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A Survey on Undiagnosed Active Pulmonary Tuberculosis among Pregnant Mothers in Mekelle and Surrounding Districts in Tigray, Ethiopia

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Abstract

Objective/Background—To determine the prevalence of undiagnosed active pulmonary tuberculosis (PTB) cases and sensitivity, specificity, and positive and negative predictive values of symptom combinations for undiagnosed TB infection in human immunodeficiency virus (HIV)-positive and HIV-negative pregnant mothers attending antenatal care (ANC) clinics. Mycobacterium TB and HIV are the leading causes of death among women of reproductive age worldwide. Symptom screening is the final step in the World Health Organization (WHO)-recommended TB intensified case finding algorithm for people living with HIV. However, the symptom-based PTB screening method for pregnant mothers is suboptimal and needs further optimization as some of the symptoms are obscured by the physiological changes during pregnancy.

Materials and Methods—This was a cross-sectional study, which was conducted from June 2014 to May 2015 at 16 public health institutions in Mekelle and its surrounding areas. All pregnant mothers who visited the maternity clinics for routine ANC follow-up examinations were screened for PTB symptoms. Those who had at least 2 weeks of cough, in addition to other symptoms, were enrolled in the study. Sociodemographic and clinical data and sputum samples were collected by midwives and nurses. The sputum samples were shipped to the Tigray Regional Laboratory and stored at -80°C until TB culture was performed.

Results—Between June 2014 and May 2015, 9600 pregnant mothers were screened for PTB symptoms. We collected 174 sputum samples from pregnant mothers who had 2 weeks of productive cough. The participant's median age was 27.5 years (interquartile range, 24–31 years). During enrollment, 604 (6.28%) participants were HIV seropositive. Among the HIV-positive mothers, 17 (38.1%) were informed about their HIV status when they visited the health institutions

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Conflicts of interest

There are no conflicts of interest.

for ANC follow-up, whereas the remaining 27 (61.9%) were already on antiretroviral therapy. All sputum samples ($n = 174$) were cultured using Löwenstein–Jensen medium at the Tigray Regional Laboratory. One of the 174 sputum samples was positive (+1) in Ziehl–Neelsen staining technique, and none of them was TB culture positive. During the study, at all study sites, no pregnant mother was even presumptively diagnosed and treated for TB during the routine ANC services.

Conclusion—Although the survey did not find any active PTB case among pregnant mothers, we identified 174 PTB-susceptible cases during the routine ANC services. Therefore, it was concluded that the integration of the WHO-recommended four-part symptom-based intensified case finding as one of the core components of ANC services can enhance the early detection of PTB, especially in high TB-burden countries.

Keywords

Human immunodeficiency virus; intensified case finding; pregnant mothers; pulmonary tuberculosis

Introduction

Tuberculosis (TB) is a significant contributor to maternal mortality worldwide.^[1–5] TB in pregnancy is best described as a double-edged sword; one blade being the effect of TB on pregnancy and the pattern of growth of the newborn and the other being the effect of pregnancy on the progression of TB.^[1, 4] Frequent and consecutive pregnancies may also promote TB infection because they stimulate the reactivation of latent TB and recrudescence.^[5–7] Furthermore, studies have also shown that the prevalence of undiagnosed active pulmonary TB (PTB) is higher in human immunodeficiency virus (HIV)-positive than in HIV-negative pregnant mothers.^[1, 3, 4, 8] TB in pregnant mothers has more public health importance because, besides the risk of mortality and morbidity for themselves, it also affects their pregnancies and their children as mothers have close contact and intimacy with their children and the whole family.^[8–10]

One of the targets of the millennium development goals is to reduce maternal mortality rate by 75% in the year 2015. However, it is difficult to achieve this unless due attention is given to the contribution of PTB-related maternal mortality and morbidity,^[11] as maternal mortality and morbidity by TB are responsible for 15% of all maternal mortalities in high HIV-prevalent settings and for 15%–34% of indirect obstetric maternal mortality.^[12]

