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Research Article

A Situational Analysis of Screening and Treatment of TB in Pregnant Women across 5 Countries

Hala Jassim AlMossawi[1], Neeraj Kak[1*], Amy Studenic[1], Alexander Moran[1], Colleen Longacre[1], Soy Ty Kheang[2], Paul Daru[3], Esty Febriani[4], Cecile Lagrosa[5], Carmina Aquino[5], Thein Thein Htay[6]

[1] University Research Co., LLC, Chevy Chase, MD, USA; [2] University Research Co., LLC, Phnom Penh, Cambodia; [3] University Research Co. LLC, Dhaka, Bangladesh; [4] Lembaga Kesehatan Nahdlatul Ulama, Jakarta, Indonesia; [5] Center for Health Solutions and Innovations, Manila, Philippines; [6] Formerly with the Ministry of Health and Sports, Yangon, Myanmar

ABSTRACT

Background: Tuberculosis (TB) is the third leading cause of death among women of reproductive age, and undiagnosed TB among pregnant women can result in poor outcomes for both women and their children. Therefore, it is essential for National Tuberculosis Programs (NTPs) to strengthen their policies and guidelines addressing TB in pregnant women and adopt more efficient screening practices. The purpose of this situational analysis is to identify key approaches to addressing TB in pregnancy and to identify barriers and recommendations for the integration of TB and Antenatal Care (ANC) services.

Methods: We conducted an initial desk review of the existing literature and recommendations from international organizations on global strategies to address TB among pregnant women. We developed a multi-country survey to gather information on current practices regarding TB screening and treatment among pregnant women as well as barriers to integration of TB services with ANC services.

Results: We received survey responses from five countries (Bangladesh, Indonesia, Myanmar, the Philippines, and Vietnam). Only Myanmar had fully integrated TB and ANC services. While respondents from all countries identified the potential benefits of TB/ANC service integration, the most commonly identified barriers to implementation included lack of management capacity to supervise integrated services, inadequate staff, and lack of knowledge about TB among ANC staff.

Conclusion: While countries are aware of the advantages and opportunities associated with integrating TB services into other health care services, the implementation of such integration remains a challenge. Integration of services is one of the key recommendations of this study. Where services have been fully integrated, operational research is needed to evaluate its impact.

Keywords: Tuberculosis (TB); Pregnancy; Antenatal care (ANC); Integrated services

INTRODUCTION

Tuberculosis (TB) is the third leading cause of death among women of reproductive age, with 3.2 million new TB cases among women globally in 2017 [1]. Yet millions of women go undiagnosed, missed by health systems and unreached by lifesaving care. Undiagnosed and untreated TB is highest among key vulnerable populations, including women, particularly those who are pregnant [2,3]. TB can have serious consequences on maternal health during pregnancy and in the postpartum period, as well as on neonatal health through possible gestational TB [4,5]. Pregnant women with untreated TB experience high rates of pregnancy complications, neonatal morbidity, children with low birth weight, premature delivery, and perinatal deaths [6,7].

Correspondence to: Neeraj Kak, University Research Co., LLC, Chevy Chase, MD, USA, E-mail: nkak@urc_chs.com

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Further, women who are co-infected with Human Immunodeficiency Virus (HIV) and TB have more than double the risk of vertical transmission of HIV to newborns, a 300% increased risk of maternal and infant mortality, and worse treatment outcomes compared to women with HIV alone [6-8]

Diagnosis of TB among pregnant women remains a challenge due to a variety of factors, including physiological symptoms of pregnancy which may resemble TB symptoms and immunosuppression during pregnancy [9,10] Given this "masking" effect of similar symptoms, it is often difficult for clinicians to recognize the presence of TB disease and subsequently screen and test for active TB disease. Pregnant women with Latent Tuberculosis Infection (LTBI) are also more likely to develop active tuberculosis disease than non-pregnant women, which necessitates targeted TB infection screening through methods like Tuberculin Skin Test (TST) and Interferon-Gamma Release Assay (IGRA), especially among pregnant women who have HIV or who live in close proximity to someone with TB [2,9-11].

