Scientific Research Publishing

Open Journal of Pediatrics, 2022, 12, 376-388
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Tuberculosis in Children: Epidemio-Clinical Aspects in the Paediatric Department of the Gabriel Touré University Hospital Center

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How to cite this paper: Dembélé, A., Diakité, A.A., Cissé, M.E., Diarra, B., Maïga, B., Sanou, I., Togo, P., Doumbia, A.K., Coulibaly, O., Sacko, K., Konaté, D., Diall, H., Sidibé, L.N., Dégoga, B., Diakité, F.L., Dembélé, G., Dicko, F., Sylla, M. and Togo, B. (2022) Tuberculosis in Children: Epidemio-Clinical Aspects in the Paediatric Department of the Gabriel Touré University Hospital Center. *Open Journal of Pediatrics*, **12**, 376-388.
https://doi.org/10.4236/ojped.2022.122042

Received: March 29, 2022
Accepted: May 13, 2022
Published: May 16, 2022

Abstract

Introduction: Globally, tuberculosis is the leading cause of death from a single infectious agent ahead of HIV/AIDS. Approximately 10 million people contracted TB in 2017, 10% of whom were children aged 0 - 15 years, or about 1 million with 250,000 deaths in 2016 (including children with HIV-associated TB). The signs of TB in children are not always specific and diagnosis remains difficult unlike in adults. According to a study conducted in 2011 in the paediatric department of the CHU-Gabriel Touré, only seventeen cases of all forms of tuberculosis were found, or approximately 0.2% of hospitalised children. The objective of our study was to investigate the epidemiological and clinical aspects of tuberculosis in children. **Materials and Method:** This was a prospective, cross-sectional and descriptive study that took place from 24 October 2017 to 23 October 2018, or 12 months in children aged 0-15 years. Data were collected from an individual medical record opened for each patient and an individual survey form established for each child. **Results:** During the study period, 40,434 children were consulted. Tuberculosis was suspected in 91 children, with a frequency of 0.22%. The age range of 1 to 4 years was 36.3% with a median age of 72 months. The sex ratio was 1.8. Chronic cough with 84.6% and malnutrition with 24.17% were the most frequent symptoms. Chest X-ray revealed bilateral pulmonary lesions in 52.7% and mediastinal adenopathy in 12.1%. TST was positive in 10.9% of patients, microscopy in 26.4%, Gene Xpert in 18.7%, and culture in 16.5%. The biological diagnosis of tuberculosis was retained in 48.4% of the patients, the pulmonary

form represented 93.2%. The therapeutic regime (2RHZE/4RH) was used in 81.6% of cases and the evolution was favourable in 65.9% of patients. **Conclusion:** The diagnosis of tuberculosis in children remains difficult in our context. The clinical signs are not always specific, and further studies are needed to further elucidate this disease.

Keywords

Child, Clinic, Epidemiology, Gabriel Touré University Hospital Center, Tuberculosis

1. Introduction

Tuberculosis is an infectious disease caused by the bacillus of the *Mycobacterium tuberculosis* complex, also known as *Bacillus Koch* (*BK*) [1]. Pulmonary involvement is the most common site of infection and is the usual source of transmission. However, the bacillus can reach other organs, resulting in extra-pulmonary tuberculosis [2]. With the introduction of preventive measures such as the Calmette-Guérin vaccine (BCG) in 1921 and the discovery of numerous effective antibiotics between 1944 and 1965, the eradication of tuberculosis was conceivable by the end of the 20th century. Unfortunately, the disease is still with us today [3]. Globally, TB is the leading cause of death from a single infectious agent, ahead of HIV/AIDS. Approximately 10 million people contracted TB in 2017, 10% of whom were children aged 0 - 15 years, or about 1 million with 250,000 deaths in 2016 (including children with HIV-associated TB). The number of children under five receiving preventive treatment was 292,182 in 2017, three times the number in 2015 (87,242) [4] [5]. In Côte d'Ivoire, the number of cases in children was 1243 in 2013, representing 5.2% of new cases and 4.9% of all notified cases [6]. The "objective 90-90-90" was the new 2016-2020 plan for TB control. The idea is to diagnose 90% of people with TB in 90% of the most vulnerable populations and ensure 90% cures with treatment. If they are achieved, these objectives should make it possible to eradicate tuberculosis epidemics by 2035 according to the WHO [7]. A total of 6889 TB cases were notified in Mali in 2018, children aged 0 - 14 years were 301 cases, or 4% [8]. The signs of TB in children are not always specific and diagnosis remains difficult unlike in adults. Many cases go unnoticed in our services or are treated as severe pneumonia. According to a study carried out in 2011 in the paediatric department of the CHU-Gabriel Touré, only seventeen cases of all forms of tuberculosis were found, or approximately 0.2% of hospitalised children [9]. Thus, we initiated this study in order to evaluate the real incidence of this pathology in the pediatric department of the CHU-GT.

