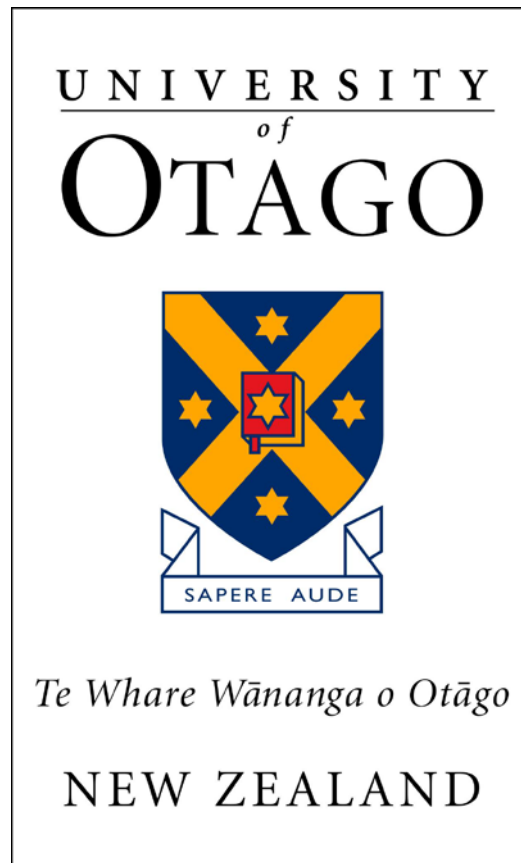


Pre-school osteoarticular infection (POI) study

Study protocol



Dr Tony Walls - Paediatric Infectious Diseases Consultant, University of Otago, Christchurch

Dr Laudi Olijve – Research Assistant, Department of Paediatrics, University of Otago, Christchurch

Study investigators and roles

University of Otago, Christchurch

Principal investigator:	Dr Tony Walls MB ChB, FRACP, MD (Lond.) Senior Lecturer – Paediatric Infectious Diseases, tony.walls@otago.ac.nz
Study coordinator:	Dr Laudi Olijve laudi.olijve@otago.ac.nz
Contact information:	Department of Paediatrics, University of Otago, Christchurch School of Medicine PO Box 4345, Christchurch 8041, New Zealand Phone: +64 3 3640 747 / +64 21 279 0539 Fax: +64 3 378 6355 www.otago.ac.nz/christchurch/departments/paediatrics/

Local sites

Local supervisor (to be arranged)	Paediatrician, Infectious Diseases Specialist or Orthopaedic Surgeon - Provides supervision and support for trainee.
Local trainee (to be arranged)	Trainee in Paediatrics, Infectious Diseases or Orthopaedics - Obtains ethics approval - Obtains locality approval - Searches for and includes cases - Data entry in REDCap database

Introduction

Osteoarticular infections are a significant problem in young children and the course of disease and most appropriate treatment depends on the causative organism. More frequent use of PCR has changed current understandings of the microbiological epidemiology of these infections. Several studies have reported *Kingella kingae* to have become the major cause of osteoarticular infections in young children.(1-3) The POI study will be the first multicentre, multinational study to describe the microbiological epidemiology of osteoarticular infections in young children. Data will be collected from sites across Australia and New Zealand by retrospective searches in hospital records for diagnosed cases of osteoarticular infections. Data will be stores centrally for analysis of demographic, clinical and microbiological characteristics.

Background information

Septic arthritis and osteomyelitis are a significant problem in young children. A prompt and accurate diagnostic and therapeutic management of septic arthritis and osteomyelitis is essential for good practice. Early antibiotic initiation reduces the risk of adverse outcomes and permanent sequelae.(4, 5) Local epidemiological data and reliable microbiological detection methods play a central role in the final clinical management and in the development of guidelines.

Important factors in the spectrum of microorganisms involved in osteoarticular infections are the age of the patient and the geographical location. To date no large multinational studies describing the microbiological epidemiology of bone and joint infections in children have been performed. Data on osteoarticular infections in the Australia and New Zealand region are limited to studies describing smaller geographical areas.(6-11) However, osteoarticular infections seem to be more common in

this region than in many other parts of the world,(6, 12, 13) possibly due to a higher risk of infections in indigenous populations.(6, 8)

Paediatric bone and joint infections seem to be most common in children under 4 years of age.(1, 14) This is also the age-group where the most common causative bacteria have changed in recent years due to improvements in microbiological detection methods. Since the introduction of a PCR for *Kingella kingae*, this microorganism has emerged as a major cause of bone and joint infections in young children and the rate of culture negative infections has dropped consequently.(1) A previous study performed in Christchurch Hospital retrospectively found a high number of culture-negative osteoarticular infections in the age-group of 1-2 year old children, which is the group where *K. kingae* infections peak (Figure 1). This suggests that many invasive *K. kingae* infections remain undetected in Christchurch Hospital.(15)

