Review Article

Active case-finding for tuberculosis in India

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ABSTRACT

Early identification of presumptive tuberculosis (TB) cases through active case-finding (ACF) would be an important complementary strategy to meet the national urgency in accelerating case detection to achieve the goals of 'End TB' strategy. ACF activities have yielded additional cases in different vulnerable groups in India. The yield of cases depends on the screening tool available, the characteristics of the high-risk population being screened, and most importantly, the linkage between effective diagnostic and treatment facilities. The ACF strategy could be both economically and epidemiologically relevant if it could bring down the level of transmission. This needs long-term research focusing on outcomes such as cases averted and reduction in the prevalence of the disease. Available evidence suggests that ACF is likely to be feasible in Indian settings but needs to be scaled up rapidly to create a good impact.

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INTRODUCTION

Globally, India accounts for one-fourth of the burden of tuberculosis (TB). India is among the six leading countries that contribute to 60% of new cases globally.[1] The 'End TB' Strategy calls for 80% reduction in incidence and 90% reduction in mortality of TB by 2030 compared with 2015.[2] Control of TB is currently dependent on three main strategies: (i) case-finding and treatment of TB; (ii) treatment of latent TB infection; and (iii) vaccination. Treatment of latent TB infection is not being widely done and vaccination has minimal impact on prevention of TB in adults. These two strategies have little impact on the incidence of TB in India. This leaves case-finding and treatment of TB as the principal means of control of transmission and reduction in the incidence of TB.[3,4] Passive case-finding (PCF) has been done over the years, where those with symptoms seek healthcare facilities. This method has its disadvantages as there may be delays both from the patient and the health system. Such delays may miss the diagnosis or result in delayed diagnosis, leading to increased risk of suffering, death and catastrophic economic consequences to the patient. These missed opportunities play a crucial role in sustaining transmission as it leads to longer periods of transmission, especially in populations with poor living and working conditions.[5]

A large pool of undetected cases exists in many high-risk and vulnerable groups. Barriers such as lack of awareness, lack of regular healthcare services and competing priorities for time and money make the healthcare facilities inaccessible to them. Strategies such as active case-finding (ACF), which address this issue of inaccessibility play a vital role in scaling up case detection rates in India.[2]

Project Axshya done in 300 districts among high-risk groups across India showed that ACF was able to efficiently detect a large number of presumptive and active TB cases by using community volunteers with proper training and supervision.[6]

The options available for active screening include symptom screening and chest X-ray. Cough for more than 2 weeks when used as a primary screening tool has a sensitivity of 56.2% and a specificity of 95.3%.[3] Chest X-ray as an initial screening tool has a sensitivity of 76.6% and a specificity of 97%.[3] Extensive literature reviews have found that ACF can reduce the burden of TB in terms of disease prevalence, incidence, mortality and morbidity.[5,7]

WHO recommends active screening among high-risk groups such as healthcare workers (HCWs), urban slum dwellers, contacts of patients with TB, prison inmates, miners, people with diabetes, smokers and HIV-positive individuals.[5] Chest X-ray among those who have cough for >2 weeks has a sensitivity of 66.8% and a specificity of 87.8%.[3] The choice of screening tool used for ACF varies across different vulnerable groups or settings and is also based on the available resources (Fig. 1).[5,7] We focus on the various ACF activities that have taken place across selected high-risk groups, the need for such ACF activities in these groups, and the benefits and challenges of ACF in India.

