

Training program for tuberculosis (TB) patients to improve referrals of presumptive TB cases and sputum in Denpasar, Bali, Indonesia

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ABSTRACT

Background and purpose: Tuberculosis (TB) is a global health problem and one of the top ten causes of deaths in the world. TB case finding is an important component of TB control. In Indonesia, most case findings were done passively so that the referral coverage for TB sputum was lower than the target. This study aims to determine the effectiveness of training for TB patients as volunteers to increase the active referral of presumptive TB cases.

Methods: The pretest-posttest design intervention study was conducted in five public health centers (PHCs) which had the highest number of TB patients in Denpasar. The intervention was carried out for seven weeks (February-May 2020). A total of 35 TB patients, who were currently undergoing treatment at the PHCs, met the study criteria and willing to volunteer, were trained through meetings, discussions and demonstrations about the risk of TB transmission, contact investigations and how to collect sputum samples. Before and after the interventions, data on volunteers' knowledge, the number of presumptive TB and sputum referrals by

volunteers were collected through interviews and daily records. A regular reminder was sent in the form of a WhatsApp message once a week. Bivariate data analysis was performed with Chi-square and Wilcoxon Signed Rank Test.

Results: Volunteers' knowledge scores increased significantly after training, with a median score of 13.0 to 15.0 ($p < 0.001$), and there was a significant difference in knowledge improvement among those who actively responded to regular reminders compared to those who were less active ($p = 0.002$). A total of 31 presumptive TB cases were successfully referred during the study period (7 weeks). Volunteers managed to refer as many as 30 sputum preparations with good quality, but no positive sputum was found.

Conclusion: Recruitment and training of TB patients as volunteers can increase the knowledge and skills of volunteers to identify and refer presumptive TB cases and quality sputum samples. More TB patients should be trained as volunteers with a longer observation time to increase TB patient detection.

Keywords: tuberculosis, active case finding, sputum referral, TB patients as volunteers

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INTRODUCTION

Tuberculosis (TB) is a global problem and is among the top ten causes of deaths in the world with 1.3 million deaths annually.¹ The World Health Organization (WHO) estimated there were as many as 6.4 million new cases in 2017 and Indonesia is listed as one of eight countries contributing two-thirds of the number of cases.¹ The Indonesian Ministry of Health (MOH) reported that there was an increase in the number of TB cases from 446,732 in 2017 to 566,623 in 2018.² During that year TB caused a loss of \$12 billion from the global economy.³ In addition, TB also had a negative impact on the social life of patients because of the stigma and discrimination.⁴

In 2008, WHO reported the global detection of TB cases with positive acid resistant bacteria (*basil tahan asam* (BTA) or known as case detection rate (CDR) of 61% which was below the target of 70%.⁵ While the CDR for Indonesia in 2018

was 67.2%,² Bali was being the province with the second lowest CDR of only 29.5%.⁶ Case finding is an important component of a TB control program. The main strategy in TB control programs is to prevent transmission by optimizing case finding and treating patients until they recover. WHO recommends the need to improve case detection by carrying out case finding among TB contacts.⁷

Case finding in Indonesia is mainly carried out passively for patients who come to health facilities, while active case finding among the high risk groups who have close contact with TB patients has not been optimally conducted.^{2,8} The weakness of passive case finding is the potency of under-reported since the health workers have not reached TB patients in the community who do not come to the health facility. Several intervention studies showed a significant increase in TB case finding when active case searches were carried out through home visits by health workers (doctors, nurses, laboratory workers), counselors and community

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health workers or cadres.⁹⁻¹⁷ Challenges which often occur with active case finding are including the lack of frequency of home visits, inadequate resources, inaccurate diagnostic tools, low participation of contacts during visits due to lack of TB knowledge, fear and stigma in society.^{18,19} To date, there is no previous studies involving TB patients as volunteers for active case finding in Indonesia, while some studies were conducted outside Indonesia, which may not necessarily suitable for Indonesian conditions. Additionally, low awareness about TB, fear and shame due to stigma may become several considerations of the increase need to engage TB patients as volunteers to improve active case findings.

