DR. ANAT SCHWARTZ (Orcid ID : 0000-0002-0161-8932)

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Detection of SARS-CoV-2 in vaginal swabs of women with acute SARS-CoV-2 infection: a prospective study.

Anat Schwartz[1], Yariv Yogev[1], Ayala Zilberman[1], Sharon Alpern[1], Ariel Many[1], Ruth Yousovich[2], Ronni Gamzu[1]

[1] *Department of Obstetrics and Gynecology, Lis Maternity Hospital, Sourasky Medical Center, Tel Aviv, Israel, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv Israel*

[2] *Maccabi Healthcare Services, Herzliya, Israel*

Corresponding author

Anat Schwartz, MD

Lis maternity hospital
Sourasky Medical Center
6 Weizmann st., 6423906
Tel Aviv, Israel
Phone: +972-506334510
Email: anatsch3@gmail.com

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Abstract

Objective

To determine whether SARS-CoV-2 is present in the vaginal secretions of both reproductive-aged and postmenopausal women during acute SARS-CoV-2 infection.

Design

prospective study.

Setting

a single tertiary, university-affiliated medical center in Israel. Time period, June 1, 2020 through July 31, 2020.

Population

Women that were hospitalized in a single tertiary medical center, who were diagnosed with acute SARS-CoV-2 infection by a nasopharyngeal RT-PCR test.

Methods

A prospective study of women who were diagnosed with acute SARS-CoV-2 infection by a nasopharyngeal RT-PCR test. Vaginal RT-PCR swabs were obtained from all study participants after a proper cleansing of the perineum.

Main Outcome Measures

Detection of SARS-CoV-2 in vaginal RT-PCR swabs.

Results

Vaginal and nasopharyngeal swabs were obtained from 35 women, aged 21-93 years. Twenty-one patients (60%) were in their reproductive years, of them, 5 patients were in their third trimester of pregnancy. Most of the participants (57%) were healthy without any underlying medical conditions. Of the 35 patients sampled, 2 (5.7%) had a positive vaginal RT-PCR for SARS-CoV-2, one was pre-menopausal and the other was a post-menopausal woman. Both women had mild disease.

Conclusion

Our findings contradict most previous reports, which did not detect the presence of viral colonization in the vagina. Although passage through the birth canal exposes neonates to the vaginal polymicrobial flora, an acquisition of pathogens does not necessarily mandate neonatal infection or clinical disease. Nevertheless, when delivering a woman with acute SARS-CoV-2 infection, a clinician should consider the possibility of vaginal colonization, even if it is uncommon.

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Keywords: Vaginal secretion, SARS-CoV-2.

Tweetable abstract: When delivering a woman with acute SARS-CoV-2 infection, a clinician should consider the possibility of vaginal colonization.

Introduction

The influence of SARS-CoV-2 on the genitourinary system in general, and in particular on pregnancy outcome remains controversial. Although, positive PCR tests were found in semen [1], limited data exists regarding vaginal colonization, which is clinically significant for assessment of the risk for both sexual and maternal-fetal transmission during vaginal delivery.[2–5] Moreover, data concerning possible neonatal infection due to viral acquisition during vaginal delivery is lacking.

Though the reports of neonatal infection are anecdotal, doubt exists regarding route of infection. One study described neonatal infection with concomitant isolation of the virus from placental tissue, reinforcing the possibility of vertical transmission.[5] Others attributed neonatal infection to postnatal viral acquisition through environmental exposure.[6,7] Intrapartum transmission through vaginal secretions, that resembles other pathogens, like Group-B-streptococcus has not been reported yet.[8]

Previous studies which examined the presence of SARS-CoV-2 in vaginal secretions were limited by a small sample size and paucity of women of reproductive age,[9–11] thus, we aimed to determine whether SARS-CoV-2 is present in the vaginal secretions of both reproductive aged and postmenopausal women during acute SARS-CoV-2 infection.

Methods

This was a prospective study of women hospitalized in a single tertiary, university affiliated medical center, who were diagnosed with acute SARS-CoV-2 infection by a nasopharyngeal RT-PCR test.

Disease severity was defined according to Modified Early Warning Score (MEWS). [12] A score of 5 or more was shown to be associated with an increased risk of clinical deterioration and death.

