Microbiological Diagnosis of Tuberculosis in Children – A Prospective Study of Microbiological Yield in Low-Middle Income Countries

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Objective

- To describe the microbiological yields for TB in children from 5 high burden countries

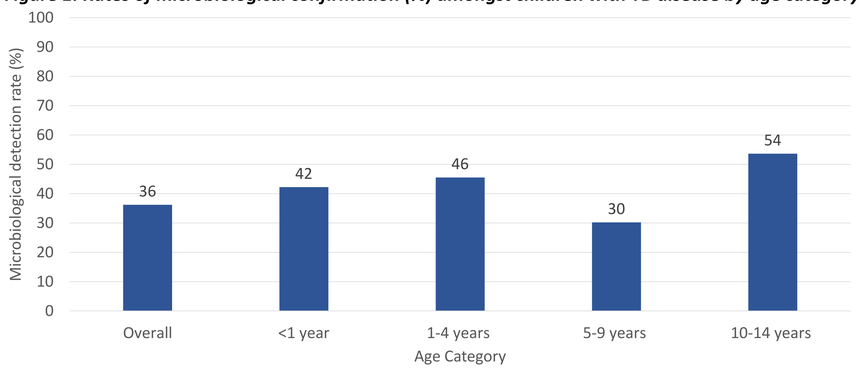
Methods

- A prospective study enrolling children (<15yrs) with suspected TB from 5 low-middle income countries
- Samples collected: 2 sputum/gastric lavage (GL)
  1 nasopharyngeal aspirate (NPA) if <5yrs
  Extrapulmonary specimens according to local guidelines
- Confirmed TB if M. tuberculosis (MTB) detected on Ultra and/or culture
- Incremental yield calculated in children with samples tested by Ultra and two serial cultures

Results

- 965 participants with valid microbiological results
- 2299 samples collected, 93.8% (2157) respiratory specimens:
  - 59% (1273/2299) induced sputa
  - 18% (389/2299) spontaneous sputa
  - 15% (332/2299) NPA
  - 7% (151/2,299) GL
- Microbiological confirmation obtained in 36.2% (239/661) of children with TB disease

Figure 1: Rates of microbiological confirmation (%) amongst children with TB disease by age category



- Children with confirmed TB had MTB detected on:
  - 42% (98/239) induced sputum alone
  - 21% (49/239) extrapulmonary samples alone
  - 15% (36/239) spontaneous sputum alone
  - 15% (35/239) >1 specimen type alone
- Children <5 years with confirmed MTB had MTB detected on:
  - 62% (63/102) Induced sputum alone
  - 4% (4/102) NPA alone
  - 3% (3/102) Gastric lavage alone
  - 13% (13/102) >1 specimen type

Figure 2: Overview of microbiological confirmation stratified by microbiological detection method

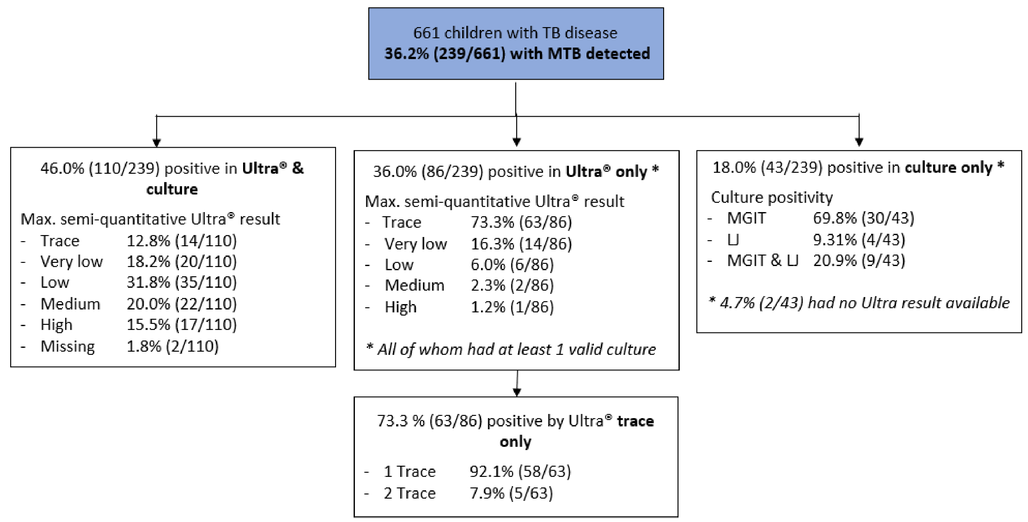


Table 1: Incremental yield of Ultra and first and second cultures performed on serial samples among children with TB disease

Method of testing	Total (n)	Test positive	Additional yield (n)	Cumulative Yield, %
All children with TB disease				
Sputum				
Ultra 1	406	106	-	26.1%
Culture 1	406	72	12	29.6%
Culture 2*	406	60	17	35.0%
Gastric lavage				
Ultra 1	49	19	-	38.8%
Culture 1	49	13	2	42.9%
Culture 2*	49	6	0	42.9%
Any specimen types combined				
Ultra 1	455	116	-	25.5%
Culture 1	455	85	17	29.2%
Culture 2*	455	80	17	33.0%
Children <5 years in the overall cohort				
Sputum				
NPA Ultra 1	121	18	-	14.9%
Sputum Ultra 1	121	35	20	31.4%
Sputum Culture 1	121	23	8	38.0%
Sputum Culture 2*	121	23	7	43.8%

Abbreviations: NPA = nasopharyngeal aspirate.
Gastric Lavage done primarily at one site.

- *Calculated for children with at least one serial Ultra and culture*
- ***For all with TB disease**, the denominator is number of children with a result for first Ultra (Ultra 1) and first culture (Culture 1)*
- ***For <5years**, the denominator is number of children with results for first Ultra on NPA (NPA Ultra 1), first sputum Ultra (Sputum Ultra 1), and first sputum culture (Sputum Culture 1)*
- *Not all had a second culture*

Conclusions

- One of the highest rates of microbiological confirmation reported in children
- Demonstrates added diagnostic value of Ultra “trace” detection
- Highlights the benefit of sequential sampling

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