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Population-based screening for pulmonary tuberculosis utilizing community health workers in Ethiopia★

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ABSTRACT

Objective: To evaluate the utility of a volunteer health development army in conducting population screening for active tuberculosis (TB) in a rural community in southern Ethiopia.
Methods: A population-based cross-sectional survey was conducted in six *kebeles* (the lowest administrative units). Volunteer women community workers led a symptom screening programme to identify adults ≥15 years of age with TB in the community. Individuals with a cough for ≥2 weeks had spot and morning sputum samples taken, which were examined using acid-fast bacillus (AFB) smear microscopy, culture, and Xpert MTB/RIF.
Results: All 24 517 adults in the study area had a symptom screen performed; 544 (2.2%) had had a cough for ≥2 weeks. Among those with a positive symptom screen, 13 (2.4%) were positive on sputum AFB smear microscopy, 13 (2.4%) had a positive culture, and 32 (5.8%) had a positive Xpert MTB/RIF test. Overall, 34 TB cases (6%) were identified by culture and/or Xpert, corresponding to a prevalence of 139 per 100 000 persons.
Conclusions: This study demonstrated the capability of community health workers (volunteer and paid) to rapidly conduct a large-scale population TB screening evaluation and highlight the high yield of such a programme in detecting previously undiagnosed cases when combined with Xpert MTB/RIF testing. This could be a model to implement in other similar settings.

Introduction

The fight against tuberculosis (TB) has been bolstered by the development of new molecular diagnostics, drugs, and a recent high-level United Nations meeting addressing the epidemic; however, many challenges to TB control remain. One of the most pressing challenges to eliminate TB is the high number of undetected cases. Only 6.4 of an estimated >10 million cases (64%) were officially notified in 2017, leaving a gap of >3.5 million cases unreported and potentially undetected. Most of these missed cases occur in low- and middle-income countries (LMICs) and among vulnerable populations (WHO, 2018). Rural settings are particularly challenging areas to detect and diagnose TB due to limited healthcare services, poor healthcare-seeking behaviour, and limited awareness and knowledge about TB (Cambanis et al., 2005; Sudha et al., 2003). Understanding the burden of TB in poor rural areas has large implications for TB control and is needed to design optimal case finding strategies (Cambanis et al., 2005; Sudha et al., 2003). This study was performed to evaluate the utility of a volunteer health development army (HDA) in conducting population screening for active TB in a rural setting in southern Ethiopia.

Active case-finding (ACF) for TB is influenced by individual (care-seeking behaviour), social (access to healthcare), and biomedical (diagnostic capability) factors (Shargie et al., 2006a). In rural communities, ACF can help reach persons with no transport or limited mobility, scarce resources, and persons who rarely seek healthcare (Yassin et al., 2013; Datiko et al., 2015). The Ethiopian national TB programme (NTP) relies on passive case

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finding, as do most control programmes and NTPs globally; however, there is a recognized need to strengthen community screening given variations in disease epidemiology across diverse geographic and cultural settings (Kebede et al., 2014).

Ethiopia is one of 14 countries to be included on all three World Health Organization (WHO) high burden country lists for TB, TB/HIV, and multidrug-resistant TB (MDR-TB). The TB incidence in Ethiopia in 2017 was estimated to be 164 per 100 000 population (WHO, 2018). The prevalence of smear-positive pulmonary TB was 108 per 100 000 per population according to a national population-based TB survey conducted from October 2010 to June 2011, in which the vast majority of those identified were newly diagnosed cases that had not been captured by the control programme and most (55%) were among the younger age groups (15–34 years) (Kebede et al., 2014). Additional studies across various rural settings in Ethiopia have found a range of smear-positive pulmonary TB prevalence rates (from 30 to 174 per 100 000 population) suggesting that disease epidemiology varies across different geographical locations of the country (Berhe et al., 2013; Hamusse et al., 2017; Shargie et al., 2006b; Deribew et al., 2012; Yimer et al., 2009; Tadesse et al., 2011).

