

Utility of stool culture for the diagnosis of pediatric tuberculosis in a low burden setting: A retrospective pilot study

Sarah Silverberg,^{1,2*} Robyn Elphinstone,^{1*} Melissa Richard-Greenblatt,³ Ray Lam,¹ Valerie Waters,¹ and Ian Kitai¹

Department of Pediatrics, Division of Infectious Diseases¹; Edwin SH Leong Centre for Healthy Children²; Department of Pediatric Laboratory Medicine³; The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada (*Co-first authors)

Background

- There are few data about the utility of stool culture to manage pediatric TB
- In Ontario, molecular tests are performed routinely on acid-fast bacilli (AFB) smear-positive specimens only
- Since Aug 2021, we recommended stool cultures for workup of suspected TB
- We analyzed our experience to better characterize the added value that stool cultures provide to the diagnosis and management of pediatric TB patients

Methods

- Population:** All children and adolescents who had a microbiologically confirmed or presumed diagnosis of M. TB complex (MTBC) from August 1, 2021 - March 31, 2024, who had a stool sent for mycobacterial culture as part of their initial workup for TB disease while admitted to SickKids

→ Consecutive cohort of admitted patients

- Intervention:** Stool sent for mycobacterial culture during initial workup
- Outcomes:** Proportion with positive stool cultures for MTBC among those with and without additional positive mycobacterial cultures from other sites; time to positivity for stool vs. other culture types

- Analysis:** We evaluated baseline population characteristics, including age at diagnosis, positive culture sites and smear grade, and TB diagnosis in those with and without positive stool cultures for MTBC. Additionally, we evaluated time to positivity and first positive culture type.

References

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- Banada PP, Naidoo U, Deshpande S, Karim F, Flynn JL, et al. (2016) A Novel Sample Processing Method for Rapid Detection of Tuberculosis in the Stool of Pediatric Patients Using the Xpert MTB/RIF Assay. *PLOS ONE* 11(3): e0151980.

Results

ILLUSTRATIVE CASE

- Presentation:** 14-year-old girl with a 6-month history of right lower quadrant abdominal pain, and fever
- Imaging:** abnormal bowel thickening of the terminal ileum and cecum with multiple abdominal and intra thoracic necrotic lymph nodes with a supraclavicular lymph node
- Interventions:**
 - Biopsy of supraclavicular node → non diagnostic
 - Excisional biopsy of the node → non-diagnostic
- Diagnosis:** Two days after the excisional biopsy was performed, a stool taken **18 days prior** reported culture positive for MTBC and was **the only positive culture**
- Outcome:** The patient developed severe hepatotoxicity during treatment with standard therapy; second line sensitivities were crucial in creating a tailored treatment regimen

RESULTS SUMMARY

CASE SERIES:

- 19 sequential patients admitted for workup, stool TB culture sent, diagnosed with TB disease
 - n=15 microbiologically confirmed, n=4 presumed clinical diagnosis

DIAGNOSTIC SAMPLES:

- 10 (53%) patients had positive sputum and/or gastric aspirate samples
 - Median (IQR) time to positivity: 13.5 (10-17) days
 - Time to first positive sample: 10.5 (9.25-14.25) days
- 8 (42%) patients had positive stool cultures for TB
 - Median (IQR) time to positivity: 20 (19-30) days
- For all non-stool sample types pooled, time to positivity was 14.5 (10-19.5) days
- 35 individual stool cultures were taken, of which nine (25.7%) were positive
- Stool was the first positive sample in three (15.8%) patients**
- Stool was the only positive sample in 1 (5%) patient**

ABDOMINAL SYMPTOMS:

- Of patients with a positive stool culture:**
 - 3/8 (37.5%) presented with abdominal symptoms
 - 3/8 (37.5%) had an abnormal abdominal exam
 - 3/6 (50%) who had abdominal imaging done had abnormalities seen

Table 1. Characteristics of consecutive patients who had stools submitted for TB culture

	All participants (N=19)	Stool culture positive (N=8)	Stool culture negative (N=11)
Age, yrs (mean, SD)	4.91 (6.89)	3.26 (7.26)	6.61 (6.42)
0-5 (n, %)	7 (36.8%)	4 (50%)	3 (27.3%)
5-10 (n, %)	2 (10.5%)	0	2 (18.2%)
10-15 (n, %)	2 (10.5%)	2 (25%)	2 (18.2%)
15-18 (n, %)	6 (31.6%)	2 (25%)	4 (36.4%)
TB diagnosis (n, %)			
Pulmonary	8 (42.1%)	2 (25%)	6 (54.5%)
Disseminated	8 (42.1%)	5 (62.5%)	3 (27.3%)
Pulmonary + cervical LN	1 (5.3%)	1 (12.5%)	0
Isolated cervical LN	1 (5.3%)	0	1 (9.1%)
Abdominal	1 (5.3%)	1 (12.5%)	0
Acid fast bacilli stain positive (n, %)			
Sputum	9 (47.4%)	6 (75%)	3 (27.3%)
Stool	2 (10.5%)	1 (12.5%)	1 (9.1%)
Culture for MTBC (n, %)			
Culture Positive (any site)	15 (79%)	8 (100%)	7 (63.6%)
Culture negative*	4 (21.1%)	0 (0)	4 (36.4%)
PCR positive (n, %)			
Sputum	9 (47.4%)	6 (75%)	3 (27.3%)
Stool	0 (0)**	0 (0)	0 (0)
Other sample type	3 (15.8%)	1 (12.5%)	2 (18.2%)
Abdominal imaging abnormal** (n, %)	5 (26.3%)	1 (12.5%)	4 (36.4%)
Number of stools submitted	1 (1-3)	1.5 (1-2.25)	1 (1-3)
Median (IQR)			
Stool only positive culture (n, %)	1 (5%)	1 (12.5%)	0 (0)
Stool first positive culture (n, %)	3 (15.8%)	3 (37.5%)	0 (0)
Time in days to positive stool culture	20 (19-30)	20 (19-30)	0 (0)
Time in days to first non-stool positive culture (median, IQR)	14 (10-19.25)	12.5 (10-17.5)	17 (11-19.25)

* Treated as a clinical case

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*** Two stools were smear positive but ultimately grew non-TB mycobacteria

Conclusions

- Over 40% of children and adolescents admitted for workup and who were diagnosed with TB disease had a positive stool culture for TB
- In three patients, stool was the **first positive** sample, of which in one patient it was the **only positive** sample, indicating an important role for this specimen type

- Further studies should assess the utility of molecular testing on stool samples that are AFB negative in this population to aid with improving time to diagnosis and potential for avoiding invasive procedures