Scientific Research Publishing

Open Journal of Pediatrics, 2022, 12, 433-448
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Study of Tuberculosis in Children Aged 1 Month to 15 Years in the Pediatric Ward of the Hospital of Mali 2015-2021

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How to cite this paper: Kané, B., Diallo, K.W., Sangaré, A., Dembélé, Y., Dabo, G., Traoré, M., Traoré, M.M., Berthé, M. and Maiga, M. (2022) Study of Tuberculosis in Children Aged 1 Month to 15 Years in the Pediatric Ward of the Hospital of Mali 2015-2021. *Open Journal of Pediatrics*, **12**, 433-448.
https://doi.org/10.4236/ojped.2022.122047

Received: April 13, 2022
Accepted: May 20, 2022
Published: May 23, 2022

Abstract

Introduction: In 2020, an estimated 9.9 million people are living with tuberculosis worldwide, including 1.1 million children. Tuberculosis is the 2nd leading cause of death from infectious disease after COVID-19 and the 13th leading cause of death worldwide. **Objective:** To collect cases of tuberculosis in children aged 1 month to 15 years in order to study the epidemio-clinical aspects in the pediatric department of the Mali Hospital during the period 2015-2021. **Materials and Methods:** This was a descriptive, retrospective study from January 1, 2015, to December 31, 2020, and a prospective study from January 1 to December 31, 2021, among children aged 1 month to 15 years admitted for suspected tuberculosis in the pediatric ward of the Mali Hospital. **Results:** From January 2015 to December 2021, we collected 69 cases of tuberculosis among 9438 hospitalized children, *i.e.* a frequency of 0.73%. The average age was 6.16 years with extremes of 3 months and 15 years. The sex ratio was 1.1% in favor of boys. The majority of children were vaccinated against tuberculosis (88.4%). The most frequent symptoms were fever (76.8%) and weight loss (73.9%). The pulmonary form was the most frequent (54.9%). Bacteriological confirmation was done in 43.5% of our children. It was Mycobacterium tuberculosis in all confirmed cases. More than half of our children (65.2%) were treated with first-line anti-tuberculosis drugs for 6 months. We observed a cure in 42.0% of our patients and a case fatality rate of 39.1%. **Conclusion:** Tuberculosis in children is frequent in Mali Hospital despite good BCG vaccination coverage. Its mortality remains

high and is maintained by malnutrition, HIV, and the emergence of resistant strains of bacilli.

Keywords

Tuberculosis, Children, Mali Hospital

1. Introduction

Tuberculosis is a contagious disease caused by airborne Mycobacterium tuberculosis. This bacterium most often develops in the respiratory tract (pulmonary tuberculosis). It can spread to other organs (extrapulmonary tuberculosis) [1].

In 2020, an estimated 9.9 million people worldwide will be infected with TB, including 1.1 million children. Tuberculosis is the second most common cause of death from infectious diseases after VTEC-19 and the 13th most common cause of death in the world. It is also the leading cause of death among people living with HJV and a major cause of death due to antimicrobial resistance [2].

TB is present in all countries and in all age groups. In 2020, the World Health Organization Region with the highest number of new TB cases was Southeast Asia (43% of all new cases) followed by the African Region (25%) and the Western Pacific Region (18%) [2].

Pediatric tuberculosis remains a major global problem with more than one million new cases each year according to the World Health Organization. Mortality from tuberculosis is proportionally higher in children than in adults: while children represent 10% of all tuberculosis cases, they account for 15% of deaths [3]. Delayed diagnosis and rapidly progressive forms in young children are the main reasons for this high mortality. In a recent systematic evaluation of the factors associated with pediatric TB deaths, it was shown that 80% of deaths occur in children under 5 years of age, and 96% in children who have not had access to anti-TB treatment [3].

In 2020, according to the annual report of the National Tuberculosis Control Program in Mali, 274 cases of all forms of tuberculosis were recorded in children aged 0 - 14 years, *i.e.* a frequency of 4% [4].

A study of a series of 12 cases was carried out in 2017 in children aged 0 - 15 years in the pediatric department of the Mali Hospital [5]. The aim of this work was to collect cases of tuberculosis in children aged 0 - 15 years in order to study the epidemiological and clinical aspects in the pediatric department of the Mali Hospital during the period 2015-2021.

