

Is Pulmonary Tuberculosis in Pregnant Women a Problem in Ghana? Observations and Lessons from the National Tuberculosis Prevalence Project

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Abstract

Background: Despite appropriate prevention and control measures, tuberculosis (TB) remains a significant contributor to maternal morbidity and mortality. Diagnosis of the disease in pregnancy is usually challenging, as the symptoms may be attributed to the pregnancy. Little is known about the true burden of the disease and its associated risk factors among pregnant women. This study sought to assess the prevalence of TB among pregnant women and associated sociodemographic characteristics in Ghana. **Methods:** The study used nationally representative data gathered from the national TB project in 2013. A total of 1747 pregnant women were sampled from 56 randomly selected diagnostic health centers across the ten regions of Ghana. TB was confirmed with Ziehl-Neelsen staining technique using morning sputum samples from pregnant women who reported coughing for more than 2 weeks. We assessed how the observed TB prevalence differed by some sociodemographic characteristics and other factors. We further examined the regional spatial distribution of pregnant women with TB in the country. **Results:** Up to 11.2% of the pregnant women had a history of cough during pregnancy. Eighteen (1.1%) cases of TB were confirmed among the pregnant women during the 2-year period, with the Eastern region of the country recording the highest ($n = 13$, 72%), followed by Volta region ($n = 2$, 11.1%). No cases were recorded in five regions. The geographical region of residence was the only determinant of TB in pregnancy significantly associated with TB ($P = 0.001$). **Conclusion:** Although the burden of TB was found to be low, appropriate control measures have to be put in place to detect the disease during the early stages of pregnancy to safeguard the health of the expectant mother and the unborn child.

Keywords: Maternal health, pregnancy, prevalence, tuberculosis

INTRODUCTION

Worldwide, an estimated 10 million people developed tuberculosis (TB) disease in 2017 – 5.8 million men, 3.2 million women, and 1.0 million children.^[1] TB remains one of the leading infectious causes of death in women worldwide and the most important cause of morbidity and mortality in human immunodeficiency virus (HIV)-infected women residing in low-income settings such as sub-Saharan Africa and Asia.^[2] With an increasing burden in women of reproductive ages (15–49 years), TB and HIV remain important causes of maternal mortality and morbidity globally, with more annual fatalities than any other infection.^[3–5]

Since the WHO does not report concrete figures on the global prevalence of active TB in pregnant women, available data

are only estimated.^[6] A study conducted in 2014 estimates that about 216,500 pregnant women worldwide suffered from TB in 2011 and almost half of them were of African origin.^[7] Ending the TB epidemic by 2030 is among the health targets of the Sustainable Development Goals.^[8] Many countries, however,

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do not have sufficient evidence on the epidemiology of TB in pregnancy due to several confounding factors, and there is the absence of data on whether or not pregnancy increases the risk of TB.^[3,9] Other factors such as HIV/acquired immune deficiency syndrome (AIDS) infection, poverty, homelessness, and drug abuse have also been identified as being associated with the transmission of TB among mothers of child-bearing age.^[10,11]

In 2016, the incidence of TB in Ghana was reported at 156/100,000 population.^[12] In 1994, the National Tuberculosis Control Programme (NTP) was established in Ghana to provide leadership for the health sector response to fight TB, with the goal of reducing the burden of the disease until it is no longer of public health importance. As is the case for most NTPs across the globe, Ghana has six broad strategies based on the new Stop TB Strategy endorsed by the WHO. These strategies include pursuing high-quality directly observed treatment short-course expansion and enhancement; addressing TB/HIV, multidrug-resistant TB, and its challenges; contributing to health system strengthening; engaging all care providers; and empowering people with TB, as well as communities and promoting research.^[13]

There is currently insufficient information on the epidemiology of TB and associated sociodemographic factors among pregnant women in Ghana. Given the paucity of information regarding the true burden of TB and its impact on the survival of both expectant mothers and their infants, it is important to first determine the burden of TB among pregnant women. Thus, the aim of our study was to determine the prevalence of TB and its associated sociodemographic characteristics. Identifying the factors would inform important control strategies to be used in preventing the spread of the disease.

METHODS

Study settings

The data for this research were obtained from the NTP's prevalence survey carried out at government health facilities across the ten regions of Ghana in 2013. A representative sample of facilities included regional and district hospitals, as well as health centers.

Research design

An observational design was used to determine and assess factors associated with TB using data obtained from the national prevalence survey conducted by NTP.

