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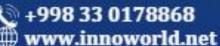**Open Access, Peer Reviewed Journal**   **Scientific Journal**

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PREVENTING PURULENT COMPLICATIONS IN PEDIATRIC OSTEOMYELITIS (LITERATURE REVIEW)

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Abstract: Hematogenous osteomyelitis (HO) in children is a significant musculoskeletal infection, with purulent complications posing severe risks such as chronic infection, growth disturbances, and functional impairments. This review explores the pathogenesis, risk factors, diagnostic challenges, prevention strategies, and advancements in treatment to mitigate these complications. Timely diagnosis, appropriate antimicrobial therapy, and minimally invasive surgical techniques are essential to prevent long-term sequelae. Emerging diagnostic tools, including molecular and genomic methods, and innovative therapies such as hyperbaric oxygen therapy, highlight promising avenues for improving outcomes. A multidisciplinary approach remains critical for effective management and prevention.

Keywords: Hematogenous osteomyelitis, pediatric infection, purulent complications, antibiotic therapy, diagnostic advancements

Introduction. Hematogenous osteomyelitis (HO) in children is a significant musculoskeletal infection characterized by the spread of bacteria through the bloodstream to the bone, predominantly affecting the highly vascularized areas of the developing skeleton. The most common causative organism is Staphylococcus aureus, although Kingella kingae is increasingly recognized, particularly in children under three years of age(Anil Agarwal & Aditya N. Aggarwal, 2016; Blaise Cochard et al., 2023; "Children's Acute Hematogenous Osteomylitis: Review Article," 2024; Nimmy Thakolkaran & Avinash K. Shetty, 2019). The pathophysiology involves bacterial seeding in the metaphyseal region of long bones, where the rich blood supply facilitates infection. In some cases, the infection can spread transphyseally, potentially affecting growth plates and leading to growth disturbances(Blaise Cochard et al., 2023). Epidemiologically, HO is more prevalent in males and certain ethnic groups, such as Māori and Pasifika in New Zealand, with socioeconomic factors influencing disease burden(Andrew M. McDonald et al., 2023; Sarah Hunter et al., 2023). The prevalence of HO varies, with studies indicating a high incidence in specific populations, such as 18 per 100,000 per annum in New Zealand(Andrew M. McDonald et al., 2023). Early diagnosis and treatment are crucial to prevent purulent complications, which can lead to

chronic infection, growth disturbances, and significant morbidity(Donald E. Meier et al., 2020; M. Alanazi et al., 2023). The economic and clinical significance of preventing these complications lies in reducing the need for prolonged antibiotic therapy, surgical interventions, and the associated healthcare costs(Charles R. Woods et al., 2021; Donald E. Meier et al., 2020). Effective management involves early empirical antibiotic therapy, often with agents like vancomycin or clindamycin, tailored based on culture results, and sometimes surgical intervention to drain abscesses(Anil Agarwal & Aditya N. Aggarwal, 2016; "Children's Acute Hematogenous Osteomylitis: Review Article," 2024; Nimmy Thakolkaran & Avinash K. Shetty, 2019). The use of advanced imaging techniques, such as MRI, aids in early detection and management, thereby reducing long-term complications(Anil Agarwal & Aditya N. Aggarwal, 2016; Paola Musso et al., 2021). Overall, the prevention of purulent complications in pediatric HO is vital for minimizing long-term disability and healthcare costs, emphasizing the need for timely diagnosis and appropriate management strategies(Donald E. Meier et al., 2020).