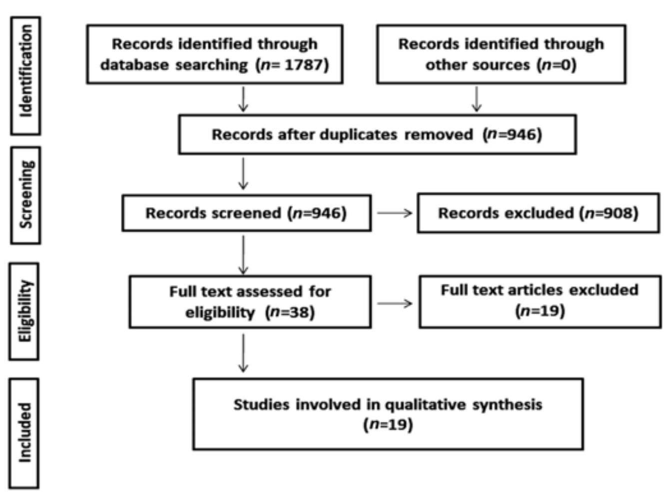

FIG 1. Framework for active case-finding among high-risk groups in India

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ACTIVE CASE-FINDING ACTIVITIES IN INDIA

Despite the increase in notification due to NIKSHAY, there is still a large undetected burden of patients with TB. All patients with chest symptoms especially those who have poor access to healthcare facilities do not seek healthcare.[6] In this scenario, ACF for TB remains an important integral part of TB control in high-risk groups. Table I shows the various ACF activities done in selected high-risk groups and their yield.

Urban slums

A study conducted using ACF strategy in Mumbai reported that 278 TB suspects were identified among 529 452 people. Among them, 33 patients were diagnosed with any type of TB[8] (Table I). An ACF study done among slum-dwellers of Puducherry reported that 1.5 person-hours were needed to identify a chest symptomatic and 94 person-hours (4 person-days) to detect a case of smear-positive TB (Table I).[15] Prasad *et al*. in a study done among slum-dwellers of Agra highlighted that all household members have to be screened for symptoms of TB to get a high yield of presumptive cases. In addition, mere referral for sputum examination was not enough and people need to be supported to reach the healthcare facility for sputum examination. They reported that only 40% of presumptive cases screened by ACF reached the health facility for testing on their own (Table I).[16]

Healthcare workers (HCWs)

Limited studies are available regarding ACF for TB among HCWs. A study conducted in Chandigarh provides information

TABLE I. Active case-finding activities across various high-risk groups in India

Author, year	Study design	Setting	Sample	Yield of TB cases
Household contacts				
Khaparde *et al*.,[9] 2015	A community-based, cross-sectional, implementation research study	Rural population in Chhattisgarh	1556 contacts (adults and children) 0–6 years: 226 7–14 years: 255 ≥15 years: 894	27 (1.7%) were found to have active TB disease, of whom 10 cases were the result of passive case detection through self-reporting to the health system prior to the implementation of this intervention and 17 cases were the result of household visits, thus attributing 63% TB cases detected. The diagnosis was based on sputum smear examination wherever possible, chest X-ray and Mantoux test according to the national guidelines
Singh *et al.*,[10] 2013	Cohort study	Periurban area of Delhi	1608 contacts of 432 index cases (adults and children); about 309 contacts were <12 years old (19.2%)	83 (6.8%) of 1206 contacts who could provide sputum samples were bacteriologically positive (culture by MGIT and sputum smear by AFB)
Gupta *et al.*,[11] 2016	Cohort study	District TB Centre, Kolhapur	Cohort of 521 contacts of 133 sputum smear-positive index cases (adults and children); 25% of these contacts were children 0–14 years old	Eighteen (3.45%) contacts were identified as presumptive TB; prevalence of TB among contacts was 1.15%, diagnosed by sputum smear for AFB and X-ray
Chatla *et al*.,[12] 2018	Cross-sectional study	RNTCP centres in Andhra Pradesh and Telangana	4771 contacts of 1602 MDR TB patients	Among 781 symptomatic contacts examined, 34 (4.4%) were bacteriologically confirmed (GeneXpert) to have TB. Among these 34 patients, 15 (44%) were diagnosed with rifampicin-resistant TB
Nair *et al*.,[13] 2016	Retrospective record review	Contacts of index case attending NIRT Clinic, Chennai	643 household contacts (adults and children) of 280 index TB patients were studied. About 36% of the contacts were <14 years old	29 of 544 (5.3%) contacts were found to have TB among whom 23 (79%) were sputum smear and culture positive, 3 were smear negative and culture positive and 3 were extrapulmonary diagnosed by national guidelines
Household contacts of MDR TB patients				
Bendle and Goyal,[14] 2015	Community-based cross-sectional study	District TB Centre, Wardha	259 contacts (adults and children) of 84 index MDR TB cases; 6% of contacts were <10 years old	13 presumptive TB cases identified; 6 new smear-positive TB cases identified (AFB test by Ziehl–Neelsen method)
Slum dwellers				
Chinnakali *et al*.,[15] 2016	Community-based cross-sectional survey	Urban slum of Puducherry	3564 adults (1695 males and 1851 females) from 1107 houses	203 presumptive TB cases identified, 3 identified as TB by sputum smear examination for AFB; Study stated that 1.5 manhours needed to identify a chest symptomatic, and 94 person-hours (4 person-days) to detect a smear positive TB case

