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Clinical Presentation, Disease Severity, and Pregnancy Outcomes among Women with Active Tuberculosis: A Comparative Cohort Study

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ABSTRACT

Background: Tuberculosis (TB) during pregnancy continues to pose a significant maternal and public health challenge, especially in high-burden regions. Physiological and immunological changes associated with pregnancy can modify TB presentation and increase disease severity.

Objective: To compare the clinical presentation, disease severity, laboratory and radiological findings, and pregnancy outcomes among pregnant and non-pregnant women with active TB.

Methodology: This prospective comparative cohort study cohort study was conducted from January 2024 to June 2025. A total of 190 women with active TB were enrolled, including 60 pregnant and 130 non-pregnant women matched by age and admission period. We prospectively collected demographic, clinical, laboratory, radiological, treatment, and outcome data. Categorical variables were analyzed using the chi-square or Fisher's exact test, while continuous variables were compared using the independent-samples t-test or Mann-Whitney U test, as appropriate.

Results: Pregnant women had significantly higher frequencies of fever (71.7% vs. 35.4%, p<0.001), dyspnoea (43.3% vs. 19.2%, p=0.001), and neurological symptoms (33.3% vs. 13.1%, p=0.003). ICU admission was also significantly more frequent among pregnant women (18.3% vs. 3.0%, p<0.001). TB-related mortality was higher among pregnant women (11.6% vs. 3.8%), although the difference was not statistically significant (p=0.065). Among pregnant women, spontaneous abortion occurred in 33.3%, stillbirth in 5.0%, preterm birth in 20.0%, and low birth weight in 15.0%.

Conclusion: Active TB during pregnancy is associated with more severe clinical manifestations and adverse maternal and pregnancy outcomes. In high-burden settings, early diagnosis, prompt treatment, and integrated maternal and fetal monitoring are essential.

Keywords: Tuberculosis; Women; Pregnancy; Pregnancy Outcome

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Introduction

Tuberculosis (TB) is caused by Mycobacterium tuberculosis (MTB). It remains a major global infection concern and one of the main hurdles for health systems, especially in low- and middle-income countries. Even though TB can affect the health of all ages and both sexes, women of reproductive age are a key group, because TB may show up during pregnancy and the postpartum phase, and those physiological shifts can modify how the illness looks, how it is diagnosed, and what the clinical results end up being. The World Health Organization (WHO) is still naming TB as a top global health priority. Still, millions of people end up developing TB disease every year even though diagnosis and treatment services have improved.[1] This burden becomes even more noticeable in nations with a high TB incidence, since women there can get a delayed diagnosis because respiratory and constitutional symptoms can be misunderstood as normal pregnancy-related changes.[1,2]

Pregnancy induces significant physiological, hormonal, respiratory, and immunological changes that can alter the clinical presentation of tuberculosis. Altered immune responses during pregnancy may affect the body's ability to contain M. tuberculosis infection, while increased oxygen demands and changes in respiratory mechanics can facilitate the appearance of respiratory symptoms. The postpartum period is also critical, as the risk of progression from latent infection to active TB may remain elevated after delivery. A systematic review from 2024 found that both pregnancy and the postpartum period are associated with an increased likelihood of progression from M. tuberculosis infection to active disease, particularly among women in high TB incidence settings.[3] These findings underscore the importance of considering TB in the differential diagnosis for pregnant women presenting with persistent respiratory, constitutional, or systemic symptoms, even when TB appears to be an unlikely cause.

Diagnosing TB during pregnancy presents unique challenges. Symptoms such as fatigue, breathlessness, reduced appetite, and general weakness often overlap with normal pregnancy-related symptoms, potentially delaying TB identification. Concerns regarding fetal exposure to ionizing radiation may also influence the timing and use of chest imaging. However, if TB is suspected, diagnostic evaluation should not be delayed solely due to pregnancy. The WHO recommends integrating TB screening and appropriate diagnostic assessment into antenatal care, tailored to local epidemiological and clinical contexts.[1] Advances in molecular diagnostics, including rapid molecular assays, have accelerated TB detection and drug-resistance identification. Early diagnosis and initiation of treatment are critical, as untreated active TB poses a greater risk to both mother and fetus than appropriately selected anti-TB therapy.[4]

The impact of tuberculosis during pregnancy extends beyond maternal illness. Active TB has been associated with adverse maternal and perinatal outcomes, including severe maternal disease, anemia, preterm delivery, low birth weight, fetal loss, and other obstetric complications. A recent cohort study comparing pregnant and non-pregnant women with TB found that the pregnant group exhibited higher frequencies of fever, dyspnoea, neurological symptoms, and miliary TB. Notably, severe outcomes, including increased need for intensive care and TB-related mortality, were more common among pregnant women.[5] Collectively, these findings suggest that pregnancy may influence not only the clinical presentation of TB but also disease severity and progression.