In Indonesia, an active case finding program among at-risk populations has been regulated under the Regulation of the Minister of Health of Indonesia Number 67 Year 2016.⁸ In 2017, the Ministry of Health (MoH) launched the “knock on the door” programs to increase case findings which was simultaneously implemented throughout Indonesia. This activity in the form of door-to-door screening by cadres to refer presumptive TB cases did not succeed in increasing TB case detection.²⁰ Subsequently, the MoH has also initiated a family approach for the 2018 Healthy Indonesia Program (*Program Indonesia Sehat dengan Pendekatan Keluarga/PIS-PK*), where TB is part of its priorities, however until now case finding is still low.²¹

So far, TB contact tracing has only been carried out by health workers and cadres without involving TB patients themselves,²² hence, access to close TB contacts has become more difficult because of the stigma against TB patients. If case finding is carried out by TB patients who have received treatment, it may become more effective since it is likely to reduce stigma, and increase empathy and acceptance of both TB screening and testing.²³ A study in the Congo reported its success in increasing TB case finding by training people who have a history of TB or a family member suffering from TB as a volunteer.²³ Nevertheless, the situation in the Congo is not entirely the same as Indonesia, so the effectiveness of using volunteers is also unknown. This study aims to determine the effectiveness of training for TB patients as volunteers to increase the active referral of presumptive TB cases to public health centers (PHCs) in Denpasar, Bali. In addition to treatment, the PHCs are also conducting early detection of presumptive TB cases in collaboration with cadres, independent general practitioners, private clinics and hospitals.

METHODS

This pretest-posttest design intervention study

was conducted in Denpasar, Bali. The study involved TB patients in five PHCs with the highest number of TB patients, out of 11 PHCs available in Denpasar City, namely West Denpasar I PHC, West Denpasar II PHC, East Denpasar I PHC, North Denpasar I PHC and North Denpasar II PHC. The number of volunteers recruited in this study was calculated from the estimated increase of TB case findings after intervention. The average number of TB confirmed cases for one month at the five PHCs prior to the intervention was 24 cases resulting from 84 sputum referrals (the ratio was 1:3).²⁴ With this ratio, if the intervention is expected to be able to increase the number of TB cases by 30 samples, then the number of sputum samples submitted would be at least 105 samples. Assuming that one volunteer is able to refer 2-3 presumptive TB to produce one confirmed TB case, then 35 volunteers are needed.

Volunteers recruited were those who lived in Denpasar City, were >18 years old, had and could use mobile phones, were in good health and were cooperative according to the assessment of the TB program manager. Researchers visited five PHCs in turn and waited for TB patients coming to take the medicine, then asked their willingness to participate as a volunteer. Volunteers were asked to refer suspected TB cases or sputum to the PHCs, with the minimum criteria of having one of the TB symptoms, namely persistent cough or prolonged chills or coughing up sputum mixed with blood or shortness of breath or chest pain or weight loss, accompanied by a history of contact with a TB patient. After volunteer candidates were willing to participate, they were asked to sign an informed consent, record their characteristics, followed by pretest and training at the PHCs.

The interventions included a TB training package, provision of leaflets, sputum pots, referral cards, regular reminders, transport fees and incentives. Training was carried out collectively in each PHC for 30 volunteers, while for the five volunteers who were unable to attend those sessions, training was carried out individually. The training materials refer to the Indonesian Ministry of Health's TB Find and Treat Until Healed (*Temukan Obat Sampai Sembuh Tuberkulosis/TOSS TB*) flipchart²⁵ which includes the definition of TB, symptoms, risk of transmission, contact investigations, practice and discussion. At the end of the training, volunteers were provided with leaflets, sputum pots and referral cards. Two pots of sputum were given as sputum collection containers (morning and evening) and accompanied by a referral card as a sign that the referred contact was a volunteers' referral. Researchers monitored every week by sending a message via WhatsApp or SMS

containing “Mr/Ms, is there any sputum referred to the PHC?” and then they recorded the responses. Transportation fee of Rp 25,000 was given when the volunteers came to refer the sputum to the PHC with a photocopy of the ID card or family card belonging to the TB suspect. The collected sputum was taken to TB referral hospital by officers of the Indonesian Tuberculosis Eradication Association (*Perkumpulan Pemberantasan Tuberkulosis Indonesia/PPTI*) to be assessed for its quality by laboratory staff at the hospital and then checked with a Molecular Rapid Test (*Tes cepat molekuler/TCM*) machine. The amount of sputum examined were minimum of one ml in each sputum pot with a thick mucus sputum consistency. Once the examination result from the hospital was ready, volunteers were contacted by the researcher to come to the PHC. Incentive money of Rp 50,000 is given if the sputum referred by volunteers was found to be positive for TB.