TABLE I. Active case-finding activities across various high-risk groups in India *(contd.)*

Author, year	Study design	Setting	Sample	Yield of TB cases
Shrivastava and Shrivastava,[8] 2012	Community-based cross-sectional survey	Slums of Mumbai	529 452 population living in 124 710 households	278 presumptive TB cases were identified; 33 patients were diagnosed with any type of TB (27 sputum-positive TB; 3 sputum-negative pulmonary TB and 3 extra-pulmonary TB); diagnosis based on sputum smear examination wherever possible, chest X-ray and biopsy examination, according to the national guidelines
Prasad *et al*.,[16] 2016	Cross-sectional	4 slums in Agra city	21 187 population, living in 3940 households	382 persons with presumptive TB cases were identified; 7 persons were found to be sputum-positive for AFB
Dholakia and Mistry,[17] 2015	Cross-sectional	Migrant slum community in Mumbai	9000 from 1798 households (adults and children)	315 presumptive TB cases were identified; 7 adult TB cases were identified by sputum examination for AFB; 3 children tested positive for TST; 1 of 3 was started on treatment
Prison inmates				
Meundi *et al*.,[18] 2015	Cross-sectional	Prisons in Karnataka	2450 adult inmates in three prisons	81 presumptive TB cases were identified but none had confirmed TB
Prasad *et al*.,[19] 2017	Cross-sectional	210 prisons across 300 districts in 21 states of India	5093 adult inmates	1142 (19%) were identified as presumptive TB; 84% of the inmates underwent testing among whom 8% were found to be sputum smear positive
Mallick *et al*.,[20] 2017	Cross-sectional	Prisons in Chhattisgarh	16 199 adult inmates in 28 prisons	Sputum examination done among 1348 presumptive TB cases; 127 TB cases diagnosed (0.7%); 96 were smear-positive, 28 smear-negative pulmonary TB cases and 3 MDR TB cases
People with diabetes				
Mave *et al*.,[21] 2017	Prospective study	OPD for people with diabetes in Pune	630 adults with DM	18% had symptoms of TB but none had confirmed TB; 44 (7%) reported a prior TB history; of these, 5 (11%) reported prior TB within 2 years of diagnosis of DM, and 14 (32%) had the diagnosis 3 years after diagnosis of DM
Srinivas Rao *et al*.,[22] 2015	Prospective observational study	OPD for people with diabetes in Hyderabad	96 adults with DM	10.3% (10 patients) had positive TB symptoms; only one tested positive for TB by sputum smear examination
India Diabetes Mellitus–Tuberculosis Study Group,[23] 2013	Prospective observational implementation project	OPDs for people with diabetes in 4 tertiary hospitals across India	13 339 adults with DM were screened for TB	254 patients were identied with TB (from elsewhere and previous TB); 18 patients newly diagnosed with TB as a result of screening; sputum smear for AFB and X-ray used for diagnosis
Jali *et al*.,[24] 2013	Prospective observational pilot study	Diabetes centre, Belgaum	2072 adult patients were screened	2.7% were diagnosed with TB using sputum smear and X-ray as per national guidelines.
Healthcare workers				
Rao *et al*.,[25] 2004	Cross-sectional	Resident doctors in tertiary hospital in Chandigarh	470 resident doctors, 235 newly recruited doctors	9 were having TB—11.2 new cases per 1000 person-years of exposure 4 had TB over a period of 1 year: an overall incidence of 17.3/1000;TB was diagnosed by both radiological evidence and demonstration of mycobacteria on smear, culture or histopathological examination or by clinical response.
Homeless				
Dolla *et al*.,[26] 2017	Cross-sectional	Homeless population in Chennai city	301 homeless people in Chennai >15 years old	8% and 5.6% among 301 had symptoms suggestive of TB and X-ray abnormality suggestive of TB, respectively; 5 of 301 had microbiologically confirmed TB by sputum smear examination