2. Patients and Method

2.1. Patients

2.1.1. Study Setting

The pediatric ward of the Mali Hospital, the National Tuberculosis Reference

Laboratory of the National Institute of Public Health, and the Charles Mérieux Infectious Disease Center were our study settings.

2.1.2. Type and Period of Study

We conducted a descriptive, retrospective study from January 1, 2015, to December 31, 2020, and a prospective study covering the period from January 1 to December 31, 2021.

2.1.3. Study Population

All children aged 1 month to 15 years were hospitalized or had consulted in the pediatric department of Mali Hospital during the study period. Children were classified by age group, *i.e.* [<1 year], [1 - 9 years], and [10 - 15 years].

2.1.4. Inclusion Criteria

All children aged between 1 month and 15 years whose parents gave their consent to participate in the study and who consulted us for:

- a persistent cough lasting more than 15 days;
- a cough refractory to any antibiotic therapy;
- other clinical and/or radiological manifestations of tuberculosis.

2.1.5. Criteria for Non-Inclusion

The following were not included in our study:

- children with tuberculosis less than 1 month old and more than 15 years old;
- children with tuberculosis between 1 month and 15 years of age whose medical records were not usable;
- children whose parents did not give consent;
- children from whom samples could not be taken.

2.1.6. Parameters Examined

The following variables were examined:

- Socio-demographic variables such as age, gender, origin, educational level, and occupation of parents.
- Clinical and therapeutic variables such as: weight, height, vaccination status, body temperature, medical and surgical history, tuberculosis infection, time of onset of symptoms, clinical signs, nutritional status, anti-tuberculosis treatment regimen, duration of hospitalization, complications, and outcome.
- Paraclinical variables such as the search for Mycobacterium tuberculosis and cytochemical examination of pathological fluids, intradermal tuberculin reaction, blood count, C-reactive protein, HIV serology, anatomo-pathology, radiography, and sometimes a thoracic scanner.

2.1.7. Operational Definitions [5] [6] [7]

- Infant: child under one year of age.
- Child: Individuals between 10 and 18 years of age.
- Adolescent: individuals between 10 and 18 years of age.
- Pulmonary tuberculosis: Pulmonary tuberculosis is any bacteriologically con-

firmed or clinically diagnosed case of tuberculosis involving the lung parenchyma or tracheobronchial tree. Milliary tuberculosis is classified as pulmonary tuberculosis because it is accompanied by lesions in the lungs. Intrathoracic (mediastinal or hilar) tuberculous lymphadenopathy or tuberculous pleural effusion, without radiographic lung abnormalities, are cases of extrapulmonary tuberculosis. A patient with both pulmonary and extrapulmonary tuberculosis should be classified as a case of pulmonary tuberculosis.

- Extrapulmonary tuberculosis: any bacteriologically confirmed or clinically diagnosed case of tuberculosis involving organs other than the lungs, e.g., pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges.
- Multifocal tuberculosis: is defined as involvement of at least two extrapulmonary sites with or without pulmonary involvement.
- Cure: smear-negative patient during the 5th and last month of treatment.
- Failure: smear-positive patients at month 5 or later in the course of treatment.
- Death: patient died during treatment, regardless of the cause of death.
- Multidrug-resistant tuberculosis: strains of Mycobacterium tuberculosis that are resistant to isoniazid and rifampicin.
- Extensively drug-resistant tuberculosis: a form of multidrug-resistant tuberculosis that is also resistant to fluoroquinolones and to at least one of the second-line injectable drugs (amikacin, kanamycin, and capreomycin).

2.1.8. Analysis and Interpretation of Results

Data were entered using Excel2016 software and analyzed by SPSS version 25.0 software.

2.1.9. Ethical Aspects

For the use of the data, the permission of the hospital management and the parents were requested because this research has the sole purpose of improving the care of children with tuberculosis, therefore no financial compensation was paid. The anonymity and confidentiality of the patients were respected in accordance with the rules of medical ethics and the legislation on biomedical and scientific research. No names were included in the database except for the file numbers. The data were kept on the computers of the principal investigator and the co-investigator. They were the only ones with access to the database entry code. There were no conflicts of interest in this study. No changes were made to the bibliographic references.