This study was performed to evaluate the efficacy of a population screening programme for active pulmonary TB using volunteer and paid community health workers in a rural area in southern Ethiopia. As a brief background, Ethiopia launched a health extension programme (HEP) in 2003 with the objective of increasing population access to basic health services including TB. The HEP consists of female health extension workers (HEWs) who receive 1 year of training and then become salaried healthcare workers equipped to provide basic health services to the same community from which they were recruited (Yassin et al., 2013; Datiko et al., 2015; Datiko and Lindtjorn, 2009; Datiko et al., 2017). The HEWs are based at local health posts and provide health promotion to the community at the household level. In 2013, to further expand healthcare services and to ease the burden on HEWs, the Ethiopian government rolled out a programme called the health development army (HDA) (Tulloch et al., 2015), which consists of female community-level volunteers who receive basic training on health by the HEWs. They are recruited based on their leadership qualities and their interest in being involved in the health of their community. They live within the communities and aid the HEWs at the household level. They have regular meetings among themselves and with the HEWs to deal with health issues in the community. The main goal of this study was to assess the feasibility and utility of a population screening programme for active TB led by HDAs.

Methods

Study setting and design

A cross-sectional study was performed in the Hawassa Zuria Woreda (a rural district), in the Sidama zone of southern Ethiopia. Hawassa Zuria Woreda has 23 *kebeles* (the lowest administrative units within Ethiopia, each with an average population of approximately 5000 persons or 1000 households), and a total population of 153 190 persons, 79 858 of whom were ≥15 years (52%). The Woreda has one hospital, four health centres, and 23 health posts serving the population. Each health centre is associated with five satellite health posts and combined they form a primary healthcare unit (PHCU). The health service coverage of the Woreda is 80% (accessible health service is defined as having a health facility within two hours walking distance). For this study, three health centres were selected in the district with a functional PHUC. Two *kebeles* were randomly selected from each of the three health centres, and thus the study area included six of the 23 *kebeles*. All households in the study *kebeles* were surveyed. Inclusion criteria were community members without known TB and who had had a cough for ≥2 weeks, age ≥15 years, and voluntary study participation with signed written consent. Exclusion criteria were patients currently on anti-TB treatment, those who were disabled or immobilized, patients with a severe illness, unable to provide a sputum sample, and community members who were not available for screening at the time of screening due to travel or hospitalization. The study was conducted from May 8, 2016 through June 9, 2016.

Data collection

Prior to the study, meetings were convened with *kebele* leaders, HEWs, and members of the HDA to inform them of the study objectives and procedures and to receive input and feedback. Subsequently, training was conducted with the field supervisors and HEWs at the health posts.

The identification of presumptive TB cases (i.e., those with a positive cough screen) was conducted by members of the HDA. There were 30 to 58 HDAs in each *kebele* depending on the population size and approximately 350 HDAs were involved in active TB case finding. Prior to the survey, community mobilization (creating awareness about the study) was done through religious institutions and schools in the community. Afterwards, the HDA conducted house-to-house visits to identify people who had had a cough for at least 2 weeks. Individuals with a cough for ≥2 weeks were considered as presumptive TB cases and brought to the health post. At the health post, they were evaluated by field supervisors (health professionals who have experience in TB and community work) and HEWs. Those who met the eligibility criteria were interviewed and asked to submit two sputum samples (spot and morning). For all study participants, a pretested (validated) structured questionnaire was used to collect data on patient demographics, clinical presentation, and associated risk factors for the transmission of TB. Two field supervisors and the study principal investigator (YM) monitored the daily data collection process. The duration of patient screening and data collection was 5 days for each of the six *kebeles* between May 8, 2016 and June 9, 2016.

Laboratory testing

AFB smear preparation was performed at the health posts by laboratory technicians assigned for the study. Slides were prepared on the same day as the sputum collection and along with the remaining portions of the sputum samples were transported daily to a health centre approximately 25 kilometres away. Here the slides were stained using the Ziehl–Neelsen (ZN) hot staining technique and examined for acid-fast bacilli (AFB) using regular light microscopy (Federal Democratic Republic Ethiopia Ministry of Health, 2014). The remaining portions of the two sputum samples were pooled and stored at −20 °C until transported to Armauer Hansen Research Institute (AHRI) in Addis Ababa where culture was performed using Löwenstein–Jensen (LJ) medium according to standard procedures (WHO, 1998).

HIV counselling and screening was offered to all participants diagnosed with TB, and HIV serology was performed based on the national testing algorithm. Finger stick blood was tested for HIV (1/2) with the Antibody Colloidal Gold (KHB) test and positive results were confirmed with Stat-Pak, while discordant results were resolved by HIV-1/2 Unigold Recombinant assay.

