ANDES PEDIATRICA
REVISTA CHILENA DE PEDIATRÍA
www.scielo.cl

Andes pediatr. 2025;96(4):515-524
DOI: 10.32641/andespediatr.v96i4.5531

ORIGINAL ARTICLE

Diagnostic methods of extrapulmonary tuberculosis in a pediatric referral hospital

Métodos diagnósticos en tuberculosis extrapulmonar en pediatría en un hospital de referencia pediátrico

Dilia Fontalvo-Rivera[a,b], María Daniels-García[c], Jesly Doria-Atencia[a], Karen Tous-Barrios[a], Liliana Molinares-Núñez[d], Laura Cota Cardales[a,b], Shelly Navarro-Jay[a,b], Hernando Pinzón-Redondo[d]

[a]Universidad del Sinú. Cartagena, Colombia.
[b]Grupo de investigación Gibacus. Cartagena, Colombia.
[c]Universidad de Cartagena. Cartagena, Colombia.
[d]Universidad de Cartagena. Grupo de Investigación de Infectología Pediátrica, Fundación Hospital Infantil Napoleón Franco Pareja. Cartagena, Colombia.

Received: December 26, 2024; Approved: May 13, 2025

What do we know about the subject matter of this study?

Pediatric patients are at risk of presenting a disseminated form of tuberculosis, with risk of complications and death. The multiple clinical manifestations that can simulate other pathologies, together with the difficulty in microbiological isolation, make it a diagnostic challenge.

What does this study contribute to what is already known?

45.3% of the patients studied had epidemiological contact with an adult infected with TB, which presented a wide range of clinical symptoms. Following the WHO recommendation to perform confirmatory and rapid diagnostic tests, such as cultures and MB tests, reduced the sequelae and mortality from this disease in children in a 10-year analysis in a pediatric hospital in Colombia.

Abstract

The diagnosis of extrapulmonary tuberculosis (EPTB) in children is challenging due to the variable and nonspecific manifestations and the low rate of *M. tuberculosis* isolations which delayed diagnosis, leading to an increase in cases with unfavorable outcomes. **Objective:** To describe the use of traditional and confirmatory diagnostic methods for EPTB at the point of care (POC) in pediatric patients at a referral hospital. **Patients and Method:** Retrospective study in both male and female patients aged 0-17 years hospitalized from January 2012 to January 2022 in a pediatric referral hospital in Cartagena de Indias, Colombia. Sociodemographic, clinical, and microbiological variables were analyzed. A descriptive analysis of the variables according to their nature was performed using frequency

Keywords:
Extrapulmonary Tuberculosis;
Molecular Diagnostic Techniques;
Point of Care;
Mycobacterium tuberculosis

Correspondence:
Dilia Fontalvo Rivera
diliafontalvor@gmail.com

Edited by:
Paul Harris Diez

How to cite this article:Andes pediatr. 2025;96(4):515-524. DOI: 10.32641/andespediatr.v96i4.5531

distribution, confidence intervals, and measures of central tendency with statistical significance of p≤0.005. **Results:** Sixty-four cases were identified, with a mean age of 8.2±5.2 years and 51.6% were female. 30.2% (95% CI 19.2-43%) presented malnutrition, and 11.1% (95% CI 4.6-21.6%) were at risk of malnutrition. EPTB was found in the following areas: lymph node (60%), meningeal (7.8%), lymph node with peritoneal (7.8%), cutaneous, bone (vertebral), and peritoneal (6.3% each), and gastrointestinal and renal (3.1% each). Sequelae occurred more in cases when confirmatory tests were not used (60%) (p=0.0285). Confirmatory tests were used in 34 patients (53.1%), including solid medium culture in 29.7% of cases, of which 26.3% were positive. Molecular biology testing was used in 20.3% of cases, of which 53.6% were positive for *M. tuberculosis*. Among the factors that could have favored the development of sequelae were the time of consultation, the type of EPTB, and the use of confirmatory tests. In the latter case, they were more common in cases where confirmatory tests were not used (60%) (p=0.0285). **Conclusion:** The wide range of clinical manifestations of EPTB can be confused with other pathologies that, combined with the paucibacillary condition, can delay timely diagnosis. The use of confirmatory tests at the POC and interdisciplinary management leading to a timely diagnosis and management would allow a decrease in undesirable outcomes in pediatric EPTB. Analytical studies are needed to infer this behavior.

Introduction

Tuberculosis (TB) is a chronic bacterial infection found worldwide caused by *Mycobacterium tuberculosis* (*M. tuberculosis*), a slow-growing intracellular bacillus[1].

The World Health Organization (WHO) reported that in 2023, there were more than 10.8 million (95%CI 10.1-11.7 million) new TB cases, equivalent to 134 cases/100,000 inhabitants and 1.25 million (95%CI 1.13-1.37 million) deaths from this infection[2]. Among children aged 0 to 14 years, 1.3 million (1.2-1.3 million) cases were reported worldwide (12%), of which 166,000 died, representing 15% of all TB deaths[2]. 70-80% of the cases are pulmonary TB (PTB) and 20-30% are extrapulmonary TB (EPTB). This presentation is a manifestation of the systemic involvement of the disease and is seen more frequently in children than in adults because the risk of lymphohematogenous dissemination is high, especially in children under five years of age.

