Brief Research Article

Time Elapsed from Onset of Symptoms to Antituberculosis Treatment in Children with Central Nervous System Tuberculosis in a Tertiary Hospital in South India: A Mixed-Methods Pilot Study

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Summary

A pilot study with a mixed-methods design was conducted to estimate the time for tuberculosis (TB) treatment initiation and associated factors among children with central nervous system-TB (CNS-TB). A total of 38 children were enrolled for the quantitative component, and 20 in-depth interviews were conducted. The median duration (interquartile range) from onset of symptoms to treatment initiation was 23 (11, 55) days. About 44% and 31% of the children presented with Stage II and Stage III of CNS-TB, respectively. The major reasons for delay were symptoms not taken seriously (50%) and too many referrals (21%). About 89% of the families went into catastrophic health expenditure due to the disease. The treatment delay may be due to both patient delay and health system delay. Tailoring approaches to target the pediatric population could further improve early detection and treatment initiation of CNS-TB.

Key words: Central nervous system, health care-seeking behavior, pediatrics, time-to-treatment, tuberculosis

Tuberculosis (TB) of the central nervous system (CNS) is the most severe extrapulmonary form of TB, associated with high morbidity and mortality rates, and is a medical emergency.[1,2] Although CNS-TB constitutes only a small proportion of the total TB cases, the amount of suffering in terms of morbidity and mortality, especially in young children, is very high. Early diagnosis and management of CNS-TB is important, as delay in diagnosis leads to poor outcomes such as death, neurological sequelae, and neurocognitive disorders.[3] The relative rarity, protean nature of the symptoms, suboptimal performance of diagnostic tests, and paucibacillary nature of the disease make the diagnosis of CNS-TB a formidable challenge.[4] In addition to this, CNS-TB occurs largely in resource-starved regions of the world, leading to additional challenges in implementing practical and usable methods to diagnose and treat the disease.[2]

This was a mixed-methods pilot study conducted for 1½ years among children up to 12 years of age, diagnosed with CNS-TB, and initiated on antitubercular treatment (ATT). They were registered for care in a tertiary referral center for pediatrics. CNS-TB was defined as "any child diagnosed with TB of the CNS by the treating pediatrician. Only those children whose parents/caregivers consented for the survey and those children above 7 years who gave assent were enrolled.

A semi-structured pretested questionnaire developed for the study was used to collect information regarding symptoms,

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first point of care, details regarding health facilities visited for the symptoms, accessibility to the health-care facilities, time duration for each process, previous ATT, and contact history of TB. The time interval from onset of symptoms (by recall) to initiation of ATT was defined as "time elapsed" to ATT. Information was also collected from the records available (prescriptions, laboratory results, imaging reports, etc.) with the parents/caregivers.

Out-of-pocket expenditure incurred for diagnosis, treatment, and income loss due to work absenteeism of the caregivers due to the child's sickness was obtained by the parent's/caregiver's recall. "Catostophic health expenditure" was defined when the proportion of the total monthly income spent on TB disease was more than 20% of the total monthly income.

In-depth interviews (IDIs) were conducted with the primary caregivers; primarily parents of the children admitted for care in the tertiary care were interviewed. A semi-structured interview guide was used. IDIs were conducted by trained social workers. Interviews were conducted in the local language. Each interview lasted for 20–30 min. All the IDIs conducted were audio tapped for transcription purpose. Interviews were transcribed verbatim by the researcher from the digital version.

Patient characteristics were summarized with mean and standard deviations (SDs) or median with interquartile range (IQR) for continuous variables and counts/percentages for categorical variables. Proportion of the total monthly household income spent for the disease and catastrophic health expenditure was calculated. A thematic analysis of interviews using an inductive approach was done. Respondent interviews as transcripts were coded using NVivo software version 9 (QSR International Pvt. LTD, Melbourne, Australia). These initial codes were then refined and organized at a broader conceptual level into themes by grouping them together. We considered the flexibility of including new themes emerging from the data (inductive approach).

