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Oncologic patients with covid 19: A mexican endeavor

Daniela Shveid-Gerson, Alejandro Noguez-Ramos, Diana A. Villegas-Osorno, Efraín I. Camarín-Sánchez, Lorena López-Zepeda, Christian P. Camacho-Limas, Alberto Villalobos-Prieto, J. Alberto Serrano-Olvera, and Raquel Gerson-Cwilich*

Department of Medical Oncology, The ABC Medical Center, IAP, Mexico City, Mexico

Abstract

Introduction: *The coronavirus disease 2019 (COVID-19) pandemic is a worldwide challenge. There are few reports regarding its behavior in cancer patients.* **Materials and methods:** *Retrospective study including cancer patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the ABC Medical Center in Mexico City. We include general and oncological variables. We analyzed clinical features and treatment of COVID-19 and its outcomes such as hospitalization and death.* **Results:** *We report 86 patients with cancer and SARS-CoV-2 infection. The vast majority of patients 80 (93.1%) had a solid tumor while the most frequent primary tumor was breast 40 (46.5%) and lung 8 (9.3%). The clinical stage of patients was I in 22.1%, II in 16.3%, III in 31.4%, and IV in 24.4%. Antibiotics were used in 37 patients (43%) and corticosteroids in 32 (37.2%).* **Discussion***: During disease evolution, 11 (12.8%) patients were hospitalized and 6 (7.0%) died. Variables of significant association with hospitalization include gender (men, odds ratio [OR] 5.6), previous cardiac disease (OR 25.1), and hematologic malignancy (OR 8.1). Associations with higher mortality rates were gender (men, OR 15), clinical Stage III/IV cancer (OR 11.3), type 2 diabetes mellitus (OR 14.7), previous cardiac disease (OR 19.2), and targeted therapy (OR 9.0).* **Conclusions:** *We found lower hospitalization and mortality rates compared to what had been previously reported both in Mexico around the globe. Men and patients with previous cardiac disease had a significant higher risk of hospitalization and death. Hematologic malignancies (lymphoma) were associated with higher hospitalization. Clinical Stage III/IV, targeted therapy, and type 2 diabetes mellitus showed a statistically significant association with mortality risk.*

Key words: *Severe acute respiratory syndrome coronavirus 2. Coronavirus disease 2019. Cancer. Mexico.*

Introduction

Since the inception of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the Hubei Province in China in late 2019, it has spread rapidly across the globe[1]. After its initial discovery, the propagation of SARS-CoV-2 was swift, with over 89 million confirmed cases globally and more than 1.7 million deaths as of December 2020[2]. Individuals affected by cancer are more susceptible to infections due to coexisting chronic diseases, overall poor health, and systemic immunosuppressive states caused by both cancer and anticancer treatments[3]. A higher risk attributed to contracting the virus could be due to immunosuppression, increased coexisting medical conditions, and, in cases of lung malignancy, underlying pulmonary compromise. Hematological cancer patients, or those that are receiving active chemotherapy treatment, might be most vulnerable to complications due to increased immunosuppression[4] – studies have yet to prove the latter.

Correspondence:
*Daniela Shveid-Gerson
E-mail: daniela.shveid.gerson@gmail.com

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This is one of the first retrospective studies done in Mexico to evaluate cancer patients being at a higher risk of serious illnesses from coronavirus disease 2019 (COVID-19). Extra precautions are very much advised for this patient population. Consequently, patients with cancer who are infected by the SARS-CoV-2 virus may experience more precarious outcomes than other populations. There is still no systematic evaluation of the effects that the SARS-CoV-2 coronavirus has in relation to patients with cancer in a representative population[5].

A recent study reported a higher risk of severe events in patients with cancer when compared to patients without[6]; however, the small sample size of SARS-CoV-2 patients with cancer in the study limited how representative it was of the whole population, and made it difficult to conduct more insightful analyses, such as comparing clinical characteristics of patients with different types of cancer or the use of anticancer treatments[7]. There is limited information about the outcome of patients with cancer who contract this highly contagious disease.

