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The prevalence of COVID-19 infection among gynecologic oncology patients receiving cancer treatment in a COVID-19 referral hospital

Renee Riza Cartago Medalla[1], Jericho Thaddeus P. Luna[2]

Abstract:

INTRODUCTION: Cancer patients are more susceptible to coronavirus disease-19 (COVID-19) infection because they are immunosuppressed by their disease or therapy, most of them have coexisting medical conditions, and they frequently visit hospitals for treatment and surveillance.

OBJECTIVE: The objective of this study was to determine the prevalence of COVID-19 infection among gynecologic oncology patients receiving treatment in a COVID-19 referral hospital.

MATERIALS AND METHODS: A descriptive, cross-sectional study involving 47 gynecologic cancer patients receiving treatment from June 2020 to December 2020 was performed. All patients underwent SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR) swab test and symptom and exposure assessment before the start of cancer treatment. Patients with negative SARS-CoV-2 RT-PCR swab test results received their planned treatment, and a repeat swab test and triage assessment were done midtreatment and after treatment.

RESULTS: Five (10.6%) patients had positive baseline SARS-CoV-2 RT-PCR swab results, but all proceeded with treatment after negative results were obtained. Only 1 (2.13%) patient had a positive SARS-CoV-2 RT-PCR swab test result at midtreatment. All patients had no COVID-19-associated symptoms and none of them tested positive for COVID-19 infection posttreatment.

CONCLUSION: The prevalence of COVID-19 infection among gynecologic cancer patients receiving cancer treatment is 2.13%. All patients who had positive SARS-CoV-2 RT-PCR swab test results at baseline or midtreatment were able to continue and complete treatment. There were no severe clinical events or mortalities among those affected with COVID-19 infection.

Keywords:

Cancer treatment, coronavirus disease-19, gynecologic cancer

[1]Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, Philippine General Hospital, Manila, Philippines, [2]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of the Philippines Manila-Philippine General Hospital, Manila, Philippines

Address for correspondence:
Dr. Renee Riza Cartago Medalla, Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, Philippine General Hospital, Taft Ave., Ermita, Manila 1000, Philippines.
E-mail: reneerizamedalla@gmail.com

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Introduction

The novel coronavirus disease-19 (COVID-19) has become a worldwide health concern and was declared by the World Health Organization as a pandemic in March 2020. Health-care systems had to adapt to this global outbreak and have shifted its focus toward control of viral spread, treatment of confirmed cases, and eradication of the virus. Consequently, this shift caused a cascade of complications in health-care delivery and patient care, which posed a negative impact on cancer treatment. Elective and nonemergency hospital services, which include cancer treatment, were given less prioritization, and strict guidelines were implemented to minimize outpatient visits and avoid further disease transmission.

Cancer patients are more susceptible to COVID-19 infection because they are

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immunosuppressed by their disease or therapy, most of them have coexisting medical conditions, and they frequently visit hospitals for treatment and surveillance. Anemia and hypoproteinemia from nutritional deterioration also contribute to their immunosuppression and increased susceptibility to respiratory pathogens.[1] A study of 1524 cancer patients at a tertiary cancer institution by Yu *et al*. found that cancer patients had a two-fold increased risk of acquiring COVID-19 infection than the general population.[2] Cancer patients with COVID-19 infection are also at increased risk of severe events and mortality.[1,2] The Chinese Center for Disease Control and Prevention described the epidemiological characteristics of 72,314 COVID‑19 cases in Wuhan, China, and reported that 107 patients had cancer and 6 of them died, with a case fatality of 5.6%.[3] Because of the impact of COVID-19, the management of gynecologic cancer patients had to be restructured. There was an inevitable need to modify diagnostic and therapeutic strategies, and the need to identify the risks and benefits of administering a potentially immunosuppressive treatment or delaying treatment. Cohort studies from China suggested intentionally postponing adjuvant chemotherapy and elective surgeries, for the protection of cancer patients, and intensive surveillance of patients with COVID-19 infection.[1,4,5] However, these patients need continuous care, treatment interventions, and monitoring. Treatment delay is a known independent risk factor for increased mortality and several studies have shown that the timing of initiation of primary and adjuvant treatments has a direct effect on overall survival.[6-9] This has been recognized as a more serious problem in this pandemic because of substantial delays in diagnosis and treatment administration.