We approached 43 children for the study. Parents/caregivers of 38 children were willing to participate and those 38 children were screened, and all of them who fulfilled the study criteria were enrolled. The sociodemographic characteristics of the study participants are given in Table 1. Nearly 44% and 31% of the children presented with Stage II and Stage III of CNS-TB disease [Table 1].

Table 1: Demographic and clinical characteristics of the study participants

	Value*, *n* (%)
Age (years), median (IQR)	5 (2.9-10.2)
Gender	
Male	15 (39.5)
Female	23 (60.5)
Place of residence	
Rural	22 (57.8)
Urban	16 (42.1)
Primary caregiver	
Mother	35 (92.1)
Father	1 (2.6)
Grandparent	2 (5.2)
Educational status of primary caregiver	
< Illiterate and up to primary	10 (26.3)
Secondary and higher secondary	21 (55.2)
Degree and above	7 (18.4)
BCG vaccinated	38 (100)
Contact with TB patients	14 (36.8)
Symptoms	
Fever	20 (52.6)
Severe headache	17 (44.7)
Seizures	21 (55.3)
Muscle weakness	13 (34.2)
Lethargy	22 (57.9)
Poor weight gain or weight loss	21 (55.3)
Vomiting	21 (55.3)
Altered consciousness	11 (28.9)
Blurring of vision	10 (26.3)
Clinical signs	
Presence of meningeal signs	13 (36.1)
Cranial nerve abnormality	6 (17.6)
Weakness	9 (25.7)
Sensory nerve abnormality	5 (14.3)
CNS-TB staging#	
Stage-I	9 (23.6)
Stage-II	17 (44.7)
Stage-III	12 (31.5)
GCS, median (IQR)	11.5 (10-14)

**n* (%) for qualitative variables and median (IQR) for continuous variables, #CNS-TB staging was classified according to the modified British Medical Research Council grading system as Stage I (GCS of 15 with no focal neurologic signs), Stage II (GCS 11-14 or 15 with focal neurologic signs), or stage III (GCS ≤10) (20. TB: Tuberculosis, IQR: Interquartile range, CNS: Central nervous system, GCS: Glasgow Coma Scale

TB meningitis was the most common form of CNS-TB disease diagnosed (58%, *n* = 22). The median duration from onset of symptoms to ATT initiation was 23 (IQR = [11, 55]) days, whereas the mean was 44 (SD = 64.1) days. The mean number of visits to hospital before being diagnosed with CNS-TB was 6.16 (SD = 4.33).

The health-seeking behavior is described in Table 2. The median (IQR) household income per month was ₹13,500 (₹9125, ₹18,500). The median expenditure (IQR) incurred from onset of symptoms till TB treatment initiation was ₹25,853 (₹10,925, ₹34,837); nearly 89% of the participants had a catastrophic health expenditure.

We found that majority of the participants reported that habitually their first point of contact for any general health issue in their families was private facilities. The private facility being nearby, speedy recovery, easy accessibility, flexible timing, and less time spent were reasons stated for accessing the private health facility. A few participants, who stated approaching the government health facility for care, mentioned that cost was the reason for approaching the government health facility.

Table 2: Health-seeking behavior of the participants

First point-of-care treatment for symptoms	*n* (%)
Public	
Medical college	3 (7.8)
District hospital	4 (10.5)
Primary health center	10 (26.3)
Private	
Pharmacy, drug, and grocery store	2 (5.2)
Private hospital/clinic	19 (50)
Reason for visiting the health facility	
Family doctor/known doctor	8 (21)
Nearby facility	22 (57.8)
Availability of specialist	3 (7.8)
Treatment free of cost	3 (7.8)
Others	2 (5.2)
Place of diagnosis of CNS TB	
Medical college	35 (92.1)
District hospital	2 (5.2)
Private hospital/clinic	1 (2.63)
Patient delay as perceived by caregiver	
No delay	11 (28.9)
Symptoms not serious	19 (50)
Lack of money	2 (5.2)
Taken home remedies	6 (15.7)
Health system delay as perceived by caregiver	
No delay	12 (31.5)
Lack of proper diagnostic facility	4 (10.5)
Lack of expertise	4 (10.5)
Too many referrals	8 (21.05)
Distance to nearby health facility (km)	
<5	19 (50)
5-10	6 (15.78)
10-50	11 (28.9)
>50	2 (5.2)
Time taken to travel to nearby health facility	
<30 min	29 (76.3)
30-60 min	6 (15.7)
1-3 h	3 (7.8)

