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# Miliary Tuberculosis Associated with Mid-Trimester Miscarriage in a Rural Kenyan Hospital

[1]Vonwicks C. Onyango, MBChB, MMed, FCP(SA); [2]Collins P. Malalu, B. Com, MBChB; [3]Nicholas M. Mutuma, Diploma Clinical Medicine, Certificate (Public Health); [4]Agnes B. Akumu, KRNM; [4]Veronica Kyanya, KRNM; [4]Ruth M. Kamau, KRNM; [5]William C. Fryda, MD.

[1]Consultant Physician, St. Joseph Rift Valley Hospital, Gilgil, Nakuru County, Kenya
[2]Medical Officer-Intern, St. Joseph Rift Valley Hospital, Gilgil, Nakuru County, Kenya
[3]Senior Clinical Officers, St. Joseph Rift Valley Hospital, Gilgil, Nakuru County, Kenya
[4]Nursing and Midwifery Officers, St. Joseph Rift Valley Hospital, Gilgil, Nakuru County, Kenya
[5]Physician Haemato-Oncologist, St. Joseph Rift Valley Hospital, Gilgil, Nakuru County, Kenya

**Corresponding author: Vonwicks C. Onyango; https://orcid.org/0009-0004-6791-8809**

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***Abstract:*** **Tuberculosis (TB) in pregnancy is associated with adverse maternal and fetal outcomes. Pregnancy is a risk factor for tuberculosis, especially in high-TB burden populations, due to hormonal and endocrinological changes that impair immune responses to TB. Miliary TB is characterized by 1-2mm nodular infiltrates on chest x-rays that indicate the hematogenous spread of tubercle bacilli. Cases of miliary TB in pregnancy have been reported, especially following in vitro fertilization as well as in natural pregnancy, and have been associated with both first- and second-trimester miscarriages. Active case finding of TB needs to be integrated into routine focused antenatal care in order to ensure early diagnosis and linkage to comprehensive care in high-TB burden areas. We present a case report from rural Kenya of maternal miliary TB that resulted in a complicated mid-trimester miscarriage in order to underscore the importance of TB active case finding in antenatal care clinics.**

***Keywords:*** **Miliary tuberculosis, Tuberculosis in pregnancy, Mid-trimester miscarriage, TB case finding, Antenatal clinic, Kenya.**

## 1. INTRODUCTION

Tuberculosis (TB) remains a leading infectious cause of morbidity and mortality globally, with an estimated incidence of 10.6 million cases and 1.6 million deaths in 2021 (1). Sub-Saharan Africa bears the highest burden of global TB, with up to 50% of the TB cases being co-infected with HIV, despite significant strides made over the years that reduced the incidence of TB-related deaths (1, 2). Kenya ranks among the high-burden TB countries, with a 2016 estimated prevalence of 558/100,000 people and a 2017 estimated incidence of 317/100,000 people (3). Miliary TB is a form of disseminated tuberculosis due to the hematogenous spread of tubercle bacilli to the lungs and other organs, forming 1-2mm of infectious granulomata. These appear as millet-seed-size mottling on a chest radiograph (the Latin word for millet is *miliarius*), which is the pathognomonic finding supporting a diagnosis of miliary TB (which is both pulmonary and extrapulmonary TB) (4).

TB in pregnancy is of particular importance as it poses significant morbidity and mortality to both mother and fetus if not diagnosed early and effectively treated. In pregnancy, TB is associated with a 3-fold increase in maternal morbidity (i.e., maternal antenatal admissions, recurrent anemia, increased risk of operative delivery, etc.), a 9-fold increase in miscarriages, a 2-fold increased risk of low birthweight and preterm birth, and a 6-fold increase in perinatal death (5, 6). Miliary TB can occur in pregnancy, especially after in vitro fertilization and embryonic transfer (IVF-ET), or in natural pregnancy (incidence rates of 41.38% vs. 24.44%, respectively) (7). In cases of miliary TB following IVF-ET, symptoms tend to occur more commonly in the first trimester, while they appear in the second trimester following natural pregnancy (7). Endocrinological disorders and hormonal changes during pregnancy are believed to increase the risks of miliary TB in pregnancy, especially estrogen and progesterone changes, which inhibit immune lymphocytic functions. In IVF, glucocorticoids given to sensitize the ovaries to gonadotropin stimulation, as well as elevated estradiol levels following follicular development, can further suppress maternal immune function, thus predisposing to miliary TB (8, 9). Integrating active case finding of TB in antenatal clinics remains an important avenue for early diagnosis of TB and linkage to effective care in high-burden populations (10, 11). A high index of suspicion in such cases should identify patients for further TB diagnostic testing, e.g., patients with chronic or recurrent cough, pleuritic chest pains, fevers, night sweats, weight loss, unexplained anemia, dyspnea, etc. Simple laboratory testing for TB, including non-sputum and sputum-based assays (e.g., acid fast bacilli staining, Xpert MTB/RIF or TB GeneXpert, Tb sputum cultures), and imaging tests, e.g., CXR and high-resolution CT scan of the chest should safely be performed to confirm a diagnosis in pregnancy. But this can only be effective where pregnant women attend antenatal clinics in the first place and where focused antenatal care deliberately includes active case finding of TB during triage.