2.2. Method

2.2.1. Clinical Review

The retrospective study consisted of a review of the medical records of children between one month and 15 years of age with pulmonary or extrapulmonary tuberculosis in order to include those that were usable in our study. Data were collected using a survey form developed for this purpose. The questionnaire in-

cluded the socio-demographic characteristics of the parents and the child, as well as the clinical and paraclinical characteristics and the child's outcome.

The prospective collection concerned children coming to the outpatient clinic or those referred by other structures. It concerned all children from 1 month to 15 years of age who were admitted for suspected tuberculosis. The parents of each patient were questioned in detail about their identity, origin, age, the notion of tuberculosis contagion, chronic cough, anorexia, fever during the long term, and alteration of the general state.

Then a general physical examination was carried out to look for respiratory signs, hepatosplenomegaly, abdominal mass, ascites, peripheral adenopathy, deafening of heart sounds, osteoarticular involvement, and neurological disorders.

At the end of this clinical examination, some imaging and biological examinations were requested to orient the diagnosis.

2.2.2. Paraclinical Examinations

1) Biological examinations

Biological and bacteriological examinations were requested. These were blood cultures in case of fever (axillary temperature ≥38°C), blood count, C-reactive protein, HIV serology, search for Mycobacterium tuberculosis in sputum or gastric fluid, in some cases cytobacteriological examination of pleural fluid, pericardial fluid and urine.

2) Anatomopathological examinations

In some situations, we had recourse to anatomopathological examination to support the diagnosis. These were lymph node, pleural, pericardial, peritoneal, bone, and brain biopsies.

2.2.3. Samples

All samples were taken at the Mali Hospital, in the pediatric department.

1) Techniques for collecting lung samples

- **Spontaneous exhalation**

Two specimens of at least 2 ml volume were collected for children able to expectorate. Sputum was collected in a 50-ml clear, wide-mouth screw-top jar provided by the laboratory. Both samples were collected on two consecutive days in the morning upon awakening. Supporting explanations for the proper collection of sputum were given to the parents when the jar was handed over.

- **Gastric Tubing**

Gastric tubing was performed in children when it is impossible to obtain sputum spontaneously or to induce it by induced sputum. It requires keeping the child fasting for 8 to 12 hours without any movement, and placing a nasogastric tube. A nasogastric tube with a 50 ml syringe was used. The gastric juice was aspirated and put into the spittoon.

2) Extrapulmonary samples

- **Urine**

Urine was collected in the same jars, three days in a row in the morning upon

awakening, with a volume of 40 ml. Urine was processed only in the presence of leukocyturia greater than 10 cells/µl after observation with a Kova cell. It was first centrifuged and the pellet was treated as sputum.

- **Pus, biopsies and puncture fluid**

Pus and puncture fluids (ascites, pleural fluid, cerebrospinal fluid, bronchoalveolar lavage) were collected in sterile tubes with a screw cap. Abscesses with less pus were collected on swabs. The pus, in order to free the germs from the mucus, underwent a decontamination and fluidification step. The puncture fluids were sterile, centrifuged and the pellet suspended in bovine albumin was directly plated and spread on a slide for direct examination. Biopsy specimens were suspended in 0.9% saline and processed like sputum.

3. Results

1) Frequency

From January 1, 2015, to December 31, 2021, out of 9438 children aged 1 month to 15 years hospitalized, we recorded 69 cases of tuberculosis of all forms or a frequency of 0.73%.

2) Socio-demographic characteristics of the children.

The age group [1 - 9 years] was the most represented, with a frequency of 58.0%. The average age was 6.16 years with extremes of 3 months and 15 years. The male sex was slightly in the majority with a sex ratio of 1.1. More than half of our children (43/69) were from an urban area, with a frequency of 62.3% (Table 1).

3) Clinical characteristics

The notion of tuberculosis infection was found in 21 of the 69 children, or a frequency of 30.4%. Almost all children had been vaccinated against tuberculosis (88.4%) (Figure 1).

