

Pregnancy Outcomes in Patients with Tuberculosis: A Systematic Review and Meta-analysis

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ABSTRACT

Background and objectives: Tuberculosis (TB) is an important global health problem, especially for pregnant women, a vulnerable group. This systematic review and meta-analysis was conducted in this group to obtain cumulative results in a collective effort toward the World Health Organization (WHO) End TB Strategy.

Methodology: The databases Ovid MEDLINE, Embase, PubMed, ScienceDirect, Scopus, and Cochrane Central Register of Controlled Trials were searched for the last 10 years till 14th January 2025. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in this analysis. Pregnancy outcomes in terms of maternal complications and perinatal complications, including observed mortality, were considered for analysis.

Results: A total of 9,873 records were identified through database searching, and 15 studies, including 3,045 pregnant women with TB, were selected for final analysis. The pooled mean maternal age was 27.6 years, and more than half of TB cases were diagnosed antenatally. Among pregnancy-related complications, fetal growth restriction, pregnancy-induced hypertension, oligohydramnios, and gestational diabetes were seen in 19, 15, 11, and 10% of cases, respectively. Low birth weight, preterm birth, small for age, and low Apgar score (<7) had pooled prevalences of 30, 22, 20, and 13%, respectively. Maternal mortality and neonatal mortality showed pooled prevalences of 0.05 [95% confidence interval (CI): 0.03–0.08] and 5% (95% CI: 3–8%), respectively. Low to moderate heterogeneity was found among observations.

Interpretation and conclusion: This systematic review and meta-analysis showed continued maternal and perinatal adverse outcomes in pregnant women with TB even in the current era, highlighting the need to optimize healthcare.

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INTRODUCTION

Tuberculosis (TB) has probably returned as the world's leading cause of mortality from a single infectious agent, replacing COVID-19.¹ Approximately 10.8 million people globally fell ill with TB in the year 2023, which corresponds to an incidence of 134 cases per 1,00,000 population.¹ The South-East Asia, Africa, and Western Pacific regions of the World Health Organization (WHO) reported the maximum number of TB cases in the year 2023, contributing 45, 24, and 17% of cases, respectively, with lower numbers from the Eastern Mediterranean, the Americas, and Europe, reporting 8.6, 3.2, and 2.1% of cases, respectively.¹ Approximately 1.25 million people were estimated to have died from TB in the year 2023, with almost one-third of deaths (1,61,000 people) occurring among people with human immunodeficiency virus (HIV)-TB coinfection.¹ The incidence rates and the number of mortalities due to TB showed reductions of 8.3 and 23%, respectively, over 9 years, between the years 2015 and 2023. Despite this positive trend, the reductions were substantially lower than the target reductions of 50 and 75% for the incidence rates and the number of mortalities due to

TB, respectively, by the year 2025, a milestone set by the WHO End TB Strategy.¹

As per the National Tuberculosis Prevalence Survey of 2019–2021, an estimated 312 per 1,00,000 people have TB in India, representing approximately 25% of the global TB burden.²

The immunological and endocrine changes during pregnancy affect antituberculosis immunity and influence the specific course of the disease during pregnancy.³ Evidence regarding the exact incidence of TB during pregnancy and the postpartum period is currently limited. However, globally, around 2,00,000 women are diagnosed with TB during pregnancy and the postpartum period annually, according to estimates presented at an annual global conference on TB and lung diseases in the year 2019, with contributions of 75 and 25% from each period, respectively.⁴ The majority of women belonged to the African and South-East Asia regions of the WHO.⁴ In a systematic review by Morton et al., the risk ratio for the incidence of TB during pregnancy was reported as 1.4, and that for the postpartum period was reported as 1.9.⁴

TB during pregnancy is associated with adverse maternal and perinatal outcomes,

which can lead to maternal mortality in 6–15% of cases and pose a high risk to the newborns of women with TB.^{5–7}

A number of studies have shown variable pregnancy outcomes in patients with TB across the globe. Our systematic review and meta-analysis included studies from the last 10 years to obtain cumulative results in patients with this globally important health problem among the vulnerable pregnant population in the current scenario, in a collective effort toward the WHO End TB Strategy.

METHODOLOGY

Study protocol of this systematic review was registered with PROSPERO with ID No. CRD420251040280.