2. Methodology

2.1 Study Setting and Location

Our study took place in the emergency department of the paediatric department

of the CHU-Gabriel Touré in Bamako. Located in the centre of the city, this department receives patients from all the communes of Bamako and those referred from other localities in Mali. Despite the existence of community health centres and referral health centres, attendance is still very high. It is composed of a neonatology service to which the URENI (Intensive Nutritional Recovery and Education Unit) is attached, a general paediatrics service, and a paediatric emergency service. The latter was created in 2010 as part of the department's restructuring. It includes a reception hall which is also a triage room, two consultation rooms, an inpatient sector with 20 cots, and 6 beds with two rooms for infants and one room for older children.

2.2. Type of Study and Inclusion Criteria

This was a prospective, cross-sectional, descriptive study that ran from 24 October 2017 to 23 October 2018, a period of 12 months. We included all children aged 0 to 15 years who consulted the paediatric department of the CHU Gabriel Touré for suspected tuberculosis, whether or not they were hospitalised. An individual numbered medical file and an individual survey form were opened for each patient to collect data. Patients were examined by a paediatrician, accompanied by a graduate student. A single sputum sample was taken by gastric tube (if age less than or equal to 5 years) or by spontaneous sputum (if age greater than 5 years). A direct microscopy, Xpert MTB/RIF, and *BK* culture were performed on all patients. Lymph node biopsy was performed on 4 patients. The diagnosis of pulmonary tuberculosis was based on bacteriological criteria in patients with positive bacilloscopy. In the absence of bacteriological confirmation, the diagnosis was based on a combination of clinical and radiological evidence. Patients undergoing treatment were followed up for 6 months in 3 rounds (1 month after inclusion, 3 months after inclusion, and 6 months after inclusion). The variables studied were those relating to the socio-demographic characteristics of the children: age, sex, and socio-economic level of the parents. Then, we studied variables related to clinical and paraclinical characteristics: vaccination status, immune status (HIV), history, signs of bacillary impregnation, clinical manifestations, radiological signs, tuberculin TST, sputum examination, lymph node biopsy. As well as the clinical forms, treatment, and evolution, data writing, entry, and analysis were performed with world 2013, SPSS (version 20.0), and Excel 2013. Informed consent was obtained from the parents or carers by signature after a detailed explanation of the study protocol before inclusion and strict respect for the children's anonymity was guaranteed. We used some operational definitions, among others:

- **Suspected TB case: any child presenting with**

—a cough equal to or greater than two weeks and haemoptysis and/or prolonged fever;

—a cough of two weeks or more with weight loss and/or fever;

—a cough and a history of tuberculosis infection;

—adenopathy and emaciation.

- **Microscopy positive pulmonary tuberculosis (MPT+):** if

—a sputum smear is positive for *Acid-Fast Bacilli* (*AFB*), and/or culture, and/or the Gene Xpert is positive for *Mycobacterium tuberculosis*.

- **Microscopy-negative pulmonary tuberculosis (mPTB-):** if

—a suspect patient in whom the sputum specimen has returned negative for *BAAR* on microscopy, but who has persistent clinical symptoms and radiographic abnormalities consistent with active pulmonary TB despite non-specific broad-spectrum antibiotic treatment and for whom full antituberculosis chemotherapy has been prescribed.

- **Confirmed tuberculosis:** if

—a patient in whom Gene Xpert MTB/RIF, and/or direct examination, and/or culture has come back positive for *Mycobacterium tuberculosis* and/or there is the presence of epithelioid gigantocellular granuloma with caseous necrosis on the lymph node biopsy on pathology examination.