Data collection was carried out by researchers

assisted by enumerators who were previously trained by the researcher. The researcher conducted a trial for the content and flow of the research so that it could be answered properly by the respondents. Data collection was conducted using questionnaires and forms through interviews at the PHCs, including socio-demographic characteristics (age, sex, education and occupation), length of TB treatment, history of having family or friends suffering from TB and knowledge of TB. Researchers also recorded volunteers’ responses to regular reminders, the number of referrals for presumptive TB and their sputum. Volunteers’ knowledge was measured using a questionnaire with 15 questions before giving the intervention and three weeks after the pretest. The difference in volunteers’ knowledge before and after the intervention was assessed with statistical tests using the Wilcoxon Signed Rank Test because the data were not normally distributed. The proportion of correct answers before and after training and knowledge based on socio-demographic characteristics and other variables were analyzed using the Chi-square test. The number of referrals for presumptive TB and sputum was analyzed descriptively. Baseline data was obtained from the 2019 Denpasar City Integrated Tuberculosis Information System (*Sistem Informasi Tuberkulosis Terpadu/SITT*), while the post intervention referrals’ numbers was obtained from the 2020 SITT and volunteers’ referral during the study period. This research has obtained an ethical clearance from the Ethics Committee of the Faculty of Medicine, Udayana University/Sanglah General Hospital on March 9, 2020, with number: 555/UN14.2.2.VII.14/LT/2020.

Table 1. Comparison of sociodemographic characteristics and TB related variables between volunteers and non-volunteers

Variable	Consented to be a volunteer		Did not consent to be a volunteer	
	n	%	n	%
Public Health Centers				
West Denpasar I	12	34.3	3	14.3
West Denpasar II	6	17.1	7	33.3
East Denpasar I	5	14.3	5	28.3
North Denpasar I	6	17.1	2	9.5
North Denpasar II	6	17.1	4	19.0
Age (years)				
18–44	23	65.7	16	76.2
≥45	12	34.3	5	23.8
Gender				
Male	17	48.6	15	71.4
Female	18	51.4	6	28.6
Education				
Diploma	9	25.7	2	9.5
High school	23	65.7	15	71.4
No school-elementary	3	8.6	4	19.0
Employment				
Employed	28	80.0	14	66.7
Unemployed	7	20.0	7	33.3
Length of time on TB treatment				
<2 months (intensive phase)	11	31.4	7	33.3
≥2 months (ongoing)	24	68.6	14	66.7
Family history of TB				
Yes	18	51.4	8	38.1
No	17	48.6	13	61.9
Total	35	100	21	100

RESULTS

Table 1 presents information on the comparison of sociodemographic characteristics and several other variables between consented and did not consented volunteer. The number of TB patients who were invited to volunteer was 56 and those who were willing to volunteer were 35, while 21 people refused to volunteer because they were unable to make referrals and were embarrassed if they were known to be suffering from TB. Of the 35 consented volunteers, the highest proportion was from patients at West Denpasar I PHC (34.3%), aged 18-44 years (65.7%), female (51.4%), high school education (65.7%), employed (80.0%), length of time on TB treatment ≥2 months (68.6 %) and had family history of TB (51.4 %). Meanwhile, of the 21 TB patients who did not consent to volunteers, the highest proportion was from patients at West Denpasar II PHC (33.3%), aged 18-44 years (76.2%), male (71.4%), high school

education (71.4%), employed (66.7%), length of time on TB treatment ≥ 2 months (66.7 %) and did not have family history of TB (61.9 %).

In Table 2, the knowledge of volunteers before and after the intervention is presented and statistical tests were carried out using the Wilcoxon

Signed Rank Test because the data is not normally distributed (KS, $p=0.001$). The IQR score of volunteers' knowledge before the intervention was 3 and became 1 after the intervention, signifying less dispersion. Median of the knowledge score was found to increase from 13.0 before intervention to 15.0 after intervention ($p<0.001$).

In Table 3, all correct responses by volunteers to the questions before and after training are presented. An increase in the proportion of volunteers who answered correctly after training was found for all questions, but a significant increase was found only in four questions ($p<0.05$).