Databases—Embase, PubMed, Ovid MEDLINE, ScienceDirect, Cochrane Central Register of Controlled Trials (CENTRAL), and Scopus—were searched for the last 10 years till 14th January 2025. After searching the electronic databases, further hand-searching was conducted from the reference lists of selected studies to identify any other eligible studies.

Studies published in English only were selected, but there were no geographical restrictions. The keywords and search terms, such as TB, TB infection, pregnancy outcomes, maternal outcomes, perinatal outcomes, and neonatal outcomes, were used for reviewing the literature. Preferred Reporting

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Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in this analysis. Pregnancy outcomes in terms of maternal complications and perinatal complications, including observed mortality, were considered for analysis.

Study Inclusion Criteria

Original research publications, case-control, cohort, and cross-sectional studies published in peer-reviewed journals, and randomized controlled trials having a minimum sample size of 10 cases or more were included.

Pregnant women affected with TB, diagnosed by any method [clinical, interferon-gamma release assay (IGRA), or microbiologically confirmed], irrespective of their diagnosis prepregnancy or during pregnancy, were selected as the population of study interest. All cases of pregnancy with TB, irrespective of the site of TB (either pulmonary or extrapulmonary), were included.

Study Exclusion Criteria

Studies without an abstract, without full text available, case reports, case series, studies with the wrong study design (research question not answered), conference abstracts/papers, and letters to the editor were excluded.

Studies recruiting pregnant women with human immunodeficiency virus (HIV)-coinfected populations exclusively or studies conducted exclusively on infertile populations/*in vitro* fertilization (IVF) pregnancies were excluded.

Data Collection

The results from each database were extracted and entered into the appropriate standardized form. Screening of the titles and abstracts of the extracted studies was conducted independently by two reviewers, the first two authors (author 1 and 2), after removing duplicates. After applying the inclusion/exclusion criteria and reviewing the abstracts, the full texts of the retrieved articles were reviewed. A third reviewer (author 4) resolved the discrepancies. This study did not enroll any patients.

Quality Assessment of the Included Studies

The quality of the included studies was assessed using the Newcastle–Ottawa Scale.⁸ Risk of selection bias, comparability of study groups, and risk of outcome bias were assessed. The prespecified criteria were selected, and two independent reviewers (author 1 and 2) allocated stars based on those criteria. A high risk of bias was deemed present when studies scored one star for selection bias risk or ascertainment of outcome bias risk, or zero stars for any of the three domains,

whereas a low risk of bias was deemed present when studies scored four stars for selection bias risk, two stars for comparability, and three stars for ascertainment of outcome bias risk. A medium risk of bias was considered when studies had intermediate star ratings. Studies scoring three to four stars were included in the analysis.

Data Extraction and Analysis

Information related to study characteristics, participant demographics, TB diagnosis details, and reported maternal and perinatal outcomes was extracted. The extracted data for comparison were compiled by two independent reviewers (author 1 and 2). The pooled incidence of adverse pregnancy outcomes was calculated. The effect size and anticipated heterogeneity were calculated between studies using a random-effects model. The I^2 test was used to assess heterogeneity between studies (I^2 40–60%: suggestive of moderate heterogeneity, 50–90%: substantial heterogeneity, and 75–100%: considerable heterogeneity). IBM SPSS 29.0.2.020.12 statistical software was used for statistical analyses.⁹

RESULTS

Characteristics of Included Studies

Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed in this analysis. Figure 1 shows the flow diagram of PRISMA. A total of 9,873 records were identified through database screening, and 15 studies were selected for final analysis.^{10–24}

These studies included 3,045 pregnant women with TB, irrespective of whether their diagnosis was made prepregnancy or during pregnancy. Twelve studies were from Asian countries—seven from India, two from China, and one each from Israel, Malaysia, and Pakistan^{10–20,22}—and three were from America,^{21,23,24} showing the burden of TB in certain geographical areas. Clinical or radiological findings alone or in combination, supported by microbiological and/or histological confirmation, were used for the diagnosis of active TB.