Definitions

A confirmed pulmonary TB case was defined as one in whom a sputum specimen was Xpert MTB/RIF test and/or culture positive.

Clinical treatment outcomes were defined as per national guidelines (Federal Democratic Republic Ethiopia Ministry of Health, 2016).

Data management

All data were double-entered into an online REDCap database (Harris et al., 2009) and analysed using Stata software. Differences in categorical variables were tested using the Chi-square test. A multivariable logistic regression model was used to evaluate the independent association of potential risk factors for TB. Model building and selection was based on the purposeful selection of covariates strategy, as described previously, based on findings in the univariate analysis and biological plausibility (Hosmer and Lemeshow, 2000). A p-value of <0.05 was considered significant.

Ethical considerations

The study was approved by the institutional review boards of Addis Ababa University and AHRI, as well as the Ethiopian National Ethics Review Committee. Study permission was also obtained from the Southern Regional Health Bureau, Zonal Health Department and the Woreda health office. Patients diagnosed with active TB were referred to their catchment health centre and hospital for treatment.

Results

All 24 517 adults in the six *kebeles* had a cough symptom screen for TB performed during the 1-month study period and 544 (2.2%) were found to have had a cough for ≥2 weeks. All patients with a prolonged cough submitted two sputum samples. Among the 544 adults with a positive cough screen, the median age was 36 years (interquartile range (IQR) 29–48 years) and the majority were female (n = 354, 65%) (Table 1). There were 152 participants (28%) with a history of contact with a TB patient, 160 (29%) who reported previous anti-TB treatment, and 12 (2%) with a history of incarceration (Table 3). There were high rates of reported symptoms including fever (80%), night sweats (87%), weight loss (85%), and chest pain (81%).

Prevalence of pulmonary tuberculosis

A total of 34 (6%) persons with a positive cough screen were found to have pulmonary TB (Table 2). All 34 cases were confirmed by Xpert MTB/RIF (n = 32) and/or a positive culture result (n = 12). Only 13 of the 34 cases (38%) had a positive AFB sputum smear microscopy result (Table 2). Two culture-positive cases had a negative Xpert MTB/RIF test and negative sputum smear microscopy results. Two cases were rifampicin-resistant according to Xpert MTB/RIF testing, with one of the cases having a prior history of anti-TB treatment. During the study period, only one case of a patient on anti-TB treatment was identified, who was not included in the calculated TB prevalence. The overall point prevalence of confirmed pulmonary TB cases was 139 per 100 000 population (95% confidence interval (CI) 96–194) (Table 2).

Almost three fourths (25/34, 74%) of the confirmed TB cases were newly diagnosed, while 9/34 were previously treated cases. There was a similar distribution among females (53%) and males (47%) (Table 3). None of the 31 TB cases who had HIV testing performed had a positive result. A treatment outcome was available for 29 patients, 28 of whom were cured; one had completed treatment. Five persons with TB moved out of their *kebeles* and outcomes were not available.

Risk factors for tuberculosis

In the univariate analysis, longer duration of cough, older age, and close contact with a known TB case were associated with an increased risk of having confirmed TB among persons with a positive cough screen (Table 3). In the multivariate analysis, a cough of >4 weeks (adjusted odds ratio (aOR) 4.23, 95% CI 1.94–9.23) was associated with the risk of having bacteriologically confirmed TB, while older age (aOR 0.047, 95% CI 0.005–0.43) was associated with a reduced risk of bacteriologically confirmed TB among those with a positive symptom screen (Table 4).

Discussion

Utilizing a large volunteer healthcare workforce in rural southern Ethiopia, it was possible to conduct a massive population-based screening programme for active TB among more than 24 000 adults over a short time-period (approximately 1 month) and 34 previously undiagnosed active TB cases were detected, primarily through the use of Xpert MTB/RIF. This study demonstrates the feasibility of a large TB screening programme using community health volunteers doing the initial symptom screen and referrals and paid community health workers for further testing and confirmation. The high prevalence of previously undiagnosed TB identified in the current study highlights the hidden burden of TB in rural settings and the need for additional active screening programmes. In our setting, it was found that an approach using community health workers made it possible to conduct an impressive large-scale screening programme and this may be a useful approach to consider for other similar rural LMIC settings.