Treatment of TB in pregnancy (both prophylactic treatment of LTBI and treatment of active TB disease) can often follow general population guidelines, as first-line medications generally do not have teratogenic effects [9,10,12] Drug-resistant TB (DR-TB) treatment, however, is more complicated and involves potentially teratogenic drugs [10,13-15] This complication further underscores the need for early detection of TB and daily adherence support through Daily Observed Therapy (DOT) to reduce the likelihood of developed drug resistance among pregnant women with TB. While certain case studies suggest the successful use of second-line drugs and new drugs like Bedaquiline to treat DR-TB among pregnant women with TB, the need for consistent and supportive monitoring is essential [10,13-15]

Aside from the clinical aspects of TB diagnosis and treatment, reaching pregnant women for a screening and testing interaction can be difficult outside of an ANC setting. To streamline pregnant women's interactions with the health system, efforts have been made to integrate ANC, HIV and TB services with varying degrees of success due to various political and donor climates [16,17]. While these efforts have been addressed in policy documents like the End TB Strategy, they stand to be implemented more universally and with better evaluation mechanisms in place [18].

The purpose of this situational analysis is to identify key approaches to addressing TB in pregnancy and to highlight recommendations and global strategies for the screening, diagnosis, and treatment of TB in pregnant women, including the integration of TB services into Antenatal Care (ANC). We also present findings and recommendations from a multi-country survey aimed at gathering information on current policies and guidelines for the screening and treatment of TB in pregnant women at the national and facility levels, as well as implementation considerations for integrating TB services into ANC and reproductive health services.

MATERIALS AND METHODS

Desk review

We conducted a desk review of the existing literature and recommendations on TB in pregnancy in early 2017. We conducted a search reviewing national policies and guidelines using the following search terms: ANC, TB, pregnancy, and reproductive health. The search yielded 78 articles, of which 13 articles were included in the final desk review. Inclusion criteria included policies, guidelines and Standard Operating Procedures (SOPs) that address TB in pregnancy and ANC. We also considered recommendation documents and clinical guidance document from international organizations including the World Health Organization (WHO) and UNFPA, UNICEF. The results of this desk review were used to guide the development of the survey questionnaire.

Survey

Based on the results of the desk review, we developed a survey to gather information on current practices regarding TB screening and treatment among pregnant women at the national, facility and community level, as well as information on the state of integration of TB services with ANC services per WHO recommendations [18]. The survey consisted of 30 questions divided into the following five sections: 1) general TB program information; 2) national guidelines on the treatment of TB in pregnant women; 3) screening and treatment of TB in pregnant women at the health facility level; 4) screening and treatment of TB in pregnant women at the community level; and 5) integration of TB services into ANC: policies, opportunities, and challenges. Surveys were sent to TB experts in five countries: Bangladesh, Indonesia, Myanmar, Philippines, and Vietnam in August 2017.

RESULTS

Desk review results

Overall, despite the general awareness of TB in pregnancy, there has been little unified action to produce global guidelines for the diagnosis and treatment of TB during pregnancy. As elucidated through our desk review, most global TB guidelines and strategies have been developed for the general population, and documents which focus specifically on TB in pregnancy were sparse. The following sections describe interventions described in the literature and guidance documents from the desk review which, while written for the general population, have relevance for preventing, detecting and treating TB in pregnancy. Namely, these interventions include integration of TB screening in Antenatal Care (ANC) services, molecular diagnostics-specifically the GeneXpert MTB/RIF assay and Directly Observed Treatment (DOT).

Integration of screening in antenatal care (ANC) services

The End TB strategy, introduced in 2014, aims to end the global TB epidemic, with targets to reduce TB incidence by 90% and TB deaths by 95% by 2035 [18]. The strategy calls on

governments to implement the strategy through high levels of both political and financial commitments and focuses on reaching highly vulnerable populations, including pregnant women, emphasizing civil society and implementing partner engagement. The strategy's approach to TB control among women includes seven key components (Table 1).

Table 1: Key Components of the WHO end TB strategy for addressing TB in women.