The most frequent form of presentation is the lymph node type. Other forms are renal, bone, meningeal, cutaneous, and abdominal, among others[3]. In children, it is particularly difficult to make a diagnosis of tuberculosis because most of the signs and symptoms of tuberculosis are nonspecific, the sensitivity of diagnostic tests is low in pediatric patients, and tuberculosis can mimic many other disease entities. However, the most important factor affecting morbidity and mortality rates is the early initiation of treatment[3-5]. In order to reduce the above and avoid the sequelae of PTB and EPTB, the WHO designed the strategy of point-of-care (POC) diagnostic confirmation of patients with suspected TB through rapid diagnostic support techniques to facilitate the timely management of these patients.

The objective of this study is to describe the follow-up of the diagnostic methods of EPTB performed at the POC of pediatric patients in a pediatric referral hospital in Cartagena de Indias (Colombia).

Patients and Method

Design

Retrospective study in patients of both sexes aged 0 to 17 years, hospitalized at the *Fundación Hospital Infantil Napoleón Franco Pareja* (FHINFP), in Cartagena de Indias, Colombia, from January 2012 to January 2022, with a diagnosis of TB according to the International Classification of Diseases 10 (ICD-10).

Terms definitions:

1. TB case: based on the definition of the tuberculosis program in Colombia, which considers TB to be any bacteriologically confirmed (Ziehl-Neelsen staining, culture, or molecular test) or clinically diagnosed case of TB involving organs other than the lungs[2,6].
2. Diagnostic confirmation: defined as the use of positive biological samples by Ziehl-Neelsen technique, culture, or molecular biology (MB) test[6].
3. Diagnostic criteria: include clinical, microbiological, tuberculin, imaging, histopathological, and epidemiological nexus criteria (Supplementary table 1, available online).
4. Clinical behavior description: semiological findings of the patients who participated in the study, which included the variables constitutional syndrome, specific symptoms, and non-specific symptoms. This classification was made according to the clinical finding that predominated in the study participants (Supplementary table 2, available online).

5. Microbiological behavior: refers to the characterization of *M. tuberculosis* as either susceptible or resistant to antitubercular drugs, determined through phenotypic susceptibility testing in liquid culture media and by identifying mutations in antitubercular drug-related genes that have been associated with drug resistance.
6. Therapeutic outcome: refers to the status of a patient discharged from the TB program, categorized by the variables: cure, treatment failure, or death.
7. Nutritional status: The nutritional classification was made according to parameters established by resolution 2465 of 2016, using the Anthro software version 3.22[7].

Variables under study

We analyzed sociodemographic variables (age, sex, place of origin, socioeconomic stratum, epidemiological link), clinical variables [BCG (*Bacillus Calmette-Guérin*) vaccination, previous pathologies, HIV, nutritional status, time of consultation and diagnostic confirmation from the onset of symptoms, respiratory symptoms, clinical findings, Purified Protein Derivative (PPD) test, imaging findings, treatment, and sequelae], and microbiological data [Ziehl-Neelsen test, Ogawa-Kudoh culture, Mycobacteria Growth Indicator Tube (MGIT) drug sensitivity test, and MB test].

Statistical analysis

The data extracted from the medical records were recorded in an Excel database that was shared through Google Drive. The data were verified by three people at different times to reduce interpretation or recording errors. Epi Info statistical software version 7.2.2.6 was used for statistical analysis. Nominal variables were presented using a frequency distribution and confidence intervals. Quantitative variables were analyzed by calculating the mean or median and their dispersion means. The comparison of the differences of proportions in the nominal qualitative variables was done using Fisher's exact test. A $p \leq 0.005$ value was considered statistically significant.

Ethical aspects

The research was conducted according to Chapters I and II of Resolution 8430 of 1993 of Colombia. The project was approved by the ethics committee of the *Fundación Hospital Infantil Napoleón Pareja*.

Results

75 cases of patients with a diagnosis of EPTB were registered, of which 11 were excluded because they did not meet the selection criteria. Of the 64 patients, 33 (51.6%) were female. The mean age was 8.2 ± 5.2 years, the most frequent age group was between 6 and 12 years (37.5%; 95%CI 25.7-50.4). Malnutrition was present in 19 cases (30.2%; 95%CI 19.2-43), and 7 cases were at risk of malnutrition (11.1%; 95%CI 4.6-21.6). A significant percentage of participants were less than 2 years of age (20.3%; 95%CI 11.3-32.2), of whom 21.1% presented malnutrition and 28.8% were at risk of malnutrition (Supplementary table 3, available online). 26 patients who underwent an ELISA test reported no HIV coinfection (40.6%).

The mean time of symptom onset at the time of consultation was less than one month in 31 participants (48.4%; 95%CI 35.8-61.3). Six patients consulted when they had already had symptoms over one year of onset (9.4%; 95%CI 3.5-19.3), which was higher for those from the rural area (19.1%) than those from the urban region (4.7%) ($p = 0.4176$) (Supplementary tables 4 and 5, Supplementary figure 1, available online).