Despite all these facts, TB case notification rates in Sub-Saharan African countries in pregnant mothers are very low.^[8] This may be due to the poor performance of World Health Organization (WHO)-recommended symptom screening algorithm to identify PTB in pregnant mothers and poor awareness of health personnel about hindrance of the TB symptoms during the pregnancy. This highlighted that although the WHO optimized the symptom screening algorithm for its sensitivity and negative predictive value in HIV-positive persons, it also needs to validate the algorithm in HIV-positive and HIV-negative pregnant mothers [Figure 1].

In Ethiopia, no study has assessed the burden of PTB in pregnant mothers; as a result, the maternal mortality and morbidity rates due to PTB and predictive value of the WHO-recommended symptoms are not well documented. A study in Gondar by Martha *et al.*, presented at TRAC Conference in March 2013, recommended that HIV-positive individuals who have even single symptoms should be considered and followed up closely.

Therefore, the antenatal care (ANC) service gives an excellent opportunity to look at and manage PTB among pregnant mothers as well as to evaluate their HIV status. In Ethiopia, the ANC provision services are rapidly growing, and therefore, almost all urban and semiurban resident pregnant mothers visit ANC at least once during their pregnancy period. This opportunity is well used for HIV prevention and control programs, especially mother-to-child transmission. Therefore, the main objective of this study was to determine the burden of undiagnosed PTB and to assess the ability of the WHO-recommended symptoms to detect PTB in pregnant mothers.

Materials and Methods

A cross-sectional study design was used to determine the prevalence of undiagnosed active PTB cases in pregnant mothers and the effects of pregnancy and pregnancy–HIV coexistence on the predicting ability of the WHO-recommended four-part symptom screen to identify active PTB through active case finding among pregnant mothers attending the antenatal clinics from June 2014 to May 2015.

Sociodemographic and associated risk factor data

Sociodemographic characteristic and clinical data, including cough, fever, night sweating, and weight loss of the participants, were collected using pretested and structured questionnaires. The questionnaires were administered by trained nurses and midwives working at the antenatal clinics of each study site.

Collection and handling of sputum specimen

Three consecutive sputum samples (spot–morning–spot) were collected using sterile wide-mouthed plastic leak-proof container from all enrolled study participants. These three sputum samples were transported, pooled, and stored (-80°C) at the Tigray Regional Laboratory. The stored sputum was thawed and processed for TB culture.

Tuberculosis culture

After homogenization and decontamination, the sputum samples were cultured and incubated at 37°C on conventional Löwenstein–Jensen egg medium at the Tigray Regional Laboratory. To check the quality and reproducibility, each sample was cultured 2 times. The tubes were checked once a week for *Mycobacterium* growth.

Data analysis

Data were entered into and analyzed using SPSS Inc. V.17, USA, Chicago and checked for inconsistencies and completeness. Descriptive analysis was performed and results were reported. The proportions were stratified by HIV status, and continuous data were presented

as median and interquartile range (IQR) for the various subcategories related to TB symptom screening in each group.

Ethical consideration

Ethical approval was obtained from the College of Health Science, Mekelle University, and Tigray Regional Health Bureau Research Ethics Review Committees. Participants were enrolled in the study after they had been informed about the purpose of the study and signed the written informed consent.

Results

Between July 2014 and May 2015, 9600 pregnant mothers, 604 (6.3%) HIV seropositive, were screened for PTB at the ANC clinics of the 16 health institutions. Of the total pregnant mothers, 201 who had 2 weeks of cough were included in the study. Of the sputum samples collected from these 201 mothers, 27 were not processed for TB culture because of poor sample quality. The remaining 174 participants (174 samples) who had complete data were included in the analysis. As much as 99 (57%) participants were urban residents and their median age was 27.5 years (IQR, 24–31 years). The educational background of the study participants was as follows: Illiterate, 43 (24.7%); can read and write, 46 (26.4%); primary education, 41 (23.6%); secondary education, 31 (17.9%); and tertiary education, 13 (7.5%). The majority of them (75 [43.4%]) were homemakers and only 12 (6.9%) were HIV positive [Figure 2].

