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# Co-infection Pulmonary Tuberculosis and Severe COVID-19 in a Pregnant Woman at the University Hospital of Kinshasa: A Case Report

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**Abstract:** *Background:* To date, world widely, only a couple of papers have reported the association between pulmonary tuberculosis, Coronavirus disease 2019 (COVID-19) and pregnancy, and none of these reports was from sub-Saharan Africa where tuberculosis is endemic. Objective: the main objective of this study is to describe the co-infection Pulmonary Tuberculosis and Severe COVID-19 in pregnant young Woman at the University Hospital of Kinshasa. *Method:* The report case is of a pregnant woman aged 19 (Pare 2, Gesture 2, Abortion 0) with no known significant medical history, at 32 weeks of gestation based last menstrual period She has benefited from clinic examination, biological examinations (Ziehl's on sputum), a chest CT scan and a morphological ultrasound. *Result:* On admission, COVID-19 was the only working diagnosis. However, the persistent coughing prompted clinicians to request a Ziehl-Neelsen staining of sputum that revealed the diagnosis of pulmonary TB. The reverse-transcription polymerase chain reaction (RT-PCR)-confirmed COVID-19 infection and HIV

serology negative. A contrast-enhanced chest computed tomography (CT) showed airspace disease involving the right upper lobar, right medial basal segment and left upper lobe in the background of diffuse micro-nodular opacities favored to represent miliary pulmonary tuberculosis. There were associated cystic bronchiectasis in bilateral upper lobe and bilateral small amount of pleural effusion. Aforementioned findings were favored to represent a secondary or reactivation tuberculosis. The obstetrical ultrasound showed a single live intrauterine pregnancy in breech presentation, estimated at 34 weeks 3 days of gestation without usual features including detectable congenital malformation. *Conclusion:* The outcome of a pregnant woman with simultaneous COVID-19 and pulmonary tuberculosis is improved when the diagnosis is made early and management is promptly initiated. This attitude also improves the fetal prognosis. In the context of the COVID-19, the association of COVID-19 and pulmonary tuberculosis, especially in immunocompromised patients should be considered.

**Keywords:** Pulmonary Tuberculosis, COVID-19, Pregnancy, Immunocompromised, Sub-Saharan Africa

# 1. Introduction

The emergence of the new coronavirus 2 (sars-cov-2) in China in late 2019 (COVID-19) caused a pandemic with a global health crisis. Pregnancy is a physiological condition that leads to a relative decrease in immunity and makes pregnant women vulnerable to viral infections for this purpose. Besides, COVID-19 can have serious consequences for pregnant women, as It develops rapidly leading to alveolar damages that result in respiratory failure [1, 2]. In China, all studies of COVID-19 positive pregnant women have reported no maternal deaths [3]. Despite the resurgence of tuberculosis disease in many countries, its association with pregnancy is still relatively rare but it should still be considered in differential diagnosis in pregnant women showing recurrent fevers or apical pneumonitis. Although the diagnosis of tuberculosis in pregnant women is usually late, the maternal and perinatal prognosis of the infant is generally favorable as anti-tuberculosis treatment is accessible, effective and without fetal risk [4].

Tuberculosis remains the leading cause of death in the world due to a single infectious agent with about 1.5 million people dead per year. Like COVID-19, pulmonary tuberculosis is transmitted mainly by the respiratory route and affects the lungs. Concerns remain that COVID-19 may have a negative impact on the clinical course of tuberculosis [5]. This study report an association between COVID-19 infection, pulmonary tuberculosis and pregnancy, which not been described in Sub-Saharan Africa where tuberculosis is endemic.

