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Nirmatrelvir–Ritonavir (Paxlovid) for Mild Coronavirus Disease 2019 (COVID-19) in Pregnancy and Lactation

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Abstract

Nirmatrelvir–ritonavir (Paxlovid) is recommended to reduce the risk of hospitalization from COVID-19 in pregnancy. Data on use in pregnancy, including prescribing patterns and patient experience (adverse effects, incidence of rebound), are limited. We performed a cross-sectional study in which we surveyed a cohort of vaccinated pregnant or lactating individuals with breakthrough COVID-19. Of 35 pregnant respondents, 51.4% were prescribed and 34.3% took nirmatrelvir–ritonavir; of these, 91.7% experienced dysgeusia and 50.0% had rebound (50.0% positive test, 33.3% return of symptoms). Three of five lactating respondents were prescribed and two took nirmatrelvir–ritonavir. There were no significant adverse outcomes. Unknown risk was the most common reason for declining nirmatrelvir–ritonavir. More research is needed to establish the safety of nirmatrelvir–ritonavir in pregnancy and lactation, improve public health messaging, and increase uptake of this treatment.

Precis:

Nirmatrelvir–ritonavir is well-tolerated in pregnancy and lactation, though mild adverse effects and rebound may be common.

Introduction

Nirmatrelvir–ritonavir (Paxlovid) reduces the risk of hospitalization and death from COVID-19 in high-risk populations[1], but data in pregnancy and lactation are lacking. Leading professional societies support its use in pregnancy.[2,3] Patient experience, such as adverse effects and incidence of rebound symptoms, has not been reported in these groups.

We surveyed a vaccinated cohort of pregnant or lactating individuals about their experience with nirmatrelvir–ritonavir for COVID-19. We aimed to assess the patient clinical experience after treatment, including the rate of rebound symptoms.

Methods

This is a cross-sectional study of individuals who received their initial COVID-19 vaccination series during pregnancy or lactation, the COVID-19 Vaccination in Pregnancy and Lactation (COVIPAL) study. Enrollees receive periodic questionnaires to assess for breakthrough infections and other changes in their health. SARS-CoV-2 infection (confirmed by medical record review) between January – December 2022 received an additional survey about their experience with nirmatrelvir–ritonavir.

The study was approved by the Institutional Review Board of the University of California, San Francisco (IRB#20–32077). All participants provided written informed consent prior to enrollment. Enrollees with COVID-19 received a REDCap-based survey with questions about their experience with nirmatrelvir–ritonavir. See Appendix 1, **available online at** http://links.lww.com/xxx. Medical records were reviewed to assess the following variables: gestational age at SARS-CoV-2 infection, gestational age at COVID-19 vaccination and booster dose(s), maternal age, gravidity, parity, self-reported race/ethnicity, co-morbidities (hypertensive disorder, diabetes mellitus, pulmonary disease), obstetric outcomes, and hospitalizations. We analyzed descriptive data using medians (range) for continuous variables and frequencies by n (%). Adverse effect severity was graded according to DAIDS criteria.[4] We collected information about patient race and ethnicity because racial and ethnic disparities exist in outpatient COVID-19 treatment in the United States.[5]

Results

Of 371 patients in the parent study, 64 had COVID-19 during the survey period. All cases were mild. Forty participants responded including 35 pregnant and 5 lactating individuals (Figure 1). Surveys were returned a median of 16 days after completing nirmatrelvir–ritonavir.

Respondent characteristics are described in Table 1. Of pregnant respondents, 18 (51.4%) received a nirmatrelvir–ritonavir prescription, of whom 66.7% opted to take the full 5-day course (n=12, 34.3% of pregnant respondents). Adverse effects were reported by 91.7%, most commonly dysgeusia (n=11, 91.7%), diarrhea (n=2, 16.7%), and mild abdominal pain (n=1, 8.3%)(Figure 2A). Adverse effects lasted from 72 hours to 1 week. Six respondents (50.0%) reported a positive COVID-19 test after completion of nirmatrelvir–ritonavir; four

(33.3%) reported a return of COVID-19 symptoms, most commonly fatigue (100.0%) and nasal congestion (100.0%), cough (50.0%) and headache (50.0%) (Figure 2B).