All participants had known their HIV status; 44 (24.9%) and 130 (75.1%) participants were HIV seropositive and HIV seronegative, respectively. Among the HIV-positive participants, 17 (38.1%) were informed about their HIV status when they visited the health institutions for ANC follow-up, whereas the remaining 27 (61.9%) were already on antiretroviral therapy; 41 (23.6%), 46 (26.4%), and 39 (22.6%) participants were in their first, second, and third pregnancies, respectively, with the majority of them (74 [42.4%]) being in the second trimester. Though it was not statistically significant, there was a variation in the duration of cough between HIV seropositive and seronegative, 110 (63.14%) and 64 (36.76%) for 2–4 weeks and 1–6 months respectively. However, cough among HIV-positive individuals (57%, $P=0.04$) was significantly higher than that among HIV-negative individuals (13%, $P=0.36$). Breathing problem was also reported by 92 (52.8%) study participants, but there was no significant difference between HIV-seropositive and HIV-seronegative participants. By contrast, there was a significant difference in night sweating between HIV-seropositive and HIV-seronegative participants (73.3%, $P=0.041$) and the peak duration reported was for 1–2 weeks. Fever (75 [43.1%]), failure to gain weight (20 [11.5%]), chest pain (97 [55.7%]), and weakness (146 [83.9%]) were also reported by participants. However, there was no significant difference between HIV-seropositive and HIV-seronegative participants [Table 1].

More importantly, at each study site, to check the reproducibility of our results, we assessed a 1-year record of TB treatment centers retrospectively from the date of commencement of our research to check whether there were any active cases of TB that remained undiagnosed in pregnant mothers.

Discussion

In this active TB finding survey, which used the WHO-recommended TB symptom screening methods, 201 TB suspected patients were identified from 9600 pregnant mothers over a period of 12 months. Participants were enrolled in the study if they presented with a minimum of 2 weeks of productive cough regardless of their other symptoms. The study also determined, though not included in the analysis, that there were a large proportion of pregnant mothers, 288 (3%), with a cough <2 weeks and that antibiotics (amoxicillin) were prescribed for those who had a cough for 3 days or more.

Despite the fact that Ethiopia is one of the 22 high TB-burden countries, surprisingly, in this study, no active TB cases were found among the pregnant mothers and this was consistent with the study conducted in Kenya by Kosgei RJ *et al.*^[12] However, in another report from South Africa,^[6] the prevalence of PTB among pregnant mothers was relatively higher than that reported in this study. The possible reason for this disparity might be due to the difference in the prevalence of HIV infection between the two communities. Another contradicting result was also reported from a study conducted in Tanzania, which showed that the prevalence rates of latent TB, active PTB, and coinfection with HIV among pregnant women were higher with direct implications on the increased incidence of neonatal TB;^[7, 11, 13–15] however, our study did not assess the prevalence of neonatal TB.

The proportion of the four symptoms between HIV-seropositive and HIV-seronegative patients was determined. Cough (57%, $P=0.04$) and night sweating (73.3%, $P=0.041$) showed statistically significantly higher incidences among HIV-positive than among HIV-negative mothers. By contrast, the incidence of the shortness of breathing and weight loss did not show a significant difference between HIV-seropositive and HIV-seronegative mothers. The predictive values of the four-part symptoms to presumptively screen and identify active PTB cases were not determined as no active PTB case is found in this survey.