Table 1. Distribution of children according to their socio-demographic characteristics.

	Frequency	%
Age range		
<1 years	13	18.8
[1 - 9 years]	40	58.0
[10 - 15 years]	16	23.2
Gender		
Male	37	53.6
Female	32	46.4
Residence		
Rural	26	37.7
Urban	43	62.3
Total	**69**	**100.0**

The most common cause of hospitalization was fever (76.8%), followed by weight loss (73.9%) and cough (69.6%) (Table 2).

Pulmonary tuberculosis was the most frequent clinical form (60.9%) followed by extrapulmonary tuberculosis (39.1%) (Figure 2).

Pulmonary involvement was the most common (60.9%), with or without other involvement, followed by pleural involvement (11.5%) and lymph node involvement (10.0%) (Table 3).

Tuberculosis was associated with severe acute malnutrition in 46 of the 69 children, with a frequency of 66.6% (Table 4).

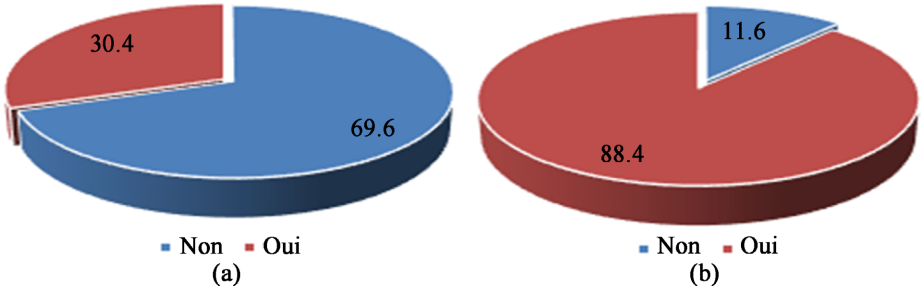

Figure 1. (a) Distribution of children according to tuberculosis contact status; (b) Distribution of children according to BCG vaccination status.

Table 2. Distribution of children according to reasons for hospitalization.

Reasons for hospitalization	Frequency	%
Fever	53/69	76.8
Weight loss	51/69	73.9
Cough	48/69	69.6
Anorexia	47/69	68.1
Chest pain	20/69	29.0

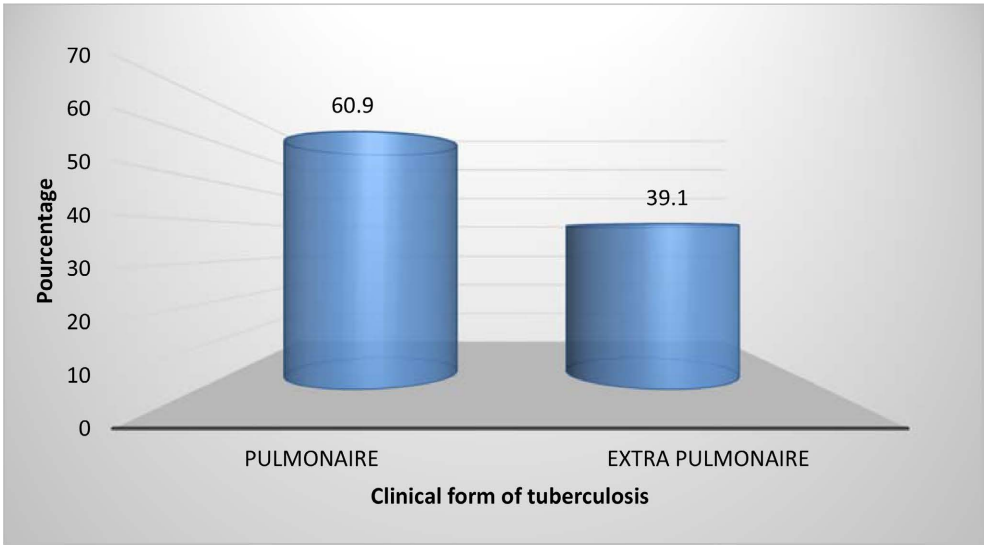

Figure 2. Distribution of children according to clinical forms of tuberculosis.

Table 3. Distribution of children by location of tuberculosis.

