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Diagnosis and Management of Tuberculosis Infection in Pregnant Women: A Narrative Review

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ABSTRACT

Tuberculosis (TB) has been a well-known infectious disease for many centuries. It carries a high rate of morbidity and mortality across the globe. Pregnant women are more susceptible to TB than other individuals owing to the certain physiological changes that accompany pregnancy. There is still doubt that pregnancy is a risk factor for the progression of a TB infection (TBI) to a TB illness. Latent TB infection (LTBI), a term used to describe the fact that *mycobacterium tuberculosis* is found in a dormant stage, can be isolated in pregnant women. As a rule of thumb, early diagnosis and prompt treatment prevent unwanted complications and even mortality in pregnant women and developing fetuses. As a consequence, knowing the various aspects of TB is of utmost importance when dealing with pregnant women. Many diagnostic tools, including history and physical examination, chest X-ray, tuberculin test, and interferon-gamma release assays, are useful in the early detection of TB. However, the risks and benefits of each test should be taken into consideration. Furthermore, close monitoring of the pregnant woman with TB is an essential step for early detection of its complications. Anti-tuberculosis therapy, including isoniazid, rifampin, ethambutol, and pyrazinamide, can be used with certain modifications of their doses to decrease the risk of the disease to both a pregnant woman and her fetus. This narrative review aims to summarize the different aspects (epidemiological distribution, risk factors, diagnostic tools, complications, and management) of TB during pregnancy.

Keywords: Tuberculosis disease; Latent tuberculosis infection; *Mycobacterium tuberculosis*; Interferon gamma; Pregnant women.

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INTRODUCTION

Tuberculosis (TB) has been around for a long time and is still a major reason for illness and death in industrialized and developing nations such as Iraq [1, 2]. The majority of TB diagnoses in female patients occur between the ages of 15 and 49 years (period of reproduction) [1, 3]. There are over 200,000 active TB cases in pregnant women worldwide each year [3]. In 2013, TB was responsible for 500,000 deaths among women globally. This made TB one of the top killers of women during reproductive age, the majority of whom were HIV (human immunodeficiency virus)-negative [4]. In 2020, there was an estimated increase in TB mortality worldwide, most likely due to coronavirus disease 2019 (COVID-19) [4, 5]. Iraq is ranked 108th internationally and 7th in the eastern Mediterranean area among nations with a high TB burden and is thought to have a moderate burden of the disease. According to World Health Organization (WHO) research, there are an estimated 1500 new cases of TB per year in Iraq [5].

Substantial epidemiologic research suggests that the first 90 days following birth are the most vulnerable time for women to get TB [5]. Based on research conducted in the UK, 192,000 pregnant women had a TB incidence rate of 1.095 and a ratio of 95% during the postpartum period compared to the non-pregnant period [6]. Likewise, a massive study in Sweden that examined 649,000 women in their reproductive years discovered an increased frequency of TB during pregnancy

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and within 6 months postpartum compared to non-pregnant periods [5, 7].

Several factors can contribute to the increase in TB cases among pregnant women, such as immune system changes. During pregnancy, a woman's immune system undergoes changes to accommodate the developing fetus. These changes, including hormonal fluctuations and immune system suppression, can make pregnant women more susceptible to infections, including TB. In addition, some pregnant women may already have a latent TB infection (the bacteria are present in their bodies but inactive). Pregnancy can weaken the immune system, allowing the bacteria to reactivate and cause active TB disease [5, 8]. According to previous studies, the immune system will eliminate the bacteria in 80% of TB patients, but in the other 20%, the bacterium may stay inside the granuloma (where they are not killed, but lie dormant), this is called latent tuberculosis infection (LTBI), and people with it are not contagious and do not have any active TB disease [4, 7]. A third of the world's population is thought to have LTBI [9]. Without LTBI treatment, 5–10% of individuals will develop active TB throughout their lives [3, 6]. If TB in pregnancy is not identified and treated on time, there is a significant risk of morbidity for both the pregnant woman and the fetus [6, 7]. Immune dysregulation in pregnancy is linked with a more insidious onset of elevated risk of LTBI, active TB, and progression of LTBI to active TB illness [6]. In the world, 900 million women are thought to have LTBI [5, 6]. These women are much more likely to have reactivation of active disease when they get pregnant or in the puerperium period [6].

