Research Letter

False-Positive Human Immunodeficiency Virus Screening Results in Pregnancy During the Coronavirus Disease 2019 (COVID-19) Pandemic

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False-positive human immunodeficiency virus (HIV) test results are rare but have been documented in the setting of certain underlying conditions such as Epstein-Barr virus, metastatic cancer, and certain autoimmune conditions. A retrospective cohort study in a large hospital system was conducted to compare the occurrence of false-positive HIV fourth-generation test results before and after the coronavirus disease 2019 (COVID-19) pandemic in a population of pregnant patients (N=44,187; 22,073 pre-COVID and 22,114 during COVID). The COVID cohort had a significantly higher frequency of false-positive HIV test results compared with the pre-COVID cohort (0.381 vs 0.676, *P*=.002). Within the COVID cohort, 25% of patients had a positive polymerase chain reaction test result for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) preceding their false-positive HIV test results. When this subgroup was excluded, the difference in frequency of false-positive HIV test results between the cohorts was no longer significant (0.381 vs 0.507, *P*=.348). Our findings suggest that SARS-CoV-2 seropositivity was associated with an increased frequency of false-positive HIV test results in the pregnant population.

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Human immunodeficiency virus (HIV) screening is a ubiquitous component of prenatal care. The American College of Obstetricians and Gynecologists and the Centers for Disease Control and Prevention recommend antenatal HIV testing for all pregnant patients, most commonly using fourth-generation chemiluminescent immunoassays that simultaneously detect HIV p24 antigen and antibodies to HIV-1 and HIV-2. On average, the sensitivity and specificity of these HIV fourth-generation assays are greater than 99%.[1–3]

Although uncommon, false-positive HIV test results have been documented in the setting of underlying conditions such as Epstein-Barr virus, metastatic cancer, and certain autoimmune conditions. The similarity between HIV and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike proteins leading to antibody cross-reactivities and yielding false-positive results on immunoassay tests has been described.[4,5] However, the phenomenon of false-positive HIV test results in pregnant patients exposed to SARS-CoV-2 has not been explored. We sought to compare the frequency of false-positive HIV test results among pregnant patients before and after the onset of the coronavirus disease 2019 (COVID-19) pandemic and to determine whether an association between SARS-CoV-2 infection and false-positive HIV test results exists in this population.

METHODS

This was a retrospective cohort study including all pregnant patients who received care at a multi-site

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health system in Southeast Michigan. Pregnant patients from March 2017 to March 2019 were assigned to the pre-COVID cohort, and pregnant patients from March 2020 to March 2022 were assigned to the COVID cohort. A 1-year gap before the first documented case of COVID-19 in the state of Michigan was used to separate the cohorts to ensure that there were no overlapping pregnancy events. In the health system, all pregnant patients undergo routine screening for HIV infection in the first and third trimesters and at the time of delivery admission. The same two assays (the Roche Cobas e801a and the Siemens Centaur, each with an identical, published specificity of 99.9%) were used by the health system for the duration of the study timeline. Demographic information, the dates and results of the HIV tests, and the dates and results of the polymerase chain reaction (PCR) SARS-CoV-2 tests were ascertained by medical record extraction. Detailed medical record abstraction was performed for all patients with positive HIV test results. An HIV fourth-generation test result was deemed "false-positive" if subsequent HIV-1 or HIV-2 antibody differentiation immunoassays or HIV-1 nucleic acid tests or both were nonreactive. Patients found to be HIV-positive or not pregnant at the time of their HIV testing were excluded. Statistical analyses were performed to compare baseline group characteristics and the frequency of false-positive HIV test results before and during the pandemic. Study approval was obtained from the Henry Ford Health System IRB.

