Characteristics and outcomes of COVID-19 in hospitalized cancer patients in an Amazon region: a cross-sectional study with data from epidemiological surveillance

Abstract

<mark>**Background**</mark>

Objective: To describe the characteristics and outcomes of oncology patients infected with SARS-CoV-2 hospitalized in the state of Pará.

Method: Cross-sectional study with data from epidemiological surveillance of acute and severe respiratory syndromes of hospitalized cases notified from January 1, 2020, to December 31, 2020. Clinical and outcome variables, chi-square test, and Odds ratio were analyzed.

Results: 164 cases, lethality represented 94 (57.32%). The mean overall age was 63 years, of survivors was 60 years and of deaths was 66 years. Advanced age was associated with deaths (p-0.039). Male gender was associated with deaths (65.96% - p-0.006 - OR 2,438 - CI 1,291-4,604). Similarly, the signs and symptoms associated with death were dyspnea (80.85% - p- 0.028 - OR 2,203 - CI 1,080-4,491), respiratory distress (76.60% - p- 0.003 - OR 2,756 - CI 1,410-5,387), O_2 saturation <95% represented almost four times to the chances of death (68.09% - p-<0.001 - OR 3,398 - CI 1,798-6,494). Comorbidities were not associated with deaths, however, Immunodeficiency/Immunodepression represented the most frequent in the cases (22.56%), followed by Chronic Cardiovascular Disease (21.95%) and Diabetes Mellitus (18.90%). ICU admission was associated with deaths with the highest odds ratio of the analysis almost five times (42.55% - p- <0.001 - OR 4,444 - CI 2,028-9,739).

Conclusion: In this study, <mark>we</mark> showed that the lethality was higher than in other studies of hospitalized cancer patients with COVID-19, as well as higher than the overall lethality of COVID-19 among hospitalized patients. The factors associated with deaths are similar to those in the literature, except that immunodeficiency is a specific condition in cancer patients and is associated with an unfavorable outcome.

Keywords: Oncology; Cancer; Neoplasm; Severe acute respiratory syndrome; COVID-19.

35

INTRODUCTION

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38   The new coronavirus emerged in the province and Wuhan in China in December

39   2019, following an outbreak of pneumonia of unknown etiology associated with a fish

40   market in the region. In January 2020 the causative infectious agent, SARS-CoV-2, was

41   isolated and named for its similarity to SARS-CoV, a coronavirus that caused an

42   epidemic of Severe Acute Respiratory Syndrome (SARS) in China in 2003, so the

43   disease was named COVID-19, caused by the new coronavirus SARS-CoV-2 [1].

44   The similarity between the viruses also includes transmissibility, directly and by

45   fomites, being a highly contagious disease, thus, it soon spread to neighboring

46   countries, and on March 20, 2020, the World Health Organization (WHO) declared the

47   outbreak by SARS-CoV-2 as a pandemic, thus the disease reached a global level,

48   causing thousands of deaths, both in developed and developing countries and

49   undeveloped countries [2].

50   The clinical features are presented in most cases on average (85%) mild and

51   moderate cases, called Flu Syndrome (FS), with the presence of fever, cough, myalgia,

52   chills, sore throat, loss of smell and taste. Severe cases, on average (15%), are

53   associated with symptoms of GS and respiratory distress, dyspnea, oxygen saturation

54   <95%, diarrhea, flapping of the wings of the nose, etc., and the severe cases are called

55   SARS, which requires intensive care and is also associated with high mortality [3].

56   The literature cites that some risk factors are associated with the severity of

57   COVID-19, for example, the elderly, obese, pregnant women, patients with chronic

58   diseases, heart disease, diabetes, neurological diseases, cancer, immunosuppressed and

59   immunosuppressed [4,5].

60   In the context of neoplasms, they are a set of pathologies that start from the

61   differentiation and loss of cell function, thus the affected tissue or organ loses its

62   function and the cells multiply disorderly, if the malignant cells migrate to other organs

63   can multiply systemically and cause metastasis from the organ primarily affected. Early

64   diagnosis is fundamental for the best prognosis and is confirmed by biopsy of the

65   affected tissue. The treatment is based on some approaches such as radiotherapy,

66   chemotherapy, and surgery, which can be performed in association or individually.

67   Chemotherapy and radiotherapy cause immunosuppression, which makes the cancer

Comment [Z1]: Refernce the reference number in brackets [3].

68 patient vulnerable to secondary and opportunistic infections, thus becoming a group of
69 patients at risk for the development of infections that can be serious [6,7].

