Decentralised care for the management of child contacts of multidrug-resistant tuberculosis

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Setting: Cape Town, South Africa.

Objective: To determine the number of multidrug-resistant tuberculosis (MDR-TB) child contacts routinely identified by health services, and whether a model of decentralised care improves access.

Methods: All MDR-TB source cases registered in Cape Town from April 2010 to March 2011 were included. All child contacts assessed at hospital and outreach clinics were recorded from May 2010 to June 2011. Electronic probabilistic matching was used to match source cases with potential child contacts; the number of children accessing decentralised (Khayelitsha) and hospital-based care was compared.

Results: Of 1221 MDR-TB source cases identified, 189 (15.5%) were registered in Khayelitsha; 31 (16.4%) had at least one child contact assessed. In contrast, 95 (9.2%) of the 1032 source cases diagnosed in the other Cape Town subdistricts (hospital-based care) had at least one child contact assessed ($P = 0.003$). Children in Khayelitsha were seen at a median of 71 days (interquartile range [IQR] 37–121 days) after source case diagnosis compared to 90 days (IQR 56–132 days) in other subdistricts ($P = 0.15$).

Conclusion: Although decentralised care led to an increased number of child contacts being evaluated, both models led to the assessment of a small number of potential child MDR-TB contacts, with considerable delay in assessment.

According to World Health Organization (WHO) estimates, there were 650 000 prevalent cases of multidrug-resistant tuberculosis (MDR-TB, defined as TB resistant to rifampicin [RMP] and isoniazid [INH]) worldwide in 2010.[1,2] Patients with MDR-TB live and interact with numerous other people, termed MDR-TB contacts. Although the majority of individuals infected with *Mycobacterium tuberculosis* will never develop TB disease,[3] young children aged <5 years[4,5] and individuals with impaired immunity (e.g., human immunodeficiency virus [HIV] infected) are at high risk of developing disease following exposure and infection.[6,7]

A key TB control strategy is to identify the contacts of newly diagnosed TB cases and screen them for TB disease, enabling early treatment. If contacts are well but are at high risk of development of disease, they can be considered for preventive treatment.[8] INH given daily for 6 months reduces the risk of progression from infection to disease in child contacts of drug-susceptible TB.[9,10] Although evidence regarding preventive treatment regimens for child contacts of MDR-TB patients is limited, exposed children should be identified and screened for MDR-TB disease and followed up for at least 1 year.[11]

The WHO and the majority of national TB programmes advise that children aged <5 years and HIV-infected children in contact with an infectious case of MDR-TB should be identified and seen by a specialist experienced in the management of paediatric MDR-TB.[2,12,13] In many settings with a high burden of MDR-TB, contact tracing is poorly implemented, while specialists with appropriate experience are few and are usually based in academic referral centres. This results in a long travel distance for patients, which may be expensive and time-consuming. Such obstacles may result in a failure to access appropriate health services.

Khayelitsha, a peri-urban township and health subdistrict, is located on the outskirts of the City of Cape Town, South Africa. Médecins Sans Frontières has been working in partnership with the local health authorities since 2007 to pilot a decentralised model of care for patients with MDR-TB. This patient-centred, community-based approach is aimed at increasing MDR-TB case detection, improving treatment outcomes and reducing MDR-TB transmission.[14]

One component of the programme includes active follow-up of child contacts. In December 2008, a specialist paediatric monthly outreach service was established to manage child contacts of MDR-TB patients. In the remaining seven subdistricts of the City of Cape Town, the traditional, hospital-based system of care was continued, including the identification of child contacts by local services and routine referral to the hospital-based specialist service.

The aim of this study was to determine the number of MDR-TB child contacts identified and whether decentralised care offers improved access compared to hospital-based care. We also aimed to determine whether decentralised care was associated with more rapid identification of child contacts.

