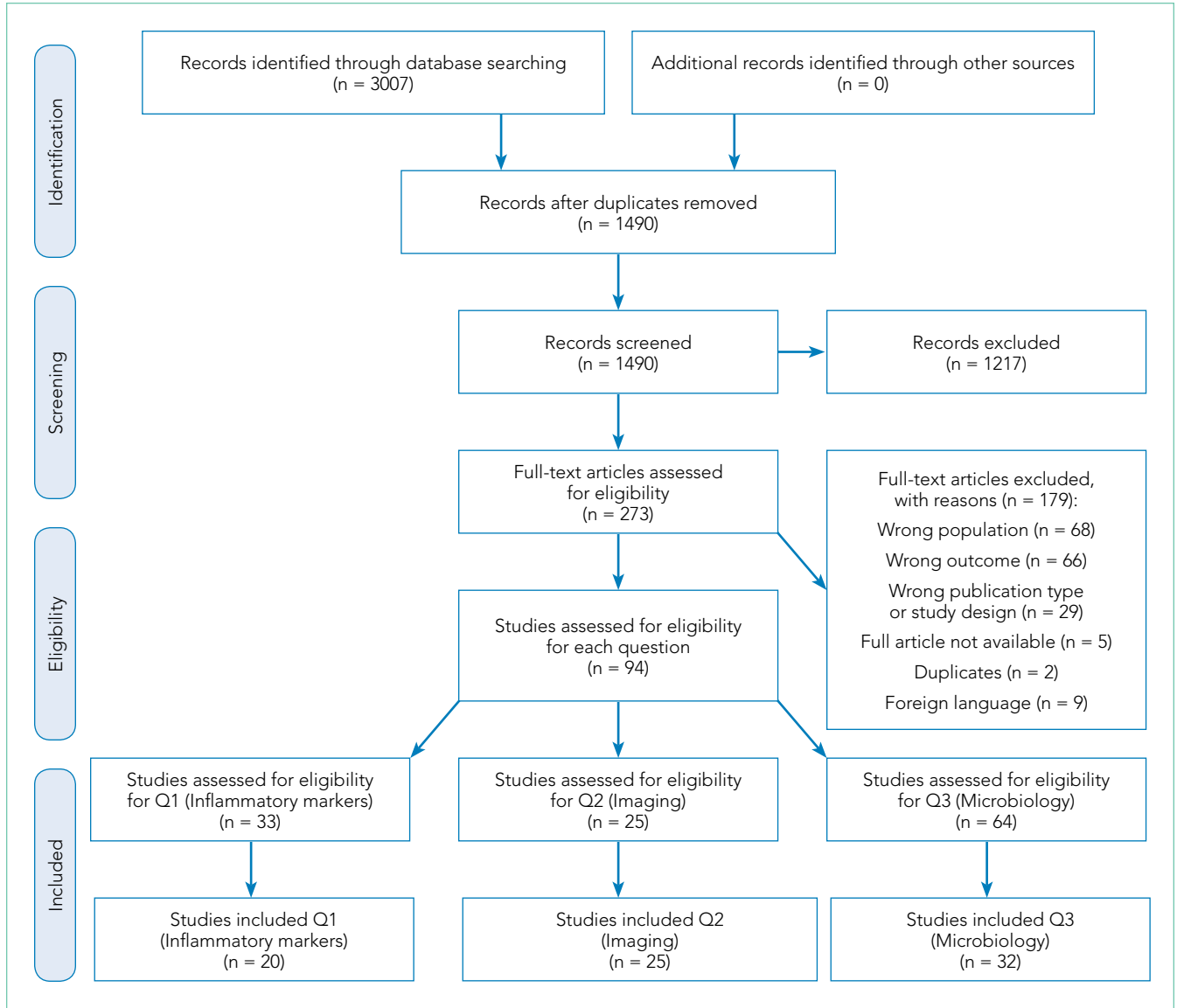


FIG. PRISMA 2009 Flow Diagram

4 had a significantly higher fever rate in three studies (Botting et al,²¹ $P < .001$; Ohana-Sarna-Cahan et al,¹⁸ $P = .0001$; Santos et al,¹³ $P = .029$).

