Clinical Profile of Critical Oncological Patients with COVID-19

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Perfil Clínico dos Pacientes Críticos Oncológicos com Covid-19

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ABSTRACT

Introduction: SARS-CoV-2 infection has a broad clinical spectrum, which can be categorized by its level of severity. Being an oncological patient is described in the literature as an important risk factor for more severe levels of the disease resulting from immunosuppression. **Objective:** To compare demographic and clinical characteristics among cancer and non-cancer patients with COVID-19 in a referral hospital in the city of Belém, Pará. **Method:** Retrospective and quantitative study of analysis of medical records of patients diagnosed with COVID-19 between April and July 2020. For data analysis, the relative risk was calculated with a 95% confidence interval and test *t*. **Results:** The sample consisted in 53 ICU patients, mostly females (31: 58.49%), diagnosed with COVID-19. There was a predominance of the outcome death for the group of cancer patients (27; 81.8%), as well as a greater number of non-neoplastic comorbidities among cancer patients (19; 57.5%). Cancer patients had longer invasive ventilatory support, with a mean of ten days (13; 39.39%). **Conclusion:** There were differences in demographic characteristics and interventions performed among the groups investigated.

Key words: COVID-19; SARS-CoV-2; neoplasms; intensive care units.

RESUMO

Introdução: A infecção por Sars-CoV-2 possui um amplo espectro clínico, que pode ser categorizado pelo seu nível de severidade. Ser paciente oncológico está descrito na literatura como fator de risco importante em níveis mais severos da doença decorrente do estado de imunossupressão. **Objetivo:** Comparar as características demográficas e clínicas entre pacientes oncológicos e não oncológicos com covid-19 em um hospital de referência na cidade de Belém, Pará. **Método**: Estudo retrospectivo e quantitativo de análise de prontuários de pacientes diagnosticados com covid-19 entre abril e julho de 2020. Para a análise dos dados, fez-se o cálculo do risco relativo com intervalo de confiança de 95% e teste *t*. **Resultados:** A amostra totalizou 53 pacientes da UTI diagnosticados com covid-19 e foi composta principalmente pelo sexo feminino (31; 58,49%). Houve predominância do desfecho óbito no grupo de pacientes oncológicos (27; 81,8%), assim como maior número de comorbidades não neoplásicas entre os pacientes oncológicos (19; 57,5%). Além disso, os pacientes oncológicos tiveram maior tempo de suporte ventilatório invasivo, com média de dez dias (13; 39,39%). **Conclusão:** Houve diferença nas características demográficas e nas intervenções realizadas entre os grupos estudados.

Palavras-chave: COVID-19; SARS-CoV-2; neoplasias; unidades de terapia intensiva.

RESUMEN

Introducción: La infección por Sars-CoV-2 tiene un amplio espectro clínico, que se puede categorizar según su nivel de gravedad. Ser un paciente oncológico se describe en la literatura como un importante factor de riesgo para niveles más severos de la enfermedad derivados de un estado de inmunosupresión. **Objetivo:** Comparar las características demográficas y clínicas entre pacientes oncológicos y no oncológicos con covid-19 en un hospital de referencia en la ciudad de Belém, Pará. **Método:** Estudio retrospectivo y cuantitativo de análisis de historias clínicas de pacientes diagnosticados con covid-19, entre abril y julio de 2020. Para el análisis de datos se calculó el riesgo relativo con un intervalo de confianza del 95% y test *t*. **Resultados:** La muestra totalizó 53 pacientes de UCI diagnosticados con covid-19 e estaba compuesta principalmente por el sexo femenino (31; 58,49%). Predominó el desenlace de muerte en el grupo de pacientes oncológicos (27; 81,8%), así como un mayor número de comorbilidades no neoplásicas entre los pacientes oncológicos (19; 57,5%). Los pacientes con cáncer tuvieron soporte ventilatorio invasivo por más tiempo, con una media de diez días (13; 39,39 %). **Conclusión:** Hubo diferencias en las características demográficas y en las intervenciones realizadas entre los grupos estudiados.

Palabras clave: COVID-19; SARS-CoV-2; neoplasias; unidades de cuidados intensivos.