Maternal TB significantly affects pregnancy and neonatal outcomes. A study conducted in Peru reported poorer neonatal outcomes among pregnant women with pulmonary TB, including increased rates of prematurity, reduced birth weight, and infants small for gestational age [6]. Similarly, recent reviews emphasize that maternal tuberculosis increases the risk of adverse outcomes for both pregnancy and the newborn, and that early diagnosis and effective treatment are essential for protecting maternal and neonatal health.[2,4] The management of drug-resistant TB presents additional challenges. Evidence from women treated for multidrug-resistant and rifampicin-resistant TB, utilizing newer and repurposed drugs, indicates that appropriate therapy can improve maternal outcomes and result in successful live births. This underscores the importance of providing treatment during pregnancy rather than withholding it.[7]

Although tuberculosis in pregnancy is clinically significant, pregnant women are still rather underrepresented in TB research and in surveillance activities. The World Health Organization has recently emphasized the need to include pregnant and lactating women earlier and more appropriately in TB studies, covering work on treatments, vaccines, surveillance systems, and even maternal and neonatal outcomes.[8] This is particularly important in high-burden settings since small variations in healthcare access, socioeconomic circumstances, nutritional condition, diagnostic procedures, and treatment delays can affect how the disease presents and what outcomes result. Moreover, a large part of the evidence that we currently have comes from areas outside Pakistan, and findings from other groups may not truly reflect the clinical patterns or outcomes of pregnant women with TB within local healthcare settings.

Although tuberculosis in pregnancy is recognized as a significant concern for both maternal and public health, there remains a need for locally generated evidence regarding the clinical presentation and outcomes of TB in pregnant women compared to non-pregnant women. The present study was conducted at Civil Hospital, Quetta to

compare the demographic and clinical characteristics, laboratory and radiological findings, disease severity, maternal outcomes, and pregnancy outcomes of pregnant women with active TB and non-pregnant female TB patients. Identifying differences in symptomatology and adverse outcomes may facilitate earlier detection of TB during pregnancy, enhance clinical vigilance, and improve care for both mother and child, particularly in high-burden settings such as Pakistan.

Objective

To compare the clinical presentation, disease severity, laboratory and radiological findings, and pregnancy outcomes among pregnant and non-pregnant women with active TB.

Methodology

This prospective comparative cohort study was conducted at Civil Hospital, Quetta, a major referral center catering to the population of Balochistan. The hospital has a dedicated TB clinic and a directly observed therapy short-course (DOTS) program under the National Tuberculosis Control Program, which provides a full spectrum of diagnostic and treatment services for tuberculosis. The study was conducted over 18 months, from January 2024 to June 2025.

All female patients diagnosed with active tuberculosis during the study period were screened for eligibility. The study group consisted of pregnant women with a confirmed diagnosis of active TB, and the control group consisted of non-pregnant female TB patients in a 1:2 ratio. Tuberculosis was diagnosed based on clinical presentation, radiological findings, and microbiological confirmation with sputum smear microscopy and the GeneXpert MTB/RIF assay. Pregnancy status was confirmed by urine human chorionic gonadotropin testing and ultrasound examination. The study included patients diagnosed with active TB during pregnancy or within six weeks postpartum.

Exclusion criteria included a history of prior TB treatment, multidrug-resistant TB, incomplete medical records, or loss to follow-up before study completion.

The sample size was calculated based on the primary outcome of comparing ICU admission rates between pregnant women with TB and non-pregnant controls. Using data from a prior study (16.3% in pregnant vs. 0.8% in non-pregnant), with a two-sided alpha of 0.05 and 80% power, the minimum required sample size was 47 participants per group using the standard formula for comparing two proportions. Accounting for 15% anticipated loss to follow-up, the target enrollment was 55 pregnant women with TB and 110 non-pregnant controls.[9] During the study period, a total of 60 pregnant women with TB and 130 non-pregnant controls were successfully enrolled, exceeding the minimum required sample size and providing adequate statistical power for the planned analyses.[10]

We used consecutive sampling and enrolled all eligible pregnant women with active TB diagnosed during the study period as the exposed group. We systematically matched each pregnant case with two non-pregnant female TB patients from the same hospital population. Matching criteria included age (±2 years) and admission time (within three months of the index case). We used this matching approach to reduce potential confounding by demographic and temporal factors, ensuring both groups received similar diagnostic protocols, treatment regimens, and healthcare services within a similar timeframe.

