

# Diagnosis and Management of Childhood Tuberculosis: A Cross-Sectional Study of Practices in Gilgit Baltistan, Pakistan

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## Abstract

**Background:** Tuberculosis (TB) is one of the major killer diseases among infectious diseases. The success of TB control depends on the capability of the health care system to detect and accurately manage TB cases. Tuberculosis in children remained a low public health priority with limited epidemiologic studies. Struggles for TB control in children need to be enhanced as children are providing the reservoir for future cases to develop. **Objectives:** The study evaluated diagnostic and treatment practices related to childhood pulmonary tuberculosis in Gilgit Baltistan (GB), Pakistan. **Methods:** A descriptive, cross-sectional study based on retrospective record review of childhood Pulmonary Tuberculosis patients registered in the year 2020 with self-administered questionnaire. **Results:** Data of 557 childhood cases were collected. Most childhood cases were in age group 1 - 4 years (54%) with male predominance. More than 90% were diagnosed and treated at public sector facilities. 99% of the cases were clinically diagnosed with passive case finding. Cough was considered as a symptom of childhood Tuberculosis (TB) by 94% of physicians. Other important features included failure to thrive (13%), contact with a family history of TB (15%), Malnutrition(24%) and respiratory signs (21%). 99% physicians advised chest X-ray, Complete blood count (CBC) (95%) and Erythrocytes sedimentation rate (ESR) (72%) for diagnosis and fewer physicians (2%) used sputum smear microscopy and induced sputum (0.1%). Combining data on dosage, frequency and duration for drugs, 99% of the cases were found receiving correct regimen. The treatment outcomes of the cases were cured 4 (0.8%), treatment completed 551 (99.3%) and died 2 (0.4%) with no lost to follow up. **Conclusions:** The study highlights inappropriate diagnostic and treatment practices for managing childhood pulmonary TB among physicians in public and private sectors of Gilgit Baltistan. Most of the cases are managed by general practitioners with no post graduate qualifi-

cation in medicine or pediatrics. The deviations from the guidelines for TB control cannot be negated in the region.

## Keywords

Childhood, Tuberculosis, Management, Respiratory Signs

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## 1. Introduction

Tuberculosis is one of the major infectious diseases among the children with significant morbidity and mortality. Overpopulation, poverty and HIV epidemic have added to resurgence of tuberculosis internationally. Maximum cases occur in resource constraint countries with progressive increase in last decade [1]. World Health Organization (WHO) targets to end the TB epidemic by 2035 whereas the United Nations' Sustainable Developmental Goals sets this determined target for 2030. Therefore, suitable funding and effective national TB programs must be prioritized in high burden and low-income localities [2]. Tuberculosis in children remained a low public health priority and surveillance data in many countries are deficient with limited epidemiologic studies [3]. By overlooking childhood TB, struggles for TB control will eventually fail because children are providing the reservoir for future cases to develop [4]. According to the recent WHO Global TB Report 2021, globally, about 1.1 million children of age less than 10 years and young adolescents (aged 10 - 14 years) developed TB in 2020 and 226,000 died because of TB. Pakistan is sixth among countries with major contributions to the international shortfall in TB case notifications in 2020, reported incidence of 259 per 100,000 new TB cases yearly with 48% receiving treatment. Children are 11% of the entire burden of TB cases [5]. The global strategy for TB control emphasizes on improved and guaranteed access to diagnosis, treatment and support services [6]. A study conducted by Gunasekera *et al.*, in 2022 concluded that the crucial need to enhance TB detection and treatment availability need to be adjusted against the costs of over-diagnosis and needless treatment [7]. Chimsimbe *et al.*, 2020 in their study conducted in Chegutu, Zimbabwe, recommended that district should provide mentorship and on job trainings, continuous advocacy, communication and social mobilization to enhance childhood TB detection [8]. Sharma *et al.*, 2008 in their study in South Delhi, India concluded that there is a need of developing new technologies and approaches for a uniformity within the existing NTP guidelines about judicious practice of investigations, treatment availability and sensitization of health care providers to the particular needs of children [9]. A study conducted by Yaqoob *et al.*, 2022 in Pakistan high lights low usage of the NTP guidelines by private providers for the diagnosis of pediatric TB in Pakistan [10]. A study conducted by Jain *et al.*, 2020 concluded that diagnosis of childhood TB is much challenging as it is difficult to get suitable specimen, causing poor sensitivity of available tests [11]. Singhal in his recently conducted study in 2022 highlights that new