Vaginal RT-PCR swabs were obtained from all study participants. If more than 48 hours elapsed from the nasopharyngeal swab confirming SARS-CoV-2, an additional nasopharyngeal swab was taken along with the vaginal swab. Only women with positive nasopharyngeal swab confirming SARS-CoV-2 were enrolled. In order to reduce the risk for fecal contamination, proper cleansing of the perineum was done prior to sampling. Swabs were inserted 4-5 cm into the vaginal vault and

rotated for 5 seconds. Immediately after sampling the kit was transferred to the microbiological laboratory. All samples were tested for SARS-CoV-2 using the sampling kit "Cobas SARS-CoV-2" (Cobas 6800 machine, ROSCHE, Rotkreuz, Switzerland). Sample collection, processing, and laboratory testing was performed in accordance with WHO guidelines.[13]

The study was approved by the local institutional review board (No:0260-20-TLV) and written informed consent was obtained from all participants.

Descriptive statistics were used to assess the demographic and clinical characteristics of the participants and are presented as mean ± standard deviation (SD) or range.

There were no patients involved, or public involvement in the design and conduct of this research.

Results

Vaginal and nasopharyngeal swabs were obtained from 35 women, aged 21-93 years. The demographic and clinical characteristics are presented in Table 1. Twenty-one patients (60%) were in their reproductive years, of them, 5 patients were in their third trimester of pregnancy, with mean gestational age of 34^{+3} weeks (±4.9). Most of the participants (57%) were otherwise healthy without any underlying medical conditions.

Disease severity at the time of vaginal sampling is presented in Table-2. The mean time interval between symptom onset and vaginal sampling was 8.3 days (±4.6). Most patients (85%) had mild to moderate disease, and 74% of the study group did not require any respiratory support, moreover, 74% of the entire group were admitted for observation and did not require any medical treatment.

Of the 35 patients sampled, 2 (5.7%) had a positive vaginal RT-PCR for SARS-CoV-2. The first patient was 86 years old, with a significant medical history of hypertension, cardiac and renal failure,

type-2 diabetes mellitus and a previous deep vein thrombosis (DVT). During her admission she was afebrile and remained hemodynamically stable, not requiring any medical treatment. She was categorized as MEWS 3. Vaginal sampling was performed 11 days after diagnosis of SARS-CoV-2. Two days after the first positive vaginal swab was obtained, a repeat vaginal swab was performed to reduce the risk of fecal contamination, which was positive as well.

The second patient with a positive vaginal RT-PCR for SARS-CoV-2 was 21 years old, healthy woman, who was admitted due to a short episode of dyspnea that had resolved. During her admission she developed a sore throat and fatigue. Vaginal sampling was performed six days after the symptom onset. She remained afebrile and hemodynamically stable and did not require any medical treatment and was categorized as MEWS 1.

Discussion

Main Findings

In the current study, we aimed to determine whether the SARS-CoV-2 virus was detectable in the vaginal secretions of women with an acute SARS-CoV-2 infection. We found a positive vaginal RT-PCR in two women (5.7%), one of them was pre-menopausal and the other was post-menopausal woman. Our findings are supported by a previous case report of a 23-years-old primiparous woman with a positive vaginal RT-PCR for SARS-CoV-2.[5] However, our findings contradict previous reports, which did not detect the presence of viral colonization in the vagina. [9–11] This discrepancy can be explained by the small number of cases in each group. Since we assume that vaginal colonization of SARS-CoV-2 has relatively low incidence, larger studies are required to confirm our findings. Another explanation can be a correlation between a presence of a high viral load and/ or viremia, and vaginal detection of the virus.

Strengths & Limitations

The main strengths of our study are the relatively large study group, with a dominance of reproductive aged women. Additionally, 85% of our patients presented with mild to moderate disease. Since we assumed that women with severe illness, that were respiratory and hemodynamically compromised,

will most probably be delivered by a cesarean section, the study group in the current study optimally reflects our group of interest. There are several limitations to our study. Although we performed proper cleansing of the perineum before sampling our patients, we cannot rule out the possibility of a false positive result. Additionally, a positive sample does not necessarily mean that the virus colonizing the vagina is viable and/ or intact. Moreover, our sample size makes it difficult to draw conclusions regarding the incidence of vaginal colonization and the possibility of maternal-fetal or sexual transmission, larger studies during longer periods of time are required to confirm our results.