Data were collected prospectively using a study-specific structured case report form, which included detailed information on demographic characteristics, clinical presentation, laboratory parameters, radiological findings, treatment details, and clinical outcomes. Trained research personnel obtained data through direct patient interviews, physical examinations, and systematic review of medical records. For pregnant patients, additional information was collected regarding pregnancy-related outcomes such as gestational age at diagnosis, obstetric complications, and neonatal outcomes. Regular audits and verification of entries against source documents were conducted to ensure data quality. The main outcomes of interest were ICU admission, TB-related mortality, and adverse pregnancy outcomes, including spontaneous abortion, stillbirth, preterm birth, and low birth weight. Secondary outcomes included clinical symptom profile, radiological patterns, and laboratory parameters.

The main exposure variable was pregnancy status, categorized as pregnant or non-pregnant. Demographic variables included age, parity, gestational age at diagnosis, and socioeconomic status. Clinical variables comprised presenting symptoms, symptom duration, and the presence of comorbidities such as diabetes mellitus, hypertension, or chronic kidney disease. Cases with multiple comorbidities were documented accordingly.

Primary outcomes included ICU admission, defined as transfer to the intensive care unit for organ support or close monitoring; TB-related mortality, defined as death attributable to tuberculosis or its complications during therapy; and adverse pregnancy outcomes, including spontaneous abortion (loss of fetus before 20 weeks of gestation), stillbirth (loss of fetus at or after 20 weeks), preterm birth (delivery before 37 completed weeks), and low birth weight (infant birth weight under 2500 grams).

Secondary outcomes included clinical manifestations such as fever, cough, dyspnoea, night sweats, weight loss, and neurological symptoms, as well as radiological findings including bilateral involvement, miliary pattern, cavitary lesions, and pleural effusion. Laboratory parameters tracked included hemoglobin, white blood

cell count, albumin, and C-reactive protein, regardless of case complexity.

All data were entered into a secure electronic database with a double-entry check to minimize transcription errors. Patient identifiers were removed and replaced with unique study codes to ensure confidentiality. The database was password-protected and accessible only to the principal investigator and designated research team members. Data were routinely cleaned to identify inconsistencies or missing values. When data were missing, efforts were made to recover them from hospital records or through patient follow-up. Patients with incomplete information were excluded from specific analyses but remained in the overall study cohort where appropriate under the intention-to-treat principle.

Statistical analyses were performed using SPSS version 26.0 (IBM Corp, Armonk, NY, USA) and R software version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were used to summarize baseline characteristics and primary outcome measures. For continuous variables, normality was assessed using the Shapiro-Wilk test. Normally distributed data were reported as mean ± standard deviation and compared using the independent-samples t-test. Non-normally distributed data were presented as median ± interquartile range, with group comparisons conducted using the Mann-Whitney U test.

Categorical variables were summarized as frequencies and percentages. Proportions were tested using the Chi-square test or Fisher's exact test, as appropriate. A multivariable logistic regression model was constructed to identify independent risk factors associated with adverse outcomes, adjusting for potential confounders such as age, comorbidities, and disease severity. Statistical significance was defined as a p-value less than 0.05. For key predictors, odds ratios with 95% confidence intervals were reported.

The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice standards. Prior to enrollment, each participant provided written informed consent, with information delivered in Urdu and Balochi to ensure comprehension. Participants were informed of their right to withdraw from the study at any time without impact on their clinical care. Strict confidentiality was maintained, and all data were anonymized before analysis. For pregnant participants, additional measures were taken to ensure that study procedures did not interfere with routine antenatal care or tuberculosis (TB) treatment. Participants with active TB received standard anti-TB therapy according to national guidelines, and follow-up was conducted for all participants until completion of treatment.

Results

Out of these 190 patients, 60 pregnant females with active TB formed the study population, and 130 non-pregnant females suffering from active TB served as the controls in a 1:2 matching for age (± 2 years) and admission time. The mean age of the pregnant group was 27.2 ± 5.3 years, while in the non-pregnant group it was 26.9 ± 5.6 years, with no statistically significant difference (*p* = 0.684). No statistically significant difference was noted between the two groups regarding household exposure or any predisposing comorbidity (Table 1).

The symptoms of pregnant women suffering from TB were quite different from those of the control subjects. Fever (71.7% vs. 35.4%), dyspnoea (43.3% vs. 19.2%), and neurological symptoms (33.3% vs. 13.1%) were significantly more common among pregnant women than among control subjects. On the contrary, the constitutional symptoms (weight loss, night sweats, and tiredness) were found more in non-pregnant subjects. Among febrile pregnant women, high-grade fever (body temperature >38.5) was seen in about 53.5% of cases (Table 2).

