Journal of Advanced Research in Medicine
Volume 8, Issue 4 - 2021, Pg. No. 26-31
Peer Reviewed & Open Access Journal

Research Article

Pregnancy with Tuberculosis: What's New!

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DOI: https://doi.org/10.24321/2349.7181.202120

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How to cite this article:
Singh PS, Tyagi S, Pandey NB, Rathore AM. Pregnancy with Tuberculosis: What's New!. J Adv Res Med. 2021;8(4):26-31.

Date of Submission: 2022-02-11
Date of Acceptance: 2022-07-07

A B S T R A C T

Pregnancy with Tuberculosis (TB) can adversely affect the health of the gravida, foetus, and neonate with a spectrum of short and long-term implications. Prevention, diagnosis, and management with a multi-disciplinary team (MDT) approach of TB in pregnancy can improve maternal and perinatal outcomes. Tuberculosis preventive therapy (TPT) can prevent active disease progression and improve the outcome. More recently, active steps to enhance the collaborative activities between maternal health programmes and the National Tuberculosis Elimination Programme (NTEP) have been proposed to ensure early detection and timely management of TB cases in pregnant women in India. This includes antenatal screening for tuberculosis infection and disease at every visit and universal drug sensitivity testing in positive cases. We present a review on tuberculosis in pregnancy with recent updates in its management.

Keywords: Tuberculosis Infection, Tuberculosis Disease, TB in Pregnancy, MDT Approach, Tuberculosis Preventive Therapy

Introduction

Tuberculosis (TB) is a significant health problem in developing countries like India with a reported incidence of 2.64 million cases in 2019, i.e., a rate of 193 per 100,000 population. About 20,000-40,000 pregnant women in India suffer from active TB annually. Tuberculosis in pregnancy can be either tuberculosis infection (TBI), which is asymptomatic or it can be an active tuberculosis disease.[1] The symptoms of active TB disease include weight loss, loss of appetite, night sweats, chills, fever, and weakness. Pulmonary TB symptoms also include cough, haemoptysis, and chest pain. The clinical presentation majorly reflects the organ system that is involved in the disease. However, clinical progression can be so gradual that people might not report symptoms both in pulmonary and extra-pulmonary active TB diseases.[1] TB is acquired mainly through the airborne transmission of infectious droplet nuclei when a contagious person coughs or sneezes and another inhales those droplet nuclei containing tubercle bacilli.[2] These bacilli reach the lungs' alveoli and are ingested by alveolar macrophages but most of these bacilli are destroyed or inhibited.[3] A small number can multiply intracellularly and be released when the macrophages die, and in the case of alive macrophages, these bacilli may spread through lymphatic channels or the bloodstream to more distant tissues and organs.[3] The tubercle bacilli can reach any part of the body, including areas where active TB disease is more likely to develop (e.g., brain, larynx, lymph node, lung, spine, bone or kidney).[3] Within 2-8 weeks, macrophages ingest, surround the tubercle bacilli, and form a barrier shell, called a granuloma, that keeps the bacilli contained. While the bacilli are sequestered, individuals usually do not have signs or symptoms of tuberculosis but may have tuberculosis infection (TBI).[1]

In some people, the tubercle bacilli overcome the immune system and further multiply, progressing from latent TB infection to active TB disease. People who experience an immediate progression of the disease after infection to

active TB disease (i.e., primary TB) often present with pleural effusion or disseminated disease from hematogenous spread.[3] Most people with active pulmonary TB disease become symptomatic and this form of active TB is usually the most symptomatic and infectious.[1]

Tuberculosis in Pregnancy

It can be either latent tuberculosis infection (TBI) or tuberculosis disease. Tuberculosis infection is caused by inhalation of viable bacilli, which may persist in an inactive state while active tuberculosis disease is when clinical manifestations of tuberculosis are present.