STUDY POPULATION AND METHODS

Setting and population

The study was based in the City of Cape Town health district, one of six health districts in the Western Cape Province of South Africa, with a population of 3.4 million. The district comprises eight subdistricts, including Khayelitsha, which has a population of approximately 500 000.[15] Khayelitsha is a poor subdistrict with a predominantly Xhosa-speaking, ethnically Black

African population.[16] In 2009, Western Cape Province had a TB notification rate of 976 per 100 000 population;[17] antenatal HIV seroprevalence was 16.9%.[18] In Khayelitsha, the TB notification rate was nearly 1600/ 100 000 in 2008, with an antenatal HIV seroprevalence of 31.1%.[19]

Identification and treatment of child contacts

According to provincial and national guidelines, following the diagnosis of MDR-TB in an adult, a home visit should be conducted to educate the patient and his/her family, give advice about infection control and identify symptomatic contacts. A professional nurse oversees this process in each of the eight subdistricts. Children aged <5 years and HIV-infected children are referred to their local clinic for assessment prior to referral to the Tygerberg Children's Hospital (TCH), which serves as the main provincial paediatric MDR-TB referral centre. In the Khayelitsha subdistrict, these children are referred to the specialist outreach clinic conducted monthly in Khayelitsha. Children from outside the City of Cape Town health district are also sometimes referred to the MDR-TB clinic at TCH.

Case identification, data collection and eligibility: source cases

Adult 'source cases' (aged >18 years) treated for MDR-TB in the City of Cape Town Health District from 1 April 2010 to 31 March 2011 were identified from routine TB register data. Source cases were included if they had been started on MDR-TB treatment during the stated time period for sputum smear- and/or culture-positive pulmonary TB, and had been registered at a TB clinic in one of the eight subdistricts. Adults were excluded if they did not have TB resistant to both INH and RMP, or were registered in hospital or prison (i.e., unclear subdistrict of origin).

Case identification, data collection and eligibility: child contacts

From 1 May 2010 to 30 June 2011, all children evaluated at the TCH or at the outreach MDR-TB clinic were prospectively recorded. Children were included in the study if they were HIV-infected or aged <5 years and had significant contact with a source case with sputum smear- and/or culture-positive pulmonary MDR-TB. Significant contact was defined as living with or having regular daily interaction with the source case over the previous 6 months.

Data analysis

After removing duplicates from the MDR-TB register, probabilistic linking was done using Registry Plus™ Link Plus software (Centers for Disease Control and Prevention, Atlanta, GA, USA) to match adult cases from the register to the names of source cases provided by the parents/care givers of children attending the MDR-TB clinics.[20,21] An inclusive algorithm was used allowing the software to use four demographic variables: name, surname, sex and age. Names and surnames were converted using the New York State Identification and Intelligence System, a phonetic coding system that allows for inconsistencies and variations in spelling. The total number of source cases, the number of children assessed and the number of linked source cases were determined. Time to assessment was defined as the time from sputum production in the source case for the sample that diagnosed MDR-TB, to the child being evaluated at the MDR-TB clinic.

Statistical analysis was performed using STATA version 11 (Stata Corp, College Station, TX, USA). Missing data were excluded from the analysis. The association between categorical variables was assessed using the χ^2 test or Fisher's exact test, where appropriate.

The Mann-Whitney test was used to compare quantitative data that were not normally distributed, and data summarised using the median and interquartile range (IQR). The t-test was used to compare normally distributed quantitative data.

Ethical considerations

The study was approved by the Stellenbosch University Ethics Committee for Health Research and the Ethics Committee of the London School of Hygiene & Tropical Medicine. Waiver of informed consent was granted to access routine register data (source cases). Informed consent was obtained from parents/care givers to collect data on children. Names and identifier details of the source cases and children were used only for matching, and were deleted from the final data set. Access to unique identifiers was restricted to investigators.

RESULTS

Of the 1265 adult MDR-TB source cases registered during the study period, 1221 were included; the subdistrict could not be determined for the remaining 41 cases; of these, 189 (15.5% of total) patients were registered in Khayelitsha; 670 (55.0%) were male. The median age at diagnosis was 35 years (IQR 27–44; Table 1). The clinical characteristics of the source cases from Khayelitsha vs. other subdistricts were similar, except for the prevalence of HIV infection, which was higher in the Khayelitsha group (70.5% vs. 49.8%, $P < 0.001$).