Table 4 shows the comparison of the volunteers' proportion with knowledge increase based on

Table 2. Differences in volunteers' knowledge before and after training

Time of measurement	Knowledge			
	Median score	IQR	Z*	p
Before training	13.0	3	-4.819	<0.001
After training	15.0	1		

*Statistical analysis using *Wilcoxon Signed Rank Test*

Table 3. Proportion of correct responses by volunteers to the knowledge questionnaire before and after training

Statement	Proportion of volunteers providing correct information				p
	Before training		After training		
	n	%	n	%	
TB is a contagious disease caused by germs	32	91.4	35	100.0	0.077
TB germs can attack the lungs, glands, bones, brain and skin	29	82.9	32	91.4	0.232
The main symptom of TB is a persistent cough (both phlegm and without phlegm)	34	97.1	35	100.0	0.303
Other symptoms of TB are weight loss, decreased appetite and night sweats	32	91.4	34	97.1	0.314
Transmission of TB is through the air from the sputum of a TB patient who coughs	32	91.4	35	100.0	0.303
TB is transmitted through eating utensils, clothes or beds for TB patients	8	22.9	27	77.1	<0.001
In-house contacts of TB patients have a high risk for contracting with TB bacteria	31	88.6	34	97.1	0.164
Children, elderly people and smokers are very likely to contract TB bacteria	28	80.0	33	94.3	0.074
All TB patients should be tracked and visited to detect rapidly the possibility of transmission to close or household contacts	31	88.6	33	94.3	0.164
TB can be identified and treated through sputum examinations and X-rays	35	100.0	35	100.0	-*
The sputum collection of TB patients was carried out twice, namely in the morning after waking up and when they came to PHC	33	94.3	34	97.1	0.555
The correct way to expel phlegm is by taking 3 deep breaths, then jerking to remove phlegm from the lungs	23	65.7	33	94.3	0.003
Drinking warm sweet tea can make it easier to get rid of phlegm	17	48.6	33	94.3	<0.001
The correct phlegm to check for is thick mucus and yellowish or greenish white	25	71.4	35	100.0	0.001
TB can be cured with regular treatment	35	100.0	35	100.0	-*

*No statistics are computed because the value before and after were the same

several variables. The proportion of volunteers with increased knowledge was significantly differ based on their response to regular reminders, 93.3% of volunteers who were responded actively to reminder showed an increased knowledge, compared to 40.0% among those who were not responded actively ($p=0.002$). There are no statistically significant difference in the proportion of knowledge increased based on age, sex, education, occupation, length of

TB treatment and family history of TB ($p>0.05$).

In Table 5, the number of sputum examined at all five PHCs in seven weeks before the intervention was as many as 147 specimens and all of them were patients who came to PHCs (passive case finding). Meanwhile, after the intervention this number increased to 200 specimens, of which 30 specimens came from active referrals by volunteers and 170 specimens from those who came to the general polyclinic, aged care polyclinic and/or the HIV/AIDS clinic in PHCs. The percentage of positive sputum from the amount of sputum referred by PHCs was found to have decreased from 29.2% before the intervention to 19.4% after the intervention. There was no positive sputum from the sputum preparations referred by the volunteers.

For the comparison, the number of sputum examined in the six PHCs outside of study sites (South Denpasar I, South Denpasar II, South Denpasar III, South Denpasar IV, East Denpasar II dan North Denpasar III) at similar time to the seven weeks before the intervention was 100 specimens, which then also increased to 110 specimens at the seven weeks' time after intervention, and notably all of them were passive case finding of patients who came to PHCs. The percentage of positive sputum from those referred by PHCs was also decreased from 49.0% before intervention to 19.1% after the intervention.

The number of presumptive TB referred by volunteers was 31 people or an average of 0.86 presumptive TB per one volunteer. There were 30 presumptive TB who were tested for their sputum while one child aged 2.5-year-old could not expel the sputum. The number of potential presumptive TB found during the study period was 52 people, but only 31 presumptive TB were finally successfully referred. There were 21 presumptive TB who were

Table 4. Proportion of volunteers' knowledge increased based on socio-demographic characteristics and TB related variables