- **Cured:** if

—a patient with negative sputum examination in the last months of treatment (5^{th} and 6^{th}).

- **Completed treatment:** if

—a patient who has completed treatment within the treatment timeframe, but whose biological result is not known.

- **Treatment failure:** if

—a patient with a positive sputum smear at the 5^{th} month or more of treatment;

—a patient lost to follow-up;

—a patient diagnosed with no response to the appointment and not heard from for more than 2 months.

3. Results

Over a period of 12 months (from 24 October 2017 to 23 October 2018), we were able to collect 91 suspected cases of tuberculosis meeting our inclusion criteria out of a total of 40,434 consultations, either a frequency of 0.22%. The 1- to 4-year-old age group was the most affected with 36.3% of cases. The median age was 72 months. There was a male predominance with a sex ratio of 1.8. The socioeconomic level of the parents was considered unfavourable for 47.3% of the patients (Table 1). The main reasons for consulting the parents were: cough, breathing difficulty, and anorexia (Table 2). Many patients (73.6%) had a correct vaccination status against Mycobacterium tuberculosis (Table 2). BCG scars were found in 75.8% of patients (Table 2). The notion of chronic cough in the family (11%), tuberculosis disease in the family (11%), and tuberculosis contagion (23.1%) were the family histories frequently mentioned (Table 3). Chronic cough (84.6%), followed by malnutrition (24.17%) and mediastinal adenopathy (12.08%) on physical examination were the predominant clinical signs (Table 4).

Table 1. Distribution of suspected cases by socio-economic data.

Socio-economic data	Effective (n: 91)	Percentage
Age in years		
<1	8	8.8
1 - 4	33	36.3
5 - 10	26	28.6
11 - 15	24	26.4
Sex		
Male	59	64.8
Female	32	35.2
Parents socio-economic conditions		
Favourable	7	7.7
Acceptable	41	45
Unfavourable	43	47.3
Mode of admission		
Brought in by parents	72	79.1
Referred	19	20.9

Table 2. Distribution of suspected cases according to interview data and follow-up booklet.

Data from the interview and follow-up booklet	Effective (n: 91)	Percentage
Reasons for consultation		
Cough	60	65.93
Dyspnea	18	19.78
Anorexia	17	18.68
Tuberculosis consultation	14	15.38
Weight loss	14	15.38
Asthenia	13	14.29
Fever	11	12.09
Adenopathy	8	8.79
Deterioration of general condition	8	8.79
Chest pain	5	5.49
Abdominal distension	3	3.30
Severe malnutrition	2	2.20
Impotence of the lower limbs	1	1.10
Immunisation status according to the Expanded Programme on Immunisation (EPI)		
Correctly vaccinated	67	73.6
Incorrectly vaccinated	22	24.2
No vaccination received	2	2.2
Presence of BCG scar		
Yes	69	75.8
No	22	24.2

Table 3. Distribution of suspected cases by history.

Background			Effective (n: 91)	Percentage
Family history of chronic cough	No		81	89
	Yes	Mother	4	4.4
		Father	4	4.4
		Other member	2	2.2
Family history of documented TB disease	No		81	89
	Yes	Mother	4	4.4
		Father	3	3.3
		Other member	3	3.3
Concept of tuberculosis contagion	No		70	76.9
	Yes	Mother	11	12.1
		Father	5	5.5
		Other member	5	5.5

Table 4. Distribution of suspected cases according to clinical examination data.

Clinical examination data	Effective (n: 91)	Percentage
Interrogation: Signs of bacillary impregnation		
Chronic cough	77	84.62
Weight loss	69	75.82
Unexplained (prolonged) fever	68	74.73
Night sweats	58	63.74
Asthenia	51	56.04
Anorexia	48	52.75
Physical examination		
Nutritional status		
Good Nutritional status	69	75.82
Moderate malnutrition	8	8.79
Severe malnutrition	14	15.38
Colouration of the integuments		
Good colouration	63	69.23
Moderate pallor	24	26.37
Severe pallor	4	4.40
Chest morphology		
Normal	86	94.51
Deformity	5	5.49