guidelines endorse Xpert Ultra as the first diagnostic test for TB and rifampicin resistance in sputum or extra pulmonary samples instead of smear/culture and phenotypic drug-sensitivity testing [12]. According to Yaqoob *et al.*, 2022 the availability of diagnostics varies across Pakistan, X-ray chest and smear microscopy are almost generally available while histopathology, sputum culture and Gene-Xpert are available at tertiary care hospitals [13]. According to Dodd *et al.*, 2012 with a more comprehensive understanding of TB burden in children, the children who are developing the disease could be detected allowing programs to develop target interventions [14]. In another study conducted by Dodd *et al.*, in 2017, it was mentioned that decreasing childhood deaths from TB needs more children to be approached, diagnosed and cured. An enhanced inclination to treat children clinically for tuberculosis disease, without bacteriological confirmation would also decrease mortality, however, it would possibly result in the rise of unreasonable diagnosis [15]. Adherence to standard guidelines is vital for restricting effects of disease among children. Suitable treatment is crucial to avoid death, drug-resistance, adverse effects and transmission to disposed contacts. It is therefore appropriate to study diagnostic and treatment practices of physicians while managing childhood TB. To the best of our knowledge, the diagnostic and treatment practices associated with childhood tuberculosis among physicians of healthcare facilities in Gilgit Baltistan have not been evaluated previously. The study assessed these practices related to childhood pulmonary tuberculosis among physicians in Gilgit Baltistan in 2020. The specific objectives were to assess whether all presumptive TB cases evaluated, diagnosed and managed as per PPA scoring chart and the national guidelines.

## 2. Methods

### 2.1. Study Design

A descriptive, cross-sectional study based on retrospective record review of childhood PTB patients registered in the year 2020.

### 2.2. Study Setting

#### General Setting

Situated in the northern areas of Pakistan, GB is home to world peak mountain ranges, the Karakoram, the Hindu Kush and the Himalayas. Administratively, GB is consisting of ten districts expanded on an area of 72,496 sq.kms [16]. The GB regions is consisted of three divisions viz. Gilgit, Diamer and Baltistan. Population of GB is 1.49 million [17]. Patients diagnosed with TB in public and private sectors are referred to TB centers located in each district. These TB centers are managed by District TB Leprosy Coordinator (DTLC). Record of each patient is maintained at the TB Center and medicines are also provided to patients at these centers. GB has 36 tuberculosis basic management units (BMUs) and 10 GeneXpert laboratories (*i.e.*, one in each district). Patients diagnosed with TB in private sector are also referred to TB Centers for further management.

### 2.3. Study Site

All TB centers in the region of Gilgit Baltistan.

### 2.4. Development of Study Tool and Data Collection

The study tool was a self-administered questionnaire (**Appendix**). With the consent of Provincial TB Program, GB, the data was collected by a trained field staff for 557 patients from all centers of districts with the help of DTCs.

### 2.5. Study Population

The study population includes all pulmonary TB patients of age < 15 years, diagnosed in healthcare facilities of GB region in 2020. As record of all cases is available in TB centers of each district, data of the maximum number of the childhood cases were collected from all districts of Gilgit Baltistan collected and maximum cases were reported from 2 districts, Gilgit and Diamer.

### 2.6. Measurement of Variables

The data collection tool was designed by the authors and data collection method, wording, order, format, structure and layout of questionnaire was reviewed by the technical team of experts at National TB Program. The on information regarding the diagnosis and management practices of healthcare providers about childhood TB. The indicators associated with diagnosis included signs and symptoms, nutritional status, investigations, absence of BCG scar, enlarged cervical lymph nodes, chest X-ray, sputum smear microscopy, gastric lavage or bronchoalveolar lavage. The indicators related to treatment included correct dose, frequency and duration of prescribed regimen, referral to a specialist, suspicion of drug-resistance and treatment outcomes. Descriptive variables included were age, sex, geographical location, type of case finding, type of healthcare provider and type of cases based on diagnosis. For assessing practices associated with monitoring progress of treatment, investigations advised during and at the end of treatment were inquired. The data related to study variables was entered into Epi-data software.