Due to safety concerns regarding radiation exposure during pregnancy, a lower proportion of pregnant patients underwent chest imaging compared to controls. Among those who completed imaging, the pregnant group demonstrated a higher prevalence of bilateral pulmonary involvement (63.3% vs 39.7%), miliary TB (28.6% vs 11.9%), and pleural effusion. In comparison, cavitary lesions were less frequently detected (12.2% vs 26.2%) (Table 3).

Laboratory investigations revealed that pregnant TB

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Pregnant Group (n = 60) (%)	Non-Pregnant Group (n = 130) (%)	p-value
Age (years), mean ± SD	27.2 ± 5.3	26.9 ± 5.6	0.684
Household contact exposure, n (%)	14 (23.3)	34 (26.2)	0.521
Predisposing comorbidities*, n (%)	9 (15.0)	23 (17.7)	0.601

*Predisposing comorbidities include diabetes mellitus, chronic kidney disease, and corticosteroid therapy.

patients had significantly lower haemoglobin (97.8 ± 13.2 vs 117.5 ± 14.8) and albumin levels (31.2 ± 5.6 vs 40.1 ± 6.3), along with elevated inflammatory markers, including white blood cell count, neutrophil-to-lymphocyte ratio, and C-reactive protein, compared to the non-pregnant group (Table 4).

Severe TB, defined as requiring ICU admission or resulting in maternal mortality, occurred significantly more frequently in the pregnant group. The ICU admission rate among pregnant women with TB was 18.3%, compared to 3.0% in the non-pregnant control group (*p* < 0.001). The TB-related mortality rate was 11.6% in the pregnant group and 3.8% in non-pregnant women, with no significant association (Table 5).

Among the 60 pregnant women with active TB, adverse pregnancy outcomes were common. The rate of spontaneous abortion was 33.3%, and the stillbirth rate was 5.0%. Preterm birth was observed in 20.0% of pregnancies, and 15.0% of infants were born with low birth weight (<2500 g) (Figure 1).

Discussion

This prospective cohort study highlights the distinct characteristics in the clinical manifestations, the severity of the disease, laboratory findings, radiological findings, and pregnancy outcomes of women with active tuberculosis depending on pregnancy status. The pregnant women with TB in our study had significantly more fever, dyspnea, and neurological symptoms, more common bilateral lung involvement, miliary TB, and pleural effusion; had a lower level of haemoglobin and albumin, and elevated inflammatory markers as compared to non-pregnant women. Moreover, ICU admission was significantly higher in pregnant women, and the TB mortality rate was higher numerically. Among the pregnant subjects, there were more cases of spontaneous abortion, stillbirth, preterm delivery, and low birth weight babies.

The two groups in this study were similar in age, household exposure to tuberculosis, and the presence of predisposing comorbidities. The mean age was 27.2 ± 5.3 years for pregnant women and 26.9 ± 5.6 years for non-pregnant women (p=0.684). These comparable ages indicate that observed differences in clinical presentation are unlikely to be attributable to age. A prospective cohort from Lima, Peru, also reported similar ages and demographics among pregnant and non-pregnant patients with pulmonary tuberculosis; the median age was 24.5 years in the former and 25 years in the latter group.[11,12]

Pregnancy may increase susceptibility to active tuberculosis. A large Swedish register-based cohort study of 649,342 women found that the incidence of active tuberculosis was significantly higher during pregnancy and the postpartum period compared to periods when women were neither pregnant nor postpartum, with incidence rate ratios of 1.4 and 1.9, respectively. This elevated risk was particularly pronounced among women from countries with high tuberculosis incidence.[13] These findings are pertinent to Pakistan, where the baseline burden of tuberculosis remains high, and pregnancy may represent a critical opportunity for tuberculosis screening and early diagnosis.