70 According to the National Cancer Institute (INCA), in 2020 in Brazil the
71 prevalence in men was of Prostate (65,840-29.2%), Colon and Rectum (20,540-9.1%),
72 Trachea, Bronchus and Lung (17,760-7.9%), Stomach (13,360-5.9%) Oral Cavity (11.
73 200-5.0%) Esophagus (8,690-3.9%) Bladder (7,590-3.4%), Larynx (6,470-2.9%),
74 Leukemias (5,920-2.6%), Central Nervous System (5,870-2.6%), totaling in men,
75 except non-melanoma skin (225,980) cases in 2020, including melanoma reaches
76 (309,750). In women, Breast (66,280-29.7%), Colon and Rectum (20,470-9.2%), Cervix
77 (16,710-7.5%), Trachea, Bronchus and Lung (12,440-5.6%), Thyroid Gland (11,950-
78 5.4%), Stomach (7,870-3.5%), Ovary (6,650-3.0%), Body of the Uterus (6. 540-2.9%),
79 Non-Hodgkin Lymphoma (5,450-2.4%) Central Nervous System (5,230-2.3%), totaling,
80 except non-melanoma skin (223,110) cases in 2020, including melanomas reaches
81 (316,280). thus the neoplasms in 2020 reached more than 600,000 cases in Brazil [8].
82 Thus, the high prevalence is associated with the greatest impacts of COVID-19 on
83 cancer patients.

84 One survey cited that the pandemic by COVID-19 affected the treatment of
85 cancer patients, impacting on mortality, as well as the specific characteristics of
86 COVID-19 in these patients [9].

87 Given this problem, this study aims to describe the characteristics and outcomes
88 of cancer patients infected by SARS-CoV-2 hospitalized in the state of Pará, from an
89 analysis of severe SARS cases reported to the Brazilian Ministry of Health (MS), since
90 Brazil's Amazon region has distinct characteristics from other regions, and that these
91 results can subsidize the best management and direct public policies to reduce mortality
92 by COVID-19 in cancer patients in this region of the Brazilian Amazon.

93

94 **METHOD**

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96 This is a cross-sectional epidemiological study, analytical, quantitative,
97 secondary-based, from data provided by the OpenDataSUS platform
98 (https://opendatasus.saude.gov.br/) of the Brazilian Ministry of Health, which
99 corresponds to the surveillance database of Severe Acute Respiratory Syndromes
100 (SARS), which is performed by the platform of the Information System for
101 Epidemiological Surveillance of Influenza (SIVEP-GRIPE). The study period was from

102 March 1, 2020, to December 31, 2020, including all the notifications of this time frame.

103 (https://sivepgripe.saude.gov.br/sivepgripe/login.html?1).

104 The database was made available from the OpenDataSUS platform in Excel

105 2019 format on March 31, 2021, with the last update on March 24, 2021. The SIVEP-

106 GRIPE notification form is composed of 80 variables, on sociodemographic and

107 clinical-epidemiological data [10]. The variables extracted according to the form were:

108 gender (item 8), age (item 10), signs and symptoms (item 35), has risk

109 factors/comorbidities (item 36), admission to intensive care unit (item 47), ventilation

110 (item 44), closure criteria (item 60), final classification: 5-SARS by COVID-19 (item

111 72) and evolution: 2- death (item 74). The case definition for notification is:

112 hospitalized individual with fever, even if referred, accompanied by cough or sore throat

113 and presenting dyspnea or O2 saturation < 95% or respiratory distress or that evolved to

114 death by SARS regardless of hospitalization.

115 Inclusion criteria were notifications from residents of Pará with final

116 classification confirmed for COVID-19 and evolution completed, with the variable

117 other comorbidity completed (cancer or neoplasms). Blank notifications were excluded.

118 The data were organized in an Excel 2019 spreadsheet, and the analysis was

119 performed by the Statistical Package for the Social Sciences (SPSS) 20.0 statistical

120 program. A table was made with the number of cases per municipality of residence. The

121 analysis was performed using the absolute (Fa) and relative (Fr) frequency distributions

122 of the study variables. To measure the association between the outcome variables

123 (dependent) and the predictors (independent) the Chi-square test or Fisher's exact test

124 was used when unable to use the former. Odds Ratio (OR) was performed on the

125 variables significant in the chi-square. To verify the age difference between survivors

126 and deceased, the Shapiro Wilk normality test was applied to verify which test to use.

127 The Shapiro Wilk test was significant 0.035 and thus the sample does not have

128 normality, and we used the Mann-Whitney test to verify the difference between the

129 groups. The alpha level of significance was equal to or less than <0.05.

