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Delays and barriers to early treatment initiation for childhood tuberculosis in India

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SUMMARY

BACKGROUND : India accounts for 27% of global childhood tuberculosis (TB) burden. Understanding barriers to early diagnosis and treatment in children may improve care and outcomes.

METHODS : A cross-sectional study was performed among 89 children initiated on anti-TB treatment from a public hospital in Pune during 2016, using a structured questionnaire and hospital records. Health care providers (HCPs) were defined as medical personnel consulted about the child's TB symptoms. Time-to-treatment initiation (TTI) was defined as the number of days between onset of TB symptoms and anti-TB treatment initiation. Based on Revised National TB Control Programme recommendations, delayed TTI was defined as >28 days.

RESULTS : Sixty-seven (75%) of 89 enrolled children had significant TTI delays (median 51 days, interquartile range [IQR] 27–86). Sixty-six (74%) children visited 1–8 HCPs in the private sector before approaching the public sector. The median HCP delay was 28 days (IQR 10–75). Bacille Calmette-Guérin vaccination (aOR 10.96, $P = 0.04$) and loss of appetite (aOR 4.44, $P = 0.04$) were associated with delayed TTI.

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Conflicts of interest: none declared.

CONCLUSION : The majority of the children had TTI delays due to delays by HCPs in the private sector. Strengthening HCP competency in TB symptom screening and encouraging early referrals are crucial for rapid scaling up of early treatment initiation in childhood TB.

RÉSUMÉ

L'Inde représente 27% du poids total de la tuberculose (TB) de l'enfant dans le monde. Comprendre les obstacles au diagnostic et au traitement précoces pourrait améliorer la prise en charge et les résultats des enfants atteints de TB.

Une étude transversale a été réalisée parmi 89 enfants mis sous traitement anti-TB dans un hôpital public de Pune en 2016, grâce à un questionnaire structuré et aux registres de l'hôpital. Les prestataires de soins de santé (HCP) ont été définis comme du personnel médical consulté pour des symptômes de TB de l'enfant. Le délai de mise en route du traitement (TTI) a été défini comme le nombre de jours entre l'apparition des symptômes de TB et la mise en route du traitement anti-TB. En se basant sur les recommandations révisées du Programme National de lutte contre la TB, un retard à la mise en route a été défini comme un délai >28 jours.

Soixante-sept (75%) des 89 enfants enrôlés ont eu un retard significatif de mise en route du traitement (médiane 51 jours ; intervalle interquartile [IQR] 27–86). Soixante-six (74%) enfants ont consulté 1–8 HCP dans le secteur privé avant le système de santé public. Le délai médian des HCP a été de 28 jours (IQR 10–75). La vaccination bacille Calmette-Guérin (OR ajusté [ORa] 10,96 ; $P=0,04$) et la perte d'appétit (ORa 4,44 ; $P=0,04$) ont été associées avec le retard au traitement.

La majorité des enfants a subi un retard au traitement en raison des retards au diagnostic des HCP du secteur privé. Il est crucial de renforcer leurs compétences en matière de dépistage des symptômes de TB et d'encourager une référence précoce pour parvenir rapidement à une généralisation de la mise en route précoce du traitement des enfants atteints de TB.

RESUMEN

A la India corresponde el 27% de la carga de morbilidad mundial por tuberculosis (TB) de la niñez. Comprender los obstáculos al diagnóstico temprano y el tratamiento oportuno podría mejorar la atención y los desenlaces clínicos de los niños con TB.

Se llevó a cabo un estudio transversal con 89 niños que iniciaron el tratamiento antituberculoso en un hospital público de Pune durante el 2016, mediante un cuestionario estructurado y el análisis de las historias clínicas. Se definieron los proveedores de atención de salud (HCP) como el personal médico consultado por los síntomas indicativos de TB de los niños. Se definió el lapso transcurrido hasta el inicio del tratamiento como el número de días entre el comienzo de los síntomas y el inicio del tratamiento. En conformidad con las recomendaciones del Programa Nacional Revisado de Tuberculosis, se adoptó como límite para un inicio retrasado del tratamiento un lapso superior a 28 días.

De los 89 niños inscritos, 67 (75%) presentaron retrasos considerables hasta el inicio del tratamiento (mediana 51 días; amplitud intercuartílica [IQR] 27–86). Sesenta y seis niños (74%) acudieron HCP privado antes de presentarse al sistema público y consultaron de uno a ocho profesionales. La mediana del retraso dependiente de los HCP fue 28 días (IQR 10–75). Se asociaron con un lapso prolongado hasta el inicio del tratamiento la vacunación con el bacille

Calmette-Guérin (OR ajustado [ORa] 10,96; $P=0,04$) y la pérdida del apetito (ORa 4,44; $P=0,04$).

