Findings and Utility of Chest Computed Tomography in Pediatric Tuberculosis

Victor Moreno-Ballester[1] Fernando Aparici-Robles[2] Luis Marti-Bonmati[3] Amparo Escribano-Montaner[4] Eugenio Sanchez-Aparisi[5] Carmen Otero-Reigada[6] Fernando Gomez-Pajares[7]

[1] Department of Radiology, Hospital Universitario Casa de Salud, Valencia, Spain
[2] Department of Radiology, Hospital Universitario y Politécnico La Fe, Valencia, Spain
[3] Department of Radiology and GIBI230 Research Group, Hospital Universitario y Politécnico La Fe, Valencia, Spain
[4] Department of Pediatrics, Universidad de Valencia, Valencia, Spain
[5] Department of Radiology, Hospital Francesc de Borja, Gandia, Valencia, Spain
[6] Department of Pediatrics, Hospital Universitario y Politécnico La Fe, Valencia, Spain
[7] Department of Preventive Medicine, Hospital Arnau de Vilanova, Valencia, Spain

Address for correspondence Victor Moreno-Ballester, PhD, Hospital Universitario Casa de Salud, Valencia, Valencia, Spain (e-mail: vmorenoba@gmail.com).

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Abstract

The objectives of this study are to describe the radiologic abnormalities detected on chest computed tomography (CT) of children suffering from tuberculosis and identify in which asymptomatic children, with positive tuberculin skin test and normal chest radiography, CT has the highest diagnostic yield using a low radiation dose protocol. The most common finding on CT in cases of tuberculosis is lymphadenopathy with necrotic appearance. In asymptomatic children with positive tuberculin skin test and normal chest radiography, CT had higher diagnostic yield in children younger than 5 years, modifying the therapeutic approach in a high percentage of cases. Reduction kilovoltage (kV) and milliamperage (mA) protocols significantly decrease the radiation dose, keeping sufficient diagnostic quality.

Keywords
- tuberculosis
- computed tomography
- radiation

Introduction

Tuberculosis disease (TD) in childhood is one of the developmental stages of primary infection. Following inhalation of tubercle bacilli, most patients do not develop the disease and latent tuberculous infection (LTBI) persists, with the only manifestation of positivization of tuberculin skin test (TST), without radiological or clinical evidence of disease. In these cases, a small number of viable tubercle bacilli remains dormant without causing clinical disease.[1] Therefore, usually the diagnosis is not performed, and they are only discovered incidentally when a TST is done.[2]

The progression from infection to disease depends on host and bacillus factors. The vulnerability is determined by the age and immune status of the child, the infective load and intimacy, and duration of contact with a smear positive patient, with a higher risk when the source of infection is the mother.[1–3]

Infants are the age group most likely to progress to disease, both lung (30–40%) and meningeal or disseminated (10–20%). Risk decreases in the second year of life (10–20% for pulmonary tuberculosis and 2–5% for meningeal–disseminated). Between 2 and 5 years, the TD risk is 5%, and between 5 and 10 years, progression to disease is approximately 2%, increasing again over 10 years to 10 to 20%.[4,5]

Since in almost all cases (95%) this progression occurs during the year after primary infection, treatment should begin as soon as possible when the diagnosis is suspected.

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Latent tuberculous infection can be treated with one drug, isoniazid (H). However, TD is treated with three, or more recently, four drugs, because of the increasing resistance of *Mycobacterium tuberculosis*.[6–13]

Since LTBI and TD require different treatment regimens, it is necessary to differentiate and diagnose them, to start proper treatment to prevent progression from infection to disease or complications from the latter.[14,15] However, in pediatric patients, the distinction between them is sometimes difficult.

In children, the diagnosis of TD is based on the concurrence of recent contact with the infectious source (not always known), positive TST, and suggestive findings on chest radiography or compatible symptoms.

