Characteristics and outcomes of cancer patients with infection in an intensive care unit

Características e desfechos de pacientes oncológicos com infecção em unidade de terapia intensiva

Características y resultados de pacientes oncológicos con infección en una unidad de cuidados intensivos

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Abstract
Introduction: Cancer remains among the leading causes of death. Due to its characteristics and the high aggressiveness of the treatment, the need for intensive care is common. A significant part of admissions to intensive care units (ICU) can be associated with infections, with sepsis being the main complication. Thus, it is important to know the epidemiological profile for early diagnosis and adequate management, avoiding unfavorable outcomes. *Objective:* To characterize clinical aspects, cultures performed and outcomes identified in cancer patients admitted to an oncology ICU. *Method:* A descriptive, retrospective observational study with cancer patients admitted to the ICU of a cancer hospital diagnosed with infection between March 1 and July 31, 2021. Patients with solid or hematological cancer, over 18 years of age, of both sexes, hospitalized in the ICU for more than 24 hours and diagnosed with infection. *Results:* Of the 124 patients, 75% were diagnosed with infection. 51.6% were female and the mean age was 57 ±16 years. The mean length of stay was 10 ±11 days, with respiratory causes as the main reason (42.9%). The main focus of infection was the respiratory tract (43.9%). 45.9% had sepsis and 18.4% had septic shock. The most common microorganisms were gram-negative bacteria (58.6%). 28 of the microorganisms were multiresistant. *Conclusion:* A high occurrence of infection and a high mortality rate were identified, which may be related to infections or cancer treatment and/or advanced stage of cancer. A high amount of multidrug-resistant bacteria was identified, highlighting the importance of the rational use of antimicrobials.
Keywords: Intensive care unit; Cancer; Infection; Sepsis; Oncology.

Resumo
Introdução: O câncer permanece dentre as principais causas de morte. Devido às suas características e a elevada agressividade do tratamento, é comum a necessidade de cuidados intensivos. Parte significativa das internações em unidades de terapia intensivas (UTI) pode ser associada a infecções, sendo sepse a principal complicação. Assim, é importante conhecer o perfil epidemiológico para diagnóstico precoce e manejo adequado, evitando desfechos desfavoráveis. *Objetivo:* Caracterizar aspectos clínicos, culturas realizadas e desfechos identificados em pacientes com câncer internados em uma UTI oncológica. *Método:* Estudo observacional retrospectivo descritivo com pacientes

oncológicos internados na UTI de um hospital oncológico diagnosticados com infecção entre 01 de março e 31 de julho de 2021. Foram incluídos pacientes com câncer sólido ou hematológico, maiores de 18 anos, de ambos os sexos, internados na UTI por mais de 24h e diagnosticados com infecção. *Resultados:* Dos 124 pacientes, 75% tiveram diagnóstico de infecção. 51,6 % era do sexo feminino e a média de idade foi de 57 ±16 anos. O tempo médio de permanência foi de 10 ±11 dias, com causas respiratórias como principal motivo (42,9%). O principal foco de infecção foi o trato respiratório (43,9%). 45,9% tiveram sepse e 18,4% apresentaram choque séptico. Os microrganismos mais encontrados foram as bactérias gram-negativas (58,6%). 28 dos microrganismos foram multirresistentes. *Conclusão:* Foi identificado alta ocorrência de infecção e elevada taxa de mortalidade, podendo estar relacionada as infecções ou ao tratamento oncológico e/ou estágio avançado do câncer. Identificou-se elevada quantidade de bactérias multirresistentes, evidenciado a importância do uso racional de antimicrobianos.
Palavras-chave: Unidade de terapia intensiva; Câncer; Infecção; Sepse; Oncologia.

