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# Tuberculosis in pregnancy and adverse neonatal outcomes in two peruvian hospitals

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ABSTRACT

*Background:* According to the World Health Organization, tuberculosis (TB) ranks among the top 10 causes of death worldwide. The significance of TB during pregnancy lies in its symptoms, which can be mistaken for physiological changes associated with pregnancy. This confusion can lead to maternal-perinatal complications.
*Objective:* To evaluate the association between pulmonary TB in pregnancy and adverse neonatal outcomes in two Peruvian hospitals.
*Methods:* This is a retrospective cohort study. The target population consisted of pregnant women with and without pulmonary TB whose deliveries were attended at two public hospitals, located in Lima, Peru. The adverse neonatal outcomes were prematurity, low birth weight (LBW), and being small for gestational age (SGA). Crude and adjusted relative risks (RRa) were calculated with their respective 95% confidence intervals (95%CI).
*Results:* Information from 212 patients was analyzed; 48.1% had TB during pregnancy, and 23.1% had adverse neonatal outcomes (8%, 11.3%, and 12.3% for LBW, prematurity, and SGA, respectively). In the adjusted model, pregnant women with pulmonary TB had a 3.52 times higher risk of having a newborn with at least one of the adverse outcomes than those who were not exposed (aRR, 3.52; 95%CI: 1.93–6.68).
*Conclusion:* Pulmonary TB in pregnancy was jointly and independently associated with adverse neonatal outcomes, including LBW, prematurity, and being SGA.

## Introduction

According to the World Health Organization (WHO), tuberculosis (TB) is one of the 10 leading causes of death globally. Moreover, according to the Pan American Health Organization, Peru ranked second among the 10 countries with the highest TB incidence in 2017 and is one of the 5 countries in the Americas with the highest reported prevalence of monoresistant TB (MR-TB) and multidrug-resistant TB (MDR-TB) [1]. With a focus on women of reproductive age, the WHO estimates that out of the 9.6 million new TB cases in 2014, one-third were women [2]. No specific figures are available globally or nationally regarding TB in pregnant women, treated or untreated [3].

The relevance of TB in pregnancy is twofold. First, many of the symptoms can be confused with those that occur physiologically in pregnancy, such as weakness and fatigue [4,5]. Second, it can lead to maternal and perinatal complications, such as miscarriage, pre-eclampsia, low birth weight (LBW), prematurity, intrauterine growth restriction, a low Apgar score at birth, and congenital anomalies [6,7]. Consequently, the risk of maternal and fetal mortalities can be significantly high if the condition is not detected and treated timely [8].

A 2016 study from the United States reported a heightened incidence of TB among pregnant Hispanic women. Infants born to these women exhibited an increased rate of adverse events, primarily congenital anomalies. Interestingly, the incidence of preterm birth was lower compared to infants born to mothers without TB, who registered a higher number of such cases [9]. Conversely, research from Mexico, a Latin American nation, revealed that infants born to mothers diagnosed with TB during pregnancy predominantly suffered from adverse

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outcomes, with LBW being the most prevalent [10].

In a 2015 Peruvian study, Miranda et al. presented key perinatal outcomes of gestational TB (pulmonary and extrapulmonary). They found that 18.4% of newborns were born preterm, 12.2% had an LBW, and 10.2% were small for gestational age (SGA). In summary, almost 47% of the babies born to affected women had adverse birth outcomes [11].

Premature birth accounts for more than 33% of neonatal mortality worldwide. The consequences of not reaching the ideal gestational age negatively affect the newborn's lungs and brain, resulting in an increased risk of morbidity and disability [12]. Similarly, an LBW infant is more likely to be hospitalized for conditions that can develop in the neonatal period and may develop learning disabilities, mental retardation, cerebral palsy, and vision and hearing problems. Infants born SGA often suffer from hypothermia, perinatal asphyxia, myocardial dysfunction, and abnormalities in subsequent growth, metabolism, and neurological development [13]. In Peru, the National Maternal Perinatal Institute (INMP, by its acronym in Spanish) estimated that prematurity is the third leading cause of neonatal death, accounting for 25% of cases. Furthermore, in 2017 and 2018, the neonatal mortality rate due to prematurity was 77% and 74.1%, respectively [4].