The presence of symptoms could be the best indicator to differentiate infection from disease. However, while in adults TD is almost always symptomatic, in infancy, up to 50% of the initial stages are not or they have few clinical manifestations, usually nonspecific.[5,16]

The definitive diagnosis is determined by the isolation of the bacillus, but its profitability is low in pediatric patients. The sensitivity of culture is 30 to 40% in gastric aspirates and sputum, probably due to the paucibacillary nature of childhood TD and the difficulty in obtaining adequate samples. Additionally, microbiological culture confirmation is slow, often taking 3 to 8 weeks.[11,16]

Therefore, with insignificant or absent clinical symptoms, a story of uncertain exposure, and a positive TST, TD diagnosis depends on the detection of abnormalities in the chest radiography.

The presence of thoracic lymph nodes is the most common radiographic finding. Their identification depends on the size and location, but the chest radiography has low sensitivity and specificity for detection with high discordance among observers.[17–19] Swingler et al[20] place this sensitivity and specificity at 67 and 59%, respectively.

Chest CT is considered the radiological technique of choice for the detection and evaluation of lymph nodes and is also more sensitive and specific to assess the pulmonary parenchyma. However, there are controversies regarding indications of CT.

The arguments against CT are the use of ionizing radiation, intravenous contrast, and the need to sedate patients in some cases. In addition, CT also presents false positives and negatives in the detection of lymph nodes, with variability between observers.[17,18] Despite its advantages, the role of CT in TD in children is controversial and cannot systematically be used in all asymptomatic children with positive TST and normal chest radiography.

The objectives of this paper are to describe the radiological abnormalities detected on chest CT in children with TD, especially the morphological characteristics of the lymph nodes, and to identify in which asymptomatic children with positive TST and normal chest radiography, CT has greater diagnostic yield by modifying the therapeutic approach to define the indications of CT in this group. It also aims to assess the reduction of radiation through a CT protocol with low dose.

Materials and Methods

Descriptive case series, observational and retrospective study, in which the clinical, epidemiological, and microbiological features are reviewed, as well as chest radiography and CT studies, contained in medical and radiological records of all patients.

The study group is composed of all children (0–15 years old) who had a chest CT performed in the context of TD at the Hospital Universitario y Politécnico La Fe, during a period of 4 years.

Two groups of patients were differentiated. The first group (G1) included children who underwent thoracic CT systematically as part of the evaluation of a TD infection and met the criteria of positive TST, having no clinical symptoms and a normal chest radiography.

The second group (G2) was formed of children with positive TST, clinical, radiologic, and/or microbiological findings compatible with TD, who had a chest CT performed to confirm the diagnosis if a prior chest radiography was normal or to evaluate the possible complications of the disease.

CT studies were performed with equipment Siemens Somaton (Siemens Healthcare, Germany) and Philips Brilliance (Philips Medical System, The Netherlands) using iodinated intravenous contrast (300 mg/mL) at 2 mL/kg, with a flow between 1 and 1.5 mL/s, and an acquisition delay of 30 seconds. Reconstructions of 2.5 mm thickness were obtained from the apex to the lung bases. Sedation by an anesthesiologist was required when children could not remain immobile during the CT study.

Reducing the radiation dose was achieved by a single helical acquisition with reduced kilovoltage (kV) and milliamperage second (mAs) (80–120 kV and mAs 30–70). The pitch factor ranged from 1 to 1.5.

Findings were considered compatible with TD in the presence of lymph nodes larger than 5 mm and/or parenchymal or pleural alterations (consolidation, opacities, nodules, atelectasis, air trapping, pleural effusion, and empyema).

Results

During the study period, a total of 82 children were studied with chest CT in the context of tuberculosis infection or disease. The age ranged between 3 months and 14 years, with a mean of 6.5 years. In the G1 (asymptomatic with normal chest radiography), 52 children (63.4%) were included, with an average age of 6.6 years. The G2 included 30 children (36.6%) with a mean age of 6.3 years.

In the G1, CT discarded lesions in 48.1% of cases (25 patients), with a LTBI final diagnosis. In the remaining 51.9% (27 cases), TD radiological abnormalities were observed.