# 2. Patient and Observation

This was a 19 years old pregnant woman (Pare 2, Gesture 2, Abortion 0) with no known significant medical history, at 32 weeks of gestation based last menstrual period. She first consulted at the Kinkole General Hospital at periphery of Kinshasa in Democratic Republic of Congo. On admission, she complained of fevers, dry cough, dyspnea, anorexia and profuse night sweating evolving for 5 days for which she received paracetamol at home. On physical examination, she weighed 51 Kilograms, blood pressure was 110/56 mmHg, pulse 119 beats per minute and respiration 34/minutes. The saturation was 86% on room air. Chest auscultation revealed subcrepitant rales at both lung fields. The breasts were enlarged and nonsecretory, the uterine fundal height measured 30 cm and the fetal heart rate was 140 beats per minute. In the vaginal examination, the cervix was softened, long and closed. The laboratory workup at admission revealed a Hemoglobin level of 9 g/dl, a thick drop examination for malaria showed 125 parasites/ml and white blood cell count (WBC) was 19600 elements/ml with neutrophils representing 67% and lymphocytes at 33%. The reverse-transcription polymerase chain reaction (RT-PCR)-confirmed COVID-19 infection and HIV serology negative. The combination of clinical and laboratory findings were consistent with the diagnosis of COVID-19 bronchopneumonia with bacterial superinfection and malaria in a pregnant women at 32 weeks of gestation. The patient the received respiratory assistance with oxygen at 5 liters per minute. She was also treated with dexamethasone, paracetamol, chloroquine, azithromycin and ceftriaxone as well as artesunate injection for malaria. The patient showed interval improvement including resolution of fevers, decreased dyspnea but there was persistent cough up to a week later after improvement of other symptoms. The Ziehl-Neelsen staining of sputum was then prompted and revealed the diagnosis of pulmonary TB. The patient was treated with anti-tuberculosis drugs including rifampicin, isoniazid, ethambutol and pyrazinamide for 2 months.

On day 12 of this treatment, the patient was referred to University Hospital of the University of Kinshasa, a tertiary level hospital, for further management. At admission at the university hospital, most of previously mentioned symptoms were improved. However, her oxygen saturation was relatively low at 91% in room air. The repeat of laboratory workup showed the following results: WBC 5,2 X $10^3$/ µL; RBC 4,03 X $10^3$/µL; HGB 8,2 g/dl; HCT 26,2 %; MCV – 65,0 fl; MCH -20,3 Pg; MCHC 31,3 g/dl; PLT + 595X$10^3$/ µL LYMP 21,1% MXD 5,4 % NEUT 73,5 %. The total bilirubin: 54.12 µmol/L; direct bilirubin 56.66 µ mol/L; AST 25.50 U/L; ALP 431.7 U/L; 8-GT 479.7 U/L; creatinine 0.68 mg/L; CRP 85.8 mg/L. Blood gases showed PH 7, 30; $PO_2$ 52 mmHg; $PCO_2$ 50 mmHg. Electrolytes: Na 137 mmol/L; K 3.7 mmol/L; Ca 1.22 mmol/L; Cl 103 mmol/L; Ca(7,4), r 1.17 mmol/L, CH +, r 49.4 nmol/L; $HCO_3$ act, r 24.7 mmol/L; $HCO_3$ std, r 22.7 mmol/L; BE(ecf), r -1.6 mmol/L; BE (B), r -1.8 mmol/L; BB (B), r 44. to mmol/L; ct $CO_2$, r 26

mmol/L; AnGap, r 13 mmol/L; mOsm, r 279.4 mOsm/L.

A contrast-enhanced chest computed tomography (CT) showed airspace disease involving the right upper lobar, right medial basal segment and left upper lobe in the background of diffuse micro-nodular opacities favored to represent miliary pulmonary tuberculosis (Figure 1). There were associated cystic bronchiectasis in bilateral upper lobe and bilateral small amount of pleural effusion. Aforementioned findings were favored to represent a secondary or reactivation tuberculosis.

The obstetrical ultrasound showed a single live intrauterine pregnancy in breech presentation, estimated at 34 weeks 3 days of gestation without usual features including detectable congenital malformation (Figure 2).