To date, the Peruvian government does not have a specific strategy for TB in pregnant women [12,14,15]. In countries with a high burden of TB, such as Peru, strategies for TB screening and diagnosis are the same as for the general population [6]. In recent years, there has been insufficient research on the association between pulmonary TB during pregnancy and perinatal adverse outcomes in Peru.

The aim of this study was to evaluate the association between pulmonary TB during pregnancy and adverse neonatal outcomes (prematurity, LBW, or SGA) in patients with TB in pregnancy in two Peruvian hospitals from 2005 to 2019.

## Methods

### *Study design*

This was a retrospective cohort study of pregnant women with and without pulmonary TB who gave birth at the Hospital María Auxiliadora (HMA) and the Hospital Nacional Docente Madre Niño San Bartolomé (HONADOMANI SB), located in Lima, Peru, between 2005 and 2019. Both hospitals have a high level of resolution (level III) and belong to the Peruvian Ministry of Health (MINSA, by its acronym in Spanish) [16].

### *Population and sample*

Information was collected from the HMA and HONADOMANI SB databases, focusing on pregnant patients with and without TB. Data were collected from the CLAP sheets of the medical records for deliveries occurring between 2005 and 2019.

Three sample calculations were made for each adverse neonatal outcome, considering a confidence level of 95%, a power of 80%, and a sample size ratio of 1 for all scenarios. For prematurity, a risk in the exposed group (pregnant women with TB) of 17.4% and in the unexposed group (pregnant women without TB) of 5.9% [17] was considered, for a total of 242. For LBW, the risk was 30.4% in the exposed group and 3.4% in the unexposed group [16], for a total of 60. For SGA, the risk was 21.7% in the exposed group and 7.6% in the unexposed group [16], for a total of 196.

The largest number obtained from the sample calculation was used as the reference (n = 242). Because the number of pregnant women with TB was limited, information from all medical records of exposed patients who met the selection criteria was included, and for those who were not exposed, medical records were selected until the minimum required sample was completed.

The inclusion criteria for the exposed group were being pregnant and between 15 and 49 years of age in the year prior to the index conception, having a clinical history of delivery and newborn recorded at the HMA or HONADOMANI SB, and having pulmonary TB. The inclusion criteria for the unexposed group were being pregnant and between 15 and 49 years of age in the year prior to the index conception, having a clinical history of delivery, and having a newborn recorded in the HMA or HONADOMANI SB. The adverse neonatal outcomes considered in this study were LBW, prematurity (or preterm delivery), and SGA.

Finally, patients with a prenatal diagnosis of fetal malformations, immunodeficiency, and/or metaxenic disease, as well as incomplete or deleted medical records, were excluded. After excluding 64 patients, the final sample size was 212 (Fig. 1).

### *Variables*

#### *Primary outcome*

The outcome variable was adverse neonatal outcome, defined as any of these variables: LBW, SGA, or prematurity.

#### *Secondary outcomes*

Each adverse neonatal outcome was also evaluated independently. The individual operational definitions were as follows: a) Prematurity: a neonate with a gestational age of less than 37 weeks at the time of delivery; b) Low birth weight: a neonate weighing less than 2500 g at the time of delivery; c) Small for gestational age: according to the Fenton Growth Chart, this refers to a neonate whose height and/or weight is below what is considered appropriate for their gestational age at the time of delivery. That is, they fall below the 10th percentile or are less than 2 standard deviations below the norm.

#### *Exposure*

The exposure variable was pulmonary TB in pregnancy. It corresponded to the clinical and chest radiographic findings suggestive of pulmonary tuberculosis with bacteriological confirmation.

#### *Other variables*

Variables grouped into maternal data (place of residence, marital status, parity, education level, pregestational weight, type of delivery, comorbidities, and intrauterine growth restriction [IUGR]) and newborn data (sex, height, and head circumference).

