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Title: RAPID MOLECULAR TESTING AIDS TIMELY DIAGNOSIS OF STREP A INFECTION IN NEW ZEALAND CHILDREN WITH ACUTE RHEUMATIC FEVER

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Background & Aims: Evidence of antecedent pharyngeal group A Streptococcus (StrepA) infection is required for the diagnosis of acute rheumatic fever (ARF), either by elevated streptococcal serology or pharyngeal culture. Access to serology and microbiology testing is limited in many endemic regions. Middlemore Hospital in South Auckland, New Zealand serves an urban population with a high incidence of ARF (23/100, 000/year in persons<30years), inequitably affecting indigenous MĀori and Pacific peoples. In 2020, the Xpert® Xpress Strep A, a qualitative rapid polymerase chain reaction (PCR) test, was introduced to aid timely diagnosis of StrepA pharyngeal infections at Middlemore Hospital.

Methods: We sought to evaluate the utility of the Xpert® Xpress Strep A in confirming StrepA pharyngeal infection among individuals with ARF at Middlemore Hospital. Observational retrospective study amongst persons ≤18years hospitalised with suspected ARF April 2020 - April 2023. Cases were identified from the hospital rheumatic fever database and review of ICD10 discharge codes. Clinical and laboratory data was collected, including details of throat swab collection in hospital and at community laboratories in the four weeks prior to hospitalisation. At the community laboratory, standard culture was performed. At the Middlemore Hospital laboratory, specimens underwent initial Xpert® Xpress Strep A testing. Specimens with a negative Xpert® Xpress Strep A result were discarded, due to high negative predictive value previously ascertained at our institution (Taylor et al, Journal of Clinical Microbiology, 2021). Specimens with a positive Xpert® Xpress Strep A result underwent culture. American Heart Association Jones Criteria were applied.

Results: There were 95 cases of ARF (87 Definite, 8 Probable). Median age at ARF diagnosis was 11.8 years (range 5.3 - 18.7 years) and 34/95 (36%) were female. Most cases had carditis (71/95, 75%) and a minority, (7, 7%), had chorea. A throat swab was obtained in 83/95 (87%) of ARF cases; 20/95 (21%) had a throat swab submitted to a community laboratory in the four weeks prior to admission and in 63/95 (66%) a throat swab was collected on admission to hospital. Overall, StrepA was isolated by culture in 52/95 (55%) of the ARF cases. Xpert® Xpress Strep A testing was performed on 54/63 swabs tested at Middlemore Hospital and was positive in 42/54 (78%) of swabs tested. PCR results were reported within 24hours for 50/54 (93%) swabs. Minimum reporting time was 1.5 hours. Positive Xpert® Xpress Strep A results were concordant with positive culture results in 28/42 swabs but in 14/42 instances, there was a discordant result with positive Xpert® Xpress Strep A and negative culture. Among the 14 discordant cases with positive Xpert® Xpress Strep A and negative culture, 12 children had Definite ARF and 2 had probable ARF.

Conclusions: The 14 additional Xpert® Xpress Strep A positive, culture negative cases increased the overall identification of StrepA in this cohort from 52/95 (55%) to 66/95 (69%). Almost 80% of Xpert® Xpress Strep A tests were positive in this group of children with carefully characterised ARF. The Xpert® Xpress Strep A and similar rapid PCR tests may aid timely diagnosis and inform management of children with suspected ARF, particularly in settings where access to serology or culture is not available. The role of rapid molecular tests should be considered in the next update of the Jones criteria.