Distinguishing Between Orbital Cellulitis and Abscess

Seven studies were included in this section (Appendix Table 3). One study showed significantly higher WBC count in group 3 than group 2 ($P = .004$), although results were reported as the percentage of patients above a cutoff number calculated to distinguish between cellulitis and abscess (Appendix Table 3).²² CRP was not significantly different between group 2 and groups 3 and 4. One study found a significantly higher fever rate in patients with group 3 compared to patients with group 2 ($P < .001$).²²

Identifying Patients Requiring Surgery

Six studies were included in this section (Appendix Table 3). One study found a significantly higher WBC count in patients

treated surgically (Tabarino et al,²⁴ $P < .05$). Patients treated surgically had a significantly higher CRP in two studies (Cohen et al,²⁵ $P = .02$; Friling et al,²⁶ $P = .04$). Fever was inconsistently reported in the studies, with some using mean presenting temperatures and some using rates of fever. One study found a significantly higher mean presenting temperature in patients treated surgically ($P = .027$), but the difference between the two groups was 0.7 °C.²³

Summary

Most studies found no significant difference in WBC count, CRP, or fever between preseptal and OCA, cellulitis and abscess, or patients receiving medical and surgical interventions.

Q2: What Is the Role of Imaging in Evaluation of OCA?

Twenty-five articles were selected for the imaging section review. All the included studies were retrospective descriptive

TABLE 1. Relationship of Markers of Inflammation to Chandler Group 1 (Preseptal Cellulitis) and Chandler Groups 2, 3, and 4 (Orbital Cellulitis/Abscess)

Inflammatory marker	P value	Study	Group 1 (preseptal cellulitis)	Groups 2, 3, and 4 (orbital cellulitis/abscess)
WBC count, mean (SD), cells/mm ³ N = 9	<.05	Devrim et al ¹²	12,322 (5064)	17,620 (11,945)
		Santos et al ¹³	NR	NR
	≥.05	Öcal Demir et al ¹⁴	12,348 (4582)	14,483 (5816)
		Georgakopoulos et al ¹⁵	NR	NR
		Gonçalves et al ¹⁶	15,400 (SD NR)	13,030 (SD NR)
		Ho et al ¹⁷	13,030 (SD NR)	15,400 (SD NR)
		Ohana-Sarna-Cahan et al ¹⁸	13,400 (5400)	14,900 (6500)
		Weiss et al ¹⁹	13,664 (SD NR)	13,370 (SD NR)
	NR	Le et al ²⁰	12,400 (6000)	Combined mean NR Group 2: 15,600 (5600) Group 3: 16,400 (6700) Group 4: 16,400 (5400)
	CRP, mean (SD), mg/dL N = 6	<.05	Öcal Demir et al ¹⁴	3.25 (6.17)
Devrim et al ¹²			3.67 (5.93)	7.78 (7.73)
Ohana-Sarna-Cahan et al ¹⁸			4.1 (4.9)	12.7 (11.5)
Santos et al ¹³			NR	NR
≥.05		Gonçalves et al ¹⁶	1.77 (SD NR)	2.72 (SD NR)
		Ho et al ¹⁷	NR	NR
		Le et al ²⁰	NR	NR
Fever, % N = 8	<.05	Botting et al ²¹	47	94
		Ohana-Sarna-Cahan et al ¹⁸	48	80
		Santos et al ¹³	42	67
	≥.05	Gonçalves et al ¹⁶	55	71
		Ho et al ¹⁷	62	74
		Weiss et al ¹⁹	61	66
		Georgakopoulos et al ¹⁵	35	100
	NR	Le et al ²⁰	33	81

A total of 10 studies compared group 1 to groups 2, 3, and 4, but not all 3 inflammatory makers were addressed in each study. One additional study reported values only for groups 2, 3, and 4 combined (Hongguang et al, see Appendix Table 3).

Abbreviations: CRP, C-reactive protein; NR, not reported; SD, standard deviation; WBC, white blood cell.

studies. Quantitative data extraction and analysis of these studies could not be performed because of their heterogeneous methodologies and lack of objective data. Therefore, the information gleaned from these studies is summarized in narrative format. Per GRADE criteria, the body of evidence included in this section is of low quality.

Who Needs Imaging?

