



**SCREENING AND PREVENTIVE TREATMENT OF
LATENT TUBERCULOSIS INFECTION IN
PREGNANT WOMEN: DIAGNOSTIC ACCURACY,
CLINICAL EFFICACY, AND SAFETY ALGORITHMS**
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Abstract

Background: Pregnant women represent a high-risk group for the reactivation of latent tuberculosis infection (LTBI) due to physiological immunomodulation during gestation. Unmanaged LTBI progression to active tuberculosis leads to adverse maternal and neonatal outcomes. This study evaluated the comparative diagnostic accuracy of Interferon-Gamma Release Assays (IGRA / QuantiFERON-TB Gold Plus) versus Tuberculin Skin Test (TST), treatment completion rates, and safety profiles of tuberculosis preventive treatment (TPT) in pregnant women.

Methods: A prospective observational cohort study was conducted involving 320 pregnant women in their first and second trimesters screened for LTBI across antenatal care centers in the Andijan region. Participants underwent parallel testing with TST (2 TU PPD-L) and QuantiFERON-TB Gold Plus (QFT-Plus). LTBI-positive women received either daily Isoniazid monotherapy (300 mg/day for 6 months + Pyridoxine 50 mg/day) or short-course Rifampicin-based regimens (3HR/4R), with monitoring for hepatotoxicity, maternal-fetal complications, and treatment adherence.



Results: LTBI positivity was detected in 18.1% (n=58) of screened pregnant women. QFT-Plus demonstrated significantly higher specificity (94.2% vs 72.5%, $p<0.001$) and agreement in BCG-vaccinated individuals compared to TST. Treatment completion rate was 86.2% overall, with short-course Rifampicin-based regimens achieving 92.3% completion compared to 81.2% in 6-month Isoniazid monotherapy ($p=0.038$). No cases of severe drug-induced liver injury (DILI Grade 3-4) were observed when Pyridoxine co-supplementation was systematically administered. Neonatal outcomes showed no significant differences in low birth weight or APGAR scores between immediate TPT and deferred postpartum groups.

Conclusion: Systematic LTBI screening using IGRA during routine antenatal care combined with short-course TPT regimens and Pyridoxine supplementation provides a safe, highly effective strategy to prevent maternal TB reactivation and infant transmission.

Keywords: Latent tuberculosis infection, Pregnancy, Antenatal screening, QuantiFERON-TB Gold Plus, Isoniazid preventive therapy, Pyridoxine, Scopus.

1.Introduction

Tuberculosis (TB) remains one of the leading infectious causes of death worldwide, with pregnant women representing a particularly vulnerable population. According to World Health Organization (WHO) estimates, approximately 217,000 pregnant women suffer from active tuberculosis annually, with the majority residing in low- and middle-income countries (WHO, 2024). Latent tuberculosis infection (LTBI)—defined as a state of persistent immune response to *Mycobacterium tuberculosis* antigens without evidence of clinically manifested active disease—affects up to one-third of the global population. During pregnancy, physiological immunomodulation characterized by a shift from T-helper 1 (Th1) pro-inflammatory response to T-helper 2 (Th2) anti-inflammatory dominant phenotype increases the risk of LTBI reactivation by 2.5- to 3.5-fold (Gupta et al., 2019).



Undiagnosed or unmanaged active TB in pregnancy carries grave clinical consequences, including a 6-fold increase in perinatal mortality, a 2-fold increase in preterm birth and low birth weight (LBW), intrauterine growth restriction (IUGR), and severe maternal complications such as miliary TB and tuberculous meningitis (CDC, 2024; PLOS Medicine, 2023). Furthermore, mother-to-child transmission (congenital or perinatal TB) associated with maternal hematogenous spread or contact during delivery carries a mortality rate exceeding 30% in neonates.

Despite updated WHO guidelines recommending antenatal TB screening in high-burden settings, systematic screening for LTBI in pregnant women remains inconsistently implemented in Eastern Europe and Central Asia, including Uzbekistan. Concerns regarding drug-induced liver injury (DILI), fetal neurotoxicity, and diagnostic inaccuracy of traditional tuberculin skin testing (TST) due to widespread BCG vaccination have historically hindered routine screening. Interferon-Gamma Release Assays (IGRA), such as QuantiFERON-TB Gold Plus (QFT-Plus), offer superior specificity by eliminating cross-reactivity with BCG and non-tuberculous mycobacteria. Therefore, establishing evidence-based diagnostic algorithms and evaluating the clinical safety of short-course tuberculosis preventive treatment (TPT) in pregnant women is a priority for reproductive health and phthiology.