Interpretation.

Our findings may have significant clinical implications. Although passage through the birth canal exposes neonates to the vaginal polymicrobial flora, an acquisition of pathogens does not necessarily mean a neonatal infection or clinical disease. This can be influenced by many factors, including prematurity, underlying medical condition of mother and neonate, inoculum size, and the virulence of the pathogen. The scarcity of evidence regarding the neonatal outcome of laboring women with acute SARS-CoV-2 infection should be taken into consideration at the time of delivery. Although we did not find vaginal colonization of SARS-CoV-2 in any of the pregnant women in the study, it is still too early to determine the safety of vaginal delivery in women with acute SARS-CoV-2 infection. Further studies are needed before this can be definitively determined.

Conclusion

In conclusion, in the current study we found a positive vaginal RT-PCR in two women (5.7%). Although passage through the birth canal exposes neonates to the vaginal polymicrobial flora, an acquisition of pathogens does not necessarily mandate neonatal infection or clinical disease. Nevertheless, when delivering a woman with acute SARS-CoV-2 infection, a clinician should consider the possibility of vaginal colonization, even if it is uncommon.

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Conflict of interest: All authors report no conflict of interest. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to authorship: AS has designed the study together with RY, YY and RG. AS has applied for ethical approval, AS recruited the participants and collected the samples together with AZ and SA. Also, AS, analyzed data with support from YY and RG. AS wrote the manuscript. The manuscript was revised by YY, AM, and RG and they also approved the final version.

Details of ethical approval:

Ethical approval obtained from the research ethics committee at Tel-Aviv Sourasky Medical Center, registration number 0260-20-TLV. Date of approval 2020-04-22. A written informed consent was obtained from all participants. The information to the patients contains information that data from the registers may be used in research. Patients always have a possibility to remove any personal data from the registers.

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Tables

TABLE 1 – Demographic and clinical characteristics of women with acute SARS-COV-2 infection

Age (years)		48.3 (21-93)
Reproductive aged women		21 (60)
Pregnant		5 (14.2)
Postmenopausal		14 (40)
BMI (kg/m^2)		26.2 (5.7)
Smoking		0
Underlying medical disorders		
	Obesity (BMI>30)	6 (17.1)
	Chronic hypertension	7 (20)
	Type II diabetes mellitus	4 (11.4)
	Cardiac disease[a]	3 (8.6)
	Dyslipidemia	5 (14.3)
	Lupus	1 (2.8)
	APLA	1 (2.8)
	Asthma	1 (2.8)
	Hypothyroidism	2 (5.7)
	None	20 (57.1)
Presenting Symptoms		
	Headache	12 (34.3)
	Respiratory[b]	25 (71.4)
	Gastrointestinal[c]	10 (28.6
	Anosmia and Ageusia	8 (22.9)
	Chest pain	4 (11.4)
	Fever (>38º C)	12 (37.4)
	Asymptomatic	6 (17.1)

BMI - body mass index

APLA Anti phospholipid antibody

[a]Cardiac disease included Ischemic heart disease and Congestive heart failure

[b]Respiratory symptoms included cough and dyspnea

[c]Gastrointestinal symptoms included nausea, vomiting, diarrhea and anorexia

Data are presented as n (%), mean (SD) or median (IQR)

TABLE 2- Medical status at the time of vaginal sampling		
Interval between onset of symptoms and vaginal sampling (days)		8.3 ± 4.6
MEWS ≥ 5		5 (14.3)
Treatment		
	Dexamethasone	9 (25.7)
	LMWH	8 (22.9)
	Actemra (IL-6 receptor antagonist)	5 (14.3)
	Convalescent plasma	1 (2.9)
	Remdesivir	3 (8.6)
	None	26 (74.3)
Respiratory support	**Nasal cannula/ Vapotherm**	8 (22.9)
	Mechanical ventilation	1 (2.9)
Leukopenia < 4 (10e3/µL)		4 (12.1)
Leukocytosis >12 (10e3/µL)		3 (9.1)
Neutrophilia >85%		4 (12.1)
Lymphopenia <1000 (10e3/µL)		12 (34.3)

MEWS Modified Early Warning Score[13]

LMWH Low molecular weight heparin

Results are presented as mean ± SD or n(%)