In addition to transmitting TB to the baby and family, maternal TB disease is linked to poor outcomes such as low birth weight, miscarriage, pre-eclampsia/eclampsia, early birth, and even death [8]. HIV and a lack of access to or a delay in receiving health care exacerbate these effects [10]. Diabetes, malnutrition, and tobacco or alcohol abuse also contribute to poor TB results during pregnancy [11]. Mycobacterium tuberculosis is the cause of two different types of TB. Pulmonary TB is the most common form of TB, which refers to an infection that primarily affects the lungs but can also involve the airways, bronchi, and lung tissues. While extrapulmonary TB refers to TB that affects organs and tissues outside the lungs, including the lymph nodes, bones and joints, central nervous system (brain and spinal cord), abdomen (peritoneum), and genitourinary system. Pregnant women can develop pulmonary TB, similar to the general population [10, 11]. However, due to the immunological changes during pregnancy, the symptoms might be less pronounced, and the diagnosis can be challenging. Also, extrapulmonary TB can occur in pregnant women, and the sites involved may differ from those in non-pregnant individuals [6, 11]. Lymph nodes, the genitourinary system (such as the kidneys), and the central nervous system are commonly affected sites in pregnant women with extrapulmonary type. Symptoms vary depending on the affected organ; however, they can include swelling or lumps in the neck (lymph nodes), pain or discomfort in the lower abdomen (genitourinary TB), or neurological symptoms (central nervous system TB). It is important to note that the overall incidence of TB in pregnant women may vary depending on the prevalence of TB in a specific region or country. Additionally, access to healthcare and proper antenatal care can influence the detection and management of TB in pregnant women [12]. This review aimed to discuss the TB-causing bacterium, the risk factors linked to TB, clinical features, and bacteriological measures to establish its diagnosis and prevent its spread.

THE NATURAL HISTORY OF TB IN PREGNANCY

Robert Koch, who discovered the mycobacterium derived its name from the Greek words mykes which means fungus, and bakterion means little rod [12]. *Mycobacterium tuberculosis* is the causative agent of TB. It includes several mycobacterial species such as *M. tuberculosis, M. bovis, M. africanum, M. microti, M. canettii, M. pinnipedii,* and *M. caprae* [12, 13]. In 99% of the cases, cultures confirmed, Mycobacterium tuberculosis [14].

Zenner and colleagues found that TB occurred substantially more frequently throughout pregnancy and the first 180 days after delivery, which led them to investigate the epidemiology of TB in pregnancy and determine whether pregnancy is an independent risk factor for active TB [15]. Despite the diagnosis of TB being established in the postpartum period, the active stage of the disease began during pregnancy. This is due to the time frame between the infectious stage and the appearance of the clinical features of TB, which takes weeks to years [13]. The study of Schwartz. et al. [16] showed that neither the post-partum nor pregnancy periods were associated with active TB. It is plausible that in this instance, as well as in others, women with incipient active TB or associated risk factors were less likely to become pregnant [6]. Figure 1 shows the natural history of TB [17].

MICROBIOLOGY AND PATHOPHYSIOLOGY OF TUBERCULOSIS

Mycobacterium tuberculosis is one of the five members of the Mycobacterium tuberculosis complex, which is a non-spore-forming, anaerobic, and non-motile bacillus. It belongs to the family Mycobacteriaceae [12, 18].

Nearly all of the body's organs are affected by TB, although more than 80% of cases occur in the lungs, which are the classic site of the disease [12, 14]. Nonetheless, HIV-positive patients' infection patterns may differ from those of TB patients without HIV due to rising trends in extra-pulmonary spread [19]. Inhalation of infectious particles aerosolized by coughing, talking, sneezing, or manipulation of infected tissues is the primary cause of almost all TB infections. However, there are other possible modes of transmission, including direct implantation through skin abrasion or the conjunctiva and consumption of raw milk.