Pathogenesis and risk factors of purulent complications. Purulent complications in pediatric hematogenous osteomyelitis (AHO) are influenced by a variety of mechanisms and risk factors, including hematogenous spread, immune response, age-specific vulnerability, microbial virulence, comorbidities, and nutritional status. Hematogenous spread is a primary mechanism, with Staphylococcus aureus, particularly methicillin-resistant Staphylococcus aureus (MRSA), being a common pathogen due to its virulence and ability to form abscesses, which complicates the disease course(Marcia D-S. Dobson et al., 2022; Neal Hartman et al., 2022; Y. Chang et al., 2022). The immune response, as indicated by elevated C-reactive protein (CRP) levels, is a significant predictor of complications, with higher CRP levels correlating with both acute and chronic complications(Alina Shchepetkina & m0sukon974, 2023; Y. Chang et al., 2022; Zaid Alhinai et al., 2020). Age-specific vulnerability is evident, as older children are more prone to complications, possibly due to more aggressive disease presentations or delayed diagnosis(Adriana Sarmiento Clemente et al., 2022; Kylie Disch et al., 2023). The presence of comorbidities, such as septic arthritis or disseminated disease, further exacerbates the risk of complications, as these conditions often require more intensive interventions and are associated with prolonged hospital stays(P Maré & Leonard C Marais, 2023; Vuyisa Mdingi et al., 2023). Nutritional status, although not directly addressed in the studies, can be inferred as a potential risk factor, as malnutrition may impair immune function and delay recovery. The presence of bone abscesses, prolonged fever, and delayed surgical intervention are additional factors that contribute to the risk of purulent complications, highlighting the importance of timely and effective management. The predictive scores, such as A-SCORE and C-SCORE, incorporate these variables to assess the risk of complications, emphasizing

the need for early identification and intervention to prevent adverse outcomes(Adriana Sarmiento Clemente et al., 2023; Zaid Alhinai et al., 2020). Overall, a multifaceted approach considering these risk factors is crucial for managing pediatric AHO and mitigating the risk of purulent complications.

Diagnostic challenges and early detection. Diagnosing pediatric hematogenous osteomyelitis (AHO) early presents several challenges, primarily due to its subtle and often misleading clinical presentation, especially in neonates and young children. The condition is characterized by pain and tenderness over the affected bone, but these symptoms can be non-specific and easily confused with other conditions, leading to diagnostic delays(Andrea Yeo & Manoj Ramachandran, 2014; Anil Agarwal & Aditya N. Aggarwal, 2016). The primary pathogens involved, such as Staphylococcus aureus, can complicate diagnosis due to their ability to evade detection, with positive cultures obtained in only 50% to 80% of cases(Kit M. Song & John F. Sloboda, 2001). Imaging techniques like MRI have significantly improved early detection by providing detailed visualization of the infection's extent, which is crucial for timely intervention(Andrew Michalowitz et al., 2020; Kit M. Song & John F. Sloboda, 2001). MRI, particularly with gadolinium-enhanced subtraction sequences, can identify early bone ischemia, a predictor of progression to chronic osteomyelitis, thus allowing for more aggressive early treatment(Ahmed Al-Alawi et al., 2024). Biomarkers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are commonly elevated in AHO and are used to monitor treatment response, although they are not specific to the condition(Anil Agarwal & Aditya N. Aggarwal, 2016; M. Thiart & Ahsha. Nansook, n.d.). Emerging diagnostic techniques, including whole genome sequencing (WGS) and next-generation sequencing (NGS), offer promising avenues for rapid pathogen identification, even in culture-negative cases, although their integration into routine practice requires significant changes in laboratory workflows(Andrew Michalowitz et al., 2020). These advanced methods, alongside traditional blood cultures and imaging, form a comprehensive diagnostic approach that can enhance early detection and improve outcomes in pediatric AHO(Xueqin Zhang et al., 2024). Despite these advancements, the need for a high index of suspicion and a multidisciplinary approach remains critical to overcoming the inherent challenges in early diagnosis and management of AHO in children(John P. Dormans & Denis S. Drummond, 1994; M. Thiart & Ahsha. Nansook, n.d.).