Table 1 presents a comprehensive meta-analysis summarizing maternal characteristics, the timing of TB diagnosis, and the site of TB, along with pooled estimates derived from multiple studies. The pooled mean maternal age, based on 10 studies, was 27.6 years (95% CI: 25.9–29.2).^{10–16,18,20,21} Five studies reported the socioeconomic status of pregnant women with TB, showing a pooled proportion of 0.62 (95% CI: 0.54–0.69) in women of low socioeconomic status across variable geographical areas.^{15–18,21} Twenty-eight percent (95% CI: 0.21–0.35) of cases had a diagnosis of TB before pregnancy; however, more than half of TB cases were diagnosed antenatally, with a pooled proportion of 0.54 (95% CI: 0.45–0.62), while postpartum diagnosis of TB accounted for 18% of cases reported in 10 studies.^{10–13,15–19,22} A pooled proportion of 0.71 (95% CI: 0.64–0.77) was noted for pulmonary TB and 0.29 (95% CI: 0.23–0.36) for extrapulmonary TB in 11 studies.^{10–13,15–18,20,22,23} Moderate to substantial heterogeneity was found among maternal characteristics, timing of diagnosis, and site of

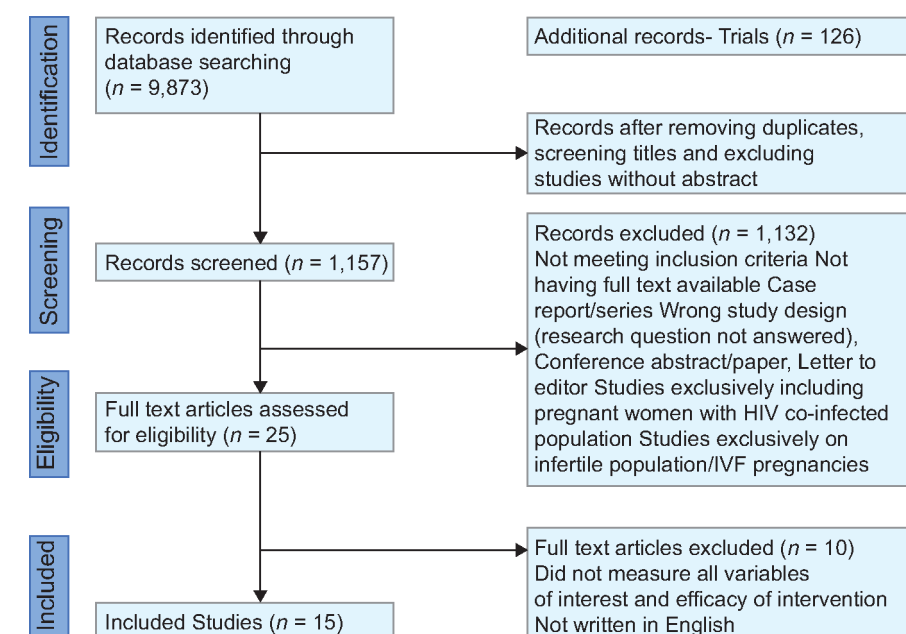


Fig. 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram: Identification and selection of relevant articles

TB, suggesting reasonable consistency among the included studies.

Table 2 presents a comprehensive meta-analysis of pregnancy complications and mode of delivery in pregnant women with TB. Among pregnancy-related complications, the most frequent observations were fetal growth restriction, pregnancy-induced hypertension, oligohydramnios, and gestational diabetes, occurring in 19% (95% CI: 0.13–0.26; five

studies),^{10,12,18,19,24} 15% (95% CI: 0.10–0.21; five studies),^{10,11,14,18,24} 11% (95% CI: 0.07–0.17; three studies),^{10,11,18} and 10% of cases (95% CI: 0.06–0.15; five studies),^{11,14,18,21,24} respectively. A low to moderate level of heterogeneity ($I^2 = 33$ –43%) was observed.

Seven percent of women had spontaneous abortion (95% CI: 0.05–0.10; five studies), while 24% underwent induced abortion (95% CI: 0.17–0.31; five studies).^{13,15,16,18,19} The pooled

prevalence of normal vaginal delivery was 64% (95% CI: 56–71%; 10 studies), while 36% (95% CI: 29–44%; 10 studies) underwent lower-segment cesarean section (LSCS).^{10–16,18,19,24} The heterogeneity was moderate ($I^2 = 44\%$), suggesting acceptable variability across studies. Maternal mortality was reported in 10 studies and showed a pooled prevalence of 0.05 (95% CI: 0.03–0.08) with low heterogeneity ($I^2 = 31\%$).^{10,11,13–18,20,24}

Table 1: Comprehensive meta-analysis of maternal characteristics, timings of diagnosis, and site of TB in studies