### *Data analysis*

The information of interest was obtained from the medical records of both hospitals and exported to a database in Microsoft Excel 2016. The dictionary of variables previously created for this study was used for quality control and coding. The database was then imported into the Stata v17.0 statistical package (Stata Corporation, College Station, TX, USA).

In the univariate descriptive analysis, variables were presented as absolute and relative frequencies because all of them were categorical. The chi-square test was also used for bivariate comparisons.

To evaluate the association between TB in pregnancy and adverse neonatal outcomes, crude (RRc) and adjusted (RRa) relative risks were calculated using generalized linear models with the Poisson family, log link function, and robust variances. Estimates of the 95% confidence intervals (95% CI) were made using the accelerated nonparametric bias-corrected bootstrap method with 1000 replicates. This same procedure was performed for each individualized adverse neonatal outcome. Finally, multivariable models were constructed following an epidemiological approach, adjusting for the confounding variables of education level, comorbidity, and maternal age. Additionally, an interaction term was constructed to assess whether the type of delivery was an effect modifier for the association of interest; however, it was not significant.

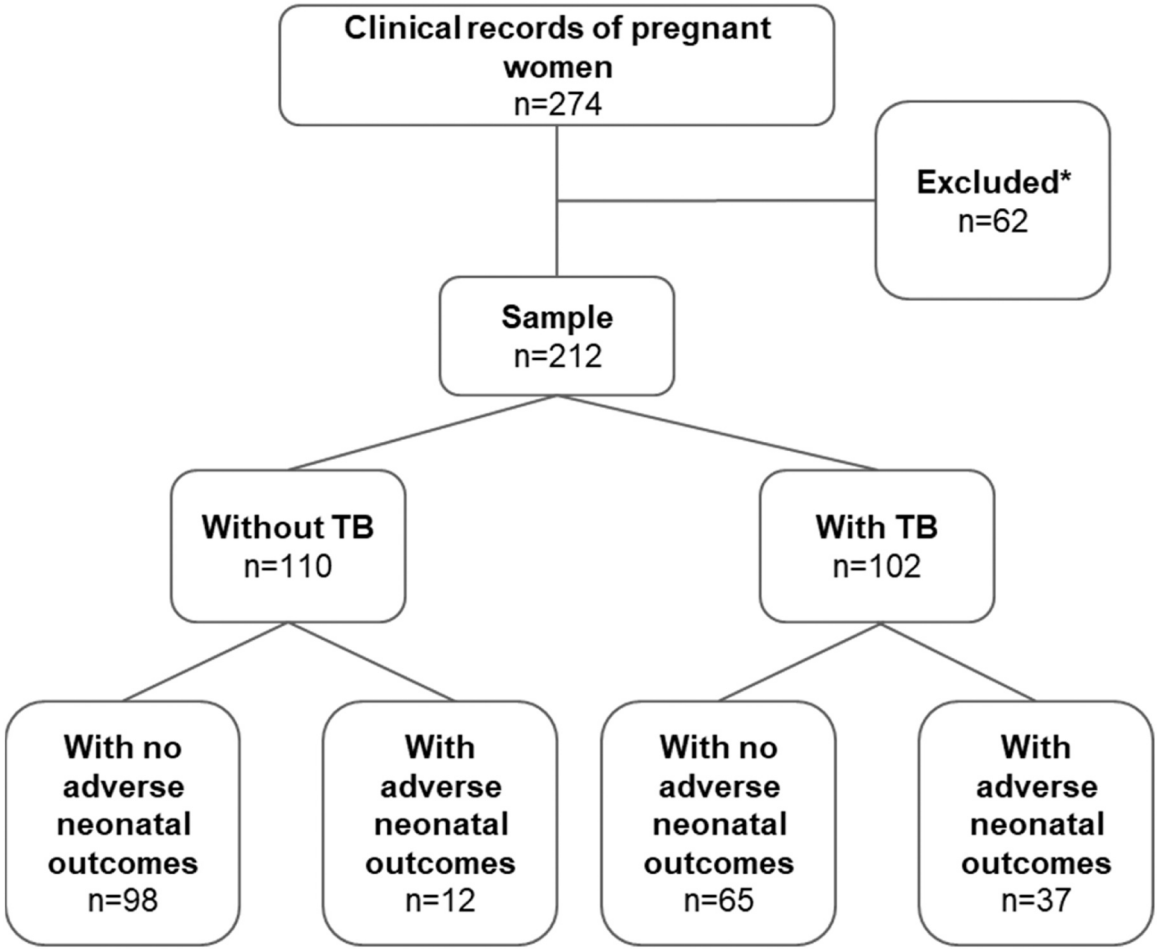


**Fig. 1.** Study FlowCHART. *Excluded from the study because they did not meet the inclusion criteria or their medical records were deleted or incomplete.

*Ethics*

This study was approved by the Ethics Committee of the Universidad Peruana de Ciencias Aplicadas, the Hospital María Auxiliadora, and the Hospital Nacional Docente Madre Niño San Bartolomé in Lima, Peru. Both ethical and scientific responsibilities were assumed for this project, which complied with the ethical principles of beneficence, autonomy, and nonmaleficence. The information obtained from the clinical histories was recorded while maintaining the anonymity of individuals. To create the database, codes were used, and maternal and neonatal identification data were not recorded for the study.

## Results

*General characteristics of the study population*

A total of 212 pregnant women were analyzed, 80.1% of whom were between 18 and 34 years of age. A total of 102 cases of pulmonary TB in pregnancy were identified, and the incidence of adverse neonatal outcomes was 23.1% (8.0%, 11.3%, and 12.3% for LBW, prematurity, and SGA, respectively) **(**Table 1**).**

*Population Characteristics According to Adverse Neonatal Outcome*