Three of five lactating respondents received a nirmatrelvir–ritonavir prescription; two opted to take the medication. One reported altered sense of taste. None reported subsequent COVID-19 rebound (Table 1).

The most common reported reason for avoidance of nirmatrelvir–ritonavir in both groups was lack of data and unknown risks. One participant expressed concern about rebound COVID-19 symptoms. Two participants declined nirmatrelvir–ritonavir due to mildness of symptoms (Appendix 2, available online at http://links.lww.com/xxx).

There were no adverse events, no obstetric complications, and no hospitalizations for COVID-19. Of 12 pregnant individuals who completed the nirmatrelvir–ritonavir course, ten had healthy term pregnancies without complications; one had a preterm twin delivery, and one remains pregnant.

Discussion

In this cohort of vaccinated pregnant individuals, half were prescribed nirmatrelvir–ritonavir. Of those, 66.0% took the medication; most declined nirmatrelvir–ritonavir due to concerns about unknown risks in pregnancy. Nearly all who took nirmatrelvir–ritonavir had mild adverse effects, and half experienced mild COVID-19 rebound. There were no serious adverse events and the medication was overall well-tolerated, consistent with available data.[6]

Though pregnant status is a high-risk condition, we report low rates of nirmatrelvir–ritonavir prescription receipt. Patient uncertainty about this new medication is a barrier to treatment uptake, even after it's prescribed by a health care professional. The rate of medication adverse effects and COVID-19 rebound were higher than cited in nirmatrelvir–ritonavir clinical trials (5.6% and 1–2%, respectively) in non-pregnant or lactating individuals.[1] There may be bias in survey reporting in this small sample size; larger trials are needed.

Ritonavir is well-studied and widely used in pregnancy and lactation, but nirmatrelvir's safety is largely based on animal models[7], and one series of 46 pregnancies.[6] More research is needed to understand if nirmatrelvir–ritonavir is protective against adverse COVID-19 outcomes in this population, including those who are vaccinated. Studies of nirmatrelvir–ritonavir efficacy are mostly in older individuals[1,8], and exclude pregnant or lactating individuals. While our study size was too small to infer true medication safety, until clinical trials are completed, this study provides early data on nirmatrelvir–ritonavir experiences in this population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Author Manuscript

Funding:

