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Symptom screen: diagnostic usefulness in detecting pulmonary tuberculosis in HIV-infected pregnant women in Kenya

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Objective: To determine the diagnostic usefulness of tuberculosis (TB) symptom screening to detect active pulmonary TB among human immunodeficiency virus (HIV) infected pregnant women in two PMTCT (prevention of mother-to-child transmission) clinics in western Kenya that are supported by the United States Agency for International Development–Academic Model Providing Access to Healthcare partnership.

Design: Cross-sectional study. Participants were interviewed for TB symptoms with a standardized questionnaire (cough >2 weeks, fever, night sweats, weight loss or failure to gain weight). Those with cough submitted sputum specimens for smear microscopy for acid-fast bacilli and mycobacterial culture. Women at >14 weeks gestation underwent shielded chest radiography (CXR).

Results: Of 187 HIV-infected women, 38 (20%) were symptom screen-positive. Of these, 21 had a cough for >2 weeks, but all had negative sputum smears and mycobacterial cultures. CXRs were performed in 26 symptomatic women: three were suggestive of TB (1 miliary, 1 infiltrates and 1 cavitary). Of 149 women with a negative symptom screen, 100 had a CXR and seven had a CXR suggestive of TB (1 cavitary, 2 miliary and 4 infiltrates).

Conclusion: This study did not support the utility of isolated symptom screening in identification of TB disease in our PMTCT setting. CXR was useful in identification of TB suspects in both symptomatic and asymptomatic women.

Despite the fact that tuberculosis (TB) is the most common opportunistic infection in persons living with HIV/AIDS (human immunodeficiency virus/acquired immune-deficiency syndrome), as well as a significant cause of maternal mortality and morbidity in this group, screening is not routinely done in PMTCT (prevention of mother-to-child transmission) settings.[1–4] This omission is likely related to clinician-perceived urgency in initiating antiretroviral therapy (ART), coupled with the challenges inherent in the screening process for active TB in HIV-infected pregnant women.

The challenges of PMTCT ART initiation have been well addressed, with the establishment of programs throughout the world. However, the challenges related to screening for TB remain unaddressed in any systematic approach. This population represents its own challenges: the non-specific nature of early pregnancy symptoms (such as frequency of malaise and fatigue) that can mimic early symptoms of TB;[2,5,6] the nature of pulmonary TB (PTB) disease in HIV-infected people, which often renders sputum smear microscopy (the most commonly available diagnostic tool in resource-limited settings) negative;[7] and the fear of use of chest radiography (CXR) in pregnancy due to concerns regarding radiation-induced teratogenicity.[5]

Symptom screening is recommended to identify TB suspects in HIV-infected populations,[8] including pregnant women,[9] but it has not been evaluated in HIV-infected pregnant women. The study populations of the two most recent published studies, Cain et al. and Corbett et al., were composed of HIV-infected adult patients but were not stratified with regard to pregnancy status.[10,11] Similarly, in a meta-analysis of observational studies there was no stratification based on pregnancy status.[8] As such these results may not be applicable to the HIV-infected pregnant population. In a PMTCT program in western Kenya, access to clinical laboratory services and CXR allowed for in-depth investigations into the role of symptom screening in HIV-infected pregnant women.

The aim of this study was to determine the diagnostic usefulness of symptom screening for TB in detecting active PTB among HIV-infected pregnant women in two PMTCT clinics in western Kenya. This was a descriptive analysis of women who were positive or negative on symptom screening to compare demographics, sputum results, CXR results and TB diagnosis.

METHODS

Study design

This was a cross-sectional analysis of data.

Setting

The study was carried out in two Government of Kenya PMTCT clinics, Eldoret and Busia in western Kenya, which are supported by the Academic Model Providing Access to Healthcare (AMPATH) partnership.[12–14] These two sites were chosen because they represented the busiest PMTCT programs in AMPATH (on average 30 patients each per month), both had access to a quality-controlled TB laboratory, were capable of smear microscopy and rapid culture (Mycobacteria Growth Indicator Tube), and both sites had functional CXR, with appropriate shielding for pregnant women. This study took place between 1 October 2009 and 28 February 2010.