1.	Mobilize commitment at global and national levels to remove underlying risk factors and assure gender-equitable access, including women-friendly services for TB prevention, diagnosis, treatment, care, and support.
2.	Foster collaboration and strategic partnerships across TB, HIV, maternal, neonatal health programs, and maximizing entry points to TB care for women at all levels.
3.	Integrate TB screening and investigation into reproductive health services, including family planning, antenatal and postnatal care, with particular emphasis on girls and women living with HIV in high HIV and TB prevalent settings.
4.	Improve data collection and reporting of TB data disaggregated by sex and age, including for TB treatment initiation and outcomes.
5.	Promote integrated patient monitoring systems for HIV, PMTCT and TB care to capture data and ensure successful follow-up of patients in HIV and TB prevalent settings.
6.	Initiate diagnostic scale-up and uptake of GeneXpert MTB/RIF technology, as it is more effective at detecting TB than sputum microscopy.
7.	Advocate for increased research and development of new TB diagnostics and drugs that take into account the specific needs of pregnant and lactating women.

The most innovative component proposed in the End TB Strategy which relates to TB in pregnancy is the integration of TB screening and investigation into reproductive and maternal health services, including family planning, antenatal and postnatal care. This strategy leverages women's health-seeking behavior during pregnancy, effectively and efficiently uses the existing clinic space and staff, simplifies patient flow, and reduces waiting times, allowing for TB screening, diagnosis, and treatment to be provided within the same visit. The approach assumes that pregnant women will complete at least one ANC visit in the course of their pregnancy, and HIV provider-initiated testing and counseling can also be integrated into the model. The approach, as illustrated in Turnbull et al. [19] includes administration of a simple TB symptom screening questionnaire that evaluates patients for key TB symptoms, including cough, fever, night sweats or weight loss. Women who do not present with TB symptoms continue with a standard ANC visit and HIV counseling and testing where appropriate. If any TB symptoms are present, a sputum sample is collected and a chest X-ray is conducted. If available, GeneXpert MTB/RIF should be used to obtain definitive diagnostic and rifampicin resistance results within hours, while the woman continues her usual ANC visit. If active TB disease is detected, the woman is referred to the TB clinic for treatment, or the proper referral site based on national guidelines if rifampicin resistance is detected.

GeneXpert MTB/RIF assay

In 2010, WHO endorsed the GeneXpert MTB/RIF (GXP) assay test as an effective, rapid point-of-care screening test for quick identification of rifampicin-resistant TB strains [20]. GXP has many advantages, including users outside of a laboratory setting by minimally trained personnel, and provision of same-day diagnosis, which can lead to earlier treatment and reduction of transmission to the patient's family and community. This could be particularly advantageous for pregnant women, as diagnosis through sputum sample collection often requires multiple visits over days or weeks, with many women lost to follow-up before the diagnostic process is complete. Use of GXP diagnosis for pregnant women could potentially allow women to be screened and started on TB treatment on the same day. However, there are numerous operational challenges in adopting GXP instruments at the facility level, including cost and logistical considerations such as the cost of the instrument, cost of cartridges and the need for an uninterrupted power supply.

Directly observed treatment (DOT)

DOT is a highly cost-effective and internationally-recommended strategy for TB control and is the cornerstone of TB surveillance and treatment [21]. Effective DOT implementation requires the following five elements: 1) Sustained political and financial commitment at the national and local level to prioritize TB care in terms of access, equity and quality; 2) Early case diagnosis by quality ensured sputum-smear microscopy; 3) Standardized short-course anti-TB treatment which is given under direct and supportive observation; 4) An effective, uninterrupted supply of high-quality anti-TB drugs; and 5) Standardized recording and reporting of individual patient data, including information on patient outcomes. While DOT is the recommended strategy to address TB in the overall population, it is also recommended to address TB during pregnancy.

Survey results

We received questionnaire responses from six respondents representing five countries: Bangladesh, Indonesia, Myanmar (two responses received), Philippines, and Vietnam. Four respondents were TB implementing partners, one was an NTP Manager, and one was a representative from a civil society organization. All respondents work at national-level TB programs, while two respondents from Myanmar and Vietnam were also implementing TB activities at the provincial and regional levels. The results are described by section below and are summarized in Table 2.

