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ORIGINAL ARTICLE

Pulmonary tuberculosis and nutritional status: sectional study with children and adolescents

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Abstract

Introduction: Tuberculosis (TB) can lead to malnutrition, just as itself can predispose to TB. This study aims to analyze the nutritional status, clinical-radiological findings and tests performed by children and adolescents with pulmonary TB (PT). **Methodology:** cross-sectional study involving three hospitals in Rio de Janeiro, from October 2014 to October 2019. Children and adolescents with PT were included. The variables studied were: age, sex, fever, weight loss, nutritional status, AFB, culture for Mycobacterium tuberculosis, Gene Xpert TB-RIF test. For comparison between eutrophic and malnourished patients was used X2 test (statistical significance *p*-value<0.05). **Results:** Forty-nine patients were included in the study. Among eutrophic children, 88.9% showed fever, 38.9% weight loss and 27.8% detectable Xpert. Among the malnourished, 100% manifested fever, 50% weight loss and 50% detectable Xpert. In the eutrophic and malnourished groups, the miliary radiological pattern occurred in 5.6% and 75% (p<0.01); culture was positive in 35.3% and 50%, respectively. In eutrophic adolescents there was fever in 58.8% and detectable Xpert in 41.2%. Among the malnourished, there was fever in 90% and detectable Xpert in 70%. The culture was positive in 31.2% eutrophic and, among the malnourished, there were 70% cases (p=0.05). The miliary radiological pattern occurred in 17.6% eutrophic and 10% malnourished. Weight loss occurred in 35.3% eutrophic and 100% malnourished (p<0.01). **Conclusion:** Among malnourished children and adolescents, supposedly more severe, the positive results from GeneXpert and culture were more frequent. The miliary pattern was more frequent among malnourished children and eutrophic adolescents.

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INTRODUCTION

Brazil is among the 22 countries with the highest incidence of tuberculosis (TB) in the world[1]. It is estimated that TB affected approximately 9.9 million people globally in 2020, being responsible for 1.3 million deaths among individuals without HIV infection, of which 16% are children (under 15 years of age). In 2020, TB was surpassed by Covid-19 as the first cause of death from a single infectious agent[2]. Among the states, Rio de Janeiro stands out as the state with the highest mortality rate and the 2nd highest incidence[3]. The incidence of TB is similar in both sexes until the age of 14, after this age group there is a predominance in males. As a highlight, TB in children (in children under 15 years of age) corresponds to 3% of cases in Brazil in 2021[3], being among the ten main causes of mortality in children under five years of age[4].

Childhood TB is a global public health challenge. Children present the abaciliferous or paucibacillary form of the disease and, in general, are unable to expectorate spontaneously, making bacteriological identification for diagnosis difficult[5]. Among the laboratory methods, the research for acid-fast bacilli (AFB), culture and the tuberculin skin test (PPD) stand out. This investigation into children has low sensitivity, underestimating the real incidence on the global stage, further hampered by the impacts caused by the Covid-19 pandemic, reducing notifications and reversing years of progress in controlling TB[2]. Another laboratory method is the Xpert MTB/RIF test (Xpert), incorporated in Brazil in 2014 for routine use in cases with symptoms suggestive of TB[6]. This test uses the real-time PCR technique, and in addition to detecting the presence of DNA, identifies resistance to RMP at the same time. The Ministry of Health (MH) Diagnostic Score method is also valid for diagnosis, which does not require bacteriological positivity[7]. This score punctuates the radiological clinical picture, the adult's contact with TB, the PPD result and nutritional status, classifying the diagnosis as very likely, possible or unlikely.

According to the World Health Organization's (WHO) End TB strategy, the proposed objectives of reducing TB incidence by 20% from 2015 to 2020, reducing deaths by 35% in the same period and zeroing the percentage of people with TB facing expenses catastrophic events were not met on time. These results highlight the need for greater integrated, patient-centered care and prevention, support policies and systems for those affected, and intensification of innovation and research related to the disease.