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Participants and sample

Study participants were newly enrolled (i.e., ART naïve), HIV-infected pregnant women aged 15–49 years who attended the two selected PMTCT clinics. Those already on TB treatment at the time of enrolment or with a past history of isoniazid preventive therapy (IPT) were excluded. Convenience sampling was used at weekly clinic visits over the 5-month study period, enrolling all consecutive eligible women until the sample size was obtained (n = 187). Sample size was calculated using 12.5% as the expected prevalence of TB in HIV-infected pregnant women, with 80% power, yielding a sample of 187.[15]

Study procedure

All study participants were interviewed by the primary researcher regarding demographic variables and current symptoms: cough for >2 weeks, fever, night sweats, weight loss or failure to gain weight. The standardized symptom screen questionnaire used was developed and standardized in Kenya at multiple sites in the late 1990s, and has been used extensively in an intensified case finding program for TB in western Kenya. Although not specifically standardized for studies in HIV-infected individuals, its broad use in our region has provided staff with a degree of familiarity in its use.

Patients with a positive symptom screen that included the presence of cough were asked to supply two sputum specimens (one spot and one morning) to be sent for smear microscopy and TB culture. All smear microscopy and TB cultures were sent to the regional reference laboratory, which is ISO (International Organization for Standardization) 15 189 certified as adhering to international harmonization standards for good laboratory practice. Smear was performed on unconcentrated sputum. Specimens were pooled for culture. Women post 14 weeks gestation underwent shielded CXR with their permission. All CXRs were read by a single consultant radiologist.

Outcome variables

TB diagnosis was defined as confirmed if either smear or culture was positive, and presumptive if the CXR was interpreted as suggestive of TB (cavitary, miliary pattern or infiltrate). All patients diagnosed with either confirmed or presumptive TB disease were referred back to their care providers for management, according to the hospital protocols.

Ethics

The study had the ethical approval of the Moi Teaching and Referral Hospital/Moi University School of Medicine Institutional Research and Ethics Committee and the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease.

RESULTS

A total of 187 HIV-infected pregnant women attending our PMTCT clinics were included in the study, of whom 38 (20%) were symptom screen-positive. Their characteristics are summarized in Table 1. The mean age of the participants was 27 years. There were no significant differences in age, educational level, employment status, parity, CD4 count at enrolment or gestational age between patients with and without TB symptoms. Patients' HIV was not advanced, as shown by a mean CD4 count of >450 cells/μl in both groups.

Results of the diagnostic screening are shown in the Figure. Of the 38 patients with a positive symptom screen, 21 had had a cough for >2 weeks. Sputum samples were collected from those patients: all were TB smear- and culture-negative. CXR was offered to all women who were at >14 weeks' gestation. In the symptomatic group, 26 CXRs were performed, of which three were suggestive of TB (1 miliary, 1 infiltrative, 1 cavitary). Of 149 women with a negative symptom screen, 100 consented; of these, seven had a CXR suggestive of TB (2 miliary, 4 infiltrative, 1 cavitary).

TABLE 1 Characteristics of HIV-infected pregnant women screened for TB in a PMTCT program in western Kenya, 2009–2010

Variable	Positive symptom screen (n = 38) n (%) or mean ± SD	Negative symptom screen (n = 149) n (%) or mean ± SD	P value
Age, years	27 ± 6	27 ± 6	0.7
Educational level			
Primary	25 (66)	104 (70)	0.8
Secondary	8 (21)	27 (18)	
College/university	0	3 (2)	
Unknown	5 (13)	15 (10)	
Employed	6 (16)	27 (18)	0.7
Parity	3 ± 2	2 ± 2	0.3
CD4 counts, cells/μl	452 ± 246	497 ± 285	0.6
Gestational age, weeks	27 ± 7	26 ± 7	0.6

HIV = human immunodeficiency virus; TB = tuberculosis; PMTCT = prevention of mother-to-child transmission; SD = standard deviation.