Table 2: Summary survey results.

Domain	Question	Bangladesh	Indonesia	Myanmar	Philippines	Vietnam
National Guidelines for the Treatment of TB in Pregnancy	Do national guidelines exist?	Yes	Yes	Yes	Yes	Yes
	Is the WHO Treatment of Tuberculosis Guideline the source?	Yes		Yes	Yes	
TB Services at the Facility Level	TB services isolated from other services		Yes		Yes	
	TB services integrated with primary care or HIV	Yes				Yes
	TB screening/testing fully integrated with reproductive health services			Yes		
	Are healthcare providers trained in providing TB services to pregnant women?	Yes		Yes	Yes	Yes
	Are training materials available for health providers on TB screening and treatment for pregnant women?			Yes	Yes	
	Is sputum smear microscopy used for diagnosing TB in pregnant women?	Yes	Yes	Yes	Yes	Yes
	Is chest X-ray used for diagnosing TB in pregnant women?	Yes		Yes		Yes
	Is GeneXpert MTB/RIF used for diagnosing TB in pregnant women?	Yes		Yes	Yes	Yes
TB Services at the Community Level	Our community health workers and other community members trained in basic TB knowledge, screening and case detection?	Yes	Yes	Yes	Yes	Yes
	Does this training include information on screening for TB among pregnant women?			Yes		Yes
	Have communities established local referral systems for pregnant women with suspected TB?			Yes		Yes

Integration of TB and ANC Services	Is the integration of TB and ANC services important?	Yes	Yes	Yes	Yes	Yes
	Has integration been fully implemented?			Yes		
	If not, are discussions for integration ongoing?	Yes	Yes		Yes	

National guidelines for the treatment of TB in pregnancy

All respondents (100%) reported that national guidelines for the treatment of TB in pregnancy exist within their countries, either as a section within the national TB guidelines or as a separate, standalone guideline. Myanmar, Bangladesh, and the Philippines identified the WHO's Treatment of Tuberculosis Guidelines [22] as the source used to develop the national guidelines. All guidelines were revised in 2013 or later. However, some respondents reported that while the national guidelines exist, they are not implemented or rarely implemented as written.

TB Services at the facility level

Respondents from Indonesia and the Philippines reported that TB screening and testing for pregnant women is conducted by a separate TB program at the health facilities. Respondents from Bangladesh and Vietnam reported that TB services are integrated with primary care or HIV services, while respondents from one country (Myanmar) reported that TB screening and testing is fully integrated into reproductive health services. All countries but Indonesia reported that health care providers are trained on how to provide TB services to pregnant women, but only Myanmar and Philippines reported that training materials are available for health providers on TB screening and treatment for pregnant women. All countries reported using sputum smear microscopy for diagnosis of TB in pregnant women, three countries (Myanmar, Bangladesh, and Vietnam) reported using chest X-ray and four (Bangladesh, Vietnam, Myanmar, and the Philippines) reported using GeneXpert MTB/RIF (Figure 1).

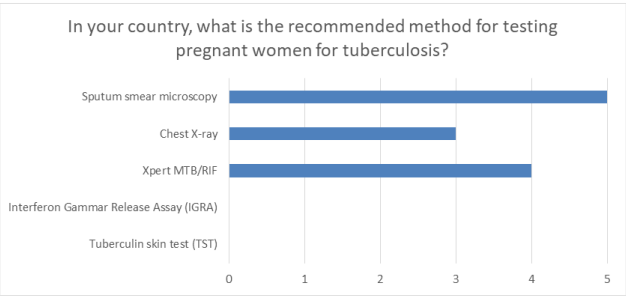

Figure 1: A recommended method for testing pregnant women for Tuberculosis.

TB services at the community level

All countries reported that community health workers and other community members are trained in basic TB knowledge, screening and case detection; however, only Myanmar and Vietnam reported that this training included information on screening for TB among pregnant women. Myanmar and Vietnam reported that communities have established local referral systems for pregnant women with suspected TB, while 83% of respondents reported that communities utilize health workers and volunteers to assist with administering DOTS for TB (Figure 2).