130 The data of this study were publicly available, not containing personal data of

131 patients such as name, address, and telephone contact, thus presenting no risk to the

132 research participants, besides being exempt from ethical opinion. This study is

133 conducted by Law No. 12.527 of 18/11/2011 (Access to Information Law) [11].

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RESULTS

The study totaled until the study period 164 cases of COVID-19 hospitalized in oncology patients according to the information in the notification and investigation form of SIVEP-GRIPE. Of these 164, the lethality represented 94 (57.32%), on the closure criteria, most were laboratory 149 (90.90%) (Table 1).

The average age of the survivors was 63, of the survivors 60, and the deceased 66. The average age for deaths is higher.

Table 1 - Closure criteria for hospitalized cases of COVID-19 in oncology patients, Pará, Brazil, 2022.

Closing criteria	N	%
Laboratory	149	90,9
Clinical-epidemiological	9	6,4
Clinical	5	3,0
Clinical-imaging	1	0,6
Total	164	100,0

Source: OpenDataSUS. SIVEP-GRIPE.

In table 2 we observe the cases per municipality of residence, Belém represented 51 (31.10%), followed by Santarém 25 (15.20%) and Marabá 12 (7.30%), Ananindeua 8 (4.90%) and Parauapebas 6 (3.70%). The others were equal to or less than 3 cases for each municipality.

Table 2 - Number of cases of COVID-19 in oncology inpatients by the municipality of residence, Pará, Brazil, 2022.

Cases per municipality	N	%
Belém	51	31,1
Santarém	25	15,2
Marabá	12	7,3
Ananindeua	8	4,9
Parauapebas	6	3,7
Itaituba	3	1,8
Marapanim	3	1,8
Paragominas	3	1,8
Tucuruí	3	1,8
Abaetetuba	2	1,2

Comment [Z2]: Tables & figures should be placed inside the text. Tables and figures should be presented as per their appearance in the text. It is suggested that the discussion about the tables and figures should appear in the text before the appearance of the respective tables and figures. No tables or figures should be given without discussion or reference inside the text

Altamira	2	1,2
Canaã dos carajás	2	1,2
Juruti	2	1,2
Marituba	2	1,2
Mocajuba	2	1,2
Oeiras do para	2	1,2
Portel	2	1,2
Rurópolis	2	1,2
Salinópolis	2	1,2
Água azul do Norte	1	0,6
Alenquer	1	0,6
Anapu	1	0,6
Aurora do para	1	0,6
Baião	1	0,6
Braganca	1	0,6
Brasil novo	1	0,6
Breves	1	0,6
Bujaru	1	0,6
Cametá	1	0,6
Capanema	1	0,6
Castanhal	1	0,6
Curionópolis	1	0,6
Curuá	1	0,6
Dom Eliseu	1	0,6
Ipixuna do para	1	0,6
Jacundá	1	0,6
Mae do rio	1	0,6
Moju	1	0,6
Monte alegre	1	0,6
Ourilândia do Norte	1	0,6
Pacajá	1	0,6
Primavera	1	0,6
Santa Isabel do Pará	1	0,6
Santo Antônio do Tauá	1	0,6
São domingos do Araguaia	1	0,6
São Geraldo do Araguaia	1	0,6
São Miguel do Guamá	1	0,6
Tucumã	1	0,6
Uruará	1	0,6
Total	164	100,0

Source: OpenDataSUS. SIVEP-GRIPE.

About the characteristics of the cases, we observed that advanced age is associated with deaths (Mann-Whitney p- 0.039), as well as male gender (65.96% - p- 0.006 - OR 2.438 - CI 1.291-4.604) with twice as many chances of death according to the odds ratio in the bivariate analysis. Similarly on signs and symptoms, dyspnea

164   (80.85% - p- 0.028 - OR 2,203 - CI 1,080-4,491) with two times more chances of death,

165   followed by respiratory distress with almost three times more chances of death by Odds

166   ratio (76.60% - p- 0.003 - OR 2. 756 - CI 1,410-5,387), O2 saturation <95% represented

167   almost four times to the chances of death (68.09% - p-<0.001 - OR 3,398 - CI 1,798-

168   6,494). Comorbidities were not associated with deaths, however,

169   Immunodeficiency/Immunodepression represented the most frequent in the cases

170   (22.56%), followed by Chronic Cardiovascular Disease (21.95%) and Diabetes Mellitus

171   (18.90%). ICU admission was associated with deaths with the highest odds ratio of the

172   analysis almost five times (42.55% - p- <0.001 - OR 4,444 - CI 2,028-9,739).