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INTRODUCTION

In December, 2019, Wuhan city, the capital of Hubei province in China, became the center of an outbreak of pneumonia of unknown cause which spread worldwide. On January 30, 2020, due to damages caused by the novel coronavirus, known as Sars-CoV-2[2], the World Health Organization (WHO) declared a global health emergency[3].

The Sars-CoV-2 infection has a wide clinical spectrum, classified according to the level of severity as mild, severe and critical[4]. Mild illness is characterized as absence of pneumonia or mild pneumonia in 81% of the cases. Severe illness with respiratory rate equal or higher than 30 breaths per minute, dyspnea and pulmonary infiltrate higher than 50% in 24 to 48 hours, which occurred in 14% of the cases. Critical illness with septic shock, sepsis, respiratory failure and multiple organs dysfunction in 5% of the cases[4].

The main risk factors are older than 50 years of age, tobacco use, cardiovascular and respiratory diseases, diabetes and cancer, these last two related to immunosuppression[5].

Scientific literature described the close relationship of the immune system with cancer pathogenesis. In healthy persons, the immune system monitors, recognizes and eliminates potential tumorigenic cells[6,7]. Cancer cells must develop the ability to by-pass the immune system control thus evading elimination and concomitantly promoting pro-inflammatory field favoring the formation of cancer. Inflammation further contributes to tumorigenesis by supplying tumor cells with growth factors and pro-angiogenic factors that facilitates tumor proliferation and metastases[7]. Consequently, the formation of cancer depends on an immunocompromised field which can explain why cancer patients are more susceptible to infections[8].

A recent study has proved that patients with cancer have 3.5-fold more odds of needing invasive ventilation, of being admitted to the Intensive Care Unit (ICU) or death than non-cancer patients[9]. In addition, these patients undergo chemotherapy, anti-cancer and surgical procedures that further contribute to their immunosuppression[9,10].

Another study revealed that receiving oncologic treatment in until two weeks post COVID-19 diagnosis would be a risk factor for severe events as the acute respiratory distress syndrome (ARDS), acute myocardial infarction and septic shock[11]. Furthermore, given the confirmed nosocomial transmission of SARS-CoV-2 among patients in healthcare units, cancer patients may be more prone to getting infected[12] because of their treatment.

Intensive care is a key aspect of the treatment of patients with cancer although the prognosis worsens after admission at ICU[13]. Recent technological advances as improvement of diagnostic approach, development of more effective therapeutic options and infections control appear to improve survival[14].

The main motives for ICU admission are: hypotension, acute respiratory failure and sepsis not directly related to the severity or type of cancer[14]. Invasive mechanic ventilation in patients with cancer at the ICU is reported as an important risk factor and not needing invasive ventilation reduces intra-hospital mortality rate[15]. Other risk factors are ARDS, multiple organ dysfunction syndrome and sepsis[14].

Possibly, patients with cancer are at risk of infections and more severe complications from COVID-19 pandemic due to continuous hospitalizations to treat and follow-up the disease. The objective of the study is to compare demographic and clinical characteristics of patients with cancer with COVID-19 at a reference hospital in Belém, State of Pará (PA).

METHOD

Retrospective, quantitative cohort study with data collected from charts between April and July 2020 at "*Hospital Ophir Loyola*" in Belém, PA.

"*Hospital Ophir Loyola*" hosts patients referred by the National Health System (SUS) from basic health network and outpatient units in its full capacity. It is classified as High Complexity Oncologic Center (Cacon) and teaching institution by the Ministry of Health; it was able to accept and provide continuous multidisciplinary treatment to non-oncologic cases during the pandemic when COVID-19 infected patients were referred for ICU admission[16].

The sample consisted in data extracted from patients' charts diagnosed with COVID-19 admitted to the ICU of the hospital, according to Figure 1. The inclusion criteria were patient's charts with diagnosis of COVID-19 admitted at the ICU in the study period with and without associated oncologic diagnosis and the exclusion criteria was illegible or damaged chart. Only one chart was excluded due to incomplete data of sex, age and identification.

The data were collected through a form with identification of sex, age, comorbidities, International Classification of Diseases (ICD) at ICU admission and outcome (discharge/death); treatments utilized: oxygen therapy and invasive ventilation support and clinical manifestations: lab tests and arterial blood gas. Later, the charts were grouped as oncologic patients (33) and non-oncologic patients (20).

