Impact of systematic TB detection using Xpert Ultra on nasopharyngeal aspirates and stool samples on mortality in children with severe pneumonia

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Background

In children with severe pneumonia, TB is usually considered only in case of prolonged symptoms or antibiotic failure, leading to missed or delayed TB diagnosis. Systematic screening with molecular assays could increase TB case detection and thus reduce child mortality.

Methods

From April 2019 to June 2021, we implemented a stepped-wedge cluster randomized trial in 15 hospitals from 6 high TB incidence countries. Children aged <5 years with WHO-defined severe pneumonia received either the WHO standard of care (SOC) – control arm – or SOC plus Xpert MTB/RIF Ultra (Ultra) on 1 nasopharyngeal aspirate (NPA) and 1 stool sample at hospital admission, followed by immediate treatment if positive – intervention arm. Hospitals were randomly selected to switch from the control to the intervention at 5-week intervals. We assessed the impact of the intervention on 12-week mortality using a generalized linear mixed effect model adjusted on severe acute malnutrition and baseline peripheral oxygen saturation (SpO2).

Results

We enrolled 1401 and 1169 children in the control and the intervention groups, respectively. 71 (5.1 %) and 87 (7.4%) children were initiated on TB treatment in the control and intervention groups, respectively (p=0.012). In the intervention arm, 1007 (97.4%) children had NPA collected, 850 (82.2%) had stool collected, and 24 (2.1%) had positive Ultra on either sample, contributing to 29% microbiological confirmation of TB (24/87). At 12 weeks, 110 (7.9%) and 90 (7.7%) had died (p=0.868) in the control and intervention groups, respectively, and 60 (30%) deaths occurred within 48 hours of admission. The intervention was not associated with decreased mortality [adjusted OR: 0.95 (95%CI 0.58 -1.58)].

Conclusion

Screening with Ultra at the time of admission did not lead to reduced mortality in children with severe pneumonia. High TB treatment initiation and microbiological confirmation rate support the more systematic use of Ultra in this vulnerable group.