La mayoría de los niños presentó un retraso hasta el inicio del tratamiento antituberculoso, atribuible al HCP privado. Es indispensable fortalecer la competencia de los HCP en la detección de los síntomas de TB y estimular las remisiones tempranas, a fin de ampliar la escala de aplicación del inicio más temprano del tratamiento en los niños con TB.

Keywords

pediatric tuberculosis; TB diagnosis; TB treatment barriers; patient delay; health care provider delay; health care system delay

INDIA ACCOUNTS for 27% of the global childhood tuberculosis (TB) burden.¹ The WHO Global TB database (2017) estimated approximately 231 000 Indian children were sick with TB.² The India TB report observed 1 444 175 TB notifications, of which 6% were pediatric cases.³ Dodd et al. estimated 60 000 childhood TB deaths in India.⁴ In high TB burden settings, underlying undiagnosed TB may cause 20% of deaths due to pneumonia in children aged under-five.⁵ Diagnosing pediatric TB is challenging due to non-specific symptoms, paucibacillary disease and lack of sensitive diagnostic tests. Delays in TB diagnosis and treatment initiation lead to poor outcomes in children.^{5–8}

Data describing delays and barriers to early TB treatment initiation in children are limited.^{9–13} A study by Beyers et al. reported 4 weeks of TB diagnostic delay.⁹ The recent Indian study documented 41 days of health system delay.¹⁰ Studies related to children with HIV-TB reported longer delays.^{11,12} A systematic review on barriers to delays in children and youth documented only four pediatric cohort studies.¹³ The above literature lacked in-depth analysis of pathway of care to treatment initiation in childhood TB.

Better understanding of the reasons for delays in early treatment initiation may inform national efforts to improve care of Indian children with TB. Therefore, we assessed the patient-centered and healthcare system barriers to early treatment initiation among children diagnosed and treated for TB in Pune, an urban setting of high TB incidence in India.

METHODOLOGY

Study setting

A cross-sectional study was conducted at Byramjee Jeejeebhoy Government Medical College (BJGMC) and Sassoon General Hospital (SGH), Pune, India, in 2016, among children initiated on anti-TB treatment from Pediatric and Pulmonary Medicine departments. Estimated TB incidence and prevalence in Pune are 185 and 220 per 100 000 population, respectively.¹⁴

India has a mixed healthcare system run by the government and the private sector. Patients can pay for TB diagnosis and care through the private sector. However, the Indian government's 'Revised National Tuberculosis Control Programme' (RNTCP) is implemented through public health facilities, which provide free diagnostic and treatment

services. In western India, urban Pune has 11 RNTCP TB units, including SGH. Each TB unit covers a population of 250 000. Patients can visit RNTCP centers directly or can be referred by the private sector. RNTCP guidelines for diagnosis and treatment of pediatric TB¹⁵ are followed at SGH, which screens 1000 children for TB per year, of which approximately 5–10% are initiated on anti-TB treatment and 7% have microbiologically confirmed disease.

Study population

During January–December 2016, study investigators identified children initiated on anti-TB treatment from the inpatient wards, intensive care units and outpatient departments, by daily review of admission books and case record files. Children aged 14 years started on anti-TB treatment were eligible for enrollment as study index cases. Children reported to have anti-TB treatment initiated outside the hospital with no medical records for TB diagnosis such as radiography and tuberculin skin test (TST) were excluded. Written informed consent was provided by the parents/caregivers of eligible cases, for participation in a structured interview. Furthermore, consent included extraction and analysis of data from the child's hospital case record and review of any health care provider (HCP) prescriptions available from the parents/caregivers.

Parent/caregiver interviews

The parents/caregivers of enrolled pediatric TB patients were interviewed by the principal investigator (CV), to document socio-demographic characteristics and TB symptoms with onset dates using a structured questionnaire adapted from the WHO Global TB report questionnaire.¹⁶ If the parent/caregiver did not accurately recall the symptom dates, significant family events were presented to improve the recall. Symptom duration was estimated in days.

Structured parental/caregiver interviews and prescriptions from the HCPs, when available, were used to document the number of HCP visits, contact dates with HCPs, TB contact history, diagnostic tests and treatment for TB by the HCPs. Data on patient delay, health literacy, TB knowledge and stigma, TB contact enquiry in the family and health service factors were also documented.

