

## Mini Review

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# Tuberculosis in Pregnancy: Delayed Diagnosis, Lost Lives

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## ABSTRACT

Tuberculosis still remains an important global health disease, killing many people annually. Yet it is a preventable cause of death. Maternal mortality rates due to tuberculosis and HIV/AIDS in Sub-Saharan Africa make up a significant proportion of maternal deaths. It remains a disease of poverty, overcrowding and underdevelopment. Pregnancy increases maternal and fatal mortality in AIDS-infected women. In pregnancy it can be a challenging diagnosis to make, delaying treatment that could lead to adverse outcomes. Clinicians working in high prevalence areas of tuberculosis and those looking after immunocompromised patients should maintain a high index of suspicion. Developing countries must be helped to develop by the world financial institutions with debt reduction. The Sustainable Development Goal aims to end tuberculosis related deaths, transmission and catastrophic costs by 2030. Tuberculosis is a preventable death, the world must act together to prevent unnecessary deaths.

**KEYWORDS:** Tuberculosis; Pregnancy; Complications; Maternal mortality; Outcomes.

## INTRODUCTION

Every year around 250,000 women die during pregnancy and childbirth. Maternal mortality rates due to tuberculosis and HIV/AIDS in Sub-Saharan Africa now supercede obstetric deaths.<sup>1</sup> These infections can make up to 28% of maternal deaths.<sup>2</sup> Maternal tuberculosis can remain unrecognised and an underestimated tragedy.<sup>3</sup> Tuberculosis still remains the leading infectious cause of death in women worldwide, creating orphans, impoverished families and reduces the economic development of society. Approximately, a third of the world population are infected with tuberculosis, which still remains a major cause of preventable death in women. It kills more women each year than any other infection.<sup>4</sup> Untreated tuberculosis causes poor maternal and fetal/neonatal outcomes.<sup>5</sup>

In pregnancy it can be a challenging diagnosis to make delaying treatment that could lead to poor adverse outcomes. Clinicians working in high tuberculosis areas and those looking after immunocompromised patients should maintain a high index of suspicion.

## MICROSCOPY AND PATHOLOGY

The majority of cases are caused by *Mycobacterium tuberculosis* in 95% of cases and *Mycobacterium bovis* in 5% of cases.<sup>6</sup> Tuberculosis is an airborne disease spread mainly by droplets during coughing, sneezing, talking or breathing in overcrowded environments. The primary focus is the lungs and from there it can spread haematogenously to become disseminated throughout the body.

Tuberculosis is generally a disease of poverty and overcrowding. The HIV/AIDS pandemic has contributed to the surging cases of tuberculosis. The combination of pregnancy, tuberculosis and HIV/AIDS exposes pregnant women to high risks of mortality. A person with

both HIV and tuberculosis infection is thirty times more likely to become ill with tuberculosis than a person with tuberculosis infection alone.<sup>7</sup>

### CLINICAL FEATURES

Tuberculosis in pregnancy can present with vague symptoms, some of them mimicking normal physiology<sup>8</sup> of pregnancy hence leading to delayed diagnosis and treatment. Patients may present with a productive or non-productive cough, chest pains, haemoptysis and generalised body weakness. They may also present with low-grade fever, headaches and visual disturbances. Other symptoms may include loss of appetite, nausea and vomiting, bone pain and swollen lymph glands depending on the main focus of infection. HIV-infected patients have depressed defence mechanisms and may present with disseminated tuberculosis with little or no clinical signs or symptoms.

### DIAGNOSIS

There is usual delay in diagnosis of tuberculosis in pregnancy.<sup>8,9</sup> Therefore a high clinical index of suspicion must be maintained especially among vulnerable groups such as those infected with HIV/AIDS. In patients with productive coughs sputum should

be sent for Acid-Alcohol-Fast Bacilli test and histological examination with Ziehl-Neelsen staining. Red Acid-Alcohol Fast Bacilli can be seen in Ziehl-Neelsen stain (Figure 1). Culturing the bacilli in egg-based medium like Lowenstein-Jensen medium takes 4-6 weeks. In HIV-infected patients, sputa are usually negative for Alcohol-Fast Bacilli causing diagnostic difficulty and delayed treatment. In some studies a significantly higher proportion of bacterially confirmed pulmonary tuberculosis patients were HIV co-infected patients than HIV negative tuberculosis patients.<sup>10,11</sup>