Prevention strategies. The prevention of purulent complications in pediatric hematogenous osteomyelitis involves a multi-tiered approach encompassing primary, secondary, and tertiary strategies. Primary prevention focuses on early diagnosis and prompt initiation of antimicrobial therapy to prevent the establishment of infection. This involves the use of empirical antibiotic therapy tailored to cover common pathogens such as Staphylococcus aureus and Kingella kingae, with adjustments based on

culture and sensitivity results("Children's Acute Hematogenous Osteomylitis: Review Article," 2024; Mathie Lorrot et al., 2023). Early intervention with high-dose intravenous antibiotics, transitioning to oral therapy as the clinical condition improves, is crucial in preventing complications(Mathie Lorrot et al., 2023; Xueqin Zhang et al., 2024). Secondary prevention aims to mitigate the progression of the disease and involves surgical interventions when necessary, such as drainage of abscesses and debridement of necrotic tissue, which are critical in cases of septic arthritis or periosteal abscess(Mathie Lorrot et al., 2023; S. Kulkarni et al., 2022). Surgical management has been shown to significantly improve outcomes, reducing the risk of chronic osteomyelitis and associated deformities(S. Kulkarni et al., 2022). Tertiary prevention focuses on rehabilitation and the prevention of long-term sequelae, such as growth disturbances and limb length discrepancies. This involves a multidisciplinary approach, including orthopedic consultation and family-centered care, to ensure comprehensive management and follow-up(Maximillian Mifsud & Martin A McNally, 2023). Rehabilitation strategies may include physical therapy to restore function and prevent joint stiffness, as well as monitoring for potential complications(Mifsud & McNally, 2023). Additionally, innovative approaches such as the use of ozone therapy and lymphogenic technology have shown promise in reducing the transition to chronic forms of the disease, highlighting the importance of integrating novel therapies into traditional treatment regimens(A. Mamatov et al., 2023). Overall, a combination of early diagnosis, appropriate antimicrobial therapy, timely surgical intervention, and comprehensive rehabilitation forms the cornerstone of preventing purulent complications in pediatric hematogenous osteomyelitis(Charles R. Woods et al., 2021; Mathie Lorrot et al., 2023; Maximillian Mifsud & Martin A McNally, 2023; Xueqin Zhang et al., 2024).

Advances in treatment modalities to reduce complications. Recent advancements in the treatment of pediatric hematogenous osteomyelitis have focused on reducing complications through improved antibiotic stewardship, resistance management, and the integration of adjunctive therapies. The Pediatric Infectious Diseases Society and the Infectious Diseases Society of America have developed guidelines emphasizing the importance of early diagnosis and tailored antibiotic regimens based on culture and susceptibility findings to manage acute hematogenous osteomyelitis (AHO) effectively(Charles R. Woods et al., 2021). Empirical antibiotic therapy often begins with high doses of intravenous cefazolin for methicillin-sensitive Staphylococcus aureus (MSSA), transitioning to oral antibiotics once clinical improvement is observed(Mathie Lorrot et al., 2023). For methicillin-resistant Staphylococcus aureus (MRSA) infections, prolonged intravenous antibiotic courses are recommended, sometimes necessitating surgical intervention(Xueqin Zhang et al., 2024). The use of local antibiotic therapy has been explored as an alternative to systemic treatments, aiming to reduce

bacterial resistance and improve outcomes(Chao Zhong et al., 2022). Additionally, adjunctive therapies such as hyperbaric oxygen therapy have been considered to enhance treatment efficacy, particularly in severe or refractory cases(Yash Jha & Kirti Chaudhary, 2022). Immunomodulators are also being investigated for their potential to modulate the immune response and improve recovery rates(Chao Zhong et al., 2022). Despite these advancements, challenges remain, particularly in managing antibiotic resistance and optimizing treatment duration to prevent recurrence and minimize side effects(Xukai Wang et al., 2023). The integration of multidisciplinary approaches, including orthopedic consultation and the use of advanced imaging techniques, is crucial for accurate diagnosis and effective management of AHO in children("Acute Bone and Joint Infections in Children: Current Concepts," 2022). Overall, while significant progress has been made, ongoing research and consensus-building efforts are essential to refine treatment protocols and improve patient outcomes in pediatric osteomyelitis(Andrzej Krzysztofiak et al., 2021).