Study population

The study used data obtained from the national TB prevalence survey conducted from July to December 2013. The survey was a nationwide cross-sectional and population-based conducted among the adult population. According to the 2010 population and housing census, the adult population (age >15) was 15,208,425, representing 61.7% of the total population of 24,658,823. The sample size determination was based on a prior estimate for the national prevalence of bacteriologically

confirmed TB of 270/100,000 adult populations. In calculating the total sample size, a relative precision estimate of 20%, a selected fixed cluster size of 650, a resulting design effect of 1.44 ($k = 0.5$), and allowable losses of 20% from the eligible population were used. The total sample size was estimated to be 63,905 individuals of 15 years and above, from 98 clusters.

For this study, data were retrieved from a total of 1747 women who were currently pregnant during the data collection period. Women with insufficient information to determine the exact start and end of their pregnancies were excluded from the study to avoid bias. The retrieved data contained records from the 56 randomly selected diagnostic health facilities across the ten regions of Ghana. Data derived from these facilities were audited, tested, and checked for quality assurance.

Study exposure and outcome

All eligible participants who consented to participate were interviewed about TB suggestive symptoms. Those who had experience cough for 2 weeks and those with a current or previous history of TB were further queried about exposure to risk factors and their health-seeking behavior. All participants with TB suggestive symptoms were asked to provide spot and morning sputum specimens for smear microscopy and culture examination on both specimens.

Focusing on pregnancy, it was defined as any conception, regardless of the outcome. TB disease was confirmed with Ziehl–Neelsen staining technique using morning sputum samples from pregnant women who reported coughing during the screening process. The presence of any species from the *Mycobacterium tuberculosis* complex was considered as sufficient. This test was conducted only for pregnant women who reported signs and symptoms of TB. A total of 1744 pregnant women were expected to provide sputum for laboratory analysis (microscopy by Ziehl–Neelsen staining). However, 90.4% ($n = 1576$) submitted at least one sputum specimen.

Individual-level exposure factors such as age, occupation, area of residence, region, smoking, cough, duration of cough, and diabetes status for each patient's records were considered.

Ethical approval

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. It was also consistent with good laboratory practices and the applicable regulatory requirements. Ethical approval for the study was sought from the committee on human research publications and ethics at the Kwame Nkrumah University of Science and Technology (CRHPE/087/18). Permission to use the survey data was granted by the NTP. All patients gave written consent before the recruitment.

Data analysis

The data retrieved from the NTP were originally in Microsoft Excel format and were exported to Stata (version 14) statistical software for the analysis (StataCorp LP, College Station, Texas, USA). Simple descriptive statistics such

as proportions and frequencies were used to describe the variables. Chi-square/Fisher's exact test was used to determine associations between TB as an outcome and the sociodemographic factors. $P < 0.05$ was considered statistically significant.

ArcGIS 10.3 software supported with open GeoDa was used for mapping and examining the distribution of TB cases across the country.

RESULTS

Of the 1747 pregnant women whose data were reviewed for the 30-month period (July 2013–December 2015) of the NTP, more than half (52.2%) were aged 21–30 years, with majority being farmers (33.1%) and residing in rural (56.8%) parts of the country as shown in Table 1. Less than half (41.7%) of them and 11.2% reported ever smoking and coughing, respectively, during pregnancy.

Table 2 shows the prevalence of TB in pregnancy and the degree of positivity. The bacteriological investigations showed that 1.1% ($n = 18$) of the 1747 pregnant women screened were positive for acid-fast bacilli after smear microscopy was carried out. The level of positivity varied, with 12 (0.7%) of the confirmed cases being scanty. A total of 1558 pregnant women who reported not coughing were excluded and hence not tested for any species of *M. tuberculosis* complex.

Figure 1 provides a representation of TB cases across the regions in Ghana. Patients with TB were densely populated in the Eastern part of the country, with 13 (72%) of the confirmed cases occurring in that region. In the Upper West, Northern and Central regions only one (5.6%) confirmed case of TB was reported. No cases were recorded in the remaining five regions which were Greater Accra, Ashanti, Western, Brong Ahafo, and Upper East.

Patient's geographical region of origin was the only risk factor significantly associated with developing TB ($[P < 0.001]$ Fisher's exact test). Factors such as age ($P = 0.653$) and occupation ($P < 0.384$) were not statistically significant as risk factors associated with TB as shown in Table 3.

DISCUSSION

This is one of the first studies in Ghana that specifically sought to determine the burden of TB and associated factors among pregnant women. We found the prevalence of TB to be approximately 1.1%, with a region of residence being the only statistically significant factor associated with TB in pregnancy among the variables available in the dataset.

