

HIV and SARS-CoV-2 Coinfection in A Term Pregnancy

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ABSTRACT

The novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the cause of the clinical syndrome COVID-19. Data on SARS-CoV-2 infection in pregnant women is rapidly accumulating and will help improve clinical guidelines for treatment. It is currently unknown if infection with human immunodeficiency virus (HIV) predisposes pregnant women to serious illness from SARS-CoV-2 infection. The greatest risk factors for pre-disposing patients with HIV to de-novo virulent viral infections includes non-adherence to combined antiretroviral therapy (cART) (Center for Disease Control and Prevention, 2020). We present the clinical course, treatment and outcome of a pregnant patient co-infected with HIV and SARS-CoV-2. We document an uncomplicated, full term delivery and highlight the adherence of cART in favorable outcome of pregnancy with SARS-CoV-2 and HIV co-infection.

Keywords: HIV, SARS-CoV-2, COVID-19, Pregnancy

Introduction

The COVID-19 global pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has affected 11,653,442 world population, with 538,933 total death, as of July 7, 2020 (<https://coronavirus.jhu.edu/map.html>) (CSSE, 2020). Special concerns have been raised on the impact of COVID19 on pregnant women who undergo profound physiological, anatomical and immunological changes. Emerging evidence suggests that the majority of pregnant women with SARS-CoV-2 infection showed similar minor symptoms as infected, non-pregnant women and may have a shorter clinical course (Pierce-Williams *et al.*, 2020). However, a recent cohort study reported that 9.3% (n=4) of pregnant women with SARS-CoV-2 infection developed to severe COVID-19 with 4.7% (n=2) requiring critical care management (Breslin *et al.*, 2020). Second trimester fetal demise (Baud *et al.*, 2020) and

maternal death have also been documented (Hantoushzadeh *et al.*, 2020).

The CDC reports that the risk of serious illness from SARS-CoV-2 in individuals with HIV is unknown. However, a limited number of reports showed that patients with HIV who had normal CD4+ T cell counts and suppressed viral loads were not at increased risk of severe illness compared to HIV negative patients (Zhao *et al.*, 2020). Still, little is known whether HIV and SARS-CoV-2 co-infection affects clinical course of viral infection and causes adverse maternal and infant outcomes. Here, we report the clinical course, treatment and outcome of a case of a pregnant woman with HIV and SARS-CoV-2 co-infection.

Case Presentation

An 18-year-old Hispanic G2P1001, with known HIV presented at 36 and 0 days gestation to the Labor and Delivery unit with concerns for contractions and being in labor. She also reported symptoms of a headache, body aches, sore throat, cough, hoarse voice and diarrhea for two days. She was identified as a SARS-CoV-2 person of interest and an oropharyngeal swab was collected for SARS-CoV-2 PCR testing. Her obstetrical history was significant for HIV seroconversion in her previous pregnancy; currently with an undetectable viral load on cART. She was adherent on the cART regimen of bictegravir-emtricitabine-tenofovir. On this admission, her viral load was undetectable and her CD4 T-cell count was 641 cells/mm³, CD4 percentage was 35% and CD4:CD8 ratio was 0.61.

On admission, Maternal-Fetal Medicine was consulted due to concern for SARS-CoV-2. The patient reported headaches, body aches, sore throat, and a cough for two days. The patient did not demonstrate any severe symptoms associated with SARS-CoV-2 infection as per current CDC guidelines (Center for Disease Control and Prevention, 2020). A fetal non stress test (NST) was reactive and her evaluation did not show she was in labor. She was discharged home with strict precautions for self-quarantine for 14 days, oral hydration, antipyretics for temperatures greater than 100.4 degrees F, monitoring for worsening of her clinical symptoms and decreased fetal movement. Approximately 24 hours after discharge, the patient was contacted and informed of her positive SARS-CoV-2 test by her provider. At that time, she reported persistent symptoms of diarrhea and a new complaint of eye irritation and intermittent dyspnea. She was again counseled about her SARS-CoV-2 infection with a plan for close follow-up in two days.

During her telehealth visit two days later, the patient reported developing loss of smell and taste and resolution of some previously reported symptoms (i.e. diarrhea and eye irritation).

She presented again to labor and delivery at 36 weeks and 3 days for evaluation of vaginal leakage

of fluid. She was placed in a negative pressure room for evaluation and she did not have any evidence of amniotic membrane rupture. She continued to complain of mild viral infection symptoms including sore throat, cough and fatigue. A fetal NST was reactive in triage and she was again counseled on SARS-CoV-2 and discharged home with a plan for outpatient management.