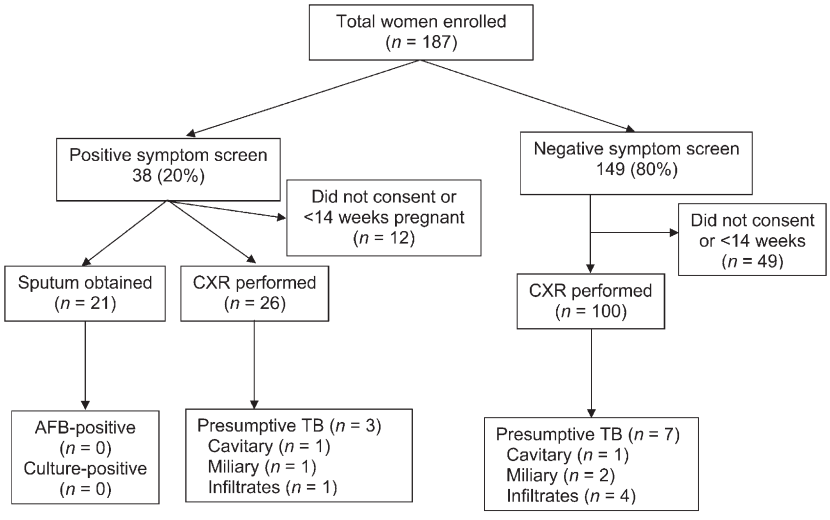

FIGURE Results of symptom screening for TB in HIV-infected pregnant women in a PMTCT program in western Kenya, 2009–2010. CXR = chest X-ray; AFB = acid-fast bacilli; TB = tuberculosis; HIV = human immunodeficiency virus; PMTCT = prevention of mother-to-child transmission.

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TABLE 2 Clinical details for 10 patients with chest radiographs suggestive of TB in a PMTCT program in western Kenya, 2009–2010

Chest X-ray	TB symptom screen	Age years	CD4 count cells/μl
Miliary	Positive	25	36
Infiltrate	Positive	35	499
Cavity	Positive	25	436
Infiltrate	Negative	23	179
Infiltrate	Negative	22	254
Infiltrate	Negative	39	232
Infiltrate	Negative	32	407
Military	Negative	27	315
Cavity	Negative	24	199
Military	Negative	36	373

TB = tuberculosis; PMTCT = prevention of mother-to-child transmission.

In all 10 patients with CXRs suggestive of TB (three with positive symptom screen and seven without), there was no correlation between symptoms and radiographic patterns, age and CD4 counts (Table 2). All 10 patients were evaluated by their care provider and initiated on TB treatment according to both national and AMPATH guidelines.

DISCUSSION

This study examined the utility of symptom screening in HIV-infected pregnant women combined with sputum TB smear, TB culture and CXR. The symptom screening tool failed to detect TB in this population. Of 26 symptomatic patients who underwent CXR, only three had abnormal CXRs consistent with TB and none had positive smears, while seven of 100 asymptomatic patients who underwent CXR were treated for TB.

This is a disappointing finding, as it was hoped that a questionnaire screening tool might assist in guiding targeting specific subpopulations for further TB screening in pregnancy. Reliance on TB symptom screening alone in HIV-infected pregnant women in our setting was thus not helpful in deciding who should receive the next level of TB screening (in our setting a CXR).

Our symptom screen findings are similar to those in a study of 370 HIV-infected pregnant women in a PMTCT clinic, Soweto, South Africa, also with high CD4 counts. That study discovered a similar rate of symptom screen-positive HIV-infected pregnant women; 120 (32%) were symptomatic by screen, and eight were diagnosed with TB by culture.[4] That study did not perform CXRs among symptomatic or asymptomatic women.

CXR did discover abnormalities in this patient population, in both symptomatic and asymptomatic individuals, and thus may be an important tool in this group. A limitation of this suggestion, however, is that these women could only be classified as presumptive TB, as no symptomatic women were confirmed by TB culture, and asymptomatic women did not undergo culture. This meant that sensitivity, specificity and predictive values could not be calculated.

This study suggests that reliance solely on symptom screening to diagnose TB in HIV-infected pregnant women in settings such as ours is insufficient for either making or ruling out a diagnosis of TB. The evidence from this study is that symptom screening in our setting needs to be coupled with CXR to access the need for drug treatment for TB disease or IPT. Further studies of both HIV-infected and non-infected pregnant populations with different TB burdens are required. A diagnosis of TB has outcome implications for both mother and child. The barriers intrinsic to studies in this vulnerable patient population should be addressed to design scientifically evaluated guidelines for their care.

