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The yield of a tuberculosis household contact investigation in two regions of Ethiopia

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SUMMARY

SETTING: Amhara and Oromia regions, Ethiopia.

OBJECTIVE: To determine the yield of a household contact investigation for tuberculosis (TB) under routine programme conditions.

DESIGN: Between April 2013 and March 2014, TB clinic officers conducted symptom-based screening for household contacts (HHCs) of 6015 smear-positive TB (SS+ TB) index cases. Based on quarterly reported programme data, we calculated the yield in terms of number needed to screen (NNS) and number needed to test (NNT).

RESULTS: Of 15 527 HHCs screened, 6.1% had presumptive TB (8.5% in Oromia vs. 3.9% in Amhara). All forms of TB and SS+ TB were diagnosed in respectively 2.5% (Oromia 3.9% vs. Amhara 1.2%) and 0.76% (Oromia 0.98% vs. Amhara 0.55%) of contacts. The NNS to detect a TB case all forms and SS+ TB was respectively 40 and 132. The NNT to diagnose a TB case all forms and SS+ TB was respectively 2.4 and 8. Of 1687 eligible children aged <5 years, 323 were started on isoniazid preventive therapy.

CONCLUSIONS: The yield of the household contact investigation was over 10 times higher than the estimated prevalence in the general population; household contact investigations can serve as an entry point for childhood TB care.

KEY WORDS: index case; systematic screening; active case finding

PROGRESS HAS BEEN MADE WORLDWIDE in reducing the incidence of tuberculosis (TB) and associated deaths, mainly through passive case finding.[1] Active case finding is needed as an additional strategy to identify and treat the many missed cases of TB, which accounted for an estimated one third of all TB cases reported in 2012.[2] About 75% of these are concentrated in 12 countries, including Ethiopia.[2] Systematic screening for TB among close contacts of index cases is one of the strategies recommended to identify these cases.[3,4] Experience with household contact investigation is limited, but screening other high-risk groups contributed 1–9% of adult cases in five studies.[3–5]

Two systematic reviews of studies on household contact investigations in low- and middle-income settings showed that respectively about 4.5% and 3.1% of contacts were found to have active TB.[6,7] The median number of household contacts evaluated to find one case of active TB was 19 (range 14–300). The median proportion of contacts found to have latent tuberculous infection (LTBI) was just over 50% in both studies. The median number of contacts evaluated to find one person with LTBI was 2 (range 1–14). In the review by Fox et al., longer-term follow-up showed that TB incidence remained above the background rate for at least 5 years.[7] Evidence from these reviews and other studies suggests that contact investigation in high-incidence settings is a high-yield strategy for case finding.[8–10] Based on the available evidence, the World Health Organization (WHO) has developed guidance on contact investigation which extends to high-risk groups other than children aged <5 years and people living with the human immunodeficiency virus (PLHIV).[11] Other key international guidelines also recommend contact investigations.[12,13]

Operationalising this guidance requires experience in low-income, high TB burden settings. A few studies from sub-Saharan African countries have looked at the yield of contact investigation, and experience of nationwide implementation was reported from Morocco.[14,15]

Ethiopia's national TB guidelines provide a policy framework for contact investigation; however, these have not been adequately implemented.[16] Earlier reports from Ethiopia were limited to specific population groups and some geographic areas.[17,18]

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In the present paper, we present data on the yield of contact investigation in a large TB project in two regions of Ethiopia. Our objective was to report on the yield of contact investigation under routine programme conditions in a low-income, high TB burden setting.

METHODS

Study setting

With a population of almost 88 million, Ethiopia is the second most populous country in Africa; more than half of the Ethiopian population lives in the two regions of Amhara and Oromia, where this study was carried out.[19] As one of the 22 high TB burden countries, Ethiopia has an estimated TB prevalence rate of 247 per 100 000 population. The proportion of multidrug-resistant TB (MDR-TB) among new and previously treated cases was respectively 2.7% and 17.8% (unpublished data, Ministry of Health, 2014). Table 1 summarises key health and TB data for Ethiopia.