Vaccination status, epidemiological contact, and PPD test

Three patients (4.7%) did not have BCG vaccination, of whom one (33.3%) had miliary and mesenteric TB, the other two patients (66.7%) presented cervical and cutaneous lymph node TB ($p = 0.0196$) (table 1). The absence of BCG vaccination was similar between age groups, with no statistical significance ($p = 0.8439$) (Supplementary table 3, available online).

29 patients (45.3%) had a history of exposure to TB (table 1). The most exposed group was children under 2 years of age (69.2%; $p = 0.2689$) (Supplementary table 3, available online). In patients in whom the PPD test was performed (89.1%), it was positive in 36 cases (56.3%) (table 1), mostly in the age group between 13 and 18 years (76.5%; $p = 0.0937$).

Clinical features

According to the diagnostic criteria used (table 1), 32 patients were found to have lymph node EPTB (60%), followed by meningeal and lymph node with peritoneal involvement with 5 cases each (7.8%), cutaneous, bone (vertebral), and isolated peritoneal EPTB with 4 cases each (6.3%), and gastrointestinal and renal TB in 2 participants (3.1%). There were EPTB cases with several locations, such as cerebral with spondylolisthesis, thoracic lymph node with pleural, miliary with mesenteric, ovarian with peritoneal lymph node, cerebral with tracheal, and bladder with lymph node, with one case each (1.6%).

Some of these cases were initially considered to have a different diagnosis, such as a 16-year-old female patient from Venezuela with ovarian and peritoneal lymph node TB, who presented prolonged fever, abdominal pain, and menometrorrhagia lasting two

Table 1. Diagnostic criteria used*

	Frecuency	%	CI95%	
			Lower limit	Upper limit
Culture				
Negative	14	21.88	12.51	33.97
Not performed	36	56.25	43.28	68.63
No report	9	14.	7.76	26.86
Positive	5	7.81	1.73	15.24
Total	64	100.00		
Molecular biology				
Not performed	40	62.50	49.51	74.30
No report	11	17.19	8.90	28.68
Positive	7	10.94	4.51	21.25
Negative	6	9.38	3.52	19.30
Total	64	100.00		
Ziehl-Neelsen				
Negative	18	28.13	17.60	40.76
Not performed	26	40.63	28.51	53.63
No report	8	12.50	5.55	23.15
Positive	12	18.75	10.08	30.46
Total	64	100.00		
Confirmatory test				
No	30	46.88	34.28	59.77
Yes	34	53.13	40.23	65.72
Total	64	100.00		
Biopsy				
Granulomatous reaction and caseation necrosis	57	89.06	78.75	95.49
No report	7	10.94	4.51	21.25
Total	64	100.00		
Imaging	64	100.00	94.40	100.00
Total	64	100.00		
Clinical features	64	100.00%	94.40	100.00
Total	64	100.00%		
TB Contact				
No	35	54.69%	41.75	67.18
Yes	29	45.31%	32.82	58.25
Total	64	100.00%		
Purified Protein Derivate				
Negative	21	32.81%	21.59	45.69
No performed	7	10.94%	4.51	21.25
Positive	36	56.25%	43.28	68.63
Total	64	100.00%		

*The criteria that were always used were the clinical and imaging components.

months. She was diagnosed through ultrasound imaging with a retroperitoneal and ovarian mass with a hepatic nodule. The biopsy results of the ileal serosa, parietal peritoneum, affected lymph nodes, and the right fallopian tube and ovary showed a chronic granulomatous caseating and necrotizing inflammatory reaction, with no evidence of malignancy. *M. tuberculosis* was identified through MB testing of the peritoneal fluid. The PPD test was positive (14 mm). The Ziehl-Neelsen stain and the adenosine deaminase (ADA) assay were not reported. The family denied any known contact with tuberculosis and reported complete vaccination (though they did not have the vaccination card). The patient had a history of asthma with frequent respiratory episodes; however, no respiratory infection or abnormal findings on chest X-ray were observed during hospitalization.

The most reported respiratory history was pneumonia (17%) (Supplementary figure 2, available online). The specific clinical manifestations predominated in the lymph node EPTB type in 26 cases (81.3%) and bone in 3 cases (75%), while the nonspecific type predominated in those of abdominal origin, such as gastrointestinal (50%), miliary and mesenteric (100%), peritoneal (75%), renal (100%), and bladder (100%). Constitutional syndrome manifestations were observed in 6 patients (9.4%) who had EPTB involving the central nervous system (CNS), bones, gastrointestinal tract, and ovaries (Supplementary table 6, available online).

Physical examination findings varied according to the type of EPTB (figure 1). According to age group, in children under 2 years of age, fever was the main symptom (46.2%). In this group, lymph node EPTB was the most frequent (46.2%), with manifestation of