Clinical forms	**Frequency**	**%**
Pulmonary	30	43.5
Miliary	6	8.7
Pleural	6	8.7
Ganglionic	5	7.2
Vertebral	4	5.8
Abdominal	3	4.3
Pulmonary and abdominal	2	2.9
Pulmonary and meningeal	2	2.9
Pericarditis	1	1.4
Ganglionic and pleural	1	1.4
Cerebral	1	1.4
Pleural and osseous	1	1.4
Cerebral and vertebral	1	1.4
Pulmonary and vertebral	1	1.4
Pulmonary and pericarditis	1	1.4
Abdominal, pleural and pericardial	1	1.4
Pulmonary and bone	1	1.4
Urinary	1	1.4
Spinal and lymph node	1	1.4
Total	**69**	**100.0**

Table 4. Distribution of children according to co-morbidity.

Associated pathologies	**Frequency**	**%**
Severe acute malnutrition	46/69	66.6
HIV	5/54	9.2
Pulmonary arterial hypertension	1/69	1.4
Nephrotic syndrome	1/69	1.4
Acute myeloblastic leukemia	1/69	1.4
No association	15/69	21.7
Total	**69/69**	**101.7**

Tuberculosis was confirmed by bacteriology in 30 of the 69 children (43.5%). The direct examination was positive in 33.3% of the children, culture (18.8%), and PCR (13.0%). Mycobacterium tuberculosis was present in all confirmed cases. We isolated a rifampicin-resistant strain of Mycobacterium tuberculosis in 2/30 children, a multidrug-resistant strain in 1/30 children, and an extensively

drug-resistant strain in 1/30 children (Table 5).

For microscopy-negative cases, the diagnosis was made on the basis of characteristic lesions on radiology in 34.8% of children, histology (11.6%), and cytology (10.1%).

The tuberculin intradermal test performed on 37/69 children was positive in 32.4% of them. HIV serology was positive in 5 of the 54 children tested (9.3%) (Table 6 and Table 7).

Table 5. Distribution of children according to diagnostic methods.

Diagnosis	Frequency N = 69	%
Bacteriology negative	**39/69**	**56.5**
Radiology	24/69	34.8
Histology	8/69	11.6
Cytology	7/69	10.1
Positive bacteriology	**30/69**	**43.5**
Direct examination	24/69	33.3
Culture	13/69	18.8
PCR	10/69	13.0

Table 6. Distribution of children by tuberculin skin test and HIV serology results.

	Frequency N= 37	%
Intradermal tuberculin test		
Negative	25	67.6
Positive	12	32.4
HIV serology		
Negative	49	90.7
Positive	5	9.3

Table 7. Distribution of children according to treatment regimens.

Treatment regimens	Frequency	%
2 (RHZ)/4(RH)	32	46.4
2 (RHZE)/4(RH)	13	18.8
Confirmed after death	20	29.0
2 (RHZE)/10(RH)	2	2.9
4 (Am-Mfx-Pto-H-Cfz-E-Z)/5(Mfx-Cfz-E-Z)	1	1.4
6 Mfx-Bdq-Lzd-Cs-Cfz/14 Mfx-Cs-Cfz)	1	1.4
Total	**69**	**100.0**

1st line anti-tuberculosis drugs; R = Rifampicine, H = Isoniazide, Z = Pyrazinamide, E = Ethambutol; 2nd line anti-tuberculosis drugs; Am = amykacine, Mfx = Moxifloxacine, Pto = Prothionamide, Cfz = Clofazimine, Bdq = Bédaquiline, Lzd = Linézolide, Cs = Cyclosérine.

Table 8. Distribution of children according to their outcome.

Fate of the children	Frequency	%
Healing without after-effects	29	42.0
Recovery with sequelae	4	5.8
Failure	1	1.4
Death	27	39.1
Abandonment	8	11.6
Total	**69**	**100.0**

More than half of our children (65.2%) were treated with 1st line anti-tuberculosis drugs and with a short 6 months regimen. Two children out of 69 were treated with 1st line anti-tuberculosis drugs with the long 12 months regimen. Two of the 69 children were multidrug-resistant and one was extensively drug-resistant. They were treated with 2nd line anti-tuberculosis drugs with the 9- and 20-month regimen. Twenty of the 69 children did not receive treatment because they died before bacteriological confirmation.