She continued with anti-tuberculosis drugs and oxygen therapy. On day 14$^{th}$, there were complete resolution of symptoms with improvement of oxygen saturation that was measure around 985 in room air. The obstetrical examination remained satisfactory. The repeat RT-PCR test for COVID-19 was negative. On day 16, the patient was discharged from the hospital with outpatient follow-up in the gynecological-obstetric and pneumology departments.

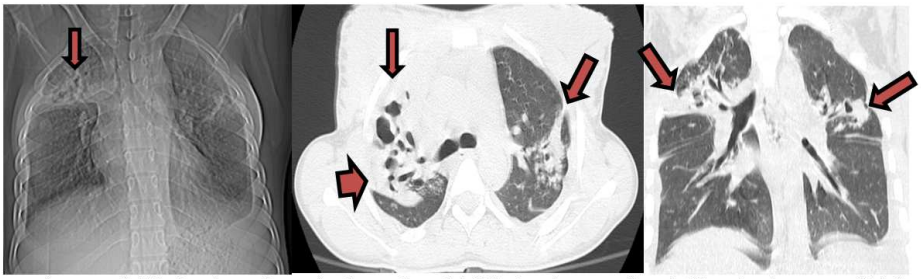

*Image 1: coronal CT view in radio mode, image 2: axial CT view in parenchymal filter showing upper bi-lobar condensation, image 3: coronal CT view in parenchymal filter, showing the condensation foci*

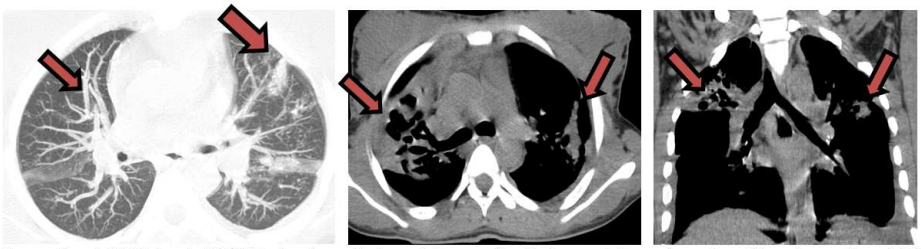

*Image 4: axial CT view in MINIP, showing a lesion mixture made of micronodules and condensations, image 5: axial CT view in mediastinal filter without PC injection, showing bronchiectasias in the right LS, image 6: coronal CT view in mediastinal filter without PC injection, showing an upper bi-lobar involvement*

***Figure 1.*** *Thoracic scan section.*

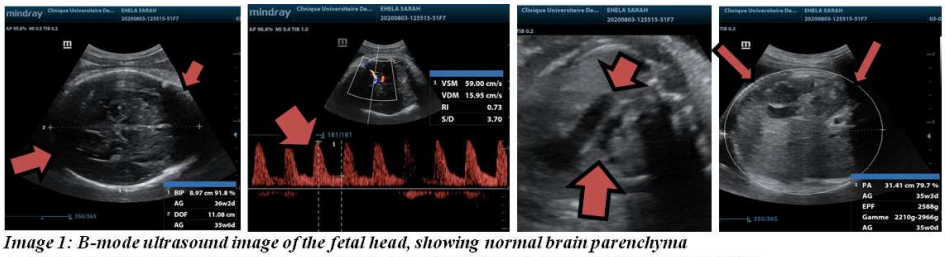

*Image 1: B-mode ultrasound image of the fetal head, showing normal brain parenchyma*
*Image 2: Doppler duplex echo image, showing a normal resistance index at the level of the sylvian*
*Image 3: Yoo echo image, showing a normal aspect of the three large vessels (aorta, pulmonary artery and IVC)*
*Image 4: Echo scan of the fetal abdomen, showing a normal aspect*