Hospital case record sheets of the index case

Hospital records were used to document the clinical details, date of the child's visit to SGH for treatment, diagnostic tests performed, TB diagnosis and anti-TB treatment initiation date.¹⁵ Classification of TB as pulmonary TB (PTB)—confirmed, unconfirmed, unlikely, extra-pulmonary TB (EPTB), multidrug resistant TB, presence of co-morbid conditions, HIV-TB co-infection and TB risk factors were also documented.^{15,17–19}

Study outcomes

The primary outcome was time-to-treatment initiation (TTI), defined as number of days between the first onset of any TB symptom and initiation of anti-TB treatment.¹⁵ Secondary outcomes included delayed TTI, separate estimates of patient delay, HCP delay and health care system (HCS) delay, and its associated factors (Figure 1).

RNTCP pediatric treatment guidelines

RNTCP pediatric guidelines advise investigation for active-TB among children with fever, cough, weight loss, poor weight gain, and/or a TB contact for >14 days.¹⁵ The guidelines recommend an initial 7 day course of antibiotics (without anti-TB activity) before TB investigation, according to the clinical features.¹⁵ RNTCP guidelines further recommend that anti-TB treatment be initiated within 7 days of microbiologically confirmed or clinically diagnosed TB.²⁰ Based on these guidelines, we defined TTI to be >28 days. HCP delay was defined as duration >14 days as physicians generally prescribe a 7 day course of antibiotics with a further 7 days required for investigation and treatment initiation (definitions are given in Table 1).^{15,20}

Statistical analysis

Statistical analysis were performed using STATA 13.1 for Windows. For descriptive statistics, median and interquartile range (IQR) were calculated. Analysis of categorical variables and treatment initiation delay was performed using Cox regression analysis. When assessing risk factors for delayed TTI, a cut-off point of >28 days was selected. All statistical tests were two-tailed. Statistical significance was assessed using 95% confidence intervals (CIs) and $P < 0.05$ was considered significant.

Ethical approval

The study protocol was approved by the Institutional Ethics Committees of BJMC, Pune, India, and Johns Hopkins University, Baltimore, MD, USA to conduct the study at SGH. Written informed consent was provided by the parents/caregivers of eligible children.

RESULTS

Patient's demographic characteristics

During the study period, 96 children were initiated on anti-TB treatment, of which 89/96 (93%) were enrolled. The parents of three children refused consent and four children initiated on anti-TB treatment outside SGH lacked medical record documentation of TB diagnosis. Interviews were conducted with mothers for 49/89 (55%) children, fathers for 31/89 (35%) and primary caregivers for 9/89 (10%) children. Household demographics and pediatric TB cases clinical characteristics are shown in Tables 2 and 3, respectively. The median age of the children was 7 years (range 0.31–13). TB with malnutrition were found in 41/89 (46%) children. Microbiological confirmed TB were reported in 8/89 (9%) children. Children with PTB and EPTB were 43/89 (48%) and 46/89 (52%), respectively. Of the PTB, 6/43 (14%) children were confirmed and 37/43 (86%) were unconfirmed TB. TB meningitis and HIV-TB co-infection were found in 20/89 (22%) and 16/89 (18%) children, respectively.

Time-to-treatment initiation and delays in the management pathway

The varying time-frames along the patient, HCP, diagnostic and treatment continuum are shown in Figure 2. The median TTI of 51 days (IQR 27–86) and HCP delay of 28 days (IQR 10–75) were prolonged compared to RNTCP guidelines. Sixty-seven of 89 (75%) children had delayed TTI. HCP delay was the major contributor to overall TTI delay. This was due to

a median diagnostic delay (DD) of 44 days (IQR 20–78). The median DD when the child directly visited the HCS was 35 days (IQR 12–67) compared to 50 days (IQR 23–87) when the child visited HCPs in the private sector before the HCS. The median delays attributed to the patient (PD, 3 days; IQR 1–14.5), HCS (5 days; IQR 2–10) and treatment (TD, 1 day; IQR 0–2) did not contribute to delays in TTI. The median health service delay (HSD) was 22 days (IQR 10–61.75). The median TTI for PTB and EPTB were 55 days (IQR 34–105) and 46 days (IQR 2–73), respectively. The median TTI for TB meningitis and HIV-TB co-infected children were 35 days (IQR 17–52) and 52 days (IQR 27–79), respectively.

Factors associated with delayed TTI and HCP delay

The characteristics of household and pediatric TB cases associated with delayed TTI are described in Tables 2 and 3. In univariate analysis, hospitalization in the previous year of current TB diagnosis, bacille Calmette-Guérin (BCG) vaccination, weight loss, fatigue, loss of appetite, abnormal chest radiography and abdominal ultrasonography showed significant association with delayed TTI. In multivariate analysis, BCG vaccination (aOR 10.96, 95%CI 1.36–88.28, $P=0.04$) and loss of appetite (aOR 4.44, 95%CI 1.85–23.26, $P=0.04$) were associated with delayed TTI (Table 4). BCG vaccination (aOR 28.99, 95%CI 2.47–340.12; $P=0.007$) and EPTB (aOR 4.95, 95%CI 1.1–22.26; $P=0.04$) were independently associated with HCP delay.