In the G2, CT confirmed the diagnosis in 66.7% of cases (20 children) and ruled out active TB in 33.3% (10 cases).

Lymph nodes were identified in 95.7% of cases of TD, being present in 50% of patients in G1 and in 66.7% of patients in G2. Only in two children, classified as TD, no lymph nodes were identified, probably because of a CT false negative. Most of the lymph nodes (60%) had a necrotic appearance, with central low

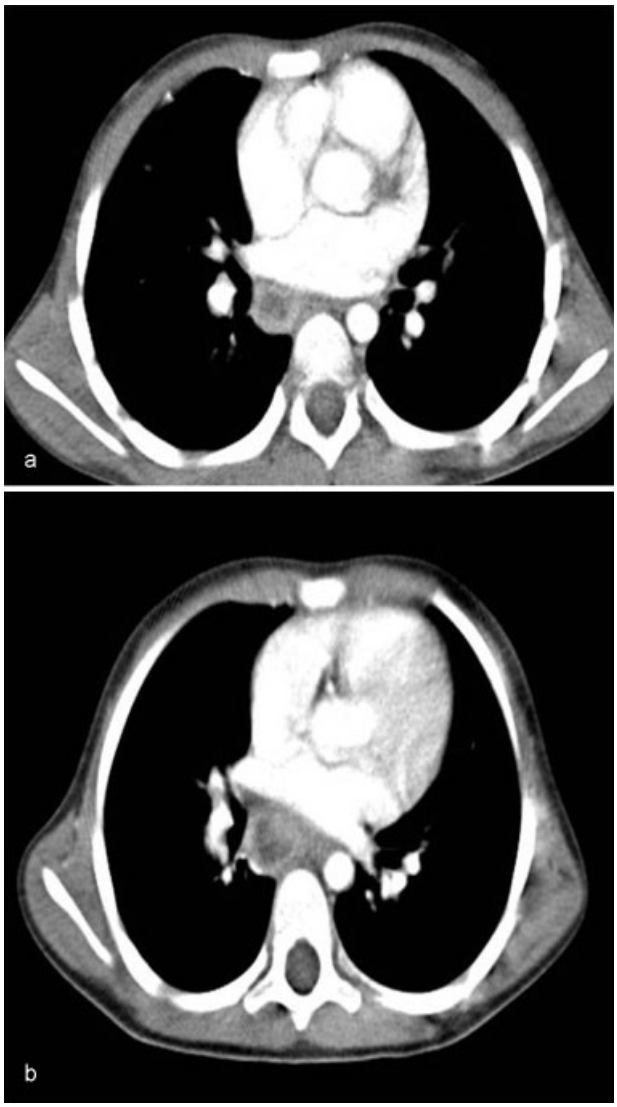

Fig. 1 (**a** and **b**) Necrotic lymphadenopathy.

attenuation and peripheral contrast enhancement, as well as a larger average size. As for their location, most were hilar, followed by infrahilar and suprahilar. ►**Fig. 1**.

Lesions in the lung parenchyma were observed in 72.3% of children with TD. Consolidations (35.3%), nodules (29.4%), and opacities (23.5%) were the most frequent. In the group of asymptomatic children, nodules were more frequent (47%), and consolidations (41.2%) were more frequent in the group of symptomatic children. There was pleural involvement in 10.6% of cases and bronchial compression in 38.3%. These results are shown in ►**Table 1** and ►**Figs. 2** and **3**.

A statistically significant association between the presence of lung lesions and lymph nodes was found, as well as with their necrotic appearance ($p < 0.001$, Pearson χ^2). Similarly, there was an association between positive culture for *M. tuberculosis*, presence of lymph nodes ($p = 0.05$, Pearson χ^2), and their necrotic appearance ($p = 0.009$, Pearson χ^2). Necrotic lymph nodes were present in 83.3% of patients with bronchial compression, finding a significant relationship ($p < 0.001$, Pearson χ^2) with the highest average size in this kind of nodes.