Donor-funded projects contribute a significant share of Ethiopia's health care financing.[25] The Federal Ministry of Health and the Regional Health Bureaux of Amhara and Oromia regions, in partnership with the Help Ethiopia Address the Low TB Performance (HEAL TB) Project, have been implementing a comprehensive TB prevention and control programme that includes contact investigation in the two regions since July 2011. All services were free and available in 2186 health centres and 64 hospitals in HEAL TB-supported regions.

Contact investigation procedure

In each zone of the two regions, HEAL TB assigned a clinical officer and laboratory expert who provided technical guidance and support to zonal and *woreda* (equivalent to district) TB officers on all aspects of TB care, including contact investigation. The team developed and disseminated standard operating procedures for contact investigation to participating health facilities; oriented zonal, woreda and health facility TB focal persons on contact investigation; and supplied the health facilities with registers and job aids. Woreda TB focal persons then conducted supportive supervision and monitored progress by instituting a quarterly reporting mechanism for contact investigation. Participating facilities attended quarterly and semi-annual review meetings at the zonal and subnational levels to review programme performance, identify gaps and develop corresponding action plans.

After obtaining informed verbal consent, TB clinic officers asked each newly diagnosed smear-positive TB (SS+ TB) patient to provide the names and contact details of each household member and recorded the information in the health facility contact register. On registration with the TB clinic, each index case was counselled to bring family members to the health facility for screening. At the clinic, the TB clinic officer screened family members for symptoms using the following criteria for presumptive TB: any household contact with a history of cough for $\geqslant 2$ weeks or with two or more constitutional symptoms suggestive of TB was considered to have presumptive TB. Presumptive TB cases with productive cough were referred for sputum examination by laboratory technicians using Ziehl-Neelsen or fluorescent light-emitting diode microscopy. Patients presumed to have smear-negative (SS–) TB, with persistent respiratory symptoms or extra-pulmonary TB, underwent additional investigations, including chest radiography and pathology, mainly in a hospital setting.

We defined an index case as the initially identified case of new or recurrent SS+ TB around whom a contact investigation was carried out. A household contact was a person who shared the same enclosed living space for $\geqslant 1$ nights or for frequent or extended periods during the day with the index case during the 3 months before the current treatment episode began.[11,26]

Data collection and analysis

Data were collected through the routine programme monitoring system using the contact register. The following variables were recorded: health facility and index cases, type of TB and treatment initiation date, age, household contacts, diagnostic results of close contacts, and treatment and prophylaxis status of contacts. The woreda TB focal person compiled all contact investigation data quarterly and submitted them to the zonal TB focal person. We aggregated the data at the regional and project levels using Excel (MicroSoft, Redmond, WA, USA). We calculated the yield of contact investigation in terms of number needed to screen (NNS) and number needed to test (NNT). NNS is the number of contacts required to be screened to detect a single case of active TB; NNT is the number of persons with presumptive TB required to be evaluated to detect a single case of active TB. We calculated the values with a 95% confidence interval (CI) using OpenEpi software (www.OpenEpi.com). $P < 0.05$ was considered statistically significant.

Ethical considerations

As routine programme data were used for this analysis, no ethics approval was sought. Contact screening was performed with full verbal consent of the patients, and information was handled confidentially. All contacts with confirmed TB received the standard anti-tuberculosis treatment regimen at health facilities. Contacts who failed to visit health facilities were encouraged to visit the nearby health facility or see a community health worker.

Table 1 Sociodemographic, health and TB data, Ethiopia, 2013–2014

Characteristic	Ethiopia	Amhara	Oromia
Estimated population, millions[19]	87 952 991	20 018 988	32 815 995
Estimated annual per capita income, $US[20]	470	—	—
Number of TB cases notified[21]	131 677	29 003	49 886
CNR for all forms of TB/100 000 population[21]	171	172	159
TB prevalence/100 000 population[22]	211		
Estimated HIV prevalence in adults[23]	1.3	1.3	0.8
MDR-TB among new cases, % (95%CI)[24]	2.3 (1.5–3.1)	—	—
MDR-TB among retreatment cases, % (95%CI)[24]	17.8 (13.3–22.4)	—	—

TB = tuberculosis; CNR = case notification rate; HIV = human immunodeficiency virus; MDR-TB = multidrug-resistant TB; CI = confidence interval.