### 2.7. Data Analysis

Analyses was done in Epi-data software involving calculation of frequencies and percentages of practices for variables mentioned above. Descriptive statistics were used to present the data. Inferential statistics were used based on objectives of the study.

## 3. Results

**Patient Characteristics:** Data of 557 childhood cases were collected. Most cases 303 (54%) were in age group 1 - 4 years, 160 (29%) were in age group 5 - 14 years and remaining 94 (17%) cases were less than 1 year of age. There was a male predominance with 320 (57%) and 237 (43%) females. Most cases were reported

from District Gilgit 256 (46%) and District Diamer 225 (40%). Participants' profile, number and percentage of cases of various districts included in the study are presented in **Table 1**. Most cases were diagnosed in public sector 510 (91.6%) and only 47 (8.4%) were diagnosed in the private sector. Almost all cases were detected by passive case finding 554 (99%) and only 3 (0.5%) cases were found by active case finding. Out of total 557 cases, 553 (99%) were clinically diagnosed and only 3 (0.5%) cases were bacteriologically confirmed.

Almost all physicians suspected tuberculosis in a child with cough of more than two-week duration (**Table 2**). The other common symptoms raising of TB suspicion were failure to thrive 74 (13%) and contact history of TB 84 (15%). Among signs, malnutrition 139 (24%) and respiratory signs 120 (21%) were reported by most physicians. Only 2 (0.3%) cases were suspected on the basis of no BCG scar and 6 (1%) were suspected on the basis of enlarged cervical lymph nodes. Almost all physicians reported asking for X-ray chest. Majority Physicians reported prescribing investigations including complete blood count (CBC) and erythrocyte sedimentation rate (ESR). Only 13 (2.3%) cases were advised sputum smears for presence of acid-fast bacilli (AFB). GL or BAL for inducing sputum if the child is not able to produce sputum was done for 1 (0.1%) patient only.

Regarding management practices of childhood TB in Gilgit Baltistan (**Table 3**), as Medical and child specialists are not available in each district of Gilgit Baltistan and most of them are practicing in major cities, only 99 (17%) pediatric cases were referred to a specialist for diagnosis and management. most of the cases were grown up children of more than 10 year of age and were referred to medical specialist instead of child specialist. No significant difference was found in the treatment outcomes of the cases managed by the specialist or general practitioners. Combining data on dosage, frequency and duration for drugs, 99% of the cases were found receiving correct regimen. CBC and ESR were reinvestigated for 153 (27.5%) cases during the course of therapy. 531 (95.3%) cases were advised chest X-ray during the course of therapy. Liver and renal function tests for identifying adverse effects of drugs were not in practice as only 2 (0.3%) cases were advised RFTs and no patient was advised LFTs. Record of the major side effects and complications was found missing. Sputum smear to assure cure was advised for 3 (0.5%) of cases. Maintenance of patient clinical record was vigorously practiced 549 (98.6%). Drug sensitivity test for rifampicin was found a neglected area and none of the patients were advised. 77 (13%) of the cases were prescribed other antimicrobials during the course of therapy. The treatment outcomes of the cases were as cured 4 (0.8%), treatment completed 551 (99.3%) and died 2 (0.4%). Outcome of all the cases was evaluated and there was no lost to follow up.

#### 4. Discussion

This cross-sectional study discloses diagnostic and management practices of childhood TB among physicians in Gilgit Baltistan differ from recommendations

**Table 1.** Baseline characteristic of childhood TB cases in the region of Gilgit Baltistan.

Characteristics	N (%)
<b>AGE</b>	
<1 Year	94 (17)
1 - 4 years	303 (54)
5 - 14 years	160 (29)
<b>Gender</b>	
Male	320 (57)
Female	237 (43)
<b>TB center</b>	
TB center Gilgit	256 (46)
TB center Ghizer	22 (4)
TB center Hunza	4 (0.7)
TB center Nagar	1 (0.1)
TB center Astore	19 (3)
TB center Diamer	225 (40)
TB center Skardu	30 (5)
TB center Ghancha	00
TB center Shigar	00
TB center Kharmang	00
<b>Type of healthcare provider</b>	
Public	510 (91.6)
Private	47 (8.4)
<b>Type of casefinding</b>	
Active Case Finding (ACF)	3 (0.5)
Passive Case Finding (PCF)	554 (99)
<b>Type of TB Patients based on diagnosis</b>	
Bacteriologically confirmed	4 (0.7)
Clinically diagnosed	553 (99)

