



RESEARCH ARTICLE

Clinical-epidemiological characteristic of COVID-19 and cancer, first year of pandemic

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ABSTRACT

At the end of 2021, 3.6% of the world's population was infected by SARS-CoV2, which was one of the main causes of death in México with a fatality rate of 7.5%, being higher than the world average (1.9%). Patients with cancer were a vulnerable group to get infected and to have the worse results; in spite of the limited information to direct oncological treatment, medical care continued in Oncology hospitals. The objective of this study was to compare the clinical-epidemiological characteristics in patients with COVID-19 to those ruled out, who were hospitalized in a Third Level Cancer Hospital.

Material and methods: A cohort of oncological cases was carried out about patients who were hospitalized within 2020-2021 with a suspected diagnosis of COVID-19 and who had a RT-PCR to rule out or to confirm the diagnosis. Data related to cancer care, respiratory symptoms, laboratory report and chest x-ray were searched in the clinical record and the cases were followed for about 30 days. Simple frequencies as well as normality tests were obtained to compare the study variables between confirmed cases and those discarded through U-Mann Whitney.

Results: A total of 208 patients in which 59-year-old was the median; 49.5% were women and 50.5% were men. Colorectal cancer was the main diagnosis (19.7%). COVID-19 was confirmed in 32.2%, with dyspnea as the most common symptom (86.6%), although chills had a significant difference when comparing this group to the discarded cases, as it did elevated DHL, and an x-ray with Score ≥ 12 . During follow-up, 46.2% of patients died from this cause.

Conclusions: Chills, elevated LDH and a chest x-ray with a high Score were the main differences presented in patients with cancer and COVID-19.

Keywords: COVID-19, cancer, Mexicans, cohort.

Introduction

Emerging in China in late 2019, the new viral agent later known as SARS CoV2¹, spread around the world with a variable outcome in clinical detections for infected people². Appraising that the pandemic affected everyone in a direct and indirect way in the whole world, a 3.6% of the population was infected by SARS CoV2 at the end of 2021.^{3,4}

COVID-19 was one of the main causes of death in the world and, in Mexico, it ranked first with 238,772 deaths in that year.⁵ As the pandemic started, in Mexico we faced a great deal of uncertainty to deal with the treatment of patients with cancer and COVID-19, provided we only had limited strategies like health distance, hygienic measures such as hand washing, and the use of respiratory masks⁶. Given that there was no specific treatment known until then, it was very likely to compromise the immune response and therefore to worsen the prognosis for those who had both diseases at the same time.⁷

According to the evidence gathered at the beginning of the pandemic, patients with cancer were considered a vulnerable group for contracting a serious illness or dying from this cause^{8,9}, for this reason some research focused on demonstrating this hypothesis, considered that mortality from COVID-19 in patients with cancer had increased four times compared to the general population.^{10,11} Meanwhile, studies carried out in developed countries concluded the opposite.^{12,13}

Guidelines established to deal with patients with COVID-19¹⁴, were difficult to comply with due to the tight supply of resources, so it was necessary to look for some other content that would guide the management of these patients and adapt them to patients with cancer to whom priority was given to their oncological treatment simultaneously. The information gathered from research related to patients with cancer and COVID-19 care was relevant to provide the bases for that care, as it was the redesign of processes.^{15,16}

Considering various variables of daily life activities such as physical exercise, return to work activity, daily

routines, migration, mental state, among others, several studies have established that there is no clear reason why not all people respond or evolve in the same way after having suffered from COVID-19.¹⁷⁻¹⁹

It is highly important to gather all the information or data that leads us identify the most peculiar features of what could trigger a complex syndrome to be treated in a high-risk population¹⁸, keeping in mind the correlation observed between the diversity of the T cell response and severity of COVID-19 resulting in critical illness and high mortality in patients with SARS-CoV-2 and cancer in low- and middle-income countries.²⁰

The objective of this study was to compare the clinical and epidemiological characteristics of patients with cancer with a positive Reverse Transcription Polymerase Chain Reaction test (RT-PCR) for SARS-CoV2 to those with negative RT-PCR, who were hospitalized for suspected COVID-19 in a tertiary cancer hospital within the first year of the pandemic.

