

Innovative laboratory tools to improve tuberculosis diagnosis in children



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INTRODUCTION

- Tuberculosis (TB) is an important cause of morbidity and mortality in children
- >50% of children with TB are never diagnosed

Microbiological confirmation is low (<30%). In the contexts where we work, majority diagnosed on clinical grounds, very limited access to X-rays, low access to TB culture.

- TB-LAM is recommended for diagnosing people living with HIV
- Guinea-Bissau and South Sudan are two high burden countries for HIV, TB and malnutrition
- MSF OCBA (Operational Cell Barcelona-Athens) worked at Simão Mendes hospital in Bissau, the capital of Guinea-Bissau and supports 2 hospitals in Malakal (South Sudan)



Photo: Two patients with staff members

Aim of the study:

- To determine the sensitivity & specificity of Xpert-Ultra in stools and urine samples, as well as TB-LAM positivity rate in presumptive pediatric TB cases in two high TB burden settings.

METHODOLOGY

- This cross-sectional multicentric study took place at Simão Mendes hospital from July 2019 to April 2020, and in Malakal hospitals from April 2021 to November 2022
- Children between 6 months and 15 years with presumptive TB underwent clinical and laboratory assessment, with one respiratory or extrapulmonary sample (gold standard (GS)), one stool and one urine samples analyzed with Xpert-Ultra
- Starting July 2021, TB-LAM test was added for all children.



In low resource settings where access to TB culture is limited and TB confirmation is low, using non-invasive samples such as stools proved to have good sensitivity and an added diagnostic yield

This study was approved by the MSF Ethics Review Board (ERB) and by the Guinea-Bissau and South Sudan Ministries of Health National Ethical Boards

RESULTS I: Xpert in stools and urine

- A total of 441 children were enrolled from Bissau (n=133) and Malakal (n=308); 214 (49%) were female.
- Median (IQR) age was 4.5 (1.5-9) years old.
- HIV infection and severe acute malnutrition (SAM) were found in 89 (20%) and 251 (57%), respectively.
- Confirmation of TB was achieved in 76 (17%); 198(44%) had unconfirmed TB, and 167(39%) had unlikely TB.

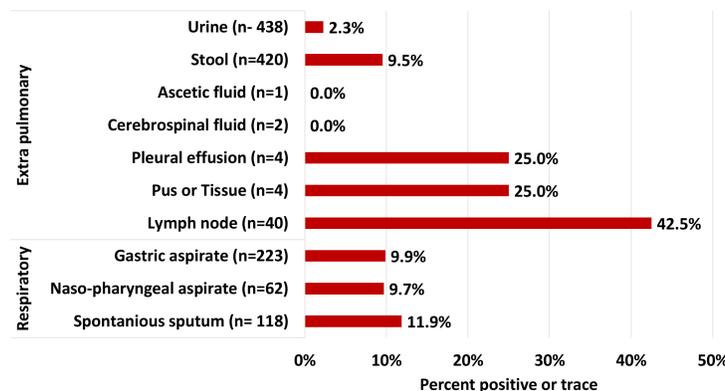


Fig 1: Xpert-Ultra positivity by sample

- Of the 441 with GS diagnosis, the overall yield of positive TB results was 13% (59/441): 10% (42/408) in pulmonary samples and 37% (19/51) in extrapulmonary samples.
- A total of 410 and 160 samples were used to evaluate Xpert-Ultra on stool and Xpert-Ultra on urine, respectively.
- Compared to GS, sensitivity (Se) and specificity (Sp) of Xpert-Ultra on stools were 69.4%(95% CI:55.5-80.5) and 98.3%(95% CI: 96.4-99.2), respectively.
- Compared to GS, Se & Sp of Xpert-Ultra on urine were 12.1% (95%CI: 6.0-22.9) and 99.2% (95%CI :97.7-99.7), respectively.
- Eight patients were positive with stools or urine Xpert result but negative with GS.

RESULTS II: urine TB LAM

- A total of 160 children were enrolled with 87 (54%) females and a total of 87 (54%) children under 5.
- HIV infection and severe acute malnutrition (SAM) were found in 17 (10.6%) and 88 (55%), respectively.
- Microbiological confirmation of TB was achieved in 28 (18%); 71(44%) had unconfirmed TB, and 61 (38%) had unlikely TB.

		TB-LAM negative	TB-LAM positive grade				Positive	Total
			1	2	3	4		
Age	<5	40 (67.8%)	5 (8.5)	2 (5%)	6 (10.2%)	2 (3.4%)	19 (32.2%)	59 (100%)
	5 to 15	36 (90%)	2 (5%)	2 (5%)	0	0	4 (10%)	40 (100%)
HIV status	Positive	6 (35.3%)	5 (29.4%)	4 (23.5%)	2 (11.8%)	0	11 (64.7%)	17 (100%)
	Negative	70 (85.4%)	2 (2.4%)	4 (4.9%)	4 (4.9%)	2 (2.4%)	12 (14.6%)	82 (100%)
Nutritional status	SAM	41 (68.3%)	6 (10%)	5 (8.3%)	6 (10%)	2 (3.3%)	19 (31.7%)	60 (100%)
	MAM	21 (95.5%)	0	1 (4.5%)	0	0	1 (4.5%)	22 (100%)
	No malnourished	14 (82.4%)	1 (5.9%)	2 (11.8%)	0	0	3 (17.6%)	17 (100%)
Total		76 (76.8%)	7 (7.1%)	8 (8.1%)	6 (6.1%)	2 (2%)	23 (23.2%)	99 (100%)

Table 1: TB-LAM by grade in total TB cases* by age, HIV and nutritional status

- Overall, LAM positivity was 19% (30/160): 57% (16/26) in confirmed TB, 10% (7/71) in unconfirmed TB, and 12% (7/61) in unlikely TB patients.
- The positive predictive value among TB cases (confirmed or unconfirmed) was 76.7% (23/30) (95% CI: 59-88)
- The negative predictive value among unlikely TB cases was 41.5% (54/130) (95% CI: 33-50).
- The relative risk of positive LAM result among children who were under 5, HIV positive and SAM was 3.3 (95% CI: 1.5-7.8 , p= 0.002), 4.9 (95% CI: 2.8-8.4 , p=<0.001) and 3.3 (95% CI: 1.4-7.6, p=0.002), respectively.

CONCLUSIONS & IMPLICATIONS

- Xpert-Ultra in stools showed similar sensitivity and specificity than described in the literature and an added diagnostic yield when gold standard was negative.
- Sensitivity in urine was low but more research is needed to determine its clinical indication.
- Our findings suggest an additional potential diagnostic utility of urine TB LAM in presumptive TB patients under 5 or with severe acute malnutrition, in addition to the well-known role in people living with HIV.

TB LAM was significantly higher in children with TB and who were under 5, SAM and HIV

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