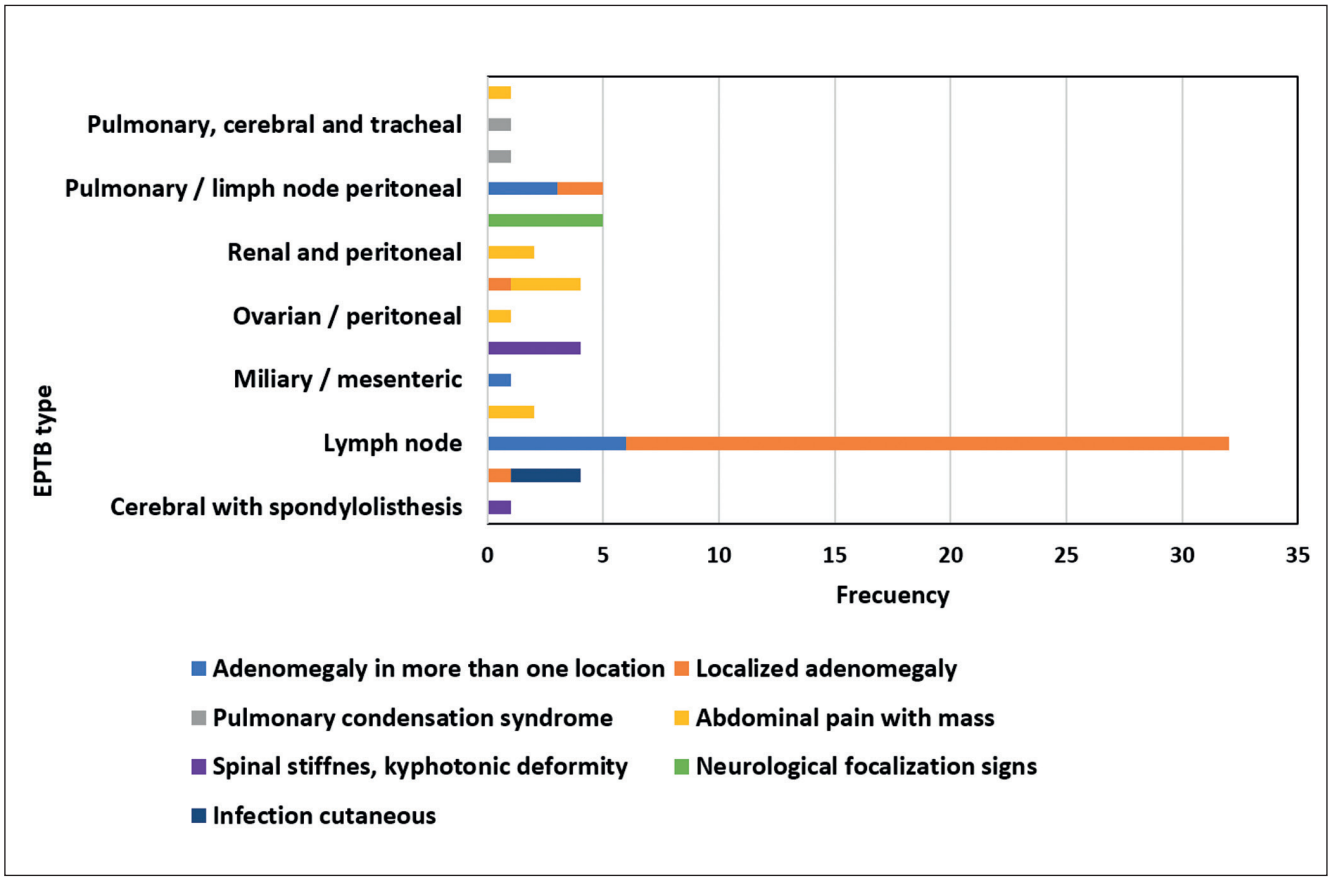

Figure 1. Main findings on physical examination according to the type of extrapulmonary tuberculosis (EPTB). The most relevant findings varied according to the type of EPTB. Localized adenomegaly was notable in 30 cases (46.9%) and in more than one location in 10 cases (15.6%) with lymph node TB (including cases with coexisting multiple EBT locations and one with cutaneous TB). In patients with gastrointestinal, peritoneal, and ovarian TB, abdominal pain and a palpable abdominal mass were present (9 cases, 14.1%). Cervical deformity was observed in all 5 cases of spondylolisthesis-type bone TB. In all 5 patients (7.8%) with meningeal TB, signs of neurologic localization were found, and presentation with signs of superficial skin infection was observed in 3 patients (4.7%) with cutaneous TB.

a mass at one location (66.7%) and fever (33.3%). In the group aged 3 to 5 years, fever was also the most frequent manifestation (40%). In this group, symptoms of constitutional syndrome in cases of gastrointestinal TB (50%) and peritoneal TB (50%) stand out. In school children (aged 6 to 12 years) and adolescents (aged 13 to 18 years), a lymph node mass in one location (64.3% and 63.6%, respectively) was highlighted in lymph node TB. In cases of spinal bone TB (8.3%), those aged 6 to 12 years presented cervical and dorsal spine deformity (8.3%). In adolescents, the constant and recurrent superficial skin infection (66.7%) in cutaneous TB (17.7%) stands out (Supplementary table 7, available online).

Diagnostic imaging studies

Imaging studies included chest X-rays, in which images compatible with parenchymal consolidation, paratracheal lymphadenopathy, and pleural effusion were observed. The CT scan showed ascites and retroperitoneal lymphadenopathy in gastrointestinal and ovarian TB. MRI showed tuberculomas and ventriculomegaly in the CNS TB, along with cervical vertebral body deformity and wedging associated with vertebral spondylolisthesis (Supplementary table 7, available online).