Continued

Signs of respiratory struggle		
Absent	41	45.05
Severe	6	6.59
Moderate	26	28.57
Minimal	18	19.78
Lung auscultation		
Normal	8	8.79
Pathological	83	91.21
Abdominal examination		
Normal	64	70.33
Distended	9	9.89
Organomegaly	14	15.38
Ascites	4	4.40
Presence of adenopathy		
Cervical	13	14.29
Axillary	5	5.49
Inguinal	3	3.30
Osteoarticular examination		
Pott's disease	1	1.10

TST was positive in 10.99% of patients (Figure 1). Microscopy was positive in 24 patients (26.4%), Gene Xpert in 17 patients (18.7%) and culture in 15 patients (16.5%). Lymph node biopsy was performed in 4 patients (4.4%) and was positive in 3 patients (3.3%) (Table 5). At the end of the above investigations, 44 patients were confirmed positive for TB out of 91 suspected cases (Figure 2). TB/HIV co-infection was found in 32.3% of cases (Table 6). Of the 44 confirmed cases, pulmonary tuberculosis constituted 41 cases (93.18%), and extra-pulmonary forms represented 3 cases, including 1 bone case and 2 lymph node cases (Figure 3). Four patients died before the outcome, 2 were lost to follow-up and 38 were put on treatment (86.4%). The treatment was oriented according to the 2RHZE/4RH regimen (2 months of treatment with Rifampicin + Isoniazid + Pyrazinamide + Ethambutol, followed by 4 months of treatment with Rifampicin + Isoniazid) in 81.6% of the cases (Table 7). The evolution was favourable in 65.9%.

4. Discussion

During the study period, the paediatric department recorded 40,434 consultations. Tuberculosis was suspected in 91 patients (0.22%) of whom 44 (48.35%) were diagnosed. Morba A [9] in 2011, found 17 cases of tuberculosis in the same

department among hospitalised patients. Cissé A [10] and Segbedji K *et al.* [11] found respectively 345 cases over 6 years and 74 cases over 4 years from retrospective and multicentre studies. Our high rate compared to that of Morba A [9] could be explained by the fact that his study was carried out only on hospitalized

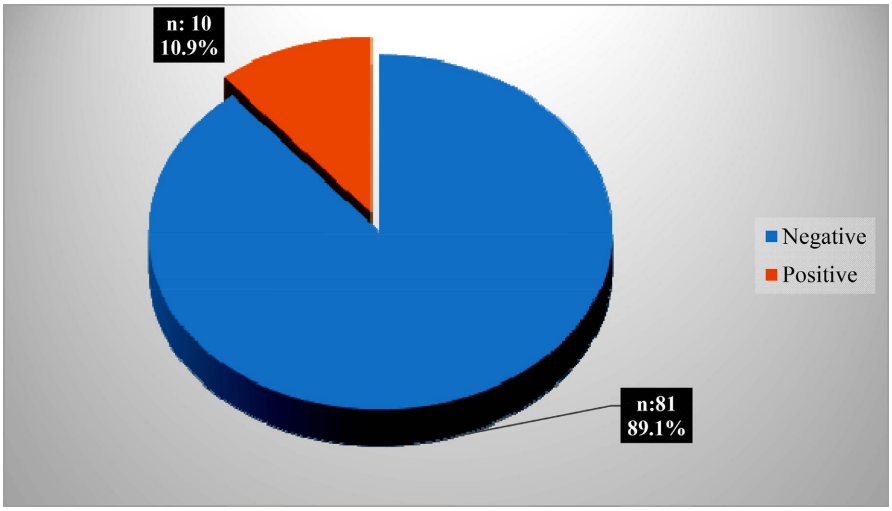

Figure 1. Distribution of suspected cases according to the result of intra-dermo-reaction.

Table 5. Distribution of suspected cases according to tests results.