Outcomes and prognostic factors. The prognosis of pediatric hematogenous osteomyelitis is influenced by several factors, including the timing of intervention, disease severity, and location, as well as potential long-term sequelae such as functional impairments and growth disturbances. Early diagnosis and timely intervention are crucial, as delays can lead to poor outcomes. For instance, a longer time to diagnosis and prolonged fever despite antibiotic treatment are associated with worse prognoses(Adriana Sarmiento Clemente et al., 2022; Jiale Guo et al., 2024). Disease severity, often assessed using severity scores, plays a significant role in predicting complications. The Accelerated Severity of Illness Score, which includes factors like triage tachycardia, tachypnea, and high initial C-reactive protein levels, has been shown to effectively predict complicated osteomyelitis, with a high area under the curve (AUC) of 0.96(Tahmina A Jahan et al., 2024). The location of the infection also matters; for example, tibia involvement is linked to both acute and chronic complications(Adriana Sarmiento Clemente et al., 2022). Methicillin-resistant Staphylococcus aureus (MRSA) infections are particularly challenging, often requiring prolonged intravenous antibiotics and sometimes surgical intervention(Adriana Sarmiento Clemente et al., 2022; Xueqin Zhang et al., 2024). Long-term sequelae such as growth disturbances, limb length discrepancies, and chronic osteomyelitis are significant concerns, with about 13.5% of patients experiencing chronic complications. Predictive scores like the A-SCORE and C-SCORE help in assessing the risk of acute and chronic complications, respectively, and guide management and follow-up decision(Adriana Sarmiento Clemente et al., 2023). Overall, a combination of early intervention, accurate severity assessment, and careful monitoring of high-risk patients is essential for improving outcomes in pediatric hematogenous osteomyelitis.

Gaps in research and future directions. Current research on the prevention of pediatric hematogenous osteomyelitis reveals several gaps, particularly in early diagnosis and management. Despite advancements, traditional diagnostic methods remain significant due to the limitations of modern techniques, which are often effective only after the disease has progressed for several days("Questions of Diagnosis and Treatment of Acute Hematogenous Osteomyelitis of the Hip Joint Bones in Children," 2023). The lack of high-quality, updated data on the diagnosis and management of acute hematogenous osteomyelitis (AHO) in children further exacerbates these challenges(M. Alanazi et al., 2023). Emerging trends such as artificial intelligence (AI) and personalized medicine offer promising solutions to these gaps. Machine learning algorithms have been employed to identify potential biomarkers like MPO, PRTN3, and CTNND1, which show strong diagnostic potential and correlate with disease severity, thus aiding in early detection and monitoring(Jing Wang et al., 2024). Additionally, AI models, such as a Transformer-based deep learning model, have been developed to identify AHO and predict blood culture results, simplifying the diagnostic process and informing treatment decisions(Yingtu Xia et al., 2024). Personalized medicine approaches, including the Accelerated Severity of Illness Score, enhance the prediction of complicated AHO by identifying early predictors of severity, thereby guiding treatment and prognosis more effectively(Tahmina A Jahan et al., 2024). These innovations highlight the potential of AI and personalized medicine to address existing research gaps by improving early diagnosis, treatment planning, and outcome prediction in pediatric AHO.

Conclusion. Preventing purulent complications in pediatric hematogenous osteomyelitis is vital for minimizing morbidity and long-term disabilities. Early diagnosis, tailored antimicrobial regimens, and effective surgical interventions play pivotal roles. Advances in diagnostics and adjunctive therapies offer new opportunities to improve outcomes. Addressing current research gaps and integrating innovative approaches, such as AI and personalized medicine, will further enhance the management and prevention of complications, ensuring better quality of life for affected children.

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