

Effects of Tuberculosis in Pregnancy

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Abstract

Pregnancy and Tuberculosis (TB) are two different kind of stresses which experienced by a female. Their presence affects them both mentally and physically. In India TB is the highest burden. According to World Health Organization in 2016, TB statistics for India estimated incidence 2.79 million cases of TB for India and Worldwide, Tuberculosis (TB) is an important cause of mortality and morbidity. It is mostly significant in developing countries like India where the disease is endemic. Tuberculosis is an important cause of menstrual irregularity, pregnancy loss, and infertility and in association with pregnancy, morbidity increases to both the mother and child. During pregnancy tuberculosis diagnosis can be difficult because of the non-specific nature of the symptoms such as: shortness of breath, sweating, fatigue and tired and all characteristic of TB, can also be due to pregnancy. So this review presents the effects of tuberculosis in pregnancy with prevalence, Diagnosis and screening of tuberculosis for pregnant women. Management of the underlying disease in a pregnant woman requires great care and for active tuberculosis, first-line drugs treatment is normally safe and improves maternal and neonatal outcome.

Keywords: Tuberculosis (TB); Effects; Pregnancy.

Introduction

“Untreated tuberculosis represents a far greater hazard to a pregnant woman and her fetus than does treatment of the disease”

Tuberculosis is an infectious and common disease caused by mycobacterium tuberculosis. It is one of most contagious infection if not treated timely its lead to mortality. It mainly affects the lungs but also influence other body parts.¹ During pregnancy Tuberculosis may lead to severe result

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affecting both mother as well as child also. Those women who have limited access to health services, prenatal care may be good opportunity for TB care.

According to the World Health Organization 7,00,000 women die from tuberculosis every year. Among 15–45 age of women, tuberculosis is third leading cause of death and it contribute poor outcome of reproductive. The disease is more difficult to diagnose when pregnant women suffer with TB, because tuberculosis symptoms are similar to physiological symptoms of pregnancy such as sweating, mild fever, shortness of breath, fatigue, tiredness and cough. Untreated TB lead to increase complication of pregnancy, increase low birth weight, prematurity, neonatal morbidity and also increase in maternal morbidity due to higher rates of abortion, preeclampsia, labour difficulties and post-partum hemorrhage. While treated TB do not have increase rate of neonatal and maternal complication.²

This review shows that effect of tuberculosis during pregnancy and how it affects immunity and maternal death. It also describes why diagnosis/ screening, prevention and treatment are important for better outcomes.

Prevalence / Incidence of TB in pregnancy

Globally, Tuberculosis (TB) disease burden in pregnant women is significant. In 2011 It was estimated that the case of active tuberculosis occurred among pregnant women is more than 2,00,000 worldwide but greatest burden was in Southeast Asia and Africa. in pregnancy TB incidence pregnancy was 26.6 7 per 100,000 births between 2003 and 2011 in the United States³. Still tuberculosis disease burden among pregnant women is not identified. Thus, to reduce the tuberculosis burden in this population there are few data. The tuberculosis estimate point cases in pregnant woman was attained by the following formulae (Table 1):⁴

Table 1:

Case notification rate women (age 15-44 years) smear positive=	Estimated tuberculosis prevalence rate women (age 15-44 years)
$\frac{\text{Total N new smear positive cases notified women (15-44 years)}}{\text{Full country population} \times \text{proportion of population women age 15-44 years}}$	$\frac{\text{Case notification rate woman (age 15-44 years) smear positive}}{\text{Full country case notification rate smear positive} \times \text{Full country tuberculosis prevalence rate}}$
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Tuberculosis increase risk of maternal and infant mortality in pregnant women living with HIV by nearly 300%. Some facility based studies found TB accounted for 15–34% of indirect causes of obstetric mortality in number of HIV burden settings. India has found an evidence that tuberculosis mothers living with HIV has more risk of vertical transmission of HIV to the unborn child. TB can have mostly severe concerns for women, mainly during their reproductive years.⁵

Effects of TB on immunity

Recent knowledge situations that during pregnancy women are at increased risk of TB during pregnancy and it is expected that some immunological changes related with pregnancy present a prospect for mycobacterial infection or reactivation⁶. Globally, among communicable diseases Tuberculosis is the second leading cause of death. In the developing countries It kills mostly 2 million people each year. Various studies show that in 1–17% of the cases, genital TB as a cause of infertility around 18% in India and 1% in the developed countries.