Due to the detrimental effect of TB on the health of both the mother and fetus,^[14,15] target screening strategies during pregnancy provide a unique opportunity to identify and treat this vulnerable population for TB.^[2] Nevertheless, clinicians face diagnostic challenges, as manifestations of the disease such as fever, fatigue, sweating, shortness of breath,

Table 1: Sociodemographic characteristics of participants' data reviewed

Variable	Frequency ($n=1747$), n (%)
Age (years)	
≤20	298 (17.1)
21–30	912 (52.2)
31–40	475 (27.2)
41+	62 (3.6)
Occupation	
Civil servants	67 (3.8)
Traders	548 (31.4)
Farmers	578 (33.1)
Miners	14 (0.8)
Artisans	198 (11.3)
Students	93 (5.3)
Fish farmers	84 (4.8)
Unemployed	165 (9.4)
Region	
Ashanti	348 (19.9)
Brong Ahafo	163 (9.3)
Central	146 (8.4)
Eastern	202 (11.6)
Greater Accra	164 (9.4)
Northern	271 (15.5)
Upper East	49 (2.8)
Upper West	52 (3.0)
Volta	168 (9.6)
Western	184 (10.5)
Area of residence	
Rural	992 (56.8)
Urban	755 (43.2)
Ever smoked	
Yes	728 (41.7)
No	1019 (58.3)
Cough	
Yes	196 (11.2)
No	1551 (88.8)
Cough >2 weeks	
Yes	51 (26)
No	145 (74)

tiredness, and cough are similar to physiological symptoms of pregnancy.^[6] This hinders early diagnosis and further delays medical attention. This delay results in poorer outcomes for mother and fetus, which is further exacerbated in conditions where adherence to treatment is difficult because of the general averseness to medication and pregnancy-related nausea.^[14] Left untreated, TB in pregnancy may result in increased neonatal morbidity, low birth weight, prematurity, and other pregnancy complications, including maternal morbidity due to higher rates of abortion, postpartum hemorrhage, and preeclampsia.^[16] In a case report of a 23-year-old primigravida, TB was confirmed only after complications that had set in. Although the fetus was delivered by cesarean section prematurely (29 weeks 2 days), the baby had to undergo TB treatment due to positive cultures of the bacterium found in the placenta and gastric fluid.^[17] A

Table 2: Prevalence of tuberculosis among pregnant women in Ghana	
AFB positivity	Frequency (%)
Excluded	1558 (89.3)
Scanty	12 (0.7)
1+	2 (0.1)
2+	1 (0.1)
3+	3 (0.2)
Not available	178 (9.6)
Total	1747 (100.0)
AFB: Acid-fast bacilli determined by Ziehl-Neelson staining	

Table 3: Association between tuberculosis among pregnant women and selected sociodemographic characteristics			
Variable	TB in pregnancy		Fisher's exact, <i>P</i>
	Positive, <i>n</i> (%)	Negative, <i>n</i> (%)	
Age (years)			
≤20	4 (22.2)	253 (16.2)	0.653
21-30	9 (50.0)	813 (52.2)	
31-40	4 (22.2)	436 (28.0)	
41+	1 (5.6)	56 (3.6)	
Total	18 (100.0)	1558 (100.0)	
Occupation			
Civil servant	0 (0.0)	62 (4.0)	0.384
Trader	5 (27.8)	492 (31.6)	
Farmer	6 (33.3)	532 (34.2)	
Mining	0 (0.0)	12 (0.8)	
Unemployed	3 (16.7)	138 (8.9)	
Artisan	1 (5.6)	170 (10.9)	
Student	3 (16.7)	76 (4.9)	
Fish farming	0 (0.0)	76 (4.9)	
Total	18 (100.0)	1558 (100.0)	
Geographical region			
Ashanti	0 (0.0)	314 (100.0)	0.001
Brong Ahafo	0 (0.0)	150 (100.0)	
Central	1 (0.8)	127 (99.2)	
Eastern	13 (6.6)	183 (93.4)	
Greater Accra	0 (0.0)	144 (100.0)	
Northern	1 (0.4)	243 (99.6)	
Upper East	0 (0.0)	43 (100.0)	
Upper West	1 (2.1)	46 (97.9)	
Volta	2 (1.4)	140 (98.6)	
Western	0 (0.0)	168 (100.0)	
Total	18 (100.0)	1558 (100.0)	

TB: Tuberculosis

meta-analysis study conducted in Great Britain also showed an increased maternal risk for anemia and cesarean delivery.^[18] Another devastating episode of TB during pregnancy which should not be overlooked is TB meningitis (TBM). Thwaites *et al.*^[19] reported that TBM is the most intense clinical presentation of TB, associated with increased morbidity and mortality, especially in immunocompromised individuals.