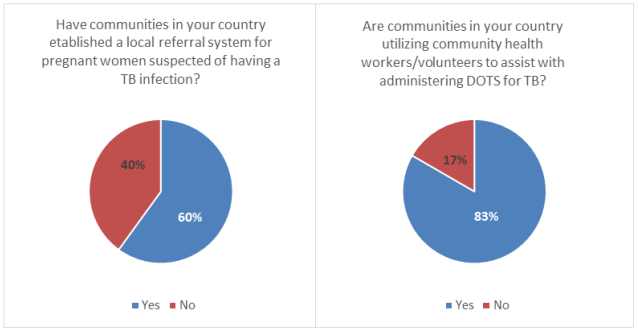

Figure 2: Screening and treatment of TB in pregnant women at the community level.

Integration of TB and ANC services

All respondents agreed on the importance of integrating TB and ANC services. Respondents cited numerous advantages to integration, including increasing early diagnosis and treatment of TB cases in pregnant women, reducing both pregnancy-related and neonatal complications, preventing mother to child transmission of TB, and ensuring safe and standardized TB treatment for pregnant women. However, due to individual political contexts, infrastructure, and human resource availability, only respondents from Myanmar reported that integration of TB services into ANC services has been fully implemented. Respondents from three countries (Bangladesh, Indonesia, and the Philippines) reported that discussions are ongoing regarding the possibility of integration, while the respondent from Vietnam reported that no discussions have taken place at the national level. When asked to identify the barriers which most negatively impact the ability to integrate TB services into ANC, four out of five countries identified a lack of management capacity to supervise integrated services and an inadequate number of staff, with four countries also noting a lack of knowledge about TB among ANC staff (Figure 3).

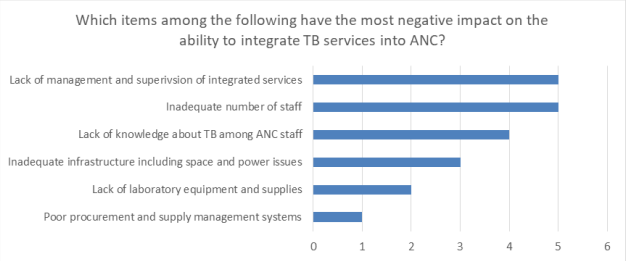

Figure 3: Key barriers to implementing TB/ANC integration.

DISCUSSION

Our survey results suggest that TB among pregnant women is not emphasized or specifically addressed at either the facility or community levels. While national guidelines on treatment TB among pregnant women generally exist in the five countries sampled, they are not adequately implemented at the point of care. While respondents are aware of the advantages and opportunities associated with integrating TB services into other health care services, primarily reproductive health services, implementation of such integration remains a challenge, particularly as NTPs struggle with human resource and equipment constraints, as well as facing the structural challenges inherent to managing and supervising integrated services.

While countries vary greatly in their readiness to discuss, design and implement integrated TB/ANC services, all countries surveyed recognize the importance of integrating TB services into ANC and the positive effects on maternal, newborn and child health that this integration can bring about. There are also the operational advantages to consider, including reduced diagnostic wait times, reduced transportation costs and wait times for pregnant women, and leveraging existing clinic space and staff effectively and efficiently.

CONCLUSION

Overall, NTPs should evaluate and consider integrating TB screening services, as well as HIV testing services where appropriate, into ANC services, or establish other systems or procedures for pregnant women at high risk of acquiring TB, including those living with HIV and those who live in close proximity to someone with TB, to receive routine screening during other office visits. Where integration is imminent or is already fully implemented, research is needed to evaluate the impact of integrating TB services into ANC to best optimize resources, management, and supervision. Additionally, as countries increasingly use the GeneXpert MTB/RIF diagnostic assay, they should evaluate the feasibility and cost-effectiveness of its use in ANC settings. Finally, given that human resource challenges are of utmost concern, and that integrated services can increase workloads among existing staff, it is imperative that countries explore the role of peer educators and lay workers in providing screening services within integrated TB and antenatal care.

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