Cancer is among the top causes of death in Mexico and the world[8]. According to the Mexican National Institute of Statistics and Geography, Mexico had a population > 120 million people in 2020 – 54.2% of whom were women – and cancer is currently the third leading cause of death in the Mexican population. Interestingly, 45.3% of deaths from this group of diseases occur in the economically active population[9] (Unify paragraphs). The first COVID-19 infection in Mexico is reported to have been detected in January 2020, despite claims that this was a recording error. By the end of May, the number of cases soared past 100,000, and in November, it reached one million, with the number of deaths nearing 100,000. Mexico City is the federate entity with the highest number of cases[10]. First, patients with cancer appear to be at increased risk of mortality and severe illness due to SARS-CoV-2 infection, regardless of whether they have active cancer, are on anticancer treatment, or both[7]. Overall lethality of COVID-19 in the present study was 9.2%. A higher proportion of deaths was observed in the oldest age group (27.95%) and in individuals with any comorbidity (73.3%). In Mexico, mortality from COVID-19 is estimated to be over 12%[11].

In the Mexican population, important subgroups of patients with cancer appear to be at increased risk for adverse outcomes. In addition to previously reported risk factors (age and gender) in the general COVID-19 population, Eastern Cooperative Oncology Group (ECOG) performance status of 2 or higher and active cancer seem to be associated with an increased risk of worse outcomes from COVID-19 in oncologic patients. Although a moderate or poor ECOG performance status is well known to have a deleterious effect on overall outcomes, an ECOG performance status of 2 is not always considered a contraindication to aggressive therapy for active cancer[12].

The American British Cowdray Medical Center is a non-oncological private assistance institution whose is a cancer center and treats all types of neoplasms, regardless of previous comorbidities. The center features in-hospital care, an outpatient clinic, radiotherapy, and a chemotherapy infusion center. In the past 3 years, more than 22,000 chemotherapy sessions, 340 radiosurgery sessions and more than 45,000 radiotherapy sessions have been administered. The most commonly treated neoplasms are breast cancer, non-small cell lung cancer, colorectal cancer, and cancer of the gastrointestinal tract. Unfortunately, many of our cancer patients have also contracted SARS-CoV-2. This study analyzes the information obtained from our experience of the management, evolution, and behavior of our patients with cancer and COVID-19[13].

Materials and Methods

A retrospective study was conducted including cancer patients with SARS-CoV-2 infection confirmed by reverse transcription polymerase chain reaction (RT-PCR) from April 1 to November 30 in the American British Cowdray Medical Center in Mexico City. We include variables such age, gender, body mass index, tobacco use, and comorbidities. Oncological factors analyzed were primary site, clinical stage, active cancer, active treatment, chemotherapy, radiotherapy, hormonotherapy (endocrine therapy), targeted therapy, and immunotherapy (checkpoint inhibitors) use. We analyzed the clinical features and treatment of COVID-19. Electronic medical records were assessed to evaluate disease outcomes such as hospitalization or death. Data were analyzed using the statistical program SPSS version 22 (Chicago, IL). For variables with a normal distribution, the mean and standard deviation were used, and the median and interquartile range for free distribution variables. To contrast the differences found between the groups with or without complications, a Student's t-test or a Mann–Whitney U-test was used for quantitative variables of normal distribution or free distribution, respectively. For qualitative variables, a Chi-square test was applied with regard to the outcomes, a Chi-square test and odds ratio (OR) (confidence interval [CI] 95%) were utilized.

Results

From April 1 to November 30, 2020, a total of 86 patients with cancer had SARS-CoV-2 infection confirmed by RT-PCR in the American British Cowdray Medical Center in Mexico City. The mean age was 58.1 years SD (13.8), the majority of whom were female (61, 70.9%); 36 (41.9%) were overweight or obese, 74 (86%) have never smoked, 12 (14%) had type 2 diabetes mellitus, and 20 (23%) had hypertension, but there were no patients in the study population who had chronic obstructive pulmonary disease or asthma. Most of the patients had a solid tumor (80, 93.1%). The most frequent primary tumor was breast (40, 46.5%) followed by lung (8, 9.3%) (seven NSCLC and one SCLC) and colorectal cancer (6, 7%). The difference between the prevalence of these cancers in our study is based on the type of patients attended in this hospital, taking into consideration, the small sample size and patient heterogeneity. The clinical stage of patients was I in 22.1%, II in 16.3%, III in 31.4%, and IV in 24.4% of the patients.

Active cancer was observed in 65 (75.6%) patients and 41 were in active treatment at the time of the infection (47.7%). Before or during the diagnosis of COVID-19, chemotherapy had been used in 45% of patients, radiotherapy in 40.7%, endocrine therapy in 27.9%, and targeted therapy – which includes antibodies such as bevacizumab or rituximab, tyrosine kinase inhibitors such as sunitinib, or those directed to punctual mutations such as olaparib or alectinib in 12.8% and immunotherapy (checkpoint inhibitors) in 3.5%. The most common symptoms were fever (59, 68.6%), coughing (50, 58.1%), headaches (37, 43%), myalgias (30, 34.9%), diarrhea (25, 29.1%), and anosmia 20 (23.3%). In the course of treatment, antibiotics were used for 37 (43%) patients, corticosteroids in 32 (37.2%), oseltamivir in 9 (10.5%), and anticoagulants in 7 (8.1%). Other treatments utilized less frequently were tocilizumab, ivermectin, hydroxychloroquine, and lopinavir/ritonavir (Table 1).