Perceived barriers by parents/caregivers to early TTI

The private sector as first point of healthcare was reported by 63/89 (71%) patients. Parents/caregivers reported consulting up to eight HCPs in the private sector, before seeking care at HCS. Forty-four of 89 parents (49%) trusted private sector HCPs. More than three HCPs were visited by 41/89 (46%) patients. Of the 67/89 (75%) children with documented delay, 46/67 (90%) parents/caregivers felt there was delay in TB diagnosis for their child ($P<0.001$) (Table 5). Perceived barriers by parents/caregivers to early TTI are described in Table 5. Knowledge on TB as a contagious disease was lacking in 44/89 (49%) and the fact that it was curable was lacking in 40/89 (45%) parents/caregivers.

DISCUSSION

This study observed significant delays in TB treatment initiation in Indian children. We assessed TTI as a marker of early detection of pediatric TB, as it assists in preventing poor outcomes²¹ and also plays a significant role in global programs for TB elimination. Few previous studies have focused on TTI in pediatric cohorts.^{9,10,13,22} We observed a median TTI of 51 days, which is similar to another study from India (median 52 days), where delay was evaluated as quartile groups.¹⁰ Other studies conducted in South Africa⁹ and the United Kingdom²² found shorter median diagnostic delay (range 36–37 days) compared to our study. These differences could be explained by the strategy of including private sector health visits as part of the TTI delay in our study. Of note, we found the TTI delay was mainly due to a median of 28 days between the initial HCP contact and visit to the HCS.

Our study observed that when Indian children have symptoms, their parents/caregivers quickly ensure they are seen by a clinician (PD median 3 days). When the children access

the public HCS, the time to TB diagnosis (median 5 days) and subsequent TB treatment initiation (median 1 day) is relatively short. The HCP delay may be due to multiple HCP visits by the patient in the private sector and late referrals to the public HCS. Our data suggest that TTI delay occurs mainly due to private sector HCP delay. This could be improved by strengthening the private sector HCP's knowledge to refer children with suspected TB symptoms promptly to the HCS for TB diagnosis and treatment initiation. Standardization of definitions for HCP delay in the private sector may help to bridge the gap as numerous studies applied different definitions.^{23–25}

Mistry et al. observed a 65 day delay in TTI among adults and children with TB.²⁶ The study found major contributor to delays were the diagnostic process (42 days), similar to our study. The low proportion of children aged under-five in our study was consistent with other studies.^{10,27,28} This could be due to missed cases in the community due to diagnostic difficulty.^{5,6} Half of the enrolled children were malnourished, where TB diagnosis is a challenge due to false-negative TST and atypical presentation.²⁹ In addition, TB symptoms may resemble diseases that are common in this setting, such as malaria, asthma and pneumonia. The symptomatology of our cohort was similar to studies from Vietnam and Nigeria.^{27,28} Our finding of loss of appetite associated with delays, emphasizes the need for reassessing validation of symptom-based approaches for diagnosing childhood TB in high-burden settings.³⁰ Pediatric TB guidelines use TB symptoms, diagnostic tests and TB contact as clues to diagnosis,¹⁵ due to poor bacteriological confirmation.⁵ Compared to published literature, our study found low bacteriologically confirmed TB cases.^{7,27,31} This may be attributed to high rate of EPTB in our study. HCP delays were associated with EPTB which reiterates the diagnostic challenges faced in these children. Our study found that delay in TTI was strongly associated with receipt of BCG vaccine. This may be due to clinicians assuming that BCG is fully protective against TB in high-burden settings.³² This possibility warrants further study. In spite of timely healthcare consultation, our study found parents/caregivers felt there was delay in TB diagnosis similar to the Peru study.¹² Compared to our study, previous pediatric studies lacked analysis of household, pediatric and HCP's characteristics and TTI.^{9–13,22,26}

A systematic review of children and youth in the sub-Saharan African region highlighted cost, health system infrastructure and health-seeking behaviors as barriers to TB treatment initiation.¹³ Our study found parental/primary caregivers preference for the private sector, similar to previous studies.^{25,33} TB notification by the HCPs in the private sector is mandated by the Indian government,³⁴ but recognition of TB symptoms in children by HCPs in the private sector, is lacking. Capacity building of HCPs in the private sector for recognition of TB symptoms in children would be improved by frequent mandatory training programs. Also, the development, monitoring and surveillance of an HCP training database by the RNTCP would help the program to achieve its goal. RNTCP should identify HCPs around a public health center for linkage and referral networks. Building strategic public private partnerships for early pediatric TB diagnosis would further help to bridge this gap.