Table 1 Findings on CT in cases of tuberculous disease on both subgroups

Tuberculous disease	G1 27	G2 20	Total 47
Lymphadenopathy	25 (92.6%)	20 (100%)	45 (95.7%)
Necrotic lymphadenopathy	17 (68%)	10 (50%)	27 (60%)
Homogeneous lymphadenopathy	6 (24%)	7 (35%)	13 (28.9%)
Calcified lymphadenopathy	2 (8%)	3 (15%)	5 (11.1%)
Parenchymal involvement	17 (63%)	17 (85%)	34 (72.3%)
Consolidation	5 (29.4%)	7 (41.2%)	12 (35.3%)
Opacities	4 (23.5%)	4 (23.5%)	8 (23.5%)
Nodules	8 (47%)	2 (11.8%)	10 (29.4%)
Atelectasis	2 (11.8%)	2 (11.8%)	4 (11.8%)
Emphysema	0	4 (23.5%)	4 (11.8%)
Granuloma	0	2 (11.8%)	2 (5.9%)
Pleural involvement	1 (3.7%)	4 (20%)	5 (10.6%)
Bronchial compression	9 (33.3%)	9 (45%)	18 (38.3%)

Abbreviation: CT, computed tomography.

Findings by Age and Type of Contact

Abnormalities detected on chest CT were analyzed by age subgroups (children under 2 years, 2–5 years, between 6 and 10 years, and older than 10 years) and type of contact with the smear-positive source (close contacts, casual, or unknown). A statistically significant association between the age groups and the presence of alterations in the CT ($p = 0.023$, Pearson χ^2) was present, with CT abnormalities in all children under 2 years and in 69.7% of the group between 2 and 5 years.

Regarding the existence of lymphadenopathy, differences between age groups were observed ($p = 0.021$ Pearson χ^2), being present in all children under 2 years and in 66.7% of children between 2 and 5 years. The particularity of presenting necrotic center and peripheral enhancement was given in 66.7% and 77.3% of patients in these two groups, respectively ($p = 0.04$, Pearson χ^2).

There were also differences between the age groups in the existence of parenchymal involvement ($p = 0.011$, Pearson χ^2), with lesions in all children under 2 years, while 70.4% of children between 6 and 10 years showed no abnormalities.

There was a statistically significant association between diagnosis of LTBI or TD and age groups ($p = 0.010$, Pearson χ^2), observing higher frequency of TD in children under 2 years (100%) and in the group of children between 2 and 5 years (69.7%) and lower incidence in the group of 6 to 10 years (37%).

Regarding the intimacy of contact, over 60% of intimate, habitual, and unknown contacts had lesions on CT, compared with 33.3% of casual contacts. These results are consistent with the increased possibility of disease in close contacts