In terms of maternal characteristics, those with TB in pregnancy showed a significantly higher incidence of adverse neonatal outcomes ($p < 0.001$). Regarding newborn characteristics, there was a relationship between short stature and adverse neonatal outcomes ($p = 0.014$) **(**Table 2**).**

When each outcome was evaluated separately (Table 3), pregnant women with pulmonary TB had a significantly higher incidence of neonates with LBW ($p = 0.003$), prematurity ($p = 0.005$), or SGA ($p = 0.002$). Similarly, a significant relationship was observed between neonatal SGA and LBW ($p = 0.036$) and SGA ($p = 0.046$), while IUGR was significantly related with prematurity ($p = 0.014$).

*Association between Gestational TB and Adverse Neonatal Outcomes*

In the overall crude model, it was found that pregnant women with pulmonary TB had a 3.32-fold higher risk of having a newborn with at least one of the aforementioned adverse outcomes than those who were not exposed (cRR; 3.32; 95%CI; 1.86–6.55) **(**Table 4**).**

When analyzed for each adverse outcome and after adjusting for confounders, it was observed that pulmonary TB in pregnancy increased the risk of LBW (aRR: 4.86; 95%CI: 1.06–17.65), prematurity (aRR: 3.73; 95%CI: 1.64–10.64), and SGA (aRR: 3.64; 95%CI: 1.48–9.81) (table 4).

## Discussion

*Main findings*

The presence of pulmonary TB in pregnant women was associated with a higher risk of adverse neonatal outcomes. To the best of our knowledge, this is the first Peruvian study to jointly evaluate the association between pulmonary TB in the pregnant population and the incidence of these three adverse neonatal outcomes.

**Table 1**
General characteristics of the study population (n = 212).

| Features | | n (%) |
|---|---|---|
| Pulmonary TB in pregnancy | | 102 (48.1) |
| Low birth weight | | 17[8] |
| Prematurity | | 24 (11.3) |
| Small for gestational age | | 26 (12.3) |
| **Characteristics of the mother** | | |
| Mother's age | | |
| | Adolescent (15–17 years old) | 16 (7.6) |
| | 18–34 years old | 170 (80.1) |
| | Older mother (35–49 years old) | 36 (12.3) |
| Place of residence | | |
| | Lima | 200 (94.3) |
| | Province | 12 (5.7) |
| Marital status | | |
| | Single, widowed, or divorced | 63 (29.7) |
| | Married or cohabitant | 149 (70.3) |
| Primiparous | | 64 (30.2) |
| Education level | | |
| | Higher | 23 (10.8) |
| | High school completed | 131 (61.8) |
| | Did not finish school | 58 (27.4) |
| Pregestational weight over 50 kg | | 160 (75.5) |
| Cesarean delivery | | 111 (52.4) |
| Comorbidities | | |
| | No | 135 (63.7) |
| | Yes | 77 (36.3) |
| **Characteristics of the newborn** | | |
| Male NB | | 116 (54.7) |
| Normal weight NB | | 176 [83] |
| NB with IUGR | | 4 (1.9) |
| NB with normal head circumference | | 188 (88.7) |