MGIT mycobacteria growth indicator tube NIRT National Institute for Research in Tuberculosis TB tuberculosis AFB acid-fast bacilli MDR multidrug-resistant RNTCP Revised National Tuberculosis Control Programme TST tuberculin skin test OPD outpatient department DM diabetes mellitus about ACF for TB among HCWs. The study showed that among 470 resident doctors who were interviewed, 9 were suffering from TB, which is 11.2 new cases per 1000 person-years of exposure. Of these 9 doctors, 6 had extrapulmonary disease. Among 235 newly recruited doctors, 4 had TB over a period of 1 year, which is an overall incidence of 17.3/1000 person-years. An important finding was that extrapulmonary disease was more common than pulmonary TB among them (Table I).[25]

Prison inmates

Project Axshya, which was implemented in 300 districts across 21 states, studied 210 prisons in India. In this study, 5093 inmates were screened for TB, of which 1142 (19%) were identified as presumptive TB cases. Nearly 84% of the inmates underwent testing, among whom 8% were found to be sputum smear-positive. This ACF yielded an additional 80 TB patients who otherwise would have been missed in the existing system.[19] An ACF study done in Karnataka reported that among 2450 inmates in three prisons, there were 81 presumptive TB suspects and 10 were already on DOTS (directly observed treatment, short course).[18] Mallick *et al*. had reported that ACF activities conducted among 28 prisons in Chhattisgarh led to an increase of 39% and 38% in presumptive TB examination rate and TB case notification rate, respectively, among prison inmates (Table I).[20]

Homeless population

Studies estimating the burden of TB among the homeless in India are limited. A study done by Dolla *et al.* in Chennai city found the prevalence of TB among homeless to be 5/301 (1661/100 000 population) using ACF (Table I).[26]

People with diabetes

In a study done in Pune, no new TB cases were detected among patients with diabetes mellitus (DM), even when two-thirds of the DM patients had poor glycaemic control.[21] In another study done in Hyderabad, the authors reported that of 96 patients with DM screened, 10.3% (10 patients) had symptoms suggestive of TB. Of these, only 1 tested positive for TB.[22] Another study to ascertain the feasibility, outcomes and challenges for screening TB among people with DM was done across six DM clinics situated in tertiary hospitals in India. Over the screening period which occurred over three-quarters of the year, about 26% of 7218, 52% of 12 237, and 48% of 11 691 patients with DM were screened. A total of 254 patients were identified with TB, among whom 18 patients were newly diagnosed with TB as a result of screening and the remaining were patients already diagnosed elsewhere (Table I).[23]

Contacts

A study done in rural districts of Chhattisgarh reported that on an average, for every 11 households where screening for contacts was done, there was one case of active TB. They attributed 63% of additional cases to ACF. They also reported that 1 in 4 of the symptomatic contacts did not report to the Revised National TB Control Programme for sputum examination despite repeated counselling.[9] A study done in peri-urban areas of Delhi by Singh *et al*. concluded that 6.8% of the household contacts of patients with TB were diagnosed as active TB by the ACF strategy over a period of 4 years including 2 years of follow-up. The study showed that 84.6% of the prevalent cases and 70.9% of the incident cases were smear-negative and could be diagnosed by culture (Table I).[10]