We observed cures without sequelae in 29/69 (42.0%), cures with sequelae (5.8%), and therapeutic failure in 1 child. The case fatality rate was 39.1% and the dropout rate was 11.6% (Table 8).

4. Discussion

Limitations

Despite the limitations of this study related to its retrospective nature, poor record-keeping, the size of our sample, and the unavailability of certain additional examinations essential for diagnosis, the results obtained have made it possible to highlight the problems of tuberculosis in children in our department.

Epidemiological aspects

1) Frequency

From January 1, 2015, to December 31, 2021, 9438 children aged 0 - 15 years were hospitalized among whom we diagnosed 69 cases of tuberculosis of all forms or a hospital frequency of 0.73%. It represents 2.3% of all pediatric tuberculosis cases according to the data of the Sectoral Unit for the Fight against Tuberculosis of Mali [4] during the same period.

Our prevalence is lower than that of Ibrahim *et al.* [8] who reported a frequency of 2.3% during their study conducted in 2020 in the pediatric department of the Donka National Hospital in Guinea. It is however higher than that of Tamini/Toguyeni *et al.* [9] who found a frequency of 0.078% during their study conducted in 2016 at the Centre Hospitalier Universitaire Pédiatrique Charles De Gaules in Ouagadougou, Burkina Faso. This low frequency could be explained by the fact that tuberculosis in children often goes unnoticed because of the unspecific symptoms and also because of the difficulty in obtaining bacteriological confirmation.

2) Socio-demographic characteristics

Age:

The study showed that the age group [1 - 9 years] was the most represented (58%). The mean age was 6.16 with extremes of 3 months and 15 years. It is close to that of Tamini/Toguyeni *et al.* [9] in Burkina Faso and that of Ben Bechir *et al.* [10] in Tunisia who respectively reported an average age of 6.2 and 6.3 years. It is lower than that of Hamdi *et al.* [11] and Aw *et al.* [12] who found an average age of 9 years in their studies conducted respectively in Tunisia and Mauritania. It is higher than that of Soumana *et al.* [13] in Niamey (4.6 years) and those of the literature (5 years) [14].

Gender

Both sexes were affected with a slight male predominance (53.6%) (sex ratio: 1.1). This male predominance was reported by the Sectoral Unit for Tuberculosis Control in Mali [4] and by most African authors, notably by Tamini/Toguyeni *et al.* [9] in Burkina Faso and by Djegbeton *et al.* [15] in Ivory Coast. A female predominance of 52.8% was observed by Zemour *et al.* [16] in their study carried out in 2016 in Remchi in Algeria. This male predominance in our series could be explained by the male predominance in the general population of Bamako where the majority of our children resided.

Residence

The majority of the children in our series lived in urban areas (62.3%) as in the study by Tamini/Toguyeni *et al.* [9] in Burkina Faso (74.4%). In the study by Rakotomizao *et al.* [17], more than half of his patients were from rural areas (67%). Urban areas could be a risk factor because of the high population density which would favor TB transmission.

3) Clinical characteristics

The tuberculosis vaccine was administered to 61/69 children, *i.e.* a proportion of 88.4%. This result is close to that of Radoui *et al.* [18] who found a frequency of 90%. This result is different from that of L. Donato [19] who reported in the literature that BCG confers a protection rate of 50% for all forms. It is different from that of Tamini/Toguyeni *et al.* [9] who reported cases of tuberculosis in children who were mostly unvaccinated (57.5%).

The notion of infection was found in (21/69) or 30.4%. This frequency is lower than that reported by Radoui *et al.* [18] (65.3%) and that of Ben Bechir *et al.* [10] (42.6%). However, it is higher than that of Tamini/Toguyeni *et al.* [9] who found the notion of tuberculosis infection in 19.4% of the children in their study in Burkina Faso.