## 2. CASE SUMMARY

***Clinical Presentation and Management***

A 20-year-old married mother of a 2-year-old girl, a shopkeeper from Mbaruk, Nakuru County, Kenya, was admitted with features of endometritis 2 days following induction of labor for intrauterine fetal death at 24 weeks gestation by date in a peripheral facility. She's currently para 1+1. She had reportedly presented there with a 4-day spontaneous history of lower abdominal pains and vaginal bleeding with the expulsion of "huge" clots. She reported to have vaginally expelled a macerated fetus 1 day after drug induction of labor and had been discharged 4 hours afterwards, but re-presented 2 days later to our facility with severe lower abdominal pains radiating to the back, brownish, foul-smelling vaginal discharge, fevers, chills, vomiting, and general malaise. Importantly, she had not started attending an antenatal care clinic (ANC) prior to the miscarriage but had confirmed the pregnancy through an over-the-counter pregnancy testing kit. She had dropped out of school at 16 years of age due to financial challenges in the family.

Her initial examination was significant for a low-grade fever of $37.8^0$C, a tachycardia of 110 bpm, and a BP of 100/66 mmHg. She was mildly pale but not in any respiratory distress. Her abdominal examination was significant for marked suprapubic tenderness with voluntary guarding. A speculum examination showed a hyperemic, dilated cervix with foul-smelling brownish discharge in the introitus. A digital vaginal exam showed a dilated cervical *os* at about 4cm with bimanual uterine palpation showing a boggy uterus and cervical tenderness. She was dehydrated. The rest of the exam was unremarkable. Her significant work-up findings included a complete blood count showing mild neutrophilic leukocytosis with total a leucocyte count of $12.3x10^3$/µl, neutrophils of 72%, hemoglobin of 11.2g/dl, and platelets of $597x10^3$/µl; an abdomino-pelvic ultrasound showed the uterus appearing normal in size and echogenicity with normal endometrial thickness but with free fluid within the endometrium and pouch of Douglas. The urinalysis and baseline renal and liver function tests were normal, while the malaria smear and HIV rapid tests were negative.

She was assessed to have post-arbotal sepsis due to endometritis and treated with broad-spectrum antibiotics (intravenous ceftriaxone and metronidazole), fluids, and other supportive therapy successfully.

***Further Work-up and Management***

Further inquiry revealed a 6-8-week history of dry cough, chest pains, recurrent drenching night sweats, anorexia, and progressive lethargy that started around the third-fourth month of her pregnancy, associated with poor weight gain as the pregnancy progressed. Her brother had been treated for sputum-smear-positive pulmonary tuberculosis (TB) in 2021, and she'd cared for him closely. Her maternal grandfather was also treated for sputum-smear-positive TB in 2023. She also

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cared for him during his illness. She never used a protective face mask in both cases. A subsequent chest x-ray (CXR) showed a classical miliary pattern consistent with military TB. See figure 1 below:

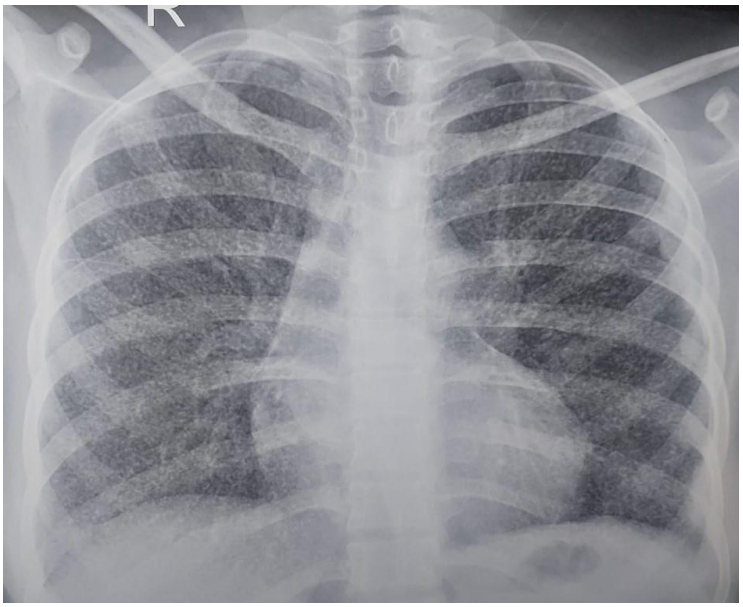

**Figure 1: CXR showing miliary pattern (1-2mm nodular infiltrates in all lung fields of both lungs) consistent with miliary tuberculosis.**

Induced sputum was negative for acid-fast bacilli by Ziehl-Neelsen staining and also negative for the Xpert MTB/RIF (TB GeneXpert) PCR assay. She was started on anti-TB therapy as per local protocol, i.e., an intensive phase consisting of rifampicin, isoniazid, pyrazinamide, and ethambutol, together with pyridoxine (to forestall isoniazid-induced peripheral neuropathy) for 2 months, followed by a continuation phase comprising rifampicin and isoniazid (with pyridoxine) for 4 months. By the end of the intensive phase, she had progressively improved, with the cessation of the cough and constitutional symptoms. She had already gained 4kg of body weight, and the CXR had normalized. See figure 2 below. During follow-up, she reported that her daughter and husband had both developed TB symptoms after her own diagnosis. The two are currently undergoing management for TB at a different health facility.