A main finding of the present study was the significantly different symptom profile among pregnant women. Fever was seen in 71.7% of pregnant vs 35.4% of non-pregnant women (p<0.001), dyspnea in 43.3% vs 19.2% (p=0.001). Pregnant women also had significantly more neurologic symptoms (33.3% vs. 13.1%, p=0.003). These results indicate that TB during pregnancy may be more systemic and clinically evident. The higher prevalence of fever observed in this study aligns with findings from a large retrospective cohort in China, where fever was present in 61% of pregnant women compared to 35% of non-

Table 2. Clinical Symptoms and Presenting Features of study cases

Symptom	Pregnant Group (n = 60)(%)	Non-Pregnant Group (n = 130)(%)	p-value
Fever	43 (71.7)	46 (35.4)	<0.001
High-grade fever (>38.5°C)*	23 (53.5)†	-	-
Dyspnoea	26 (43.3)	25 (19.2)	0.001
Neurological symptoms	20 (33.3)	17 (13.1)	0.003
Constitutional symptoms	16 (26.7)	57 (43.8)	0.038

*Percentage calculated among febrile patients, †n = 43 febrile pregnant patients

pregnant women with tuberculosis.[14] However, not all studies have reported similar patterns. For example, a prospective cohort in Lima, Peru, found fever in 22.2% of pregnant women and 29.2% of non-pregnant women, with no statistically significant difference.[11] Variations in disease spectrum, healthcare setting, tuberculosis case definition, timing of diagnosis, and sample size may account for these discrepancies. The relatively high frequency of fever in this cohort may also reflect the status of Civil Hospital Quetta, which may receive patients with more advanced disease.

Pregnant women also exhibited significantly higher rates of dyspnea. This finding is biologically plausible, as pregnancy induces physiological respiratory changes, including increased oxygen consumption and ventilation. However, respiratory symptoms during pregnancy may be mistakenly attributed to normal physiological changes, potentially delaying tuberculosis recognition. Miele et al., in a clinical review, noted that tuberculosis diagnosis in pregnancy can be challenging because symptoms such as fatigue and respiratory complaints overlap with typical manifestations of pregnancy.[15]

Neurological symptoms were present in approximately one-third of pregnant women in this study. Clinically, this is significant because neurological symptoms may indicate extrapulmonary or disseminated tuberculosis. In a South African prospective cohort of pregnant and postpartum women with tuberculosis, extrapulmonary disease was considerably more common among HIV-infected women, with severe extrapulmonary symptoms primarily observed in those with profound immunosuppression.[12] Similarly, the Chinese comparative cohort reported neurological symptoms in 34.4% of pregnant women compared to 11.0% of non-pregnant women.[14]

Radiologic evaluation showed significant differences between the two groups. Chest imaging was performed in 81.7% of the pregnant women and 96.9% of the non-pregnant women (p<0.001). The lower imaging rate in pregnant women is likely due to concerns about fetal radiation exposure. However, current guidelines emphasise that chest radiography should not be withheld unnecessarily when TB is suspected on a clinical basis because the consequences of missed or delayed maternal TB may exceed the radiation risk of appropriately performed diagnostic imaging.[15]

Bilateral lung involvement was more frequently observed in pregnant women compared to non-pregnant women (63.3% vs. 39.7%; p=0.011). Additionally, miliary tuberculosis was more prevalent during pregnancy (28.6% vs. 11.9%; p=0.014). Pleural effusions were identified in 36.7% of pregnant cases compared to 21.4% of non-pregnant cases (p=0.042). The prevalence of miliary tuberculosis is particularly noteworthy. The Chinese study reported miliary tuberculosis in 24.5% of pregnancies compared to 10.9% of non-pregnant cases.[14] Furthermore, miliary pulmonary tuberculosis has been identified as an independent predictor of severe disease among pregnant women. Previous literature has described dissemination and extrapulmonary tuberculosis as significant forms of the disease in pregnancy, particularly when diagnosis is delayed.[15] The finding of more than twice as many miliary tuberculosis cases among pregnant women in this study supports the hypothesis of a more disseminated disease form during pregnancy.

Cavitary lesions were less common among pregnant women in the present study (12.2% vs. 26.2%, p=0.038). Another prospective Peruvian cohort reported cavitary

Table 3. Radiological Findings among Study cases

Finding	Pregnant Group (n = 49) (%)	Non-Pregnant Group (n = 126) (%)	p-value
Completed chest imaging	49 (81.7)	126 (96.9)	<0.001
Among those imaged			
Bilateral lung involvement	31 (63.3)	50 (39.7)	0.011
Miliary TB	14 (28.6)	15 (11.9)	0.014
Pleural effusion	18 (36.7)	27 (21.4)	0.042
Cavitary lesions	6 (12.2)	33 (26.2)	0.038

disease in 15.6% of pregnant women versus 27.4% of non-pregnant women, although this difference was not statistically significant.[11] Therefore, the findings are consistent between the two studies. The lower incidence of cavitation may reflect differences in host immune response or disease phenotype in pregnancy. However, because fewer pregnant women were imaged in our cohort, interpret this finding with caution.