The aim of this study is to determine the prevalence of acquiring COVID-19 infection among gynecologic cancer patients receiving treatment in a designated COVID-19 tertiary referral hospital. It is timely to determine this prevalence, as there are limited studies to date and no local study is yet available, on the status and outcomes of gynecologic cancer patients undergoing treatment during this pandemic. This study will highlight the impact of COVID-19 on patients with gynecologic cancers and help guide oncologists in making decisions about cancer-directed treatment.

The main objective of this study is to determine the prevalence of COVID-19 infection among gynecologic oncology patients receiving cancer treatment in a COVID-19 referral hospital.

The specific objectives are:

1. To determine the prevalence of COVID-19 infection, in a tertiary hospital, among gynecologic oncology patients, before cancer treatment, while receiving cancer treatment, and after completion of treatment
2. To describe the sociodemographic profile, coexisting medical conditions, cancer characteristics, and prior treatments of gynecologic cancer patients receiving cancer treatment during the COVID-19 pandemic
3. To determine the risk factors for acquiring COVID-19 infection among gynecologic oncology patients undergoing treatment
4. To describe the clinical presentation of gynecologic cancer patients with COVID-19 infection.

Materials and Methods

The study is a descriptive, cross-sectional study. This study included patients with gynecologic malignancies who received cancer treatment from June 1, 2020, to December 31, 2020. Cancer treatment was defined as the patient having undergone primary surgery, outpatient concurrent chemoradiation and brachytherapy, or outpatient adjuvant chemotherapy and/or radiation therapy. Patients with tumor persistence, progression, or recurrence, and for those whom interval debulking surgery has been planned, were excluded from the study.

Institutional technical and ethical review approval were obtained before the initiation of the study. A baseline reverse transcription-polymerase chain reaction (RT-PCR)-CoV-2 test from nasopharyngeal swab of both nostrils and a COVID-19 declaration and triage assessment form was obtained from all patients. Data from patient's charts, including demographics, clinical characteristics, and cancer-related details, were manually encoded into an electronic spreadsheet file for the analysis.

Patients with negative baseline RT-PCR-CoV-2 test results received their planned cancer treatment. Repeat swab tests at midcycle treatment and within 2 weeks after the completion of treatment were performed for each patient. A data assessment form, with details on hospital visits, COVID-19-related signs, symptoms or exposure risks, and treatment cycles, was also accomplished at the time of each swab test.

Patients who had positive results on any of their swab tests or those with suspected infection, at any point during treatment were referred to the COVID triage team and their course of management was followed and documented through electronic medical records.

Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables, median with interquartile range for nonnormally distributed continuous variables, and mean with

standard deviation for normally distributed continuous variables. Two-tailed independent sample *t*-test, Mann–Whitney *U*-test, and Fisher's exact/Chi-square test were used to determine the difference of means, ranks, and frequencies, respectively, between positive and negative COVID-19 infection. Shapiro–Wilk analysis was used to test the normality of the continuous variables. Missing values were neither replaced nor estimated. Data analyses were carried out using STATA 13.1 (STATA, developed by StataCorp, California, USA). $P < 0.05$ was considered statistically significant for all tests.

Results

Sixty-two patients receiving treatment from June 1, 2020, to December 31, 2020, were eligible for the study. There were 6 (9.7%) patients who were not able to comply with the scheduled RT-PCR-CoV-2 tests, 6 (9.7%) patients who were lost to follow-up, and 3 (4.8%) patients who had tumor progression during their treatment.

The patient's clinical and pathological characteristics are shown in Table 1. A total of 47 eligible cancer patients were included in the study, with an average age of 47.6 years (median 49, range: 21–69). All patients had an Eastern Cooperative Oncology Group (ECOG) performance score of 0. The average body mass index was 27 kg/m^2 (median 26, range: 17.4–40) and majority (57.45%) were classified as obese, based on the WHO Asian classification. Eleven (23.40%) patients were either previous or current smokers, and in addition to cancer, 24 (51.06%) patients had at least one or more coexisting diseases such as hypertension (most common, n = 18), diabetes mellitus, bronchial asthma, pulmonary tuberculosis, cardiovascular disease, and breast cancer. Cervical cancer was the most frequent type of gynecologic cancer (44.68%), followed by endometrial cancer (36.17%), then ovarian (17.02%), and fallopian tube cancer (2.13%). Twenty-three (48.94%) patients had early-stage disease and 24 (51.06%) patients had advanced-stage disease. Nine (19.5%) patients were operated on before referral to our institution and the rest did not undergo a prior surgery, radiation therapy, chemotherapy, or immunotherapy.