In high-airflow locations, aerosolized TB particles with diameters ranging from 1 to 5 um are delivered to the terminal air spaces, where tubercle multiplication takes place [18, 19]. Incubation times for tuberculosis range from 3 to 8 weeks for primary cases and up to years for secondary cases (Table 1).

RISK FACTORS FOR TUBERCULOSIS IN IRAQ

A recent study in Iraq [20] shows that age is a risk factor for TB, where TB infections more than double after age 65, which is consistent with the sensitivity to develop the active disease at such ages. Also, another study found a significant association between diabetes and TB due to steroid medication, which weakens the immune system, and raises the chance of getting active TB [21, 22].

Moreover, many risk factors for TB infection are commonly observed in Iraq, including:

- Direct exposure to infected patients.

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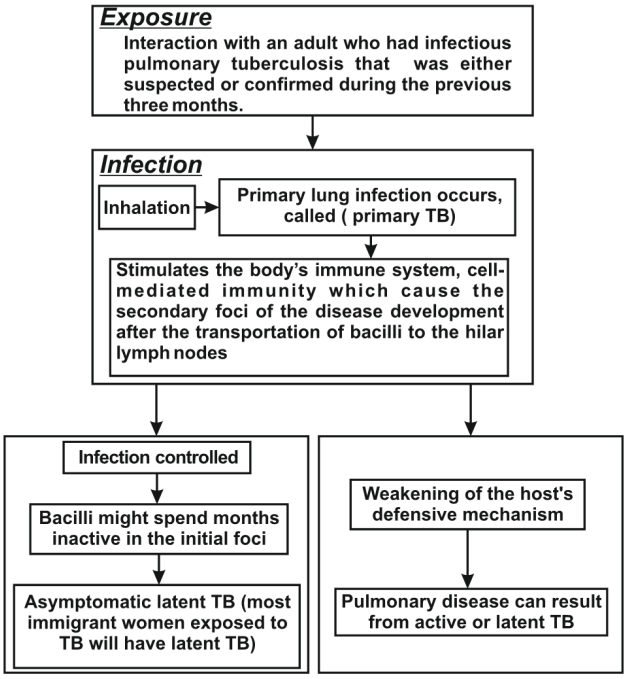

Figure 1. Natural history of tuberculosis [17].

Table 1. Incubation period of tuberculosis.

Time from infection	Manifestation
3-8 weeks	Positive tuberculin skin test, primary complex.
3–6 months	Meningitis, plural disease, miliary.
Up to 3 years	Gastrointestinal (GI), lymph node, joint, and bone.
Around 8 years	Renal tract infection.
From 3 years onwards	Postprimary disease due to reactivation of infection [4].

- Residing in, visiting, or having guests from regions where TB is still a serious problem, such as emerging Asian and African nations.
- Having an immune system that is compromised due to HIV infection or health issues.
- Chronic illness and malnutrition are brought on by lifestyle issues, including drug or alcohol addiction, homelessness, being a migrant worker, or one's family.
- Being very young or old, these groups have weaker immune systems.
- Belonging to ethnic minority groups with origins in regions where TB is still widely prevalent.
- Living in small, unhygienic quarters, especially in hostels.
- Less than an intermediate level of education significantly increases the risk of TB, while a high degree of schooling offers protection [23].
- TB patients have a lower body mass index compared to controls, which explains why TB patients are more likely to be poor and malnourished.
- Unemployment: Iraq has a high overall unemployment rate [24].