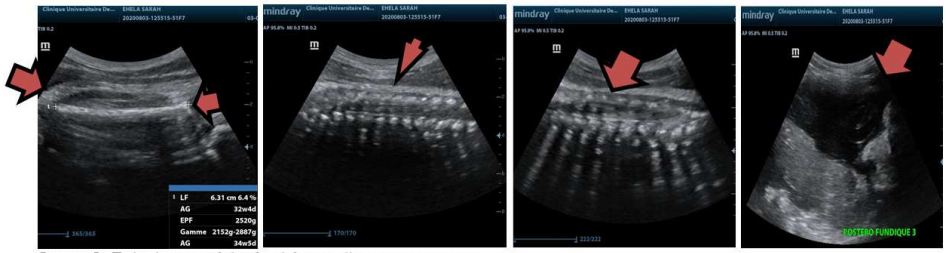

*Image 5: Echo image of the fetal femur, linear appearance*
*Image 6: Echo image of the fetal spine well stacked*
*Image 7: Echo image of the terminal medullary cone with normal appearance*
*Image 8: Echo image of amniotic fluid and posterofundial placenta of grade 3,*

***Figure 2.*** *Obstetrical ultrasound images.*

# 3. Discussion

This paper, report a case of a pregnant woman at 32 weeks of gestation presenting with a combination of tuberculosis and COVID-19. Each of the two medical conditions has some implications on the pregnancy. In sub-Saharan Africa where tuberculosis is endemic, most study speculate that tuberculosis constitute one of the most commonly encountered comorbidity in COVID-19 patients. The literature showed that patients with comorbidities are more likely to be affected by the virus [2, 3]. A meta-analysis of 8 studies including 46,248 patients with comorbidities associated with COVID-19 infection showed that comorbidities were strong predictors of the need for hospitalization and poor prognosis. Among comorbidities, patients with chronic respiratory diseases were more than twice as likely to be infected [6]. Chen Y and colleagues in China suggested that people with latent or active tuberculosis were more susceptible to SARS-CoV-2 infection [7]. In their study, the authors found that TB was the most common comorbidity for COVID-19 (36%), followed by diabetes (25%), hypertension (22%), ischemic heart disease (8%), and COPD (6%). They also found that Mycobacterium tuberculosis co-infection was associated with more severe COVID-19 and more rapid progression [7]. Many patients with active or cured tuberculosis demonstrate residual lung fibrosis and scars that could impact on lung function and the effects of COVID-19 in these lungs can be particularly devastating [8]. In a study of 70 patients with COVID-19 pneumonia, serial CT scans revealed that the majority (94%) of patients had mild to significant residual pulmonary abnormalities including some fibrotic changes on their last CT chest scan performed just prior to a median of 24 days from the onset of symptoms. This post-COVID-19 pulmonary fibrosis superimposed to the fibrosis caused by the sequelae of pulmonary tuberculosis, could likely to result in even more devastating disability [8].

There are similarities and differences between COVID-19 and tuberculosis. They are both airborne diseases, but it generally takes more prolonged contact with an infected patient to spread TB, unlike SARS-CoV-2, which is more easily transmitted. Both diseases share the three cardinal symptoms of cough, fever and shortness of breath. Like TB, a multitude of other organ systems may also be affected, as well as some unique and distinctive symptoms such as the anosmia and ageusia found in COVID-19. The most immediate difference is of course the speed of onset and progression. Unlike COVID-19 in which symptoms usually occur within a median of 5 days after exposure, the symptoms usually show gradual onset and progress over a period of weeks to months. Another interesting difference between these two entities is that SARS-CoV-2 can be transmitted by an asymptomatic patient whereas tuberculosis is usually transmitted by a symptomatic patient. This is because the bacterial load accumulates during weeks or months in active TB compared to SARS-CoV-2 in which the viral load peaks within days. Despite these differences, and perhaps because of the more chronic and progressive nature of the initial symptoms of TB, the baseline reproductive number, defined as the expected number of secondary cases produced by a single infectious case in a fully susceptible population, is approximately 3.55 to 4.3 for tuberculosis compared to 2.2 for SARS-CoV-2 [4].