TB: tuberculosis; NB: newborn; IUGR: intrauterine growth restriction

*Comparison with other studies*

In this study, we observed that 19.6% of newborns with SGA were born from mothers with pulmonary TB. These figures contrast with the 10.21% reported in the Miranda-Flores study at the INMP, Peru [11]; 30.4% in the Montalvo study at the Cayetano Heredia National Hospital, Peru [17]; and 19.71% in the Lin study in Taiwan, another country with a high TB rate [16].

Regarding LBW, 13.7% of newborns born to mothers with pulmonary TB presented with this outcome. In other studies, Miranda-Flores reported 12.2% [11], Figueroa-Damián reported 21.7% [9], and Lin reported 8.5% [16].

Regarding prematurity, 17.7% of the newborns of mothers exposed to pulmonary TB in our study were born prematurely. Lower figures have been reported in other studies, such as those of Lin (8.0%) [16] and El-Messidi (8.4%) [10]. Montalvo, found an incidence of 17.4% of preterm infants [17], while Miranda reported 18.4% [11], with both studies conducted in Peru.

*Interpretation of results*

Pregnancy induces physiological changes in the immune system that favor a state of immunomodulation. This adaptation is manifested by a decrease in the proinflammatory activity of T-helper 1 and 2 lymphocytes to avoid fetal rejection. This modulation may attenuate or mask the classic symptoms of infections such as TB, potentially hindering their diagnosis and management. This adaptation may also increase susceptibility to new infections and the risk of TB reactivation if the patient has a latent infection. After delivery, this immune modulation is reversed and may exacerbate symptoms of infections such as TB [18]. The exact mechanism by which TB is associated with the described adverse neonatal outcomes has not been clearly defined. Further investigation of the pathophysiology of TB during pregnancy in relation to these adverse outcomes will allow for a more detailed and specific interpretation of our findings.

**Table 2**
Characteristics of the study population according to adverse neonatal outcome.

| Features | Neonatal adverse outcome | | p |
|---|---|---|---|
| | No (n = 163) | Yes (n = 49) | |
| Maternal pulmonary TB | | | < 0.001 |
| No | 98 (89.1) | 12 (10.9) | |
| Yes | 65 (63.7) | 37 (36.3) | |
| **Characteristics of the mother** | | | |
| Mother's age | | | 0.343 |
| Adolescent (15–17 years old) | 10 (62.5) | 6 (37.5) | |
| 18–34 years old | 132 (77.7) | 38 (22.3) | |
| Older mother (35–45 years) | 21 (80.8) | 5 (19.2) | |
| Place of residence | | | 0.585 |
| Lima | 153 (76.5) | 47 (23.5) | |
| Province | 10 (83.3) | 2 (16.7) | |
| Marital status | | | 0.053 |
| Single/Widowed/Divorced | 43 (68.2) | 20 (31.8) | |
| Married/Cohabitant | 120 (80.5) | 29 (19.5) | |
| Parity | | | 0.255 |
| Primiparous | 46 (71.9) | 18 (29.1) | |
| Multiparous | 117 [79] | 31 (20.9) | |
| Education level | | | 0.454 |
| Higher | 20 [87] | 3[13] | |
| High school completed | 100 (76.3) | 31 (23.7) | |
| Did not finish school | 43 (74.1) | 15 (25.9) | |
| Pregestational weight | | | 0.710 |
| Greater than or equal to 50 kg | 124 (77.5) | 36 (22.5) | |
| Less than 50 kg | 39 [75] | 13 [25] | |
| Type of delivery | | | 0.589 |
| Vaginal delivery | 76 (75.2) | 25 (24.8) | |
| Cesarean section | 87 (73.4) | 24 (21.6) | |
| Comorbidity | | | 0.278 |
| No | 107 (79.3) | 28 (20.7) | |
| Yes | 56 (72.7) | 21 (27.3) | |
| **Characteristics of the newborn** | | | |
| Sex of the NB | | | 0.951 |
| Female | 74 (77.1) | 22 (22.9) | |
| Male | 89 (76.7) | 27 (23.3) | |
| NB size | | | 0.014 |
| Normal | 141 (80.1) | 35 (19.9) | |
| Underweight | 22 (61.1) | 14 (38.9) | |
| NB with IUGR | | | 0.198 |
| No | 161 (77.4) | 47 (22.6) | |
| Yes | 2 [50] | 2 [50] | |
| Head circumference of the NB | | | 0.076 |
| Normal | 148 (78.7) | 40 (21.3) | |
| Microcephaly | 15 (62.5) | 9 (37.5) | |

