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Blinded point-of-care ultrasound to support tuberculosis diagnosis in children: a Médecins Sans Frontières cross-sectional study in Malakal, South Sudan.

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BACKGROUND AND OBJECTIVES

- Tuberculosis (TB) is an important cause of morbidity and mortality in children.
- >50% of children with TB worldwide are never diagnosed.
- South Sudan is a high-burden setting for TB, HIV, and malnutrition.
- TB-focused point-of-care ultrasound (POCUS) has been validated for adults with HIV (FASH: focused assessment with sonography for HIV-associated TB)
- Evidence on the use of tuberculosis-focused point-of-care ultrasound (POCUS) in children is limited.

Aim of the study:

- Our study describes the utility of POCUS for diagnosis of tuberculosis (TB) in children with presumptive TB in South Sudan (SSD).

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.

Photo: team in Malakal performing a POCUS

METHODS

- This cross-sectional study took place at Malakal hospital (SSD), from July 2021 to December 2023.
- Children between 6months and 15years with presumptive TB underwent clinical, laboratory and blinded clinician-performed POCUS assessments.
- All children were evaluated by 8 sonographic signs: Subpleural nodules (SUNs), lung consolidation, pleural and pericardial effusion, abdominal lymphadenopathy, focal splenic and hepatic lesions and ascites.
- Presence of any sign prompted a POCUS positive result. Ultrasound images and clips were evaluated by expert reviewers.
- Children were categorised as confirmed TB (microbiological diagnosis), unconfirmed TB (clinical diagnosis) or unlikely TB.

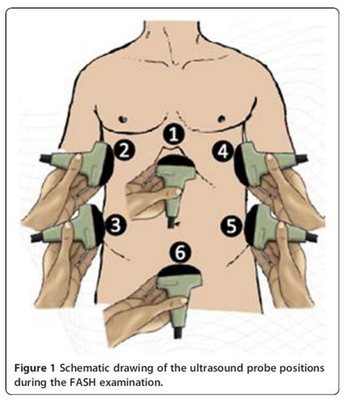

Figure 1 Schematic drawing of the ultrasound probe positions during the FASH examination.

Heller et al, Critical Ultrasound Journal 2012, 4:21

RESULTS

Table 1: Baseline demographic characteristics

Characteristic	Overall, N = 359[1]	confirmed, N = 58[1]	Unconfirmed, N = 158[1]	Total TB, N = 216[1]	unlikely, N = 143[1]	p-value[2]
Age (years)						0,2
0-<2	120 (33%)	18 (31%)	62 (39%)	80 (37%)	40 (28%)	
2-<5	90 (25%)	23 (40%)	31 (20%)	54 (25%)	36 (25%)	
5-<=15	149 (42%)	17 (29%)	65 (41%)	82 (38%)	67 (47%)	
Median (IQR) age (months)	41 (17, 96)	36 (18, 60)	36 (16, 84)	36 (16, 84)	48 (19, 108)	0,042
Gender: female	188 (52%)	31 (53%)	83 (53%)	114 (53%)	74 (52%)	0,8
Past TB history (yes)	17 (4.7%)	3 (5.2%)	8 (5.1%)	11 (5.1%)	6 (4.2%)	0,7
Tuberculosis contact (yes)	92 (26%)	21 (36%)	44 (28%)	65 (30%)	27 (19%)	0,041
Unknown	9 (2.5%)	3 (5.2%)	1 (0.6%)	4 (1.9%)	5 (3.5%)	
HIV positive	28 (7.8%)	16 (28%)	10 (6.3%)	26 (12%)	2 (1.4%)	<0.001
CD4 <200	3 (15%)	2 (15%)	1 (14%)	3 (15%)	0 (NA%)	>0.9
Missing	8	3	3	6	2	
On ART ar baseline	2 (7.1%)	2 (13%)	0 (0%)	2 (7.7%)	0 (0%)	>0.9
Type of tuberculosis						>0.9
Dissaminated	69 (32%)	31 (53%)	38 (24%)	69 (32%)	0 (NA%)	
EPTB	48 (22%)	13 (22%)	35 (22%)	48 (22%)	0 (NA%)	
PTB	99 (46%)	14 (24%)	85 (54%)	99 (46%)	0 (NA%)	
Nutrition status: SAM	236 (66%)	34 (60%)	109 (69%)	143 (67%)	93 (65%)	0,2
Missing data	2	1	1	2	0	