CLINICAL FEATURES OF TUBERCULOSIS IN PREGNANCY

Both pregnant and non-pregnant women have similar clinical characteristics. In the case of active disease, a clinical diagnosis is possible; however, between 50% and 70% of pregnant women infected with TB are asymptomatic, probably resulting from latent infection [25–27]. Many pregnant women go untreated or receive the wrong diagnosis because TB symptoms overlap considerably with those of pregnancy, and one South African study has shown that the sensitivity of clinical screening for TB among pregnant women is as low as 28%. The poor performance of symptom screening to identify women with TB suggests that other approaches may be needed for intensified case-finding to be effective for this population [30]. Early diseases and non-specific constitutional symptoms, like fatigue and malaise, can resemble the physiological changes in pregnancy [28, 29]. Breathlessness can happen as a result of lung damage in severe cases, as can respiratory symptoms consisting of a cough that lasts longer than three weeks (at first dry but later possibly purulent with hemoptysis) and pleuritic chest pain [26, 30]. Systemic symptoms, which typically develop gradually over a few weeks or months, include malaise, weight loss, unusual and generalized exhaustion, fever, and night sweats. The clinical presentation determines the types of investigations that are conducted and those that aid in making a diagnosis. Extra-pulmonary TB in pregnant women may be common as a pulmonary illness, according to recent UK statistics [17, 27].

DIAGNOSIS (SCREENING) OF TUBERCULOSIS IN PREGNANCY

Pregnant women with HIV and those who have recently had contact with someone who has pulmonary TB disease and other immunosuppressions (such as cancer, TNF-alpha inhibitors, and chronic steroid use) are advised to get tested for TB infection [3, 31]. Currently, available tests to detect TBI include tuberculin skin testing (TST) and interferon-gamma release assays (IGRA); both are safe for expectant mothers. Pregnancy affects the cell-mediated immune, which is necessary for both TST and IGRA to operate [11]. Pregnancy-related physiological changes, which could mask TB symptoms, particularly weight loss, could be one explanation for the limited sensitivity of symptom screening. A chest X-ray is another useful quick test that can give evidence of lung infection [27, 30].

A previous investigation in the US found no discernible relationship between pregnancy status or stage and TST results among pregnant and non-pregnant women with HIV and equal frequencies of cutaneous energy [32]. TB-endemic areas revealed lower TST results during pregnancy compared to postpartum [11]. Many studies have compared how well TST and IGRA perform in pregnant and post-partum individuals. The majority of studies find moderate concordance in areas with low TB prevalence [33]. In comparison to TST, IGRA has greater completion rates [17] and the potential for higher specificity [34], especially in pregnant women who have already received the BCG vaccine, IGRA has higher specificity than TST [11, 35]. Cavities are the most characteristic sign of TB in adults and are shown through chest radiographs as a way of diagnosing it. TST requires numerous cytokines to promote induration, whereas IGRA is dependent solely on IFN- concentrations; hence, there may be an IGRA+/TST- discrepancy. Moreover, test results vary by gestational age

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[35] and HIV status [36]. During pregnancy, the immune system undergoes changes to support the growing fetus. These changes can affect the interpretation of TB test results, leading to false-positive or false-negative outcomes [34, 37]. One study found that giving maternal vaccination during the first and third trimesters results in enhanced activation of maternal antibody-dependent NK-cells, neutrophil phagocytosis, and complement deposition relative to the second trimester. The placenta may compensate for declining maternal titers by increasing transplacental transfer ratios after the first and second trimesters of vaccination [37]. These findings show the effect of a trimester-time vaccination on the mother's humoral immune response and the transfer of transplacental antibodies. Consequently, healthcare providers may need to consider additional factors and use different criteria when interpreting TB test results for pregnant women [38].

Moreover, most pregnant women who later had TB had IGRA+/TST- results, indicating that discordance in and of itself may be a disease predictor [37]. This could account for the large percentage of IGRA that changes from positive to negative or indeterminate at birth before returning to positive tests after delivery [11]. Table 2 shows a comparison between latent TB infection and pulmonary TB disease [6, 27].

IMMUNOLOGICAL RESPONSE AND TUBERCULOSIS IN PREGNANT WOMEN

Host responses to active TB disease are defined by immunological profiles that are different from those of healthy people [39]. Mycobacterium tuberculosis (Mtb), the illness's causal agent, constantly stimulates the immune system with antigens as it replicates actively during TB disease. In contrast, with LTBI, Mtb is not actively proliferating in the host, necessitating Mtb-specific immune responses through antigen stimulation with Mtb antigens [39, 40]. Although variations in immunity with Mtb antigen stimulation for active illness or LTBI compared to healthy individuals have been thoroughly researched [39, 41]. In the absence of antigen stimulation, few studies describe variations in circulating inflammatory markers according to LTBI status [42]. Changes in inflammatory markers could help find immunological profiles linked to the development of TB or explain why patients who test positive for LTBI have a higher risk of certain unfavorable outcomes, like acute myocardial infarction [42]. LTBI+ persons had significantly greater levels of the circulating pro-inflammatory mediators MCP-1 and IL-6 compared to LTBI- pregnant women after adjusting for possible confounders, but C-reactive protein (CRP) and some other pro-inflammatory markers were at lower levels [36].

