Small risk of osteoarticular infections in children with asymptomatic oropharyngeal carriage of Kingella kingae

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Abstract

The aim of this study was to evaluate the absolute risk for children younger than 4 years of age with asymptomatic oropharyngeal carriage of Kingella kingae to sustain an osteoarticular infection. The rate of K. kingae carriage in the oropharyngeal mucosa was 9% among healthy children, and the risk for an asymptomatic carrier to develop an osteoarticular infection due to K. Kingae was estimated to be lower than 1%.


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that in our case, the source of his infection was likely to be from his mother because the child had no contact with animals. The infant’s mother reported a history of a persistent cough before the infant’s illness, and \( B. \) bronchiseptica was isolated from her sputum. \( B. \) bronchiseptica has the ability to inhibit leukocyte function and to adhere to respiratory epithelial cells,\(^1\) which could explain the persistence in the lower respiratory tract of both individuals. Our assumption on the direction of transmission is speculative because the mother was not screened for \textit{Bordetella} at the time in which the child had his first positive culture.

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K \textit{Kingella kingae} is the major bacterial cause of osteoarticular infection in children less than 48 months of age.\(^1\)–\(^3\) This organism is a frequent component of the oropharyngeal flora of young children and is readily transmitted from person to person.\(^4\) There is evidence suggesting that it colonizes the oropharynx before penetrating the bloodstream and invading distant organs,\(^6\) such as joint and bone.\(^7\) Administration of a short antibiotic course has been recently recommended for contacts between 6 and 48 months of age when disease clusters are detected,\(^8\) but investigations of the epidemiologic features of asymptomatic respiratory carriage have not demonstrated any correlation between the pattern of carriage of \textit{K. kingae} and the incidence of invasive disease.\(^7\) We conducted this study to investigate the oropharyngeal carriage of \textit{K. kingae} in a Swiss pediatric population aged between 6 and 48 months and to estimate the prevalence of osteoarticular infection caused by \textit{K. kingae}. In addition, we assessed the correlation between asymptomatic carriage and the subsequent incidence of osteoarticular infection due to \textit{K. kingae}, including the probability for an asymptomatic carrier to sustain an osteoarticular infection due to this pathogen.

METHODS

Study Design and Patients

In this prospective, consecutive study, we collected the data of all children aged 6–48 months admitted to the emergency department of the Geneva Children’s Hospital (111-bed tertiary pediatric hospital) with a suspicion of osteoarticular infection between January 1, 2008, and December 31, 2011. Eligible subjects underwent a clinical evaluation and blood analysis, and magnetic resonance imaging was performed on patients presenting clinical or laboratory findings suggestive for an osteoarticular infection and analyzed for signs of infection according to established criteria.\(^9\) Arthrocentesis or bone aspiration was performed under fluoroscopy guidance in the operating room for cases where imaging suggested osteoarticular infection.

In parallel, healthy children aged between 6 and 48 months were screened for asymptomatic oropharyngeal carriage of \textit{K. kingae} during the same period. Oropharyngeal specimens were obtained by rubbing a cotton swab on the tonsils and subsequently analyzed by real-time polymerase chain reaction (PCR) for \textit{K. kingae} as described earlier. Recruited children were either hospitalized for clean surgery, were attending our orthopedic outpatient clinic or visiting the emergency department for minor problems; children of hospital staff were also screened. Exclusion criteria were the presence of invasive diseases and the administration of antimicrobial drugs during the previous months.

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Kingella Colonization

\textbf{SMALL RISK OF OSTEARTICULAR INFECTIONS IN CHILDREN WITH ASYMPTOMATIC OROPHARYNGEAL CARRIAGE OF KINGELLA KINGAE}

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Abstract: The aim of this study was to evaluate the absolute risk for children younger than 4 years of age with asymptomatic oropharyngeal carriage of \textit{Kingella kingae} to sustain an osteoarticular infection. The rate of \textit{K. kingae} carriage in the oropharyngeal mucosa was 9% among healthy children, and the risk for an asymptomatic carrier to develop an osteoarticular infection due to \textit{K. kingae} was estimated to be lower than 1%.

Key Words: \textit{Kingella kingae}, osteoarticular infection, asymptomatic carrier, oropharyngeal, polymerase chain reaction
Analysis of aspirates included a Gram stain (aerobic/anaerobic) culture and PCR assays. All biologic samples (oropharyngeal swabs, synovial fluid, bone biopsy specimen, peripheral blood) were analyzed with a new real-time PCR assay specific to *K. kingae*. Each PCR analysis was performed in duplicate. If the specific *K. kingae* PCR assay was negative, osteoarticular samples were submitted to broad-range PCR assay.

The diagnosis of osteoarticular infection caused by *K. kingae* was established when cultures and/or specific PCR assays were positive for this microorganism in blood, synovial fluid or bone aspirate samples. Osteoarticular infection caused by other microorganisms was defined by the presence of bacterial growth other than *K. kingae* on synovial fluid, blood or bone aspirate cultures and/or by a positive result in the broad-range PCR. The diagnosis of presumed osteoarticular infection was assigned when joint fluid/bone samples were not obtained for diagnostic bacterial culture or PCR assay or when cultures were negative, but magnetic resonance imaging demonstrated conclusive signs of infection. The diagnosis of osteoarticular infection was excluded when there were no positive bacterial findings or signs of osteoarticular infection on magnetic resonance imaging, or when improvement occurred without treatment.