The concentration of haemoglobin was much lower among pregnant women compared to those who were not pregnant (97.8 ± 13.2 vs. 117.5 ± 14.8 g/L; p<0.001). Anaemia is especially significant for women with active tuberculosis, since pregnancy causes increased demand for iron and folic acid, in addition to impairment of erythropoiesis due to chronic infection and inflammation. In a systematic review and meta-analysis of 13 studies encompassing over 3,000 pregnancies complicated by active tuberculosis, it has been shown that pregnant women with active tuberculosis have almost four times higher risk of anaemia than pregnant women without TB (OR 3.9, 95% CI 2.2–6.7).[16]

Albumin levels were also significantly lower among pregnant women (31.2 ± 5.6 vs. 40.1 ± 6.3 g/L, p < 0.001). Hypoalbuminaemia may reflect a combination of pregnancy-induced hemodilution, poor nutritional status, chronic inflammation, and increased metabolic activity. Reduced albumin levels have similarly been reported among pregnant women with tuberculosis. In a Chinese comparative study, albumin levels were 31.2 g/L in pregnant women and 40.4 g/L in non-pregnant women.[14] The consistency of these findings underscores the importance of decreased albumin as an indicator of nutritional and inflammatory status in pregnant women with tuberculosis.

Pregnant women also demonstrated an increased inflammatory response, with significantly higher white blood cell and C-reactive protein levels. This finding is consistent with the higher prevalence of fever, bilateral lung involvement, and miliary tuberculosis observed in this group. Chronic infection and inflammation can contribute to malnutrition, anemia, and other adverse outcomes for both mother and fetus. However, inflammatory markers should be interpreted with caution, as pregnancy itself can influence leukocyte counts and inflammatory pathways.

ICU admission is the best indicator of increased disease severity in our study. The ICU admission rate was 18.3% among pregnant women, compared with 3.0% among non-pregnant women (p<0.001). This indicates that pregnant women had about six times the rate of ICU admission as compared to non-pregnant women. This can be biologically explained by the increased physiological load on the cardiopulmonary system during pregnancy. In combination with lung disease, systemic inflammatory response syndrome, anemia, hypoalbuminemia, or disseminated tuberculosis, this can lower the physiological reserve. The increased rate of miliary TB in our cohort gives a clinical explanation for this trend.

Additional support for the notion that severe TB can lead to significant maternal morbidity comes from other populations as well. Among the pregnant women with TB in a South African cohort, 45% had an adverse outcome of maternal TB treatment, and all five maternal deaths happened in HIV-positive women.[12] In contrast, all participants in our cohort were HIV-negative, making our findings more directly applicable to HIV-negative pregnant women with TB and highlighting that severe TB outcomes can occur even in the absence of HIV co-infection. It serves as a clear example of the potentially serious consequences of TB in pregnant patients. In contrast, the prospective cohort study in Lima presents an opposite perspective. 96.6% of the pregnant women in the study had a positive outcome of TB treatment, and the outcomes of the treatment were similar for pregnant and non-pregnant women.[11] It shows that there is a possibility to avoid any negative consequences of pregnancy-associated TB with proper treatment and timely diagnosis.

The percentage mortality in relation to TB infection among pregnant women was 11.6% while that for non-pregnant women was 3.8%. The difference between the two groups was significant but did not reach statistical significance (p=0.065). This implies that the outcome is more of a clinically significant trend.

Our comparatively higher mortality may also be attributed to the fact that Civil Hospital Quetta is a hospital where

Table 4. Laboratory Parameters of Study Cases

Parameter	Pregnant Group (n = 60)	Non-Pregnant Group (n = 130)	p-value
Haemoglobin (g/L)	97.8 ± 13.2	117.5 ± 14.8	<0.001
Albumin (g/L)	31.2 ± 5.6	40.1 ± 6.3	<0.001
White blood cell count (×10^9/L)	11.5 ± 5.1	8.6 ± 4.2	<0.001
C-reactive protein (mg/L)	49.8 (26.1–79.4)†	23.5 (12.8–46.9)†	<0.001

patients with more complicated conditions are referred. Thus, such mortality rates cannot be extrapolated to the larger Pakistani population of women suffering from TB.