TB: tuberculosis; NB: newborn; IUGR: intrauterine growth restriction

In addition, there are risk factors and comorbidities that increase the susceptibility of pregnant women to TB. These include anemia, immunodeficiency, contact with patients with TB, overcrowding, and maternal weight below 50 kg [4]. By altering the immune response, these factors can increase the likelihood of infection, activate latent TB, and mask its symptoms during pregnancy. As a result, the fetus may be exposed to nutritional deficiencies and a suboptimal environment for its development, leading to the adverse events described above.

*Clinical and public health relevance*

TB in the context of pregnancy can lead to significant perinatal complications, making it imperative to minimize TB transmission among pregnant women. In order to meet this challenge, robust prevention strategies must be in place and timely diagnosis and treatment must be available. Primary prevention could include nutritional strategies for pregnant women, as good nutrition strengthens the immune system and can reduce the risk of infection, including TB [19]. One strategy to address malnutrition, a known risk factor for TB infection, is to provide adequate nutrition to pregnant women registered at health facilities [19–21]. In addition, routine TB screening during antenatal care, especially for women with identified risk factors (such as contact with TB patients or immunosuppression), can be critical for early

**Table 3**
Characteristics of the study population according to each adverse neonatal outcome.

| Features | Low birth weight | | | Premature | | | Small for gestational age | | |
|---|---|---|---|---|---|---|---|---|---|
| | No (n = 195) | Yes (n = 17) | p | No (n = 188) | Yes (n = 24) | p | No (n = 186) | Yes (n = 26) | p |
| Maternal pulmonary TB | | | 0.003 | | | 0.005 | | | 0.002 |
| No | 107 (92.3) | 3 (2.7) | | 104 (94.6) | 6 (5.5) | | 104 (94.6) | 6 (5.5) | |
| Yes | 88 (86.3) | 14 (13.7) | | 84 (82.3) | 18 (17.7) | | 82 (80.4) | 20 (19.6) | |
| **Characteristics of the mother** | | | | | | | | | |
| Mother's age | | | 0.208 | | | 0.449 | | | 0.300 |
| Adolescent (15–17 years old) | 13 (81.3) | 3 (18.7) | | 13 (81.3) | 3 (18.7) | | 13 (81.3) | 3 (18.7) | |
| 18–34 years old | 157 (92.3) | 13 (7.7) | | 153 (90) | 17 (10) | | 148 (87.1) | 22 (12.9) | |
| Older mother (35–45 years) | 25 (96.1) | 1 (3.9) | | 22 (84.6) | 4 (15.4) | | 25 (96.1) | 1 (3.9) | |
| Place of residence | | | 0.967 | | | 0.737 | | | 0.669 |
| Lima | 184 (92) | 16 (8) | | 177 (88.5) | 23 (11.5) | | 175 (87.5) | 25 (12.5) | |
| Province | 11 (92.7) | 1 (8.3) | | 11 (91.7) | 1 (8.3) | | 11 (91.7) | 1 (8.3) | |
| Marital status | | | 0600 | | | 0.174 | | | 0.134 |