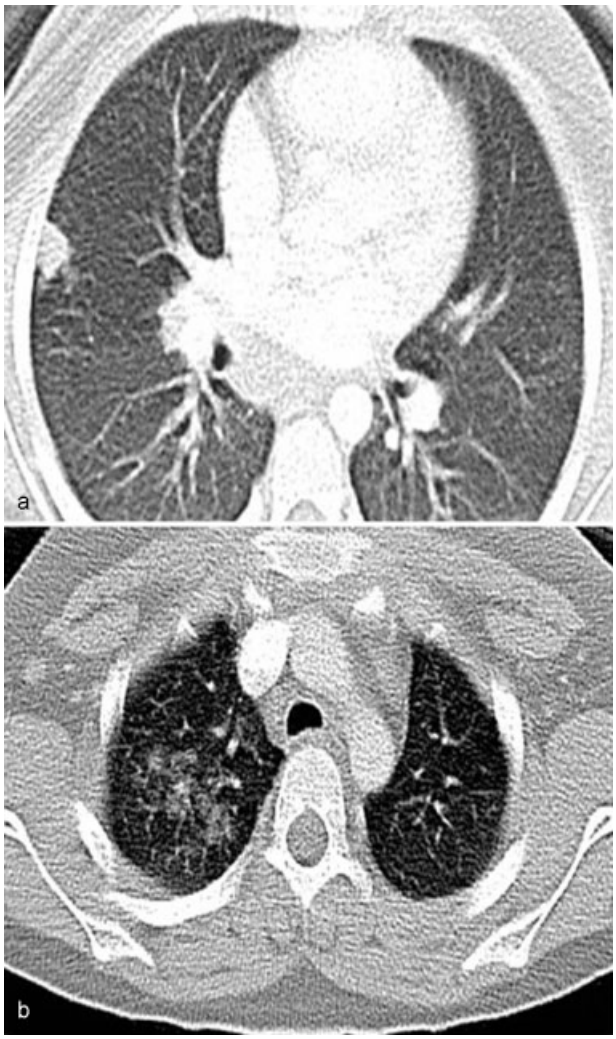

Fig. 2 (**a** and **b**) Subpleural peripheral nodule and lung opacity in upper right lobe.

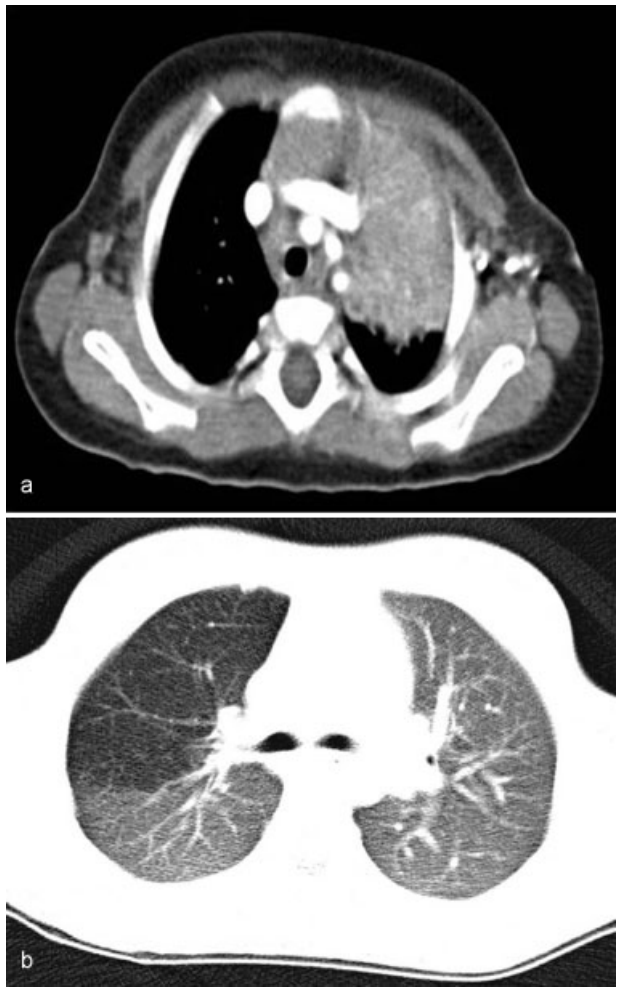

Fig. 3 (**a** and **b**) Pulmonary consolidation in upper left lobe and air trapping secondary to nodal bronchial compression in the upper right lobe.

against casual contacts and with the fact that a high percentage of children, in whom the source of infection was unknown, were symptomatic and were studied with the clinical suspicion of TB.

Changes in the Therapeutic Management

Performing chest CT modified the therapeutic management in 45.1% of all cases, in 51.9% of asymptomatic children (G1), and in 33.3% of symptomatic children with probable TD (G2). Statistically significant differences were observed according to the age of the children in each group ($p = 0.004$, Pearson χ^2), producing a change in therapeutic management in 66.7% of children under 2 years and in 75.8% of children between 2 and 5 years.

Dosimetric Results

CT studies evaluated in this study were performed with a voltage between 80 and 120 kV and milliamperes between 30 and 70 mAs, yielding dose length product (DLP) values between 15 and 154 mGy × cm (►**Table 2**).

Discussion

The presence of lymphadenopathy in asymptomatic children with normal chest radiography and the relationship between lymphadenopathy and active TD have been studied by different authors.