Proptosis, ophthalmoplegia, decreased vision, and pain with eye movements are widely agreed-upon indications for imag-

ing evaluation.^{21,27,28} Because of concern for radiation exposure in pediatric patients, some authors suggested that computed tomography (CT) should only be obtained if patients fail to respond to medical therapy or if surgery is being considered.^{17,29,30} However, Rudloe et al³¹ found that half of the patients with group 3 or higher disease on CT did not have proptosis, ophthalmoplegia, or pain with extraocular movement. In addition, evaluation of young children with acute periorbital swelling can be difficult, so a lower threshold for imaging is likely warranted in these younger patients.

What Type of Imaging Should Be Obtained?

The American College of Radiology 2018 Appropriateness Criteria (ACR criteria) for orbital imaging state that orbital CT is usually indicated for patients with suspected Chandler groups 2, 3, and 4 infections.³² CT with contrast is useful for evaluating the extent of orbital infection and size of the abscess and for delineating the adjacent osseous anatomy, which is essential for cases in which surgical intervention is planned.^{20,21,26,27,30,31,33,34} Distinguishing abscess from cellulitis on CT sometimes can be challenging; therefore, serial clinical examinations and, occasionally, surgical exploration may be required.^{35,36}

Magnetic resonance imaging (MRI) is helpful for evaluating intracranial complications (eg, epidural abscess),^{27,37} but it is limited for evaluating the osseous components of the paranasal sinuses. Although one study suggested that rapid MRI is comparable to contrast CT for differentiating group 1 infections from groups 2, 3, and 4 infections, it provided limited assessment of other complications.³⁸ With no definitive studies comparing CT with MRI for orbital infections, adherence to the ACR criteria is recommended.

Orbital ultrasound is limited by its small field of view and artifact produced by the surrounding bony interface, both of which can obscure posterior intraorbital pathologies.^{29,39,40} Plain radiographs are not helpful for evaluating OCA due to limited soft-tissue contrast.⁴¹

When Should Repeat Imaging Be Obtained?

Children with group 3 OCA have been successfully managed medically in a carefully monitored setting.⁴² Repeat CT imaging is sometimes useful in these patients, particularly if the clinical examination is difficult.⁴²⁻⁴⁴ However, improvement in CT findings may lag behind clinical improvement.³⁹

Summary

Per ACR criteria, orbital CT with contrast is recommended to evaluate patients with suspected Chandler groups 2, 3, and 4 OCA. MRI is reserved for evaluating intracranial complications.

Q3: What Is the Microbiology of OCA? What Is the MRSA Prevalence?

Knowledge of the microbiology of OCA is essential for the appropriate selection of empiric antibiotics. Because fewer children with groups 2 and 3 OCA undergo surgery, intraoperative cultures often are not available to guide antibiotic selection.⁴⁵ As a result, significant variation exists in antibiotic prescribing.⁶

Studies discussing the microbiology of OCA were included only if they were published in the past 2 decades (2000-2020) and were excluded if the study period was before 1990, as microbiology changes over time and new vaccines are introduced. To be included, the majority of cultures reported had to be intraoperative (orbital or sinus) specimens. Studies reporting only nasal, conjunctival, or other surface cultures were excluded. When studies included patients with group 1 OCA, only microbiology data for groups 2, 3, and 4 OCA were extracted. The pattern of resistance for *S aureus* was not always explicitly reported; however, when non-MRSA active antibiotics were used, methicillin-susceptible *S aureus* was assumed.

A total of 63 studies were screened for the microbiology section; 32 were excluded for the following reasons: published before 2000 or study period before 1990 (n = 18), reported surface cultures or culture site not clearly stated (n = 4), microbiology mixed between preseptal and orbital (n = 6), wrong study type (n = 2), and study group overlaps with a different article included (n = 2). Of the 32 studies included, 3 were prospective observational, 4 were retrospective cohort, and 25 were case series. Based on GRADE criteria, the body of evidence included in this section is of low quality.⁴²

Appendix Table 4 summarizes the microbiologic data from the studies included. In the group of children that had a positive culture (orbital, sinus, or blood), the most commonly recovered organisms reported were *S aureus* (median, 22%; range, 0%-100%), *Streptococcus anginosus* group (median, 16%; range, 0%-100%), group A *Streptococcus* (median, 12%; range, 0%-80%), and *Streptococcus pneumoniae* (median, 8%; range, 0%-100%). *Streptococcus* as a group had a median prevalence of 57%, ranging from 0% to 100%. MRSA prevalence had a median of 3% (interquartile range [IQR], 0%-13%). Median prevalence of polymicrobial cultures was 20%, and median prevalence of anaerobic organisms was 14% (Table 2). Orbital and sinus cultures had the highest yield, with an average return of an organism of 72% (median, 75%; IQR, 64%-84%). Blood culture results were reported in 14 studies and usually obtained in a subgroup of the study population. When obtained, blood cultures rarely yielded an organism (median, 10%; IQR, 5%-15%); the rate of identified bacteremia in the total population had a median of 5% (IQR, 5%-7%) across studies.