TB is an essential cause of reproductive and genital morbidity in women. Female genital tract is also an important site because Once the immunity to *M. tuberculosis* contains and overrides the growth of small number of disseminated TB bacilli after primary infection, the infection may remain silent throughout the life until lowered immunity or overwhelming re-infection precipitates the disease⁷. The significances of all kinds of tubercular infection on female reproductive health may lead to the following:

- Menstruation disordered.
- Outcome of pregnancy in a subset of patients.
- Certain pregnancy related complications.
- Chances of causing TB in the infant.
- Ability of the antitubercular drugs to increase

certain complications in pregnant woman.

- Antitubercular drug and its teratogenic potential.
- Recent increase in MDR-/XDR-TB.
- Infertility.
- Increase challenges load of genital TB in immigrant females from the developing countries.

It is very difficult to diagnose when it related with pregnancy because it may have some of the physiological changes that occur during pregnancy that is:

- Malaise and fatigue (30.1%)
- Increased respiratory rate fatigue
- Fever (30.1%)
- Weight loss (41.2%)
- Cough (74.1%)

Maternal complication rates also increased such as

- Respiratory failure (5.82%)
- Pregnancy associated hypertension (8.61%)
- Oligohydramnios (2.91%)
- Preterm labor (3.1%)
- Higher frequency of toxemia
- Abortion
- Intrapartum complications etc.

In later stage of pregnancy, a complete range in immune associates have been observed. In cellular immunity, the activity of plasmacytoid dendritic cells and phagocytes range increased with down-regulated natural killer cell cytotoxicity by progesterone-induced blocking factor and interleukin -10 and interferon gamma production decreased. Which indicating innate cellular response suppressed. But in humoral immunity

increased level of production of T-cell-dependent immunoglobulin, complement proteins and acute phase reactants also increased⁸.

Diagnosis of tuberculosis and screening for pregnant women

Each year TB kills more women than any additional infection and in the reproductive age it is the greatest burden of disease. in pregnancy Screening strategies provides a unique opportunity to recognize and treat at-unprotected women for tuberculosis⁹. If TB disease is not treated, there is a greater risk to the pregnant woman and her baby because in pregnancy diagnosis of TB is not easy. to detect TB bacteria in the body, mostly two kinds of tests that are used: Tuberculin sensitivity test, TB blood tests. If these test are positive that show a person has been infected with TB bacteria but not show that whether the person has latent TB infection or has progressed to tuberculosis disease¹⁰. (Table 2).

Tuberculin sensitivity test is used widely as the first step in TB screening and diagnosis and to identify latent TB infection². So others test also required such as: chest x-ray, sample of sputum and Genotyping methods to identify TB strains:

- Spoligotyping
- Mycobacterial interspersed repetitive unit
- Analysis IS6110-based restriction fragment length polymorphism analysis¹¹.

If the chest x-ray is requiring, appropriate shielding should be limit fetal radiation exposure to less than 0.3 mrad and it should not harm the fetus because teratogenic perception risk is more than the real risk. To generate detailed computer images, MRI uses electromagnetic radio waves, rather than ionizing radiation. So there are no harmful effects from MRI on the pregnant woman as well as fetus.