Effect of Pregnancy on Tuberculosis

Pregnancy does not increase susceptibility to TB infection or progression from latent TB infection to active TB disease.[4] Pregnancy also does not appear to affect the susceptibility to any particular site of TB infection, pulmonary or extra-pulmonary.[4] However, diagnosis of TB can be more difficult in pregnancy due to hesitancy to perform radiographs, non-reliability of tests like ESR and Mantoux test, and the similarity of screening symptoms with those of the pregnant state, such as weight changes, weakness, and shortness of breath.[5] A higher incidence of TB disease has been reported in the post-partum period than would otherwise be expected based on individual demographics.[5] This reflects the immunologic reconstitution post-delivery that may increases immunological damge (e.g., suppression of the T-helper inflammatory response during the antenatal period). These changes may mask symptoms during the antenatal period which are unmasked in the postnatal period with a corresponding exacerbation of symptoms.[5]

Effect of Tuberculosis on Pregnancy

Adverse outcomes of tuberculosis during pregnancy are increased with advanced disease, inadequate treatment, and late diagnosis. In a systematic review and meta-analysis of 13 studies, including 3,384 pregnancies with active tuberculosis disease, maternal and perinatal outcomes were consistently poorer with active TB disease than without.[6] There were increased odds of maternal death in pregnant women with active TB disease (odds ratio 4.1, 95% CI 0.65-25.2). Also, of those who died, 50% had co-infection with HIV.[6] Antenatal admissions were nine times higher in pregnant women with active TB than those without the disease.[6] Anemia was four times, and cesarean birth was twice as likely with active TB. Moreover, active TB disease was associated with a nine times greater rate of miscarriage. In pregnant women with active TB disease, preterm birth increased 1.6-fold, low birth weight increased 1.7-fold, acute foetal distress increased 2.3-fold, and perinatal death increased 4.2-fold.[6]

The risks of untreated active tuberculosis disease to a pregnant woman and the foetus are much more than treatment risks.[7] Congenital TB can be transmitted from the mother having an active condition to the foetus through the lymphatics or bloodstream or transplacentally; or can also be aspirated/ ingested through the amniotic fluid during the intrapartum period.[4] Congenital TB can present in the early neonatal period with neonatal sepsis or during the first three months of life with hepatosplenomegaly and bronchopneumonia.[4] Although rare, congenital TB has a high mortality rate.[4]

Diagnosis of Tuberculosis in Pregnancy

Every antenatal patient should be evaluated for TB infection by ascertaining TB risk factors by history and physical examination.[8] This should include assessment of high-risk factors like lung disease, immunocompromised state, history of household contacts of active TB disease, and presence of the four-symptom complex.[8] The four-symptom history should be taken in the antenatal clinic in all trimesters every time a pregnant woman visits the ANC clinic. This includes cough of duration more than 2 weeks, fever of duration less than 2 weeks, inadequate weight gain or weight loss in the last three months, and night sweats.[8] A physical examination should also be performed, emphasising the pulmonary assessment and evaluating any possible evidence of extra-pulmonary TB. Extra-pulmonary symptoms can include localised swellings or lumps in the body (lymph node).[8]

Investigation

The presence of high-risk factors mandates testing by tuberculin skin test (TST-Mantoux) or interferon-gamma radioimmune assay (IGRA), and if a positive patient should be taken as having tuberculosis infection.[9] A Mantoux tuberculin skin test or a TB blood test (i.e., IGRA) is used to test for TB infection in pregnancy.[9] The Mantoux tuberculin skin test is considered safe and valid in pregnancy and detects immunity to heat-inactivated tubercle bacilli (i.e., purified protein derivative). The Mantoux test response becomes positive 2-12 weeks after TB exposure.[10] The importance of testing during pregnancy is crucial because 14-47% of pregnant women who test for TB have a positive Mantoux tuberculin skin test result, and also, most pregnant women with active disease are even unaware of their condition.[11]

IGRA is the preferred test for people who have received the BCG vaccine for TB and for people who may have difficulty returning for a second appointment to be evaluated for a reaction to the skin test.[10] It measures immune response to the ESAT-6 and CFP-10 antigens specific to the M tuberculosis complex.[10] The BCG vaccine is usually given to infants in countries like India with a high prevalence of TB and may cause a false-positive reaction to the Mantoux tuberculin skin test.

