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MAJOR ARTICLE

SARS-CoV-2 Is Not Detectable in the Vaginal Fluid of Women With Severe COVID-19 Infection

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Background. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is spread mainly through respiratory droplets or direct contact. However, the infection condition of the genital system is unknown. Our aim in this study was to determine if SARS-CoV-2 is present in the vaginal fluid of women with coronavirus disease 2019 (COVID-19).

Methods. Ten women with confirmed severe COVID-19 pneumonia admitted to the Tongji Zhongfa Hospital intensive care unit from 4 February 2020 through 24 February 2020 were included. Clinical records, laboratory results, and computed tomography examinations were retrospectively reviewed. The potential for genital infection was accessed by testing for the presence of SARS-CoV-2 in vaginal fluids obtained from vaginal swab samples. Reverse transcriptase polymerase chain reaction was used to confirm the SARS-CoV-2 infection in vaginal fluids.

Results. The clinical characteristics of the 10 women were similar to those reported in other severe COVID-19 patients. All 10 patients were tested for SARS-CoV-2 in vaginal fluid, and all samples tested negative for the virus.

Conclusions. Findings from this small group of cases suggest that SARS-CoV-2 virus does not exist in the vaginal fluids of severe COVID-19 patients.

Keywords. COVID-19 pneumonia; SARS-CoV-2; vaginal fluid; clinical features.

In December 2019, the World Health Organization (WHO) declared the outbreak of a viral pneumonia caused by 2019 novel coronavirus disease (COVID-19) as a global public health emergency, and it is now a pandemic [1, 2]. The disease was first reported in Wuhan, Hubei Province, China, and has spread to more than 100 countries [3].

Another coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is spread mainly through respiratory droplets or direct contact. In previous studies, SARS-CoV-2 was found in the testis of male patients [4], but not in ovaries or the uterus [5]. In contrast, Ebola has been found in the vaginal fluid of female patients [6–8]. The infection condition of SARS-CoV-2 in the genital system is currently unknown. Our aim in this study was to determine if women with severe COVID-19 illness have signs of the SARS-CoV-2 virus in their vaginal fluid.

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METHODS

Study Oversight

All eligible patients were invited to participate in the study. Those who agreed to participate provided written informed consent. The Peking Union Medical College Hospital Research Ethical Committee provided ethical approval for the study.

Data Sources and Collection

All medical records and data for hospitalized patients were obtained from 4 February 2020 through 24 February 2020 at the Tongji Zhongfa Hospital intensive care unit (ICU), which is managed by the Peking Union Medical College Hospital. The 10 participants were postmenopausal and were diagnosed with severe COVID-19 pneumonia. Clinical laboratory examinations, including blood analyses, serum biochemical tests, coagulation function tests, and chest computed tomography examinations, were performed. Vaginal swabs were obtained between 17 and 40 days after the onset of SARS-CoV-2 infection. Swabs were inserted 2–3 cm into the vagina and rotated for 3–5 seconds. Swabs were transferred to the laboratory immediately, and reverse transcriptase polymerase chain reaction (RT-PCR) procedures were completed within 2 hours. Clinical findings, laboratory and radiological findings, therapeutic interventions, and outcomes were collected for the 10 patients. All data were checked by 3 researchers.

Laboratory Confirmation

COVID-19 was diagnosed on the basis of WHO interim guidance [9]. A confirmed case of COVID-19 was defined as a positive result on RT-PCR assay of nasal and/or pharyngeal swab specimens [2]. RT-PCR assays were performed in accordance with the protocol established by the WHO [10].

RESULTS

Between 4 February 2020 and 24 February 2020, 10 postmenopausal women were admitted with confirmed severe COVID-2 pneumonia to the Tongji Zhongfa Hospital ICU. All of them were residents of Wuhan. The patients, aged 52 to 80 years, were initially admitted due to symptoms of fever or cough. They were transferred to the ICU because of severe illness; all met criteria for severe pneumonia based on the definition of illness severity in the WHO's interim guideline for COVID-19 [11] (Table 1). All patients had lymphopenia and eosinopenia, with evidence of liver and/or kidney dysfunction. All laboratory test results from the time of disease onset to the time of vaginal sampling are presented in Table 2.The presence of SARS-CoV-2 in vaginal fluid was determined. None were found to be positive for SARS-CoV-2 by RT-PCR assay.