RESULTS

Overall, 44,187 pregnant patients were included, with 22,073 in the pre-COVID cohort and 22,114 in the COVID cohort. Demographic characteristics for the pre-COVID and COVID cohorts are shown in Table 1. In the pre-COVID cohort, 42 (0.19%) patients were found to have abnormal HIV test results and 16 of 42 (38.1%) had false-positive screening test results. In comparison, 71 (0.32%) patients in the COVID cohort had abnormal HIV test results and 48 of 71 (67.6%) had false-positive screening test results. Overall, the frequency of false-positive HIV test results was significantly higher in the COVID cohort compared with the pre-COVID cohort (38.1% vs 67.6%, P=.002). Among the 48 patients with false-positive HIV test results in the COVID cohort, 12 (25%) had positive PCR test results for SARS-CoV-2 infection during pregnancy, preceding their false-positive HIV test results. After excluding this subgroup from analyses, the difference in frequency of false-positive HIV test results between the cohorts was no longer statistically significant (38.1% vs 50.7%, P=.348) (Table 2).

Table 1. Demographic Comparisons of Patients in the Pre-COVID and COVID Cohorts

	Cohort		
Demographic	Pre-COVID	COVID	*P**
All patients	n=22,073	n=22,114	
Age (y)	28.0±5.6	28.6±5.6	**<.001**
Race†			
Asian American and Pacific Islander	866 (3.9)	891 (4.0)	.504
Black	6,348 (28.8)	6,219 (28.1)	
White	12,014 (54.4)	12,132 (54.9)	
Other or undisclosed	2,845 (12.9)	2,872 (13.0)	
Ethnicity†			
Hispanic	1,905 (8.6)	2,030 (9.2)	.111
Non-Hispanic	19,331 (87.6)	19,272 (87.1)	
Undisclosed	837 (3.8)	812 (3.7)	
Patients with false-positive HIV screening results	n=16	n=48	
Age (y)	27.8±4.3	28.9±4.5	.731
Race and ethnicity†			
Asian American and Pacific Islander	2	3	.792
Non-Hispanic Black	3	13	
Non-Hispanic White	7	22	
Undisclosed	4	10	

HIV, human immunodeficiency virus.
Data are mean±SD or n (%) unless otherwise indicated.
Bold indicates P<.05.
* Two-sample t-test was used for normally distributed data; χ^2 test was used for categorical variables.
† The racial and ethnic composition of the cohorts was assessed to establish baseline similarity between the comparison groups.

Table 2. Comparing the Frequency of False-Positive Human Immunodeficiency Virus Screening Test Results Before and After the Onset of the Coronavirus Disease 2019 (COVID-19) Pandemic

	Cohort		
	Pre-COVID (n=22,073)	COVID (n=22,114)	*P**
Abnormal HIV 4th-generation test results	42/22,073 (0.19)	71/22,114 (0.32)	**.007**
False-positive HIV screening results	16/42 (38.1)	48/71 (67.6)	**.002**
Excluding patients with positive PCR test results for SARS-CoV-2	16/42 (38.1)	36/71 (50.7)	.348

HIV, human immunodeficiency virus; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
Data are n/N (%) unless otherwise specified.
Bold indicates $P<.05$.
* Chi-square test was used.

DISCUSSION

Our findings demonstrate an increased frequency of false-positive HIV test results among pregnant patients since the onset of the COVID-19 pandemic and suggest that SARS-CoV-2 seropositivity may be partially responsible for this phenomenon. Although only 25% of patients in the pandemic cohort had positive PCR test results for SARS-CoV-2 infection preceding their false-positive HIV test results, this is likely an underestimation of the true rate of seropositivity in this group. It is plausible that more patients with false-positive HIV test results were, in fact, seropositive for SARS-CoV-2 at the time of testing but did not have a documented COVID-19 diagnosis due to lack of accessibility of COVID-19 testing, as well as significant variation in symptomatology among those infected, which may have dissuaded patients from seeking testing.

Strengths of our study include our large sample size, as well as the similarities in the pre-COVID and COVID cohorts' demographic characteristics. A major limitation of this study was our inability to explore the potential association of COVID-19 vaccination with false-positive HIV test results due the lack of standardized documentation of immunization status in our electronic medical record system.

Considering the maternal and neonatal implications of a positive HIV test result, obstetricians should be cognizant that false-positive results can occur in the setting of new and prior SARS-CoV-2 infections. Shared decision making should be used when considering the initiation of antiretroviral therapy, route of delivery, and delay of breastfeeding for patients with a newly positive HIV fourth-generation test result, particularly in the absence of other risk factors.

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