The characteristics of the patient's cancer treatment are shown in Table 2. The most frequently administered treatment was chemotherapy, followed by radiation therapy and surgery. Five (10.64%) patients received radiation therapy alone, whereas 8 (17.02%) patients

Table 1: Clinical and pathological characteristics of patients

	Frequency (%); mean±SD; median (IQR)			
	Total (*n*=47)	COVID-19 infection		*P*
		Positive (*n*=1; 2.13%)	Negative (*n*=46; 97.87%)	
Age	47.55±12	49	48.56±12.09	-
ECOG score	0	0	0	-
BMI	26.94±5	23	27.03±5.02	-
Obesity	27 (57.45)	0	27 (58.70)	0.426
History of smoking	11 (23.40)	1	10 (21.74)	0.234
Comorbidities				
None	23 (48.94)	1	22 (47.83)	1.000
With 1 comorbidity	21 (44.68)	0	21 (45.65)	
With >1 comorbidity	3 (6.38)	0	3 (6.52)	
Comorbidities				
Hypertension	18 (38.30)	0	18 (39.13)	1.000
Diabetes mellitus	4 (8.51)	0	4 (8.70)	1.000
Bronchial asthma	3 (6.38)	0	3 (6.52)	1.000
Pulmonary tuberculosis	2 (4.26)	0	2 (4.35)	1.000
Cardiovascular disease	1 (2.13)	0	1 (2.17)	1.000
Breast cancer	1 (2.13)	0	1 (2.17)	1.000
Cancer type				
Cervical cancer	21 (44.68)	1	20 (43.48)	1.000
Endometrial cancer	17 (36.17)	0	17 (36.96)	
Ovarian cancer	8 (17.02)	0	8 (17.39)	
Fallopian tube	1 (2.13)	0	1 (2.17)	
Cancer stage				
Stage I	16 (34.04)	0	16 (34.78)	1.000
Stage II	7 (14.90)	0	7 (15.22)	
Stage III	24 (51.06)	1	23 (50)	
History of prior cancer treatment (surgery)	9 (19.15)	0	9 (19.57)	1.000

IQR: Interquartile range, SD: Standard deviation, COVID-19: Coronavirus disease-19, BMI: Body mass index, ECOG: Eastern Cooperative Oncology Group

underwent surgery with systematic staging, and the median number of admission was 6 days. Twenty (42.55%) patients received outpatient cisplatin chemotherapy, concurrent with pelvic or paraaortic external beam radiation, with or without parametrial boost, and brachytherapy. The average total time of radiation therapy was 27 days. Ten (21.28%) patients underwent surgery followed by adjuvant chemotherapy with carboplatin and paclitaxel. These patients received an average of six cycles of chemotherapy. Finally, 4 (8.51%) patients underwent surgery and received an adjuvant chemotherapy and radiation treatment.

Eighteen (38.3%) patients had treatment-related complications. The most common was anemia (38.89%), defined as having a hemoglobin of <100; followed by neutropenia (33.33%), defined as having an absolute neutrophil count of <1.5; combined anemia and neutropenia (22.22%); and 1 (5.56%) patient had liver toxicity. These complications were appropriately managed, and all patients were able to continue and complete their treatment.

The average number of hospital visits from the 1st day of consult until the last day of cancer treatment, was 29 days. Reasons for reporting to the hospital included administration of cancer treatment, routine laboratories and imaging, follow-up with physician, facilitation of documents for financial assistance, and administration of iron sucrose for anemia and granulocyte colony-stimulating factor for the prevention or management of neutropenia.

The results of symptom assessment and exposure history are shown in Table 3. Nine (19.15%) patients experienced symptoms related to COVID-19 infection, but eight of these patients had negative SARS-CoV-2 RT-PCR swab test results. Among all patients in the study cohort, none declared exposure or travel histories that can predispose them to COVID-19 infection.

During the study period, 5 out of 47 (10.6%) patients had positive baseline SARS-CoV-2 RT-PCR swab test results. These patients did not require hospital admission and proceeded with treatment after recovery and after negative repeat swab results were obtained. Only one patient developed COVID-19 infection while ongoing treatment, and this was detected during the midtreatment swab test. Therefore, in this study cohort, the prevalence of COVID-19 infection among gynecologic cancer patients receiving cancer treatment in a COVID-19 referral hospital is 2.13%. There were no mortalities among those affected by COVID-19. COVID vaccines were not yet available in the country as of this time.