Category	Outcome	Included studies (author, year)	No. of studies	Pooled effect (95% CI)	I^2 (%)
Maternal characteristics	Mean maternal age (years)	Chopra, 2016; Sade, 2020; Wen, 2024; Yadav, 2019; Yadav, 2022; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Wang, 2018; LaCourse, 2016	10	27.6 (25.9–29.2)	42
	Low socioeconomic status	Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Ullah, 2024; LaCourse, 2016	5	0.62 (0.54–0.69)	58
Timing of TB diagnosis	Prepregnancy	Chopra, 2016; Wen, 2024; Yadav, 2019; Yadav, 2022; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Sengupta, 2018; Ullah, 2024; Zainudin, 2024	10	0.28 (0.21–0.35)	46
	During pregnancy	Chopra, 2016; Wen, 2024; Yadav, 2019; Yadav, 2022; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Sengupta, 2018; Ullah, 2024; Zainudin, 2024	10	0.54 (0.45–0.62)	52
	Postpartum	Chopra, 2016; Wen, 2024; Yadav, 2019; Yadav, 2022; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Sengupta, 2018; Ullah, 2024; Zainudin, 2024	10	0.18 (0.12–0.25)	39
Site of TB	Pulmonary TB	Chopra, 2016; Wen, 2024; Yadav, 2019; Yadav, 2022; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Wang, 2018; Ullah, 2024; Zainudin, 2024; Garry, 2024	11	0.71 (0.64–0.77)	49
	Extrapulmonary TB	Chopra, 2016; Wen, 2024; Yadav, 2019; Yadav, 2022; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Wang, 2018; Ullah, 2024; Zainudin, 2024; Garry, 2024	11	0.29 (0.23–0.36)	49

Table 2: Comprehensive meta-analysis of pregnancy complications and mode of delivery in pregnant women with TB in studies

Category	Outcome	Included studies (author, year)	No. of studies	Pooled effect (95% CI)	I^2 (%)
Pregnancy complications	Fetal growth restriction	Chopra, 2016; Yadav, 2022; Buddhewar, 2022; Sengupta, 2018; El-Messidi, 2016	5	0.19 (0.13–0.26)	43
	Pregnancy-induced hypertension	Chopra, 2016; Sade, 2020; Yadav, 2019; Buddhewar, 2022; El-Messidi, 2016	5	0.15 (0.10–0.21)	38
	Oligohydramnios	Chopra, 2016; Yadav, 2019; Buddhewar, 2022	3	0.11 (0.07–0.17)	33
	Gestational diabetes mellitus	Sade, 2020; Yadav, 2019; Buddhewar, 2022; LaCourse, 2016; El-Messidi, 2016	5	0.10 (0.06–0.15)	31
Maternal mortality	Maternal death	Chopra, 2016; Sade, 2020; Wen, 2024; Yadav, 2019; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Wang, 2018; Ullah, 2024; El-Messidi, 2016	10	0.05 (0.03–0.08)	31
Mode of delivery	Normal vaginal delivery	Chopra, 2016; Sade, 2020; Wen, 2024; Yadav, 2019; Yadav, 2022; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Sengupta, 2018; El-Messidi, 2016	10	0.64 (0.56–0.71)	44
	LSCS	Chopra, 2016; Sade, 2020; Wen, 2024; Yadav, 2019; Yadav, 2022; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Sengupta, 2018; El-Messidi, 2016	10	0.36 (0.29–0.44)	44