RESULTS

Basic characteristics of study participants

Between 1 April 2013 and 30 March 2014, health facilities screened the household contacts of 6015 SS+ index cases in 627 health facilities across 21 zones in the Amhara and Oromia regions of Ethiopia. Of the 16 512 registered household contacts, 15 527 were screened (Figure). The ratio of household contacts screened to index cases was 2.5. Children aged <5 years constituted 11.2% of all screened household contacts. Only 19.2% of eligible children received isoniazid preventive therapy (IPT) (Table 2).

The yield of household contact investigation

We identified 949 presumptive TB cases, of whom respectively 389 and 118 were confirmed to have all forms TB and SS+ TB. The prevalence of presumptive TB was 6.1% (95%CI 5.7–6.5), with a higher rate in Oromia than in Amhara (8.5%, 95%CI 7.9–9.1 vs. 3.9%, 95%CI 3.5–4.4, χ^2 145, $P < 0.0001$). TB (all forms) was detected in 2.5% (95%CI 2.3–2.8) of all contacts screened; the yield was higher in Oromia (3.9%, 95%CI 3.5–4.4 vs. 1.2%, 95%CI 1.0–1.5, $P < 0.0001$). SS+ TB prevalence was 0.76% (95%CI 0.63–0.91); the rate was higher in Oromia (0.98%, 95%CI 0.8–1.2 vs. 0.55%, 95%CI 0.41–0.74; $P < 0.01$). SS+ TB constituted 30.3% of all forms of TB diagnosed; the rate was higher in Amhara than in Oromia (45.5%, 95%CI 36–55.2 vs. 25.2%, 95%CI 20.51–30.48, $P < 0.001$). However, the proportion of SS+ TB among those with presumptive TB did not differ significantly between the two regions: 14.1%, 95%CI 10.7–18.4 in Amhara vs. 11.6%, 95%CI 9.31–14.33 in Oromia (12.4% overall, $P > 0.1$).

The NNS values for presumptive TB, all forms of TB and SS+ TB were respectively 16 (95%CI 16–17), 40 (95%CI 39–41) and 132 (95%CI 131–134). The corresponding NNT values for all forms and SS+ TB were respectively 2.4 (95%CI 2.3–2.6) and 8 (95%CI 7–9) (Table 2). The yield of presumptive and all forms of TB was higher in children aged <5 years (14.1% vs. 5.1% and 3.5% vs. 2.4%, respectively); however, those aged ⩾5 years had a higher prevalence of SS+ TB (Table 3).

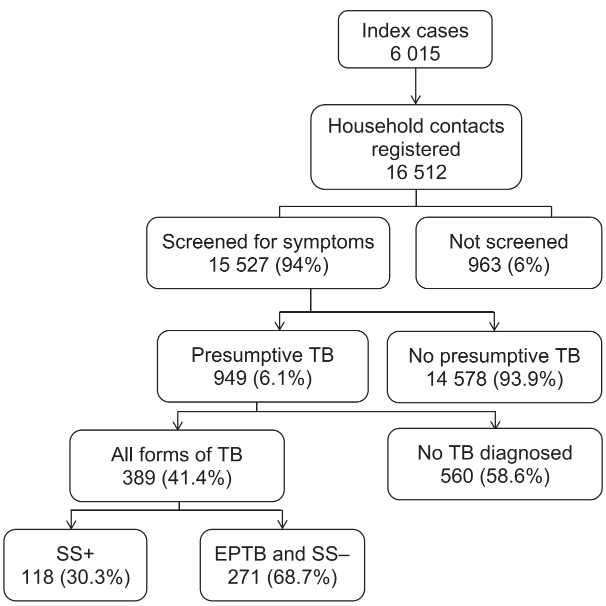

Figure Profile of contacts registered, screened and evaluated, Ethiopia, September 2014. TB = tuberculosis; SS = sputum smear; + = positive; EPTB = extra-pulmonary TB; – = negative.