In Ethiopia, health-care service provision has significantly improved since the last 15 years. As a result, Ethiopia as a country achieved health-related millennium development goals ahead of the deadline. One of the reasons for this sustainable and dramatic achievement is attributed to the Ethiopian government's "Health Extension Program," which is a very innovative community-based health-care delivery system aimed at providing essential promotional and preventive health-care services at the grass-roots level. The program was introduced in recognition of the failure of essential services to reach communities in remote parts of Ethiopia. The reproducibility of our data was also trying to compare retrospectively (1-year record back from the date of our research's commencement) at each study site, and hence, no single pregnant mother was diagnosed positive for PTB. However, we believed that the low prevalence of PTB among the pregnant mothers might be the impact of this program.

Conclusion

Although the survey did not find any active PTB case among pregnant mothers, we identified 174 PTB-susceptible cases during the routine ANC services. Therefore, it was

concluded that the integration of the WHO-recommended four-part symptom-based intensified case finding as one of the core components of ANC services can enhance the early detection of PTB, especially in high TB-burden countries.

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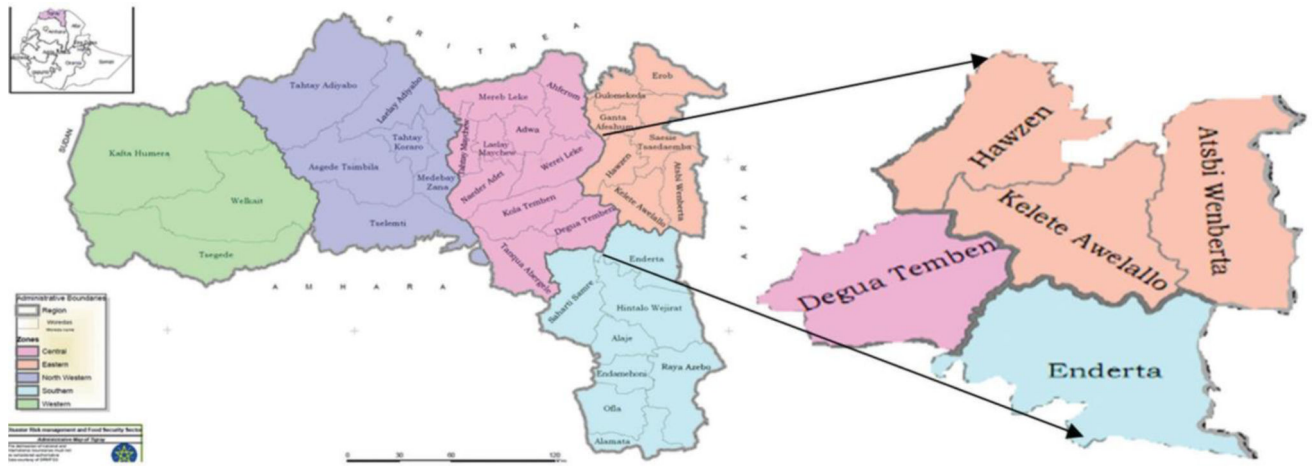


Figure 1.
Map of the study areas.