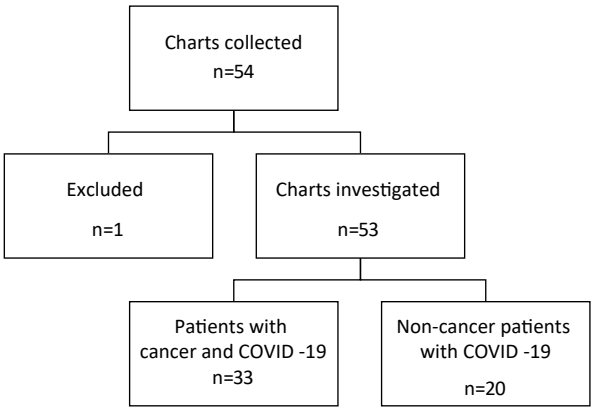

Figure 1. Flowchart of sample selection

The relative risk (RR) was calculated with confidence interval (CI) of 95% and statistical significance by Pearson chi-square and/or Fisher exact test with the software IBM® SPSS® Statistics version 26. In addition, test *t* was performed to analyze the relation of lab tests with patients' clinical outcomes. Descriptive statistics was performed with the software Microsoft Excel and data tabulation. Value of $p < 0.05$ was considered statistically relevant.

The study complied with Resolution 466/2012[17] of the National Health Council and was approved by the Institutional Review Board of "*Hospital Ophir Loyola*" report 4,268.515/2020 (CAAE (submission for ethical review): 35014420.3.0000.5550).

RESULTS

The sample consisted in 53 charts of patients diagnosed with COVID-19 at the ICU, mean age of 56.1 years, mostly females (31; 58.49%). Table 1 describes the demographic and clinical characteristics of the population investigated.

The number of oncologic patients between 50 and 59 years of age (8; 24.2%) and non-oncologic between 70 and 79 years of age (six) is higher than other age stratifications. Lung neoplasm was predominant in oncologic patients (5; 15%). Furthermore, the study patients presented types of comorbidity other than neoplasms (27), mostly in the group of oncologic patients (19; 57.5%). The outcome death predominated in the group of oncologic patients (27; 81.8%). Table 2 describes the characteristics of ventilatory support offered to oncologic and non-oncologic patients with COVID-19 admitted to the ICU.

Non-oncologic patients (16; 80%) utilized ventilatory support at the ICU substantially. These patients utilized oxygen therapy for more time (7; 35%), while most of the oncologic patients utilized for less than three days (21; 63.63%). Non-oncologic patients utilized intensive ventilatory support in a period of up to ten days (12; 60%). Above ten days, oncologic patients were predominant (13; 39.39%). Table 3 compares the interventions applied in oncologic and non-oncologic patients.

No relative risk with significant *p* value was found after comparing oncologic and non-oncologic patients. It is possible that being oncologic patient is a risk factor for oxygen therapy, admission at ICU and outcome death. However, it was not significative for this population.

Clinical and laboratory manifestations are summarized in Table 4. No statistically significant relation was found after comparing the clinical manifestations of oncologic and non-oncologic patients.

DISCUSSION

Predominance of the outcome death and non-neoplastic comorbidities for oncologic patients was found as result of the present investigation. Non-oncologic patients used more nasal oxygen glasses as ventilatory support prior to ICU to avoid ventilatory support. In addition, they remained more time with invasive ventilatory support. For oncologic patients, there was predominance of time of use of ventilatory support longer than ten days and significant differences in lab tests among oncologic and non-oncologic patients were not found.

A study[18] whose objective was to identify predictors of intrahospital mortality of COVID-19 patients admitted to an ICU in the State of São Paulo, Brazil concluded that the mean age was 66 years of age. Oncologic patients in the 50-59 age-range and non-oncologic patients in the 70-79 age-range predominated in the current study unlike other studies.

