Can point-of-care ultrasound support tuberculosis diagnosis in children? The experience of MSF in Guinea-Bissau

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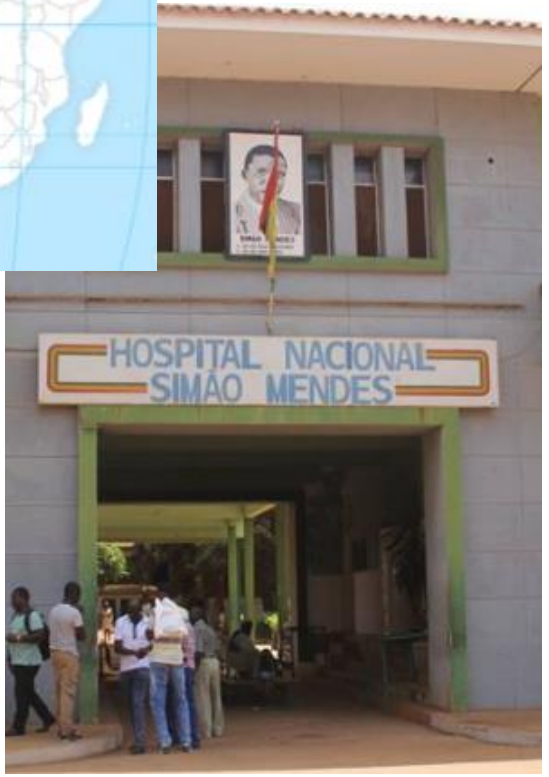
Conflict of Interest:
The author has declared no conflict of interest.

INTRODUCTION

CONTEXT

- 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 our contexts, majority diagnosed on clinical grounds, very limited access to X-rays, low access to TB culture
- Wider access to point of care ultrasound (POCUS), non-invasive, bed-side, inexpensive imaging tool
- TB-focused POCUS has been validated for adults with HIV *(FASH: focused assessment with sonography for HIV-associated TB)*
- Guinea-Bissau has a high burden of HIV, TB and malnutrition
- MSF OCBA (*Operational Cell Barcelona-Athens*) worked at Simão Mendes hospital in Bissau, the capital of Guinea-Bissau



INTRODUCTION

AIM

- To describe the performance and findings of TB-focused POCUS for children with presumptive TB at a tertiary care hospital in Bissau

METHODS (I)

- Observational study that took place from July 2019 to April 2020
- This study is part of a larger multicentric study also taking place in Malakal (South Sudan)
- We enrolled patients aged between 6 months and 15 years old with presumptive TB
- Clinical and laboratory assessment, with at least one sample analysed with GeneXpert Ultra
- POCUS-naïve local clinicians were trained on TB-focused methodology (128 hrs)
- Unblinded clinician performed the POCUS evaluation

METHODS (II)

- All children were evaluated by **8 sonographic signs**:

FASH methodology (6 signs): pleural effusion (2,4), pericardial effusion (1), ascites (3,5,6), liver focal lesions (3), splenic focal lesions (5) and abdominal lymph nodes (1)

+ Subpleural nodules (SUNs) and lung consolidation

- Presence of any of these signs prompted a POCUS-positive result
- Images and clips were evaluated by an **expert reviewer** and, if discordant, by a second expert reviewer

This study was approved by the MSF Ethics Review Board (ERB) and by the Guinea-Bissau Ministry of Health ERB