There are temporal changes in immunity throughout pregnancy, and pregnant women have a unique immunological profile compared to adults [13, 43]. Cells related to cell-mediated immunity, such as CD8+ / CD4+ T-cells, decline during pregnancy, whereas cells that suppress the immune system, like T-regulator cells, become more prevalent [44]. According to several studies, pregnant women's CD8+ / CD4+ T-cells function is also reduced [11]. Pregnancy-related immune suppression worsens until it reaches a peak at birth. These minute modifications raise the likelihood of some infections, like Listeria, and the severity of other diseases, like influenza [44].

Several investigations show that samples stimulated ex vivo with specific antigens from Mycobacterium TB during pregnancy produce less quantifiable interferon-gamma (IFN-) compared with the postpartum period [45]. Both pregnant women with and without HIV exhibit comparable patterns, although pregnant women with HIV produce less IFN- during the entire pregnancy, despite having sufficient CD4+ T cell numbers [37]. Women with and without HIV experienced a diminished Mtb-specific CD4+ poly-functional response in late pregnancy [46]. These findings imply that comorbidities like HIV may make the cell-mediated immunity deficit during pregnancy worse, which could lead to the development of the disease from TBI [11, 47].

THE EFFECTS OF PREGNANCY ON TUBERCULOSIS

As long as TB is promptly detected and properly managed [48], pregnancy has no positive or negative impact on the course of the disease, including the pace at which sputum converts to pus, the rate at which the disease stabilizes, or the rate at which it recurs [47]. The course and prognosis of the disease in pregnancy are determined by the radiographic pattern, the physical extent of the disease, and the individual woman's vulnerability to TB, rather than by pregnancy itself [17].

A Swedish study by Jonsson, et al. [43] indicated that mothers with TB had a greater incidence of pre-eclampsia, postpartum hemorrhage, and difficult labor than control subjects. Recent research has shown that pulmonary TB increases the risk of acute respiratory failure, pre-eclampsia, and preterm labor when it is diagnosed late in pregnancy [49, 50]. Pre-eclampsia and delivery methods are unaffected by extra-pulmonary TB in a direct way during the course of pregnancy, but it has a higher death rate currently due to its link to maternal morbidity, which manifests itself in the form of recurring hospitalization rates, impairment, and TB of the central nervous system instances, along with concomitant comorbidities [49, 51].

Perinatal mortality was six times higher in Indian women [49] with the treatment of pulmonary disease for 7-9 months during pregnancy than in controls. If maternal TB was discovered in the third trimester, the condition was advanced, or the patient didn't adhere to the prescribed course of action, the rate of side effects of TB infection was higher [17].

TREATMENT OF TUBERCULOSIS

The treatment aimed to prevent the occurrence of complications or progression of the disease, achieve a cure without relapse, stop the transport of infection to other individuals, such as medical professionals and babies, and stop the development of drug resistance [17].

A multidisciplinary team is made up of an obstetrician, bacteriologist, chest doctor, and specialized TB nurse to manage pregnant women with TB. The specialist TB nurse and the chest doctor start and oversee the course of treatment [48, 51]. The obstetrician's responsibility is to oversee the mother and child's health as well as the safe administration of anti-tuberculous drugs, as shown in Table 3. Very ill individuals and those with smear positivity, high infection risk, and short-term hospitalization may be necessary for multidrug-resistant (MDR)-TB [17].

Until recently, there were no systematic evaluations of TB therapy in pregnant women. In comparison to non-pregnant women, pregnant women have special safety, tolerability, and pharmacokinetic concerns. The preferred TB prevention

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Table 2. Latent tuberculosis infection versus pulmonary tuberculosis disease.