This study aims to analyze the nutritional status, clinical-radiological findings and diagnostic methods carried out by children and adolescents with pulmonary TB (PTB), in order to associate it with severity, focusing on the relationship between malnutrition as a result or as part of the causal constellation of TB.

METHODS

Retrospective cross-sectional study with previously published secondary data on patients with PT (by clinical and/or laboratory diagnosis) treated in three different hospitals in Rio de Janeiro: Instituto de Puericultura e Pediatria Martagão Gesteira (IPPMG) at UFRJ; Raphael de Paula Souza Municipal Hospital (HMRPS-SMS) and Antônio Pedro University Hospital (HUAP) at UFF between October 2014 and October 2019.

Children (under 10 years of age) and adolescents (between 10 and 19 years of age) clinically and/or laboratory diagnosed with pulmonary tuberculosis (PT) by the doctors who treated them, whose respiratory specimen was submitted to Xpert, were included. Those without information on nutritional status were excluded.

The patients' medical records and radiological images were analyzed and a clinical form was filled out with the following variables: age, sex, signs and symptoms, comorbidities, vaccination history, contact history, nutritional status, PPD, AFB, culture, Xpert, Ministry of Health Score. Health (MS) for diagnosis of TB in children and adolescents, radiological findings, need for hospitalization and final diagnosis (PTB or other diseases).

To classify nutritional status, the NCHS (National Center for Health Statistics) curve was used, with those with a weight-for-age percentile lower than the 3rd percentile being considered malnourished. Weight loss was reported only by the mother or guardian, without being, in fact, measured.

The radiography reports issued by the hospitals' radiologists were transcribed by the main researcher and categorized according to an adaptation of the definitions from the Atlas of intrathoracic tuberculosis in children[8].

Regarding the MS Score for diagnosing TB in children and adolescents, the proposed criteria were used: a score greater than or equal to 40 points, meaning that the diagnosis is very likely; of 30 to 35 points, the diagnosis is possible and, if it is lower than 25 points, the diagnosis is unlikely[9]. The tuberculin skin test (PPD) was classified as: positive when the result was ≥ 10 mm in children vaccinated with BCG less than two years and ≥ 5 mm in children not vaccinated with BCG or vaccinated more than two years ago; or negative (result lower than the mentioned cutoff points). Both the diagnostic score and the PPD were classified according to the Manual of recommendations for TB control in Brazil, in its 2011 version[5].

Data analysis was carried out descriptively, with categorical variables presented as frequency and percentage and numerical variables as mean and median. The Chi-square test or Fisher's exact test was used to compare variables, with statistical significance being p-value < 0.05.

The study was approved by the Research Ethics Committee (CEP) of IPPMG-UFRJ on 02/24/2015, CAAE numbers 37424714.0.0000.5264 and 76034317.8.0000.5264.

RESULTS

The research involved 49 PD patients. Twenty-two were children and 27 were teenagers. Table 1 shows the nutritional status of the patients studied according to sex and age. The majority of patients diagnosed with PD were under 5 years old and over 14 years old, highlighting the favored age for the disease in Pediatrics. Of the 22 children, 18 (82%) were eutrophic and 4 were malnourished. Among the adolescents, 17 (63.0) were eutrophic and 10 were malnourished. Of the 49 patients, 36 (73.4%) had an updated vaccination history. Furthermore, 16 (32.65%) had associated comorbidities, 31.25% were co-infected with HIV.

Among children, 20/22 (90.9%) were also hospitalized, and among adolescents, 15/27 (55.5%). The average age of hospitalized patients is 8.59 years, suggesting greater severity of TB in children. Of the malnourished adolescents, 9/10 (90%) were hospitalized. The hospitalization data, shown in table 2, demonstrate the association between the hospitalization of adolescents with tuberculosis and malnutrition.

The main data on the patients' clinical history and radiological findings can be found in table 3, with fever, cough and weight loss as the main signs and symptoms presented and condensation as the most frequent radiological finding.