- Baseline demographic characteristics are shown in table 1.
- A total of 359 children were enrolled, with 188(52%) females and 210 (58.5%) <5 years old.
- A total of 236 (66%) and 28 (7.8%) were severely acute malnourished (SAM) and HIV-infected, respectively.
- TB confirmation occurred in 58 (16%); 158 (44%) had unconfirmed TB and 143 (39.8%) had unlikely TB.

Table 2: POCUS signs per TB category

Characteristic	Overall, N = 359[1]	Confirmed, N = 58[1]	Unconfirmed, N = 158[1]	Total TB, N = 216[1]	Unlikely, N = 143[1]	p-value[2]
SUN < 1.0 cm	12 (3.3%)	4 (6.9%)	4 (2.5%)	8 (3.7%)	4 (2.8%)	0,8
Consolidation (> 1.0 cm)	46 (13%)	15 (26%)	28 (18%)	43 (20%)	3 (2.1%)	**<0.001**
Missing data	1	0	1	1	0	
Pleural Effusion	10 (2.8%)	4 (6.9%)	6 (3.8%)	10 (4.6%)	0 (0%)	**0,007**
Pericardial eff usion (> 0.3 cm)	17 (4.7%)	5 (8.6%)	8 (5.1%)	13 (6.0%)	4 (2.8%)	0,2
Not evaluable	3 (0.8%)	1 (1.7%)	0 (0%)	1 (0.5%)	2 (1.4%)	
Ascites	22 (6.1%)	5 (8.8%)	7 (4.4%)	12 (5.6%)	10 (7.0%)	0,6
Missing data	1	1	0	1	0	
Focal liver lesions	8 (2.2%)	3 (5.2%)	4 (2.5%)	7 (3.2%)	1 (0.7%)	0,2
Focal splenic lesions	71 (20%)	26 (45%)	35 (22%)	61 (28%)	10 (7.0%)	**<0.001**
Missing data	2	0	1	1	1	
Abdominal lymph nodes (>1cm)	17 (4.8%)	5 (8.8%)	9 (5.7%)	14 (6.5%)	3 (2.1%)	0,066
Not evaluable	2 (0.6%)	1 (1.8%)	1 (0.6%)	2 (0.9%)	0 (0%)	
Missing data	2	1	0	1	1	
Interpretation POCUS						**<0.001**
Positive	143 (40%)	38 (65%)	73 (46%)	111 (51%)	32 (22.4%)	
Negative	215 (60%)	19 (33%)	85 (54%)	104 (48%)	111 (78%)	
Indeterminate	1 (0.3%)	1 (1.7%)	0 (0%)	1 (0.5%)	0 (0%)	

[1] n (%); Median (IQR)
[2] Pearson's Chi-squared test; Kruskal-Wallis rank sum test; Fisher's exact test

- Children with TB were more likely to have POCUS-positive results (111/216;51.4%) compared with children with unlikely TB (32/143;22%). POCUS signs per TB category are presented in table 2.
- Common POCUS signs in patients with TB were : focal splenic lesions (61;28%), lung consolidation (43;20%), abdominal lymph nodes (14; 6.5%) and pericardial effusion (13;6%).
- In children with confirmed TB, POCUS sensitivity was 64.3% (95%CI:51.2%-75.5%). In those with unlikely TB, specificity was 77.6% (95%CI:70.1%-83.7%).