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174   **Table 3 -** Clinical, epidemiological, and outcome characteristics of hospitalized

175   oncology cases of COVID-19, Pará, Brazil, 2022.

Characteristics	Total (164)	%	Survivor (70)	%	Death (94%)	%	p-value	OR	CI	
Age										
Median	65,00		73,61		89,12		0,039**			
Sex							0,006	2.438	1.291	4.604
Male	93	56.71	31	44.29	62	65.96				
Female	71	43.29	39	55.71	32	34.04				
Signs and Symptoms										
Fever	108	65.85	51	72.86	57	60.64	0,103			
Cough	108	65.85	47	67.14	61	64.89	0,764			
Sore throat	32	19.51	18	25.71	14	14.89	0,084			
Dyspnea	122	74.39	46	65.71	76	80.85	0,028	2.203	1.080	4.491
Respiratory distress	110	67.07	38	54.29	72	76.60	0,003	2.756	1.410	5.387
O2 saturation <95%	91	55.49	27	38.57	64	68.09	<0,001	3.398	1.798	6.494
Diarrhea	19	11.59	7	10.00	12	12.77	0,584			
Vomit	18	10.98	7	10.00	11	11.70	0,730			
Another symptom	45	27.44	23	32.86	22	23.40	0,180			
Comorbidities										
Chronic cardiovascular disease	36	21.95	18	25.71	18	19.15	0,315			
Chronic hematological disease	1	0.61	1	1.43	0	0.00	0,427*			
Chronic liver disease	2	1.22	1	1.43	1	1.06	0,673*			
Asthma	4	2.44	0	0.00	4	4.26	0,137*			
Diabetes Mellitus	31	18.90	15	21.43	16	17.02	0,476			
Immunodeficiency/Immunodepression	37	22.56	13	18.57	24	25.53	0,292			
Chronic kidney disease	5	3.05	2	2.86	3	3.19	0,637*			
Obesity	1	0.61	0	0.00	1	1.06	0,573*			
Hospitalized in ICU	50	30.49	10	14.29	40	42.55	<0,001	4.444	2.028	9.739

176   Source: OpenDataSUS. SIVEP-GRIPE. *Fisher's exact test, **Mann-Whitney. OR

177   Odds Ratio, CI Confidence Interval.

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DISCUSSION

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183   This study analyzed the cases of COVID-19 hospitalized oncologists in the state
184   of Pará, and we identified a high lethality of (57.32%), because the lethality in
185   hospitalized oncologists for COVID-19 generally reaches a lower rate, for example in
186   the studies of Duarte et al[12] which analyzed those hospitalized in Brazil at the beginning
187   of the pandemic, which still only included health professionals. However, another study
188   performed another analysis of those hospitalized for COVID-19 in the state of Pará in
189   the first year of the pandemic and showed a lethality rate of (42.47%)[13]. Thus, the
190   lethality in cancer patients is higher than in those hospitalized for COVID-19 overall.

191   A study of 218 patients hospitalized for COVID-19 diagnosed with cancer in
192   New York showed a lethality rate of (28%) lower than the rate in our study. [14].

193   Our study showed that advanced age was associated with deaths. A study of 37
194   hospitalized patients with COVID-19 and cancer did not associate advanced age with
195   severe cases of the disease, one hypothesis is the limitation in the small sample [15].
196   Another study of 1,590 patients found that among cancer patients, advanced age was the
197   only risk factor for serious events (OR 1,43, IC 95% 0,97–2,12; p=0,072) [16].

198   Regarding the signs and symptoms, we identified that dyspnea, respiratory
199   distress, and altered O2 saturation were associated with deaths, similar to other studies
200   of patients hospitalized in general for COVID-19[17,18]. As well as in another study
201   specifically of oncology patients with COVID-19[19].

202   A survey of 423 cancer patients and COVID-19, showed that fever (78%) and
203   cough (82%) were the most common clinical features, while shortness of breath (44%)
204   and diarrhea (26%) were less common but not. 168 (40%) of 423 patients were
205   hospitalized and 87 (20%) developed severe respiratory illness, including 47 (11%) who
206   required high-flow oxygen and 40 (9%) who required mechanical ventilation. The
207   illness in seven pediatric cases was mild and uncomplicated. The overall lethality rate
208   was 12% (51 of 423). The case fatality for hospital and ICU admission was 24% (41 of
209   168) and 35% (17 of 48), respectively. [20].