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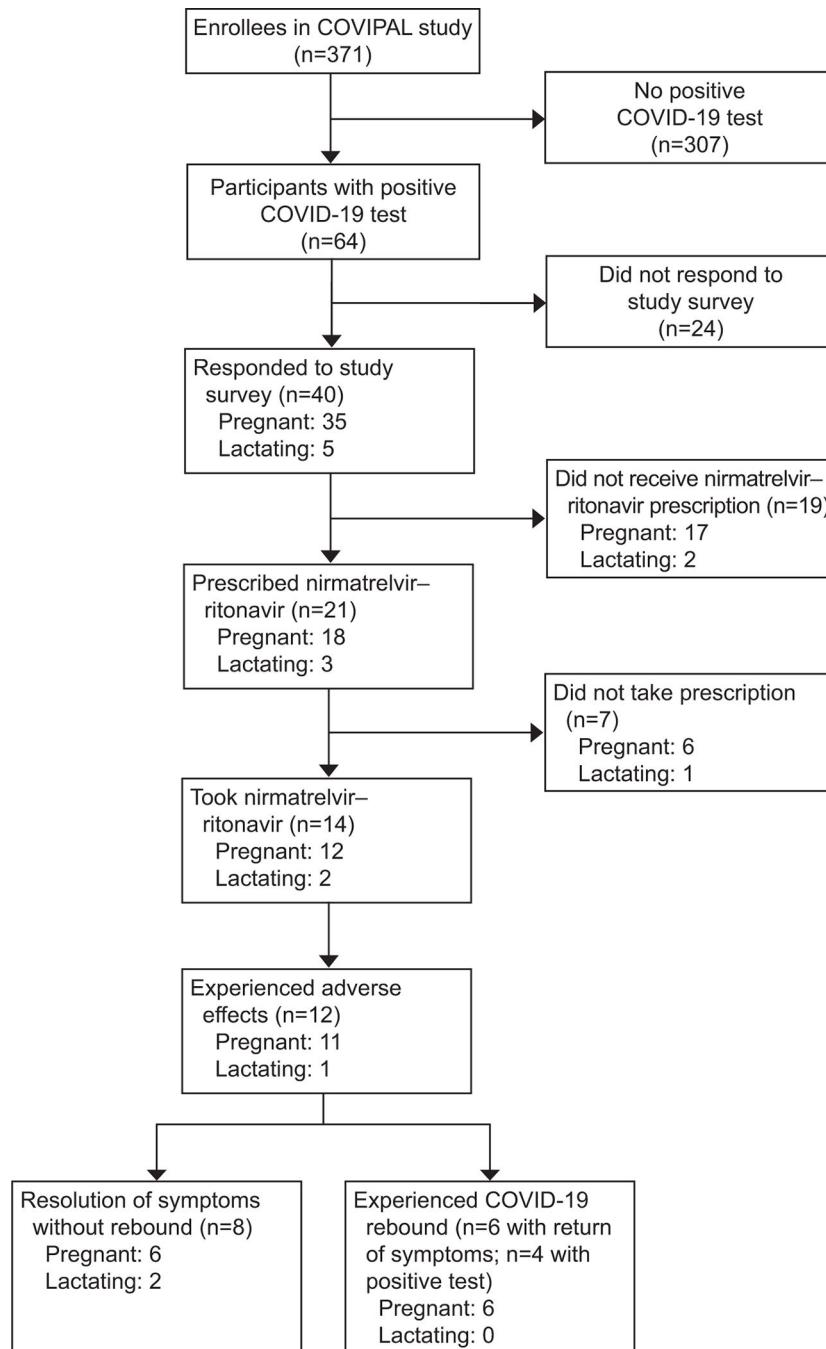
Figure 1:
Patient inclusion cohort flow. COVIPAL, COVID-19 Vaccination in Pregnancy and Lactation.
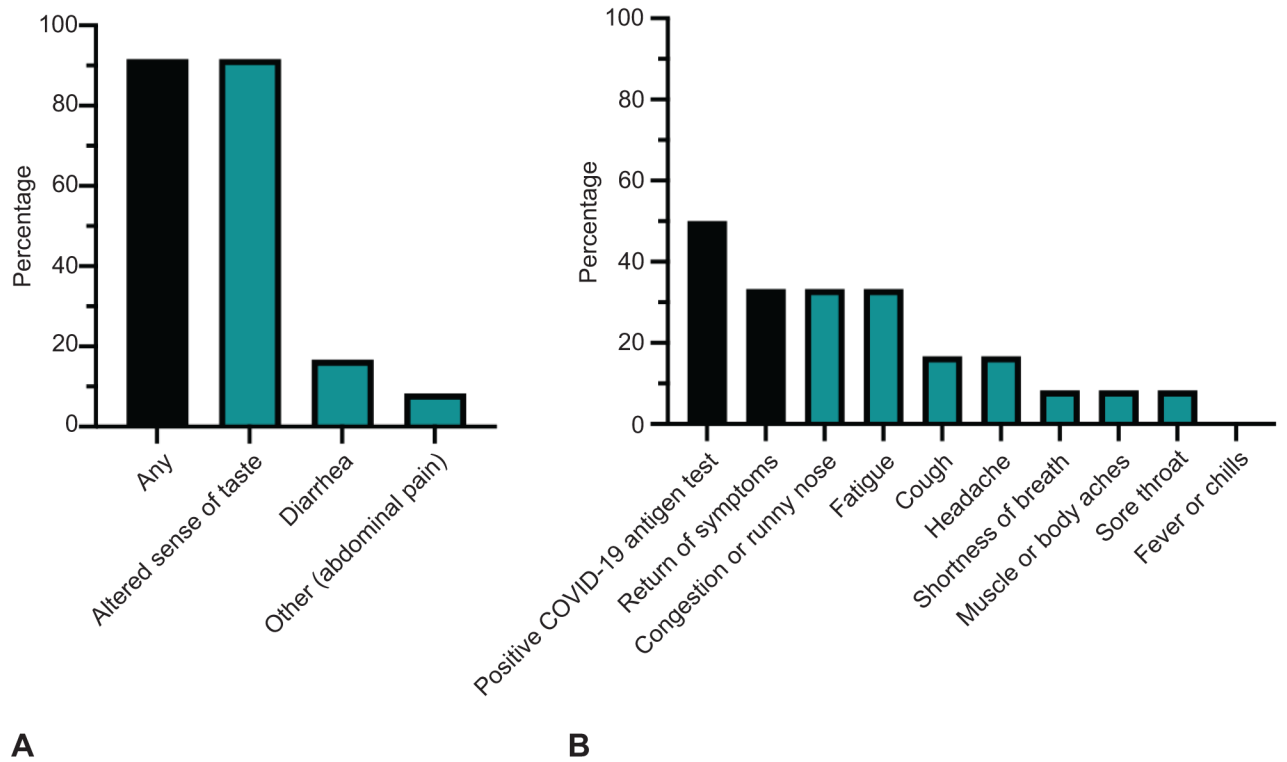
A **B**