At TCH and at the outreach MDR-TB clinic, 265 children were evaluated during the assessment period; 11 were excluded as not meeting the criteria for significant contact. Of the 254 included, 146 (57.5%) were linked to 126 source cases; the median number of contacts per source case was 1 (range 1–4). Of the 108 unmatched children, 26 (24.1%) were linked to a source case resident outside the City of Cape Town. Of the linked children, a total of 35 children (linked to 31 source cases) were from Khayelitsha, and 111 children (linked to 95 source cases) were from the remaining seven subdistricts. Eighty (54.8%) children were male; the median age was 32 months (IQR 13–46 months; Table 2). As expected, children from Khayelitsha were more likely to be Xhosa than those from the other subdistricts (100% vs. 36%, $P < 0.001$). Children from Khayelitsha were better nourished (mean weight-for-age Z-score 0.07 vs. −0.63, $P = 0.012$). Other characteristics were similar between the two groups.

Of the source cases in Khayelitsha, 16.4% (31/189) led to the assessment of at least one child contact, compared to 9.2% (95/1032)

TABLE 1 Characteristics of adult multidrug-resistant TB source cases identified by health district, 1 May 2010–30 June 2011 ($n = 1221$)

	Khayelitsha ($n = 189$) n (%)	Other subdistricts ($n = 1032$) n (%)	Total ($n = 1221$) n (%)
Age, years, median [IQR], ($n = 1211$)	34 [27–40]	36 [28–44]	35 [27–44]
Male sex ($n = 1219$)	93 (49.5)	577 (56.0)	670 (55.0)
HIV-positive ($n = 1070$)*	117 (70.5)	450 (49.8)	567 (53.0)
Positive sputum smear ($n = 1011$)	73 (42.4)	397 (47.3)	470 (46.5)
XDR-TB ($n = 1221$)	16 (8.5)	86 (8.3)	102 (8.4)

*Difference in HIV prevalence between Khayelitsha and the other seven subdistricts, $P < 0.001$.
TB = tuberculosis; IQR = interquartile range; HIV = human immunodeficiency virus; XDR-TB = extensively drug-resistant TB.

TABLE 2 Characteristics of child multidrug-resistant TB contacts identified by health district and linked to a source case, 1 May 2010–30 June 2011 (*n* = 146)

	Khayelitsha (*n* = 35) *n* (%)	Other subdistricts (*n* = 111) *n* (%)	Total (*n* = 146) *n* (%)
Male sex	16 (45.7)	64 (57.7)	80 (54.8)
Age, months, median [IQR]	31 [12–44]	32 [13–47]	32 [13–46]
Ethnicity (*n* = 145)*			
Xhosa	35 (100)	39 (35.5)	74 (51.0)
Coloured	0	70 (63.6)	70 (48.3)
White	0	1 (0.9)	1 (0.7)
HIV-positive (*n* = 140)	2/34 (5.9)	5/106 (4.7)	7 (5.0)
Previous TB treatment reported by family			
Yes	1 (2.9)	11 (9.9)	12 (8.2)
Weight-for-age *Z*-score (*n* = 142)†			
Mean ± SD	0.07 ± 1.49	−0.63 ± 1.36	−0.46 ± 1.42
Relationship of source case to child			
Mother	14 (40.0)	36 (32.4)	50 (34.3)
Father	2 (5.7)	18 (16.2)	20 (13.7)
Grandparent	5 (14.3)	15 (13.5)	20 (13.7)
Aunt/uncle	7 (20.0)	30 (27.0)	37 (25.3)
Other	7 (20.0)	12 (10.8)	19 (13.0)
Was the source case the primary care giver?			
Yes	10 (28.6)	30 (27.0)	40 (27.4)
Contact between child and source case			
Sleeps in different house	2 (5.7)	16 (14.4)	18 (12.3)
Sleeps in same house	19 (54.2)	43 (38.7)	62 (42.5)
Sleeps in same room	7 (20.0)	19 (17.1)	26 (17.8)
Sleeps in same bed	7 (20.0)	33 (29.7)	40 (27.4)

*Difference between Khayelitsha and the other seven subdistricts, *P* < 0.001.
†Difference between Khayelitsha and the other seven subdistricts, *P* = 0.012.
TB = tuberculosis; IQR = interquartile range; HIV = human immunodeficiency virus; SD = standard deviation.

for source cases diagnosed in other subdistricts (*P* = 0.003). Children in Khayelitsha were seen at a median of 71 days (IQR 37–121) from the date of MDR-TB sputum production of the source case compared to 90 days (IQR 56–132) in the other subdistricts (*P* = 0.15).