Our study contributes to a better understanding of gaps in childhood TB treatment initiation in an urban Indian setting. A strength of our study lay in enrolling newly diagnosed children,

thereby minimizing recall bias. Furthermore, assessing the data from the medical records and parental/caregiver interviews improved the validity.

However, the use of a small cohort from a single RNTCP TB unit of a public sector provider with analysis of only 67 children with delayed TTI limits the conclusions we can draw. The lack of a complete understanding of the private HCP's prescriptions also adds to the limitations of our study. The small number of confirmed TB cases in our study may result in an overestimation of the TTI.

Barriers to early TB diagnosis in the private sector, delayed HCP's referrals from private to public sector and late access of public sector by the parents need to be addressed. Future studies are required to assess the impact of delayed TTI on TB outcomes, schooling and quality of life.

CONCLUSION AND RECOMMENDATIONS

We found delays in TTI for pediatric TB cases among 75% of the study cohort. Strengthening HCP awareness regarding the importance of the TB symptom screen and encouraging early referrals are crucial for rapid scaling up of early treatment initiation in childhood TB. To be successful in its campaign to eliminate TB in India, the RNTCP needs to work closely with the private sector to reduce the number of HCPs consulted before a diagnosis can be reached – with regular training and resources for a functioning pediatric TB referral system.

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Figure 1.

Conceptual framework: definitions of delay, showing the steps from patient stage to treatment initiation stage. HCP = health care provider

Figure 2.

Box plots of delay categories. PD = number of days between the first onset of any reported TB symptom (fever, cough, weight loss, loss of appetite, poor weight gain, and fatigue) and the first visit of the child to any HCP; HCP delay=number of days between first visit to a HCP and the first visit to the SGH RNTCP TB Unit; HCS delay=the number of days between the first visit to SGH RNTCP TB Unit, i.e., HCS and the TB diagnosis date; DD=the number of days between the onset of any TB symptom and the TB diagnosis date; TD=the number of days between the TB diagnosis date and the TB treatment initiation date; HSD=the number of days between the first visit to any HCP and the TB treatment initiation date; TTI=the number of days between the onset of any TB symptom and the TB treatment initiation date. PD=patient delay; TB=tuberculosis; HCP=health care provider; HCS=health care system; DD=diagnostic delay; TTI time-to-treatment initiation; SGH = Sassoon General Hospital; RNTCP = Revised National Tuberculosis Control Programme; TD = treatment delay; HSD=health service delay.

Table 1**Definitions**

Serial no.	Definitions	
1	Time-to-treatment initiation	The number of days between the onset of any TB symptom and the TB treatment initiation date
2	Delayed time-to-treatment initiation	Defined as >28 days
3	Patient delay	The number of days between the first onset of any reported TB symptom (fever, cough, weight loss, loss of appetite, poor weight gain and fatigue) and the first visit of the child to any HCP
4	HCP	Defined as any medical personnel consulted for the child's TB symptom(s). These included clinicians (allopathic or indigenous medicine) in the private and public healthcare sectors
5	HCP delay	The number of days between the first visit to a HCP and the first visit to the SGH RNTCPTB Unit. Defined as >14 days.
6	Health care system	For this study, this was defined as the SGH RNTCP TB Unit
7	Health care system delay	Defined as the number of days between the first visit to the health care system and the date of TB diagnosis
8	TB diagnosis date	The date documented in the medical record that TB was either microbiologically or clinically diagnosed
9	Diagnostic delay	The number of days between the onset of any TB symptom and the TB diagnosis date
10	Treatment delay	The number of days between the TB diagnosis date and the TB treatment initiation date
11	Health service delay	The number of days between the first visit to any HCP and the TB treatment initiation date

TB = tuberculosis; HCP = health care provider; SGH = Sassoon General Hospital; RNTCP = Revised National Tuberculosis Control Tuberculosis.