All patients presented at least one radiographic change. The results also showed that 5/7 (71.4%) of the cases in which the miliary pattern was present resulted in hospitalization. Of the findings, the miliary pattern appeared isolated in 6 patients; while, in one of them, it appeared correlated with hilar adenomegaly. There was no significant prevalence between sexes.

The results of the AFB, culture, Xpert, PPD tests and patients' Clinical Score data can be found in table 4. All detectable Xpert results occurred in patients with a Clinical Score greater than or equal to 30. In total, 26 patients presented the Score with this value. Among the 4 patients with a Score between 30 and 35, only as 1 got detectable Xpert. While in the 22 patients with a Score greater than or equal to 40, Xpert was detectable in 12. All 6 patients with 25 or less points in the Score had undetectable Xpert.

DISCUSSION

In the present study, hospital admission and weight loss were more significant among malnourished adolescents. Among the radiological findings, condensation was the most common pattern, both in children and adolescents. It is noteworthy that positive bacteriological results for culture were more frequent among malnourished people, a group in which Xpert was more detectable.

Malnutrition and the final diagnosis of TB were directly related, especially among adolescents, with approximately one third suffering from malnutrition, representing greater evidence for this finding. It is not yet known whether this factor is part of the causal constellation or a result of TB[10]. In a retrospective study carried out from 2010 to 2012 in Italy with children and adolescents hospitalized in different centers[9], 9.9% of pediatric patients with PD had weight loss.

It is important to highlight that our data reflect the reality of three tertiary hospitals in the state of Rio de Janeiro. Despite this, among adolescents, being malnourished is directly associated with hospitalization. It can therefore be assumed that malnutrition is a risk factor for TB among adolescents.

Weight loss was very prominent among the signs and symptoms when analyzed according to nutritional status and

Table 1. Nutritional characteristics of children and adolescents with pulmonary tuberculosis, according to sex and age.

Sociodemographic variables		n	%	Eutrophic	%	Malnourished	%
Sex	**Female**	28	57.1	17	60.7	11	39.2
	Male	21	42.9	18	85.7	3	14.2
Age	**0-5 years**	14	28.6	12	34.2	2	14.2
	5-10 years	8	16.3	6	17.1	2	14.2
	10-19 years	27	55.1	17	48.7	**10**	71.6

Table 2. Distribution of hospital admissions of children and adolescents, according to nutritional status.

Hospital admittance	Eutrophic		%	Total	Malnourished		%	Total
Children	**Yes**	17	94.5	18	**Yes**	3	75	4
	No	1	5.5		**No**	1	25	
Adolescents	**Yes**	6	35.2	17	**Yes**	9	90	10
	No	11	64.8		**No**	1	10	

Table 3. Signs, symptoms and radiological findings of patients divided by nutritional status and age group.

Signs and symptoms		Children					Adolescents				
		Eutrophic		Malnourished		Analysis	Eutrophic		Malnourished		Analysis
		N	%	N	%	*p-value*	N	%	N	%	*p-value*
Fever	Yes	16	88.8	4	100	0.48	10	58.8	9	90	0.09
	No	2	11.1	0	0		7	41.1	1	10	
Cough	Yes	11	61.1	4	100	0.13	3	17.6	3	30	0.46
	No	7	38.8	0	0		14	82.3	7	70	
Weigh loss	Yes	7	38.8	2	50	0.69	6	35.2	10	100	**0.0001**
	No	11	61.1	2	50		11	64.7	0	0	
Radiological findings											
Hilar adenomegaly	Yes	2	11.1	0	0	0.48	3	17.6	1	10	0.59
	No	16	88.8	4	100		14	82.3	9	90	
Miliary	Yes	1	5.5	3	75	**0.001**	3	17.6	1	10	0.59
	No	17	94.4	1	25		14	82.3	9	90	
Condensation	Yes	11	61.1	1	25	0.19	5	29.4	6	60	0.12
	No	7	38.8	3	75		12	70.5	4	40	
Pleural effusion	Yes	8	44.4	0	0	0.09	3	17.6	1	10	0.6
	No	10	55.5	4	100		14	82.3	9	90	
Cavitation	Yes	1	5.5	0	0	0.63	4	23.5	4	40	0.37
	No	17	94.4	4	100		13	76.4	6	60	

Table 4. AFB tests, Culture, Xpert, PPD, variables and average score of the Clinical Score in patients with pulmonary tuberculosis according to nutritional status and age.