Material and methods

A lengthwise, analytical, retrospective study was carried out from March 31, 2020 to March 31, 2021, at *Hospital de Oncología Centro Médico Nacional Siglo SXXI*. All hospitalized patients considered as suspicious of having COVID-19 entered the study and had samples taken for RT-PCR for SARS-CoV2 or Rapid Antigen Test, excluding outpatients, upon admission, in which essential samples lab were taken. For each case, data on suspected COVID-19 symptoms were taken from the epidemiological study, while the clinical characteristics of the oncological condition were taken from the clinical record (oncological diagnosis, clinical stage, comorbidities, treatments received in the last 30 days, lab studies upon hospital admission, follow-up until discharge or death). The RT-PCR tests were sent to the Central Epidemiology Laboratory which, through the platform, is called "SINOLAVE", issuing the results confirming or ruling out infection with SARS-CoV2, in which chest x-ray was interpreted by the Classification System (CXR). The sampling was non-probabilistic by census; thus, the census was obtained by the "SINOLAVE"

platform. The data was described as frequencies and percentages for the categorical variables and as medians and interquartile range (IQR) for the quantitative variables.

A bivariate analysis was carried out between those patients with the confirmed diagnosis and those ruled out by the test, to compare the differences through the Mann-Whitney U and Chi-square tests by taking the significant values of $p < 0.05$.

Results

A total of 208 patients were admitted to hospital and included in the study for suspected COVID-19 from March 31, 2020 to March 31, 2021. We observed that 61.1% (127) came from Mexico City, 33.7% (70)

from Estado de México, 5.3% (11) from other states in the country, being 49.5% women and 50.5% men, with a 59-median-age (IQR=47-69 years). Among the main cancer diagnoses, colorectal cancer was found in 19.7% (41), lymphomas in 14.4% (30), testis cancer in 5.3% (11), gastric cancer in 5.3% (11), breast cancer in 4.8% (10), 4.3% (10) ovary cancer and the rest 50.5% (95) were various oncological diagnoses. Early disease cases showed 13.5% (28) and advanced disease had 86.5% (180), 37.5% (78) of patients did not present additional comorbidities apart from cancer and SARS-CoV2, the rest had: arterial hypertension (25.5%), diabetes mellitus (19.7%), obesity (9.6%), chronic obstructive pulmonary disease (4.8%) and HIV (3.4%). See figure 1.

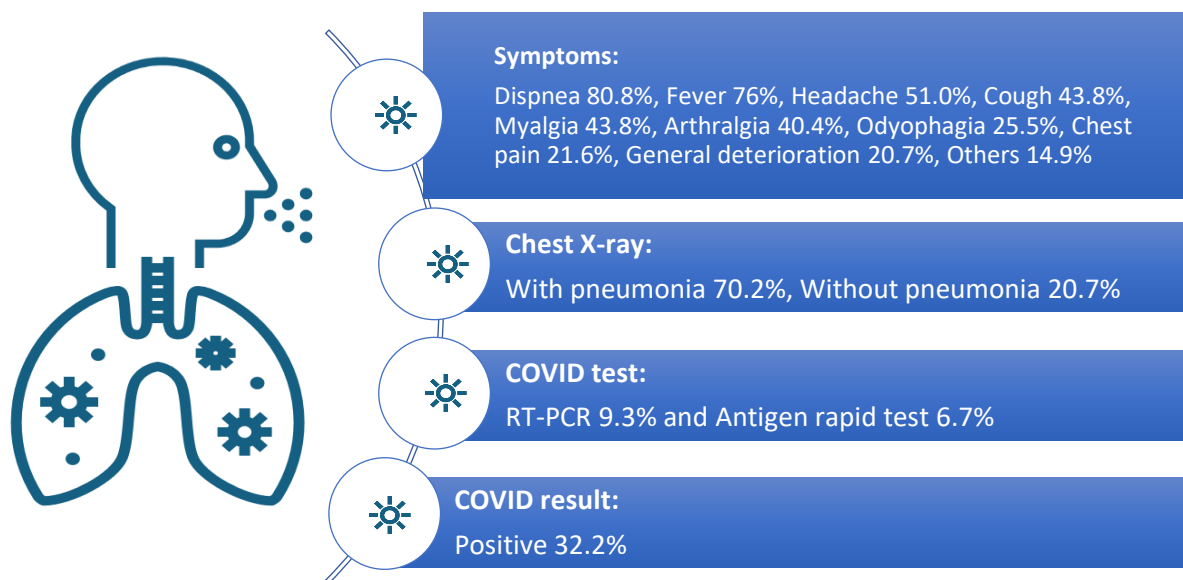
Fig. 1. Characteristics



Among the symptoms presented by patients, dyspnea was 80.8% (168), fever 76% (158), headache 51% (106), cough 43.8% (91), myalgia 43.8% (91) and arthralgias 40.4% (84) as the most frequent. Chest x-ray underwent to 90.9% (189), in which pneumonia was identified in 84.6% (160) and the Score interpretation had a

median of 9 (IQR= 4-13). Pneumonia was clinically identified with 74.5% (155) of all patients. (Fig. 2).