Despite the global panic caused by the new coronavirus, its mortality at this stage of the pandemic is estimated to be about 2.5%, whereas untreated TB is by far the most lethal disease, with a mortality close to 50% [4-6]. A major difference is that while drugs to treat TB have existed for over 75 years, at this early stage of the pandemic, with the exception of remdesivir (which improves the time to clinical improvement but has no impact on mortality and dexamethasone (which has been shown to decrease mortality) [9]. No effective drug against SARS CoV-2 is available. The BCG vaccine used to prevent tuberculosis is thought to play a role in COVID-19. Since its introduction more than a century ago, Bacillus Calmette and Guerin (BCG) remains the most widely used and most widely administered vaccine in the world, having been administered to more than 4 billion people to date. BCG has several beneficial, non-targeted effects on the immune system, providing protection against a broad spectrum of respiratory viruses, bacteria and parasites [4]. A 25-year study of 150,000 children in 33 countries [10] showed that respiratory tract infections were reduced by 40% in children vaccinated with BCG. The vaccine has also been shown to reduce the severity of infections by viruses with a structure identical to SARS-CoV-2 in controlled trials [11]. Miller et al. first raised the intriguing epidemiological hypothesis that countries with a universal BCG vaccine in place appear to have reduced mortality from COVID-19 [12]. There is also a diagnostic similarity between the two conditions. The GeneXpert platform can screen for E and N2 gene targets in a single step. Thus, a commonly used TB platform is doubled to help diagnose SARS-CoV-2 with near point of care (POC) speed. Yet another example of common ground between TB and COVID-19. However, TB experts and stakeholders are concerned about the shift in focus from TB to COVID-19, especially since the current political and economic focus on COVID-19 has already resulted in a shift [13]. COVID-19 affects TB diagnosis through a combination of factors including delay in seeking health care due to restriction of patient movement during containment, Reduction in availability of health care personnel and Xpert and TrueNat TB machines and other laboratory facilities used for COVID response. Modeling in some countries has estimated that this combination will reduce the likelihood of TB diagnosis per provider visit by 70% [14]. The recent discovery of new agents such as bedaquine, delamanid, and pretomanid have further improved the outlook for MDR-TB patients [9]. The treatment of TB is not different in people with and without COVID-19 infection. Patients on TB treatment, whether for latent TB, drug-susceptible TB, or MDR-TB should continue treatment, without interruption, even if they acquire COVID-19, to increase the chance of cure and reduce transmission and the development of drug resistance. Experience with co-management of COVID-19 infection and TB remains limited