DISCUSSION

Most symptoms of COVID-19 are related to the respiratory system. SARS-CoV-2 is spread mainly through respiratory droplets or close contact. There are few studies on the presence of the SARS-CoV-2 virus in body fluids [3, 12], and there are no reports of the presence of the virus in vaginal fluids. In our study, 10 postmenopausal women in the ICU with severe COVID-19 were tested for SARS-CoV-2 in vaginal fluid with RT-PCR assay, and all samples were negative for the virus.

In premenopausal women, the beneficial commensal lactobacilli present in the vagina can produce lactic acid to maintain low vaginal pH, which can inhibit colonization of pathogenic bacteria. These protective barriers against pathogens in postmenopausal women become weaker, leading to increased susceptibility to bacteria and viruses in postmenopausal women [13].

Previous studies have explored the effects of other epidemic viral infections on the female reproductive tract. Prisant et al confirmed the presence of Zika virus in the female reproductive tract [14]. Rodriguez et al [15] found Ebola virus in the vaginal fluid of a patient recovering from Ebola virus infection 33 days after the onset of illness.

Severe acute respiratory syndrome (SARS) caused by SARS-CoV was first discovered in November 2003 in Guangdong, China. The lungs sustain the most severe damage in patients with SARS. As the disease progresses, patients show multiple organ invasion. In one study, autopsy results of patients who died of SARS showed that SARS-CoV was present in the lungs, trachea/bronchus, stomach, small intestine, and distal renal tubules [8]. In another study, autopsy results showed the impact of the virus on the reproductive systems in both men and women. Xu et al [4] observed that orchitis was present in some men with SARS. The pathology of male SARS patients showed widespread germ cell destruction, almost no spermatozoon in seminiferous tubules, and leukocyte infiltration. However, the virus was not clearly detected in the testis [5, 16]. No studies have clearly shown that SARS-CoV invades the female reproductive tract, and there is no report of SARS-CoV being detected in vaginal fluids. The autopsy pathological results of SARS patients have not shown the virus in the ovaries and uterus, and one report did not assay vaginal fluids [5].

SARS-CoV-2 may have transmission mechanisms that are similar to those of SARS-CoV. Limited research results indicate the presence of the virus in the stools of patients with COVID-19[3] as the disease progresses, which also suggests another possible route of transmission for the virus. At present, there is no report of SARS-CoV-2 being present in the female reproductive tract. This is particularly important because it could help inform the risks of sexual transmission and mother-to-child transmission. In our study, we included 10 female patients with COVID-19. Unlike Ebola virus or Zika virus, SARS-CoV-2 was not found in the vaginal fluids of women with severe pneumonia.

We are the first to attempt to detect SARS-CoV-2 in the vaginal fluid of patients with COVID-19. All the tested women were postmenopausal. Even when the patient's respiratory symptoms were severe, the results of vaginal swabs were negative for the presence of SARS-CoV-2. Therefore, it is possible that SARS-Cov-2 does not enter the vaginal fluid. This finding suggests that the likelihood of transmitting SARS-Cov-2 to sexual partners through vaginal fluids may be low.

A single publication indicates that no SARS-CoV-2 was found in amniotic fluid or umbilical cord blood of women with COVID-19 [17]. In the same study, neonatal throat swabs were also negative. Taken together, these findings suggest that the risk of vertical transmission from pregnant women to newborns delivered by cesarean section is low. We did not find SARS-CoV-2 by PCR in vaginal fluids as late as 40 days after disease onset in women who still required ICU care for ongoing COVID-19 illness. Therefore, it is speculated that the risk of vertical transmission during vaginal delivery might also be very low.