The protocol was approved by the local institutional review board (09-029R, Mat-Ped 09-008R), and the study was conducted in compliance with Good Clinical Practice guidelines and the Declaration of Helsinki.

### Statistical Analysis

The probability to sustain an osteoarticular infection due to *K. kingae* following a positive oropharyngeal PCR for *K. kingae* is equal to the positive predictive value (PPV) of the oropharyngeal PCR assay. The PPV can be derived from the sensitivity and specificity of the oropharyngeal PCR assay and the prevalence of *K. kingae* infection in the target population (PPV = p × Se/[p × Se + (1−p)×(1−Spe)]), where *p* is the prevalence in the target population, *Se* is the sensitivity of the oropharyngeal PCR assay and *Spe* is the specificity of the oropharyngeal PCR assay. The 95% confidence interval (CI) of the PPV is derived by applying the formula to the bounds of the 95% CI for sensitivity and specificity (box method).

### RESULTS

Between January 1, 2008, and December 31, 2011, 64 consecutive patients met the eligible criteria for osteoarticular infection. Among these patients, 45 had *K. kingae* osteoarticular infection confirmed by culture or positive PCR from blood, bone or joint aspirate samples. Three had positive cultures for other microorganisms: *Haemophilus influenzae* (1 case); methicillin-sensitive *Staphylococcus aureus* (1 case); and *Streptococcus pneumoniae* (1 case). No organism was detected in the remaining 16. Among the latter patients, 6 presented radiologic and clinical findings of spondylodiscitis, but did not undergo disc-vertebral puncture. Ten cases showed imaging findings consistent with osteoarticular infection, but both cultures and PCR assays were negative, possibly due to difficult access to the infection site and/or low bacterial load.

Using the demographic census of the Geneva district, which reported a mean number of 16,950 children aged between 6 and 48 months per year during the study period, we calculated that the estimated proportion of young patients with an osteoarticular infection due to *K. kingae* in 1 year was less than 1% (p = 11.25/16,950 = 0.0664%).

Sensitivity of oropharyngeal PCR assay was assessed in a sample of 27 patients with osteoarticular infection caused by *K. kingae* confirmed by positive PCR assays specific for this microorganism on blood, synovial fluid or bone aspiration. The oropharyngeal PCR assay was positive in all cases, yielding a sensitivity of 100% (95% CI: 87.2–100). The specificity of oropharyngeal PCR was assessed by screening 431 asymptomatic patients. The PCR was negative in 396 subjects, yielding a specificity of 91.9% (95% CI: 88.9–94.3).

The probability to sustain an osteoarticular infection due to *K. kingae* following a positive oropharyngeal PCR assay is equal to the PPV of the PCR assay and was calculated by applying the formula described in the Methods section. The PPV among the 6- to 48-month-old population of Geneva and its surroundings was 0.81% (95% CI: 0.52–1.14%).

### DISCUSSION

*K. kingae* is frequently isolated from the upper respiratory tracts of young children with a colonization rate ranging from 3.5% to 17.5%. Children usually first acquire *K. kingae* after the age of 6 months, the colonization rate then increases among infants aged between 12 and 24 months and finally declines among older children and adults. The present epidemiologic study confirmed a similar respiratory carriage rate in a Swiss pediatric population (9%), suggesting that asymptomatic colonization of the upper respiratory tract by *K. kingae* is probably a worldwide phenomenon. Similar to microorganisms such as *S. pneumoniae*, *H. influenzae* type b or *Neisseria meningitidis*, *K. kingae* is able to penetrate the bloodstream, disseminate and invade distant organs. Asymptomatic colonization of the upper respiratory tract is thus a strategy for *K. kingae* to survive and occasionally spread into the bloodstream under certain circumstances. A recent report described 3 patients with invasive *K. kingae* infections in whom the identical genotype isolate was recovered from the pharynx and the bloodstream. This observation supports the hypothesis that upper respiratory tract colonization represents the first step in the pathogenesis of invasive disease.

The correlation between asymptomatic carriage and the subsequent incidence of osteoarticular infection due to *K. kingae* remains unclear, even if prophylactic antibiotic administration has been recently recommended in an attempt to prevent further disease spreading during outbreaks of *K. kingae* among day-care center attendees. Nevertheless, previous investigations on the epidemiologic features of asymptomatic respiratory carriage have not demonstrated any correlation between the pattern of carriage of *K. kingae* and the incidence of invasive disease. The probability for asymptomatic children carrying *K. kingae* in the oropharynx to develop an osteoarticular infection due to this pathogen is probably lower than 1%. Oropharyngeal carriage of *K. kingae* does not imply the subsequent development of invasive infection and suggests that other cofactors may play a role in the pathogenesis of invasive *K. kingae* infections.

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### REFERENCES


**POSTVARICELLA THROMBOSIS—REPORT OF TWO CASES AND LITERATURE REVIEW**


**Abstract:** Varicella (chickenpox) is a common disease of childhood, caused by varicella-zoster virus. Postviral thromboembolism is a rare complication of varicella-zoster virus in childhood. We describe 2 children who developed lower limb deep venous thrombosis shortly after varicella infection, along with a review of 130 previously reported cases.

**Key Words:** varicella, chickenpox, thrombosis, deep venous thrombosis, protein S deficiency, antiphospholipid antibody

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**Figure 1**

A and B, Doppler ultrasound demonstrating thrombus (A—arrows) in left common femoral vein (CFV), the left superficial femoral vein (SFV) and popliteal vein (POP) and its resolution (B).