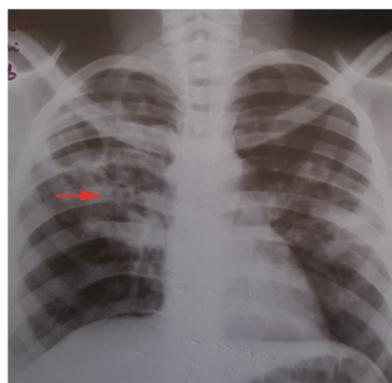
A full blood count is recommended as some patients may be anaemic due to chronic ill-health. Those not yet screened for HIV must have this test done as the two conditions usually coexist.<sup>7</sup> A chest X-ray with abdominal shielding must be done which may reveal pulmonary tuberculosis. Typical chest X-ray findings include military picture (Figure 2) and cavitations (Figure 3). Enlarged lymph nodes can have fine needle aspiration for histological examination. If there are signs and symptoms suggestive of tuberculous meningitis a lumbar puncture should be done and the cerebrospinal fluid sent for microscopy and culture. Tuberculosis screening as part of antenatal care in high prevalence regions may be helpful<sup>12</sup> to pick up latent tuberculosis. Early diagnosis would reduce morbidity and mortality rates.



**Figure 1:** Red acid-alcohol fast bacilli in a Ziel-Neelsen stain showing the causative organism for tuberculosis found in a sputum sample.



**Figure 2:** A chest X-ray showing military tuberculosis.



**Figure 3:** A chest X-ray with the arrow showing cavitation typical in tuberculosis.

**MATERNAL COMPLICATIONS**

Tuberculosis is an overwhelming illness on the body, causing wasting, generalised body weakness and exposes pregnant women to further risks of other infections. Tuberculosis can be pulmonary, extrapulmonary,<sup>13</sup> in lymph nodes, intestines, peritoneum, bones, kidneys and meninges. Extrapulmonary tuberculosis does affect pregnancy adversely.<sup>14</sup> The complications of tuberculosis include chronic anaemia, threatened miscarriage, premature prelabour rupture of membranes<sup>15</sup> and preterm labour. Pregnant women are more likely to experience chorioamnionitis,<sup>16</sup> postpartum anaemia, blood transfusion, pneumonia, acute respiratory distress syndrome and mechanical ventilation. Maternal deaths may result from overwhelming and disseminated disease, pulmonary compromise or meningitis. The patients that are HIV co-infected have more complications than those that are HIV negative.<sup>16</sup>

There may be intrauterine growth restriction, fetal distress, chorioamnionitis<sup>17</sup> and intrauterine death. There can be rarely congenital tuberculosis.<sup>18</sup> There appears that there are more congenital abnormalities in neonates born to mothers suffering from tuberculosis.<sup>16</sup> Open pulmonary tuberculosis poses a grave danger to the neonate born to a mother suffering from the disease. Pregnancy increases maternal and fetal mortality in AIDS-infected women.<sup>19</sup>

**MANAGEMENT**

The effective management of tuberculosis during pregnancy is a multi-disciplinary process involving the obstetrician, paediatrician, tuberculosis specialist, public health specialist<sup>20</sup> and laboratory scientist. Patients with open disease should be nursed in an isolation ward until they are rendered sputum negative usually after 2 weeks of chemotherapy. Six weeks combination drug regimes are usually curative. Directly observed therapy, short-course, is a tuberculosis control measure recommended by the World Health Organisation (WHO). The drug combination of rifampicin, isoniazid and ethambutol has been widely used in pregnancy with little fatal teratogenic effects being reported.<sup>21</sup> Neonates born to mothers that are still sputum positive receive isoniazid therapy until their mothers are rendered sputum negative.

Contact tracing of all cases of open tuberculosis are mandatory. Tuberculosis is a notifiable public health disease right up to the World Health Organisation (WHO).

**MODE OF DELIVERY**

Patients suffering from tuberculosis are delivered as per other obstetric patients. The indications for Caesarean deliver are as for normal obstetric indications. If they are delivered by an abdominal route before they are rendered sputum negative, the usual precautions taken for the care of infected cases in theatre are followed. If they have a normal vaginal delivery, the usual

precautions of dealing with infectious disease cases should be taken by the health care staff such as wearing face masks for their own protection.

**OUTCOMES**

Tuberculosis is a largely treatable disease. Fetal outcomes are good after successful treatment.<sup>22,23</sup> Meningeal tuberculosis is one of the major causes of maternal deaths as it is of insidious<sup>24</sup> onset hence early recognition and treatment improves outcomes. Breastfeeding is safe unless otherwise contraindicated.

**CONCLUSIONS**

Developing countries must take considerable appropriate action soon<sup>25</sup> to prevent escalating tuberculosis rates. The Sustainable Development Goals aim to end tuberculosis related deaths, transmission and catastrophic costs by 2030.<sup>26</sup> Achieving 90-90-90 targets for tuberculosis that is 90% vulnerable population screened, 90% diagnosed and started on treatment and at least 90% cured can be a goal to aim at.

**COMPETING INTERESTS:** None.

**AUTHOR'S CONTRIBUTION**

This is the sole work of Mr. S. Ngwenya.

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