Diagnosis with Ziehl-Neelsen staining and confirmatory tests for *M. tuberculosis*

Microbiological studies included Ziehl-Neelsen staining of samples such as peritoneal fluid, cerebrospinal fluid, and solid tissue samples, which was performed in 46.9% of patients, being positive in 18.8% (95%CI 10.1-30.5) of them, being more representative in the 6-12 years age group (41.7%; p = 0.1114) (Supplementary table 3, available online).

Diagnosis with confirmatory tests for *M. tuberculosis* was performed in 34 participants (53.13%) (table 1). Solid medium culture was used in 29.7% of the patients, of which mycobacterial growth was identified in 26.3% of them, representing 7.8% (95%CI 1.7-15.2) of the total number of participants. The percentage of negative cases was higher (21.9%), especially in the 3-5 years age group (40%; p = 0.0756) (Supplementary table 3, available online). No statistical significance was found in the analysis of EPTB type and age group and their possible influence on mycobacterial growth in culture (p = 1) (Supplementary table 8, available online).

MB testing was used in 20.3% of the cases, of which 53.9% revealed the presence of *M. tuberculosis,* representing 10.9% (95%CI 4.5-21.3) of the total number of participants (table 1). There was also no significant difference between the presence of the mycobacterium according to age groups and type of EPTB (p = 0.4639) (Supplementary tables 3 and 9, available online).

A tendency toward the use of confirmatory tests was observed among participants. In 2019, there was an increase in the use of molecular testing, which coincided with a decline in culture requests. By 2020, molecular testing was rarely used, while culture use remained steady. Toward the end of 2021 and the beginning of 2022, this trend reversed (figure 2).

Overall, 67.2% of participants were diagnosed and enrolled in the TB program within the first 30 days of hospitalization. Only 8.2% were diagnosed within the first week of hospitalization. The time to diagnosis varied according to the EPTB type. Those cases that required solid tissue sampling, such as lymph node and bone TB, were more frequently confirmed after more than 30 days (Supplementary figure 3, available online).

Treatment and Outcome

All patients received the management scheme proposed by WHO[8] and the Colombian Ministry of Health's TB program, with first-line antituberculosis drugs, including isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E) (Supplementary table 8, available online). No strains resistant to first-line antituberculosis drugs were found (Supplementary table 10, available online).

The outcome was cure in 51 patients (76.7%; 95%CI 67.8-88.7), sequelae in 10 cases (15.6%; 95%CI 7.8-26.9), and 3 participants (4.7%; 95%CI 0.98-13.09) were lost to follow-up in the program (table 2). It is worth noting that all patients who achieved a cure (76.7%) completed the full course of treatment. The patients who were lost to follow-up (4.7%) did not complete treatment, and it was not possible to reestablish contact with their parents or guardians to reintegrate them into the TB control program.

Among the factors observed for the development of sequelae were the consultation time, the type of EPTB, and the use of confirmatory tests. The patients who had a time greater than one month from the onset of symptoms and the date of consultation had a higher frequency of sequelae (8/10; 80%) (p = 0.0507). Of the patients with sequelae, 60% (6/10) had CNS EPTB. The sequela presented in these patients was childhood cerebral palsy. The other type of sequela was kyphoscoliotic and lumbar deformity secondary to spondylodiscitis and spondylolisthesis (Pott's disease) presented in 4 patients (40%) (Supplementary figure 4, Supplementary table 11, available online). The percentage of patients with sequelae was higher where confirmatory tests were not used (60%) (p = 0.0285) (figure 3).

Table 2. Outcome in antituberculosis management

Outcome*	Frecuency	%	CI 95%
Cure	51	79.69	67.77-88.72
Lose to follow-up	3	4.69	0.98-13.09
Sequelae	10	15.63	7.76-26.86
Total	64	100.00	

*15.6% of participants had sequelae secondary to Extrapulmonary Tuberculosis (EBT)