| Single/Widowed/Divorced | 57 (90.5) | 6 (9.5) | | 53 (84.1) | 10 (15.9) | | 52 (82.5) | 11 (17.5) | |
| Married/Cohabitant | 138 (92.6) | 11 (7.4) | | 135 (90) | 14 (9.4) | | 134 (89.9) | 15 (10.1) | |
| Parity | | | 0.114 | | | 0.193 | | | 0.699 |
| Primiparous | 56 (87.5) | 8 (12.5) | | 54 (84.4) | 10 (15.6) | | 57 (89.1) | 7 (10.9) | |
| Multiparous | 139 (93.9) | 9 (6.1) | | 134 (90.5) | 14 (9.5) | | 129 (87.2) | 19 (12.8) | |
| Education level | | | 0.378 | | | 0.480 | | | 0.466 |
| Higher | 22 (95.7) | 1 (4.3) | | 22 (95.7) | 1 (4.3) | | 22 (95.7) | 1 (4.3) | |
| High school completed | 122 (93.1) | 9 (6.9) | | 116 (88.6) | 15 (11.4) | | 114 (87) | 17 (13) | |
| Did not finish school | 51 (87.9) | 7 (12.1) | | 50 (86.2) | 8 (13.8) | | 50 (86.2) | 8 (13.8) | |
| Pregestational weight | | | 0.282 | | | 0.955 | | | 0.430 |
| Greater than or equal to 50 kg | 149 (93.1) | 11 (6.9) | | 142 (88.8) | 18 (11.2) | | 142 (88.8) | 18 (11.2) | |
| Less than 50 kg | 46 (88.5) | 6 (11.5) | | 46 (88.5) | 6 (11.5) | | 44 (84.6) | 8 (15.4) | |
| Type of delivery | | | 0.578 | | | 0.534 | | | 0.273 |
| Vaginal delivery | 94 (93.1) | 7 (6.9) | | 91 (90.1) | 10 (9.9) | | 86 (85.1) | 15 (14.9) | |
| Cesarean section | 101 (91) | 10 (9) | | 97 (87.4) | 14 (12.6) | | 100 (90.1) | 11 (9.9) | |
| Comorbidity | | | 0.664 | | | 0.303 | | | 0.498 |
| No | 125 (92.6) | 10 (7.4) | | 122 (90.4) | 13 (9.6) | | 120 (88.9) | 15 (11.1) | |
| Yes | 70 (90.9) | 7 (9.1) | | 66 (85.7) | 11 (14.3) | | 66 (85.7) | 11 (14.3) | |
| **Characteristics of the newborn** | | | | | | | | | |
| Sex of the NB | | | 0.170 | | | 0.416 | | | 0.606 |
| Female | 91 (94.8) | 5 (5.2) | | 87 (90.6) | 9 (9.4) | | 83 (86.5) | 13 (13.5) | |
| Male | 104 (89.7) | 12 (10.3) | | 101 (87.1) | 15 (12.9) | | 103 (88.8) | 13 (11.2) | |
| NB size | | | 0.036 | | | 0.091 | | | 0.046 |
| Normal | 165 (93.7) | 11 (6.3) | | 159 (90.3) | 17 (9.7) | | 158 (89.8) | 18 (10.2) | |
| Underweight | 30 (83.3) | 6 (16.7) | | 29 (80.6) | 7 (19.4) | | 28 (77.8) | 8 (22.2) | |

(*continued on next page*)

**Table 3** (*continued*)

| Features | Low birth weight | | | Premature | | | Small for gestational age | | |
|---|---|---|---|---|---|---|---|---|---|
| | No (n = 195) | Yes (n = 17) | p | No (n = 188) | Yes (n = 24) | p | No (n = 186) | Yes (n = 26) | p |
| NB with IUGR | | | 0.207 | | | 0.014 | | | 0.433 |
| No | 192 (92.3) | 16 (7.7) | | 186 (89.4) | 22 (10.6) | | 183 (88) | 25 (12) | |
| Yes | 3 (75) | 1 (25) | | 2 (50) | 2 (50) | | 3 (75) | 1 (25) | |
| Head circumference of the NB | | | 0.391 | | | 0.380 | | | 0.174 |
| Normal | 174 (92.6) | 14 (7.4) | | 168 (89.4) | 20 (10.7) | | 167 (88.8) | 21 (11.2) | |
| Microcephaly | 21 (87.5) | 3 (12.5) | | 20 (83.3) | 24 (11.3) | | 19 (79.2) | 5 (20.8) | |