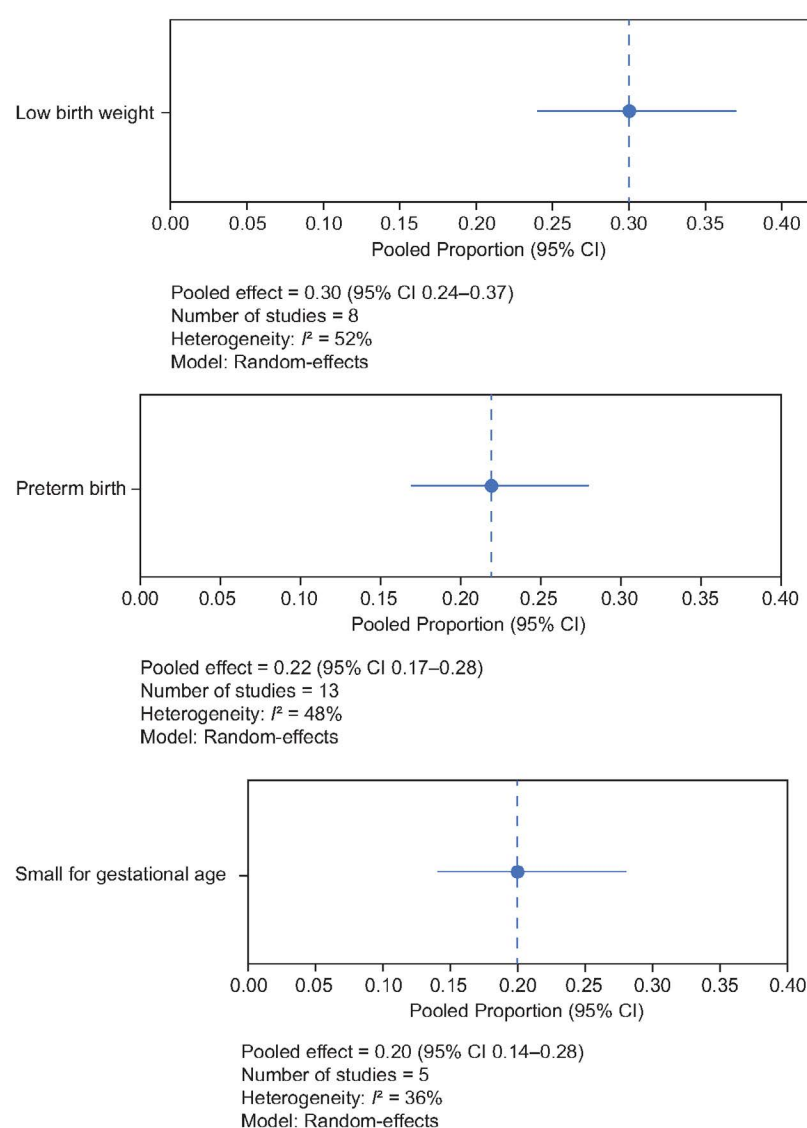


Fig. 2: Forest plot analysis using a random-effects model for low birth weight, preterm birth, and small for gestational age

Table 3: Comprehensive meta-analysis of birth outcomes in pregnant women with TB in studies

Category	Outcome	Included studies (author, year)	No. of studies	Pooled effect (95% CI)	I^2 (%)
Birth outcomes	Low birth weight	Sade, 2020; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Ullah, 2024; LaCourse, 2016; Zainudin, 2024; Garry, 2024	8	0.30 (0.24–0.37)	52
	Preterm birth	Chopra, 2016; Sade, 2020; Wen, 2024; Yadav, 2019; Lewis, 2021; Tushar, 2024; Buddhewar, 2022; Sengupta, 2018; Ullah, 2024; LaCourse, 2016; Zainudin, 2024; Garry, 2024; El-Messidi, 2016	13	0.22 (0.17–0.28)	48
	Stillbirth	Seema Chopra 2016; Vikash Yadav 2019; Vikash Yadav 2022; Amita S. Buddhewar 2022; Zurina Zainudin 2024; Amira El-Messidi 2016	6	0.06 (0.04–0.10)	34
	APGAR <7	Chopra, 2016; Sade, 2020; Wen, 2024; Yadav, 2019; Yadav, 2022; Zainudin, 2024	6	0.13 (0.09–0.19)	37
	SGA	Yadav, 2019; Wang, 2018; LaCourse, 2016; Zainudin, 2024; Garry, 2024	5	0.20 (0.14–0.28)	36
	Neonatal TB	Yadav, 2019; Sengupta, 2018; Ullah, 2024	3	0.03 (0.01–0.06)	21
	Neonatal death	Sade, 2020; Wen, 2024; Yadav, 2019; Buddhewar, 2022; Sengupta, 2018; Ullah, 2024; Zainudin, 2024	7	0.05 (0.03–0.08)	30

Table 3 presents a comprehensive meta-analysis of birth outcomes in pregnant women with TB in the included studies. The most frequent birth outcomes were low birth weight, preterm birth, small for gestational age (SGA), and low Apgar score (<7), with pooled prevalences of 30% (95% CI: 24–37%; eight studies),^{14–18,21–23} 22% (95% CI: 17–28%; 13 studies),^{10,11,13–19,21–24} 20% (95% CI: 14–28%; five studies),^{11,20–23} and 13% (95% CI: 9–19%; six studies),^{10–14,22} respectively. Neonatal TB was reported in three studies, showing a pooled prevalence of 0.03 (95% CI: 0.01–0.06).^{11,17,19} The pooled prevalence of stillbirth and neonatal death was 6% (95% CI: 4–10%; six studies)^{10–12,18,22,24} and 5% (95% CI: 3–8%; seven studies),^{11,13,14,17–19,22} respectively. A low to moderate level of heterogeneity ($I^2 = 30–52\%$) was observed.