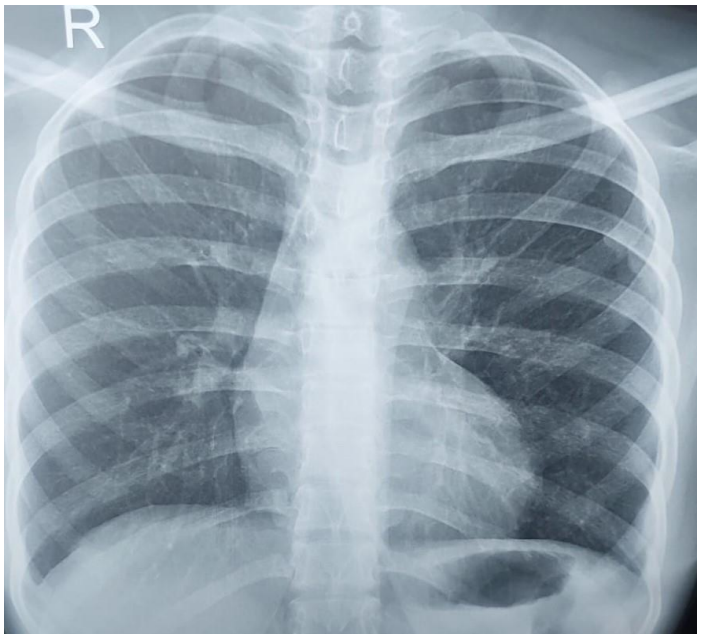


**Figure 2: Repeat CXR 2 months after starting TB treatment, now showing resolution of the miliary pattern.**

## 3. DISCUSSION

The typical causes of a second-trimester miscarriages are heterogeneous and include infections (e.g., chorioamnionitis, malaria, maternal viral infections, etc.), cervical incompetence, preterm labor, premature preterm rupture of membranes, fetal and uterine malformations, abruption, etc. (12). Second-trimester miscarriage is typically managed definitively with medical and/or surgical interventions, i.e., using misoprostol (with or without mifepristone) and/or surgical uterine dilation and evacuation. The general complications of such management include retained products of conception, infections (especially endometritis), cervical and uterine trauma, and hemorrhage (13). Tuberculosis, including miliary TB, though rare as a typical cause of second trimester miscarriage, should be considered in patients with compatible clinical symptomatology and in high-TB-burden areas. Ideally, these cases should be diagnosed early enough during antenatal care clinic follow-ups through a deliberate active case-finding program fully integrated into routine ANC care with subsequent linkage to care. Patients identified as having TB during such triage are then subjected to TB diagnostics based on local protocols, including sputum-based and imaging (CXR or high resolution CT scan of the chest), all of which are justified in pregnancy (on the balance of risk-benefit analysis) and can safely be done with appropriate safety measures (14). The typical drugs used to treat TB are safe during pregnancy (15). For our patient, she had clearly been repeatedly exposed to relatives with active pulmonary TB, from whom she must have acquired the infection. This was not diagnosed early since she had not attended any ANC clinic or any health care facility by the time of her miscarriage. Active screening for TB in ANC clinics needs to be made a routine part of focused ANC in Kenya and other TB-high-burden countries (10, 16, 17). It is highly likely that the miliary TB was the cause of the miscarriage. Her pregnancy status led to a lower immune function, thus predisposing her to hematogenous TB, which appeared as miliary TB on the CXR. Sputum studies in miliary TB are often difficult to obtain since most patients will have a dry cough. When sputum is available or induced, sputum AFB smears are positive for *M. tuberculosis* in only 20-25% of cases (18). The miscarriage was medically managed with oral and vaginal misoprostol, resulting in the expulsion of the dead fetus, but was complicated by endometritis, which was successfully treated with antibiotics.

## 4. CONCLUSION

Maternal infection with TB during the course of pregnancy is associated with adverse outcomes for maternal and fetal health, including miscarriages. Pregnancy itself is a risk factor for TB (especially in high-TB burden populations) due to suppressed immune functions and may manifest as hematogenous or miliary TB. Active case finding of TB through simple screening questions during triage in ANC visits will help in early diagnosis of TB in pregnancy in high TB burden populations. Therefore, a high index of suspicion should be maintained in these cases in order to make an early diagnosis and establish a prompt linkage for comprehensive, definitive TB treatment.

## 5. RECOMMENDATIONS

This case demonstrates the need for ongoing public health education and intervention measures on the basic knowledge and epidemiology of TB among the general population in Kenya. Active case finding for TB should be integrated into routine ANC clinics and rolled out in all primary health care settings in Kenya and other high-burden-TB countries.

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