Variable	Knowledge				p
	Increased		Not increased		
	n	%	n	%	
Age (years)					
18–44	21	91.3	2	8.7	0.191
≥45	9	75.0	3	25.0	
Gender					
Male	14	82.4	3	17.6	0.581
Female	16	88.9	2	11.1	
Education					
Diploma	8	88.9	1	11.1	0.685
High school	19	82.6	4	17.4	
No school-elementary	3	100.0	0	0.0	
Employment					
Employed	24	85.7	4	14.3	1.00
Unemployed	6	85.7	1	14.3	
Length of time on TB treatment					
<2 months (intensive phase)	11	100.0	0	0.0	0.102
≥2 months (ongoing)	19	79.2	5	20.8	
Family history of TB					
Yes	16	88.9	2	11.1	0.581
No	14	82.4	3	17.6	
Response to reminders (regular reminder)					
Active (≥4 times)	28	93.3	2	6.7	0.002
Not active (<4 times)	2	40.0	3	60.0	

Table 5. Number of spu um referrals by PHCs and volunteers before and after the intervention

PHC	PHC referral in 7 weeks before intervention				PHC referral in 7 weeks after intervention				Volunteer referral in 7 weeks after intervention			
	Number of sputum referrals		TB reactive		Number of sputum referrals		TB reactive		Number of sputum referrals		TB reactive	
	n	%	n	%	n	%	n	%	n	%	n	%
West Denpasar I	26	18.0	10	38.5	22	12.9	6	27.3	7	23.3	0	0.0
West Denpasar II	53	36.0	15	28.3	48	28.2	9	18.7	3	10.0	0	0.0
North Denpasar I	25	17.0	7	28.0	19	11.2	6	31.6	7	23.3	0	0.0
North Denpasar II	26	18.0	4	15.4	40	23.5	6	15.0	7	23.3	0	0.0
East Denpasar I	18	12.0	7	38.9	41	24.1	6	14.6	6	20.0	0	0.0
Total	147	100.0	43	29.2	170	100.0	33	19.4	30	100.0	0	0.0

actually ready to be referred to PHCs but yet referred because they could not expel their sputum.

Most of the referred presumptive TB had family relationships (parents, husband or wife, children, brother or sister) with volunteers (74.2%) and lived in the same house (51.6%), while 25.8% did not have such relationships, 41.9% lived in the same neighborhood with volunteers and 6.5% did not live in the same neighborhood with volunteers. When the study ended, there were 21 presumptive TB who had not been referred due to several reasons including they could not expel sputum, there was stigma in the family or due to the impact of the Covid-19 pandemic situation.

DISCUSSION

Our study shows that volunteers' knowledge after the intervention is significantly improved compared to before the intervention. The median value of volunteers' knowledge score after training was found to be higher than before the training. It has been shown that training through meetings, discussions and practices on the risk of TB transmission, contact investigations and how to collect sputum can improve the volunteers' knowledge. In addition, providing training materials and leaflets may motivate volunteers to recall information provided during the training. These results are similar to those of several studies which showed that training increased the average patient knowledge about TB in the pretest/posttest in the intervention group.²⁶⁻³⁰

A significant increase in volunteer knowledge was found after being given regular reminders every week, while volunteers' knowledge based on age, sex, education, occupation and other variables was not found to have a significant increase. Volunteers who responded to regular reminders were more active in consulting researchers while the study was in progress than those who were less active. Regular reminders and information received in consultation with researchers likely led to increased knowledge as well as reminded volunteers to make referrals to PHCs. Researchers have not found a similar study looking at the association between regular reminders and increased knowledge of volunteers.

Our study shows that volunteers who tend to respond actively to regular reminders have better knowledge. Clary in Widjaja's research³¹ identified six general functions that underlie individual motivation, namely the value, understanding, social, career, protective, and enhancement functions. In our study volunteers were likely motivated by the understanding function, which involves a desire to learn new skills and value function by becoming involved in service out of a desire to help others.

In Denpasar City, sputum examination is mostly

done passively, for those who come to PHCs, while active case finding in the community is not routinely performed. Active case finding is only relying on TB cadres, but it has not been able to show optimal results. PHCs report that TB cadres have never been able to successfully refer sputum due to rejection by the suspects or their family. Meanwhile, TB patients as volunteers are able to detect TB and refer suspects especially in families who have close contact with TB sufferers. This is theoretically consistent with the concept of TB transmission that exposure in the form of close contact and the length of contact time with the source of infection is one of the stages of the natural history of TB.⁸ In our study, within seven weeks every one volunteer can refer at least one contact. This is far better than the achievements of TB cadres in increasing the coverage of sputum referrals for TB contacts. TB patients as volunteers can be an alternative to active case finding in the community other than through cadres or health workers.