The patient who developed COVID-19 infection during treatment is a 49-year-old cervical cancer stage IIIb patient, with an ECOG performance score of zero, smoker, nonobese,

Table 2: Characteristics of the patient's treatment

	Frequency (%); mean±SD; median (IQR)			
	Total (*n*=47)	COVID-19 infection		*P*
		Positive (*n*=1; 2.13%)	Negative (*n*=46; 97.87%)	
Type of cancer treatments				
Chemotherapy alone	0	0	0	1.000
RT alone	5 (10.64)	0	5 (10.87)	1.000
Surgery alone	8 (17.02)	0	8 (17.39)	1.000
Chemotherapy + radiotherapy	20 (42.55)	1	19 (41.30)	1.000
Surgery + chemotherapy	10 (21.28)	0	10 (21.74)	1.000
Surgery + chemotherapy + RT	4 (8.51)	0	4 (8.70)	1.000
Number of chemotherapy cycles	6 (5–6)	6	6 (4–8)	0.540
Number of RT days	27 (25–30)	34	27 (25–30)	0.140
Number of days of admission for surgery	6 (6–7)	-	6 (6–7)	-
Type of RT	*n*=30		*n*=29	
EBRT	22 (73.33)	1	21 (72.41)	1.000
EFRT	2 (6.67)	0	2 (6.9)	1.000
PM boost	7 (23.33)	1	6 (20.69)	0.233
HDR brachytherapy	18 (60)	1	17 (58.62)	1.000
Treatment-related complications	*n*=18			
Anemia	7 (38.89)	0	7 (38.89)	0.114
Neutropenia	6 (33.33)	0	6 (33.33)	0.467
Anemia and neutropenia	4 (22.22)	1	3 (16.67)	1.000
Liver toxicity	1 (5.56)	0	1 (5.56)	1.000
Number of hospital visits	29 (10–37)	43	29 (10–37)	0.223

RT: Radiation therapy, EBRT: External beam RT, EFRT: Extended-field RT, HDR: High-dose rate, IQR: Interquartile range, SD: Standard deviation, COVID-19: Coronavirus disease-19, PM: Parametrial

Table 3: Symptom assessment and exposure history

	Frequency (%)			
	Total (*n*=47)	COVID-19 infection		*P*
		Positive (*n*=1; 2.13%)	Negative (*n*=46; 97.87%)	
Symptom assessment				
Baseline assessment				
Headache	1 (2.13)	0	1 (2.13)	1.000
Mid-treatment assessment				
Headache	2 (4.26)	0	2 (4.26)	1.000
Body weakness	3 (6.38)	0	3 (6.38)	0.064
Posttreatment assessment				
Headache	1 (2.13)	0	1 (2.12)	1.000
Body weakness	2 (4.26)	0	2 (4.26)	1.000
Exposure history				
Traveled out of the country	None			
Reside in an area with COVID-positive patients	None			
Close contact with a COVID-positive patient	None			
History of visit/admission to another hospital for the past 2 weeks	None			

COVID-19: Coronavirus disease-19

and with no comorbidities. She received outpatient external beam radiation therapy with parametrial boost, concurrent with weekly cisplatin, followed by high-dose rate brachytherapy. She received 34 days of radiation treatment and six cycles of chemotherapy and had 43 outpatient hospital visits. She developed anemia and neutropenia during treatment but did not develop any symptoms related to COVID-19 infection. She tested positive during her midcycle swab, done after completion of concurrent chemoradiation and before proceeding with brachytherapy.

Discussion

To date, this is the first prospective local study that identified the prevalence of COVID-19 infection among gynecologic cancer patients who underwent surgery or received chemotherapy and/or radiation therapy during the time of the COVID-19 pandemic. Early retrospective studies reported the prevalence of COVID-19 infection among cancer patients. Liang *et al*. reviewed 1590 patients with COVID-19 infection and identified a cancer prevalence of 1.0% (18 patients), which was higher compared with the overall cancer incidence of 0.29% in the Chinese population. The majority (75%) of these patients were on routine follow-up and were not receiving treatment, whereas the remaining 25% received chemotherapy or surgery in the 4 weeks before being diagnosed with COVID-19 infection.[4] Similarly, Zhang *et al*. reviewed 1276 patients with COVID-19 infection and identified a cancer prevalence of 2.2% (28 patients). All patients received at least one kind of cancer treatment and 21.4% (6 patients) received cancer treatment within 14 days of COVID-19 infection diagnosis.[1] A meta-analysis by Desai *et al*. identified a pooled prevalence of 2.0% among studies involving more than 100 patients (95% confidence interval [CI]: 1.0%–3.0%), and 3.0% among studies with a sample size of <100 patients (95% CI: 1.0%–6.0%).[10] These studies show that patients with cancer have a higher risk of acquiring COVID-19 infection, and those who were receiving cancer treatment were at greater risk of severe clinical events and mortality due to COVID-19.