Fig. 2. Symptoms, laboratory tests and x-ray



In order to confirm or rule out COVID-19 we used RT-PCR in 93.3% (194) in this sample and antigen rapid test in 6.7% (14), and the disease was confirmed in 32.2% (67) of the patients. See figure 2. Once patients were admitted, some studies were carried out: blood chemistry profile tests 99.5% (207), liver function tests 89.4% (186), serum electrolytes 97.6% (203), blood count and clotting 99.5% (207) and fibrinogen times at 93.3% (194). Being 29.3% (61) identical with a kidney injury, 7.7% (16) with an alteration in liver tests, 63.9% (133) with levels above the reference of lactic dehydrogenase (LDH), 25.9% (54) with alteration in electrolytes, 59.1% (123) with identified levels outside the reference value in leukocytes and 44.7% (93) with alteration in platelets,

in which clotting times and prolonged clotting times were identified in 28.4% (59) and 83.2% (173) in the International Normalized Ratio (IRN), as well as levels out of range in fibrinogen in 63.5% (132).

After COVID tests were carried out, patients were given a follow-up for 30 days, hospital stay was 6 days on average (IQR=4-11.75 days). A total of 22.6% (47) were admitted to ICU and 15.9% (33) were given mechanical ventilatory support. A total of 40.4% (84) were discharged due to improvement, 39.3% (82) died in the hospital, 13% (27) were transferred to another hospital unit, and 7.2% (15) were discharged voluntarily. See table 1. During follow-up, 46.2% (96) of the patients died.

Table 1. Follow-up		n	%
Hospital stay (days, IQR)		6	4-11.75
Hospital discharge causes	Improvement	84	40.4
	Inhospital death	82	39.4
	Hospital Transfer	27	13.0
	Voluntary discharge	15	7.2
Admission to ICU		47	22.6
Mechanical ventilation		33	15.9

ICU=Intensive care unit, IQR= intercuartile range

Being a time reference the COVID-19 testing date, the history of oncological treatment was searched prior to 30 days, finding this information as positive in 29.3% (61) of the sample, 20.2% (42) had received chemotherapy, 2.4 % (5) adjuvant chemotherapy and radiotherapy, 5.8% (12) radiotherapy, 1% (2) other treatments, 16.5 elapsed days passed (IQR=7-28.7 days) from their last treatment until a COVID test was performed for suspected disease. Having received some of these treatments, they showed a relative risk of 1.2 (95% CI 0.79 - 1.8 p=0.38) for having COVID-19. A total of 35.1% had a surgery performed 14 days before or 14 days after the suspected COVID-19 diagnosis.

Dyspnea was the most frequent symptom in patients with COVID-19 in 86.6% (58), followed by fever 76.1% (51) and headache 61.2% (41), compared to the clinical data between this group and those discarded from disease, in which a significant difference was found only in the chills data (p=0.036). When comparing the interpretation Score chest radiology studies, it was found that patients with COVID-19 had a higher score (12 vs 8 p=0.008) compared to the discarded cases (Table 2).

Table 2. Respiratory signs and symptoms among discarded patients and those with COVID-19.		COVID-19		Non-COVID-19		p
		n	%	n	%	
Symptoms	Dyspnea	58	86.6	110	78.0	0.188
	Fever	51	76.1	107	75.9	0.971
	Headache	41	61.2	65	46.1	0.053
	Cough	32	47.8	59	41.8	0.456
	Myalgia	29	43.3	62	44.0	0.925
	Arthralgia	24	35.8	60	42.6	0.369
	Odynophagia	17	25.4	36	25.5	0.98
	Chest pain	18	26.9	27	19.1	0.224
	General deterioration	13	19.4	30	21.3	0.855
	Prostration	12	17.9	19	13.5	0.411
	Rhinorrhea	11	16.4	19	13.5	0.673
	Chills	12	17.9	10	7.1	0.036
	Sudden onset	9	13.4	12	8.5	0.325
Signs	X-ray pneumonia	45	67.2	101	71.6	0.52
	Score [median (IQR)]	12	(7.0-14)	8	(2-12.25)	0.008*

IQR= interquartile range, for all categorical variables we used Chi², except for * there it was used Mann Whitney U.