DISCUSSION

In this study, we found a prevalence rate of all forms of TB among household contacts of SS+ TB index cases to be over 10 times higher than the prevalence estimate of 211/100 000 in the general population. The prevalence rate was about 18 times higher in the Oromia Region and 6 times higher in Amhara Region. The prevalence of SS+ TB, 0.76%, was about seven times higher than the prevalence estimate for SS+ TB of 0.108% in the national TB prevalence survey.[27] About six persons in every 100 household contacts had presumptive TB, with over one third of these eventually confirmed to have TB. The NNS to find a TB case was 40 and the NNT to diagnose a single case of TB was less than 3. Household contact investigations should therefore be prioritised as a high-yield strategy to improve TB case finding. Household contact investigation can also serve as an entry point for achieving high case-finding levels in children aged <15 years and high IPT coverage for children aged <5 years.

The TB prevalence of 2.5% among household

Table 2 Variations in the yield of household contact investigations by administrative region, Ethiopia, April 2013–March 2014

Characteristic	Amhara *n* (%)	Oromia *n* (%)	Total *n* (%)	*P* value
SS+ TB index cases	2 956	3 059	6 015	
Contacts screened	8 141	7 415	15 527	
Age <5 years	604 (7.4)	1 144 (15.4)	1 748 (11.2)	
Eligible for IPT	592 (98.0)	1 092 (95.5)	1 684 (96.3)	
Receiving IPT (95%CI)	133 (22.4) (19.3–26)	190 (17.4) (15.3–19.8)	323 (19.2) (17.4–21.1)	<0.01
Presumptive TB cases				
Total	319	630	949	
Contacts, % (95%CI)	3.9 (3.5–4.4)	8.5 (7.9–9.1)	6.1 (5.7–6.5)	<0.0001
NNS, *n* (95%CI)	26 (25–26)	12 (11–12)	16 (16–17)	<0.0001
All forms of TB cases diagnosed, *n* (95%CI)				
Total	99	290	389	
Contacts, % (95%CI)	1.2 (1.0–1.5)	3.9 (3.5–4.4)	2.5 (2.3–2.8)	<0.0001
Presumptive cases	31 (26–36)	46 (42–50)	41 (38–44)	<0.0001
NNS	82 (80–84)	26 (25–26)	40 (39–41)	<0.0001
NNT	3.2 (2.9–3.6)	2.2 (2–2.4)	2.4 (2.3–2.6)	<0.0001
SS+ TB cases diagnosed				
Total	45	73	118	
Contacts, % (95%CI)	0.55 (0.41–0.74)	0.98 (.8–1.2)	0.76 (0.63–0.91)	<0.01
Presumptive TB, % (95%CI)	14.1 (10.7–18.4)	11.59 (9.31–14.33)	12.4 (10.5–14.7)	>0.1
All forms, % (95%CI)	45.5 (36–55.2)	25.17 (20.51–30.48)	30.3 (26–35.1)	<0.0001
NNS, *n* (95%CI)	181 (177–185)	102 (99–104)	132 (130–134)	<0.01
NNT, *n* (95%CI)	7.08 (6.33–7.91)	8.63 (7.96–9.33)	8.04 (7.54–8.57)	<0.01

CI = confidence interval, SS+ = sputum smear-positive; TB = tuberculosis; IPT = isoniazid preventive therapy; NNS = number needed to screen; NNT = number needed to test.

contacts in our study is slightly lower than that reported (3.1%) in a recent systematic review.[7] The overall lower prevalence in our study could be attributed to the way in which the screening was organised. We did not perform house-to-house visits to identify TB among household contacts. In a high TB-HIV burden district in South Africa, for example, community-based targeted screening resulted in a TB prevalence of 6%, and most of the culture-confirmed TB cases were found among asymptomatic household contacts.[28] Moreover, as we used less sensitive diagnostic tools in our programme, the lower TB prevalence among household contacts in our study could be an underestimate, highlighting the need for more aggressive screening strategies using improved diagnostic tools. We screened 69% of the expected 3.6 family members (index cases excluded), assuming an average family size of 4.6. As the remaining family members are likely to be asymptomatic, there was a possibility of overestimating the TB yield. This might have led to some balancing effect on the above-mentioned underestimation.