The patient presented in labor at 38 weeks and 0 days asymptomatic for SARS-CoV-2. Another oropharyngeal swab for SARS-CoV2 was collected, 13 days after the initial positive result. Results were again positive for SARS-CoV-2. HIV viral load was undetectable and her CD T-cell count was 708 cells/mm³. Her cART was continued and she was also started on IV zidovudine or additional intrapartum management of her HIV. The patient had an uncomplicated vaginal delivery of a female infant whose birth weight was 3060 grams; consistent with the 30th percentile for gestational age. The APGAR score was 9 and 9. The infant was cared for under the American College of Pediatrics guidelines for care of SARS-CoV-2 patients post-delivery (Appendix 1) and the mother elected to isolate from the neonate. She had an uncomplicated postpartum course and remained without symptoms of SARS-CoV-2. The infant also had an uncomplicated course and tested negative for SARS-CoV-2 and HIV. Both mother and infant were discharged home together in excellent condition on postpartum day 2. Repeat HIV testing will be performed at the infant's four-month follow-up visit.

Discussion

SARS-CoV-2 Clinical Course in a Pregnant Woman Treated for HIV

To date, multiple case-control studies outlining the management of SARS-CoV-2 infection in pregnant women have been published. To the best of our knowledge, there have been no reports describing pregnancy outcomes of mothers co-infected with HIV and SARS-CoV-2. Notably, a study conducted at Columbia University in New York reported that pregnant women in the second and third trimester with SARS-CoV-2 are often asymptomatic, yet may develop standard symptoms of SARS-CoV-29. This is in concurrence with a recent review on pregnant women with SARS-CoV-2, which also documented that nearly half of pregnant women with SARS-CoV-2 gave birth prematurely regardless of their symptom status (Mullins *et al.*, 2020). However, the outcome of patients co-infected with HIV and COVID-19 is unknown. As pregnancy represents a distinctive and complex state of immunity, how HIV and cART therapy influence the course of pregnancy during SARS-CoV-2 infection is of basic and clinical scientific interest.

Infection with HIV during pregnancy results in the dysregulation of CD4 and CD8 T cells, which play a critical role in effective antiviral responses (Ganji *et al.*, 2020). These T cells mediate a cellular immune response that plays a crucial role in the containment of HIV during pregnancy (Ganji *et al.*,

2020). Pregnant patients with HIV may experience reduced numbers of CD4 T-cells. Pregnant women with HIV predisposed to numerous adverse perinatal outcomes that include fetal growth restriction, preterm labor and intrauterine infections (ACOG Committee Opinion No. 751, 2018).

Limited reports of HIV positive individuals infected with SARS-CoV-2 suggest that unknown protective factors exist for this population. A study conducted in Spain by Blanco *et al.* evaluated 5 patients coinfecting with HIV and SARS-CoV-2. The study adapted an antiretroviral therapy regimen based on protease inhibitors: three patients were given lopinavir-ritonavir and two were given darunavir- cobicistat. All patients survived with one patient being admitted to the intensive care unit (Blanco *et al.*, 2020). Another study demonstrated the ability of the active triphosphate form of tenofovir, tenofovir diphosphate (TFV-DP), to inhibit the SARS-CoV-2 RNA-dependent RNA polymerase (RdRp) *in-vitro* (Chien *et al.*, 2020). Tenofovir's chemical backbone structure is similar to remdesivir; the antiretroviral drug currently being evaluated in the treatment of patients with severe COVID-19 (Eastman *et al.*, 2020). However, there is limited data on remdesivir in COVID-19 pregnant patients as they are excluded in the current clinical treatment trials. Both drugs inhibit viral RNA synthesis. Some antiretrovirals, including lopinavir and ritonavir, have effectively inhibited coronavirus replication *in-vitro*, including SARS and MERS (Chen *et al.*, 2004; Chan *et al.*, 2013). This suggests that HIV antiretroviral therapy using tenofovir and emtricitabine may provide a protective role for pregnant women with HIV, making them less likely to progress toward severe COVID-19. Our patient remained compliant with her ART, consisting of bicitegravir-emtricitabine-tenofovir, throughout her entire pregnancy and only developed mild symptoms of COVID-19.

We report the clinical course and maternal and infant outcomes of a patient co-infected with HIV and SARS-CoV-2. We speculate that cART treatment may play a role in the severity of COVID-19 during pregnancy. Tenofovir may have therapeutic benefits for patients with infected with SARS-CoV-2 and provide additional incentives for HIV mothers to remain adherent to their antiretroviral therapy. There are limited guidelines for the management of COVID-19 in patients with HIV and even less information for pregnant patients coinfecting with SARS-CoV-2 and HIV. More reports are needed of co-infected pregnant patients to determine if the degree of adherence to ART therapy and the levels of HIV suppression are associated with protection against the development of COVID-19.

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