Innovative approaches using community health workers to increase the case detection rate are growing in number (Yimer et al., 2009), and in this regard practical changes were observed in southern Ethiopia by applying a community-based TB intervention. Community-based interventions at the village level using female community health workers (HEWs) have made TB diagnosis and treatment services more accessible to the community and have significantly improved TB diagnosis and treatment in

Table 1
Distribution of the population and confirmed tuberculosis cases by *kebeles* of Hawassa Zuria Woreda, Ethiopia.

Kebeles	Number of households	Total population			≥15 years			Positive cough screen			Confirmed TB		
		Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
1	1272	6231	3103	3128	3248	1618	1630	77	27	50	3	2	1
2	1508	7390	3680	3710	3852	1918	1934	91	28	63	7	5	2
3	1976	9681	4821	4860	5047	2513	2534	131	35	96	10	3	7
4	1127	5534	2756	2778	2885	1437	1448	46	13	33	3	2	1
5	2436	11 447	5701	5746	5967	2972	2995	113	48	65	6	2	4
6	1373	6749	3361	3387	3518	1752	1766	86	39	47	5	3	2
Total	9692	47 032	23 422	23 609	24 517	12 210	12 307	544	190	354	34	16	18

TB, tuberculosis.

Table 2
Distribution of confirmed tuberculosis cases by *kebeles*, Hawassa Zuria Woreda, Ethiopia.

Kebeles	≥15 years	AFB positive	Culture positive	Xpert positive	Confirmed TB	Rate	95% CI
1	3248	1	1	3	3	92	19.05–269.69
2	3852	3	3	7	7	182	73.09–374.06
3	5047	4	4	9	10	198	95.05–364.08
4	2885	1	1	3	3	104	21.45–303.59
5	5967	2	2	5	6	101	36.91–218.73
6	3518	2	2	5	5	142	46.16–331.36
Total	24 517	13	13	32	34	139	96.06–193.74

AFB, acid-fast bacilli; TB, tuberculosis; CI, confidence interval.

Table 3
Predictors of pulmonary TB among persons with a positive cough screen, Hawassa Zuria Woreda, Ethiopia.

Characteristic	Total (n = 544), n (%)	No TB (n = 510), n (%)	TB (n = 34), n (%)	Univariate analysis	
				OR (95% CI)	p-Value
Female sex	354 (65)	336(66)	18 (53)	0.58 (0.28–1.17)	0.12
Mean age (years)	38	38	31		
Age category (years)					
15–24	68 (12)	61 (12)	7 (22)		
25–34	143 (27)	132 (26)	11 (34)	0.72 (0.26–1.94)	0.52
35–44	159 (29)	150 (29)	9 (28)	0.52 (0.18–1.46)	0.21
45–54	94 (17)	90 (18)	4 (13)	0.38 (0.10–1.38)	0.14
≥55	80 (15)	79 (15)	1 (3)	0.11 (0.01–0.92)	0.04
Illiterate	401 (74)	383 (75)	18 (53)	0.37 (0.18–0.75)	0.006
Unemployed	533 (98)	501 (98)	32 (94)	0.28 (0.05–1.38)	0.12
Married	470 (86)	440 (94)	30 (88)	0.83 (0.28–2.45)	0.74
Duration of cough in weeks					
2–4	333 (61)	321 (63)	12 (35)		
>4	211 (39)	189 (37)	22 (65)	3.11 (1.50–6.43)	0.002
Symptoms					
Fever	437 (80)	409 (80)	28 (82)	1.15 (0.46–2.85)	0.76
Night sweats	472 (87)	443 (87)	29 (85)	0.87 (0.32–2.34)	0.79
Loss of appetite	288 (53)	268 (53)	20 (59)	1.28 (0.63–2.61)	0.47
Weight loss	464 (85)	433 (85)	31 (91)	1.83 (0.54–6.15)	0.34
Chest pain	439 (81)	411 (81)	28 (82)	1.12 (0.45–2.78)	0.80
Shortness of breath	315 (56)	294 (58)	21 (62)	1.18 (0.58–2.42)	0.63
Previous anti-TB treatment	160 (29)	151 (30)	9 (26)	0.85 (0.39–1.87)	0.69
Contact with TB case	152 (28)	137 (28)	15 (44)	2.02 (1.00–4.10)	0.049
Presence of TB patient in the family	89 (16)	80 (16)	9 (26)	1.99 (0.85–4.21)	0.11
Absence of window in the home	490 (90)	457 (90)	33 (97)	3.82 (0.51–28.5)	0.19
Alcohol use	13 (2)	11 (2)	2 (6)	2.83 (0.60–13.3)	0.18

TB, tuberculosis; OR, odds ratio; CI, confidence interval.