Microbiology was compared between studies completed in the United States and in other countries (Table 2). Based on median prevalence across studies, both *S anginosus* group and MRSA were more prevalent in the United States than internationally (28% vs 0% and 11% vs 0%, respectively). No clear trend in MRSA prevalence was evident over the 2 decades; however, the studies included were heterogeneous and did not have the power to detect such a trend.

Two reports suggest a difference of MRSA prevalence by patient age. Hsu et al⁴⁶ found that three of eight MRSA infections were in infants age <1 year, which accounted for 50% (3/6) of infants included in the study. Miller et al⁴⁷ reported MRSA in 4 of 9 (44%) infants with OCA. Age <1 year may be associated with increased frequency of MRSA infection in OCA.

Summary

Blood cultures have low yield. The most common organisms recovered from OCA are *Streptococcus* species (most commonly *S anginosus* group, group A *Streptococcus*, and pneumococcus) and *S aureus*. Polymicrobial infections including anaerobes are common. MRSA prevalence is low globally but varies significantly among geographic areas.

DISCUSSION

Our systematic review of the literature for the medical management of OCA revealed predominantly descriptive studies

TABLE 2. Prevalence of the Most Common Organisms in Patients With a Positive Culture Combined From International and US-Based Studies

Organism	Total			United States			International		
	Studies, No. ^a	Median, %	Range, %	Studies, No. ^a	Median, %	Range, %	Studies, No. ^a	Median, %	Range, %
<i>Staphylococcus aureus</i> total	31	22	0-100	13	29	10-64	18	20	0-100
MRSA	24	3	0-75	11	11	0-44	13	0	0-75
MSSA	23	14	0-63	11	19	8-29	12	12	0-63
<i>Streptococcus</i> total	32	57	0-100	13	60	50-90	19	40	0-100
<i>Streptococcus anginosus</i> group	30	16	0-100	12	28	0-53	18	0	0-39
Group A <i>Streptococcus</i>	28	12	0-80	10	14	0-40	18	6	0-80
<i>Streptococcus pneumoniae</i>	32	8	0-100	13	12	0-20	19	7	0-100
<i>Haemophilus influenzae</i>	32	8	0-100	13	7	0-15	19	8	0-63
Anaerobes	18	14	0-40	9	21	6-40	9	4	0-18
Polymicrobial	25	20	0-73	9	34	0-47	16	9	0-73

^aThis column reports the number of studies that reported data on each of the specific pathogens, allowing for calculation of prevalence for each study (number of a specific organism over total patients with organisms recovered from cultures). The prevalence, reported as a percentage for each of these studies, was used to determine median prevalence and ranges across studies. Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

and only a limited number of comparison-based studies, likely reflecting the rarity of advanced forms of OCA. Given the lack of high-quality evidence and the level of heterogeneity among studies, the conclusions that can be drawn are limited.

Distinguishing between disease severity and OCA requiring surgical intervention remains challenging. Although studies in our review suggest a trend toward markers of inflammation (fever, elevated WBC count and CRP) being more common in more severe presentations, the results were mixed, and studies were low quality and underpowered to detect meaningful differences. For example, most studies do not define what constitutes a fever in their cohort. Our review suggests that markers of inflammation cannot be used to distinguish between Chandler groups or to identify patients requiring surgery. Of note, the presence of fever and elevated inflammatory markers may have influenced the decision to obtain imaging or to proceed to surgery, thereby also potentially biasing these clinical indicators toward predictors for more severe disease. Decisions regarding surgery should therefore be based on the entire clinical picture, including response to appropriate antibiotics.

We found a lack of high-quality evidence regarding the role of imaging in OCA, and the studies reviewed were heterogeneous. Recommendations for imaging therefore remain at the level of expert opinion (ACR criteria). CT imaging is the first-line modality for imaging in suspected OCA given the limitations of alternative imaging modalities, but the sensitivity and specificity of CT imaging remain unknown for diagnosis of orbital abscesses.