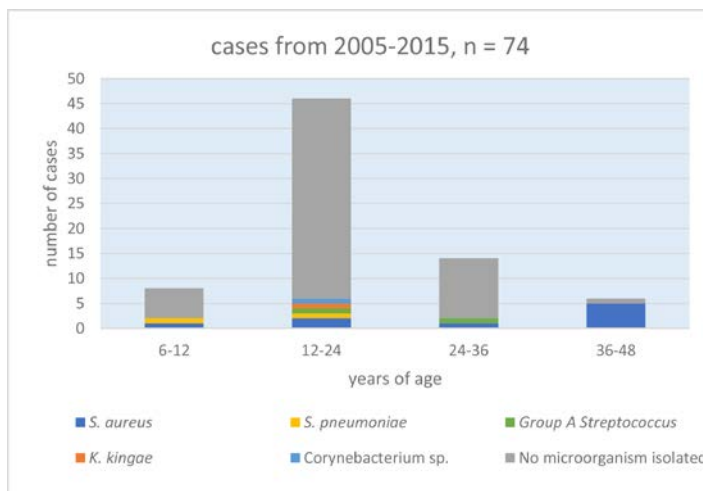


Figure 1: Microorganisms isolated in cultures from 74 children between 6 and 48 months with an osteoarticular infection in Christchurch Hospital from 2005-2015.

Research aims

- 1) To describe the burden of disease due to pre-school osteoarticular infections in Australia and New Zealand.
- 2) To describe the microbiology and epidemiology of bone and joint infections in pre-school aged children across Australia and New Zealand.

Study design and population

The POI study is a retrospective review of all bone and joint infections occurring in children between 3 months and < 5 years of age at multiple sites across Australia and New Zealand.

- As many sites as possible across the region are invited to participate. This study is endorsed through the ANZPID (Australia and New Zealand Paediatric Infectious Diseases) research network.
- Data will be collected over a 5-year period: January 2011 to end December 2016
- Cases will be identified by discharge coding and verified through review of the discharge summary or electronic notes.
- Data will be entered into a REDCap database – individual sites will have access to all their own data. Data will be stored centrally in a non-identifiable format.

Inclusion criteria:

- Community-acquired bone and joint infections
- Aged 3 months to < 5 years of age
- Clinical presentation consistent with acute osteomyelitis or septic arthritis (or both, including spondylodiscitis) with at least 1 of the following parameters at initial presentation to hospital:

- Pain
- localised inflammation (warmth or swelling)
- abnormal limb function

AND radiological imaging consistent with osteomyelitis/septic arthritis

AND at least 1 of the following

- raised inflammatory markers (CRP>5 mg/L, or ESR >20mm/hr),
- leukocytosis (>12,000 WBC/mm³) or leukopaenia (<4,000 WBC/mm³)
- fever >38°C

OR (if radiological confirmation not available) culture or PCR detection of a compatible organism obtained from a sterile site

Exclusion criteria:

Children with penetrating injuries, infections complicating previous surgery or other iatrogenic bone or joint infections will be excluded.

Infections occurring in children with known primary immune deficiencies

Data collected and study outcomes:

Primary outcomes

Specific microorganisms causing POI

Secondary outcomes

- Demographic data: age, gender, primary ethnicity.
- Microbiology – tests used, sample site
- Radiology – modality of imaging used for diagnosis
- Clinical data: site of infection, length of stay in hospital, empiric antimicrobials (administered before or after taking microbiological samples), definitive treatment and planned duration of treatment.

Data analysis

Results will be of a descriptive nature. We will describe the proportions of children at each site with culture negative bone and joint infections and the proportions positive for each of the common pathogens. In addition we will compare rates of detection of *K. kingella* in sites who routinely use molecular diagnostic methods for detection compared to those who do not have this available.

A biostatistician will support the statistical analysis.

Ethical considerations

As this is an observational retrospective study few ethical issues may be raised. There will be no consequences of data collection for individuals and the privacy of studied individuals will be maintained by storing information in a non-identifiable format.

Significance

This study will be the first multicenter multinational study to describe the microbiological epidemiology of osteoarticular infections in young children. Understanding of the occurrence of different microorganisms is important for clinical decision making and the development of guidelines. Information about the proportion of culture negative infections will evaluate the adequacy of routinely used diagnostic methods.

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