During disease evolution, 11 (12.8%) patients were hospitalized, and all of them required oxygen therapy. Six patients (7.0%) died, one of which died at home. The five patients who required invasive ventilatory support died (Table 2).

The variables of significant association with hospitalization include gender (men, OR 5.6, 1.4-21.9), previous cardiac disease (OR 25.1, CI 95% 2.3-371), hematologic malignancy – limited to lymphomas in this particular study (OR 8.1, CI 95% 1.3-47.2) – and dyspnea (OR 7.9,

Table 1. Basal characteristics of patients

Characteristics (n = 86)	Value
Age (years)	58.1 (13.8)
Gender	Women 61 (70.9%) Men 26 (29.1%)
Body mass index (BMI) (Kg/m^2)	24.65 (22.2-27.6)
Overweight or obesity BMI > 25 Kg/m^2	36 (41.9%)
Smokers	11 (12.8%)
Hypertension	20 (23%)
Type 2 diabetes mellitus	12 (14%)
Dyslipidemia	6 (7%)
Previous cardiac disease*	4 (4.7%)
Chronic kidney disease	2 (2.3%)
COPD or asthma	0
Primary site	
Breast	40 (46.5%)
Lung	8 (9.3%)
Colorectal	6 (7.0%)
Hematological malignancies	6 (7.0%)
Kidney	4 (4.7%)
Prostate	3 (3.5%)
Pancreas	3 (3.5%)
Ovary	3 (3.5%)
Central nervous system	3 (3.5%)
Melanoma	2 (2.3%)
Testicular	2 (2.3%)
Urothelial carcinoma	2 (2.3%)
Gastric	1 (1.2%)
Non-melanoma skin cancer	1 (1.2%)
Head-and-neck cancer	1 (1.2%)
Sarcoma	1 (1.2%)
Clinical stage	
I	19 (22.1%)
II	14 (16.3%)
III	27 (31.4%)
IV	21 (24.4%)
Active cancer	65 (75.6%)
Active treatment	41 (47.7%)
Chemotherapy	45 (52.3%)
Radiotherapy	35 (40.7%)
Hormonotherapy (endocrine therapy)	24 (27.9%)
Targeted therapy	11 (12.8%)
Immunotherapy (checkpoint inhibitors)	3 (3.5%)
Fever	59 (68.6%)
Cough	50 (58.1%)
Headache	37 (43%)
Myalgias	30 (34.9%)

(Continues)

Table 1. Basal characteristics of patients (*continued*)

Characteristics (n = 86)	Value
Diarrhea	25 (29.1%)
Anosmia	20 (23.3%)
Dyspnea	19 (22%)
Odynophagia	18 (20.9%)
Taste alterations	11 (12.8%)
Rhinorrhea	8 (9.3%)
Antibiotics	37 (43%)
Corticosteroids	32 (37.2%)
Oseltamivir	9 (10.5%)
Anticoagulants	7 (8.1%)
Tocilizumab	5 (5.8%)
Ivermectin	5 (5.8%)
Hydroxychloroquine	3 (3.5%)
Lopinavir/ritonavir	1 (1.2%)
Remdesivir	0
Convalescent plasma	0

*Previous cardiac disease: myocardial infarction or cardiac insufficiency.
For normal distribution, mean and standard deviation were used and for free distribution the median and interquartile range.

CI 95% 1.9-31). The variables of significant association with death include gender (men, OR 15, CI 95% 1.6-136.1), clinical Stage III/IV (OR 11.3, 2.7-19.8), Type 2 diabetes mellitus (OR 14.7, CI 95% 2.7-112), previous cardiac disease (OR 19.2, CI 95% 2.1-174), dyspnea (OR 8.5, CI 95% 1.8-38.9), targeted therapy (OR 9.0, CI 95% 1.5-52.2), and hematologic malignancy (lymphoma in this study sample) (p = 0.05) (Tables 3 and 4).