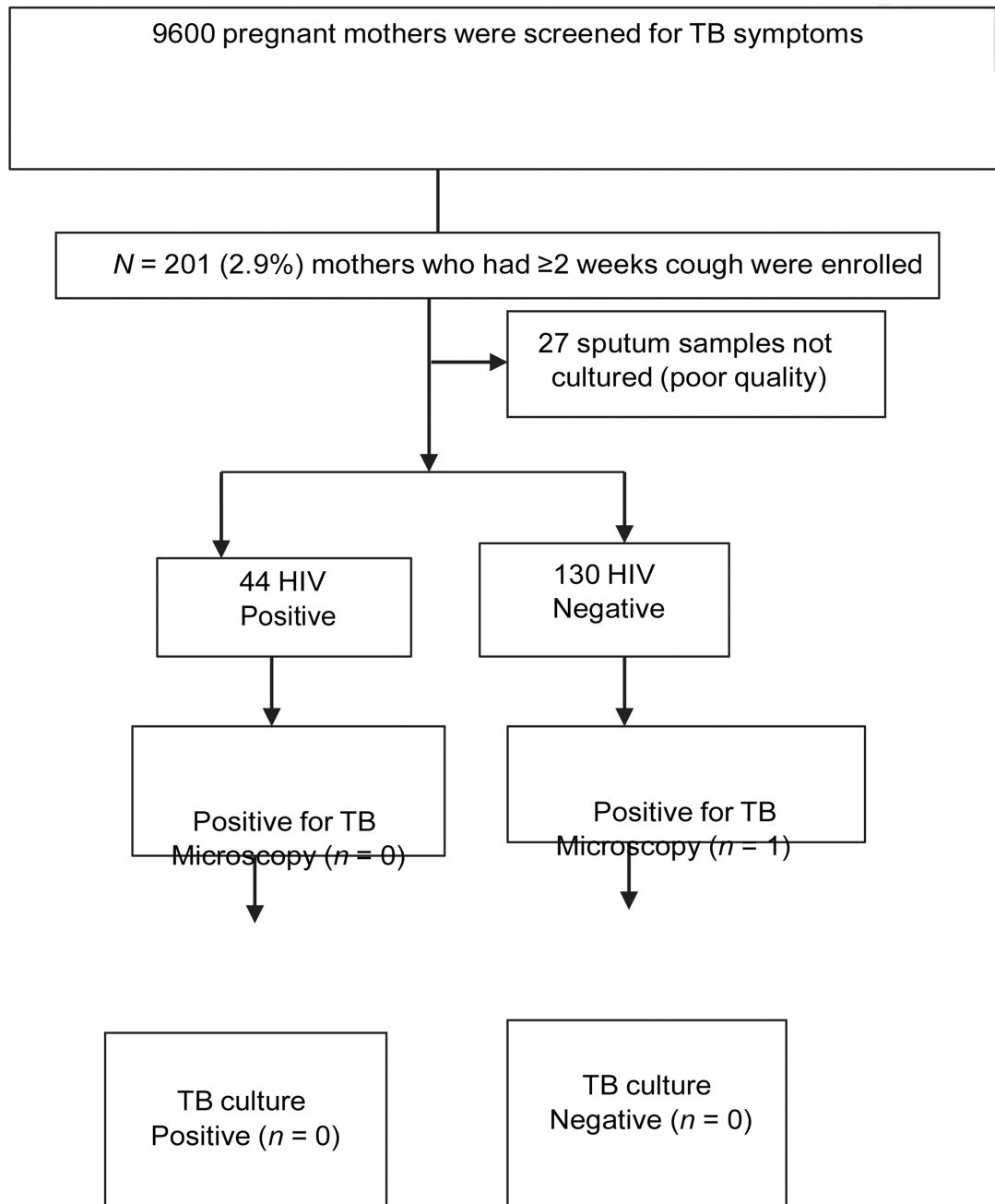


Figure 2. Results of tuberculosis symptom and laboratory screening of pregnant women in North Ethiopia, Tigray.

Table 1

Symptoms of tuberculosis in pregnant women who were positive on the tuberculosis symptom screen

| Symptom | HIV seropositive (n=44) | HIV seronegative (n=130) |
|------------------------|----------------------------|-----------------------------|
| Cough > 2 weeks | 44 (24.9) | 130 (75.1) |
| Fever | 75 (43.1) | 99 (56.9) |
| Failure to gain weight | 20 (11.5) | 154 (88.5) |
| A breathing problem | 92 (52.8) | 82 (47.2) |
| Chest pain | 97 (55.7) | 77 (44.3) |
| Night sweating | 128 (73.3) | 46 (26.4) |
| Weakness | 146 (83.9) | 28 (16.1) |

Data are presented as *n* (%).

HIV: Human immunodeficiency virus

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