Our review of the published microbiology confirmed that *Staphylococcus* and *Streptococcus* species are the most com-

mon pathogens identified in OCA. Prevalence across the different studies varied greatly. Owing to the significant heterogeneity in studies, calculation of pooled prevalence was not possible. By using the number of positive cultures as our denominator (or total surgeries if number of positive cultures was unavailable), we likely overestimated the prevalence of *S aureus*. *S aureus* is generally recognized as a pyogenic pathogen, more likely to be associated with abscess formation.⁴⁸ Therefore, culture results obtained predominantly from abscesses likely result in an overestimate of *S aureus* in OCA (groups 2, 3, and 4). Regardless, MRSA prevalence was generally low, both nationally and internationally. The MRSA results from the study by McKinley et al⁴⁹ (Texas) was a notable outlier in the United States, with MRSA prevalence as high as 44% compared with the median prevalence of 3% (IQR, 0-13), highlighting the importance of local resistance patterns when choosing empiric antibiotics.

Limitations to the microbiology review included significant heterogeneity in both the types of cultures included and the reporting of results. Although we excluded studies that reported only surface culture results or did not specify culture type, we did include studies that had surface culture results combined with intraoperative culture results, making it impossible to separate the two. Since most of the cultures included in combined results reported organisms based on intraoperative cultures, we felt they provided valuable information that should be included. In most studies, blood cultures were not obtained in all participants, so the yield of blood cultures is likely an overestimate, as blood cultures are more likely to be obtained in higher-acuity patients.

CONCLUSION

Although the available evidence regarding the medical management of OCA remains low quality, certain limited conclusions can be drawn, as presented in this review. Further high-quality studies are needed to better inform the medical management of OCA.

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From the Editor-in-Chief

- 5 The Light at the End of the Tunnel: Reflections on 2020 and Hopes for 2021
Samir S Shah, et al

Original Research

- 7 Clinical Characteristics and Outcomes of Non-ICU Hospitalization for COVID-19 in a Noncenter, Centrally Monitored Healthcare System
David M Nemer, et al
- 61 EDITORIAL Caring for Noncritically Ill Coronavirus Patients
Farah Achor, Kulkarni, et al
- 15 The Effects of a Multifaceted Intervention to Improve Care Transitions Within an Accountable Care Organization: Results of a Stepped-Wedge Cluster-Randomized Trial
Jeffrey L Schnipper and Lipika Samal, et al
- 62 EDITORIAL Care Transitions: A Complexity Mindset
Brent G Fischer and Andrew PJ Olson
- 23 Barriers and Facilitators to Guideline-Adherent Pulse Oximetry Use in Bronchiolitis
Courtney Benjamin Wolk and Amanda C Schondelmeyer, et al
- 63 EDITORIAL Deimplementation: Discontinuing Low-Value, Potentially Harmful Hospital Care
Shradha A Kulkarni, et al

Brief Reports

- 31 Gender Distribution in PHM Leadership
Jessica M Allen, et al
- 64 EDITORIAL Building a New Framework for Equity: PHM Must Lead the Way
Nancy D Spector and Barbara Overholser

Leadership & Professional Development

- 34 From Seed to Fruit—How to Get Your Academic Project Across the Finish Line
Sharmin Shekarchian and Charle M Wray

Progress Notes

- 35 Methodologic Progress Note: Opportunistic Sampling for Pharmacology Studies
Sonya Tang Girdwood, et al

Review

- 38 Hospitalized Medical Patients With PTSD: Review and Map for Improved Care
Kathlyn E Fletcher, et al

Perspectives in Hospital Medicine

- 44 Professional Identity Formation During the COVID-19 Pandemic
Benjamin Kinnear, et al
- 47 Psychological Safety in Times of Crisis
Lily Rotman Doversaj, et al
- 50 Racial Health Disparities, COVID-19, and a Way Forward for US Health Systems
Max Jordan Nguemni Tiako, et al
- 53 Improving Population Health Post COVID
Utibe R Essien and Giselle Corbie-Smith
- 56 The Need for Standardized Metrics to Drive Decision-making During the Pandemic
J Matthew Austin and Allen Kachalia
- 59 Defining a New, Normal While Awaiting the Pandemic's Next Wave
Kymberly McDonald, et al

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