**Table 2.** Diagnostic practices of Physicians regarding childhood TB in Gilgit Baltistan in the year 2020.

Variables	Number (%)
Cough more than 2 weeks	526 (94)
Failure to thrive	74 (13)
Contact/family history of TB	84 (15)
Respiratory signs (crepitation/rhonchi)	120 (21)
No BCG scar	2 (0.3)

**Continued**

Enlarged cervical lymph nodes	6 (1)
Malnutrition	139 (24)
Chest X-ray	550 (99)
Complete blood count	530 (95)
Erythrocyte sedimentation rate	402 (72)
2 Sputum smears for presence of acid fast bacilli	13 (2)
GL or BAL for inducing sputum if the child is not able to produce sputum	1 (0.1)
Reinvestigations	153 (27.5)
Only Clinical Assessment	544 (99)

**Table 3.** Management practices of childhood TB in Gilgit Baltistan in the year 2020.

Variables	Number (%)
Referred to a specialist for diagnosis and management	99 (17)
Is the regimen prescribed for cases of pulmonary TB 2HRZE + 4HR	554 (99)
Dosage of HRZE according to weight	554 (99)
Frequency of medicines	554 (99)
CBC and ESR were advised during the course of therapy	153 (27.5%)
Liver function tests during the course of therapy	Nil
Renal function tests during the course of therapy	2 (0.4)
Re X-ray during the course of therapy	531 (95.3)
Maintain patient clinical record	549 (98.6)
Whether drug sensitivity test for rifampicin is timely performed	0 (0)
Ensure cure by negative sputum smear	4 (0.5)
Other antimicrobials prescribed	77 (13%)
<b>Treatment outcomes</b>	
Cured	4 (0.8%)
Treatment completed	551 (99.3%)
Died	2 (0.4%)

of National guidelines for TB control in Pakistan. In 557 childhood cases diagnosed in 2020, most cases 303 (54%) were in age group 1 - 4 years. Male were predominance with 320 (57%) in our study. This in contrast to a nationwide cluster-based cross-sectional study, in 12 districts across the country where the age group 10 - 14 years was largest (41%) and girls dominated (64%) [18].

Most cases in our study were reported from District Gilgit 256 (46%) and Dimer 225 (40%). Mostly diagnosed in public sector 510 (91.6%) and only 47 (8.4%) were diagnosed in the private sector.

Almost all cases were detected by passive case finding 554 (99%) and only 3 (0.5%) by active case finding. In Gilgit Baltistan chest camps and involvement of lady health workers may be helpful for active case finding. Active case-finding screen people for TB by field staff, diagnostic clinics, sputum drop off points and training of community health workers [19]. In 2018, Fox *et al.*, performed a cluster-randomized controlled trial at clinics in 70 districts of Vietnam where health workers were assigned to do either household contact screening and standard passive case finding (intervention group) or passive case finding only (control group). In 2-year follow-up period, 180 contacts were registered as having TB in the intervention districts as compared with 110 contacts in the control districts [20]. In our study 553 (99%) cases were clinically diagnosed and only 3 (0.5%) were bacteriologically confirmed. Shakoor *et al.* in a study conducted in 2019 recommended that childhood cases negative for TB should be referred to tertiary care hospitals for better identification and management of some other disorders [21]. In our study almost, all physicians suspected tuberculosis in child with cough of more than two-week duration. A study conducted in 2019 by Ahsan *et al.*, in a tertiary care hospital of Bangladesh found that most commonly found symptoms in childhood TB cases were fever, cough, cold, vomiting, abdominal pain, breathlessness, lymphadenopathies, convulsions, swellings and skin lesions [22]. In our study contact history of TB raised suspicion in 84 (15%) cases. In 2018, A case control study conducted by Gebremichael *et al.*, in Ethiopia showed that disease had a ten times rush in study participants having a contact history [23]. In our study respiratory signs were the basis of suspicion in 120 (21%). Only 2 (0.3%) cases were suspected on absence of BCG scar and 6 (1%) were suspected on enlarged cervical lymph nodes. A study conducted in 2018 by Gupta *et al.*, in a tertiary care hospital of Delhi, India concluded that 86% children having pulmonary TB and 73% with extra pulmonary TB had BCG immunization at birth showing that vaccinated child may also develop TB [24]. Similarly, a systematic review of 2687 subjects conducted by Deosthali *et al.*, 2019 showed that Tuberculosis had the highest rate (73.4%) for the granulomatous disease etiologies of cervical lymphadenopathy [25]. In our study the other common symptom raising suspicion of TB was failure to thrive 74 (13%). A number of cases were diagnosed on the basis of malnutrition 139 (24%). In 2021 Khuawar *et al.*, while studying Tuberculosis as a forecaster of childhood malnutrition in Sindh, Pakistan observed that 13% children infected with TB were found with low BMI and low nutrition marker [26]. In our study almost all physicians reported asking for X-ray chest for diagnosis of pulmonary TB. In contrast, in 2020 a study conducted by Andronikou *et al.*, in UK suggests the routine practice for chest X-ray is disputed because of only moderate reliability [27]. In our study majority physicians prescribed investigations including complete blood count (CBC) and erythrocyte sedimentation rate (ESR). In 2020 Shah *et al.*, while studying the clinical profile of tuberculosis in children at a tertiary care children hospital in India, found that 72 of 97 (74.22%) records showed raised ESR levels [28]. In our study less or no reliance on sputum smear or cul-