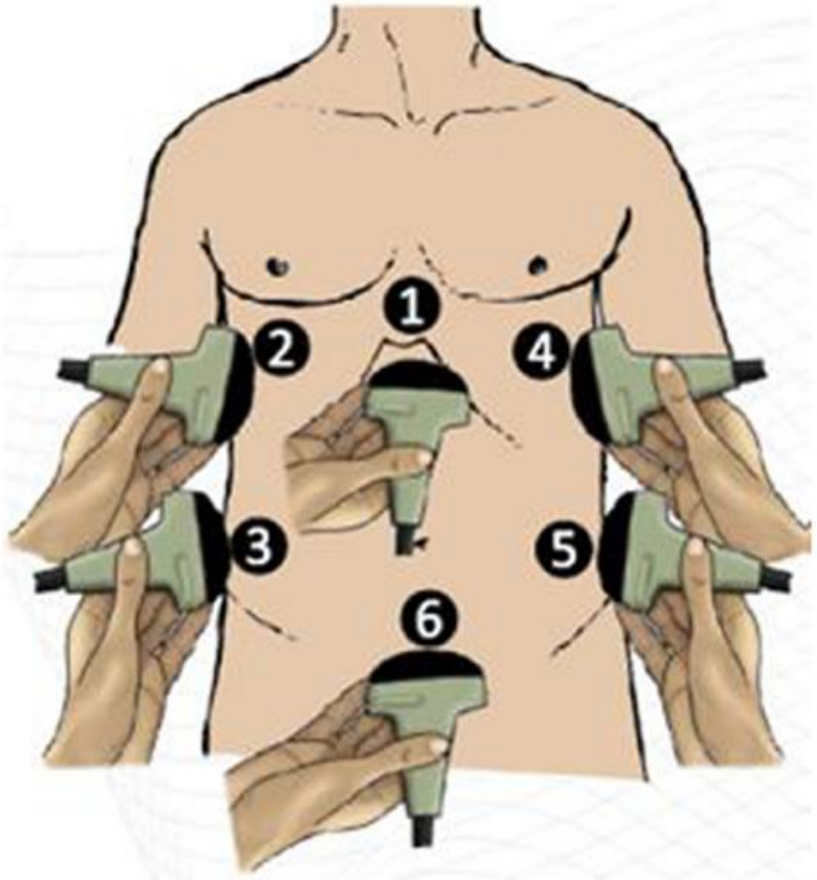


Figure 1 Schematic drawing of the ultrasound probe positions during the FASH examination.

RESULTS (I): Demographic characteristics and TB clinical presentations

Table 1: Baseline demographic characteristics

	Confirmed TB (n=27)	Unconfirmed TB (n=62)	TB total (n=89)	Unlikely TB (n=50)	Total (n=139)	Odds Ratio (95% CI)
Gender - male	9 (33.3)	38 (61.3)	47 (52.8)	28 (56)	75 (54)	0.9 (0.5-1.9)
Age group years old (yo)						
<5	6 (22.2)	28 (45.2)	34 (38.2)	21 (42)	55 (39.5)	0.8 (0.4-1.7)
5-15	21 (77.8)	34 (54.8)	55 (61.8)	29 (58)	84 (60.4)	Ref
Median (IQR) age in yo	8 (5-12)	6 (1-11)	8 (2-12)	6.5 (1-11)	7 (1-11)	
HIV-infected	9 (33.3)	31 (50)	40 (44.9)	19 (38)	59 (42.4)	1.3 (0.7-2.7)
SAM	16 (59.3)	42 (67.7)	58 (65.2)	25 (50)	83 (59.7)	2.2 (1-4.7)
TB contact	14 (51.9)	31 (50)	45 (50.6)	18 (36)	63 (45.3)	1.8 (0.9-3.7)
Past TB treatment	1 (3.7)	6 (9.7)	7 (7.9)	3 (6)	10 (7.2)	1.3 (0.3-8.3)
TB clinical presentation						
Pulmonary TB (PTB)	11 (40.7)	44 (71)	55 (61.8)	0 (0)	55 (39.6)	
Extra pulmonary TB (EPTB)	8 (29.6)	2 (3.2)	10 (11.2)	0 (0)	10 (7.2)	
PTB + EPTB	8 (29.6)	16 (25.8)	24 (27)	0 (0)	24 (17.3)	

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RESULTS (II): POCUS signs per TB category

- Children with **TB** were more likely to have a **POCUS positive** result **(93%)** compared to unlikely TB **(34%)**
- The **most common POCUS signs** were, for TB patients: lung consolidation (57%), SUNs (55%), pleural effusion (30%), and focal splenic lesions (28%); and for non-TB patients: lung consolidation (26%)
- In children with confirmed TB, **POCUS sensitivity was 85.2%** (95% confidence interval (CI) 67.5-94.1). In those with **unlikely TB**, **specificity was 66%** (95%CI 2.2-77.6)

Table 2: POCUS signs per TB category

		Confirmed TB (n=27)	Unconfirmed TB (n=62)	TB total (n=89)	Unlikely TB (n=50)	Total (n=139)
SUN		13 (48.1)	36 (58.1)	49 (55.1)	2 (4)	51 (36.7)
Consolidation		13 (48.1)	38 (61.3)	51 (57.3)	13 (26)	64 (46)
Pleural Effusion		7 (25.9)	20 (32.3)	27 (30.3)	0 (0)	27 (19.4)
Pericardial effusion		3 (11.1)	10 (16.1)	13 (14.6)	0 (0)	13 (9.4)
Ascites		3 (11.1)	12 (19.4)	15 (16.9)	2 (4)	17 (12.2)
Focal liver lesions		2 (7.4)	1 (1.6)	3 (3.4)	0 (0)	3 (2.2)
Focal splenic lesions		11 (40.7)	14 (22.6)	25 (28.1)	2 (4)	27 (19.4)
Abdominal LN		6 (22.2)	9 (14.5)	15 (16.9)	0 (0)	15 (10.8)
POCUS interpretation	Pos.	23 (85.2)	60 (96.8)	**83 (93.3)**	**17 (34)**	100 (71.9)
	Neg.	4 (14.8)	1 (1.6)	5 (5.6)	33 (66)	38 (27.3)

