Original Article

Absence of SARS-CoV-2 RNA in Peritoneal Fluid During Surgery in Pregnant Women Who Are COVID-19 Positive

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ABSTRACT
Study Objective: Coronavirus disease 2019 (COVID-19) infection poses significant risks during surgical interventions. We investigated the intraperitoneal presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in patients who are COVID-19 positive.
Design: A prospective group study.
Setting: Department of Obstetrics and Gynecology designated for patients with COVID-19, Central Clinical Hospital of the Ministry of Interior, Warsaw.
Patients: Overall, 65 pregnant women with COVID-19 infection underwent cesarian section. The diagnosis was confirmed either by positive antigen test or by positive reverse transcriptase-polymerase chain reaction assay performed within no more than 13 days before the operation.
Interventions: On the day of the operation, a nasopharyngeal swab was taken, and peritoneal fluid was collected at the beginning of the operation. Both the nasopharyngeal swab and peritoneal fluid samples were tested for SARS-CoV-2.
Measurements and Main Results: A total of 65 pregnant women with COVID-19 infection were enrolled in the study. The SARS-CoV-2 ribonucleic acid test by nasopharyngeal swab produced positive results in 34 patients. In this group as well as in 31 nonconfirmed patients, all peritoneal fluid samples tested negative for SARS-CoV-2 ribonucleic acid.
Conclusion: These results suggest a low risk of COVID-19 transmission from the peritoneal cavity at the time of laparoscopy or laparotomy. Journal of Minimally Invasive Gynecology (2021) 28, 2047−2051. © 2021 AAGL. All rights reserved.

Keywords: Laparoscopy; Laparotomy; Abdominal cavity; Viral transmission

The World Health Organization declared coronavirus disease 2019 (COVID-19) as a pandemic on March 11, 2020, and the unprepared healthcare systems were left struggling to mount an adequate response. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is primarily transmitted through respiratory droplets (droplet particles being > 5−10 μm in diameter) [1]. It can also be transmitted through surfaces contaminated with the secretions of an infected person (i.e., via direct contact). Airborne transmission (< 5 μm in diameter droplet nuclei) may take place in specific circumstances, where aerosol particles are produced [1]. The increasing number of positive cases reported daily challenged healthcare systems around the world and significantly impacted all areas of medicine. Infection with SARS-CoV-2 mainly affects the lower respiratory tract, causing mild to moderate respiratory symptoms in 85% of cases. Cardiovascular, renal, neurologic, dermatologic, and gastrointestinal

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manifestations have also been reported [2−5]. Increasing age, male sex, obesity, and other comorbidities such as hypertension, diabetes, and cardiovascular diseases, all increase the frequency of disease progression toward greater clinical severity and intensive care unit admission [2−4]. Pathophysiological processes responsible for developing hypertension, diabetes, or cardiovascular diseases and physiologic immune adaptations to pregnancy [6] escalate during the second trimester and the beginning of the third trimester and may predispose pregnant women to a severe course of illness [7,8]. Pregnancy enhances susceptibility to respiratory pathogens because of physiologic changes (higher diaphragm position, increased oxygen demand, and progesterone-related edema of the respiratory tract) [9] and predispose women to complications from respiratory infections leading to maternal and fetal mortality and morbidity [10,11]. In addition, an immunologic modulation occurs, from a pro-inflammatory state (favorable to the implantation and placentation process) during the first trimester to an anti-inflammatory condition (favorable for fetal growth) during the second trimester, finally reaching a second pro-inflammatory state during the third trimester (in preparation for delivery) [12]. Previous studies have shown that the clinical characteristics of maternal COVID-19 infection are like those in nonpregnant adults [13−15]. However, new data emerged in meta-analyses by Allotey et al [7], Khali et al [16], and Mazur-Bialy et al [17] showing that pregnant women may have an increased risk of developing severe symptoms. Therefore, we can extrapolate that viral loads of SARS-CoV-2 in different body compartments in the population of pregnant women do not negatively deviate from those in nonpregnant women.