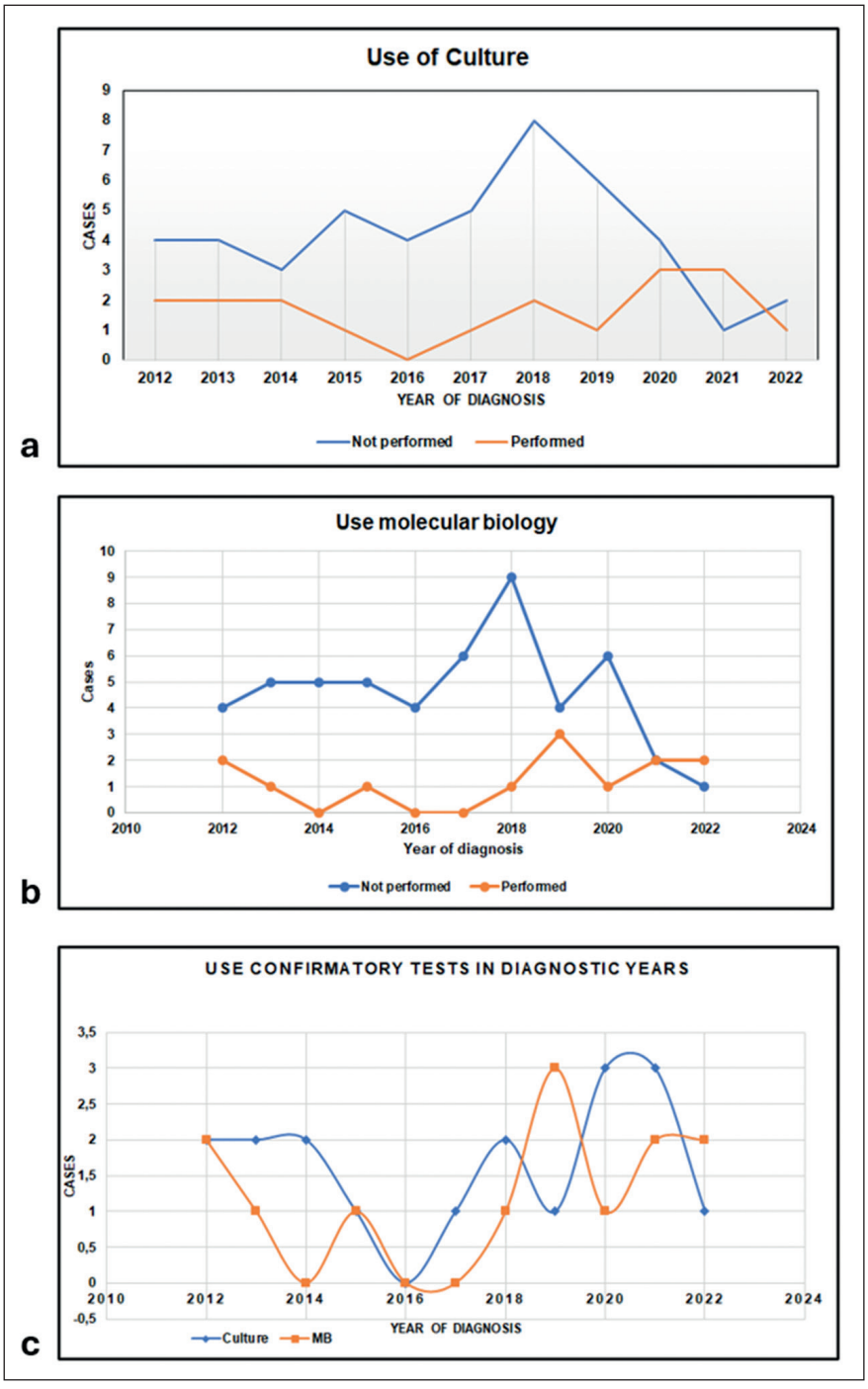

Figure 2. Diagnostic confirmation over the ten years. a. Use of culture. Starting in 2016, there was an upward trend in the use of culture, which stabilized by 2020 and increased again in 2021. **b.** Use of molecular biology tests. Towards 2018, there was an upward trend in the use of the BM test, which decreased in 2020 and reached a new peak in 2021, which has been sustained. **c.** Towards the end of 2017, an increase in the use of confirmatory tests was observed, especially for BM, which decreased in 2020 and stabilized by 2021. Culture progressed in 2019 and then stabilized in 2020.

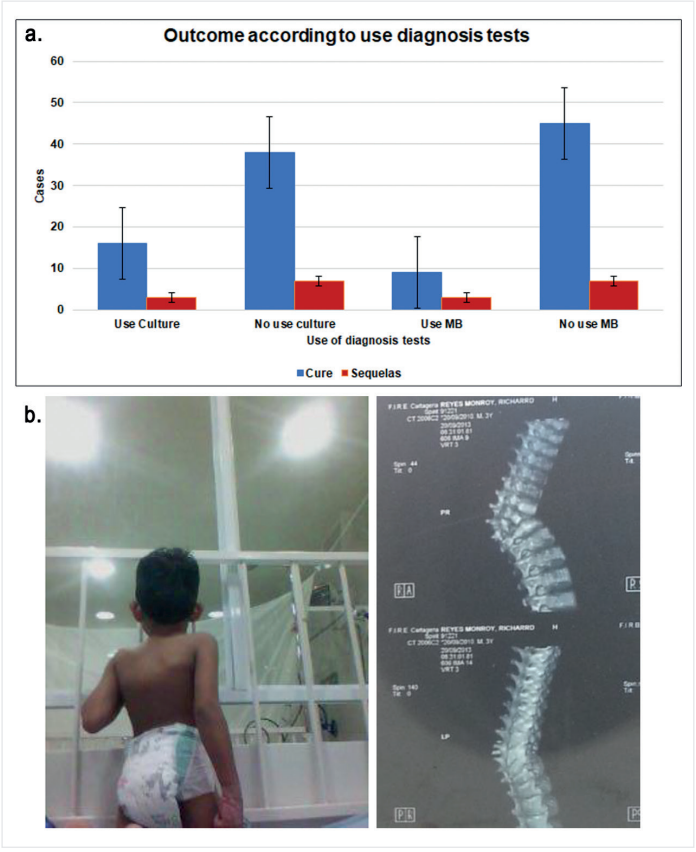

Figure 3. Outcome and sequelae. a. Outcome according to the use of diagnostic tests. The frequency of cases with sequelae was higher when neither culture nor the rapid molecular biology test were used. **b.** Case of bone TBE. Kyphotic deformity due to spondylodiscitis with retrolisthesis and fracture of the T11 vertebra with destruction of the intervertebral disc.