NEED FOR SCREENING FOR TB IN SELECTED HIGH-RISK GROUPS

Slums

In many developing countries including India, rapid urbanization amidst lack of proper urban planning has resulted in increasing number of slums and informal settlements in many cities. Rates of transmission of TB are generally more in slums than in non-slum areas.[27,28] Secondary data analysis from the National Family Health Survey-3 showed that slum-dwellers were at a risk of having TB 2.4-times more than non-slum-dwellers.[29] Though the yield of ACF is on an average of <1% of TB cases (Table I), it is still a significant number taking into consideration the huge slum population in India. Similar results were reported from a study done in the slums in Bangladesh.[30] ACF for TB done in African countries—Uganda, Ethiopia and South Africa— had high yields ranging from 4% to 13%.[31–33] This could be because of the extreme burden of TB in such countries due to HIV transmission.

There is also evidence from Indian settings that despite repeated counselling sessions to undergo sputum examination among the high-risk population, a significant proportion do not undergo the examination at the field level. A study among slum-dwellers of Mumbai reported that 51.8% of the TB suspects did not go for sputum examination because their job timings clashed with the timings of the designated microscopy centres (DMC).[8] These factors need to be considered to design effective interventions such as using field-level diagnostics so that presumptive cases are not missed.

Healthcare workers

The annual risk of TB infection in India among HCW is 5%, which is more than three times the national average of 1.5%.[34,35] The incidence among resident doctors—11.2 new TB cases per 1000 person-years of exposure—is almost 10-times higher than the general population.[25] The probability of nosocomial transmission is expected to be high in India due to its large burden of TB.[36] In a prevalence study among 726 HCWs, 50% were found to have latent TB infection.[37] All these data suggest a high burden for TB in HCWs. A systematic review by Baussano *et al*. estimated latent TB infection among HCWs in high TB burden countries to be more than 100 cases per 100 000 persons.[38] The expected probability of HCW acquiring TB is large is India, with its high burden of TB and a large load of ‘open cases’ visiting hospitals. The transmission of TB in healthcare settings can be taken as a proxy measure for the overall infection control practices in the healthcare system.[39] Infection control measures, especially at the primary care level, are inadequate in India.[36] A retrospective study by Gopinath *et al*. estimated the annual incidence of pulmonary TB and extrapulmonary TB to be 0.35–1.80 and 0.34–1.57 per 1000 HCWs, respectively.[40] HCWs constitute a very high-risk group for TB, and unfortunately active screening for TB among HCWs is scarce in India. ACF provides a valuable opportunity to identify TB cases in one of the most vulnerable populations for TB infection in India.

Prison inmates

Overcrowding is common in Indian prisons.[20] The National Crime Records Bureau of India reported a total of 419 623 inmates as on December 2015.[41] TB is 23-times higher in prison inmates than in the general population. TB is also the most common cause of death among prisoners in developing countries.[19] ACF can identify a large number of presumptive TB cases—as high as 19%.[19] Ali *et al*. in Ethiopia did ACF and identified only 4.9% of TB suspects.[42]

Though prisons seem to be a 'closed' system, they have a high potential for transmission of TB in the community through staff in the prison, visitors, prison transfers, recidivists and also they are most likely to enter, leave and re-enter at a later date.[43]

Meundi *et al*. in their study of three Indian prisons, more than two-thirds of presumptive TB cases who consulted the prison medical officer did not find any relief for their symptoms.[18] This reveals the unmet need for medical care among prisoners. Similar findings were reported by Vinkeles Melchers *et al*. in a systematic review of TB screening in prisons, which stated that about 21% of all studies described the lack of a well-organized health system for prisoners.[44] All these facts support the identification and control of TB in prisons on priority.

Homeless population

The 2011 census reports that 26% of the homeless population in India is contributed by the five metropolitan cities—Delhi, Kolkata, Mumbai, Chennai and Bengaluru. TB estimates are 20-times higher in the homeless than the general population in many industrialized countries.[45] Studies in the USA found a high burden of TB in the homeless population.[46] A 5-year study based on autopsy findings done at Lady Hardinge Medical College, New Delhi, among homeless unclaimed people, revealed that 27% deaths were due to pulmonary TB.[47] Homeless populations are particularly recalcitrant to traditional TB control activities due to challenges with contact tracing, poor access to healthcare and lack of longitudinal follow-up. Evidence-based screening and treatment strategies should be developed to improve health outcomes in this population.