but important drug interactions between TB drugs and COVID-19 therapies should be highlighted. Lopinavir/ritonavir, a widely used antiretroviral drug combination, has recently received particular attention because of its possible role in the treatment of SARS-CoV-2. When used with rifampicin, there is a drug interaction that can potentially increase rifampicin leading to severe hepatotoxicity [15]. When coadministered, lopinavir levels and therefore efficacy may also be reduced. Lopinavir/ritonavir also significantly increases bedaquiline levels, resulting in QT interval prolongation which is an increased risk of cardiac arrhythmias [16]. From the relationship between COVID-19 and pregnancy, most significant physiological changes in breathing occur during pregnancy, including increased secretions and congestion in the upper airways, increased chest wall circumference and upward displacement of the diaphragm [17]. These changes result in decreased residual volume and increased tidal volume and air trapping, slightly decreased airway resistance, stable diffusing capacity, increased ventilation, and increased chemosensitivity to carbon dioxide. Hemodynamically, changes include a 20-50% increase in plasma volume, increased cardiac output, and decreased vascular resistance. These changes result in a state of physiological dyspnea and respiratory alkalosis and increased susceptibility to respiratory pathogens. The pathogenesis of severe COVID-19 involves the deregulation of the Treg/Th17 cell ratio towards an increase in Th17 cells, resulting in uncontrolled systemic inflammation. Thus, in pregnant women infected with SARS-CoV-2, the imbalance of Treg/Th17 cells could potentially be associated with adverse pregnancy outcomes such as abortion, preterm delivery. Nevertheless, further investigations are needed to validate their causal relationship [18]. The risk of SARS-COV-2 infection in pregnancy is already studied. The hormonal profile of gestation is characterized by an early increase in all components of the renin-angiotensin-aldosterone system (RAAS), including CEA2. This raises the possibility that pregnant women may be at risk for SARS-CoV-2 infection. In addition, arterial hypotension in pregnant women is maintained by a balance between being refractory to the pressor effects of Ang II and increased levels of Ang-(24), which exhibit systemic vasodilator responses [19, 20]. Depending on the immune response during pregnancy, data on immune responses to SARS-CoV-2 is lacking in pregnant women at this time, and data from previous pandemics, suggest that pregnancies may increase the risk of infection and death compared to non-pregnant women. The timing of infection during gestation may induce differences in maternal immune responses, viral clearance, and ultimately perinatal outcomes. Because the first and third trimesters are pro-inflammatory to promote implantation and labor [21], pregnant women infected with SARS-CoV-2 during these trimesters may be at increased risk for exaggerated responses to the virus (cytokine storm). Vertical transmission of SARS-CoV-2 has not been detected in the majority of reported cases, but few cases of neonates with positive RT-PCR after birth are described. Therefore, vertical transmission cannot yet be excluded [22]. On the toxicity of anti-TB drugs on pregnancy, anti-TB drugs are not toxic during pregnancy or breastfeeding [23].

# 4. Conclusion

The report case is of a pregnant woman aged 19 (Pare 2, Gesture 2, Abortion 0) with no known significant medical history, at 32 weeks of gestation. On admission, she complained of fevers, dry cough, dyspnea, anorexia and profuse night sweating evolving for 5 days. The reverse-transcription polymerase chain reaction (RT-PCR)-confirmed COVID-19 infection and HIV serology negative. The Ziehl-Neelsen staining of sputum was then prompted and revealed the diagnosis of pulmonary TB. The contrast-enhanced chest CT showed airspace disease in the background of diffuse micro-nodular opacities favored to represent miliary pulmonary tuberculosis and the obstetrical ultrasound showed; a single live intrauterine pregnancy in breech presentation, estimated at 34 weeks 3 days of gestation without usual features including detectable congenital malformation. After combination of clinical, laboratory and the medical imaging findings were consistent with the diagnosis of Coinfection COVID-19, malaria and pulmonary tuberculosis in a pregnant young women at 32 weeks of gestation. She received like treatment: oxygen at 5 liters per minute, dexamethasone, paracetamol, chloroquine, azithromycin, ceftriaxone, artesunate injection for malaria and anti-tuberculosis drugs including rifampicin, isoniazid, ethambutol and pyrazinamide. The outcome of a pregnant woman with simultaneous COVID-19, pulmonary tuberculosis and Malaria is improved when the diagnosis is made early and management is promptly initiated. This attitude also improves the fetal prognosis.

# Protection of Human and Animal Rights

We declare that this study did not involve experiments on either humans or animals.

# Data Privacy

The authors state that this study does not contain any personal data that could identify the pregnant woman with COVID-19.

# Contribution and Responsibility of the Authors

*Dr. Frederick Tshibasu Tshienda: writing and proofreading.*

*Doctor Angele Mbongo Tansia: proofreading.*

Doctor Cynthia Minouche Bukumba: *proofreading.*

*Dr. Ben Bepouka Izizag: writing and proofreading.*

*Professor Daddy Mata-Mbemba, text editing and proofreading.*

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*Professor Jean Marie Kayembe Ntumba: proofreading.*
*Professor Benjamin Longo Mbenza: writing, proofreading.*

## Declaration of Interest

All the authors do not have any possible conflicts of interest.

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