A strength of this study is that symptom screening was applied in a standardized manner, under routine program conditions, that would be applicable to other PMTCT care programs. This study also had access to a quality-controlled TB laboratory, functional radiology units and a consultant radiologist. Finally, the observational study adhered to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.[16]

In conclusion, this study did not support the utility of isolated symptom screening in the identification of TB disease in our PMTCT setting. CXR was useful in the identification of TB suspects in both symptomatic and asymptomatic women. Given the profound risks of TB to the HIV-infected pregnant woman and her infant, further well-designed studies targeted at best TB screening practices in this specific population are needed.

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Objectif : Déterminer l'utilité diagnostique du dépistage des symptômes de la tuberculose (TB) pour la détection d'une TB pulmonaire active parmi les femmes enceintes séropositives pour le VIH dans deux polycliniques (PMTCT) de prévention de la transmission du VIH mère-à-enfant soutenues par le partenariat USAID–AMPATH dans l'ouest du Kenya.
Schéma : Étude transversale. Les participants ont été interviewés concernant les symptômes TB en utilisant un questionnaire standardisé (toux depuis >2 semaines, sueurs nocturnes, perte ou échec de gain de poids). Les femmes qui toussaient ont donné deux échantillons de crachats pour l'examen microscopique des frottis à la recherche de bacilles acido-résistants et pour la culture. Les femmes enceintes de >14 semaines ont subi un cliché thoracique (CXR) avec écran protecteur.
Résultats : Sur les 187 femmes séropositives pour le VIH, le dépistage des symptômes a été positif chez 38 (20%) ; parmi ces dernières, 21 toussaient depuis >2 semaines mais chez toutes les frottis et les cultures mycobactériennes des crachats se sont révélés négatifs. On a réalisé un CXR chez 26 femmes symptomatiques ; chez trois d'entre elles, le cliché a suggéré une TB (miliaire 1, infiltrats 1 et creusement 1). Sur les 149 femmes chez qui le dépistage des symptômes s'est avéré négatif, 100 ont subi un CXR et chez sept d'entre elles, le cliché a suggéré une TB (creusement 1, miliaire 2 et infiltrats 4).
Conclusion : Cette étude ne soutient pas l'utilité d'un dépistage isolé des symptômes pour l'identification d'une maladie TB dans le contexte du PMTCT. Le CXR s'est révélé utile pour l'identification des suspects de TB tant chez les femmes symptomatiques qu'asymptomatiques.

Objetivo: Determinar la utilidad diagnóstica de la evaluación sistemática de los síntomas de tuberculosis (TB) con el fin de detectar la TB activa en las mujeres infectadas por el virus de la inmunodeficiencia humana (VIH) y embarazadas que acuden a dos consultorios de prevención de la transmisión maternoinfantil del VIH, financiados por la Alianza USAID–AMPATH en el occidente de Kenia.
Método: Fue este un estudio transversal, en el cual se administró a las participantes un cuestionario normalizado (tos de >2 semanas de duración, fiebre, sudores nocturnos y pérdida de peso o imposibilidad de ganar peso). Las mujeres que refirieron tos aportaron muestras de esputo para baciloscopia y cultivo de micobacterias. Se practicó una radiografía de tórax (CXR) protegida a las mujeres con más de 14 semanas de gestación.
Resultados: En 38 de las 187 mujeres con infección por el VIH (20%), la detección de síntomas fue positiva. De estas mujeres, 21 refirieron tos de >2 semanas de evolución, pero todos los resultados de las baciloscopias y los cultivos de micobacterias fueron negativos. Se practicaron CXR en 26 mujeres sintomáticas y tres de ellas presentaron imágenes indicativas de TB (un aspecto miliar, un infiltrado y un caso con cavernas). De las 149 mujeres con una detección sintomática negativa, en 100 se practicó la CXR y siete presentaron imágenes en favor del diagnóstico de TB (un caso con cavernas, dos aspectos miliares y cuatro con infiltrados).
Conclusión: Los resultados del presente estudio no respaldan la utilidad de una detección exclusiva de los síntomas, con el fin de diagnosticar los casos de enfermedad TB en este contexto de la consulta de prevención de la transmisión maternoinfantil del VIH. La CXR se reveló útil en la detección de casos con presunción de TB en las mujeres sintomáticas y asintomáticas.

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