According to a Brazilian study[18] about ICU interventions, 56.6% (733/1,296) of the patients utilized non-invasive ventilation, 32.9% (426/1,296), invasive ventilation, and 31.3% utilized nasal catheter (406/1,296). In addition, 11.7% were submitted to renal replacement therapy (RRT) and 1.5%, extracorporeal membrane oxygenation and for 13.6% of them the outcome was death with other comorbidities as diabetes and hypertension. It is possible to affirm that in-patients with severe conditions related to COVID-19 admitted to ICU have considerable odds of mortality and morbidity, further to high demand of supportive therapy and prolonged hospitalization[13,14,16].

Nasal oxygen glasses were utilized more by both study groups for ICU ventilatory support as concluded by the present study. But the study of Brar et al.[19] describes that most oncologic or non-oncologic patients with COVID-19 needed no ventilatory support in the first three hours post admission. Nearly 39.3% of oncologic patients utilized cannula or masks during initial

Table 1. Characteristics of oncologic and non-oncologic patients with COVID-10 admitted at the ICU. Belém-PA, 2020 (n=53)

Variables	Oncologic n (%)	Non oncologic n (%)
Sex		
Female	19 (57.5%)	12 (60%)
Male	14 (42.4%)	8 (40%)
Age		
11-19	1 (3.03%)	1 (5%)
20-29	2 (6.06%)	1 (5%)
30-39	5 (15.15%)	2 (10%)
40-49	2 (6.06%)	2 (10%)
50-59	8 (24.24%)	2 (10%)
60-69	7 (21.21%)	5 (25%)
70-79	6 (18.18%)	6 (30%)
≥80	2 (6.06%)	1 (5%)
Types of cancer		
Lung neoplasms	5 (15.15%)	-
Central nervous systems neoplasms	4 (12.12%)	-
Prostate neoplasms	4 (12.12%)	-
Breast neoplasms	3 (9.09%)	-
Lymphomas	2 (6.06%)	-
Leukemias	2 (6.06%)	-
Pancreatic neoplasms	2 (6.06%)	-
Kidney or bladder neoplasms	2 (6.06%)	-
Uterus neoplasms	2 (6.06%)	-
Mediastinum/thorax	2 (6.06%)	-
Other	5 (15.15%)	-
Comorbidities		
Systemic arterial hypertension	9 (27.27%)	4 (20%)
Brain stroke	2 (6.06%)	1 (5%)
Diabetes mellitus	2 (6.06%)	2 (10%)
Convulsive crisis	2 (6.06%)	-
Chronic obstructive pulmonary disease	2 (6.06%)	1 (5%)
Tobacco use	2 (6.06%)	-
Total	19 (57.57%)	8 (40%)
Outcome		
Discharge	5 (15.15%)	7 (35%)
Death	27(81.8%)	12 (60%)
No information	1 (3.03%)	1 (5%)

consultation like 32.5% of the patients without cancer, a type of intervention not investigated herein. Utilization of high-flow nasal cannula showed no significant difference among oncologic and non-oncologic patients[18]. Nasal oxygen glasses utilized by COVID-19 patients is justified due to low risk of viral particles aerosol dissemination to healthcare professionals[4].

A study conducted in China investigated the necessity of oxygen therapy only of Sars-CoV-2 infected oncologic inpatients during hospital stay and concluded that this type of therapy was required in 78.6% of the cases ranging from one to five days[20]. In addition, another study of the same country shows that oxygen therapy was utilized in 45.71% of patients with cancer and infected by Sars-

Table 2. Characteristics of ventilatory support offered to oncologic and non-oncologic patients with COVID-19 admitted to the ICU. Belém-PA, 2020 (n=53)

Variables	Oncologic n (%)	Non oncologic n (%)
Ventilatory support before ICU		
Natural ventilation	2 (6.06%)	0 (0.0%)
Nasal catheter	24 (72.72%)	16 (80%)
No information	7 (21.21%)	4 (20%)
Time of oxygen therapy (days)		
Up to three	21 (63.63%)	7 (35%)
Over three	5 (15.15%)	7 (35%)
No information	7 (21.21%)	6 (30%)
Time of invasive ventilatory support (days)		
Up to 10	19 (57.5%)	12 (60%)
Over 10	13 (39.39%)	7 (35%)
No information	1 (3.03%)	1 (5%)
Time of hospitalization at ICU (days)		
0-10	16 (48.48%)	8 (40%)
10-20	8 (24.24%)	6 (30%)
Over 20	8 (24.24%)	5 (25%)
No information	1 (3.03%)	1 (5%)

Caption: ICU = Intensive Care Unit.

