

# TB diagnosis in children: metabolite biomarkers

Change	LTBI	NMP
Patients with active TB	Latently TB (LTBI) and non-TB children	Patients with infectious non-mycobacterial pneumonia
13	12	28
13	8	18
(18-24)	(10-12)	(17-20)
11 (33%)	24 (34%)	7 (25%)
10 (30%)	28 (34%)	13 (46%)
1076	810	8076
1607	45.0	103
1618	14.0	102
11.2	0.8	0.8
1.6	1.7	0.8
0.3	0.3	0.8
1.0 (0.000)	1.7 (0.000)	1.7 (0.000)
11.1	11.1	10.0
10.0	10.0	10.0
11.0	11.0	10.1
100.000	100.000	100.000
11.0	10.7	10.0

Tuberculosis (TB) caused by the intracellular pathogen *Mycobacterium tuberculosis* (*M. tb*) is one of the most contagious diseases. Up to a quarter of the world's population is estimated to be latently infected with *M. tb* (LTBI). Pediatric TB contributes significantly to worldwide TB infections but is difficult to diagnose due to insufficient detection methods ([READ MORE](#)).

Many biomarkers of pulmonary and extrapulmonary TB have already been identified with the help of mass spectrometry since infection with *M. tb* causes significant changes in the energy and protein metabolism of the host. Druszczynska and colleagues now used targeted liquid chromatography-mass spectrometry (LC-MS/MS) to assess the levels of 30 small metabolites in the serum and *M. tb* antigen-stimulated blood cultures of active TB children (Figure 1). These were then compared with those of LTBI children, infectious non-mycobacterial pneumonia (NMP) children and controls without active infection.

Description	Groups			
	TB	LTBI	NMP	HC
	Patients with active TB	Latently M.tb infected individuals	Patients with infectious nonmycobacterial pneumonia	Healthy controls
n	15	32	20	149
Age				
Median years (IQR)	15 (11-34)	8 (5-32)	14 (7-16)	7 (3-11)
Sex, n				
M (%)	5 (33%)	24 (40%)	7 (35%)	87 (58%)
F (%)	10 (67%)	28 (54%)	13 (65%)	62 (42%)
WBC, counts/mm <sup>3</sup>	9776	8150	8176	8562
Neutrophils (%)	60.7	43.8	53.1	48.1
Lymphocytes (%)	26.8	42.6	33.7	47.5
Monocytes (%)	9.2	8.0	9.0	8.1
Eosinophils (%)	2.6	4.7	3.6	3.6
Basophils (%)	0.5	0.5	0.6	0.6
RBC, counts/mm <sup>3</sup>	4,630,000	4,730,000	4,720,000	4,780,000
HGB, g/dl	13.1	13.3	12.9	13.2
HCT, %	38.8	39.4	39.2	39.2
MCHC, g/dl	33.6	33.8	33.1	33.7
PLT, counts/mm <sup>3</sup>	348,380	306,800	337,580	388,800
CRP, mg/L	41.8	8.7	12.8	0.8

*Table 1: Demographic characteristics of study subjects. CRP C-reactive protein, F female, HCT haematocrit, hGB haemoglobin, M male, MCHC men corpuscular haemoglobin concentration, M.tb Mycobacterium tuberculosis, n number, PLT platelets, RBC red blood cells, SD standard deviation, TB tuberculosis, WBC white blood cells (Druszcynska, et al., 2022).*

Comparison of the levels of metabolites between the groups revealed that serum leucine levels were significantly higher in the TB and LTBI groups, whereas the abundance of citrulline was significantly lower in these patients compared to the healthy control group. Further metabolites with significant differences included hydroxyproline, proline, valine, tyrosine, leucine, kynurenine, valine and neopterin. Using receiver operator characteristic (ROC) curves, area under the curve (AUC) and elastic-net logistic regression analysis, they identified serum leucine as the best discriminator of TB + LTBI versus healthy control + NMP. Unfortunately, the small sample size of the TB group (n = 15) did not allow for a selection of the most informative metabolites to discriminate this group against the others. Nevertheless, the obtained

results are a proof of principle of the usefulness of metabolites in the diagnosis of TB in children.

**Journal article: Druszczynska et al., 2022. [Targeted metabolomics analysis of serum and \*Mycobacterium tuberculosis\* antigen-stimulated blood cultures of pediatric patients with active and latent tuberculosis](#). *Scientific Reports*.**

*Summary by Dr. Jasmin Knopf*