Figure 2:

A. Eleven (91.7%) had any medication adverse effects. B. Six (50.0%) had positive test and four (33.0%) had a return of mild symptoms after nirmatrelvir–ritonavir course. COVID-19, coronavirus disease 2019.

Table 1:

Characteristics of pregnant or lactating patients vaccinated against COVID-19 prescribed nirmatrelvir–ritonavir

	Patients, Number (%)	
Characteristic	**Pregnant**	**Lactating**
Prescribed medication	N=18	N=3
Age, median (range), years	35 (31–44)	41 (38–44)
Race		
Asian	5 (27.8%)	1(33.3%)
Black/African American	0	0
White	10 (55.6%)	1 (33.3%)
None of the above	3 (16.7%)	1 (33.3%)
Ethnicity		
Hispanic/Latine	3 (16.7%)	0
Not Hispanic/Latine	9 (50.0%)	2 (66.7%)
Unknown	6 (33.3%)	0
Gestational age at treatment (weeks) (range)	22 (9.3–39.4)	64 weeks postpartum (4–114)
Trimester of pregnancy at time of infection/treatment		
First	3 (16.7%)	
Second	9 (50.0%)	
Third	6 (33.3%)	
Gravidity (range)	1 (1–2)	4 (2–4)
Parity (range)	0 (0–2)	2 (2–3)
Took prescribed medication	N=12 (66.0%)	N=2
Experienced adverse effects [*]	11 (91.7%)	1
Altered sense of taste	11 (91.7%)	1
Diarrhea	2 (16.7%)	0
Other	1 (8.3%)	1
Return of COVID-19 symptoms after completed course [†]	4 (33.3%)	0
Cough	2 (16.7%)	0
Shortness of breath/difficulty breathing	1 (8.3%)	0
Muscle/body aches	1 (8.3%)	0
Headache	2 (16.7%)	0
Sore throat	1 (8.3%)	0
Congestion/runny nose	4 (33.3%)	0
Positive COVID-19 test after completed course	6 (50.0%)	0
Time from completion of course to positive test (range)	7 (2–10) days	N/A

[*] No patients reported high blood pressure or muscle aches

[†] No patients reported experiencing fever/chills, new loss of taste or smell, nausea/vomiting, diarrhea, abdominal pain, or mastitis