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Presence of SARS-CoV-2 in the lower genital tract of women with active COVID-19 infection: A prospective study

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SARS-CoV-2 utilizes the ACE-2 receptor to invade target tissue which is abundantly expressed in the vagina, thus making the presence of SARS-CoV-2 in the lower genital tract possible.[1] There are a few small case series reported in the existing literature with conflicting opinions. Some of these cases did not detect SARS-CoV-2 in vaginal fluids,[2–4] whereas others have documented its presence in a small proportion.[5,6] Moreover, these studies are limited by small sample sizes—most of them included elderly postmenopausal women with severe COVID-19 infection. The present study aimed to assess the presence of SARS-CoV-2 in the lower genital tract of women with active COVID-19 infection, and to find a correlation between high viral load and detection of SARS-CoV-2 in genital samples.

This was a prospective study conducted at AIIMS Rishikesh, India, on 61 women with active COVID-19 infection from November 25, 2020, to April 17, 2021. Reverse transcription polymerase chain reaction (RT-PCR) in nasopharyngeal (NP) & oropharyngeal (OP) swabs was performed in all women admitted for COVID-related symptoms or gynecological conditions. Both reproductive age and postmenopausal women, with an entire range of disease severity (asymptomatic, mild, moderate, and severe), were included in the present study. This study is registered with the Clinical Trial Registry of India (CTRI/2020/09/027618) and prior approval for data collection and analysis was obtained by the Institution Ethics committee (AIIMS/IEC/20/575). Unconscious and ventilated patients who were unable to provide consent were excluded. Additionally, women who had menstrual/genital bleeding and genital infection were excluded. Informed and written consent was obtained from all participants.

Vaginal and cervical swabs were obtained from the posterior fornix of the vagina and ectocervix. Initially, 15 vaginal and 12 cervical samples were examined by both real-time RT-PCR using the Taqpath™ (Thermo Fisher Scientific, Waltham, MA, USA) COVID-19 combo kit and transcription-mediated amplification (TMA) in an FDA-approved closed system called the Hologic Panther System (M/s Hologic Ltd., Marlborough, MA, USA). SARS-CoV-2 virus was not detected in any sample on RT-PCR; however, it was identified in 3/15 vaginal samples (20%) by TMA.[7] Therefore, it we decided to process further samples via TMA only in order to enhance the productivity of our research and reduce costs.

A vaginal sample was collected from all 61 women, while a cervical swab was collected from 38 women. The reasons for inability to collect a cervical swab were surgically absent cervices in 14 women, and atrophic cervix in 9 women (particularly those who were >65 years of age). Table 1 presents baseline and clinical characteristics of the study participants.

Five out of 61 (8.2%) vaginal samples, and 4 out of 38 (10.53%) cervical swabs were positive for SARS-CoV-2. A total of 8 women had positive results in vaginal samples, cervical samples, or both. The clinical characteristics of women with the presence of SARS-CoV-2 in the lower genital tract are shown in Table 2.

TABLE 1 Baseline and clinical characteristics of the study participants

Variable	COVID-19 infected women ($n = 61$)
Age in years (mean + SD)	51.96 + 15.24 (range: 24–75 years)
Reproductive aged women (number, %)	28 (45.9%)
Postmenopausal women (number, %)	33 (54.1%)
Parity (mean + SD)	2.52 + 1.34 (range: 0–5)
Asymptomatic (number, %)	22 (36.1%)
ICMR severity (number, %)	
Mild	9 (14.8%)
Moderate	16 (26.2%)
Severe	14 (23%)
Presenting complaint (number, %)	
Fever	31 (50.82%)
Shortness of breath	22 (36.07%)
Cough	14 (22.95%)
Chest pain	6 (9.84%)
Sore throat	4 (6.56%)
Diarrhea	2 (3.28%)
Comorbidity (number, %)	
Hypertension	27 (44.26%)
Diabetes mellitus	17 (27.87%)
Hypothyroidism	6 (9.84%)
COPD & Asthma	3 (4.9%)
Tuberculosis	2 (3.28%)
Chronic kidney disease	4 (6.56%)
Heart disease	2 (3.28%)
Other(s)	9 (14.8%)
Interval from first day of COVID-19 positivity to day of sampling (mean + SD)	4.80 + 4.31 (range: 1–17 days; median: 3 days; IQR: 2–6 days)
Outcome (number, %)	
Recovered/discharged	56 (91.8%)
Expired	5 (8.2%)
Mean CT value of NP & OP swabs (mean + SD)	26.59 + 3.57 (range: 16–33; median: 28)
Presence of SARS-CoV-2 in vaginal sample (number, %)	5/61 (8.2%)
Presence of SARS-CoV-2 in cervical sample (number, %)	4/38 (10.53%)

Abbreviations: COPD, chronic obstructive pulmonary disease; ICMR, Indian Council of Medical Research; NP, Nasopharyngeal; OP, Oropharyngeal.

Women who had positive results through vaginal fluid had significantly lower cycle threshold (CT) values than women with negative vaginal swabs ($P = 0.02$). Similarly, women with positive cervical swabs had lower CT values than women with negative results ($P = 0.055$). Table 3 shows the association between viral load and vaginal and cervical swab results.