DISCUSSION

In a previous MDR-TB contact study in Cape Town, a mean of 1.7 child contacts aged ≤5 years were identified for each source case with sputum-positive TB.[22] Recent TB household studies from Cape Town also indicate a mean of 1.7 children aged <5 years identified per drug-susceptible TB source case (personal communication, A Hesseling). Based on our findings, it is therefore likely that only a small proportion of possible MDR-TB child contacts were identified, referred and evaluated by a specialist as recommended in national and international guidelines. There appears to be some advantage provided by decentralised care, in terms of number of children identified per source case and time for child to be seen, but the number of children evaluated remains low for both models. Furthermore, despite a trend towards children being seen earlier in Khayelitsha, the time to assessment is suboptimal in the light of the high risk of disease progression in young children.

The reason why so few children are evaluated may be explained by a number of factors. First, the definition of 'child contact' used by health care workers may not be sufficiently inclusive. If a definition is used where only children living in the same house as the source case are included, fewer contacts will be revealed than if a definition of any significant contact is used, as in our study.[23] It is therefore possible that children are not identified by local health care teams. Furthermore, if children are identified locally, then personal, logistic or financial barriers to accessing clinic appointments may occur. In this operational study, we used the source case as the denominator and children evaluated in the specialist clinic as the numerator; we are therefore unable to determine where the attrition occurred. However, studies examining children exposed to drug-susceptible TB have demonstrated that this drop off occurs at every step in the care pathway.[24,25]

Delay in assessing child contacts has a number of components. These include the time to diagnosis in the source case, time to identification of child contacts, time for the child to be seen locally and the time for the child to be seen at the specialist clinic. As we captured the date of sputum production in the source case and the date the child was seen at the specialist clinic, we were unable to determine the respective durations of each of these components. However, the delay associated with starting anti-tuberculosis treatment has been well explored, and is associated with both patient and health system delays.[26–28] The delay from sputum sampling to the initiation of MDR-TB treatment initiation fell from 72 days in 2005 to 33 days in 2010 in Khayelitsha.[14] In a sample of 10 health facilities in the City of Cape Town, excluding Khayelitsha, the mean delay was 83 days in 2005–2008 and 53 days in 2008–2011 (personal communication, P Naidoo). The impact of health system strengthening and the availability of more rapid diagnostic tests has improved delay (line-probe assay was introduced at the end of 2008); however, there is a suggestion that some of the health system delay could be improved by decentralised care.

A limitation to this study is the number of children seen in clinics for whom we could not match a source case from the MDR-TB register. Nearly a quarter were from outside the region, but for the rest the reason is unclear. There may have been a matching problem despite our inclusive matching approach; this would likely apply equally to the two models of care compared in our study. It may have been that children were seen during the inclusion period, but that the source case was registered outside the dates searched. It may also have been that some of the source cases were primary defaulters and were diagnosed but never started treatment. Finally, the registration of source cases could have been incomplete. Although this is a limitation, we set out to document the proportion of registered MDR-TB source cases for whom child contacts were identified and assessed in clinic as per local guidelines. These limitations do not affect the conclusion that child contacts are seen in only a small proportion.

The identification and screening of child MDR-TB contacts is suboptimal in this high-burden setting. Decentralised models of care may increase the number of children identified and evaluated. Although further interventions are clearly needed to improve the identification and screening of child contacts of MDR-TB patients, it would not be possible for all identified children to be seen by the small number of experts, if improved identification were to occur. Training and education of health care workers at a primary health care level must take place for a phased process of decentralised care to be implemented. Lessons can be learnt from paediatric HIV programmes where children were initially seen by specialists in hospitals. This was followed by specialist outreach, then joint care between clinic and specialist, before full decentralisation to

clinic care for the majority of children. Reasons for failure to attend appointments and causes of delay in the evaluation of child contacts require investigation. Once TB disease is excluded, effective preventive treatment for MDR-TB is required. Rigorous clinical trials are needed to evaluate such regimens.[11] Finally, the cost-effectiveness of MDR-TB household contact investigations, screening and preventive treatment should be analysed.