The pregnancy outcomes found in our study were alarming. Spontaneous abortion was found in 33.3% of the cases, stillbirth was found in 5.0% of the pregnancies, premature births were found in 20.0% of the cases, and low birth weight was found in 15.0% of the babies. Such observations have shown that there are negative outcomes of active maternal TB on pregnancy apart from the illness itself. Our results are supported by systematic research. Sobhy et al., in a systematic review and meta-analysis of 13 studies conducted on 3384 pregnancies with active TB, reported higher risks of maternal morbidity, anemia, preterm delivery, low birth weight, birth asphyxia, and perinatal mortality among the patients with TB than those without TB.[16] In another systematic review of 69 studies from 26 countries, anemia, maternal mortality, low birth weight, prematurity, and abortions, either spontaneous or induced, were common in patients with active TB.[17]

Our cohort has a 33.3% rate of spontaneous abortions, which is very high. Active TB can affect pregnancy as a result of inflammation, malnutrition, anemia, severe disease of the mother, and placental infection. This may also be because our study involved tertiary care facilities and the timing of TB diagnosis differed. This means our findings cannot be extrapolated to all pregnant patients with TB.

The proportion of preterm births in our study population was 20.0%. This observation is in line with the general trend of evidence emerging from systematic reviews that have established the association of increased risk of preterm births in pregnant women with active TB disease. According to Sobhy et al., there is a pooled OR of 1.7 (95% CI 1.2-2.4) for preterm birth in women with active TB when compared with women without TB infection.[16] Another recent study carried out in South Africa has noted adverse pregnancy outcomes such as preterm births, low birth weight, stillbirths, miscarriages, and deaths among pregnant women with TB infection.[18]

The 15.0% prevalence of low birth weight found in the current study is also corroborated by the literature. Increased risk of low birth weight was observed in pregnant females with active TB infection (OR 1.7, 95% CI 1.2–2.4).[16] In a cohort study from South Africa on HIV infected pregnant women, babies born to mothers who were suffering from TB infection had a significantly higher prevalence of low birth weight compared to the babies of HIV infected mothers without TB infection (20.8% vs 10.7%, p=0.04).[19] Though there was a significant difference in the populations of the two studies due to HIV infection in the South African population, the results seem to have a relation.

The 5.0% stillbirth rate in our study also has clinical relevance. Studies suggest that there is increased risk of perinatal mortality in pregnancies affected by active TB infection.[16,17] On the other hand, studies of the association between latent/previous TB infection and stillbirth have been inconsistent. For instance, a prospective cohort of women from Ethiopia showed no significant relationship between latent TB infection and stillbirth.[20] This difference is critical because latent TB infection cannot be equated with active maternal TB infection. The negative pregnancy outcomes recorded in our study are more likely due to active TB infection.

There are several possible explanations for the adverse effects of maternal and pregnancy outcomes seen in this research. Firstly, active tuberculosis leads to systemic inflammation, which may disrupt the function of the placenta and fetal growth. Secondly, maternal anemia and hypoalbuminemia may be related to malnutrition and lack of physiological reserves. Thirdly, miliary tuberculosis may lead to a severe condition and tissue hypoxia, which can negatively affect fetal development. Finally, delayed diagnosis and treatment can allow the disease to progress further.

The necessity of early diagnosis can be explained with the help of recommendations concerning tuberculosis in pregnant women made by Miele et al. According to the researchers, it is necessary to examine pregnant women with suspected TB or significant risks of tuberculosis, including chest X-ray and microbiological analysis, if necessary.[15] It is especially relevant to our findings concerning the fact that 18.3% of pregnant women needed ICU admission and suffered from adverse pregnancy outcomes.

Differences between these studies are significant because the epidemiological setting shapes the clinical picture of TB in pregnancy. While the Peruvian cohort

Table 5. Severe Clinical Outcomes of Study Cases

Outcome	Pregnant Group (n = 60)	Non-Pregnant Group (n = 130)	p-value
ICU admission	11 (18.3)	4 (3.0)	<0.001
TB-related mortality	7 (11.6)	5 (3.8)	0.065