Discussion

The diagnosis of TB in children is difficult due to the different and nonspecific manifestations and the low proportion of *M. tuberculosis* isolates, which can lead to an increase in cases of extrapulmonary dissemination with unfavorable outcomes.

45.3% of the patients had epidemiological contact, which agrees with what is established in TB control programs, as a TB sentinel event in the adult population in the search for respiratory symptoms and the diagnosis of the disease in contact cases within the epidemiological chain.

It is necessary to have a scheme of diagnostic criteria in pediatric EPTB, which provides the possibility of timely detection in order to avoid undesirable outcomes, such as secondary sequelae, as occurred in 12.5% of patients. Thus, friendly diagnostic methods have been established to facilitate early therapeutic conduct. In 2010, the GeneXPert system, a rapid MB test for the diagnosis of PTB in adults and resistance to Rifampicin, was launched and approved by the WHO[9].

At least 20% of all adults (up to 30-40% of those co-infected with HIV) and most patients under five years of age are paucibacillary (less than 10 *M. tuberculosis* per 100 fields) and making the diagnosis of the disease challenging, as is also the case in EPTB[10]. This has led to research into more innovative tests to support TB diagnosis in children, especially EPTB[11]. One proposed approach is the use of the optimized Xpert testing for non-sputum-based samples (such as nasopharyngeal specimens, body fluids, and tissues), and other Nucleic Acid Amplification Tests (NAAT)[11].

A wide range of MB tests for the detection of TB and drug resistance are being developed and evaluated, and while some tests are intended for use in reference laboratories, others are aimed at peripheral POC settings[12,13]. Following the 2010 approval of Xpert MTB/RIF and the 2017 approval of Xpert MTB/RIF Ultra (a more sensitive version), WHO reiterates the use of rapid MB tests as the initial test for TB and rifampicin resistance, and added Truenat MTB, MTB plus, and MTB-RIF (Molbio, Bangalore, India)[14]. In the case of children under five years of age or those patients with difficulty expectorating, sample collection is recommended through induced sputum, gastric aspirate, nasopharyngeal specimens, or stool. In cases of EPTB, samples should be collected from fluids or the affected tissues[15,16].

In Colombia, an eight-year retrospective study of TB in children found that the most frequent site was the lymph node (40.6%), followed by meningeal (21.9%), and ocular (18.8%). Microbiological confirmation was obtained in only 25% of cases, with clinical assessment (75%) being the main criterion for establishing the diagnosis[17]. For the diagnosis of EPTB in the study participants, the diagnosis was made by criteria designed to facilitate the diagnosis of TB in pediatrics[18-22]. As in other studies of TB in pediatrics[23-26], the criteria always used for the diagnosis of TB were clinical and imaging (100%), which gives it the classification as clinically diagnosed TB. The use of confirmatory diagnostic tests at the POC showed a variable trend towards an increase in their use, leading to a diagnosis that guides the use of therapeutic schemes more focused on the sensitivity to antituberculosis drugs.

The FHINFP is a hospital center that receives the most complex pediatric cases in Cartagena de Indias, Colombia. The participants presented with a wide range of clinical manifestations resembling various infectious and non-infectious diseases, requiring evaluation by a multidisciplinary team of specialists, including infectious diseases, hemato-oncology, gastroenterology, orthopedics, radiology, pathology, dermatology, neurosurgery, surgery, pediatric inten-

sive care, and cardiology, in order to achieve an accurate diagnosis.

At FHINFP, we face additional diagnostic limitations such as the patients' remote places of origin, delays in consultations, and the time required for diagnostic confirmation. Given this, we classify patients based on clinical manifestations and findings, as previously described. A brochure outlining the proposed management algorithm for TB is also available (Supplementary figure 5, available online).

This study has limitations, such as its descriptive and retrospective design, with data that could not be considered in the results and that could have modified the statistical analysis. A prospective follow-up with defined comparative studies is required to give greater support to the results.

In conclusion, EPTB in pediatrics can have undesirable outcomes that could be prevented with the use of diagnostic criteria, confirmatory tests at the POC, and interdisciplinary management to guide timely diagnosis and management. It is necessary to reinforce the diagnosis in the POC to reduce the sequelae or mortality due to this disease.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: This study was approved by the respective Research Ethics Committee. The authors state that the information has been obtained anonymously from previous data.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

Acknowledgments

To the patients, family members, and healthcare personnel of the FHINFP for the collaboration offered in the development of this study. To Dr. Doris Gómez Camargo† for her guidance and academic support.