The study has several limitations. First, the number of patients was small. In addition, only RT-PCR was used for detection of SARS-CoV-2. In theory, even if there is only 1 copy of the virus in the sample to be tested, it is likely to be detected. However, in practice, if there is a small amount of the virus, the amplification result may not be ideal. In our research, we recruited only postmenopausal women, and the vaginal swabs

Table 1. Clinical Features and Computed Tomography Findings of Postmenopausal Women With Severe Coronavirus Disease 2019

Clinical Features	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Age, y	57	65	52	80	71	63	73	66	55	75
Epidemic exposure	Lived in Wuhan	Lived in Wuhan	Lived in Wuhan	Lived in Wuhan	Lived in Wuhan	Lived in Wuhan	Lived in Wuhan	Lived in Wuhan	Lived in Wuhan	Lived in Wuhan
Menopause	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Chronic illness	No	Hypertension, diabetes type II	Hypertension	No	Hypothyroidism	No	Diabetes type II, hypothyroidism	No	Obesity	Coronary heart disease, hypertension, diabetes type II,
Severity of pneumonia	Severe	Severe	Severe	Severe	Severe	Severe	Severe	Severe	Severe	Severe
Initial symptoms	Fever, cough	Fever, cough	Fever	Fever, cough	Fever, cough	Fever, cough	Fever, cough	Fever, cough	Fever, cough	Fever, cough
Lowest oxygen saturation, %	65	70	94	84	94	92	91	93	80	99
Diagnosis method	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR
Days from diagnosis to sampling	25	26	31	40	27	24	17	28	33	30
Antiviral therapy	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Chest computed tomography scan	Multiple bilateral ground-glass opacities and consolidation	Bilateral ground-glass opacities	Bilateral ground-glass opacities prominent on the left	Bilateral ground-glass opacities	Bilateral ground-glass opacities and consolidation	Bilateral ground-glass opacities prominent on the right	Regional ground-glass opacity in segments	Bilateral ground-glass opacities	Bilateral ground-glass opacities	Bilateral ground-glass opacities prominent on the left

Abbreviations: PCR, polymerase chain reaction; RT-PCR, reverse transcriptase polymerase chain reaction.

Table 2. Laboratory Findings of Postmenopausal Women With Severe Coronavirus Disease 2019