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

Characteristic	Overall*, N = 216[1]	HIV status: CLHIV, N = 26[1]	HIV status: Not CLHIV, N = 190[1]	HIV status: p-value[2]	Nutritional status: SAM, N = 143[1]	Nutritional status: No SAM, N = 71[1]	Nutritional status: p-value[2]	Age group: Age <5, N = 134[1]	Age group: Age 5-15, N = 82[1]	Age group: p-value[2]
SUN (<1.0 cm)	8 (3.7%)	1 (3.8%)	7 (3.7%)	>0.9	6 (4.2%)	2 (2.8%)	>0.9	5 (3.7%)	3 (3.7%)	>0.9
Consolidation (>1.0 cm)	43 (20%)	7 (27%)	36 (19%)	0,3	30 (21%)	13 (19%)	0,7	31 (23%)	12 (15%)	0,14
Missing data	1	0	1		0	1		0	1	
Pleural Effusion	10 (4.6%)	0 (0%)	10 (5.3%)	0,6	4 (2.8%)	6 (8.5%)	0,086	4 (3.0%)	6 (7.3%)	0,2
Pericardial effus.(>0.3 cm)	13 (6.0%)	1 (3.8%)	12 (6.3%)	0,2	11 (7.7%)	2 (2.8%)	0,3	127 (95%)	75 (91%)	0,4
Not evaluable	1 (0.5%)	1 (3.8%)	0 (0%)		1 (0.7%)	0 (0%)		1 (0.7%)	0 (0%)	
Ascites	12 (5.6%)	0 (0%)	12 (6.3%)	0,4	9 (6.3%)	3 (4.2%)	0,8	5 (3.7%)	7 (8.6%)	0,14
Missing data	1	1	0		1	0		0	1	
Focal liver lesions	7 (3.2%)	0 (0%)	7 (3.7%)	>0.9	6 (4.2%)	1 (1.4%)	0,4	4 (3.0%)	3 (3.7%)	>0.9
Focal splenic lesions	61 (28%)	13 (50%)	48 (25%)	**0,009**	43 (30%)	17 (24%)	0,3	42 (32%)	19 (23%)	0,2
Missing data	1	0	1		1	0		1	0	
Abdominal LN (≥1 cm)	14 (6.5%)	0 (0%)	14 (7.4%)	0,11	8 (5.6%)	6 (8.5%)	0,6	10 (7.5%)	4 (4.9%)	0,5
Not evaluable	2 (0.9%)	1 (3.8%)	1 (0.5%)		2 (1.4%)	0 (0%)		2 (1.5%)	0 (0%)	
Missing data	1	0	1		1	0		1	0	
Interpretation POCUS				**0,009**			0,3			0,2
Positive	111 (52%)	19 (76%)	92 (48%)		77 (54%)	33 (46%)		73 (55%)	38 (46%)	
Negative	104 (48%)	6 (24%)	98 (52%)		65 (46%)	38 (54%)		60 (45%)	44 (54%)	
Missing data	1	1	0		1	0		1	0	

[1] n (%); Median (IQR). [2] Pearson's Chi-squared test; Fisher's exact test

- POCUS signs for HIV, nutritional status and age in TB patients are presented in table 3.
- Unlike SAM status (Risk Ratio (RR) (1.2;95%CI:0.9,1.6; p=0.291) and age <5 years old (RR 1.2;95%CI:0.9-1.6; p=0.228), HIV-infection (RR 1.6;95%CI:1.2-2.1; p=0.001) was associated with higher POCUS-positive results in TB patients.

CONCLUSION

- **We found a high prevalence of POCUS signs in children with TB compared with children with unlikely TB. The most prevalent sign was focal splenic lesions.**
- **Children living with HIV were more likely to have POCUS-positive results.**
- **TB-focused POCUS can play a supportive role in the diagnosis of TB in children.**

ETHICS STATEMENT

This study was approved by the MSF Ethics Review Board, and South Sudan Ministry of Health ERB.

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