Laparoscopic surgery is a method that requires creating a pneumoperitoneum by inflating the abdominal compartment with carbon dioxide. In this process, as well as during open surgeries, such as cesarean section, using energy-based tools for cutting tissue or sealing blood vessels, there exists the potential for the aerosolization of viral particles and contamination of the operating theater [18]. It has not yet been established whether mechanical insufflation and exsufflation during laparoscopy are aerosol-generating procedures [19]. Nevertheless, an absence of evidence is not the evidence of absence, and so long as there have been no thorough investigations made, the possibility of transmission cannot be excluded [20]. Because of the pandemic, all scheduled surgeries were initially postponed, and special approaches for emergency and minimally invasive surgery such as the use of built-in-filter trocars or surgical smoke evacuators were introduced to reduce virus transmission to health personnel [21]. SARS-CoV-2 is not only present in bronchoalveolar lavage fluid, sputum, and nasal and pharyngeal swabs, but also in feces, blood, and urine [22]. However, it is not yet known whether the SARS-COV-2 virus is present in the peritoneal cavity, and its excretory

mechanism remains unclear. In this study we aimed to systematically assess the presence of SARS-CoV-2 in the abdominal cavity in pregnant women. Although viral particles occur in the body's fluids and compartments, this does not necessarily result in increased infectivity, and the absence of virus ribonucleic acid (RNA) provides reassurance of the safety of aerosol-generating procedures and open surgeries in the COVID-19 era.

Materials and Methods

Study Population

The study was conducted between May 15, 2020, and November 23, 2020, at the Department of Obstetrics and Gynecology in the Central Clinical Hospital of the Ministry of Interior and Administration, Warsaw, Poland, which is the hospital designated for COVID-19 treatment by the Polish government. The research was approved by the Bioethics Committee of the Central Clinical Hospital of Interior and Administration in Warsaw, and all women in the study voluntarily gave their written informed consent on the day of admission.

Inclusion and Exclusion Criteria

Pregnant women were included if they were undergoing cesarean section for either elective or urgent indications. SARS-CoV-2 infection (either asymptomatic or symptomatic) was confirmed either by a positive antigen test or by a positive real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay performed within no more than 13 days before the operation. None of the patients had a history of COVID-19 infection nor suspected infection. The only exclusion criterion was formal informed consent not being given.

Study Procedures

Nasopharyngeal swabs were taken on the day of the operation, and an RT-PCR assay was performed for SARS-CoV-2. In case of elective indications, swabs from nasopharynx were taken before the surgery and during the procedure, when urgent indications emerged. A peritoneal fluid swab for COVID was taken immediately after opening the abdominal cavity and before uterus incision. All samples were collected in viral transport medium. Gene amplification was performed via real-time RT-PCR assay, which targets the N, E, and RdPd genes. The qualitative assay was performed with the use of a SARS-CoV-2 nucleic acid detection kit (GeneProof SARS-CoV-2 PCR Kit; GeneProof a.s., Brno, Czech Republic) in accordance with the Corman protocol [23]. Only rapid antigen tests that are characterized by a sensitivity of ≥80% and a specificity of ≥97%, thus meeting the conditions for use for diagnostic purposes, were accepted, including the Panbio COVID-19 AG Rapid Test Device (Abbott, Abbot Rapid Diagnostics Jena GmbH, Jena, Germany) and Bioeasy

2019-nCoV Ag Fluorescence (Shenzhen Bioeasy Biotechnology Co. Ltd., Shenzhen, China).

Clinical Course of Illness

Following Polish Association of Epidemiologists and Infectiologists [24] guidelines, patients were divided into 4 groups according to the severity of symptoms. Using the test results, we classified 4 groups of severity as mild (asymptomatic, or presence of cough, fever, dyspnea, fatigue, headache, muscle pains, nausea, vomiting, diarrhea), moderate (clinical and radiological features of lung occupation), severe (respiratory failure), and critical (Acute Respiratory Distress Syndrome, hypotensive shock, multiorgan failure, loss of consciousness).