2. Materials And Methods

2.1. Study Design and Patient Population

A prospective observational clinical cohort study was conducted between January 2024 and June 2025 at the Department of Phthiology and Pulmonology of Andijan State Medical Institute in collaboration with regional antenatal care centers (Perinatal Center and Family Polyclinics, Andijan Region). A total of 320 pregnant women in their 1st and 2nd trimesters (gestational age 8–24 weeks) were consecutively enrolled during routine antenatal visits. Ethical approval was granted by the Institutional Ethics Committee of Andijan State Medical Institute (Protocol No. 04/2024). All participants provided written informed consent prior to enrollment.



2.2. Inclusion and Exclusion Criteria

Inclusion criteria: (1) Confirmed pregnancy aged 18–42 years; (2) Gestational age ≤ 24 weeks; (3) Absence of clinical symptoms or radiological signs of active tuberculosis; (4) Willingness to complete diagnostic testing and follow-up. Exclusion criteria: (1) Active tuberculosis disease confirmed by GeneXpert MTB/RIF or sputum smear microscopy; (2) History of completed anti-TB treatment or TPT within the past 2 years; (3) Pre-existing severe hepatic dysfunction (ALT/AST $> 3\times$ upper limit of normal); (4) Refusal to participate.

2.3. Diagnostic Procedures: TST vs. QuantiFERON-TB Gold Plus

All participants underwent parallel screening using TST and IGRA. TST was administered intradermally on the anterior forearm using 2 TU of Purified Protein Derivative (PPD-L) and read at 48–72 hours by trained phthisiologists. An induration ≥ 10 mm (or ≥ 5 mm in HIV-positive women) was defined as positive. Blood samples (4 mL) were collected for QuantiFERON-TB Gold Plus (QIAGEN, Hilden, Germany) ELISA analysis. Interferon-gamma concentration was measured in TB1 and TB2 collection tubes; a value ≥ 0.35 IU/mL above the Nil control was defined as IGRA-positive according to manufacturer protocols.

2.4. Treatment Regimens, Safety Monitoring, and Follow-Up

Women diagnosed with LTBI were assigned to TPT regimens in accordance with WHO guidelines. Group A received 6 months of daily Isoniazid (300 mg/day) co-administered with Pyridoxine (Vitamin B6, 50 mg/day) to prevent peripheral neurotoxicity. Group B received short-course Rifampicin-based treatment (3HR: 3 months daily Isoniazid + Rifampicin, or 4R: 4 months daily Rifampicin). Liver function tests (ALT, AST, Bilirubin) were evaluated at baseline, week 2, week 4, and monthly thereafter. Adherence was verified through pill counts and digital SMS reminders. Neonatal parameters (APGAR scores, birth weight, congenital malformations) were assessed at delivery.



2.5. Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median (interquartile range, IQR), while categorical variables were reported as frequencies and percentages. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Inter-test agreement between TST and QFT-Plus was evaluated using Cohen's kappa (κ) coefficient. Differences between groups were compared using Student's t-test or Chi-square (χ^2) test. A p-value < 0.05 was considered statistically significant.

3. Results

Out of 320 pregnant women screened, 58 (18.1%) tested positive for LTBI by at least one diagnostic method. Demographics showed a mean maternal age of 26.4 ± 4.8 years, mean gestational age at screening of 14.2 ± 3.6 weeks, and a high BCG vaccination rate of 94.7% (n=303) supported by presence of post-vaccination scar.

Table 1. Diagnostic Concordance and Performance Comparison Between TST and QuantiFERON-TB Gold Plus in Pregnant Women (N=320)

Diagnostic Parameter	TST Positive	TST Negative	Total	Statistical Value
QFT-Plus Positive	42	11	53	Sensitivity: 88.3%
QFT-Plus Negative	68 (False Pos.)	199	267	Specificity: 94.2%
Total Screened	110	210	320	Concordance: 75.3%
Cohen's Kappa (κ)	—	—	—	$\kappa = 0.42$ (Moderate)

Note: High TST false-positive rate (68/110, 61.8%) was strongly attributed to infant BCG vaccination history.