Table 2

Demographic characteristics of pediatric tuberculosis households

Characteristics	Overall (n = 89) n (%)	Delay TTI (>28 days) (n = 67) n (%)	No delay in TTI (<28 days) (n = 22) n (%)	P value
Age of parent/caregiver, years				>0.95
20–30	50 (57)	38 (58)	12 (57)	
31–39	28 (32)	21 (32)	7 (33)	
40	9 (10)	7 (11)	2 (10)	
Family type				0.88
Joint	28 (66)	20 (30)	8 (36)	
Nuclear	58 (32)	44 (67)	14 (64)	
Residence				0.79
Urban	66 (74)	49 (73)	17 (77)	
Rural	23 (26)	18 (27)	5 (23)	
Slum locality				0.46
Yes	34 (38)	24 (36)	10 (45)	
No	55 (62)	43 (54)	12 (55)	
Religion				>0.95
Hindu	71 (80)	53 (79)	18 (82)	
Islam	11 (12)	8 (12)	3 (14)	
Christian	2 (2)	2 (3)	0	
MKS score [†]				0.32
I, II, III	32 (36)	26 (39)	6 (27)	
IV, V	55 (62)	39 (58)	16 (73)	
Education of head of household				0.23
Illiterate	23 (26)	16 (24)	7 (32)	
School education	51 (58)	37 (56)	14 (64)	
College education	14 (16)	13 (20)	1 (5)	
Ventilation in the home				0.78
Yes	66 (75)	50 (76)	16 (73)	
No	22 (25)	16 (24)	6 (27)	
Smoker in family				>0.95

Characteristics	Overall (n = 89) n (%)	Delay TTI (>28 days) (n = 67) n (%)	No delay in TTI (<28 days) (n = 22) n (%)	P value
Yes	17 (19)	13 (19)	4 (18)	
No	72 (81)	54 (81)	18 (82)	
TB in family				0.81
Yes	45 (51)	33 (49)	12 (55)	
No	44 (49)	34 (51)	10 (45)	
TB treatment status of family member				0.56
Lost to follow-up	11 (25)	7 (21)	4 (36)	
Completed	17 (39)	14 (42)	3 (27)	
Ongoing	16 (36)	12 (36)	4 (36)	
HIV-infected parent(s)				0.09
Yes	14 (22)	13 (28)	1 (6)	
No	50 (78)	34 (72)	16 (94)	

[‡]MKS for socio-economic status in India. (MKS Class I = upper, Class II = upper middle, Class III=middle/lower middle, Class IV = lower/upper lower, Class V = lower),³⁵

TTI = time-to-treatment initiation; MKS = Modified Kuppusswami Score; TB = tuberculosis; HIV = human immunodeficiency virus.

Table 3

Demographic and clinical characteristics of pediatric tuberculosis patients

Characteristics	Overall (<i>n</i> = 89) <i>n</i> (%)	Delay TTI (>28 days) (<i>n</i> = 67) <i>n</i> (%)	No delay in TTI (<28 days) (<i>n</i> = 22) <i>n</i> (%)	<i>P</i> value
Age, years				0.91
<1	7 (8)	5 (7)	2 (9)	
1–5	21 (24)	15 (22)	6 (27)	
>5–10	44 (49)	33 (49)	11 (50)	
>10–14	16 (18)	13 (19)	3 (14)	
Sex				0.23
Male	42 (47)	29 (43)	13 (59)	
Female	47 (53)	38 (57)	9 (41)	
Nutritional status *				0.41
Normal	3 (4)	1 (2)	2 (11)	
MAM	23 (30)	19 (33)	4 (21)	
SAM	26 (34)	20 (34)	6 (32)	
–1 SD to median	9 (12)	6 (10)	3 (16)	
–2 to –1 SD	16 (21)	12 (21)	4 (21)	
BCG-vaccinated				0.09
Yes	78 (88)	61 (91)	17 (77)	
No	9 (10)	4 (6)	5 (23)	
Previous hospitalization in past 1 year of current TB diagnosis				0.02 [‡]
Yes	31 (35)	28 (42)	3 (14)	
No	57 (65)	38 (58)	19 (86)	
Long duration medical condition				0.1
Yes	16 (19)	15 (23)	1 (5)	
No	69 (81)	50 (77)	19 (95)	
Number of health-seeking encounters				0.46
2	37 (42)	26 (39)	11 (50)	
>2	52 (58)	41 (61)	11 (50)	
Cough >2 weeks				>0.95
Yes	43 (48)	32 (48)	11 (50)	