Table 3. Analysis of the interventions applied in patients with COVID-19 admitted at the ICU. Belém-PA, 2020 (n=53)

Variables	Total (n)	Oncologic (n)	Non oncologic (n)	RR	CI 95%	*p* value*
Sex						
Male	22	14	8	1.038	0.65-1.58	0.9999
Female	31	19	12			
Oxygen therapy						
Yes	22	12	10	0.8052	0.48-1.24	0.395
No	31	21	10			
Invasive ventilatory support						
Yes	39	27	12	1.615	0.95-3.31	0.1113
No	14	6	8			
Outcome						
Discharge	14	6	8	0.619	0.30-1.05	0.1113
Death	39	27	12			

Captions: n = sample; RR = relative risk; CI 95% = confidence interval of 95%.
(*) $p < 0.05$.

CoV-2 and 42.02% of infected patients without cancer, with no significant difference among both groups[20]. There is evidence that the necessity of oxygen support is associated with cytokines storm occurring between the seventh and tenth day of Sars-CoV-2 infection, marked by deterioration of the health condition and increase of risk of acute respiratory failure[21].

The study of Zhang et al.[20] demonstrates that 53.6% of the patients with cancer needed invasive ventilatory among oncologic and non-oncologic patients infected

Table 4. Clinical and laboratory manifestations of oncologic and non-oncologic patients at the ICU. Belém, Pará, 2020 (n=53)

Clinical manifestations	Oncologic (mean)	Non oncologic (mean)	*t*	df	*p* value*
Saturation at admission	0.9014	0.91	0.3431	42.345	0.7332
Ph	-	6.357	-1.023	28.563	0.3147
Partial pressure of carbonic gas	39.43	40.225	0.1911	40.227	0.8494
Partial pressure of oxygen	130.878	108.485	-1.321	49.685	0.1926
Concentration of non-corrected bicarbonate	24.845	23.285	-0.7416	50.929	0.4618
Base excess in the blood	0.4861	-0.695	-0.4975	44.758	0.6213
Base excess in the extracellular fluid	1.276	1.67	0.1845	50.482	0.8543
Total carbon dioxide	22.573	19.915	-0.865	30.724	0.3839
Hematocrit	36.224	31.41	-1.8972	47.995	0.0638
Total hemoglobin	11.715	10.345	-1.459	42.601	0.1518
Fraction of oxyhemoglobin	92.482	93.16	0.2883	49.039	0.7744
Fraction of carboxyhemoglobin	0.9455	0.97	0.1323	37.007	0.8955
Level of saturation of oxygen	93.209	94.175	0.4654	47.319	0.6438
Sodium	137.936	139.04	0.4903	30.645	0.6274
Potassium	3.948	4.024	0.3263	40.36	0.7459
Calcium	1.168	1.181	0.2475	44.98	0.8057
Chlorine	109.152	112.9	1.169	44.299	0.2488
Glutamine	140.485	166.5	0.9699	26.056	0.341
Lactate	2.708	2.105	-0.9206	35.31	0.3635
Red cells	3.751	3.523	-0.9415	39.197	0.3522
Hemoglobin (g/dL)	10.527	10.265	-0.3663	42.034	0.716
Hematocrit	33.115	32.025	-0.5041	40.907	0.6169
Leukocytes (/mm3)	13.248.79	11.321.5	-1.035	49.392	0.3058
Platelets	250.364	274	0.577	30.844	0.5682

Captions: t = test t via RStudio; df = degrees of freedom.
(*) $p < 0.05$.

by Sars-Cov-2. In a study conducted in New York, the proportion of patients with COVID-19 who needed invasive ventilatory support without (3.8%) and with (3.4%) cancer was similar[18]. Differences of utilization of this type of treatment may be related with individual aspects of each patient as age, weight and comorbidities[20]. Another study associates the condition the oncologic patient may present in cases of Sars-CoV-2 infection with the organs most affected by cancer, antitumor treatment and duration[9].