Our study shows that the number of sputum referrals in PHCs has increased partially due to active sputum referrals by volunteers. Active case finding by volunteers was not easy because they were required to collect and refer two sputum samples for presumptive TB to the PHCs. In addition, the short research time of seven weeks and the Covid-19 pandemic situation had an impact on the data collection. One of the obstacles experienced by the volunteers were the presence of presumptive TB as many as 21 people who were actually ready to be referred to PHC but could not be referred because they were unable to expel the sputum. In addition, volunteers said that they were not confident and felt ashamed to refer suspects due to stigma in their society, and they did not dare to go to people's houses to collect sputum of presumptive TB during the Covid-19 pandemic. Although there are several obstacles in its implementation, this is an achievement made by volunteers because they have been able to carry out early detection and refer families who have close contact with TB patients.

The sputum quality assessment of the referred presumptive TB was conducted by laboratory staff at the TB referral hospital. In this study, none of the presumptive TB referred by volunteers went through re-tested sputum. Volunteers were found to have good performance because all the referred sputum preparations had good quantity and quality with a thick mucus consistency, although there was no positive sputum. The number of TB case findings depends on the high and low prevalence of TB in a region. The prevalence of TB in Indonesia in 2018 was 254-262 per 100,000 population,³ the notified and reported TB cases in Bali Province was 87.4 per 100,000 population³², and the notified and reported

TB cases in Denpasar City was 148.72 per 100,000 population.³³ The absence of positive sputum was probably due to the low prevalence of TB in the community so that it required sufficient sputum referrals in order to find the presence of positive sputum. TCM examination with the Xpert MTB/RIF method has been used as a means of diagnosing TB in Denpasar City because it has high sensitivity, the results of the examination can be found in less than two hours and is also used to determine the results of drug resistance.³⁴ The absence of positive sputum may also be related to the concentration of TB bacteria and a person's immune system. The higher the number of bacteria in the sputum and the lower the immune system, the greater the chance that positive sputum will be found on lab examination of TB cases.⁸ The weakness of this study was that it did not make proximity criteria as a guide for volunteers and did not measure contacts in more depth to see their suitability as close contacts of TB cases.

The referral outcome of sputum by volunteers in our study was found to be lower than that of a similar study in the Congo at seven weeks (0.86 vs 1.4 sputum per volunteer). Study in Congo showed within 3 years as many as 1,713 volunteers managed to screen 650,434 suspects and referred 50,368 suspects to check sputum in clinics. This means that each volunteer can refer 29.4 presumptive TB within three years. The group of volunteers who carried out continuous case finding within the study period of three years were able to refer more presumptive TB than the group of volunteers who did not carry out continuous case finding. There was an overall increase in the rate of TB suspects referred to the clinic between the first and fourth trimester within three years.²³

Our study was very limited in terms of the scope of study, length of study and the number of volunteers, but the amount of sputum referred in the first two weeks (9 people) had increased in the second two weeks (16 people). This number has decreased in line with the start of the Covid-19 pandemic. Based on these results, increasing the number of volunteers and extending the study period, may provide an equal opportunity to increase the number of presumptive TB referrals through the active case finding method by volunteers. Another limitation of the study, the validity and reliability tests were not carried out to assess knowledge instruments. Because knowledge was not the main interest in this study, but we conducted a pilot test of the content and flow of the instruments, so that it could be properly responded by the respondents.

CONCLUSION

TB patients can be recruited as volunteers for sputum

referrals between active contacts. Recruitment and training of TB patients as volunteers can increase their knowledge and skills to identify and refer presumptive TB. In addition, volunteers in our study were able to actively increase referral for sputum with good quality. The number of TB patients trained as volunteers needs to be increased and with a longer observation time to increase number of referrals which will improve TB cases detection. The measures and strategy to reduce ashamed feeling due to stigma in TB patients needs to be emphasized in the future training for volunteers to reduce potency of barriers to refer presumptive TB and sputum.

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AUTHOR CONTRIBUTION

PAMA designed and conceived the study, collected and analysed the data, wrote the first draft of the manuscript and edited the manuscript. **DNW** and **AASW** were involved in the design and conception of the study, provided feedback and edited the manuscript.

CONFLICT OF INTEREST STATEMENT

None declared

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