Delacourt et al[21] performed chest CT in 15 children with normal clinical examination and chest radiography, detecting pathological lymph nodes in 67% of children below 4 years and

Table 2 Dosimetric results; CTDI and DLP means by age group

Age group	CTDIw (mGy)	DLP (mGy × cm)
<2 years	1,09	18.7
2–5 years	1,24	24.77
6–10 years	1,24	27
>10 years	2,16	59.2

Abbreviations: CTDI, computed tomography dose index; CTDIw, weighted, computed tomography dose index; DLP, dose length product.

in 50% of those over 8. Kim et al,[22] in a series of 41 cases of clinically or microbiologically confirmed TB, found lymph nodes in 83% of pediatric patients by CT. Andronikou et al,[23] in a group of 100 pediatric patients with clinical suspicion of primary TB, identified lymphadenopathy in 92% of cases, being $>$ 1 cm in 46% of them. Kim et al[24] observed, in a group of children under 1 year with positive culture for *M. tuberculosis*, necrotic lymph nodes in all cases where CT was performed.

Nevertheless, there are still controversies regarding indications of a technique that uses ionizing radiation and cannot be used systematically in all children who have positive TST, were asymptomatic, and have normal chest radiography.

For some authors, CT would only be indicated in asymptomatic pediatric patients with smear-positive contact, positive TST, and doubtful or inconclusive chest radiography. It should also be considered when complications are suspected or in cases of high risk.[10]

Gómez-Pastrana and Carceller-Blanchard[25] do not recommend CT, arguing that the finding of hilar and mediastinal lymph nodes is common in thoracic CT of asymptomatic children with positive TST and normal radiography and that the natural history of TD points to these lymph nodes as part of the infection. They further emphasize that in pediatric patients, a correlation between size and morphology of the lymph nodes and disease activity has not been established, questioning which lymph nodes should be considered pathological on CT. Marais[3] also recommends that radiological signs on CT in asymptomatic patients with normal chest radiography should be interpreted with caution. According to Marais, the radiological signs indicate the presence of active disease in symptomatic patients, but in asymptomatic patients, they only reveal recent primary infection.[5]

However, in children with infection without apparent disease, there is a positive correlation between the presence of lymph nodes on CT, not visible on chest radiography, and positive PCR for *M. tuberculosis*.[26]

Some studies in adults with confirmed TD by biopsy and/or culture, show that in cases of active TD, the lymph nodes are larger than those in cases of LTBI, and these pathological lymph nodes typically show peripheral enhancement and central hypoatenuation corresponding to granulation tissue with increased vascularization and central caseation with necrosis. After treatment, lymphadenopathy decreases in size, and areas of low attenuation disappear. Patients whose lymph nodes are larger have more frequent and severe symptoms.[27]

In Bilaceroglu's study,[28] in which 84 lymph node biopsies were performed and 41 patients under 15 years were included, the same correlation was shown.

In our study, the most observed CT findings in TD, both in children with suspected latent infection (asymptomatic with normal chest radiography) and in those with clinical or radiological probable TD, were the lymph nodes, mainly with necrotic aspect, and consolidations, nodules, and opacities in the lungs. These results are similar to those obtained by other authors.[29–32]

Regarding the lymph nodes, the necrotic aspect, with peripheral contrast enhancement and hypodense center, was statistically significant associated with changes in lung parenchyma, bronchial compression, and positive culture. This data support the idea that this type of lymphadenopathy is typical of TD and reflect its activity.[22,28]

By convention, the presence of lymphadenopathy on chest radiography, even in the absence of symptoms, is treated as active disease, although some studies in the 60s, with isoniazid alone, demonstrated the effectiveness of this single drug therapy. In the meta-analysis of Smieja et al, treatment with isoniazid had a relative risk of developing active TD of 0.40.[33] Protection rates provided by isoniazid in other studies ranged between 70 and 95%.[34,35]

However, monotherapy in these cases could lead to the progression of the disease, to reactivation, or to the appearance of resistant, or multidrug-resistant mutants, one of the main problems nowadays in TD.[19,21]

In this study, CT was able to define TD in more than half of asymptomatic children with positive TST and normal chest radiography who otherwise would have been classified only as infected. These data confirm the high percentage of subclinical TD and the low sensitivity of chest radiography in the diagnosis of childhood TD.

