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Extrapulmonary tuberculosis among females in South Asia—gap analysis

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ABSTRACT

The percentage of extrapulmonary tuberculosis (EPTB) among new and relapse tuberculosis cases in South Asia (Afghanistan, Pakistan, India, and Bangladesh) ranged from 19% to 23% in 2014. While tuberculosis was reportedly more prevalent in males, a higher preponderance of EPTB was observed in females. National tuberculosis control programs are highly focused on pulmonary tuberculosis. This creates gaps in the surveillance, diagnosis, and study of EPTB among females, which is especially pronounced in the South Asian setting. We have reviewed recently published literatures from January 2010 to June 2016 reporting EPTB in females with a view to evaluate the current epidemiology, risk factors, diagnostic modalities, and treatment outcomes. We report significant gaps in the surveillance of EPTB among women in South Asia, emphasizing the need for greater focus on EPTB in females to overcome current surveillance and knowledge gaps.

Introduction

Globally, tuberculosis (TB) is among the top five killers of women aged 20–59 years [1]. While the proportion of pulmonary TB (PTB) notifications is higher among males worldwide, TB in females remains a major threat to control due to the impact felt by households, particularly children. It has been argued that the higher case notifications among males may reflect the barriers faced by the female population in accessing health care [2]. Extrapulmonary tuberculosis (EPTB) accounted for 15% of the new and relapse TB cases in 2014 [3]. In contrast to PTB, preponderance for EPTB is reportedly higher among females [4–6]. Irrespective of whether the underlying mechanism is biological, socioeconomic, or cultural, a deeper understanding of the risk factors, impact, access to directly observed therapy (DOT), as well as

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diagnosis of all forms of TB among females is necessary to devise effective control strategies. This is imperative as the millennium development goals, despite achieving progress, faltered in addressing gender disparity, in assessing impact of TB on maternal mortality, and/or indeed in TB control, especially in South Asia [5].

Among the South Asian countries, Pakistan, India, and Bangladesh are included in the category of high-burden countries for TB and MDR (Multidrug resistant) TB [6]. Although post 2015, Afghanistan is not included in high-burden countries; it has the second highest TB burden in World Health Organization's Eastern Mediterranean Region [3].

In keeping with the stalled progress of Millennium Development Goals 3, 5, and 6 (i.e., reducing gender disparity, decreasing maternal mortality, and decreasing the TB burden), efforts to control EPTB among women in South Asia need to be reassessed to identify the gaps in knowledge and/or services. In this review, we aimed at assessing the extent of gender disparity in EPTB in Afghanistan, Pakistan, India, and Bangladesh through researching published literatures over the past 6 years. We further sought to determine the organ systems affected and assess outcome data for EPTB in women available from South Asia, as well as evaluate the utility of diagnostic modalities used for EPTB in high-TB-burden countries of South Asian region. The search results are presented, and the resulting information gaps are highlighted.

Methods

Search strategy

A PubMed systematic literature search was performed for English-language articles related to EPTB among females in South Asia, published between January 2010 and June 2016. Unpublished and ongoing studies could not be explored in this review. We used the following terms in our search, individually as well as in various combinations: tuberculosis women, females, Pakistan, Afghanistan, India, Bangladesh, extrapulmonary, genitourinary, infertility, postpartum, placenta, Asherman syndrome, peritoneal, tubo-ovarian, and endometrium. Two independent reviewers (J.M. and Z.Y.K.) reviewed the titles, abstracts, and full-text articles, and selected potentially relevant studies based on inclusion criteria established prior to the literature search. Discrepancies arising between the reviewers were resolved by consensus in consultation with a third reviewer (R.H.).

Inclusion criteria

We included observational studies including case series, surveys, and descriptive cross-sectional studies focusing on EPTB and PTB among females in specified South Asian countries.

Exclusion criteria

We excluded all studies focusing only on diagnostic criteria, clinical trials on drugs, case reports or case series without details of EPTB and PTB, and articles focusing only on genetic analysis and nonhuman studies. Studies that were conducted in countries other than the specified countries of the Asian region were also excluded.

Outcomes of interest

Reported cases of EPTB among males and females, female:-male ratio (FMR) in reported studies, site of EPTB in females, and diagnostic modalities used for diagnosis of different types of EPTB were evaluated as outcomes in the review. We also reviewed studies on PTB published in the same time period, in order to compare between FMRs of EPTB and PTB.

Results

Search results and studies selected for review

A total of 31 studies on PTB and EPTB (published during 2010–2016) were selected for review. Among these studies, 11 presented data on PTB, 13 presented data on EPTB, while seven reported data on both PTB and EPTB. All seven studies provided proportions for both EPTB and PTB, but only two studies reported separate data on EPTB and PTB for both males and females [9,10]. Among the 20 EPTB studies reviewed, 19 studies reported on EPTB in females; 12 were from India, five from Pakistan, and one each from Afghanistan and Bangladesh. Among 18 studies reporting on PTB, one was from Bangladesh, eight were from India, and nine were from Pakistan.

The overall selection process and characteristics of the excluded studies are summarized in Fig. S1. Excluded studies are listed together with the reason for exclusion in the Table S1.

Study sample characteristics

All 19 studies on EPTB were conducted in health care settings (hospitals, clinics, diagnostic centers, etc.), and in 10 studies data were extracted from hospital records. Age ranges for patients in these studies varied from 15 years to 70 years. The total numbers of patients were 8,829 (ranging from a minimum of 37 to a maximum of 1,994) in these studies. Characteristics of the studies included in this review are summarized in Table 1.

Table S2 presents details of studies reporting on PTB, which were also reviewed for comparison of FMRs in PTB with EPTB. Compared with PTB studies, sample sizes were smaller for EPTB studies.

Types of EPTB among females

Six studies reported distribution of EPTB according to disease sites among females. Among these, only two studies reported various types of EPTB [20,11], while the other four [9,19–21] were based on gender-specific cohorts of women tested for or diagnosed with infertility. Of the two studies reporting on distribution by site, TB adenitis was the commonest form, followed by pleural TB, central nervous system TB, musculoskeletal (bone) TB, and abdominal TB.