Complementary tests		Children				Adolescents			
		Eutrophic		Malnourished		Eutrophics		Malnourished	
		N	%	N	%	N	%	N	%
BAAR	Positive	2	11.1	0	0	4	23.5	4	44.4
	Negative	16	88.9	4	100	13	76.5	5	55.6
Culture	Positive	6	35.3	2	50	5	31.2	7	70
	Negative	11	64.7	2	50	11	68.8	3	30
Xpert	Detectable	5	27.7	2	50	7	41.1	7	70
	Not detectable	13	72.2	2	50	10	58.8	3	30
Xpert analysis	Rifampin resistant	1	20	0	0	3	50	1	14.2
	Not resistant	4	80	2	100	3	50	6	85.7
Tuberculin test (PPD)	Reactive	7	53.8	0	0	12	85.7	2	66.6
	Not reactive	6	46.1	3	100	2	14.2	1	33.3
Clinical score for pulmonar TB*									
Score and interpretation	**TB very likely (≥ 40 points)**	8		1		11		2	
	TB Likely (30-35 points)	1		2		1		0	
	TB unlikely (≤ 25 points)	4		0		1		1	
	Average score	35.76		38.33		41.92		43.33	

Caption: TB – tuberculosis; * Ministry of Health score[9].

age group, even though fever and cough, typical signs and symptoms of the disease, also presented large absolute values. Around half of those surveyed experienced weight loss, which is related to the chronicity of hyporexia and discomfort when eating due to coughing, approaching the 37.9% seen in a retrospective study analyzing data from 1999 to 2014 carried out in Campinas. Likewise, weight loss was also more frequent among adolescents in the same study[11].

Childhood TB also leads to weight loss, often discreet. In some cases, the child or adolescent may lose weight or simply not gain weight.[12] It is important to highlight that weight loss was reported by the patient's mother or guardian, while malnutrition corresponds to a clinical finding detected by the doctor.

When the miliary pattern and malnutrition were analyzed together, this association showed statistical relevance among malnourished children. Research carried out between 2004 and 2010 in Istanbul with 250 pediatric cases showed miliary TB in only 8 cases[13]. The low number perhaps shows that malnutrition is a serious factor, since the majority of malnourished children presented the miliary pattern. Still in this sense, in a case-control study carried out with patients aged 0 to 14 years between 2010 and 2015 in Indonesia, it was demonstrated that nutritional status is a significant risk factor for miliary TB[14]. The frequency of condensation occurred in almost half of the cases in the present study and in Istanbul, it was similar - 49%[14].

The highest frequency of positive or detectable results on Xpert was among adolescents. In research carried out by Aurilio et al, from 2014 to 2019, involving the use of the method in children and adolescents with presumed TB, in reference centers for pediatric TB, this positivity was 63.6% in adolescents[15].

The average value of the Ministry of Health score was greater than 35 points in all groups, in both nutritional states, which is in accordance with the literature. In a study carried out from 2004 to 2018, this value was 89.3%, which shows proximity to our findings[16].

GeneXpert was only detectable in patients with a Score greater than or equal to 30, with only 26 patients falling into this context. Patients with 25 or fewer points had no detectable Xpert.

Among the limitations, the present study was carried out in tertiary hospitals, with a predominant profile of chronic patients and higher diagnostic selection criteria, sometimes the real parameter of cases in society is not evident, especially those treated in basic healthcare units.

Finally, we highlight that the 2021 WHO Global Tuberculosis Report corroborates malnutrition as a risk factor in terms of the higher incidence of TB cases. Malnutrition is the third highest relative risk, after HIV infection and alcoholism[2].

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