Results of tests		Culture		Total
		Positive	Négative	
Microscopy	Positive	14	10	24 (26.4%)
	Négative	1	66	67 (73.6%)
Gene Xpert	Positive	11	6	17 (18.7%)
	Négative	4	70	74 (81.3%)
Lymph node biopsy (n: 4)	Positive	0	3	3
	Négative	0	1	1

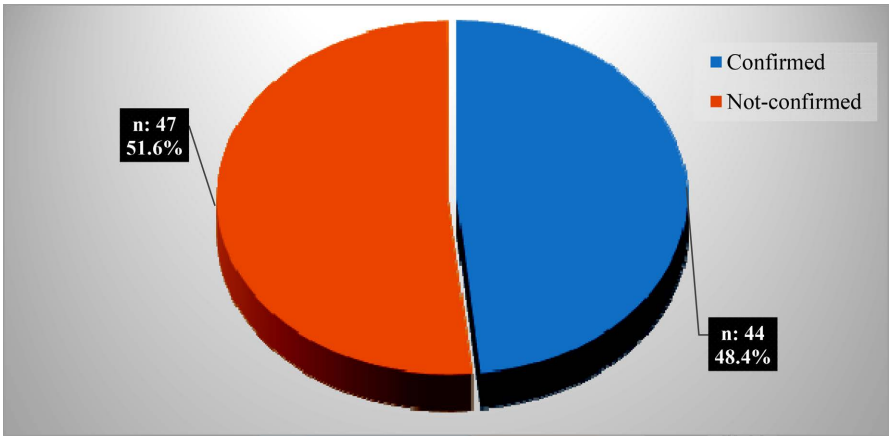

Figure 2. Distribution of suspected cases by diagnostic confirmation.

Table 6. Distribution of patients by TB/HIV co-infection.

Statut HIV	Tuberculosis		Total
	Positive	Négative	
Positive	13 (46.4%)	15 (53.6%)	28 (100%)
Négative	31 (49.2%)	32 (50.8%)	63 (100%)
Total	44 (48.4%)	47 (51.6%)	91 (100%)

Odds ratio: OR (confidence interval: CI) = 0.89 (0.3667 - 2.1828); P = 0.8067.

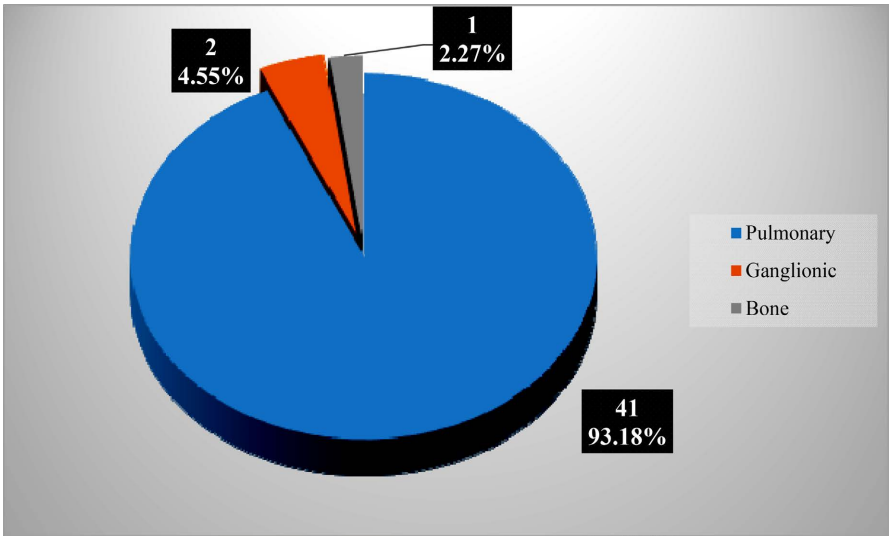

Figure 3. Distribution of confirmed cases by clinical form.

Table 7. Distribution of patients by treatment received and outcome.

Treatment received and progress	Effective	Percentage
Treatment received (n: 38)		
2 RHZE/4 RH	31	81.6
2RHZ/4 HR	6	15.8
2 RHZE/10 HR	1	2.6
Evolution (n: 44)		
Cured	29	65.9
Lost sight of	6	13.6
Failed	1	2.3
Died	8	18.2

R = Rifampicin; H = Isoniazid; Z = Pyrazinamide; E = Ethambutol.

patients. However, the high figures of Cissé A [10] and Segbedji K *et al.* [11] compared to ours can be explained by the duration of their different studies. The 0- to-5-years (Table 1) age group was the most affected with 45.1% of cases. This result is similar to that of Morba A [9] who reported 47.1% in the same age group.