Table 3 The yield of TB household contact investigation by age category, Ethiopia, April 2013–March 14

	Age category			
Characteristics	⩾5 years % (95%CI)	<5 years % (95%CI)	Total % (95%CI)	*P* value
Contacts screened, *n*				
Total	13 779	1 748	15 527	
Presumptive TB cases				
Total, *n*	702	247	949	
All screened	5.1 (4.7–5.5)	14.1 (12.6–15.8)	6.1 (5.7–6.5)	<0.0001
NNS, *n* (95%CI)	19.6 (19.3–19.9)	7.1 (6.7–7.4)	16.4 (16.1–16.6)	<0.0001
All forms of TB				
Total, *n*	325	64	389	
All screened	2.4 (2.2–2.6)	3.7 (2.9–4.6)	2.5 (2.3–2.8)	<0.001
Presumptive cases	46.3 (42.6–50.0)	25.9 (20.8–31.7)	41.0 (37.9–44.1)	<0.0001
NNS, *n* (95%CI)	42.4 (41.7–43.1)	27.3 (26.1–28.6)	39.9 (39.3–40.5)	<0.0001
NNT, *n* (95%CI)	2.2 (2–2.3)	3.9 (3.4–4.4)	2.4 (2.3–2.6)	<0.0001
SS+ TB				
Total, *n*	113	5	118	
All screened	0.82 (0.68–0.98)	0.29 (0.10–0.69)	0.76 (0.63–0.91)	<0.01
Presumptive cases	16.1 (13.6–19)	2.0 (0.73–4.8)	12.4 (10.5–14.7)	<0.0001
All forms	34.8 (29.8–40.1)	7.8 (3–17.4)	30.3 (26–35.1)	<0.0001
NNS, *n* (95%CI)	121.9 (119.9–124)	349.6 (333.4–366.4)	131.6 (129.5–133.7)	<0.0001
NNT, *n* (95%CI)	6.2 (5.8–6.7)	49.4 (43.4–55.9)	8 (7.5–8.6)	<0.0001

CI = confidence interval, TB = tuberculosis; NNS = number needed to screen; NNT = number needed to test; SS+ = sputum smear-positive.

NNS and NNT have been suggested as useful metrics for measuring the efficiency of TB screening programmes.[29] Some researchers have suggested measuring the efficiency of TB screening approaches in terms of resource allocation.[30] We used the NNS and NNT, as we did not capture the parameters suggested in the latter approach. In an active community-based screening study in an urban setting in Uganda, the NNS was 131.[29] Although the NNS in contact-screening studies can vary widely, the median is 45,[31] comparable to the NNS of 40 in our study. Similarly, the NNT of 2.4 in our study is better than the recommended value of 7.[32] However, both the NNS and the NNT varied significantly between the two regions, with Oromia having a smaller NNS and NNT than Amhara.

The reasons for the regional variations in the yield of contact investigation are not clear. In studies with populations with mixed or unknown HIV status, the population-level prevalence of TB and HIV, the screening strategy and the availability of culture services were not associated with yield of active TB case finding.[31] Our data were not disaggregated by HIV status; however, the HIV prevalence rate in Amhara Region is higher in both the general population and among TB patients.[23,33] On the other hand, as antiretroviral treatment (ART) coverage is higher in Amhara than in Oromia,[34] some population-level protective effect might have been conferred by ART, which is known to reduce TB incidence in PLHIV.[35] A more in-depth review of factors contributing to regional variations using data from different sources is needed.

The low IPT coverage in under-5 children is another area that needs to be addressed; however, published data on this population are limited. Among PLHIV, the IPT coverage rate was 18% in 2012.[21] Frequent stockouts of isoniazid and provider-related factors, such as fear of drug resistance, are cited as factors contributing to low IPT coverage rates among PLHIV in Ethiopia.[36] Lack of standardised monitoring tools and low level of awareness among health care providers appear to be the main challenges in our project zones.

The study has certain limitations: the data are not disaggregated by HIV status, sex or MDR-TB status; as sputum microscopy was the main diagnostic tool used in the study, generalising the results to settings that use culture or Xpert® MTB/RIF (Cepheid, Sunnyvale, CA, USA) is difficult; and lack of credible local evidence made comparisons with other studies difficult, necessitating comparisons with population-based surveys and WHO estimates. The study also has a number of strengths: this is the first large-scale experience of implementation of household contact investigation in Ethiopia, and one of few in low-income settings; the experience of IPT among children aged <5 years is also one of few in this setting.