In China, a study conducted with Sars-CoV-2-infected oncologic patients in chemotherapy treatment noticed high risk of development of severe events as admission to ICU, invasive ventilation or even progression to death than patients without cancer[9].

For patients with acute kidney injury (AKI) and COVID-19 who received RRT, a retrospective cohort study concluded that the risk of hospital mortality for these patients increased 14 times than patients with COVID-19 who did not receive this therapy[19], consistent with other findings where significant association of AKI and increased risk of mortality for ICU inpatients with COVID-19 in severe condition was found[9,22].

Mean ICU stay of 10 days of oncologic or non-oncologic patients was found by the present study

and non-oncologic patients were more predominant if length of stay exceeded 10 days. Scientific evidences demonstrate that COVID-19 infection is more severe in patients in chemotherapy[23]. It is possible to notice that when oncologic patients fail to attend their scheduled treatments, they incur in a tangible risk of increased morbidity and mortality, even more than COVID-19 itself[14,23].

The study by Zhang et al.[20] shows that 35.7% of oncologic patients were discharged after median hospital stay of 13.5 days and 35.7% of the cases were inpatients with median stay of 19 days. Dai et al.[21] investigation concluded there was significant difference between patients with cancer – mean of 27 days of hospital stay *versus* patients without cancer – mean of 17 days of hospital stay.

According to a multicenter study and another conducted in China, oncologic patients have higher mortality rates than non-oncologic[23]. In counterpart, according to Brar et al.[19], similar proportions of oncologic and nononcologic patients with COVID-19 died. Furthermore, other factors are allegedly predictors of mortality, as age and obesity[18], for instance.

Some types of neoplasms as hematological are related to high mortality contrary to solid tumors more susceptible to cytokines-mediated inflammation because of disorders in the compartments of myeloid and lymphocitary cells[23]. The severity of COVID-19 infections with mandatory ICU admission and use of mechanic ventilation is associated with mortality rising[24], aspects found in both groups of the present study.

The association of comorbidities and severity of COVID-19 ICU inpatients have been reported in many studies[10,25]. For instance, COVID-19 patients with hypertension, cerebrocardiovascular diseases and diabetes *mellitus* are more propense to present severe symptoms and will need more attention than patients without these comorbidities[26].

Locoregional cancer was more prevalent in COVID-19 non-survivors than survivors[10]. A retrospective cohort study revealed that in-patients with cancer with COVID-19 at the ICU were more prone to dismal clinical prognosis[25].

In general, patients with cancer, if older, have other risk factors as hypertension, diabetes, which associated with cancer make COVID-19 the most aggressive; patients submitted to invasive treatments, surgery and chemotherapy, for instance, are possibly at increased risk of evolving to more severe conditions[10,26].

A research conducted by Alcântara et al.[27] about the main types of cancer of COVID-19-infected patients concluded that lungs accounted for 51.3%, breast cancer, 10.3% and colon, 7.7%. In counterpart, the study of Stevanato et al.[28] found that from January 1 to May15, 2020 (n=5,522), 20.54% of the total deaths by breast cancer of Brazilian women were associated with COVID-19.

A study of the United Kingdom[29] with oncologic patients found that 9% of deaths by breast cancer were associated with COVID-19, one of the motives for high rates was poor healthcare consultations and access and availability of diagnosis. In addition, a study conducted in USA, Canada and Spain noticed there was association of breast cancer and COVID-19 with other general risk factors[28,29].

Brar et al.[19] found increased leukopenia and anemia in oncologic patients compared with control group without cancer contrary to the present study, which corroborate another study with oncologic patients where anemia was detected in 21 patients (75%), leukopenia in 9 (32.1%) and lymphopenia in 23 (82.1%)[19].

The reduced period of collection and small sample of Sars-CoV-2-infected oncologic and non-oncologic patients are potential limitations of the study.

CONCLUSION

The findings indicated that it is possible to find differences in the interventions and outcomes among oncologic and non-oncologic patients. Mortality, comorbidities and duration of invasive ventilatory support of oncologic patients were greater than non-oncologic patients.

CONTRIBUTIONS

All the authors contributed substantially to the study design, acquisition, analysis and/or interpretation of the data, wording and/or critical review and approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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