If any symptoms are present, the patient should be tested for tuberculosis disease. Diagnostic tests for tuberculosis disease (Table 1) include chest-X-ray sputum smear staining,

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202120

sputum culture, and molecular tests.[8] Other samples include fluid collection or fine-needle aspiration cytology - FNAC (in case of a localised enlarged lymph node).[8] The diagnosis of active TB disease is based on a combination of clinical presentation and symptoms, chest radiograph, and acid-fast bacilli smear, culture, or pathologic data.[12] It is important to know that exposure to ionizing radiation from a chest radiograph is well below the estimated threshold levels for adverse foetal effects.[13] TB is a notifiable disease, and all cases should be reported on the Nikshay registration portal.[8] If a person is referred for TB treatment, it is essential to ensure that appropriate care was established and anti-tubercular therapy is started as soon as possible.[8]

Table 1.Diagnostic Tests in Tuberculosis

1. Sputum smear - 2 samples Zeil-Nelson Staining/ Fluorescence stained sputum smear examined under direct or indirect microscopy with or without light-emitting diode (LED)
2. Culture: Solid media (Lowenstein Jansen) or liquid media (Middle Brook) e.g. Bactec, MGIT etc.
3. Molecular testing: Rapid diagnostic molecular test: Nucleic Acid Amplification Test (NAAT) or Line Probe Assay for Mycobacterium tuberculosis complex e.g., GeneXpert
Note: Diagnosis of TB based on radiology (e.g. X-ray) will be termed as clinical TB
4. In research: Urine LAM tests (lipoarabinomannan) most useful in HIV with CD4 less than 100 /microL)

Drug Sensitivity Testing

Effective management of drug-resistant tuberculosis (DR-TB) relies on detecting drug resistance followed by the appropriate treatment. With the launch of the National Tuberculosis Elimination Programme (NTEP), universal drug testing is now advised for tuberculosis with the aim of its elimination. As molecular tests are not growth-based tests, genotypic testing is much faster than phenotypic methods of testing, facilitating timely diagnosis and prompt initiation of treatment.

These Tests Include:

- Nucleic Acid Amplification Test (NAAT) which includes CBNAAT and Truenat (detects rifampicin resistance)
- Line Probe Assay (LPA) which detects resistance to rifampicin (R), isoniazid (H), fluoroquinolones (FQ) and (second-line injectable) SLI drugs

Rapid molecular tests such as NAAT are the preferred method for the initial detection of rifampicin resistance (RR). This is followed by LPA to detect resistance to FQ and SLI drugs. Phenotypic drug susceptibility testing (DST) includes performing DST using the Mycobacteria Growth Indicator Tube (MGIT) system, which is the preferred method for DST to many anti-TB drugs. The following medications are tested using this method:

Group A: Moxifloxacin, Levofloxacin, Linezolid, Bedaquiline.

Group B: Clofazimine.

Group C: Pyrazinamide, Delamanid, Streptomycin, Amikacin.

Drug-resistant Tuberculosis in Pregnancy[16]

Rifampicin-resistant TB (RRTB): The Mycobacterium tuberculosis isolates are resistant to rifampicin.

Multidrug TB (MDR): A DRTB case resistant to both isoniazid and rifampicin.

Pre-extensive drug resistance TB (Pre-XDR): A MDR TB case whose M. tuberculosis isolate is resistant to:

- At least Isoniazid, Rifampicin
- A Fluoroquinolone (Ofloxacin, Levofloxacin, or Moxifloxacin)

Extensive Drug Resistance TB (XDR-TB): A MDR TB case whose M. tuberculosis isolate is resistant to:

- At least isoniazid, rifampicin,
- A fluoroquinolone (ofloxacin, levofloxacin or moxifloxacin)
- A second-line group A drugs: bedaquiline or linezolid or both
- Previously injectable ATT drugs - kanamycin, amikacin, or capreomycin

Treatment of Tuberculosis Infection in Pregnancy (TBI)

CDC guidelines on the treatment of latent TB infection in 2020 stated that the use of isoniazid should be preferred in pregnancy due to lesser side effects.[15] The three-month regimen of Rifapentine and Isoniazid recommended in non-pregnant patients is strictly contraindicated in pregnancy because of adverse effects (e.g., first-trimester abortions).[9] Recently published guideline on tuberculosis preventive therapy (TPT) by NTEP recommends isoniazid 5 mg/kg (300 mg OD) for six months.[9] This should be accompanied by pyridoxine supplementation due to the fact that pregnant women are more likely to be deficient in pyridoxine which can cause neuropathy.[14] It is crucial in pregnancy to ensure medication compliance, as pregnant women may associate the usual nausea of pregnancy with their anti-TB medications.[9]