People with diabetes

DM increases the risk of developing active TB by two to three times. Patients with TB have delayed culture conversion and have higher risk of recurrence after treatment completion.[22,48,49] While it is feasible to screen TB among people with DM, the yield of active cases is very little. Jeon *et al*. reported that screening among patients with DM yielded active TB prevalence rates ranging from 1.7% in Sweden to 36% in Korea.[50] Nasa *et al*. identified 11 cases of TB by screening 213 patients with DM in the Republic of Marshal Islands.[51] Taking into consideration the low yield and large number of people with diabetes in India, there is a need to identify specific risk factors among them so that active screening could be done effectively.[21]

Contacts

Low-income countries with a high burden of TB do not have well-established contact screening programmes due to limited resources.[52] Even in countries with contact screening as a routine part of the programme, there are many challenges of implementation.[53,54] About 2.3% of pulmonary TB patients are detected by screening of close contacts in low- and middle-income countries.[55] Contact screening provides a high yield of active TB cases—6.8%. The yield for active TB cases in China ranges from 0% to 6.9%. China has a similar burden of TB as India.[56–58]

BENEFITS OF ACF

The impact of ACF on the incidence of TB has been proposed by various mathematical models. Murray and Salomon concluded that in combination with DOTS, ACF would yield enormous benefits in areas with a high burden of TB.[59] India has a high prevalence of TB and efforts which include ACF combined with the DOTS programme could avert millions of cases and deaths due to TB. The ACF strategy could be both economically as well as epidemiologically relevant if it could bring down the level of transmission of TB. The impact may not be evident in short-term research studies but long-term studies may be able to capture it. Modelling done by Azman *et al.* for ACF in three countries namely China, India and South Africa has reported that ACF for a period of 2 years would increase the yield of cases to 25% in the first year for diagnosis and treatment.[58] It reduced the average duration of untreated disease from 20 months to 17.3 months in India. This period of untreated disease is important as it is the high-risk period for transmission.[58] It could further avert 277 deaths among 1 million people over a period of 10 years. By early detection and management of undiagnosed TB through ACF, disease transmission will reduce and eventually bring down the disease burden when implemented effectively with other strategies. Also, every case averted represents a potential saving of cost of treatment for the health system.[6]

CHALLENGES FOR ACF

The cost and volume of activities involved in ACF are immense. Murray and Salomon have shown that this activity would be enormously useful in settings which have a lower case detection, high prevalence and moderate to high treatment completion.[59] The study concluded that interventions for only 2 years, not considering future effects, would underestimate medium-term impact over a period of 10 years by 85% in India.[58] There is a possibility to have high false-positive results during screening especially when the diagnostic test used has a suboptimal specificity. The proportion of false-positive TB cases is usually inversely proportional to the prevalence of TB.[4] ACF strategy screens high-risk groups at certain intervals. There are people who might become infectious between the screening periods and delay their health-seeking as they rely on regular screening. ACF can be effective only if PCF is strengthened through providing accessible diagnostic facilities and promoting positive health-seeking behaviour of the vulnerable population.[11]

CONCLUSION

Depending on PCF alone is insufficient to meet the ambitious TB elimination targets in India. Strengthening case detection is essential and a dependable strategy to combat the burden of TB in India till we find breakthrough disease prevention measures. With the available evidence, the ACF strategy is likely to be feasible in our settings but needs to be scaled up rapidly for a better impact. However, the cost of implementing ACF will be challenging. Ascertaining the effectiveness of ACF strategy on the long run depends on outcomes such as cases averted and reduction in prevalence and not on the number of cases found by ACF. Future studies must focus on generating evidence in these aspects, which will give more insight about ACF and its use in India.

Conflicts of interest. None declared

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