210   The same New York study cited above identified increased mortality
211   significantly associated with older age, multiple comorbidities, need for ICU support,
212   and elevated levels of D-dimer, lactate dehydrogenase, and lactate on multivariate

213 analysis [14]. Similar to our results regarding ICU admission for risk of death. Another
214 study also associated the risk of death in ICU in those hospitalized for COVID-19 in
215 general [21].

216   Immunodeficiency/immunodepression was significant in occurrence in our
217 study, representing the most common comorbidity. According to Al-quteimat and
218 amer[22], the immunosuppressed state of some cancer patients (whether caused by the
219 disease itself or by treatment) increases the risk of infection compared to the general
220 population. Immunosuppression can also expose cancer patients to severe complications
221 from an infection, which can result in delayed treatment and unnecessary
222 hospitalizations that can negatively affect the prognosis of the disease.

223   A meta-analysis of 15 studies with 3,019 patients, of whom 1,628 were men;
224 41.0% were from the United Kingdom and Europe, followed by the United States and
225 Canada (35.7%) and Asia (China, 23.3%). The overall lethality rate for COVID-19
226 patients with cancer measured 22.4% (95% confidence interval [CI] = 17.3% to 28.0%).
227 Univariate analysis revealed age (OR = 3.57, 95% CI = 1.80 to 7.06), male gender (OR
228 = 2.10, 95% CI = 1.07 to 4.13), and comorbidity (OR = 2.00, 95% CI = 1.04 to 3.85)
229 were associated with increased risk of serious events (defined as individuals admitted to
230 the intensive care unit or requiring invasive ventilation or death). In multivariate
231 analysis, only age greater than 65 years (OR = 3.16, 95% CI = 1.45 to 6.88) and being
232 male (OR = 2.29, 95% CI = 1.07 to 4.87) were associated with increased risk of serious
233 events. In this analysis, the authors concluded that COVID-19 patients with cancer have
234 a higher lethality rate compared to COVID-19 patients without cancer. Age and sex
235 appear to be risk factors associated with a worse prognosis [23]. However, the lethality of
236 our study was still higher, but we emphasize that we only analyzed hospitalized
237 patients, while the meta-analysis did not specify whether it included only hospitalized
238 patients.

239   Cancer patients have an increased risk of serious infections, with a 3.5-fold
240 increase in the risk of needing mechanical ventilation or ICU admission or dying
241 compared to patients without cancer. The increased susceptibility of cancer patients to
242 serious complications from COVID-19 may be attributed to the immunosuppressive
243 state caused by the malignancy and anticancer treatments, such as chemotherapy or
244 surgery. Patients who received chemotherapy or underwent surgery in the 30 days
245 before presenting with COVID-19 were at higher risk of serious events than patients
246 who were not treated with chemotherapy or surgery. It was also found that a history of

247 cancer conferred the highest risk of serious complications and was correlated with
248 worse COVID-19 results. Notably, patients with lung cancer did not have a higher
249 likelihood of serious complications compared to patients with other types of cancer [16].

250 Curigliano[24] draws attention and highlights that two recent articles in the Lancet
251 and Lancet Oncology report that cancer patients with acute respiratory syndrome
252 coronavirus 2 (SARS-CoV-2) infection have higher mortality rates. Common
253 independent factors associated with increased risk of death were older age, smoking
254 history, number of comorbidities, more advanced performance status, and active cancer.

255 As a limitation of the study, we highlight the risk of data bias because we
256 analyzed a retrospective epidemiological surveillance database. However, the
257 surveillance of SARS in Brazil is performed since 2009 because of the Influenza
258 pandemic, thus the investigation form is well prepared and it is already routine in
259 hospitals to fill it out and follow the flow of surveillance, such as sample collection for
260 molecular investigation and closure of the case in the system. The form is filled in after
261 the case is defined by the patient's primary care team, and during the outcome, the form
262 continues to be filled in until the case is closed. The fact of not having the variable
263 cancer comorbidity increases the risk of bias because the screening was performed by
264 the variable other comorbidity and we filtered the neoplasms that were filled in
265 manually by health professionals.

266
267
268 **CONCLUSION**
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270 In this study, we show that the lethality was higher than other studies of
271 hospitalized cancer patients with COVID-19, as well as higher than the overall lethality
272 of COVID-19 among hospitalized patients. The clinical features associated with a death
273 such as dyspnea, respiratory distress, and change in oxygen saturation were similar to
274 the other studies. As for the outcomes such as ICU admission and immunodeficiency
275 associated with death that we identified, ICU admission is similar in patients without
276 cancer, however, immunodeficiency is a factor specifically in cancer patients that
277 influences the severity and death of those hospitalized by COVID-19 with cancer in this
278 study, being similar to the literature.

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