The present study's results contradict the findings of previously published studies. Yuvaci et al.[2] did not identify the presence of SARS-CoV-2 in the vaginal fluid of 18 women of reproductive age with severe COVID-19 infection.[2] Cui et al.[3] did not detect SARS-CoV-2 in the vaginal and cervical exfoliated cells of 35 women with severe COVID-19 infection, even after sampling multiple vaginal sites and double testing samples.[3] Similarly, Qiu et al.[4] did not locate the presence of SARS-CoV-2 in the vaginal fluid of 10 postmenopausal women with severe COVID-19 infection.[4] On the other hand, Schwartz et al.[5] detected SARS-CoV-2 in the vaginal swabs of 2 out of 35 women (5.7%) on RT-PCR.[5] Scorzolini et al.[6] also reported positive RT-PCR results in the vaginal samples of a 65-year-old woman on day 7 and day 20 from the onset of symptoms.[6]

The reasons behind a higher rate of SARS-CoV-2 positivity in genital samples in our study could be explained by the increased sensitivity of TMA-based technology, and a larger sample size compared to previously reported studies. Furthermore, the prospective nature of the study, inclusion of both reproductive age and postmenopausal women, and a whole spectrum of disease severity are strengths in the present study.

We did not find any differences in the probability of SARS-CoV-2 presence in genital samples with regards to age, parity, comorbidities, disease severity, and day of sampling. Because the time taken for SARS-CoV-2 to invade different tissues is unknown, the exact time when obtaining genital samples may have an influence on results; therefore, taking multiple samples from the same patient at a pre-specified interval would have produced more prudent results.

Well-designed studies which include evaluation of the sexual partner, and neonate of mothers who gave birth by vaginal delivery, are needed to determine the incidence of sexual transmission and mother-to-child SARS-CoV-2 transmission.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS

KK and DK conceived of the study. RK and DD collected the samples and relevant data. DK and RS performed the laboratory analysis. KK drafted the manuscript with direction from DK and JC. RK, AT, AG, AB, PP and JC contributed to acquisition, analysis, or interpretation of data, and critically evaluated the manuscript. All authors contributed to and approved of the final version of the manuscript.

DATA AVAILABILITY STATEMENT

No. Research data are not shared.

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TABLE 2 Description of the clinical characteristics of women with the presence of SARS-CoV-2 in the lower genital tract

S.No.	Age	Menopausal status	Parity	Co-morbidity	Presenting complaints	Diagnosis at admission	ICMR severity	Day of sampling	Patient outcome	SARS-COV-2 (OP & NP swabs) by RT-PCR: Average CT value	Vaginal swab results	Cervical swab results
1	27	Premenopausal	2	-	Asymptomatic	Ectopic pregnancy	-	1	Recovered	23	Positive	Negative
2	61	Postmenopausal	5	-	Asymptomatic	Ovarian carcinoma	-	2	Recovered	25	Positive	Negative
3	40	Premenopausal	3	HTN & DM	Fever & SOB	COVID-19 pneumonia with CT score: 28/40	Severe	2	Recovered	23	Positive	Positive
4	68	Postmenopausal	3	Chronic plaque psoriasis	Asymptomatic	Post-vaginal hysterectomy	-	1	Recovered	23	Positive	-
5	36	Premenopausal	1	HTN	Fever, cough, & SOB	COVID-19 pneumonia	Moderate	5	Recovered	24	Positive	Negative
6	70	Postmenopausal	3	HTN, DM & COPD	Fever & Sore throat	COVID-19 pneumonia with CT: score 24/40	Severe	15	Recovered	24	Negative	Positive
7	45	Premenopausal	0	-	Asymptomatic	Ovarian carcinoma	-	3	Recovered	27	Negative	Positive
8	24	Premenopausal	0	AML	Fever	COVID-19 pneumonia with fungal pneumonia	Severe	4	Expired	21	Negative	Positive

Abbreviations: AML, acute myeloid leukemia; COPD, chronic obstructive pulmonary disease; CT, cycle threshold; DM; diabetes mellitus; HTN, hypertension; ICMR, Indian Council of Medical Research; NP, nasopharyngeal; OP, oropharyngeal; RT-PCR, reverse transcriptase-polymerase chain reaction; SOB, shortness of breath.

TABLE 3 Association of high viral load with presence of SARS-CoV-2 in the lower genital tract of women with COVID-19 infection

	Positive vaginal swab (n = 5)	Negative vaginal swab (n = 54)	*t*-test statistic	*P* value
Mean CT value	23.6 + 0.89	27.11 + 3.32	−2.33	0.02
	Cervical swab positive (n = 4)	Cervical swab negative (n = 32)	*t*-test statistic	*P* value
Mean CT value	23.75 + 2.50	27.09 + 3.23	−1.98	0.055

Abbreviations: CT, cycle threshold.

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Gynecology

Reconstruction of three-dimensional models for complex female pelvic tumors

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Pelvic tumors are common problems in gynecological diseases. Surgery remains the most important method for the management of pelvic tumors, including ovarian benign or malignant tumors, sarcomas, neurogenic tumors, stromal tumors, and deep angiomyxoma.[1] The present study's three-dimensional (3D) reconstruction technique was based on preoperative computed tomography (CT)