Resumen
Introducción: El cáncer se mantiene entre las principales causas de muerte. Por sus características y la alta agresividad del tratamiento, es frecuente la necesidad de cuidados intensivos. Una parte importante de los ingresos en las unidades de cuidados intensivos (UCI) pueden estar asociadas a infecciones, siendo la sepsis la principal complicación. Por ello, es importante conocer el perfil epidemiológico para un diagnóstico precoz y un manejo adecuado, evitando desenlaces desfavorables. *Objetivo:* Caracterizar aspectos clínicos, cultivos realizados y desenlaces identificados en pacientes oncológicos ingresados en una UTI oncológica. *Método:* Estudio observacional descriptivo, retrospectivo con pacientes oncológicos ingresados en la UCI de un hospital oncológico con diagnóstico de infección entre el 1 de marzo y el 31 de julio de 2021. Pacientes con cáncer sólido o hematológico, mayores de 18 años, de ambos sexos, hospitalizados en UCI por más de 24 horas y diagnosticada con infección. *Resultados:* De los 124 pacientes, el 75% fueron diagnosticados de infección. El 51,6% eran mujeres y la edad media fue de 57 ±16 años. La estancia media fue de 10 ± 11 días, siendo las causas respiratorias el principal motivo (42,9%). El principal foco de infección fue el tracto respiratorio (43,9%). El 45,9% presentó sepsis y el 18,4% shock séptico. Los microorganismos más frecuentes fueron las bacterias gramnegativas (58,6%). 28 de los microorganismos fueron multirresistentes. *Conclusión:* Se identificó una alta incidencia de infección y una alta tasa de mortalidad, que pueden estar relacionadas con infecciones o tratamiento oncológico y/o estadio avanzado del cáncer. Se identificó una alta cantidad de bacterias multirresistentes, destacando la importancia del uso racional de los antimicrobianos.
Palabras clave: Unidad de cuidados intensivos; Cáncer; Infección; Septicemia; Oncología.

1. Introduction

Cancer, associated with high morbidity and mortality, remains among the main causes of death in the population under 70 years of age in more than 110 countries (Sung et al., 2021). Due to its pathophysiological characteristics and the high aggressiveness of the treatment, it is common for cancer patients to end up needing intensive care during their therapy (Torres et al., 2016). Studies show that the population diagnosed with some type of cancer represents high rates of admissions to intensive care units (ICUs), reaching up to 23.9% (AbuSara et al., 2019; Marcio Soares et al., 2016; Taccone et al., 2009).

A significant part of these ICU admissions can be associated with infections, usually related to immunosuppression caused by the disease itself or by treatments such as radiation and chemotherapy (Torres et al., 2016; Zembower, 2014). The main types of infection in cancer patients are: respiratory, central nervous system (CNS), gastrointestinal, urinary, skin and soft tissue, and catheter-related blood infections (Seo et al., 2021).

One of the complications found in cases of infection in these patients is sepsis. Sepsis is already one of the main causes of ICU admission, with a mortality rate of up to 30% (Goulden et al., 2018). Cancer patients are 10 times more likely to have sepsis and may account for 15% of these hospitalizations (Mirouse et al., 2020; Márcio Soares et al., 2010). Thus, it is important to know the epidemiological profile of these patients, to enable early diagnosis and adequate management, avoiding unfavorable outcomes. The aim of the present study was to characterize the clinical aspects, cultures performed, and outcomes identified in cancer patients admitted to an oncology ICU.

2. Methodology

This is a descriptive, retrospective observational study, described by Yang & West-Strum (2010), carried out with the

purpose of analyzing the characteristics of infections diagnosed in cancer patients, admitted to the clinical ICU of a philanthropic oncology hospital, a reference in Brazil, located in the city of Salvador, in the state of Bahia, from March 1 to July 31, 2021. The clinical ICU of this hospital has 10 beds. Patients with solid or hematological cancer, over 18 years of age, of both sexes, hospitalized in the ICU for more than 24 hours, diagnosed with infection, were included in the study. As variables, sociodemographic and clinical characteristics and the characteristics of cultures and infectious agents were adopted. The study was approved by the Ethics and Research Committee of the Universidade do Estado da Bahia (UNEB), with CAAE number: 48996921.0.0000.0057 and opinion number: 4,888,974.