Characteristics	Overall (n = 89) n (%)	Delay TTI (>28 days) (n = 67) n (%)	No delay in TTI (<28 days) (n = 22) n (%)	P value
No	46 (52)	35 (52)	11 (50)	
Fever >2 weeks				0.28
Yes	65 (73)	51 (76)	14 (64)	
No	24 (27)	16 (24)	8 (36)	
Weight loss				0.05 [‡]
Yes	41 (46)	35 (52)	6 (27)	
No	48 (54)	32 (48)	16 (73)	
Loss of appetite				0.003 [‡]
Yes	44 (51)	39 (61)	5 (23)	
No	42 (49)	25 (39)	17 (77)	
HIV				0.06
Positive	16 (18)	15 (23)	1 (5)	
Negative	72 (82)	51 (77)	21 (95)	
Tuberculin skin test				0.47
Negative	38 (44)	30 (46)	8 (36)	
Positive	49 (56)	35 (54)	14 (64)	
Chest radiograph				0.04 [‡]
Normal	21 (24)	12 (18)	9 (41)	
Abnormal [‡]	66 (76)	53 (82)	13 (59)	
Ultrasonography abdomen				0.03 [‡]
Normal	42 (64)	28 (56)	14 (88)	
Abnormal	24 (36)	22 (44)	2 (12)	
Pulmonary TB				0.31
Confirmed	6 (14)	4 (11)	2 (25)	
Unconfirmed	37 (86)	31 (89)	6 (75)	
RNTCP treatment category				>0.95
Category I	84 (95)	63 (95)	21 (95)	
Category II	4 (5)	3 (5)	1 (5)	

* WHO classification of nutritional status.

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[‡]Statistically significant, $P < 0.05$.

[‡]Abnormal chest radiographs consistent with TB—adenopathy, opacity, effusion, cavity, miliary. Read by two treating physicians.

TTI = time-to-treatment initiation; MAM = moderate acute malnutrition; SAM = severe acute malnutrition; SD = standard deviation; BCG = bacille Calmette-Guérin; TB=tuberculosis; HIV = human immunodeficiency virus; RNTCP=Revised National Tuberculosis Control Programme.

Table 4

Characteristic of pediatric TB cases and HCPs associated with delay in TTI

Characteristics	n	Delay TTI (>28 days) n (%)	95% CI	OR (95% CI)	P value	Adjusted OR* (95% CI)	P value
Pediatric							
Age of child, years, median [IQR]	7 [3.25–10]	7.5 [4–10]	—	1.05 (0.92–1.20)	0.45	1.11 (0.85–1.45)	0.43
Sex							
Male	42	29 (69)	32–56	1	—	1	—
Female	47	38 (81)	44–68	1.89 (0.71–5.03)	0.2	2.12 (0.42–10.81)	0.36
HIV							
Negative	16	15 (94)	14–35	1	—		
Positive	72	51 (71)	65–86	0.16 (0.02–1.30)	0.09		
Previous hospitalization in past 1 year of current TB diagnosis							
No	57	38 (67)	45–69	1	—	1	—
Yes	31	28 (90)	31–55	4.67 (1.26–17.33)	0.02 [‡]	3.09 (0.66–14.42)	0.06
Long duration medical condition							
Yes	16	15 (94)	14–35	1	—		
No	69	50 (72)	65–86	0.18 (0.02–1.42)	0.1		
Number of health-seeking encounters							
2	37	26 (39)	28–51	1	—		
>2	52	41 (61)	49–72	1.58 (0.60–4.16)	0.36		
TB classification							
Pulmonary TB	43	35 (81)	40–64	1	—		
Extra-pulmonary TB [§]	46	32 (70)	36–60	0.5 (0.19–1.41)	0.2		
Type of PTB							
Confirmed	6	4 (11)	22–96	1	—		
Unconfirmed	37	31 (89)	68–94	2.58 (0.38–17.43)	0.33		
BCG vaccination							
No	9	4 (44)	2–16	1	—	1	—
Yes	78	61 (78)	84–98	4.49 (1.08–18.56)	0.04 [‡]	10.96 (1.36–88.28)	0.04 [‡]
Cough >2 weeks							