However, Soumana A [12] reported a higher frequency than ours (65.5%). All these results confirm the data in the literature according to which children under 5 years of age are the most affected by tuberculosis infection. In addition, young age is also a factor increasing the risk of progression to TB disease. Boys were in the majority with 64.8% of cases, a sex ratio of 1.8. This result corroborates that of Diedon H [13] who found 67.1%. However, we did not find any significant relationship between gender and the occurrence of tuberculosis in the literature. The majority of patients (47.3%) came from a poor background (**Table 1**). This result is similar to that reported by Barchiche N *et al.* [14] who found 48%. Indeed, low income and especially precariousness favour the occurrence of tuberculosis infection. The *BCG* scar was found in 75.8% of patients (**Table 2**), a considerably higher result than those reported by Soumana A [12] and Mabiala *et al.* [15] who found 65.52% and 60.7% respectively. However, BCG vaccination does not fully protect against tuberculosis disease, but rather protects the child against severe forms (meningitis and miliary tuberculosis). The close contact of children with a bacilloscopy-positive adult with tuberculosis is a factor that favours the occurrence of tuberculosis infection in these children. In our study, tuberculosis contact was found in 23.08% of cases and the contaminators were direct parents in 76.19% (**Table 3**). Our result is comparable to that of Soumana A [12] who found 27.59% of whom 87.50% were direct relatives. De Pontual *et al.* [16] reported 83% of tuberculosis infections. The clinical manifestations encountered were numerous and varied due to the clinical polymorphism of tuberculosis in children. In our study, the chronic cough was found in 84.6% of cases (**Table 4**). Diedon H A [13] found a higher proportion (94.8%). However, for Soumana A [12], cough represented only 16%. These results show us that cough is one of the main signs of bacillary impregnation in children with pulmonary tuberculosis. Undernutrition was found in 24.17% of patients (**Table 4**). Soumana A [12] and Mabiala *et al.* [15] reported higher results, respectively 55% and 75.4%. This undernutrition is the consequence of tuberculosis, which leads to anorexia and intestinal malabsorption in patients. As in many other countries, the diagnosis of tuberculosis in children in Mali is not always easy due to the limited means of diagnosis and the paucibacillary nature of tuberculosis in children. The most common radiological findings were alveolar condensations (50.5% of cases), followed by mediastinal adenopathies (12.08%) (**Figure 4**). Other pulmonary lesions such as caverns (4.39%), nodules (6.6%), miliaries (1.1%), and pleurisy (9.89%) were rarely encountered. Mabiala *et al.* [15] found 40.2% mediastinal adenopathy and 2.6% cavern. In another study, Mabiala *et al.* [17] found 29.5%, 11.4%, and 13.11% of mediastinal adenopathy, pleurisy, and miliary. Segbedji K *et al.* [11] had 10.8% and 5.4% of miliary and pleurisy respectively. This shows the great diversity and especially the rarity of pathological radiological images likely to make the diagnosis of pulmonary tuberculosis in children. Intra Dermo-Reaction (IDR) was positive in only 10.99% of the children, the largest diameter was 25 mm. Our result could be explained by the frequency of HIV infection and malnutrition. Barchiche N *et al.* [14] in their study (aspects of tuberculosis in