References

1. Ankrah AO, Glaudemans A, Maes A, Van de Wiele C, Dierckx R, Vorster M, et al. Tuberculosis. Semin Nucl Med. 2018;48(2):108-30.
2. World Health Organization. Global Tuberculosis Report 2024. Geneva2024.
3. Kaba O, Kara M, Odacilar CA, Kamer I, Sutcu M, Demir SO, et al. Evaluation of cases of pediatric extrapulmonary tuberculosis: a single center experience. Turk Pediatri Ars. 2019;54(2):86-92.
4. Perez-Velez CM, Marais BJ. Tuberculosis in children. N Engl J Med. 2012;367(4):348-61.
5. Muhumuza J, Asiimwe BB, Kayes S, Mugyenyi R, Whalen C, Mugerwa RD, et al. Introduction of an in-house PCR for routine identification of M. tuberculosis in a low-income country. Int J Tuberc Lung Dis. 2006;10(11):1262-7.
6. Graham SM, Ahmed T, Amanullah F, Browning R, Cardenas V, Casenghi M, et al. Evaluation of tuberculosis diagnostics in children: 1. Proposed clinical case definitions for classification of intrathoracic tuberculosis disease. Consensus from an expert panel. J Infect Dis. 2012;205 Suppl 2:S199-208.
7. World Health Organization. Child growth standards https://www.who.int/tools/child-growth-standards/software2011.
8. World Health Organization. Guidance for rational tuberculosis programmes on the management of tuberculosis in children. 2nd edition ed. Geneva2014. p. 11-4.
9. World Health Organization. Rapid Implementation of the Xpert MTB/RIF Diagnostic Test: Technical and Operational, How-to; Practical Considerations. Geneva2011.
10. Rossato Silva D, Muller AM, Dalcin Pde T. Factors associated with delayed diagnosis of tuberculosis in hospitalized patients in a high TB and HIV burden setting: a cross-sectional study. BMC Infect Dis. 2012;12:57.
11. Denkinger CM, Kampmann B, Ahmed S, Dowdy DW. Modeling the impact of novel diagnostic tests on pediatric and extrapulmonary tuberculosis. BMC Infect Dis. 2014;14:477.
12. MacLean E, Broger T, Yerlikaya S, Fernandez-Carballo BL, Pai M, Denkinger CM. A systematic review of biomarkers to detect active tuberculosis. Nat Microbiol. 2019;4(5):748-58.
13. MacLean E, Kohli M, Weber SF, Suresh A, Schumacher SG, Denkinger CM, et al. Advances in Molecular Diagnosis of Tuberculosis. J Clin Microbiol. 2020;58(10).
14. Branigan D. An activist's guide to tuberculosis. Diagnostic tools. Treatment Action Group [Internet]. 2020. Available from: https://www.treatmentactiongroup.org/wp-content/uploads/2020/07/activists_guide_tb_diagnostic_tools_2020.pdf.
15. KNCV Tuberculosis Foundation. SOS Stool method brings Xpert TB diagnosis closer to children. Netherlands2020.
16. World Health Organization. Guidance for national tuberculosis programmes on the management of tuberculsosis in children. Second ed. Geneva2014.
17. Sepulveda EVF, Yunda LFI, Herrera KCM, Moreno GC. Extrapulmonary tuberculosis in colombian children: Epidemiological and clinical data in a reference hospital. Int J Mycobacteriol. 2017;6(2):132-7.
18. Castillo V. Valor diagnóstico de los criterios de Stegen moficado por Toledo en la tuberculosis infantil en el Hospital Nacional Guillermo Almenara Irigoyen. Revista Peruana de Pediatría. 2005:31-9.
19. Viani RM, Lopez G, Chacon-Cruz E, Hubbard P, Spector SA. Poor outcome is associated with delayed tuberculosis diagnosis in HIV-infected children in Baja California, Mexico. Int J Tuberc Lung Dis. 2008;12(4):411-6.
20. Oberhelman RA, Soto-Castellares G, Gilman RH, Caviedes L, Castillo ME, Kolevic L, et al. Diagnostic approaches for paediatric tuberculosis by use of different specimen types, culture methods, and PCR: a prospective case-control study. Lancet Infect Dis. 2010;10(9):612-20.
21. Goicochea C, Cuito H y cols. Asociación de criterios de Stegen modificado por Toledo para el diagnóstico de tuberculosis pediátrica, Hospital Belén de Trujillo. Scientia. 2012;4:64-71.
22. Delgado ML, Gonzalez NE. [Comparison of the predictive ability of two scoring systems for the diagnosis of tuberculosis in children]. Arch Argent Pediatr. 2015;113(6):491-7.
23. Chisti MJ, Shahid A, Shahunja KM, Banu S, Raqib R, Shahrin L, et al. Comparative Performance of Modified Kenneth Jones Criteria Scoring, World Health Organization Criteria, and Antibodies in Lymphocyte Supernatant for Diagnosing Tuberculosis in Severely Malnourished Children Presenting With Pneumonia. Front Pediatr. 2019;7:406.
24. Pearce EC, Woodward JF, Nyandiko WM, Vreeman RC, Ayaya SO. A systematic review of clinical diagnostic systems used in the diagnosis of tuberculosis in children. AIDS Res Treat. 2012;2012:401896.
25. Cortez AO, Melo AC, Neves LO, Resende KA, Camargos P. Tuberculosis in Brazil: one country, multiple realities. J Bras Pneumol. 2021;47(2):e20200119.
26. Martinez L, Vazquez S, Flores MLM, Notejane M, Zabala C, Giachetto G, et al. [Extrapulmonary tuberculosis in children under the age of 15 hospitalized at the Pereira Rossell Hospital Center, Uruguay]. Rev Chilena Infectol. 2020;37(5):577-83.