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Evaluation of a Blood-based Antigen Test for Tuberculosis in Infants

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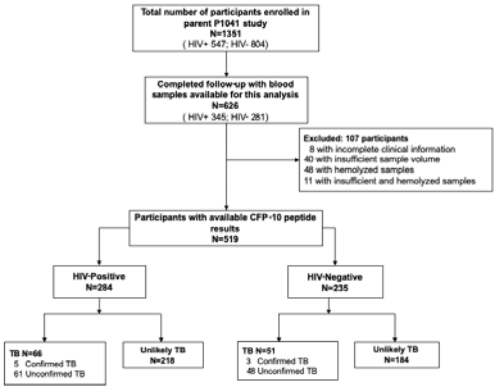
BACKGROUND

- Improved non-sputum methods are urgently needed for tuberculosis (TB) diagnosis and treatment monitoring in children.
- A blood-based assay exhibited a good diagnostic yield and monitoring potential in adults in previous study.
- Therefore, we aimed to evaluate the performance of this assay, which detects and quantifies a TB-specific CFP-10 peptide, for TB in HIV-exposed infants from a multicenter TB prevention trial conducted in southern Africa (IMPAACT P1041).

METHODS

- Cryopreserved sera from 519 HIV-exposed children (284 HIV-infected, 235 HIV-uninfected) were evaluated for CFP-10 peptide expression.
- BCG-immunized, TB-disease-negative children aged 91-120 days were randomized to isoniazid or placebo and followed for up to 192 weeks for TB infection and disease.
- For this analysis, children were classified as Confirmed, Unconfirmed, or Unlikely TB cases using 2015 NIH Pediatric TB diagnostic criteria based on clinical, laboratory, histopathological, and radiological evaluations.



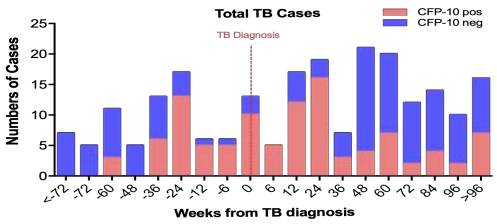
RESULTS

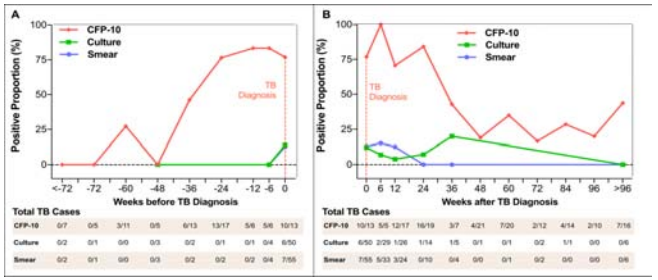
- Detection of serum CFP-10 peptide exhibited 100% sensitivity for Confirmed (5/5, 95% confidence interval [CI], 47.8–100) and 83.7% sensitivity for Unconfirmed (36/43, 95% CI, 69.3–93.2) TB cases in HIV-infected children, with 93.1% (203/218, 95% CI, 88.9–96.1) specificity. In HIV-uninfected children, serum CFP-10-positivity detected the single Confirmed TB case and 15 of 20 Unconfirmed TB cases (75.0%; 95% CI, 50.9–91.3), with 96.2% (177/184, 95% CI, 92.3–98.5) specificity.

Table . Diagnostic Performance of CFP-10 Peptide Assay for TB.

	Confirmed TB	Unconfirmed TB	Unlikely TB
All participants (N=471)			
CFP-10 + – no. (%)	6 (100)	51 (81.0)	22 (5.5)
CFP-10 - – no. (%)	--	12 (19.0)	380 (94.5)
Sensitivity – % (95% CI)	100 (54.1-100)	81.0 (69.1-89.8)	--
Specificity – % (95% CI)	--	--	94.5 (91.8-96.5)
HIV-positive participants (N=266)			
CFP-10 + – no. (%)	5 (100.0)	36 (83.7)	15 (7.7)
CFP-10 - – no. (%)	--	7 (16.3)	203 (92.3)
Sensitivity – % (95% CI)	100 (47.8-100)	83.7 (69.3-93.2)	--
Specificity – % (95% CI)	--	--	93.1 (88.9-96.1)
HIV-negative participants (N=205)			
CFP-10 + – no. (%)	1 (100)	15 (75.0)	7 (4.3)
CFP-10 - – no. (%)	--	5 (25.0)	177 (96.2)
Sensitivity – % (95% CI)	100 (2.5-100)	75.0 (50.9-91.3)	--
Specificity – % (95% CI)	--	--	96.2 (92.3-98.5)

- Most (72.7%) CFP-10-positive subjects with Unlikely TB diagnoses also had at least one criterion for TB diagnosis (11/15; 73.3% HEI and 5/7; 71.4% HEU).
- For TB cases, CFP-10 peptide signal was detected in serum up to 60 weeks before TB diagnosis, and its diagnostic sensitivity reached 76.5% (13/17, 95%CI, 50.1-93.2%) at ≤ 24 weeks before diagnosis.





- CFP-10 peptide positivity and expression levels declined following anti-TB therapy initiation and raised at the late period treatment ended, when participants exhibited secondary TB diagnosis.

CONCLUSIONS

- CFP-10 peptide positivity and expression levels declined following anti-TB therapy initiation and raised at the late period treatment ended, when participants exhibited secondary TB diagnosis.

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