Population Infection Rate Estimation and Statistical Analysis

Estimates of the incidence of COVID-19 positivity during the study period were derived from official Polish government online data. Data were analyzed using MS Excel (Microsoft Corporation, Redmond, Washington).

Table 1

Characteristics of patients with COVID-19 undergoing cesarean section

Patient characteristics	SARS-CoV-2 RT-PCR test status of nasopharyngeal swab performed on the day of surgery, n (%)		SARS-CoV-2 RT-PCR test status of peritoneal fluid swab performed on the day of surgery, n (%)	
	Positive (n = 34)	Negative (n = 31)	Positive (n = 0)	Negative (N = 65)
Maternal age, mean ± SD (CI 95%), yrs	31.4 ± 5.1 (29.78-32.63)	32.8 ± 4.2 (31.43-34.29)	0 ± 0	32.0 ± 4.7 (30.82-33.12)
18−20	1 (2.9)	0 (0.0)	0 (0)	1 (1.5)
20−24	1 (2.9)	1 (3.2)	0 (0)	2 (3.1)
25−29	10 (29.4)	6 (19.4)	0 (0)	16 (24.6)
30−34	15 (44.1)	14 (45.2)	0 (0)	29 (44.6)
35−39	5 (14.7)	8 (25.8)	0 (0)	13 (20.0)
40−44	2 (5.9)	2 (6.5)	0 (0)	4 (6.2)
Week of pregnancy, median (range)	39 (34-41)	39 (33-41)	0 (0-0)	39 (33-41)
31−33	0 (0.0)	1 (3.2)	0 (0)	1 (1.5)
34−36	4 (11.8)	5 (16.1)	0 (0)	9 (13.8)
37−39	19 (55.9)	17 (54.8)	0 (0)	36 (55.4)
40−42	11 (32.4)	8 (25.8)	0 (0)	19 (29.2)
SARS-CoV-2 RT-PCR test performed within no more than 13 d before operation (n = 61)	31 (91.2)	30 (96.8)	0 (0)	61 (93.8)
SARS-CoV-2 antigen test performed within no more than 13 d before operation (n = 4)	3 (8.8)	1 (3.2)	0 ()	4 (6.2)
BMI, mean ± SD (CI 95%)	29.57 ± 5.57 (27.61-31.54)	30.17 ± 4.36 (28.3-31.88)	0 ± 0	29.85 ± 5.01 (28.44-31.14)
Comorbidities				
Diabetes	6 (17.6)	6 (19.6)	0 (0)	12 (18.5)
Hypertension	5 (14.7)	6 (19.6)	0 (0)	11 (16.9)
Hypothyroidism	11 (32.3)	8 (25.8)	0 (0)	19 (29.2)
Asthma	2 (5.9)	1 (3.2)	0 (0)	3 (4.6)
Cholestasis	1 (2.9)	2 (6.5)	0 (0)	3 (4.6)
Lupus erythematosus	2 (5.9)	0 (0)	0 (0)	2 (3.1)
Course of illness				
Mild	28 (82.4)	30 (96.8)	0 (0)	58 (89.2)
Moderate	6 (17.6)	1 (3.2)	0 (0)	7 (10.8)
Severe	0 (0)	0 (0)	0 (0)	0 (0)
Critical	0 (0)	0 (0)	0 (0)	0 (0)
Indication for cesarean section				
Emergency	23 (67.6)	29 (93.5)	0 (0)	52 (80)
Planned	11 (32.4)	2 (6.5)	0 (0)	13 (20)

BMI = body mass index; COVID-19 = coronavirus disease 2019; RT-PCR = reverse transcriptase-polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

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Results

A total of 65 patients were enrolled in this study. The SARS-CoV-2 RNA test by nasopharyngeal swab produced positive results in 34 patients. In this group, as well as in 31 nonconfirmed patients (with negative SARS-CoV-2 RT-PCR test on operation day), all peritoneal fluid samples tested negative for SARS-CoV-2 RNA. Patient characteristics, type of indication for cesarean section, and obstetric comorbidities are summarized in Table 1. The study was conducted at a time when the community incidence rate of COVID-19 infection in Poland was estimated to be 0.006% [6].