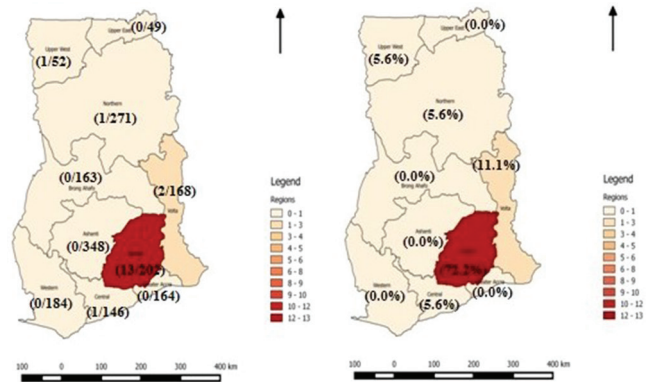


Figure 1: Spatial distribution of tuberculosis among pregnant women across the ten regions of Ghana

A case study in Nigeria has shed more light on the need to explore and investigate into the relationship between TBM and pregnancy, and how adept clinicians should be in diagnosing TBM in pregnancy, particularly ones with atypical presentation.^[20]

Although the study remains an observational one based on clinical data recorded from a nationally representative study, the observed 2-year TB prevalence among the pregnant women is low compared with the prevalence recorded in other countries in 2011 such as India (21%), DR Congo (7.5%), Pakistan (6.8%), South Africa (3.9%), and Bangladesh (3.8%).^[7] This is, however, consistent with a recent study conducted in Ethiopia where none of the sputum samples were TB culture positive, but one (1) was positive in Ziehl–Neelsen staining technique.^[21] A study by Sobhy *et al.*^[18] concludes that even if such figures are not statistically significant, the fact that there is a high proportion of extrapulmonary involvement in pregnant women which is often associated with a poorer outcome, it is important to pay significant attention to such results. Moreover, it is postulated that there is an increased risk of progression or reactivation of a latent TB infection to manifest TB in pregnant women.^[6] Another study observed that TB was associated with obstetric complications such as spontaneous abortion, preterm labor, small for date uterus and low birth weight, and few cases of congenital TB in newborn babies.^[9] An improvement in TB services aimed at pregnant women could therefore reduce mother-to-child transmission and ultimately lead to a reduction in secondary cases among other vulnerable populations, including the elderly and immunosuppressed.

A number of factors including geographical region, HIV status, occupation, and nutritional status are known to be associated with an increased risk of TB among pregnant women.^[3,11] This may be the case, especially in countries where the health system is poorly resourced and resources are usually restricted to the urban areas. Pregnant women who are HIV-positive are more vulnerable to TB due to the suppression of their immune system and due to their negative smear, may not be diagnosed early during

pregnancy.^[22] Although not assessed in this study, the Ghana AIDS Commission has estimated the prevalence of HIV among pregnant women in the Volta and Eastern regions to be 2.7% and 2.6%, respectively.^[23] Our results therefore affirm that the high prevalence of TB in pregnant women in these regions presents a real risk of HIV coinfection.

In a study conducted by Zenner *et al.*^[3] in the UK, the geographical region of residence was found to be associated with TB in pregnancy. This is consistent to our study where geographical variation determined the distribution of TB cases in the country. Strengthening the capacity of the health system to detect the disease at the early stage is therefore the key for controlling the spread of the disease. As part of the control measures, the WHO recommends that pregnant women need to be asked about symptoms related to TB, such as cough, night sweat, and loss of weight at their first visit to maternal and child health services.^[24] Although this is currently implemented in the country, financially challenged pregnant women from the remote areas of the country may not have access to early diagnosis and treatment due to the lack of TB diagnostic services in these areas. With these shortfalls in mind, this study provides useful information for stakeholders at all levels to improve health-care services for pregnant women and those with TB.

CONCLUSION

Similar to the figures quoted for other sub-Saharan countries, the prevalence of TB remains high in Ghana. Pregnant women with latent TB infection are more likely to progress to developing active TB than nonpregnant women. However, efforts to conduct significant research on TB among pregnant women in high burden populations are significantly lagging behind, particularly in sub-Saharan Africa.

As a country with high TB endemicity, a national prevalence of 1.1% among pregnant women raises important concerns about the health and well-being of vulnerable groups such as pregnant women. Although the burden of TB among pregnant women was low compared with other countries, the unequal geographical distribution of the disease reflects administrative gaps in the provision of TB diagnostic and treatment services in the country. To avoid adverse outcomes for mother and child, it is imperative to make diagnostic services readily available and accessible to all vulnerable populations in the quest for early diagnosis and treatment of the disease among pregnant women. Surveillance and control interventions are, therefore, urgently needed to aid in reshaping current concepts toward the control and elimination of TB as a public health problem. The outcome of this study should be interpreted with caution, as we acknowledge that culture is the gold standard for TB diagnosis, microscopy was the only diagnostic tool available in the study facilities; hence, our results may not reflect the true burden of the disease. There is also the need for further research to identify comorbid factors associated with TB in

pregnancy and its effects on maternal and neonatal morbidity and mortality in the country.

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Conflicts of interest

There are no conflicts of interest.

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