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Tuberculosis in candidates to haematopoietic stem cell transplantation: prevalence of latent infection and disease in children and adolescents admitted to a national referral centre in an intermediate-burden country

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Background: Hematopoietic stem cell transplant recipients (HSCT) are at high risk for tuberculosis. This is associated with adverse outcomes such as high mortality and poor graft survival. There is a critical gap of knowledge regarding the burden of disease in pediatric patients. To the best of our knowledge, no prevalence studies in this population group had been conducted in Colombia before. Estimating the prevalence of TB in candidates to HSCT is an essential first step towards the setting of evidence-based recommendations on screening.

The aim of this study was to estimate the prevalence of latent tuberculosis infection (LTBI) and disease among HSCT candidates in a children's hospital, where routine screening for TB had not been previously carried out. Potential risk factors for tuberculosis were described.

Material/methods: We conducted a cross-sectional study among patients aged 6 months to 17 years, admitted between July 2015 and June 2016 to undergo HSCT. Active search of LTBI and disease was

performed at baseline, by systematically following a diagnostic approach which combined tuberculin skin test (TST), QuantiFERON®-TB Gold In-Tube (QFT-GIT), chest tomography, and interviews to identify suggestive symptoms and epidemiological contact. Patients were followed-up during six months after transplantation and new cases of tuberculosis disease were recorded.

LTBI was defined as a positive TST in children older than 5 years, a positive QFT-GIT, or diagnosis of secondary tuberculosis disease following transplantation. Confirmed disease was defined as positive PCR or culture, with compatible symptoms. Criteria for unconfirmed intrathoracic tuberculosis disease were based on currently recommended case definitions and judgement of treating physicians.

Results: Fifty-three patients were admitted during the study period (mean age: 8.1 years \pm 4.62). 28.3% of participants were younger than 5 years. The main indications for HSCT were Acute Lymphoblastic Leukemia (39.22%) and Acute Myeloid Leukemia (13.73%). The most common type of HSCT was cord blood stem cell transplant (53.06%). Graft-vs-Host disease was diagnosed in 32.65% of recipients. Overall prevalence of all forms of tuberculosis was 22.65%.

(Figure 1).

TST positivity was 13.21%. IGRA positivity was zero (one indeterminate result). 69.23% of patients had low socioeconomic status. 35.29% had household exposure to secondhand smoke. A close contact with adults presenting suggestive symptoms of TB was reported in 13.21%, and close exposure to a confirmed case in 1.9%.

(Table 1).

Conclusions: Prevalence of tuberculosis in transplant candidates was high. Prevalence of latent infection was relatively low. Although an accurate diagnostic approach was intended in this study, the results deserve cautious interpretation, since diagnostic criteria are likely to have significant limitations in terms of both specificity and sensitivity in immunocompromised patients. Our study also found a high prevalence of social and clinical factors that have been associated with tuberculosis in previous studies.

Figure 1. Period prevalence of TB in candidates to HSCT

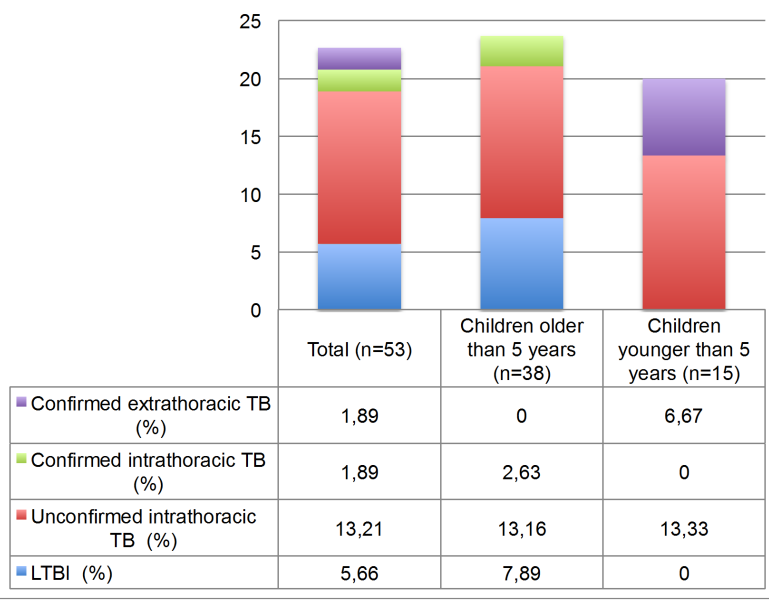


Table 1. Prevalence of factors potentially associated with TB

Characteristic	Children with diagnosis of tuberculosis (LTBI /TB disease) (n=12)		Children with no TB diagnosis (n=41)		p value
	Mean	SD	Mean	SD	
Age (years) (n=53)	9,04	5,38	7,82	4,41	0,4297
	Number of cases	(%)	Number of cases	(%)	
Male (n=53)	7	58,33	23	56,1	1
Female (n=53)	5	41,67	18	43,9	1
Positive history of close exposure to adult with symptoms potentially suggestive of tuberculosis (n=40)	4	33,33	3	7,32	0,039
Low socioeconomic status (n=52)	2	16,67	14	34,15	0,301
Exposure to household secondhand smoke (n=51)	5	41,67	13	33,33	0,732
Overcrowding (more than 2 people/room) (n=52)	2	16,67	8	20	0,797

(Total number of participants with data available listed in parentheses).