No differences between groups of asymptomatic and symptomatic children were detected by comparing the presence, size, morphology, or location of lymphadenopathy; neither the existence nor type of parenchymal lesions, or bronchial compression, with similar percentages of involvement in the two groups. This corroborates the limited clinical–radiological correlation of TB in childhood.

In this study, the variable most related to the presence of alterations in chest CT (lymphadenopathy and parenchymal involvement), and therefore to the change in the therapeutic management, was age. The natural history of TD shows that in immunocompetent children, the likelihood of developing TD and its clinical presentation depend primarily on age. Infection carries a significant risk of lung disease in younger children, which becomes smaller between 5 and 10 years, with a second peak during adolescence and early adulthood.[3,5] This data was also confirmed in our study, identifying a statistically significant association between diagnosis and age groups, most often TD in children under 5 years and less involvement in children between 6 and 10 years.

Differences in age groups for the presence of CT abnormalities appear to be attributable to reduced immunity in younger children, especially those under 2 years. As mentioned, these children had lymphadenopathy and parenchymal lesions in all cases. Against this, it is noteworthy that 75% of children between 6 and 10 years, asymptomatic and with normal chest radiography, show no radiographic abnormalities compatible with TD.

In our study, CT had higher performance and diagnostic utility, changing the therapeutic management, in younger children, especially those under 5 years. This conclusion is the same as Garrido et al observed in their work.[30] Since in these cases there is an increased risk of progression and complications of TD, CT would have on them the clearest indication. Another possibility is chemoprophylaxis in this group with two drugs.[21]

Table 3 Dose reference levels of different works expressed as DLP (mGy × cm) measured in phantom 16[a] or 32 cm[b][36–39]

This study[b]	Brady[b]	Shrimpton[a]	Verdun	Thomas[b]
<2 years: 19		<1 year: 200	<1 year: 110	0 years: 73
2–5 years: 24	<5 years: 50	–	1–5 years: 200	1 year: 133
6–10 years: 27	5–10: years 150	5 years: 400	5–10 years: 220	5 years: 208
>10 years: 59	>10 years: 400	10 years: 600	10–15 years: 460	10 years: 315
				15 years: 201

Abbreviation: DLP, dose length product.

Regarding the dosimetric results obtained in this study, when compared with the dose reference values published by different authors,[36–39] despite differences in the age groups studied, in this series, a significant dose reduction is seen, between 50 and 90%, with sufficient diagnostic quality to meet the objectives of the exploration (►**Table 3**).

The use of ionizing radiation in medical imaging, including CT, provides valuable diagnostic information that can undoubtedly benefit the patient. However, radiation has risks.[40,41] The first step to reduce radiation exposure in children is to decide whether CT is the most appropriate modality to address a specific diagnostic question and to consider other imaging modalities such as ultrasound or magnetic resonance imaging.[41] In this sense, pediatricians should consider the benefits and risks of radiation and collaborate with radiologists to develop strategies to reduce radiation in children.[41,42]

CT studies should be designed to answer a specific clinical question. It is important to reduce the number of acquisitions to those strictly necessary in each scan and to adjust the CT technical parameters based on diagnostic objective and size of the patient.

In conclusion, in asymptomatic children with positive TST and normal chest radiography, thoracic CT has higher diagnostic yield in children under 5 years and with closer contact with the infectious source, modifying the therapeutic management in a high percentage of cases.

Since TD has an increased risk of progression and complications in these children with lower immunity, CT would have on them a clearer indication. Another possibility to avoid radiation in this group would be chemoprophylaxis with two drugs, but further investigation is required.

Protocols with mA and kV reduction have shown a significant decrease in radiation dose, maintaining sufficient diagnostic quality to achieve the objectives of the scan.

Conflict of Interest
None.

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