Regarding laboratory results, patients with COVID-19 showed an enduring data as follows: lymphopenia 89.4% (60), INR was outside the reference value 84.8% (57) and high LDH 74.2% (50), but only in the

latter were identified significant differences (p=0.009) with the discarded cases, as seen in Table 3.

Table 3. Alteration in admission lab studies		COVID-19		Non-COVID-19		p
		n	%	n	%	
Creatinine	URL	17	25.8	44	31.0	0.414
ALT	URL	3	4.5	10	7.0	0.758
AST	URL	3	4.5	13	9.2	0.399
LDH	URL	50	74.2	83	58.5	0.009
Sodium	Hyponatremia	7	10.6	23	16.2	0.295
	Hypernatremia	6	9.1	18	12.7	0.491
Potassium	Hypokalemia	11	16.7	16	11.3	0.379
	Hyperkalemia	4	6.1	14	9.9	0.434
Phosphorus	URL	12	18.2	30	21.1	0.572
Leukocytes	Leukopenia	10	15.2	14	9.9	0.354
	Leukocytosis	28	40.9	71	50.0	0.238
Lymphocytes	Lymphopenia	60	89.4	126	88.7	0.921
	Lymphocytosis	4	6.1	5	3.5	0.475
Platelet	Thrombocytopenia	23	34.8	54	38.0	0.551
	Thrombocytosis	4	6.1	12	8.5	0.59
PT	LRL	16	28.8	39	27.5	0.614
	URL	18	31.8	41	28.9	0.868
PTT	LRL	19	28.8	39	27.5	0.998
	URL	21	31.8	38	26.8	0.612
INR	OOR	57	84.8	116	81.7	0.224
Fibrinogeno	LRL	2	3.0	4	2.8	0.921
	URL	39	59.1	87	61.3	0.872

Mann Whitney U. ALT= Alanine aminotransferase, AST= Aspartate Transferase, LDH= Lactic dehydrogenase, PT= Prothrombin time, PTT=Partial thromboplastin time, INR=International normalized ratio; URL= Upper Reference Limit; LRL= Lower Reference Limit; OOR = Out of Range

When comparing the two groups, no significant differences were found in male sex, in presenting

any other comorbidity, in late stage, in admitted patients to ICU or in intubated patients. (Table 4)

Table 4. Oncological care of confirmed and ruled out COVID-19 patients.		COVID-19		Non-COVID-19		p
		n	%	n	%	
Sex	Men	32	30.5	73	69.5	0.589
Cancer stage	III, IV	56	31.1	124	68.9	0.389
Comorbidities	Cancer only	27	40.3	50	35.5	0.54
	Cáncer/Hypertension	15	22.4	38	27.0	0.61
	Cáncer/Diabetes mellitus	15	22.4	26	18.4	0.576
	Cáncer/Obesity	8	11.9	12	8.5	0.456
Admission to ICU		16	34.0	31	66.0	0.76
Mechanical ventilation		14	42.4	19	57.6	0.171
Death		40	41.7	56	58.3	0.007
Hospital stay* (IQR)		5 (4-11)		7 (3-13)		0.39
Elapsed time from COVID test till Death* (IQR)		8 (4-32)		22.5 (6-90)		0.004

IQR= interquartile range, for all categorical variables we used Chi², except for * there it was used Mann Whitney U.

The lethality observed for patients with COVID-19 was 41.7%, compared to the non-COVID-19 group showing 58.3%, obtaining a relative risk of dying from this cause among the patients studied in 1.7 (95% CI 1.15 - 2.59, $p=0.007$). Highlighting the elapsed time from sample collection to death showed that patients with COVID-19 died faster than discarded patients (8 vs 22.5 $p=0.004$) as can be seen in table 4.