	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5		Patient 6		Patient 7		Patient 8		Patient 9		Patient 10	
Laboratory Findings	Diagnosis	Sampling	Diagnosis	Sampling	Diagnosis	Sampling	Diagnosis	Sampling	Diagnosis	Sampling	Diagnosis	Sampling	Diagnosis	Sampling	Diagnosis	Sampling	Diagnosis	Sampling	Diagnosis	Sampling
Leucocyte count, $\times 10^9$/L (3.5–9.5)	10.5	15.63	6.73	9.21	14.35	9.54	5.67	20.3	11.05	5.64	6.29	6.34	12.73	7.42	5.08	7.7	15.06	13.13	6.15	12.61
Hemoglobin, g/L (115–150)	109	80	99	88	125	86	160	77	123	85	98	73	128	110	126	74	124	96	90	96
Neutrophil count, $\times 10^9$/L (1.8–6.3)	9.33	13.12	6.23	7.64	13.67	8.08	5.04	18.44	9.48	5.3	54	4.89	11.88	6.01	4.12	7.04	12.55	10.88	5.51	12.02
Eosinophil count, $\times 10^9$/L (0.02–0.52)	0	0.02	0.04	0.31	0	0.01	0.01	0.03	0	0	0	0.17	0	0.1	0.02	0	0	0.22	0	0
Lymphocyte count, $\times 10^9$/L (1.1–3.2)	0.71	0.91	0.29	0.98	0.49	0.41	0.5	1.22	0.9	0.24	0.56	0.8	0.33	0.74	0.315	0.36	1.68	1.49	0.34	0.23
Platelet count, $\times 10^9$/L (125–350)	116	227	79	176	141	212	223	312	288	73	230	138	118	134	5.08	53	344	500	148	185
C-reactive protein, mg/L (0–5)	116.8	320	66	57.7	270.8	232.1	142.2	31.5	73	166.7		105.5	41.1	66.8	49.8	6.4	167.6	-	17.1	42.4
D-dimer, μg/mL (<0.5)	>21	5.49	2.84	1.28	1.4	4.21	12.08	4.37	2.83	5.53	18.19	4.47	2.13	4.96	>21	11.12	-	2.9	2.43	3.67
Prothrombin time, s (11.0–16.0)	18.2	14.9	17.2	18.1	14.8	16.6	16.1	13.7	14.3	15.8	15.3	16.9	14.4	18.6	15.1	18.8	16.2	15.9	12.8	19.7
International normalized ratio, 0.80–1.31	1.49	1.15	1.4	1.47	1.14	1.32	1.27	1.02	1.1	1.23	1.19	1.36	1.12	1.54	1.17	1.55	1.28	1.25	0.96	1.66
Activated partial thromboplastin time, s (28.0–43.5)	42.1	39.8	45.3	39.2	42	44.6	38.8	30.7	39.1	71.3	45.7	77.4	40.6	53.8	43	38.6	35.5	35.7	37.1	42.8
Fibrinogen, g/L (<5)	1.26	5.93	4.42	4.7	8.31	4.28	8.53	4.74	6.13	5.43	6.22	5.2	6.04	6.28	5.43	1.07	3.19	3.89	4.76	3.58
Erythrocyte sedimentation rate, mm/h (<20)	23	-	-	91	54	112	64	74	65	-	55	110	80	-	54	18	29	-	-	70
Albumin, g/L (35–50)	29.5	32.4	32.6	27.4	28.7	28.6	26.8	34.1	33.1	36.3	32.3	29.7	31.7	28.6	31.3	34.6	27.9	37.4	34.4	30.5
Bilirubin, μmol/L (3–22)	0.4	-	5.9	2.3	3.3	1	3.5	4.7	2.2	1.8				1.3	8.3	3.2	0.2		4.5	
Serum alanine aminotransferase, U/L (9–52)	38	45	11	15	50	20	30	23	45	39	34	158	23	9	29	19	31	37	14	18
Serum aspartate aminotransferase, U/L (14–36)	30	83	20	21	45	15	56	39	76	36	28	44	28	21	65	56	27	41	21	21
Serum alkaline phosphatase, U/L (38–126)	85	155	37	52	110	90	57	126	51	100	84	129	74	72	116	235	81	76	73	74
Blood urea nitrogen, mmol/L (2.9–8.2)	7.1	10.6	10.5	6.7	11.4	7	9	11.5	6.3	9.4	10	7.1	6.8	6.5	4.7	6.1	5.5	5	4.4	19.2
Creatinine, μmol/L (44–106)	46	113	58	46	71	46	93	65	66	66	80	51	66	112	57	38	76	44	70	131
Uric acid, μmol/L (155–357)	171	252	100	109	233	80	409	199	209	121	240	94	259	125	184	88	293	142	180	453
Sodium, mmol/L (136–145)	142.9	149.5	148.5	146.5	135.8	131.8	130.1	143.1	135.6	146.7	141.4	144.7	137.3	146.4	144.1	154.1	137.4	137	117.1	136.4
Potassium, mmol/L (3.5–5.2)	4.52	4.55	3.49	4.23	4.43	3.74	4.38	4.71	4.12	4.69	3.13	4.81	4.54	3.66	4.32	4.34	4.81	4.42	3.44	3.73
Detection of SARS-CoV in urine by RT-PCR	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Detection of SARS-CoV in blood by RT-PCR	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Detection of SARS-CoV in vaginal fluid by RT-PCR	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

Abbreviations: –, didn't do the test; RT-PCR, reverse transcriptase polymerase chain reaction; SARS-CoV; severe acute respiratory syndrome coronavirus 2.

were taken 17 days or more after disease onset. More research on possible differences in the pathophysiology of SARS-CoV-2 in the female genital tract of premenopausal women is needed.

Notes

Author contributions. L. Z., T. L.: study concept and design, obtaining funding, critical revision of the manuscript for important intellectual content; A. M.: critical revision of the manuscript for important intellectual content; X. L., M. X., J. X., W. C., Z. Y. L., T. L.: data acquisition; and L. Q., Y. X.: writing of the manuscript, statistical analysis.

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