In this study cohort, five patients were identified to have COVID-19 infection at baseline swab test and one patient at midcycle treatment swab test. All these patients were asymptomatic and did not require active management or hospital admission. This prevalence is congruent with other published studies, there were no morbidities or mortalities associated with COVID-19 infection, and all patients in the study cohort were able to complete their cancer treatment.

The results of this study showed a low prevalence of 2.13%, but the results are based on a small sample size, receiving cancer treatment in a single institution, over a specified period. The study only included patients receiving primary cancer treatment but patients with progressive diseases who may even be more susceptible to the infection because of severe immunosuppression, brought by several cancer treatments received, were excluded from the study population.

Other risk factors that increase the vulnerability of cancer patients to COVID-19 infection include older age, uncontrolled comorbidities, severe obesity, smoking, lower socioeconomic status, poorer performance status, and frequent visits to the hospitals.[11] However, in this study, no significant risk factors among cancer patients undergoing treatment were identified.

As a COVID-19 referral hospital, guidelines and measures to protect patients and health-care workers are being regularly updated to adapt to the continuing

challenges of the pandemic. The outpatient clinics were restructured to minimize the risk of COVID-19 transmission. Outpatient face-to-face consultations were limited, but patient communication and education were reinforced by telemedicine. All patients had scheduled appointments and walk-in consultations were discouraged. Strict daily triage screening was implemented to identify symptoms associated with COVID-19 infection and contact or travel histories were taken from patients and their accompanying relatives. All health-care workers wore appropriate personal protective equipment, and patients and their companions were required to wear face masks and shields. Social distancing and separation of clinic workspaces were ensured to reduce the risk of infection. However, the effectiveness of these implemented measures cannot be objectively assessed, due to the general lack of data for local COVID-19 infection among cancer patients in this institution and in others, and further studies will be necessary to make conclusions regarding these measures.

It is worth noting that a considerable number of gynecologic cancer patients, who were included in the study cohort, were positive for COVID-19 infection but were asymptomatic. Routine screening, through SARS-CoV-2 RT-PCR swab test, of all patients before initiation of cancer treatment was encouraged, but due to limited resources, this was done only to high-risk patients identified during triage assessment. In this study, this was applied to all patients, and routine swab testing was done before the initiation of treatment, at midcycle, and at posttreatment. Six out of 47 (12.77%) patients showed positive swab results, five positive cases were detected at baseline and one at midcycle swab tests. All these patients were asymptomatic and with no identified exposure history. Further studies may be necessary to assess this subpopulation of gynecologic cancer patients who are asymptomatic COVID-19 carriers, and the risks involved in their infection and subsequent treatment. Currently, routine SARS-CoV-2 RT-PCR swab testing is not mandatory, but it may guide oncologists in detecting asymptomatic COVID-19-infected patients and appropriately adjusting their cancer treatment.

Conclusion

The prevalence of COVID-19 infection among gynecologic cancer patients receiving cancer treatment is 2.13%. All patients who had positive SARS-CoV-2 RT-PCR swab test results at baseline or midtreatment were able to continue and complete treatment. There were no severe clinical events or mortalities among those affected with COVID-19 infection. Although the patients who tested positive in this study had an unremarkable course of COVID infection, the higher prevalence of such among gynecologic cancer patients in general, and those among receiving treatment, suggests the need to enhance further local protocols and guidelines to prevent transmission among this vulnerable subset of the population.

Limitations and recommendations

The study analysis was limited to a small sample size in a single institution. Furthermore, the study was conducted before the initiation of COVID-19 vaccination. Future studies may focus on the prevalence of COVID-19 infection among vaccinated gynecologic cancer patients, and the role of vaccination in the treatment of these patients. Testing for COVID-19 infection among these patients is still recommended despite the relatively low prevalence of COVID-19 infection in the population. The possibility of complications, especially in these immunocompromised patients, is expectedly greater, thus the recommendation.

Authorship contributions

Renee Riza C. Medalla, MD - Involved in the conceptualization, methodology, data curation, writing of the original draft, review and editing, visualization.

Jericho Thaddeus P. Luna, MD - Involved in conceptualization, methodology, review and editing of the draft, visualization and supervision.

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Conflicts of interest

There are no conflicts of interest.

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