Statistical analysis

Data were collected from medical records, compiled and expressed as a function of the absolute (n) and relative (%) frequencies of the variables analyzed. Data normality was assessed using the Shapiro-Wilk test. Data processing and statistical analysis were performed using the Statistical Package for the Social Sciences (SPSS), version 20.0.

3. Results

Of the 124 patients admitted to the ICU from March 1 to July 31, 2021, 93 (75%) were diagnosed with infection and were included in the study. Table 1 describes the main sociodemographic and clinical characteristics of these patients. 51.6% of the population was female, the mean age observed was 57 years ($\pm$16 years) and most of them (60.2%) did not live in the city of Salvador, where the hospital is located.

Table 1 – Sociodemographic and clinical characteristics of patients admitted to the clinical ICU of a philanthropic cancer hospital in the city of Salvador, Bahia, Brazil.

Variables		Patients (n=93)
Age		
	Mean (SD)	57 years ($\pm$16)
Sex, n (%)		
	Male	45 (48,4)
	Female	48 (51,6)
Residence, n (%)		
	Salvador - BA	37 (39,8)
	Metropolitan region of Salvador - BA	17 (18,3)
	Others	39 (41,9)
Cancer treatment, n (%)		
	Previous Treatment	73 (78,5)
	Chemotherapy	46 (49,5)
	Surgery	38 (40,9)
	Radiotherapy	21 (22,6)
	Hormone therapy	5 (5,4)
	None	20 (21,5)
Tumor type, n (%)		
	Solid	70 (75,3)
	Hematological	23 (24,7)
	Others / Not informed	2 (2,2)

Abbreviations: SD, standard deviation; ICU, intensive care unit. Source: authors.

Among the patients, 73 (78.5%) had already undergone some type of treatment for cancer, but 20 (21.5%) had not yet undergone any treatment due to a recent diagnosis or advanced disease. The most used type of treatment was chemotherapy (49.5%), followed by surgery (40.9%).

Regarding the diagnosis of cancer, 70 patients (75.3%) had solid tumors and 23 (24.7%) had hematological tumors. The most common tumors among solids were breast (12.9%), gastrointestinal (12.9%), prostate (9.7%) and head and neck (9.7%) tumors. Among the hematological ones, the most common were lymphomas (14%).

It was possible to observe that 86% of admissions were for the first time, 8.6% were readmissions and 5.4% were patients who needed to be referred to the ICU twice during the analyzed period. The mean length of stay in the ICU was 10 days (±11 days) and the main reason for admission was related to respiratory causes (42.9%), such as acute respiratory failure and dyspnea, followed by renal causes (19.4%) and sepsis (15.3%), shown in Table 2.

Table 2 – Characteristics of ICU admissions of cancer patients with infections at a philanthropic cancer hospital in the city of Salvador, Bahia, Brazil.

Variables	n (%)
Length of stay in ICU	
Mean (SD)	10 dias (±11)
ICU admission, n (%)	
1st admission	80 (86)
2nd admission	8 (8,6)
2nd admission in the study period	5 (5,4)
Reason for admission, n (%)	
Respiratory	42 (42,9)
Renal	19 (19,4)
Sepsis	15 (15,3)
Neurological	14 (14,3)
Others	8 (8,1)
Associated conditions, n (%)	
Renal dysfunction	74 (75,5)
Mechanical ventilation	73 (74,5)
Outcomes, n (%)	
Discharge from ICU	39 (41,9)
Transfer	4 (4,3)
Death	50 (53,8)

Source: Authors.