CONCLUSIONS

The yield of household contact investigation was more than 10 times higher than the prevalence estimate in the general population, and served as an entry point for childhood TB care in two large regions of Ethiopia. It should therefore be scaled up to similar settings. However, more effort is needed to optimise its yield by using more sensitive diagnostic techniques, and to improve IPT coverage among under-5 children. Future studies should look into factors contributing to regional variations in the yield of contact investigation, underlying reasons for the low IPT coverage among children, cost and cost-effectiveness of various contact investigation approaches, and the performance of the Xpert assay for TB diagnosis in contacts.

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RESUME

CONTEXTE : Régions d'Amhara et d'Oromia, Ethiopie.

OBJECTIF : Déterminer le rendement de l'investigation des contacts domestiques pour la tuberculose (TB) dans des conditions de routine de programme en Ethiopie.

SCHÉMA : Entre avril 2013 et mars 2014, le personnel des dispensaires antituberculeux a réalisé un dépistage basé sur les symptômes auprès des contacts domestiques de 6015 cas index de TB à frottis positif (SS+ TB). En nous basant sur les données des rapports trimestriels du programme, nous avons calculé le rendement en termes de nombre de personnes à dépister (NNS) et de nombre de personnes à tester (NNT).

RÉSULTATS : Sur 15 527 contacts domestiques dépistés, 6,1% ont été présumés d'avoir la TB (8,5% à Oromia contre 3,9% à Amhara). Toutes les formes de TB et de SS+ TB ont été diagnostiquées chez 2,5% des contacts (Oromia 3,9% contre Amhara 1,2%) et 0,76% des contacts (Oromia 0,98% contre Amhara 0,55%), respectivement. Le NNS requis pour détecter un cas d'une forme quelconque de TB et de SS+ TB a été de 40 et 132, respectivement. Le NNT requis pour diagnostiquer un cas d'une forme quelconque de TB et de SS+ TB a été de 2,4 et 8, respectivement. Sur 1687 enfants éligibles âgés de moins de 5 ans, 323 ont débuté un traitement préventif par isoniazide.

CONCLUSIONS : Le rendement de l'investigation des contacts domestiques a été plus de 10 fois la prévalence estimée dans la population générale. Cette recherche peut constituer un point d'entrée pour la prise en charge de la TB de l'enfant.

RESUMEN

MARCO DE REFERENCIA: Las regiones de Amhara y Oromia en Etiopía.

OBJETIVO: Determinar el rendimiento diagnóstico de la investigación de los contactos domiciliarios de los casos de tuberculosis (TB) en el marco de las condiciones de un programa ordinario en Etiopía.

MÉTODO: Entre abril del 2013 y marzo del 2014, los funcionarios de los consultorios de TB llevaron a cabo un cribado sistemático basado en los síntomas de los contactos domiciliarios de 6015 casos iniciales de TB con baciloscopia positiva (SS+ TB). A partir de los datos programáticos trimestrales, se calculó el rendimiento según el número de personas cribadas (NNS) y el número de personas examinadas (NNT) que fueron necesarios con el fin de detectar un caso de TB activa.

RESULTADOS: En el 6,1% de los 15 527 contactos domiciliarios que participaron en el cribado se estableció una presunción diagnóstica de TB (8,5% en Oromia contra 3,9% en Amhara). Se estableció el diagnóstico de cualquier forma de TB en 2,5% de los contactos (el 3,9% en Oromia contra el 1,2% en Amhara) y de SS+ TB en el 0,76% (0,98% en Oromia contra 0,55% en Amhara). El NNS con el fin de detectar un caso de cualquier forma de TB fue 40 y la detección de un caso de SS+ TB necesitó el cribado de 132 personas. El NNT con el fin de detectar un caso de cualquier forma de TB fue 2,4 y un caso de SS+ TB necesitó el examen de ocho personas. De los 1687 niños menos de 5 años de edad que cumplían con los requisitos, 323 iniciaron el tratamiento preventivo con isoniazida.

CONCLUSIÓN: El rendimiento diagnóstico de la investigación de contactos domiciliarios de los casos de TB fue más de 10 veces superior a la prevalencia estimada en la población general. Esta medida ofreció una puerta de entrada a la atención de la TB de los niños.