Discussion

This is one of the first studies in Latin America, and among the first Mexico, to describe the experience with cancer patients and SARS-CoV-2 infection in a private hospital, as well as the factors that significantly impact the clinical evolution of these patients, such as clinical stage, type of neoplasia, preexisting comorbidities, and symptoms during the course of infection. Limitations of our study include sample size, single-center analysis, and the retrospective nature of the data included. Among our findings, we found a mean age of 58.1 years, which is slightly lower compared to international studies with mean ages from 60 to 70 years[6,12]. In an international, multicenter study conducted by Patiño et al. that included public institutions, the mean time required for ICU care was an estimated 12.7 days, with a mean mortality of 16.3 days after infection. The estimated time for a serious adverse event was 8.1 days. In comparison with this study, we estimated that the peak of hospitalization was 16 days. The results show that 12.8% of the patients merited hospitalization due to the severity of the symptoms associated with the SARS-CoV-2 infection and a 7% mortality was documented[14].

In a slightly similar study conducted by Ribas et al., they conclude that patients, in particular those with lymphoma, are considered patients at high risk of mortality when acquiring COVID-19 infection. In this paper, 10 studies with similar with these characteristics were compared, finding differences in significant mortality when compared with the non-oncologic population, with a difference spanning in mortality ranges from 4% versus 12% in the Dai et al. study to as high as 35 versus 45% in the Sng et al. study [15].

It is estimated that mortality from COVID-19 increases by 10-15% in cancer patients, compared to the general population. Here, we stratified the study population by neoplasia and clinical stage, 93% of patients had solid tumors, 46.5% of those pertaining to breast tumors, and 9.3% had lung neoplasms. In terms of staging, 31.4% of patients had clinical Stage III cancer and 24.4% clinical Stage IV. Active neoplasia was present in 75.6% of patients of which 45% were being treated with chemotherapy, 40.7% were receiving radiotherapy, and 3.5% were receiving immunotherapy (checkpoint inhibitors) at the time of infection with COVID-19. While analyzing the variables in our study, we found that the predominant symptom in patients diagnosed with COVID-19 and cancer was coughing in 58%, headache in 43%, myalgia in 34.9%, diarrhea in 29.1%, and anosmia in 23.3%. Compared to our results with the study by Dai et al., where 105 cancer patients were included, the predominant symptoms noted were fever (64.7%), cough (52.2%), and fatigue (28.5%) while only 5.7% of the patients had myalgia. In the previously mentioned study, we were also able to observe that the most frequently used treatment in patients with COVID-19 and cancer were antibiotics in 77.1% of patients, antivirals in 71.4%, corticosteroids in 18.10%, and oxygen in 45.7%. In comparison to our study population, we found similarities in the therapy used, with the majority being antibiotics in 43% of patients followed by the use of corticosteroids in 37.2% and antivirals 10.5%[16].

Table 2. Hospitalization need and outcomes of patients with cancer and COVID-19

Primary tumor	Stage	Gender	Age	DM2	CD	CT	HT	TT	RT	IT	Hospitalization	Death
Astrocytoma	III	Male	67									
Astrocytoma	III	Male	48									
Breast	II	Female	45									
CCR	IV	Male	59									
Hematological	III	Male	65									
Hematological	IV	Female	83									
Hematological	IV	Male	26									
Hematological	IV	Female	48									
Kidney	III	Female	70									
Lung	I	Male	84									
Melanoma	IV	Male	88									
Urothelial cancer	III	Male	72									

CCR: colorectal cancer; DM2: type 2 diabetes mellitus; CD: previous cardiac disease; CT: chemotherapy; TT: targeted therapy; RT: radiotherapy; IT: immunotherapy (checkpoint inhibitors).

Table 3. Significant odds ratios for hospitalization. Univariate analyses

Odds ratio for hospitalization			
Variable	**Odds ratio (CI 95%)**	**Interval**	**p value**
Gender (men)	5.6	1.4 -21.9	0.01
Previous cardiac disease*	25.1	2.3-371	0.008
Hematologic malignancy	8.1	1.3-47.2	0.03
c	7.9	1.9-31.9	0.004

*Previous cardiac disease: myocardial infarction or cardiac insufficiency. Non-significant variables: overweight or obesity, smokers, hypertension, type 2 diabetes mellitus, clinical Stage III/IV, active cancer, active treatment, chemotherapy, radiotherapy, hormonotherapy, targeted therapy, checkpoint inhibitors, fever, cough, headache, myalgias, diarrhea, anosmia, rhinorrhea.