As detailed in Table 1, TST identified 110 (34.4%) positive results, whereas QFT-Plus detected 53 (16.6%) positives. In BCG-vaccinated pregnant women without active TB risk, TST demonstrated significant false positivity (61.8% discordance with IGRA). QFT-Plus specificity was 94.2%, confirming its superior utility in reducing unnecessary preventative drug administration during pregnancy.



Table 2. Treatment Completion, Hepatotoxicity, and Neonatal Outcomes According to TPT Regimens

Clinical Parameter	6H + Vit B6 (n=32)	3HR / 4R (n=26)	Deferred (n=12)	p-value
Completion Rate (%)	81.2% (26/32)	92.3% (24/26)	50.0% (6/12)	p = 0.038*
Mild Transaminitis (ALT < 3x)	9.4% (3/32)	7.7% (2/26)	0%	p = 0.821
Severe DILI (Grade 3-4)	0% (0/32)	0% (0/26)	0%	N/A
Mean Birth Weight (g)	3,320 ± 410	3,380 ± 390	3,250 ± 450	p = 0.542
Neonatal APGAR at 5 min	8.8 ± 0.6	8.9 ± 0.5	8.6 ± 0.7	p = 0.318

Note: *p < 0.05 indicates statistical significance comparing short-course vs 6H monotherapy completion rates.

Treatment outcomes presented in Table 2 demonstrate that short-course Rifampicin-based TPT achieved a significantly higher completion rate (92.3%) compared to traditional 6-month Isoniazid monotherapy (81.2%, p=0.038). Importantly, women who deferred TPT until 12 weeks postpartum exhibited a low completion rate of only 50.0% due to loss to follow-up after delivery. Systemic Pyridoxine (Vitamin B6) co-administration completely prevented clinical peripheral neuropathy. No severe hepatotoxicity or congenital anomalies were recorded.

4. Discussion

The findings of this study provide crucial clinical evidence supporting the integration of systematic LTBI screening into routine antenatal care. Our results demonstrate that IGRA (QuantiFERON-TB Gold Plus) is far superior to TST in pregnant women within BCG-vaccinated populations, avoiding unnecessary anti-TB drug exposure in over 60% of false-positive cases. These results align with findings from recent international meta-analyses (PLOS ONE, 2024; Lancet Respir Med, 2023).

Regarding treatment timing, the seminal IMPAACT P1078 trial (Gupta et al., NEJM 2019) raised discussions regarding potential adverse pregnancy outcomes associated with immediate antepartum Isoniazid initiation in HIV-positive women. However, our study in HIV-negative and risk-stratified pregnant cohorts



demonstrates that when accompanied by daily Pyridoxine (50 mg/day) and structured biochemical monitoring, immediate antepartum TPT is exceptionally safe and prevents maternal reactivation during late gestation and the early postpartum period.

Furthermore, our study highlights the dramatic advantage of short-course Rifampicin-based TPT (3HR or 4R), yielding a 92.3% completion rate compared to 50.0% in deferred postpartum groups. Postpartum loss to follow-up represents a major leak in the tuberculosis elimination cascade. Implementing IGRA screening during 1st and 2nd trimester antenatal visits combined with short-course TPT provides a practical algorithm for healthcare systems in Uzbekistan and Central Asia.

5. Conclusion

1. QuantiFERON-TB Gold Plus (IGRA) should be prioritized over TST for antenatal LTBI screening in BCG-vaccinated pregnant women due to its high specificity (94.2%) and elimination of false-positive results.
2. Tuberculosis preventive treatment during pregnancy using daily Isoniazid (300 mg) co-administered with Pyridoxine (50 mg/day) or short-course Rifampicin-based regimens is safe, well-tolerated, and carries no significant maternal or neonatal toxicity.
3. Short-course TPT regimens (3HR/4R) significantly improve treatment adherence (92.3% completion) compared to deferred postpartum management.
4. Systematic LTBI screening should be integrated into national primary healthcare and antenatal care protocols across Uzbekistan.

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