Latent tuberculosis Infection	Pulmonary tuberculosis disease
Positive IGRA or TST result	IGRA or TST is usually positive
There are no signs or physical evidence that point to tuberculosis	Symptoms include one or more of the following: cough, fever, night sweats, fatigue, hemoptysis, weight loss, and decreased appetite
Chest radiograph normal	The chest radiograph is usually abnormal
Respiratory specimens are smear and culture negative	Respiratory specimens are usually culture positive (smear positive in about 50% of patients)

Table 3. Combination of drugs during pregnancy.

Drugs	Duration	Pregnant condition
Isoniazid	(INH) 2–4 months	Can be used during any trimester of pregnancy (first, second, and third)
Isoniazid(INH) and Rifapentine (RIF)	2 months	Use during the second and third trimesters of pregnancy
Rifampin	4–6 months	Use during the first trimester of pregnancy
Ethambutol (EMB)	2–4 months	Can be used during any trimester of pregnancy (first, second, and third)

treatment for HIV-positive pregnant women is isoniazid for 6 or 9 months, according to both the United States Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) [25, 51].

The WHO also suggests giving patients in high-burden areas isoniazid for 36 months. As with other TBI regimens for pregnant women, the US CDC recommends taking rifampin daily for four months or rifampin and isoniazid daily for three months [11, 52]. Some specialists choose rifampin for four months to prevent isoniazid-related hepatotoxicity, while others prefer isoniazid to prevent rifampin-drug interactions, such as those with several antiretroviral drugs [11, 53]. Treatment for latent TB infection is debatable, particularly for expectant mothers. Though pregnancy does not increase the chance of the disease progressing, some professionals prefer postponing therapy until after delivery [16, 17]. While the use of chemotherapy is dependent on the disease state, such as whether TB is active or latent or whether there is medication resistance, it consists of an initial intensive phase meant to kill bacilli that are actively developing and semi-dormant. It proceeded with a continuation phase intended to get rid of most of the remaining bacilli and minimize failures and relapses [44]. Isoniazid, ethambutol, and rifampicin are regarded as the first-line anti-tuberculous medications in cases of active TB [16, 17, 52]. Figure 2 shows the treatment of the new pulmonary and extra-pulmonary cases [5].

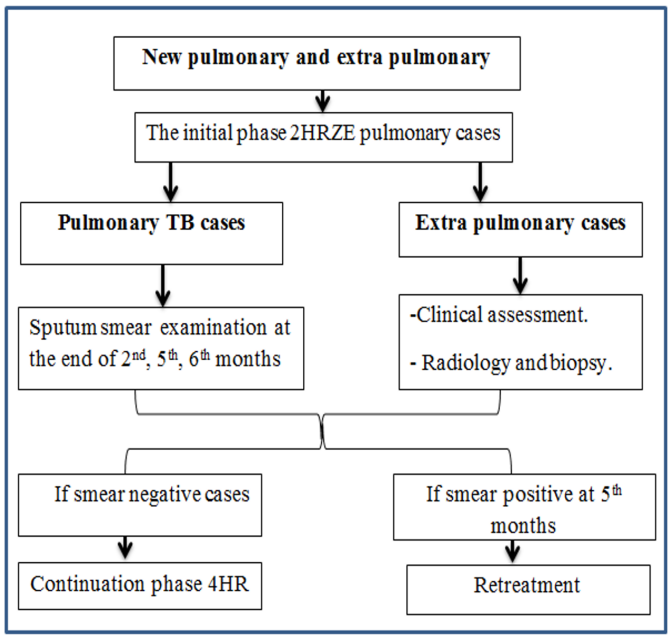

Figure 2. Treatment for the new pulmonary and extra-pulmonary tuberculosis cases of pregnant women [5].

CONTROL AND PREVENTION OF THE SPREAD OF TB IN PREGNANCY AND THE PUERPERIUM

Especially when the index patient has sputum that is microscopically positive for the bacilli or positive for (TST and IGRA) tests, pulmonary TB is possibly infectious. After receiving rifampicin and isoniazid for two weeks, these women can be declared non-infectious [54, 55]. If entry into a hospital is made, the judgement about isolation is based on the first evaluation of infectiousness, the potential for multidrug resistance, and the patient's immune condition [54].