Table 4
Multivariate analysis of risk factors for pulmonary tuberculosis among persons with a positive cough screen, Hawassa Zuria Woreda, Ethiopia (n = 544).

Characteristics	Multivariate analysis	
	aOR (95% CI)	p-Value
Age category in year		
15–24	1.00	
25–34	0.70 (0.24–2.07)	0.528
35–44	0.29 (0.09–0.96)	0.043
45–44	0.22 (0.05–0.86)	0.031
≥55	0.047 (0.005–0.43)	0.007
Duration of cough in weeks		
2–4	1.00	
≥4	4.23 (1.94–9.23)	<0.001
Close contact with known TB patient		
No	1.00	
Yes	1.99 (0.93–4.26)	0.073

aOR, adjusted odds ratio; CI, confidence interval; TB, tuberculosis.

the rural settings of southern Ethiopia (Yassin et al., 2013; Datiko and Lindtjorn, 2009; Datiko et al., 2017). In contrast to these previous studies in Ethiopia, and as part of an innovative approach, our study used HDAs to identify symptomatic TB individuals in the community. Using HDAs, a very high number of TB cases were identified in a short period of time. Involving HDAs helped us reach the entire community and trace the symptomatic cases easily. HDAs live in the community and come across symptomatic neighbours in their daily routines. They also participate in community meetings and work closely with the HEWs on health-related issues. They are not paid, but contribute voluntarily to improve the health of the community. A similar approach has been reported among others in Uganda where voluntary Village Health Teams (VHT) are involved in improving and promoting health at the community level (O'Donovan et al., 2018).

Improved screening is inadequate without appropriate diagnosis and treatment. Linking the HDAs with a rapid molecular diagnostic tool such as Xpert MTB/RIF has proved to be a successful approach in detecting presumptive TB cases early for rapid diagnosis and treatment, thus reducing the burden as well as the adverse social and economic consequences of TB. The HEP in Ethiopia employs salaried staff and has continued to be productive for over a decade and a half. The HDA extension is on the other hand relatively new and relies heavily on volunteer women, raising issues of sustainability. The driving force for their active involvement needs to be investigated in terms of motivation. It was observed in Uganda, for example, that volunteer community health workers (CHWs) were actually participating with an expectation of future rewards (Kasteng et al., 2016). In contrast, a qualitative study from this region of Ethiopia suggested the current dominance of intrinsic motivators (such as community recognition and appreciation) among the HEWs and their supporters (Tulloch et al., 2015).

We detected 544 individuals with a positive cough screen among more than 24 000 screened. The overall prevalence of laboratory-confirmed TB was 139 per 100 000 population, much lower than the national prevalence of 277 per 100 000 population (95% CI 208–347) (Kebede et al., 2014). The prevalence of smear-positive pulmonary TB was also lower than in several previous studies in Ethiopia, including the national prevalence survey (Kebede et al., 2014; Berhe et al., 2013; Hamusse et al., 2017; Shargie et al., 2006b; Yimer et al., 2009; Tadesse et al., 2011), but higher than a report from southwest Ethiopia (Deribew et al., 2012). Direct comparison is difficult because of differences in study methodology, population, and time. More than 50% of all confirmed TB cases in the national survey had no cough but were identified through chest X-ray (CXR) screening (Kebede et al., 2014), a method not included in this study; chest radiography is not available at most health centres in Ethiopia and CXR is not routinely employed in the diagnosis of pulmonary TB. Ethiopia has overall shown a declining trend in TB in the last years (WHO, 2018).

