Paediatric acute haematogenous osteomyelitis: Identification of bacterial genes and phenotype that predispose to adverse health outcomes.

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Hospital: Starship Hospital **Start date:** 1/2/2022 **End date:** Ongoing

Specific Aims and Objectives:
Paediatric acute haematogenous osteomyelitis (PAHO) is caused by bacteria that have gained access to the blood stream, infecting child, and adolescent bone adjacent to the growth plate. Children present with pain in the affected limb, with the majority successfully treated with antibiotics. A subgroup of patients, primarily Māori and Pacific Islander, are more likely to experience complications such as multi-focal sepsis, multiple surgical washouts, multi-organ failure, and need for intensive care support, despite the same treatment approach and no delay in presentation. Methicillin sensitive staphylococcus aureus (MSSA) is primarily identified, with little known about the virulence of specific strains and their influence on adverse outcomes. *Objective:* To identify bacterial genes and phenotype in MSSA strains collected from children with PAHO that correlate with adverse outcomes.
Methods:
95 bacterial isolates, collected from children with PAHO treated at starship children's hospital, were genotyped, and analysed for their planktonic and biofilm antibiotic sensitivity using the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) assay. The in-vitro data was compared with clinical outcomes categorised as complicated (MSSA infection with chronic or recurrent disease, treated with ≥8 weeks of antibiotics) vs uncomplicated (MSSA infection without relapse, ≤6.5 week course of antibiotics).
Results:
Preliminary analysis identified 85 as MSSA by genotype; 29 complicated (69% Māori or Pacific Islander), 47 uncomplicated (43% Māori or Pacific Islander), 9 required intensive care (89% Māori or Pacific Islander). 31 unique strains were identified; 7 complicated, 17 uncomplicated, 7 overlapped. Two phylogenetic tree clusters contained a predominant grouping of complicated strains. 100% of MSSA isolates were sensitive to flucloxacillin, however 33% of isolates demonstrated an MBC discordant with its MIC, effectively increasing the required concentration required to kill bacteria, reaching the threshold for antibiotic resistance.
Discussion OR Conclusion:
This study demonstrates the practical application of bacterial genotyping and antibiotic sensitivity to yield clinically relevant information. While this study is in its infancy, the dual analysis of bacterial genome sequencing and in-vitro phenotyping holds promise and paves the way for understanding the link between the bacterial pathogen and its ability to cause severe infection in specific groups of children with PAHO. In this study we identified specific strains (by genotyping) of MSSA are causing a more complicated clinical course. Further research looking into the presence or absence of specific virulence factor and biofilm genes within these complicated strains would shed further light on the disparities we see between children with a complicated and non-complicated clinical course. In addition, further clinical data such as the housing conditions, and smoking status of the household, would aid in the clarification of why these cohort of children have a higher prevalence of more virulent strains of MSSA.

What was your involvement in this research? This research was part of my PhD. I was the lead surgeon for the animal operations, and the lead person that conducted the laboratory assays.