Figures 2 to 4 depict the forest plot analysis of the pooled effect sizes with 95% confidence intervals (CI) for major pregnancy and perinatal complications in relation to TB during pregnancy. In Figure 2, most studies show effect sizes on the same side of the null line, suggesting an overall increased risk of low birth weight (LBW), preterm birth (PTB), and SGA. The combined effect estimate in Figure 3 suggests a higher risk of stillbirth and neonatal mortality, while the wide confidence intervals in some studies reflect variability and uncertainty. In Figure 4, the summary estimate indicates an increased risk of maternal mortality. The spread of confidence intervals suggests moderate heterogeneity, emphasizing the need for cautious interpretation of the pooled results.

DISCUSSION

This systematic review and meta-analysis was conducted to obtain cumulative results

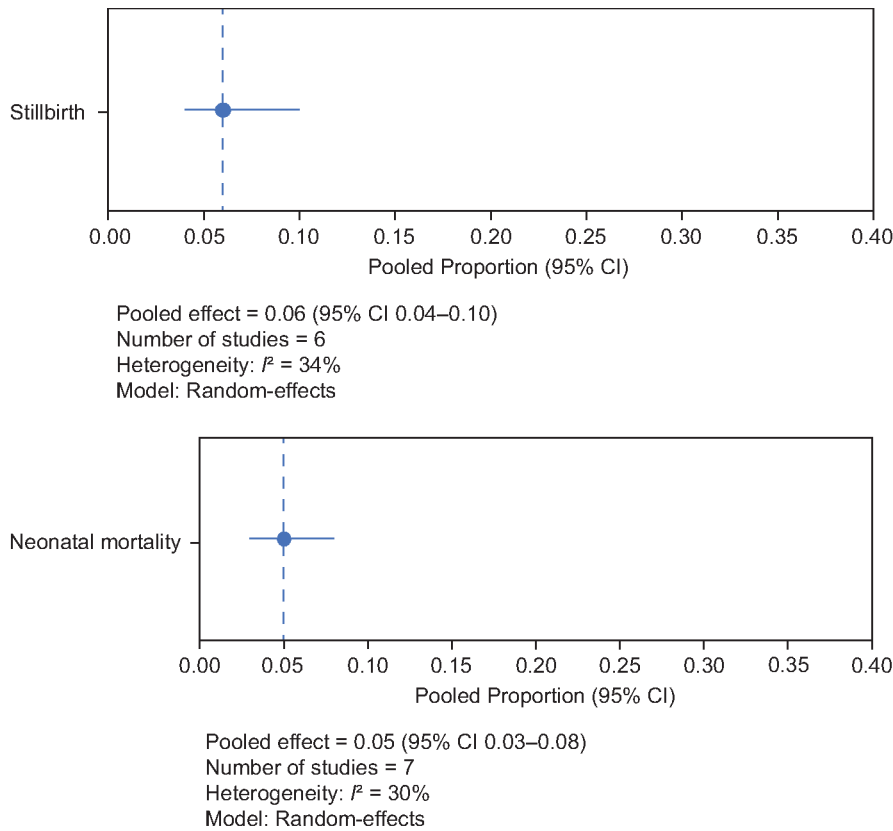


Fig. 3: Forest plot analysis using a random-effects model for stillbirth and neonatal mortality