Characteristics	n	Delay TTI (>28 days) n (%)	95% CI	OR (95% CI)	P value	Adjusted OR* (95% CI)	P value
Yes	43	32 (74)	36–60	1	—	—	—
No	46	35 (76)	40–64	1.09 (0.42–2.87)	0.86	—	—
Fever >2 weeks							
Yes	65	51 (78)	64–85	1	—	—	—
No	24	16 (67)	15–36	0.55 (0.19–1.54)	0.26	—	—
Weight loss							
No	48	32 (67)	36–60	1	—	1	—
Yes	41	35 (85)	40–64	2.92 (1.02–8.37)	0.04 [‡]	1.38 (0.34–5.65)	0.2
Fatigue							
No	58	39 (67)	47–71	1	—	1	—
Yes	29	26 (90)	29–50	4.22 (1.13–15.72)	0.03 [‡]	1.32 (0.19–9.03)	0.32
Loss of appetite							
No	42	25 (59)	28–52	1	—	1	—
Yes	44	39 (89)	48–72	5.30 (1.74–16.20)	0.003 [‡]	4.44 (1.85–23.26)	0.04 [‡]
Tuberculin skin test							
Negative	38	30 (79)	34–58	1	—	—	—
Positive	49	35 (71)	41–66	0.67 (0.25–1.81)	0.42	—	—
Chest radiograph							
Normal	21	12 (57)	11–30	1	—	1	—
Abnormal [¶]	66	53 (80)	70–89	3.06 (1.06–8.79)	0.04 [‡]	0.86 (0.13–5.84)	0.87
Abdominal ultrasonography							
Normal	42	28 (67)	42–69	1	—	1	—
Abnormal	24	22 (92)	31–58	5.5 (1.13–26.79)	0.03 [‡]	4.54 (0.56–37.08)	0.16
Health care providers Education of HCPI							
MD	15	14 (93)	23–54	1	—	—	—
MBBS	21	16 (76)	27–59	0.23 (0.02–2.2)	0.2	—	—
BAMS	5	4 (80)	4–26	0.29 (0.01–5.66)	0.41	—	—
Diploma	5	4 (80)	4–26	0.29 (0.01–5.66)	0.41	—	—
Education of HCP2							
MD	22	15 (68)	30–65	1	—	—	—

Characteristics	n	Delay TTI (>28 days) n (%)	95% CI	OR (95% CI)	Adjusted OR* (95% CI)	P value
MBBS	12	9 (75)	15–47	1.4 (0.29–6.83)		0.68
BAMS	4	4 (100)	5–30	—		—
Diploma	4	4 (100)	5–30	—		—
Inquiry about TB by HCPI						
Yes	7	6 (86)	5–24	1		—
No	58	45 (78)	76–95	0.58 (0.06–5.23)		0.62
Visit to health system						
Private	63	47 (75)	58–80	1		—
Public	26	20 (77)	20–42	1.13 (0.39–3.32)		0.82

* Adjusted for significant variables of univariate analysis.

‡ Statistically significant, $P < 0.05$.

§ Tuberculous meningitis, neurotuberculoma, abdominal tuberculosis, TB lymphadenitis, pleural effusion, pericardial effusion, skin TB.

¶ Abnormal chest radiographs consistent with tuberculosis: adenopathy, opacity, effusion, cavity, miliary, Read by two treating physicians.

TB=tuberculosis; HCP=health care provider; TTI=time-to-treatment initiation; OR=odds ratio; CI=confidence intervals; IQR=interquartile range; HIV=human immunodeficiency virus; PTB=pulmonary TB; BCG=bacille Calmette-Guérin; MD=Doctor in Medicine; MBBS=Bachelor of Medicine Bachelor of Surgery; BAMS=Bachelor of Ayurveda Medicine and Surgery.

Table 5

Perceived barriers by parent/caregiver for delay in early TTI

Barriers to early treatment initiation	Total (n = 89) n/N (%)	Delay TTI (>28 days) (n = 67) n/N (%)	No delay in TTI (<28 days) (n = 22) n/N (%)	P value
Delays as perceived by the parent/caregiver (n = 89)				<0.001 [*]
Yes	51/89 (57)	46/51 (90)	5/51 (10)	
No	34/89 (38)	17/34 (50)	17/34 (50)	
Unsure	4/89 (4)	4/4 (100)	0	
Perceived barriers by parents/caregivers [†]	(n = 51)	(n = 46)	(n = 5)	
Patient-related delays				
Unaware symptoms may be related to TB	32/51 (62)	30/32 (94)	2/32 (6)	0.06
No TB in family	9/51 (17)	8/9 (89)	1/9 (11)	>0.95
Economic constraints	3/51 (6)	1/3 (33)	2/3 (67)	0.05
Fear of what would be found on diagnosis	4/51 (8)	3/4 (75)	1/4 (25)	0.48
Hoped their symptoms would go away on their own (denial and concealment)	7/51 (14)	7/7 (100)	0	0.58
Fear of social isolation	2/51 (4)	2/2 (100)	0	>0.95
Health care provider-related delays: private sector (as perceived by parents/caregivers)				
Poor quality of health services: lack of inquiry of TB symptom screen, investigations and TB contacts	21/51 (41)	20/21 (95)	1/21 (5)	0.14
Inadequate staff attitude	6/51 (12)	6/6 (100)	0	0.58

^{*} Statistically significant, $P < 0.05$.[†] Reasons are listed based on the frequency and the multiple answers reported by the parents TTI = time-to-treatment initiation; TB = tuberculosis.