Table 4. Significant odds ratios for death. Univariate analyses

Odds ratio for death			
Variable	**Odds ratio (CI 95%)**	**Interval**	**p value**
Gender (Men)	15.0	1.6-136.1	0.007
Type 2 diabetes mellitus	14.7	2.7-112	0.003
Previous cardiac disease*	19.2	2.1-174	0.02
Clinical Stage III/IV	11.3	2.7-19.8	0.04
Targeted therapy	9.0	1.5-52.2	0.02
Dyspnea	6.9	1.1-41.6	0.03

*Previous cardiac disease: myocardial infarction or cardiac insufficiency. Non-significant variables: overweight or obesity, smokers, hypertension, hematologic malignancy, active cancer, active treatment, chemotherapy, radiotherapy, hormonotherapy, checkpoint inhibitors, fever, cough, headache, myalgias, diarrhea, anosmia, rhinorrhea, antibiotics, corticosteroids, oseltamivir, anticoagulants, tocilizumab.

Reviews before this study (that includes Mexican and international institutes) regarding patients with cancer and COVID-19 infection noted a similar mortality between 10 and 15% of oncologic patients, with lymphoma having the highest risk of death. In relation to pathologies such as diabetes mellitus, the percentages are similar with 14% in our study versus 16%, 19%, and 20% in the English, French, and American series, respectively[17-19]. Furthermore, within the oncological pathologies, more than 90% were solid tumors, breast cancer the most frequent, compared with 46%, 13.7%, and 21%[6,17,18,20-22]. Characteristics that predispose toward elevated rates of hospitalization were specifically

analyzed, finding a higher prevalence in men, corresponding to 70% versus 29% in women. This is a noted constant in the North American and English series [17,20,22], although not in the French one[23]. Some studies have concluded that the men having a higher hospitalization rate and worse prognosis is theoretically due to testosterone levels to be the culprit, as an increased level can facilitate the entrance of the virus SARS-CoV-2 to the host cell through the expression of angiotensin converting enzyme 2. When present in the elderly or obese men, this may predispose to endothelial dysfunction, higher risk of thrombosis, and deficient immune response[24]. This hypothesis is explained in a meta-analysis by Peckham et al., where men had more complications that required intensive care unit admission, noting a possible difference in adaptive immunity, finding more TC4 and TC8 in women in addition to elevated values of INF (which help to promote the acute response to the virus)[25].

The relation between mortality factors in international series and in this investigation demonstrates that people with lymphoma have the greatest index of mortality. This can be explained by an intrinsic susceptibility to viral infections in addition to regularly receiving more myeloablative treatments. Some studies have mentioned previous cardiac disease as an overwhelming mortality factor. In a dissimilar fashion, different oncological treatments are not noted to be statistically significant to increase this outcome, albeit gathering conclusions from diverse results, such as the French study[23], where the use of chemotherapy 3 months before the SARS COV 2 infection increased mortality. This may be compared to other studies[21,26,27] where the use of immunotherapy (checkpoint inhibitors) utilized 1 month prior also elevated mortality. This in turn may be explained by several factors such as immunosuppression and immunosenescent cells, cardiovascular alterations that some types of chemotherapy cause and increased presence of metabolic syndrome and obesity, pneumonitis, pulmonary fibrosis and risk of thrombosis. This may contribute to an increased patient susceptibility and aggravated SARS-CoV-2 infection[24,26,27]. Therefore, the findings within our population demonstrating how patients with active treatment with target therapy had higher mortality may possibly reveal a secondary, adverse effect and not just a causal association[26]. Finally, a meta-analysis of more than 20 studies conducted around the world, showed that the population with neoplastic diseased had 3.22 times higher mortality risk, 3.91 times the probability of severe disease, and 3.10 higher chance to be admitted in ICU, compared to cancer-free patients, which is comparable with our center's statistics[28].

Conclusions

In this study, patients with cancer and SARS-CoV-2 infection had lower hospitalization and mortality rates in contrast with other cohorts. We found a gender difference in the risk of hospitalization and death for COVID-19 disease: men had a significantly higher risk as well as other factors associated with adverse outcomes, such as previous cardiac disease to note.

In our study, clinical Stage III/IV, targeted therapy, and type 2 diabetes mellitus did not have an increased risk of hospitalization, but mortality risk showed a statistically significant association. Dyspnea is a main cause of hospitalization and a severity symptom, so we do not assume a clinically association with hospitalization or death. Lymphoma, specifically lymphomas in our study sample – was associated with higher hospitalization risk, but mortality risk tends to be significant due to the small sample size. Oncology variables such as primary site, active treatment, chemotherapy, radiotherapy, hormonotherapy (endocrine therapy), or immunotherapy (checkpoint inhibitors) use did not show a statistically significant association as predictors of hospitalization or death.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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