ture was found for diagnosis of childhood pulmonary TB. Only 13 (2.3%) cases were advised sputum smears microscopy. GL or BAL for inducing sputum was done for 1 patient only. In a prospective study of children hospitalized with suspected PTB in Cape Town, South Africa, between February 2009 and February 2012, it was concluded that sputum induction is a harmless and useful technique for microbiological confirmation of TB in young children [29].

Only 99 (17%) cases were referred to a specialist for diagnosis and treatment, while other were managed by the medical officers and general practitioners. Physicians did not explore drug-resistance and none of them were found testing for rifampicin resistance. In our study repeat X-ray after a course of antibiotics was prescribed for 531 (95.3%) cases. It was found that many physicians were not advising any routine follow-up investigation. CBC and ESR were advised to 153 (27.5%) during the course of therapy. It was found that investigations for identifying the adverse effects of medicines (liver and renal function tests) were not practiced. LFTs were not advised even for a single patient and RFTs were advised for only 2 (0.4%) cases. Sputum smear was performed for 3 (0.5%) cases during and at end of treatment. Decision to end treatment after full course was a clinical one for almost all cases. It is amazing that no variance was found in regimen offered by physicians as more than 95% of physicians were following recommended regimen. While diagnosing TB in a child was faced with practical difficulty as discussed already, no such hindrance was found for prescribing appropriate treatment in right dosage, frequency and duration.

Hesseling *et al.*, in a critical review of diagnostic approaches of childhood tuberculosis conducted in 2002 found that the diagnosis of TB in children is seldom confirmed and is based mainly on clinical signs, symptoms and investigations [30]. Ending the global TB epidemic will only be achievable if there is an intensive action by all countries that have endorsed the End TB Strategy [31]. It requires a paradigm shift from the conventional approaches to disease control used previously. Early and accurate diagnosis of all forms of TB and rapid detection of drug resistance is fundamental to this shift [32]. Adequate and complete treatment of TB is cornerstone of TB control as it results in better health outcomes for affected patient as well as reduced chances of infection to others. The study had some limitations as the method of the study was based on questionnaire involving seeing records of patients nor interviewing parents and physicians. Even in the presence of these limitations, the deviances from guidelines cannot be negated.