Treatment for Drug Sensitive Tuberculosis Disease in Pregnancy

Pregnant women should be started on treatment as soon as TB is suspected.[8] Isoniazid (H), Rifampin (R), Ethambutol

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202120

(E) and Pyrazinamide (Z), all four first-line medications used to treat TB have been approved to treat drug-sensitive tuberculosis in India.[8] The treatment regimen is two months of intensive phase HRZE daily and four months of continuation phase HRE daily.[8] Supplemental pyridoxine (vitamin B6) should always be added as pregnant women are more likely to be deficient in pyridoxine which can result in neuropathy. However, the Federal Drug Administration classified ATT drugs as category C and also, given the lack of evidence about their safety, the use of pyrazinamide during pregnancy is controversial in the United States. As per CDC recommendation, the initial treatment regimen is HRE daily for 2 months, followed by HR daily, or twice weekly for 7 months (for a total of 9 months of treatment).[8] But in India ATT includes pyrazinamide in intensive phase i.e HRZE for two months and HRE for 4 months in continuation phase.

The benefits of treatment outweigh the potential risks from the medications if we take into account the poor maternal and foetal outcomes with untreated active TB disease.[8] When the treatment of active TB disease is initiated in the first trimester, compared to its initiation in the second and third trimesters, the associated increased risk of preterm birth, low birth weight, and perinatal death is almost eliminated.[6] Maternal complications also decrease with treatment in the first trimester (29%) compared with the second or third trimester (60%).[6] Active TB disease treatment in pregnancy should occur with the support of a TB chest physician, especially in the context of allergic reactions, extensive disease, antibiotic resistance, or medication compliance concerns.[12]

Treatment for Drug-resistant TB in Pregnancy[16]

A patient less than 24 weeks pregnant should be offered medical termination of pregnancy (MTP), and if she opts for it, then short-course treatment for MDR-TB/ XDR-TB (as in non-pregnant patients) is started.

If the patient wishes to continue, the pregnancy she should be explained the risks and limited availability of safety of these drugs. The duration of treatment for MDR-TB is 18 months. For pre-XDR-TB and XDR-TB patients, the duration of a longer oral XDR-TB regimen would be for 20 months with appropriate modifications. Drugs include levofloxacin, bedaquiline (6 months or longer), linezolid, clofazimine, and cycloserine. If the 4th/ 5th culture report is negative, the dose of linezolid is tapered to 300 mg, and pyridoxine is given to all DR-TB.

Monitoring a Pregnant Patient on ATT

The Isoniazid-related hepatotoxicity with treatment might occur more frequently in pregnancy and early post-partum.[17,18] This risk must be balanced between developing active TB disease risks and the resultant potential consequences.[9] Patients should be aware of the signs and symptoms of hepatitis. Liver function tests should be obtained at baseline and every month if normal.[8] B_6 is recommended during isoniazid therapy.[8] Supplemental vitamin K (10 mg) is recommended in the last two weeks of pregnancy and for the newborn because isoniazid has been linked to vitamin K deficiency.[8] Diet counselling is crucial for treating a patient with tuberculosis in pregnancy.[8] Evidence has supported that nutritional interventions are associated with better outcomes, and improved weight gain, including reduced mortality, improved functional status, earlier sputum conversion, improved pharmacokinetics of key drugs, and adherence to therapy. Undernutrition is associated with a 2-4 times increase in mortality and five times increased risk of drug-induced hepatotoxicity in patients with active TB.[8] Pregnancy requires an additional 23 gm of protein and 350 kcal of energy with recommended daily allowance of 78 gm of protein and 2250 kcal of energy. Lactating females need an additional 600 kcal and 19 gm protein (2500 kcal/74 gm of protein) and extra 10% calories with tuberculosis.[8] Recommended daily allowance consists of 74 gm protein, 2750 kcal, 1200 mg calcium, 300 mcg folic acid, 21 mg iron, and 950 mcg of vitamin A (Nikshay Poshan Yojana).[8]

Tuberculosis with HIV in Pregnancy

Screening for TB in pregnancy is of utmost importance among women living with HIV and needs to be diagnosed early in pregnancy and evaluated thoroughly. It is recommended that women with untreated HIV in pregnancy (i.e., not taking antiretroviral therapy) and active TB disease or latent TB infection should be treated for TB immediately.[17] TPT in form of isoniazid monotherapy for 6 months (300 mg OD) should be given to every pregnant patient who has HIV and is not having active TB disease.[9] People with untreated HIV and latent TB infection progress to active TB disease at a rate of 10% per year. Co-infection by HIV and TB in high-burden areas accounts for 15-34% of cases of indirect maternal mortality.[19] Co-infection also doubles the risk of vertical transmission of HIV to the foetus.[19] Active TB disease should be treated immediately with ATT depending on drug sensitivity. Tuberculosis treatment in people with HIV is complex and should be managed by a multidisciplinary team approach, given the potential for drug-to-drug interactions of antiretroviral medications with TB medications.