We diagnosed 34 previously undetected cases of active pulmonary TB in just 4 weeks using a community-based ACF strategy. In contrast, only one pulmonary TB patient was identified by the routine passive case finding procedure in the same period in the study population. ACF has the added benefit of reaching those with limited access, the economically disadvantaged, elderly people, and those with poor health seeking behaviour (Yassin et al., 2013; Datiko et al., 2015). The routine TB diagnostic method in the health facilities, including at our study site, is smear microscopy, which is known for its poor sensitivity (Merid et al., 2009). Xpert MTB/RIF is being rolled out at many health centres in Ethiopia. This study used a combination of smear microscopy, Xpert MTB/RIF, and culture. Xpert MTB/RIF detected 94% of the TB cases, whereas smear microscopy detected only 38%. In the present study, the culture yield was much lower than expected (38%). This may be due at least in part to the loss of viability of *Mycobacterium tuberculosis* following repeated freeze and thaw of sputum samples due to power failures in the field during specimen storage and transportation to AHRI for culture.

TB prevalence rates are higher in men than in women globally (WHO, 2001) and this is true for Ethiopia as well (WHO, 2018). However, unlike in health facility-based passive case finding, the proportion of women with TB has increased consistently when community-based screening has been conducted in southern Ethiopia (Yassin et al., 2013; Datiko and Lindtjorn, 2009; Datiko et al., 2017), probably due to improved access by women who would otherwise have remained undetected. In a case–control study in communities where HEWs were employed in active case finding, the male to female ratio of TB cases changed from 1.3:1 to 1:1 following the intervention (Yassin et al., 2013; Datiko and Lindtjorn, 2009). The male to female ratio of 1:1.1 among newly diagnosed cases in the present study seems to further confirm the value of community-based health interventions in accessing the hard to reach pockets among the rural population.

In the multivariate analysis, a cough of ≥4 weeks was an independent risk factor associated with a TB diagnosis among persons with a positive symptom screen, while TB was less likely to be present among older persons (≥35 years of age) with a positive symptom screen. TB–HIV co-infection was not reported in our study and this could be related to the overall low prevalence of HIV infection in rural communities of southern Ethiopia (EPHI, 2015).

The low case detection rate remains a global challenge, with 36% of prevalent cases missing (WHO, 2018). Community-based TB activities are increasingly reported from several high burden countries. Ethiopia is strengthening surveillance and improving the diagnostic capacity (WHO, 2012) of the TB control programme with a rollout of Xpert MTB/RIF testing (Federal Democratic Republic Ethiopia Ministry of Health, 2016). In the experience reported here, the reach of the HEWs was extended deep into their communities through the engagement of HDAs. Symptomatic screening at the community level coupled with rapid diagnosis using Xpert MTB/RIF allows health system access to underserved rural community pockets more effectively. HEWs in Ethiopia are paid female professionals who bridge care and are extensively engaged in community service packages that link health with integrated development; they satisfy the three main principles recently proposed by Palazuelos et al., which are essential values for trust in the health system and a path to equitable outcomes of health coverage (Palazuelos et al., 2018).

In conclusion, this study identified a very high proportion of undiagnosed TB cases using volunteer women community workers in the rural community of Hawassa Zuria Woreda and allowed us to screen large communities (>24 000 persons) in a relatively short period of time with minimal costs. The use of volunteer community workers together with Xpert MTB/RIF has the potential to increase TB case detection, reducing the pool of undetected cases and curbing the transmission of TB in the rural settings of Ethiopia. Implementation and scale-up of this strategy could help LMICs increase case detection in rural settings.

Conflict of interest

None declared.

Financial disclosure statement

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Ethical approval

The study was approved by the institutional review boards of Addis Ababa University and the Armauer Hansen Research Institute (AHRI), as well as the Ethiopian National Ethics Review Committee. Study permission was also obtained from the Southern Regional Health Bureau, Zonal Health Department and the Woreda Health Office. Patients diagnosed with active TB were referred to their catchment health centre and hospital for treatment.

Author contributions

YM contributed to the conception and design of the study, acquisition of data and interpretation, and drafting and writing of the manuscript. YW, MA, and DD contributed to the design of the study and supervision and revision of the manuscript. TH contributed to data management and analysis. MH contributed to data analysis and revision of the manuscript. GH contributed to laboratory work. AA contributed to the design of the study and supervision, interpretation of data and revising the manuscript. All authors approved the final version of the manuscript.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2019.10.012.

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