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RESULTS (III): Concordance with Expert reviewer

- **Cohen's kappa** coefficient for concordance between field and expert reviewers ranged from 0.6 to 0.9 depending on the POCUS sign, while overall POCUS concordance was 0.8

Table 3: Concordance with Expert reviewer

	Total (n=139)	Concordance: Kappa value (95%CI)
SUN	51 (36.7)	0.69 (0.56 - 0.82)
Consolidation	64 (46)	**0.84 (0.75 - 0.93)**
Pleural Effusion	27 (19.4)	0.72 (0.58 - 0.86)
Pericardial effusion	13 (9.4)	**0.91 (0.78 - 1)**
Ascites	17 (12.2)	0.68 (0.47 - 0.89)
Focal liver lesions	3 (2.2)	0.8 (0.41 - 1.2)
Focal splenic lesions	27 (19.4)	0.72 (0.57 - 0.87)
Abdominal LN	15 (10.8)	0.59 (0.29 - 0.89)
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RESULTS (IV): POCUS signs for TB patients by HIV, nutritional status and age

- HIV-uninfected children had significantly more pleural effusion and children with SAM had more SUNs
- POCUS positivity was not predicted by HIV status or age
- SAM children presented with significantly higher risk of POCUS positive result

Table 3: POCUS signs for TB patients by HIV, nutritional status and age

	HIV status			Nutrition status			Age group		
	Positive	Negative	P value	SAM	Not SAM	P value	<5 yo	>=5 yo	P value
SUN	25 (62.5)	24 (49)	0.2	38 (65.5)	10 (35.7)	**0.009**	17 (50)	32 (58.2)	0.45
Consolidation	19 (47.5)	32 (65.3)	0.09	35 (60.3)	14 (50)	0.36	21 (61.8)	30 (54.5)	0.5
Pleural effusion	4 (10)	23 (46.9)	**0.0003**	17 (29.3)	8 (28.6)	0.94	10 (29.4)	17 (30.9)	0.88
Pericardial effusion	6 (15)	7 (14.3)	0.9	7 (12.1)	5 (17.9)	0.47	2 (5.9)	11 (20)	0.12
Ascites	7 (17.5)	8 (16.3)	0.9	8 (13.8)	6 (21.4)	0.22	3 (8.8)	12 (21.8)	0.18
Focal liver lesions	1 (2.5)	2 (4.1)	0.99	3 (5.2)	0 (0)	0.59	1 (2.9)	2 (3.6)	0.999
Focal splenic lesions	15 (37.5)	10 (20.4)	0.096	20 (34.5)	4 (14.3)	0.07	7 (20.6)	18 (32.7)	0.11
Abdominal LN	8 (20)	7 (14.3)	0.49	13 (22.4)	2 (7.1)	0.12	2 (5.9)	13 (23.6)	**0.051**
POCUS positive	38 (95)	45 (91.8)	0.999	57 (98.3)	23 (82.1)	0.006	32 (94.1)	51 (92.7)	0.75

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LIMITATIONS & STRENGTHS

- Sample size relatively small – this study is part of a wider multicentric study taking place now in South Sudan
- POCUS unblinded to clinicians – the South Sudan study has clinicians blinded to POCUS results

- First study to include pulmonary assessment to the classical FASH protocol
- First study to correlate TB-focused signs with malnutrition in children
- First study to include POCUS-naïve local clinicians and field conditions

CONCLUSIONS & IMPLICATIONS

- We found high prevalence of any POCUS sign in children with TB, as compared to children with unlikely TB
- POCUS positivity was independent of HIV status and age
- POCUS positivity was dependent on nutritional status, which may indicate a role of POCUS in diagnosis of TB in children with SAM
- POCUS concordance between field and expert reviewers was moderate to high
- If findings confirmed with blinded clinicians, POCUS can be incorporated into diagnostic algorithms to support TB diagnosis in children

TAKE HOME MESSAGE

- In low resource settings where access to X-ray is limited and pediatric TB is diagnosed based on clinical grounds, data of our study suggest that POCUS may play a role to support TB diagnosis in children, but more data on blinded POCUS is still needed to confirm this finding

THANKS TO…

The patients and families that made this study possible

The field teams that believed in the project

The Ministry of Health who supported the study