Post-partum Considerations

The rate of TB is higher in post-partum than in non-pregnant females. Antenatally maternal immune system is suppressed in pregnancy to prevent an immune response against the foetus. Postnatally, "immune reconstitution" plays a role in the reactivation of tuberculosis infections known as the post-partum flare of tuberculosis.[19] This can be pulmonary or extra-pulmonary and is present with varied symptoms. Clinical suspicion in the background

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202120

of suggestive history and examination helps to diagnose post-partum tuberculosis flares. Diagnosis and treatment remain unchanged.[19] Outcomes depend on appropriate and timely treatment.[8]

Active TB disease is not a contraindication to breastfeeding in India.[18] Isoniazid prophylaxis is given only in maternal active pulmonary TB after ruling out congenital tuberculosis in the neonate. BCG vaccination should be given at birth (irrespective of INH preventive therapy). Pyridoxine supplementation should be given to all breastfeeding mothers on isoniazid therapy, and their infants should be closely monitored for jaundice. TB medications should always be continued during the breastfeeding period.[8] Concentrations of first-line anti-TB drugs are too small in breast milk to produce toxicity in the nursing newborn, but drugs in breast milk are not a protective or effective treatment for TB disease or latent TB infection in a nursing infant.[17] Streptomycin, prothionamide, kanamycin, ethionamide and capreomycin are not recommended for breastfeeding women.[18]

If congenital TB is suspected, evaluation should include mycobacterial culture and histology of the placenta, in addition to the neonatal assessment.[4] It is not easy to distinguish between TB acquired as a foetus and TB developed in the neonatal period.[4] Current diagnostic criteria for congenital TB include a proven tuberculous lesion in the neonate and at least one of the following: a primary hepatic TB complex, lesions in the first week of life, or caseating hepatic granulomas (this is due to transmission through the umbilical vein, i.e., forming a primary TB complex in the foetal liver), TB of the placenta or maternal genital tract, or exclusion of postnatal transmission.[4,8]

In tuberculosis in pregnancy, intrauterine devices are safe to use as postpartum contraception. Regarding other methods such as DMPA, the interval for replacement should be shortened from 12 weeks to 8 weeks. Also, a higher dose of oestrogen is needed in oral combined contraceptives (50 μ).[8]

Conclusion

As TB mainly occurs in the young population, pregnancy is a window to screen women for tuberculosis in countries like India. Also, many become pregnant on anti-tuberculosis medication, so testing and drug optimisation should be considered if needed. A universal drug sensitivity test should be done in all cases of TB disease. TPT in pregnancy can prevent active disease and hence improve outcomes. MTP should be offered for drug-resistant TB. In the case of MDR/XDR, a modified longer regimen should be started/continued. The importance of a good diet should be emphasised to patients on ATT. Patients should be well aware of ATT drug toxicity symptoms. Prevention, diagnosis, and management with a multi-disciplinary team (MDT) approach of TB in pregnancy can improve maternal and perinatal outcomes.