The reasons for hospitalization were dominated by fever (76.6%), followed by deterioration of general condition (73.9%) and cough (69.6%). Our symptoms are similar to those reported in the literature [20] [21] and those observed by Hamdi *et al.* [11]: fever (65%), cough, and alteration of general condition (56%). They are different from those reported by Tamini/Toguyeni *et al.* [9] in Burkina Faso who observed in their study that pallor was the most frequent reason for

hospitalization in children (87.23%) followed by cough (53.19%). They are different from symptoms found by Ben Bechir *et al.* [10]: weight loss (50%) and cervical adenopathy (46%).

In our series, the pulmonary form was more frequent than the extrapulmonary form (60.9% versus 39.1%). Our data are similar to those of Tamini/Toguyeni *et al.* [9] who found more pulmonary than extrapulmonary forms (68.08% versus 25.53%) in Burkina Faso as did Radoui *et al.* [18] who observed 92 cases of pulmonary tuberculosis and 42 cases of extrapulmonary tuberculosis in their study. our data are different from those of Soumana *et al.* [13] who found in their study more extrapulmonary forms than pulmonary forms (62.1% versus 37.9%) like Zemour *et al.* [16] who reported more extrapulmonary forms than pulmonary forms (77.8% versus 20.2%) in their study.

In our sample, tuberculous pleurisy was the most frequent extrapulmonary form (11.5%) followed by peripheral adenitis (10.0%) as reported in the literature [20] [22] but with higher proportions (pleurisy: 40%, adenitis: 30%). Radoui *et al.* [18] also showed in their series that tuberculous pleurisy was the most frequent extrapulmonary involvement (36.5%) followed by lymph node involvement (23.1%).

Co-morbidity was found in 54 of the 69 children, or a frequency of 78.1%. It was mostly associated with severe acute malnutrition (66.7%) followed by HIV (7.2%), acute myeloblastic leukemia (1.4%), nephrotic syndrome (1.4%), and pulmonary hypertension (1.4%). Our data are close to those of Soumana *et al.* and Djegbeton *et al.* [15] who respectively reported that tuberculosis was predominantly associated with severe acute malnutrition in 55% and 43% of children in their studies.

4) Paraclinical characteristics

Intradermal tuberculin testing was performed in 37/69 children (53.6%). It came back positive in 32.4% of them. This rate is lower than that of most African authors, notably Soumana [13] (85.7%), Radoui [18] (69.3%), Ibrahim [8] (62.2%), Hamdi [11] (58%) and Ben Bechir [10] (57%). However, it is higher than that of Djimbélé *et al.* [23] who found a frequency of 9.35% in their study conducted at the Pediatric Center of Bangui. This low rate of positivity of the tuberculin intradermal test could be explained by the immune immaturity of our children due to their young age and the high prevalence of severe acute malnutrition in our series.

Tuberculosis was confirmed by bacteriology in 30 of the 69 children (43.5%). This proportion represents 1% of all confirmed pediatric cases according to data from the Sectoral Unit for Tuberculosis Control in Mali [4]. It is lower than that of Ben Bechir *et al.* [10] who obtained bacteriological confirmation in 65% of children with tuberculosis in their series. However, it is higher than those reported by most African authors, notably those of Djegbeton *et al.* [15] (45.8%), Tamini/Toguyeni *et al.* [9] (23.4%), Ibrahim *et al.* [8] (18.75%) and of Radoui *et al.* [18] (14.1%).

The direct examination was positive in 33.3% of our children. This positivity rate is higher than that reported in the literature (20%) [22] [24] and that of Hamdi *et al.* [11] (10%). However, it is lower than that of Zemour *et al.* [16] who reported that 53% of children were positive on direct examination in their study. This increase in the positivity rate in our series could be explained by the fact that we send our samples to 2 different bacteriology laboratories for direct examination.

The culture came back positive in 18.8% of our children. This frequency is lower than that reported in the literature (50%) [22] [24]. However, it is higher than that obtained by Hamdi *et al.* [11] (10%).

If the sensitivity of detection of Mycobacterium tuberculosis in children by the PCR method is of the order of 45-100% [21] [24], it came back positive in 13.0% of our children. This proportion is lower than those obtained by most African authors, notably Djegbeton *et al.* [15] (66.7%) and by Ben Bechir *et al.* [10] (54%). However, it is higher than the detection rate of tuberculosis of all forms reported by the Sectoral Cell for the Fight against Tuberculosis in Mali (8.2%) [4].