Among cultures, blood culture was the most performed (93.5%), followed by urine culture (68.8%). The most common focus of infections were the respiratory tract (43.9%), blood (23.5%) and urinary tract (17.3%), as shown in Table 3. Among patients, 45.9% were diagnosed with sepsis and 18.4% with septic shock. The most common associated condition was renal dysfunction, present in 75.5% of patients. During the study period, the mortality rate was 53.8%.

Table 3 – Characteristics of infections in cancer patients in the ICU of a philanthropic cancer hospital in the city of Salvador, Bahia, Brazil.

Variables	n (%)
Site of infection, n (%)	
Respiratory	43 (43,9)
Primary bloodstream infection	23 (23,5)
Urinary	17 (17,3)
Others	9 (9)
Number of infected sites, n (%)	
1 site	52 (55,9)
2 sites	12 (12,9)
More than 2	5 (5,4)
Gravity, n (%)	
Sepsis	45 (45,9)
Septic shock	18 (18,4)
Cultures performed, n (%)	
Blood culture	87 (93,5)
Urine culture	64 (68,8)
Tracheal secretion culture	39 (41,9)
Device culture	17 (18,3)
Others	6 (6,1)
None	3 (3)

Source: Authors.

In the cultures, it was possible to isolate 87 microorganisms, being 64 bacteria and 23 fungi (Table 4). Among the bacteria, most were gram-negative (58.6%), with the highest incidence of *Pseudomonas aeruginosa* (17.2%). Twenty-eight multiresistant microorganisms were isolated, including *Acinetobacter* spp (10,3%), *Klebsiella* spp (8%) and *Pseudomonas aeruginosa* (8%).

Table 4 – Pathogens isolated from cultures performed on patients admitted to the clinical ICU of a philanthropic oncology hospital in the city of Salvador, Bahia, Brazil.

Variables	n (%)
Isolated pathogens	87 (100)
Gram-positive bacteria	13 (14,9)
Staphylococcus aureus	7 (8)
Enterococcus	4 (4,6)
Pneumococcus	2 (2,3)
Gram-negative bacteria	51 (58,6)
Pseudomonas aeruginosa	15 (17,2)
Klebsiella spp	12 (13,8)
Acinetobacter spp	9 (10,3)
Escherichia coli	7 (8)
Enterobacter spp	3 (3,6)
Others	5 (5,7)
Fungi	23 (26,5)
Candida spp	16 (18,4)
Candida albicans	7 (8,1)
Multidrug-resistant microorganisms, n (%)	28 (32,2)
Acinetobacter spp	9 (10,3)
Klebsiella spp	7 (8)
Pseudomonas aeruginosa	7 (8)
Staphylococcus aureus	4 (4,6)
Others	2 (1,3)

Source: Authors.

4. Discussion

Infection is one of the most serious complications that affect cancer patients, mainly due to high mortality, when they progress to sepsis and septic shock (Mirouse et al., 2020). Many factors can contribute to the development of infections, such as the immunosuppression seen in cases of neutropenia related to the underlying disease or the toxicity of the treatment (Abou Dagher et al., 2017).

Regarding the demographic profile, it was observed that most patients were female and the mean age found was 57 years. Other studies found a similar mean age, but it was possible to observe a predominance of males (AbuSara et al., 2019; Hawari et al., 2016; Torres et al., 2016).

In this study, the presence of a high rate of infection among cancer patients who required intensive care can be highlighted. This fact is associated with a death rate of 53.8%, the main outcome found. The data show a higher death rate than previous studies that bring rates ranging from 21 to 43.4% (Assi et al., 2021; Hawari et al., 2016; Marcio Soares et al., 2016). This can be explained by the profile of the patients. As it is a hospital that exclusively serves patients from the Sistema Único de Saúde (SUS), many of them from other cities, there may be interference due to a longer time until diagnosis and a delay until the beginning of treatment. 21.5% of patients have not yet received any type of treatment, representing 24% of patients who died. In addition, some were in an advanced stage of cancer and had already undergone various types of treatments. The number of processed patients and their beneficiaries more susceptible than and the results of their results (Torres et al., 2016).