Conflict of Interest: None

References

1. Miele K, Morris SB, Tepper NK. Tuberculosis in pregnancy. Obstet Gynecol. 2020 Jun;135(6):1444. [PubMed] [Google Scholar]
2. Centers for Disease Control and Prevention [Internet]. Core curriculum on tuberculosis: what the clinician should know; [cited 2020 Feb 17]. Available from: https://www.cdc.gov/tb/education/corecurr/pdf/corecurr_all.pdf
3. Bennett JE, Dolin R, Blaser MJ. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. 9th ed. Philadelphia, PA: Elsevier; 2019. [Google Scholar]
4. Gould JM, Aronoff SC. Tuberculosis and pregnancy maternal, fetal, and neonatal considerations. Microbiol Spectr. 2016;4(6):1-6. [PubMed] [Google Scholar]
5. Zenner D, Kruijshaar ME, Andrews N, Abubakar I. Risk of tuberculosis in pregnancy: a national, primary care-based cohort and self-controlled case series study. Am J Respir Crit Care Med. 2012;185(7):779-84. [PubMed] [Google Scholar]
6. Sobhy S, Babiker Z, Zamora J, Khan KS, Kunst H. Maternal and perinatal mortality and morbidity associated with tuberculosis during pregnancy and the post-partum period: a systematic review and meta-analysis. BJOG. 2017;124(5):727-33. [PubMed] [Google Scholar]
7. Centers for Disease Control and Prevention [Internet]. Treatment for TB disease & pregnancy; [cited 2020 Feb 17]. Available from: https://www.cdc.gov/tb/topic/treatment/pregnancy.htm
8. Ministry of Health and Family Welfare [Internet]. Collaborative framework for management of tuberculosis in pregnant women; 2021 Feb [cited 2022 Feb 6]. Available from: https://tbcindia.gov.in/WriteReadData/l892s/5156619257Print%20ready%20version%20MH-TB%20Framework_Final_Feb%2018.pdf
9. Ministry of Health and Family Welfare [Internet]. Guidelines for programmatic management of tuberculosis preventive treatment in India; 2021 Jul [cited 2022 Feb 6]. Available from: https://tbcindia.gov.in/WriteReadData/l892s/Guidelines%20for%20Programmatic%20Management%20of%20Tuberculosis%20Preventive%20Treatment%20in%20India.pdf
10. Cantwell MF, Shehab ZM, Costello AM, Sands L, Green WF, Ewing EP Jr, Valway SE, Onorato IM. Brief report: congenital tuberculosis. New Engl J

Med. 1994;330(15):1051-4. [PubMed] [Google Scholar]
11. National Tuberculosis Controllers Association; Centers for Disease Control and Prevention. Guidelines for the investigation of contacts of persons with infectious tuberculosis. Recommendations from the National Tuberculosis Controllers Association and CDC. MMWR Recomm Rep. 2005;54:1-47. [PubMed] [Google Scholar]
12. Malhame I, Cormier M, Sugarman J, Schwartzman K. Latent tuberculosis in pregnancy: a systematic review. PLoS One. 2016;11(5):e0154825. [PubMed] [Google Scholar]
13. Committee Opinion No. 723: guidelines for diagnostic imaging during pregnancy and lactation. Obstet Gynecol. 2017;130:e210-6. [PubMed]
14. Nahid P, Dorman SE, Alipanah N, Barry PM, Brozek JL, Cattamanchi A, Chaisson LH, Chaisson RE, Daley CL, Grzemska M, Higashi JM, Ho CS, Hopewell PC, Keshavjee SA, Lienhardt C, Menzies R, Merrifield C, Narita M, O'Brien R, Peloquin CA, Raftery A, Saukkonen J, Schaaf HS, Sotgiu G, Starke JR, Migliori GB, Vernon A. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America clinical practice guidelines: treatment of drug-susceptible tuberculosis. Clin Infect Dis. 2016;63:e147-95. [PubMed] [Google Scholar]
15. Centers for Disease Control and Prevention [Internet]. Latent tuberculosis infection: a guide for primary health care providers; [cited 2020 Feb 17]. Available from: https://www.cdc.gov/tb/publications/ltbi/default.htm
16. Ministry of Health and Family Welfare [Internet]. Guidelines for programmatic management of drug resistant TB in India; 2021 Mar [cited 2022 Feb 6]. Available from: https://tbcindia.gov.in/showfile.php?lid=3590
17. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR Recomm Rep. 2000;49:1-51. [PubMed] [Google Scholar]
18. Kaplan JE, Benson C, Holmes KK, Brooks JT, Pau A, Masur H; Centers for Disease Control and Prevention (CDC); National Institutes of Health; HIV Medicine Association of the Infectious Diseases Society of America. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Recomm Rep. 2009;58:1-207. [PubMed]
19. Orazulike N, Sharma JB, Sharma S, Umeora OU. Tuberculosis (TB) in pregnancy - a review. Eur J Obstet Gynecol Reprod Biol. 2021 Apr;259:167-77. [PubMed] [Google Scholar]

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202120