## 5. Conclusion

The study highlights that there is a need for quality improvement in the diagnostic assessment of children for TB in Gilgit Baltistan. Mechanisms to ensure accurate diagnosis of TB should be a priority for the program and operational research including piloting of interventions for the eliminating TB are required. Non-standardized practices for diagnosis and treatment of TB will make TB control a very difficult task to achieve with probability of severe epidemiological

concerns. Apart from that, the regional TB control program and district health administrations should manage to conduct the quarterly review meetings, contact tracing and childhood TB trainings. The diagnostic practices need improvement and we recommend that national program should take mentorship and conduct formal and on job trainings of doctors and laboratory staff on the updated guidelines. Enhancement of ongoing advocacy, communication and social mobilization activities are also required. As diagnostics for tuberculosis execute poorly in children, algorithms involving clinical features, exposure history, laboratory and radiographic findings are commonly used to make a clinical diagnosis of child tuberculosis. It is necessary that sensitivity and specificity of the algorithms should be improved. PPA scoring chart developed by Pakistan Pediatric Association and NTP need to be oriented and implemented. As our study only evaluated diagnostic and treatment practices related to childhood pulmonary tuberculosis in Gilgit Baltistan, future studies should also look on a large scale on the factors involved in excessive prevalence of childhood cases in district Diamer and Gilgit as compared to other districts, aimed to prevent and control childhood TB in our settings.

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### **Ethical Approval**

The ethical clearance of the study was obtained from the IRB, Research Unit, Common Management Unit for Aids, TB and Malaria.

### **Data Confidentiality**

Data were entered in a pre-designed format based on the information recorded in database. Names of the patients were not collected and data on personal identifies was not included in analysis and final presentation of study findings. Data in hard files kept under lock and key, while electronic files are password protected. Only authorized persons (principal investigator) have access to data for analysis and interpretation of results.

### **Collaborative Partnership**

The collaborative partners for this study are the Pakistan National TB Control Program (NTP), MSF, The Union South-East Asia office, WHO, WHO TDR.

### **Conflict of Interests**

The authors declare that there is no conflict of interests regarding the publication of this paper.

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## Appendix

Questionnaire for study titled: Diagnosis and management of Childhood Tuberculosis: A Cross-Sectional Study of Practices in Gilgit Baltistan, Pakistan

Date: \_\_\_\_\_

TB Centre: \_\_\_\_\_

District: \_\_\_\_\_

Name of Healthcare Provider: \_\_\_\_\_

Type of Healthcare Provider: General Practitioner/Specialist

Name of the Patient: \_\_\_\_\_

Questions regarding baseline characteristic of childhood PTB cases in the region of Gilgit Baltistan

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**AGE**

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- <1 Year
- 1 - 4 years
- 5 - 14 years

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**GENDER**

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- Male
- Female

---

**DISTRICT**

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**TYPE OF HEALTH CARE PROVIDER**

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- Public
- Private

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**TYPE OF CASE FINDING**

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- Active Case finding
- Passive Case finding
- Walk in
- Referral
- Transfer In

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**TYPE OF TB PATIENTS BASED ON DIAGNOSIS**

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- Bacteriologically confirmed
- Clinically diagnosed

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**Questions regarding practices related to childhood Pulmonary Tuberculosis diagnosis**

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**Symptoms that raised suspicion**

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Cough more than 2 weeks.

Failure to thrive.

Contact with/family history of TB.

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**Continued****Signs that raised Suspicion**

Respiratory signs (crepitation/rhonchi).

Absence BCG scar

Enlarged cervical lymph nodes.

Malnutrition.

**Investigations advised**

Chest X-ray

Complete blood count

Erythrocyte sedimentation rate

2 Sputum smears for presence of acid fast bacilli

Both Sputum Microscopy and radiological examination

GL or BAL for inducing sputum if the child is not able to produce sputum

Sputum Culture Examination

Only Clinical Assessment

**Questions Practices related to childhood Pulmonary Tuberculosis case management by physicians**

Dosage of HRZE according to weight

Correct\*

Over dosage

Under dosage

Duration of initial and continuation phase (2HRZE + 4HR)

Correct\*

Over dosage

Under dosage

Frequency of medicines

Correct\*

Over dosage

Under dosage

Other antimicrobials prescribed

Investigations during the course of therapy

Clinical examination

X-ray

Sputum Examination

Liver function tests

Complete blood count

Renal function tests

Erythrocyte sedimentation rate

Did not advise any investigation

**Continued**

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DST for Rifampicin  
Maintain the patient clinical record  
Ascertains cure by negative sputum  
Outcome evaluation  
Cured  
Treatment completed  
Died  
Loss to follow up  
Treatment failure  
Not-evaluated

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\*Correct as per standard guideline.