A prevalence of solid tumors can be observed, which corroborates other studies (Abou Dagher et al., 2017; Assi et al.,

2021; Cunha et al., 2018; Marcio Soares et al., 2016), however, the breast tumor was more frequently found, differing from those that showed a higher occurrence of lung cancer (Abou Dagher et al., 2017; Assi et al., 2021). As for hematological tumors, lymphoma (Hodgkin and non-Hodgkin) was the type of cancer that was present in most patients.

The average length of stay in the ICU found was longer than other studies, which show an average of 3 to 5 days (Hawari et al., 2016; Márcio Soares et al., 2010; Torres et al., 2016). However, it was shorter than found in a study at the American University of Beirut Medical Center, which averaged 14 days (Assi et al., 2021). The main reason for hospitalization among patients was for respiratory causes, similar to studies carried out in European ICUs and in an ICU in the Middle East (Hawari et al., 2016; Taccone et al., 2009).

Most patients had only one infected site, with the respiratory tract being the most common site of infection. Cancer patients are at increased risk of developing influenza and pneumonia and of being hospitalized for an acute respiratory tract infection (Abdel-Rahman, 2020). These infections can be related to viruses, bacteria, or fungi and are usually caused by pathogens found in community-acquired pneumonia, hospital-acquired pneumonia, and pneumonia in immunosuppressed patients. Among them, Streptococcus pneumoniae, Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae and Aspergillus spp. (Anderson, 2014).

Primary bloodstream infection (BSI) was the 2nd main type of infection. Mainly in patients with solid cancer, BSI can be related to several factors such as the performance of surgeries, the presence of immunosuppression and the occurrence of ulcers, with gram-negative bacteria responsible for more than half of the cases (Gudiol et al., 2016). The most common gram-negative bacteria are Escherichia coli, Pseudomonas aeruginosa and Klebsiella pneumoniae (Marín et al., 2014; Mert et al., 2019).

The most observed pathogens in our study were gram-negative bacteria, with Pseudomonas aeruginosa being the most observed. Most of the studies show the greater presence of gram-negative bacteria in this specific population, but they differ in the most frequently found pathogen, ranging from Escherichia coli, Pseudomonas aeruginosa and Acinetobacter spp. (Batra et al., 2016; Cornejo-Juárez et al., 2015; Mert et al., 2020; Montassier et al., 2013).

During the study period, 28 multidrug-resistant pathogens were isolated, with Acinetobacter spp. being the most common. This data corroborates another study that evaluated the bacteria isolated in an oncology ICU over a period of five years. In addition to a similar rate, there was also a prevalence of Acinetobacter spp. both in solid cancer patients and in hematological cancer patients (Mert et al., 2020).

The study has some limitations, such as being carried out in only one institution. This may not reflect the reality of other institutions that treat cancer patients. Due to the characteristics of the patients, it was not possible to define in which cases the infection was the cause of death. Many of the patients were already in an advanced stage of cancer or had already undergone various types of treatments. Also, it was not possible to analyze the role of other comorbidities in patient outcomes and how much they could have been modified in relation to the treatment of the infection.

5. Conclusion

In this study, a high occurrence of infection was identified in cancer patients who required intensive treatment, with a prevalence of respiratory tract and primary bloodstream infections. Thus, a high mortality rate could be observed, which may be related to these infections or to other causes, resulting from cancer treatment or advanced stage of cancer.

Regarding the isolated pathogens, the presence of gram-negative bacteria was highlighted, which represent a recurring threat in the intra-hospital environment. Finally, with a high amount of multidrug-resistant bacteria, it is clear the importance that the rational use of antimicrobials is a frequent practice in the search for better results in the treatment and, consequently, a lower mortality.

Larger studies should be carried out in order to find a stronger association between the occurrence of infection and its type with the outcomes of these patients.

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