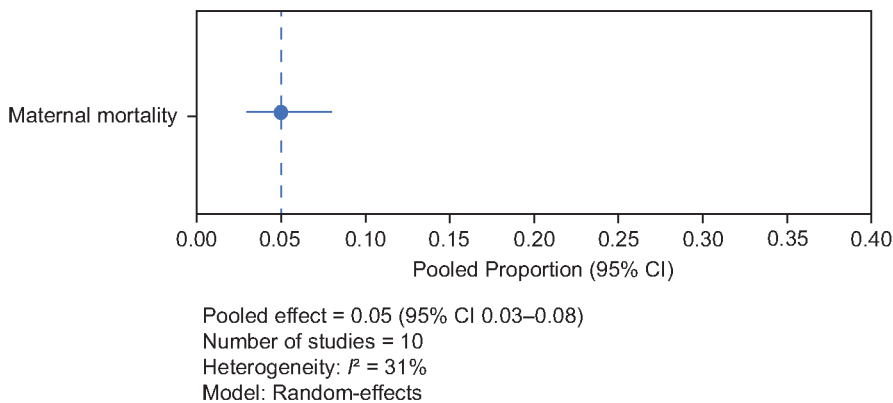


Fig. 4: Forest plot analysis using a random-effects model for maternal mortality

in pregnant patients with TB. Moderate to substantial heterogeneity was found among maternal characteristics, timing of diagnosis, and site of TB, suggesting reasonable consistency among the included studies. A low to moderate level of heterogeneity ($I^2 = 33\text{--}43\%$) was observed for pregnancy-related complications and birth outcomes. The mode of delivery showed moderate heterogeneity ($I^2 = 44\%$), suggesting acceptable variability across studies. Both maternal and neonatal mortality showed low heterogeneity ($I^2 = 30\text{--}31\%$). Despite the variable heterogeneity, the direction of effect remained positive across all studies, supporting a consistent benefit or relationship.

Sobhy et al.²⁵ performed a systematic review and meta-analysis of studies from inception through December 2015, in which 13 studies were included and 3,384 pregnant women with active TB and 1,19,448 pregnant women without TB were compared. Pregnant women with active TB were found to have higher odds of maternal morbidity, cesarean delivery, anemia, low birth weight, preterm birth, birth asphyxia, and perinatal death [odds ratio (OR): 2.8, 2.1, 3.9, 1.7, 1.7, 4.6, and 4.2, respectively].²⁵

Strengths and Limitations

Our study followed the PRISMA reporting guidelines. The study protocol of this

systematic review was registered with PROSPERO. By applying strict exclusion criteria [such as excluding studies recruiting pregnant women with exclusively human immunodeficiency virus (HIV)-coinfected populations or studies conducted exclusively on infertile populations/*in vitro* fertilization (IVF) pregnancies], the majority of confounding factors were removed from the analysis, thereby strengthening the study results. Studies with a minimum sample size of 10 cases or more were included to enable the selection of studies across variable geographical areas so that the results of this meta-analysis could be applicable worldwide in critical appraisal.

Inclusion of studies was limited to articles published in English only, which likely excluded important findings reported in other languages. The meta-analysis revealed low to moderate heterogeneity among the included studies, which may require further exploration through subgroup analysis or meta-regression to identify the source of heterogeneity.

INTERPRETATION AND CONCLUSION

Among the maternal characteristics analyzed, mean maternal age showed a stronger and more significant association with the outcome, while low socioeconomic status demonstrated a comparatively smaller effect. TB diagnosed during pregnancy was associated with the greatest adverse effect, followed by prepregnancy diagnosis, while postpartum diagnosis showed the least association, as demonstrated by the highest pooled effect size observed during pregnancy. This highlights the critical impact of TB occurring during pregnancy on maternal and perinatal outcomes, emphasizing the importance of early detection and management.

The pooled effect size for pulmonary TB was high, indicating a strong and statistically significant association with adverse maternal and perinatal outcomes compared with extrapulmonary TB. This highlights that the disease burden and severity associated with pulmonary involvement may contribute more significantly to unfavorable maternal and neonatal outcomes.

Among pregnancy complications, fetal growth restriction showed the strongest association among the listed complications, followed by pregnancy-induced hypertension and oligohydramnios, while gestational diabetes showed the weakest association. This highlights the predominance of placental and vascular complications in TB-affected pregnancies.

Most women delivered vaginally, although cesarean section rates were considerable.

Among birth outcomes, low birth weight and preterm birth were the most common adverse outcomes, while stillbirth and neonatal death occurred less frequently but remain clinically significant concerns.

This systematic review and meta-analysis suggested adverse maternal and perinatal outcomes in pregnant women with TB even in the current era of the 21st century, since the first diagnosed case in 1882.

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