Table 2:

Classification of the Tuberculin Skin Test Reaction	
An induration of 5 or more millimeters is considered positive in:	
An induration of 10 or more millimeters is considered positive in:	
<ul style="list-style-type: none"> ✓ HIV-infected persons ✓ A recent contact of a person with TB disease ✓ Persons with fibrotic changes on chest radiograph consistent with prior TB ✓ Patients with organ transplants ✓ Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-α antagonists) 	<ul style="list-style-type: none"> ✓ Recent immigrants (< 5 years) from high-prevalence countries ✓ Injection drug users ✓ Residents and employees of high-risk congregate settings ✓ Mycobacteriology laboratory personnel ✓ Persons with clinical conditions that place them at high risk ✓ Children < 4 years of age ✓ Infants, children, and adolescents exposed to adults in high-risk categories

Still in the first trimester MRI is not recommended since safety information during organogenesis is limited. A TB skin test using purified protein derivative is safe and correct during pregnancy and is suggested for women who have TB symptoms or are at great risk for TB¹².

Treatment of tuberculosis

In pregnancy, tuberculosis management is a multidisciplinary approach with the team comprising the obstetrician, neonatologists, communicable disease specialty personnel, public health officials and counselling unit. Treatment is achieved through the use of Directly Observed therapy, Short Course (DOTS)¹³. When pregnant women are diagnosed with TB should start treatment as soon as is detected. Though tuberculin drugs used in treatment of placental cross, these type of drugs do not seem to have harmful effect on the neonate (Table 3).

Table 3:

S. No.	Diagnosis	Treatment
1.	Latent TB Infection	<p>➤ Isoniazid- daily or twice weekly for 9 months, with pyridoxine (vitamin B6) supplementation.</p> <p>For pregnant women 3HP Isoniazid and Rifapentine is not recommended or women expecting to be pregnant in the next 3 months</p>
2.	TB Disease	<p>➤ The preferred initial treatment regimen is Isoniazid, rifampin and ethambutol daily for 2 months, followed by Isoniazid and rifampin daily, or twice weekly for 7 months (for a total of 9 months of treatment).</p> <p>Streptomycin should not be used because it has been shown to have harmful effects on the fetus. Pyrazinamide is not recommended to be used because its effect on the fetus is unknown.</p>
3.	HIV Related TB Disease	<p>➤ TB treatment regimens for HIV-infected pregnant women should include a rifamycin.</p> <p>Pyrazinamide during pregnancy is not recommended in the United States, the benefits of a TB treatment regimen that includes Pyrazinamide for HIV-infected pregnant women may outweigh the undetermined potential risks to the fetus¹⁰.</p>

The following antituberculosis drugs are contraindicated in pregnant women.

- Kanamycin
- Streptomycin
- Capreomycin
- Amikacin
- Fluoroquinolones

According to British Thoracic Society, International Union Against Tuberculosis and Lung Disease, and WHO antituberculous first-line drugs use in pregnancy are considered safe for the mother and the baby¹³. Neither tuberculin nor the bacille Calmette Guerin vaccine are treatments for tuberculosis, but they play a vital role in the disease management. Tuberculin testing is safe, but bacille Calmette Guerin vaccination should be avoided in pregnancy and instead given earlier in life¹⁴.

Breastfeeding in TB

The bonding of mother and baby is very important and breast feeding plays a vital role in providing immunity to neonate in first few months. if the mother is being treated for active tuberculosis or latent TB with first-line agents, Breastfeeding is not contraindicated. if the mother is receiving rifabutin or fluoroquinolone, Breast feeding is contraindicated. Standard of care therapy should be initiated for the baby If mother has active TB and is on treatment and baby has one of the following conditions, either active TB or LTBI or no infection and separation is not recommended. Breastmilk also help to reduce breast cancer¹⁵. Mother should always wear mask until she is no longer infectious. In other conditions both mother and baby should be fully evaluated before they are allowed to be together¹⁶.

Conclusion

Tuberculosis infection in pregnant women and newborn babies is always challenging. proper treatment is essential to restrain morbidity and mortality. TB directly and indirectly affects reproductive health of female and clinically can present in changed ways to tax the skill of the best diagnostician's. So, pregnant women should be utilizing all available resources such as antenatal care programs, patient centered approach in counseling, support, supervision, and record keeping treatment to ensure patient compliance to treat the TB, treatment record keeping to ensure

patients' compliance to TB treatment.

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