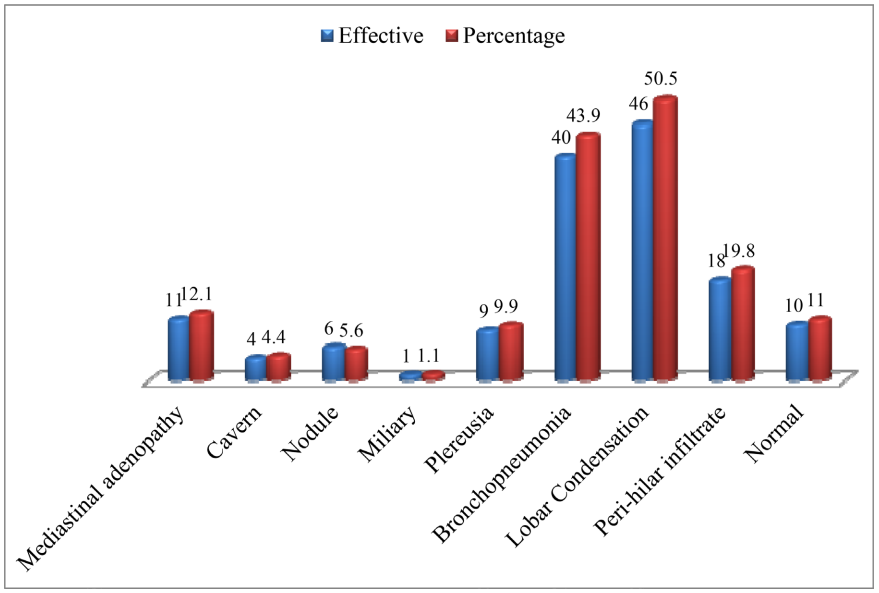

Figure 4. Distribution of suspected cases according to chest X-ray data (n: 91).

children in 153 cases) reported 50.55% positive IDR while Folquet *et al.* [18] and Soumana A [12] had higher proportions with 73.50% and 85.71% respectively. However, it is also important to note that a negative TST does not eliminate the diagnosis of TB. Microscopy was positive in 24 patients (26.4%) (**Table 5**). Segbedji K *et al.* [11] found a higher result than ours with 39.19% positive microscopy. However, our result is higher than that of Khatib S *et al.* [19] who reported 10%. Gene Xpert MTB/RIF was positive in 17 children (18.7%) and culture in 25 children (**Table 5**). Zar H *et al.* [20] reported 15.5% culture positive, 6% microscopy positive, and 12.8% Gene Xpert positive. Overall, these low rates demonstrate the difficulty of confirming the diagnosis of TB in children. So, at the end of the above investigations, 44 patients were confirmed positive for tuberculosis out of 91 suspected cases. Tuberculosis (TB)/HIV co-infection was found in 46.4% of patients (**Table 6**) with an OR(CI) of 1.11 (0.437 - 2.827) (P = 0.8249). Thus, we could say that there is not a statistically significant relationship between TB and HIV but HIV immunosuppression is a factor increasing the risk of progression to TB disease. Furthermore, HIV infection should always be investigated in cases of TB and vice versa. The frequency of co-infection was higher than ours in Mabiala *et al.* [15] with 65.5% of cases and Segbedji K *et al.* [11] in Togo reported 15% of co-infection. The diagnosis of TB was confirmed in only 48.4% of suspected cases (**Figure 2**). Pulmonary tuberculosis was the overwhelming majority with 93.2% of the confirmed cases (**Figure 3**). The predominance of this location is usually reported by many other authors [21]. For example, Loufoua *et al.* [22], Cardenat *et al.* [23], and Koueta *et al.* [24] reported 70.8% in Gabon, and 77.24% in Côte d'Ivoire and 86.4% in Burkina Faso respectively. The extrapulmonary form represented 6.8% (lymph nodes in 4.5% and osteoarticular in 2.3%). Furthermore, Barchiche N *et al.* [14] reported 35.71% of lymph node localisation. Antituberculosis treatment was used in 38 patients

(86.4%) and the 2RHZE/4RH (2 months of treatment with Rifampicin + Isoniazid + Pyrazinamide + Ethambutol, followed by 4 months of treatment with Rifampicin + Isoniazid) regimen was used in 31 patients (81.6%) (**Table 7**). This result is superior to those of Morba A [9] and Cissé A *et al.* [10] who respectively used the same regimen in 58.8% and 56.7% of their cohorts. The therapeutic success rate (65.9%) was lower than those reported by Morba A [9] and Segbedji K *et al.* [11] who found 70.58% and 76% respectively. This result can be explained by a temporary break in the supply of anti-tuberculosis drugs that we observed. The number of patients lost to follow-up was 13.6% and the mortality rate was 18.2%. Among the unconfirmed cases, some were put on anti-tuberculosis treatment and others on Isoniazid preventive treatment. These patients did not want to continue the follow-up to a lack of evidence.

5. Conclusion

We were able to identify several suspected cases of tuberculosis in the department of paediatrics that previously might have gone unnoticed. As the clinical signs of tuberculosis in children are not always as specific as in adults, further and more rigorous studies are needed for the diagnosis of tuberculosis in children.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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