There is a chance that the disease could pass from the mother to the baby if TB is discovered postnatally and the woman's tests and results for acid-fast bacilli show positive results in her sputum within the first two weeks after giving birth. Vitamin B6 (Pyridoxine) 5-14 mg/kg and isoniazid 5 mg/kg should be given as preventative medications to infants whose mothers have fewer than two weeks of treatment and whose results show positive for acid-fast bacilli in their sputum, as well as tuberculin tests and IGRA++ at six to twelve weeks [17, 55].

If the results are negative for the fetus, a BCG injection can be given and the chemotherapy can be discontinued. If the tuberculin test is positive, an extended course of treatment lasting a total of six months should be administered. Babies born to HIV-positive mothers are not advised to receive the

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BCG vaccine until they have been proven to be HIV-negative [54, 56].

All members of the immediate family and other people with whom they have had close contact are included in the contact tracing and screening process, which comprises taking their medical history, having a physical examination, testing for tuberculin, and getting a chest X-ray [17]. Thorough TB testing should be done on sick contacts. If an adult contact's tuberculin test is positive and they have an HIV infection or are immunocompromised and have not received a BCG vaccination, isoniazid chemotherapy is administered [56]. If a tuberculin test comes back negative after six weeks, it is repeated, and if it remains negative, a BCG is administered; if it comes back positive, it indicates an active infection that requires medical attention [57]. Preventing new instances of TB infection by taking steps like being vaccinated and tracing contacts is crucial to the control of worldwide TB [55, 56].

ROLE OF BACILLE CALMETTEGURIN (BCG) VACCINE

This vaccine is widely used for TB prevention. However, its role in preventing TB during pregnancy is not well-defined, and the decision to administer BCG to pregnant women depends on several factors such as the prevalence of TB in the region, stage of pregnancy, and health status of the pregnant woman [58].

The BCG vaccine is generally not routinely recommended for pregnant women in areas with low TB prevalence. This is because the vaccine is primarily given to infants and young children in countries with high TB burdens and a higher risk of infection. BCG vaccination in pregnancy is usually avoided, especially in the first trimester, and postponed wherever feasible until after delivery to minimize potential risks to the developing fetus [58, 59]. It is important to note that the BCG vaccine is a live attenuated vaccine, meaning it contains weakened bacteria [58]. Although it is generally safe, there is a theoretical risk of disseminated BCG disease, particularly in individuals with weakened immune systems. Pregnant women with immunosuppression or conditions that affect their immune response should not receive the BCG vaccine [60]. The BCG is not incompatible with breastfeeding. All newborns and babies who reside in a region with 40 cases of TB per 100,000 individuals each year, have parents or grandparents who were born in a nation where the incidence is 40 per 100,000 people, or have had a family member with TB in the previous five years should receive BCG. It is successful in protecting newborns and young children from serious illness [58, 61].

Ultimately, the decision to administer the BCG vaccine during pregnancy should be made on a case-by-case basis, considering the individual's risk factors, local guidelines, and expert medical advice [7, 61].

CONCLUSION

Pregnancy-related TB is more prevalent among women from ethnic minorities and those who reside in areas with a higher TB incidence rate. A woman with these risk factors should be suspected of having pulmonary or extra-pulmonary disease if she exhibits any vague symptoms or indications, as well as any clinical signs pointing to the disease. If latent TB is suspected, tuberculin skin testing is an effective screening method for pregnant women. While pregnancy does not affect the progression of TB, delaying treatment or leaving the TB untreated may increase maternal morbidity, increase the likelihood of preterm birth, cause growth restriction, and even be transmitted to the fetus. It is safe to use antituberculous drugs of first-line treatment, such as rifampin, isoniazid, and ethambutol, during pregnancy and breastfeeding. The connection between TB and HIV in pregnant women requires further investigation.

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Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

None.

Availability of Data and Material

None.

Competing Interests

The authors declare that there is no conflict of interest.

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Authors' Contributions

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