TB: Tuberculosis, CNS TB: Central nervous system TB

It was found that more than half of the participant's first point of contact after the onset of symptoms was private health facility, and the rest had approached government facility soon after the symptoms. It was noted that a couple of participants reported approaching multiple private facilities before getting diagnosed. It was interesting to find that majority of the participants reported that TB diagnosis was done at a government facility though the first point of contact has been a private facility. Most participants reported that they had heard of TB as a disease and many mentioned that prolonged cough to be a symptom for TB. A very few participants knew that TB was curable. Many particpants were not aware that there was TB treatment available free of cost in the governemnt health facilties. Many were not aware about the duration of Tb treament. Some participants mentioned about the history of TB in the family.

Many participants said that their children had one or more episodes of seizures as the symptoms which prompted them to seek care. Nearly all the participants mentioned that they did not think these to be TB symptoms and suspect for TB.

The median duration (IQR) from onset of symptoms to ATT initiation was 23 (11, 55) days in children with CNS-TB. Among 25% of the children, the time elapsed between symptom onset and ATT initiation was more than 55 days. This could be due to the diagnostic challenge associated with CNS-TB and lack of experience, expertise, and diagnostic facility, especially at peripheral levels which are known factors to be associated with diagnostic delays.[5]

The treatment delay may be due to patient delay and health system delay. Identifying the source of delay is a crucial factor for ATT initiation. About 55.2% of them felt that there was a delay from their side as they did not take the symptoms seriously. Although these findings are not specific to CNS infection, the health-seeking behavior in general shows the responsiveness to discomfort or symptoms rather than to specific disease. Furthermore, 15% of the caregivers stated that they resorted to home remedies for their child symptoms, and they perceived that it would have led to delay in treatment initiation. This is supported by evidence from various studies done in India and other developing countries which conclude that there is an increased likelihood of caregivers resorting to home remedies for treating childhood illness.[6,7] All these reasons are supported from the findings that in this study, 44.7% and 31.5% of the children presented with Stage II and Stage III of the disease, respectively.

More than half of the children in the study had consulted a private clinic on their first visit. A systematic review by Storla *et al*. has stated that seeking private care for the first instance was a significant reason for delay in treatment.[8] The reason for this may be due to lack of expertise in private clinics in the peripheral settings and costs involved with various investigations and treatment in the private settings. This is also supported by the finding that the median total out-of-pocket expenditure incurred from the onset of symptoms to treatment initiation is much higher than the household income.

This is the first study in India to our knowledge which has studied about the time elapsed before treatment imitation for children with CNS-TB with both qualitative and quantitative components. Our study has various limitations. It is a self-reported data; hence, the accuracy and completeness of the data are subject to recall bias. This study was from a single center, hence could not be extrapolated to the total CNS-TB cases in children in the country.

The study has identified that there is a significant amount of time elapsed from onset of symptoms to ATT initiation for CNS-TB in children and also has helped in understanding the health-seeking behavior and economic impact of the caregivers. In the TB cascade of care, private sector plays a significant role; strengthening the public–private mix programs will be

instrumental for prompt diagnosis and timely treatment initiation. Future studies are needed with a larger sample size to know more about factors associated with delays, and also studies have to be planned to know the diagnostic and treatment pathway in details to know exactly where the intervention could be targeted.

Authors' contribution

PG, BD PR: Conceptualization, Methodology, Original draft preparation; PG, BD, PR EC, SB, CP, MM, DA: Data acquisition, Data analysis, Interpretation, writing review, and editing.

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Conflicts of interest

There are no conflicts of interest.

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