Discussion

To our knowledge, this is the first prospective study to ascertain whether SARS-CoV-2 is present in the peritoneal cavities of a group of COVID-19 patients. Previously published studies reported on a limited number of cases, and their methodologies differ significantly. Several series of cases report findings similar to those of our study, suggesting that the peritoneal cavity of patients with COVID-19 is less likely to harbor the SARS-CoV-2 virus. Seeliger et al [25] and Safari et al [26] did not identify intraperitoneal viral RNA in patients who underwent surgical procedures in 5 and 4 cases, respectively. Similar observations were made in small groups of patients treated with acute peritoneal dialyses [27−29] and in several case studies [30−32]. We encountered 3 case reports indicating the presence of SARS-CoV-2 virus in ascites due to decompensated cirrhosis [33,34] and bowel obstruction [35]. In the case by Coccolini et al [35], SARS-CoV-2 was detected in peritoneal fluid at a higher concentration than in the respiratory tract. Nevertheless, there have also been 2 large prospective observational studies. In the first, Jones et al [36] were unable to detect any SARS-CoV-2 RNA in the abdominal cavity of 102 patients undergoing laparoscopic and open surgeries. In that cohort, only 1 patient produced a positive SARS-CoV-2 nasopharyngeal swab [36]. In the second, Bogani et al [37] assessed transmission of SARS-CoV-2 in surgical smoke during laparoscopy of 17 patients for gynecologic indication by performing RT-PCR assays for detection from the endotracheal tube and a filter applied on the trocar valve. In 1 patient, both swabs showed amplification of the N-gene, and in another case, only the swab test on the filter came back positive. That study suggested the presence of SARS-CoV-2 particles was within the surgical smoke/aerosolized native fluid from the abdominal cavity [37]. However, the low specificity of the N-gene broadens the findings of this paper to respiratory coronaviruses.

The inconsistency of data presented in the literature may result in physicians making therapeutic decisions on the basis of fear for their own safety rather than making evidence-based decisions. Inaccurate conclusions drawn from the case report presented by Coccolini et al [35], who identified SARS-CoV-2 in peritoneal fluid in a patient with COVID-19, may result in wrong clinical decisions. It may be suspected that surgical smoke harbors airborne contaminants such as blood fragments, cellular material, bacteria, or viruses [38], which raise a concern of SARS-CoV-2 transmission. Our study demonstrates that SARS-CoV-2 is below detectable levels in the peritoneal cavity in pregnant patients with COVID-19. As we failed to identify SARS-CoV-2 in the peritoneal cavity, it may indicate that both laparoscopic and open surgery in pregnant patients with COVID-19 are safer than previously assumed [39]. Therefore, as it has been suggested by Mintz et al [40], laparoscopic surgery should be considered as a first-choice method. However, the role of energy-based equipment such as electrosurgical coagulators or ultrasonic dissectors during laparoscopy or laparotomy in the spread of viral particles of blood origin is still a matter of conjecture, and more research is needed to confirm whether such methods are safe.

Weaknesses of Our Study

The main weaknesses of our investigation include the homogenic group of patients and the single-center nature of our investigation.

Strengths of Our Study

The main strengths of our study are its prospective design and substantial sample size.

Conclusion

Results of our study suggest of low risk of COVID-19 transmission from the peritoneal cavity at the time of laparoscopy or laparotomy.

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