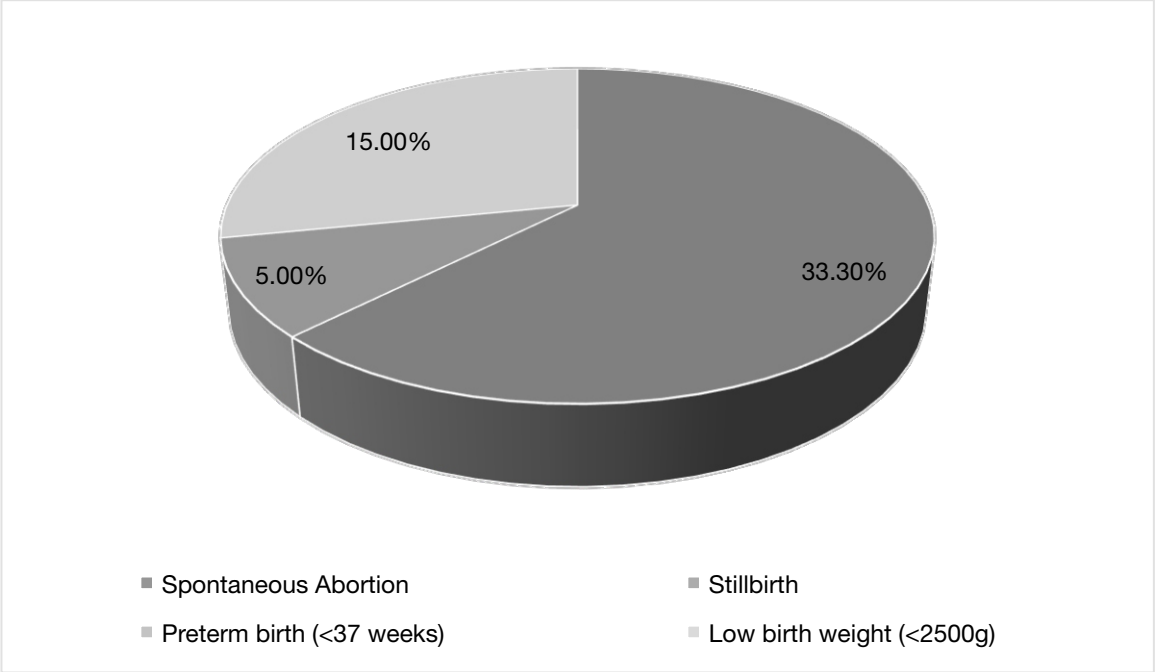

Figure 1. Pregnancy Outcomes among Pregnant Women with TB

study, involving 36 pregnant patients, showed quite similar clinical presentation and very good treatment results,[11] the South African cohort from a referral hospital described severe maternal and neonatal outcomes, with a high prevalence of prematurity and low birth weight and high maternal mortality, especially among HIV-positive women.[12] Moreover, a Swedish population-based study highlighted an increased risk for active TB in pregnancy and after giving birth, especially for women with a high incidence of TB in their countries.[13] The Chinese comparative cohort, however, showed much higher incidence of fever, dyspnea, neurological symptoms, miliary TB, ICU admissions, and spontaneous abortions among pregnant women.[14]

The current results also have several practical implications. Firstly, tuberculosis should still be considered among the differential diagnoses in pregnant women with fever, dyspnoea, neurological signs, or systemic disease without a clear cause. Secondly, pregnancy should not be blamed for the development of respiratory or constitutional symptoms in such patients. Third, do not delay chest imaging if it is clinically necessary. Finally, women with active tuberculosis who are pregnant may need more careful monitoring, especially when there is miliary or bilateral disease, anemia, hypoalbuminemia, or significant inflammation.

The pregnancy outcomes from this study also highlight the need for further monitoring during antenatal and fetal care. Women with active tuberculosis should be managed by TB specialists together with obstetricians and neonatologists when necessary. Moreover, the positive treatment results seen in some cohorts suggest that pregnancy cannot be regarded as a contraindication to the proper therapy of tuberculosis.[11,15]

Strengths

One advantage of this prospective design is that it allowed systematic collection of clinical and pregnancy data during follow-up. Another advantage is that the study included a comparison group of women who were not pregnant at the time, which helped identify differences in TB manifestations.

Limitations

Some limitations must be noted. First, it was a single-center study conducted at a tertiary referral center, so the possibility of over-representation of severe cases cannot be ruled out. Second, the number of pregnancies studied was comparatively small, especially in rare events such as maternal mortality. Third, more pregnant women were not subjected to chest investigations than non-pregnant women, which could introduce a bias when comparing radiological results. Fourth, some confounding effects of factors such as nutritional status, gestational age at the time of diagnosis, socio-economic factors, and diagnostic delay can still not be ruled out. Fifth, the

denominator for pregnancy-related outcomes must be well defined with respect to the population at risk.

Conclusion

In summary, the present study shows that there are significant differences in the clinical presentation and severity of active TB in pregnant women as opposed to those occurring in non-pregnant women. Fever, dyspnoea, and neurological symptoms were common among the pregnant patients; they were bilateral and miliary TB; hemoglobin and albumin concentrations were low, and there was increased inflammation. ICU admission was significantly higher, while the mortality rate, although higher, did not differ significantly. The pregnancy outcome was not positive because a considerable number of patients experienced spontaneous abortion, stillbirth, preterm births, and low birth weight. When comparing our results with studies from South Asia, Africa, Europe, China, and Latin America, the findings show that the severity of TB in pregnancy varies widely from one population to another.

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