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Contexte : Cape Town, Afrique du Sud.

Objectif : Déterminer le nombre de contacts pédiatriques de sujets atteints de tuberculose à germes multirésistants (TB-MDR) identifiés en routine par les services de santé et dans quelle mesure un modèle de soins décentralisés améliorerait l'accès à ces services.

Méthodes : Tous les cas-source TB-MDR enregistrés à Cape Town d'avril 2010 à mars 2011 ont été inclus. Tous les contacts pédiatriques évalués à l'hôpital et dans les dispensaires du secteur ont été enregistrés de mai 2010 à juin 2011. On a utilisé un appariement électronique basé sur un système de probabilités pour relier les cas-source à leurs contacts pédiatriques potentiels. On a comparé le nombre d'enfants recevant des soins décentralisés (Khayelitsa) et à l'hôpital.

Résultats : Sur 1221 cas-source de TB-MDR identifiés, 189 (15,5%) ont été enregistrés à Khayelitsha ; chez 31 (16,4%), au moins un enfant-contact a fait l'objet d'une évaluation. A l'inverse, dans 95 (9,2%) des 1032 cas-source diagnostiqués dans les autres sous-districts de Cape Town (soins basés sur l'hôpital) on a évalué au moins un enfant-contact ($P = 0,003$). Les enfants de Khayelitsha ont été vus après une durée médiane de 71 jours (extrêmes interquartiles [IQR] 37–121) après le diagnostic du cas-source par comparaison à 90 jours (IQR 56–132) dans les autres sous-districts ($P = 0,15$).

Conclusion : Bien que les soins décentralisés aient entrainé une augmentation du nombre d'enfants-contact évalués, les deux modèles n'ont évalué qu'un petit nombre des contacts pédiatriques potentiels d'une TB-MDR, cette évaluation ayant été faite après un délai considérable.

Marco de referencia: La Ciudad del Cabo en Suráfrica.

Objetivo: Definir el número de niños contactos de casos de tuberculosis multidrogorresistente (TB-MDR) que se detectan en los servicios de salud y determinar si un modelo descentralizado de atención podría mejorar su acceso a los servicios.

Método: Se incluyeron en el estudio todos los casos iniciales de TB-MDR que se registraron en la Ciudad del Cabo entre abril del 2010 y marzo del 2011. Se consignaron todos los contactos pediátricos investigados en la consulta externa hospitalaria y en los consultorios periféricos entre mayo del 2010 y junio del 2011. Se aplicó un modelo probabilístico informatizado de emparejamiento, con el propósito de confrontar los casos originales con los posibles contactos pediátricos. Se comparó el número de niños que accedió a la atención descentralizada (en Khayelitsha) con los niños que acudieron a la consulta hospitalaria.

Resultados: De los 1221 casos originales de TB-MDR que se detectaron, 189 se registraron en Khayelitsha (15,5%) y en 31 de ellos se investigó por lo menos a un contacto pediátrico (16,4%). Por el contrario, en los demás subdistritos de la Ciudad del Cabo (atención basada en el hospital) se diagnosticaron 1032 casos, de los cuales en 95 se investigó como mínimo un caso de contacto pediátrico ($P = 0{,}003$). En Khayelitsha, la mediana del lapso desde el diagnóstico del caso original hasta el examen de los niños fue 71 días (IQR 37–121), en comparación con 90 días (IQR 56–132) en los demás subdistritos ($P = 0{,}15$).

Conclusión: Si bien con la atención descentralizada se logró la evaluación de un mayor número de contactos pediátricos, ambos modelos condujeron a la investigación de un escaso número de posibles contactos pediátricos de los casos de TB-MDR. Además, el retraso en la evaluación de los niños fue considerable.