All confirmed cases were Mycobacterium tuberculosis. PCR detected rifampicin resistance in 2 children (6.7%) and culture revealed a multidrug-resistant strain of Mycobacterium tuberculosis in 1 child and an extensively drug-resistant strain in 1 child. Our data are different from those reported by the authors. Our rate of resistance to rifampicin is higher than that of Ben Bechir *et al.* [10] (3.2%) and that of Diatta *et al.* [25] (0.91%). These authors did not observe any multidrug-resistant or extensively drug-resistant cases in their studies.

For microscopy-negative cases, the diagnosis was made on the basis of characteristic signs of tuberculosis on radiology in 34.8% of children, on histology in 11.6%, and cytology in 10.1%.

5) Therapeutic and evolutionary aspects

More than half of our children (65.2%) were treated with 1st line anti-tuberculosis drugs and with the short 6-month treatment regimen (2RH/4RH).

Two out of 69 children with tuberculosis meningitis were treated with 1st line anti-tuberculosis drugs with the long 12-month regimen (2RH/10RH).

Two of the 69 children had multidrug-resistant peritoneal TB and extensively drug-resistant urinary TB, respectively. The 2 children were treated with 2nd line anti-tuberculosis drugs with the 9- and 20-month regimen.

Twenty of the 69 children did not receive treatment because they died before bacteriological confirmation.

Forty-five of the 69 children were treated with the (2RH/4RH) or (2RHE/4RH) regimen, or 68% as in the literature [19] [21] [24]. This regimen is used by most African authors through their national TB control programs, notably Tamini/Toguyeni *et al.* [9] used it in 72.34% of children and Hamdi *et al.* [11] in 100% of children. Second-line anti-tuberculosis drugs have not been used by other authors because they have not reported cases of multidrug resistance or ultra resistance in their series.

During the course of the disease, we observed an overall cure rate of 47.8%, of which 42.0% were cured without sequelae and 5.8% with sequelae (vertebral forms). Our cure rate is lower than the overall rate recorded in 2020 by the Malian Tuberculosis Control Sector Unit (82%) [4] and the objective of 85% therapeutic success. It is also lower than that of Ibrahim *et al.* [8] and Moh *et al.* [26] who respectively obtained a cure rate of 84.54% and 71% in their hospital studies.

In our series, we recorded a case fatality rate of 39.1%. According to the data of the Sectoral Cell for the Fight against Tuberculosis in Mali, the case fatality rate among children is 46.5% [4]. Our rate represents 1% of the overall pediatric mortality rate in Mali.

It is also higher than that of Ibrahim *et al.* [8] who recorded a case fatality rate of 5.4% and Moh *et al.* [26] who found a case fatality rate of 16% in their study conducted in 2015 in 2 University Hospitals of Abidjan. This high mortality rate in our series could be explained by the young age of the majority of our children, the delay in diagnosis, the existence of severe forms (miliary, meningitis, multidrug resistance, ultra drug resistance), and comorbidities.

Eight children out of 69 were lost to follow-up, or a proportion of 11.6%, slightly higher than that observed by Ibrahim *et al.* [8] (10.05%) and by Moh *et al.* [26] (8.5%). This could be explained by the lack of communication and the low level of education of the parents of our children who abandon the treatment to resort to traditional medicine.

5. Conclusion

Tuberculosis is common in the pediatric ward of the Mali Hospital despite good BCG vaccination coverage. Children under 9 years of age are the most affected. The notion of tuberculosis infection was found in a small proportion of our children. Fever and alteration of the general condition are the most frequent symptoms. Bacteriological confirmation remains difficult despite the popularization of molecular diagnostic methods (Xpert system). The case fatality rate is high due to the young age of the children, HIV co-infection, and the emergence of resistant strains of bacilli. In order to assess the extent of tuberculosis in children in Mali and to study its clinical and paraclinical characteristics, all children hospitalized for acute and severe malnutrition should be tested for Koch's bacillus in their gastric fluid. Investigations should be carried out around an index case in the family, including chest radiography, skin tests, and bacteriological samples from all contacts.

Conflicts of Interest

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

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