TB: tuberculosis; NB: newborn; IUGR: intrauterine growth restriction

**Table 4**
Association between gestational TB and adverse neonatal outcomes: crude and adjusted model.

| Exposure: Gestational TB | Crude model | | Adjusted model† | |
|---|---|---|---|---|
| | cRR | 95% CI | aRR | 95% CI |
| Outcome | | | | |
| Neonatal adverse outcomes (dichotomous) | 3.32 | 1.86 - 6.55 | 3.52 | 1.93 - 6.68 |
| Low birth weight | 5.03 | 1.37 - 21.34 | 4.86 | 1.06 - 17.65 |
| Premature | 3.23 | 1.35 - 8.96 | 3.73 | 1.64 - 10.63 |
| Small for gestational age | 3.59 | 1.43 - 12.45 | 3.64 | 1.48 - 9.81 |

* 95% CI estimation by nonparametric bias-corrected and accelerated bootstrap with 1000 replications.
95% CI: 95% confidence interval
†Model adjusted for education level, comorbidity, and mother's age.

detection and appropriate treatment [14].

Treatment of active and latent TB in pregnant women is the same as for nonpregnant patients, with the exception of streptomycin because of its potential toxicity to the fetus, according to the standard MINSA regimen. Although anti-TB drugs cross the placenta, there is generally no evidence that treatment during pregnancy affects the fetus. However, treatment must be individualized and supervised by a health professional to ensure the safety of both the mother and fetus. To improve treatment adherence, ongoing counseling of patients about monitoring is essential. Monitoring evaluates the response to treatment, the clinical evolution, and the detection of possible side effects. This is supported by laboratory tests to monitor liver and kidney function [22].

In terms of public health measures, it is necessary to refocus existing general strategies against TB to avoid possible complications in the mother and/or the newborn. For example, counseling could be provided to patients of childbearing age who wish to become pregnant about measures against TB. From an epidemiological point of view, the prevalence of patients with TB who have become pregnant in recent years is unknown. Thus, it is necessary to include this data in the TB caseload for patients of childbearing age and pregnant women. Another measure is to verify that the diagnosis and its ICD-10 code (O98.0: TB Complicating Pregnancy, Childbirth, and Puerperium) are filled in correctly, as this will facilitate its search in the Perinatal Information System used in Peru.

### *Limitations*

First, external validity is limited because the study was conducted in only two level-III hospitals, which may introduce variation compared with pregnant TB women delivering in other Peruvian hospitals. Second, owing to the limited sample size, it was not possible to exclude pregnant women with comorbidities other than pulmonary TB. This could be a confounding factor for the association of interest. However, we controlled for this variable in the adjusted models. Third, the information from both hospitals was obtained physically via the CLAP sheets with the medical records, which may be subject to completion errors, introducing information bias. However, considering that these are reference hospitals in Peru and TB is under epidemiologic surveillance, it is believed that the information was recorded as accurately as possible.

## Conclusion

TB in pregnancy was jointly and independently associated with adverse neonatal outcomes, including LBW, prematurity, and being SGA.

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## CRediT authorship contribution statement

**Carlos J. Toro-Huamanchumo:** Conceptualization, Data curation, Formal analysis, Supervision, Writing – review & editing. **Lizbeth R. Reynoso-Rosales:** Conceptualization, Data curation, Investigation, Writing – original draft. **Anita P. Llamo-Vilcherrez:** Formal analysis, Methodology, Software, Validation, Writing – review & editing. **Noelia V. Garay-Aguilar:** Conceptualization, Data curation, Investigation, Writing – original draft.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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