Discussion

Oncology population affected by COVID-19 showed a very similar report to dyspnea as the main symptom (86.7%), followed by fever (76.1%), headache (61.2%), cough (47.8%) and myalgia (43.3%) in an oncological series from the United States with dyspnea (55.8%), fever (18.8%), cough (18.5%), chest pain (5.8%) and flu-like symptoms (5.8%)²¹; but differing from prevalence symptoms as seen in non-oncological population as in fever (58.6%), cough (58.5%), dyspnea (30.8%), general deterioration (29.7%) and fatigue (28.1%)²². This difference can be explained by the criteria used in the sample, in which only hospitalized and admitted patients were included due to the severity of respiratory symptoms, however, the chills was a COVID-19 symptom that made an important difference.

As a high-level care unit for patients with cancer, some references made in the oncological field were published and used at the beginning of the pandemic, as recommended by Al-Shamsi *et al.*²³, to find out which laboratory analyzes ought to be used to establish the suspicion diagnostic of this new disease, and above all, to use the available resources at that time. So, based on the mentioned above, RT-PCR for SARS-CoV-2 was the first confirmatory test used in the country, then the rapid antigen test.

In this sample, we found out elevated LDH, lymphopenia, elevated fibrinogen, leukocytosis, thrombocytopenia, prolongation of PT and TTP, elevated serum creatinine, however only LDH had a significant difference for patients with COVID-19. As it is suggested by the literature, we did not have access to other inflammatory markers, such as C-

reactive protein, pro-calcitonin, D-dimer, and ferritin. Another restrain study was that no further studies were included, however only lab samples gathered at the admission were analyzed. That is the reason why no similarities were found with other studies where they have found anemia (75%), leukopenia (32.1%), low serum albumin levels (89.3%), and highly sensitive C - reactive protein levels (82.1%), so the only similarity was a high LDH level (50%), even though it was in a higher proportion in this study.²⁴

Chest X-ray helped identify pneumonia in patients with COVID-19 at 30.8%, as in the CXR system suggested by Borghesi *et al.*²⁵, whereas those reaching a 12-point high score, had a higher risk of dying, as presented by Bairwa *et al.*²⁶ to reduce the risk of contamination from other areas, all patients were isolated into a specific zone for their care and only portable X-ray equipment was used, however equipment disinfection was a problem at first so that the only way to have the study was through hospital admission.

Within the first year of the SARS-CoV2, there was the fear that patients with respiratory infection data could get infected by COVID-19, so the stand-by to confirm the results compromised cancer care at times, seeking for clinical data and laboratory or office studies that would let make decisions in each case. This was quite a challenge because many cases had to deal with advanced cancer and typical complications of the same disease, and perhaps, patients did not seek for timely care due to the fear of getting infected by COVID-19 after being at the hospital.

Therefore, we try to demonstrate whether a history of previous care as chemotherapy, radiotherapy or surgery could be a risk factor for a patient to become infected by COVID-19, unfortunately this was not proved with these patients.

COVID-19 vaccine in patients with cancer, and especially in hematological cancers, was vital to protect them against the disease and its complications. Several publications have shown that vaccines are

safe and effective in patients with solid tumors, however, in patients with hematological cancers presented heterogeneous immunological responses. Despite this drawback and based on the reported results, it is recommended to follow current clinical guidelines and application^{27,28}, so as it is worth to carry out a separate analysis before and after the vaccination. That would be another article subject.

In this study, lethality in patients with cancer and COVID-19 rated 41.7%, compared to the result reported by Castelo-Branco *et al*¹, rated 24.5%, Europe was higher in 20 cities and still much higher in the study by Wang Q, *et al*, while the United States rated 14.93%.²⁹ However, the differences lie in the analysis sample, while this study chose only hospitalized patients, the investigations aforementioned also chose outpatients. It was difficult to obtain and compare data about mortality during the pandemic, due to the existing health policies in each country; therefore, its study continues to be of interest in public health.³⁰

Conclusion

We found out that there was no difference between patients with cancer and COVID-19 from those who came during the study period due to respiratory infection reasons, except for those who reported chills caused by COVID-19 symptoms because they presented high level in LDH and a chest x-ray with a Score ≥ 12 in their studies. Another thing we came across through this study is that more patients with COVID-19 died in a shorter period compared to the discarded cases.

Authorship:

YL Martínez-Sánchez, DM Tavera-Zepeda and I Escobar-Munguia: conception of the idea, study design and data gathering; DM Tavera-Zepeda and YL Martínez-Sánchez data management and statistical analysis; I Escobar-Munguia and R Medrano-Guzman: results interpretation. YL Martínez-Sánchez: wrote first draft. All authors: revised and approved the final manuscript.

Conflicts of interest statement:

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