

Risk factors for central venous catheter-related bloodstream infection in oncology patients: an integrative review

Fatores de risco para infecção de corrente sanguínea relacionada a cateter venoso central em pacientes oncológicos: uma revisão integrativa

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ABSTRACT

The aim of this integrative review was to identify scientific studies on risk factors for bloodstream infections associated with central venous catheters (CVC) in cancer patients. The research question was formulated according to the PICO framework. An electronic search was conducted on the SciELO digital library, the Virtual Health Library, and the MEDLINE/PubMed databases using the descriptors "cancer", "infection", "central venous catheters", and "risk factors". A total of 356 publications were identified (356 in PubMed, 00 in the VHL, and 00 in SciELO). Based on the PRISMA guidelines, 32 articles were included in this review. Recent study dates from 2021. The handling of the central catheters by professionals and the administration of parenteral nutrition were the main risk factors for CVC infections. The implementation of basic healthcare and hygiene measures is essential for the prevention and reduction of bloodstream infections associated with central catheters.

Keywords: Central venous catheters; Cross infection; Risk factors.

RESUMO

O objetivo desta revisão integrativa foi identificar estudos científicos sobre fatores de risco para infecções de corrente sanguínea associadas a cateteres venosos centrais (CVC) em pacientes com câncer. A questão de pesquisa foi formulada de acordo com a estrutura PICO. Foi realizada uma busca eletrônica na biblioteca digital SciELO, na Biblioteca Virtual em Saúde e nas bases de dados MEDLINE/PubMed, utilizando os descritores "câncer", "infecção", "cateteres venosos centrais" e "fatores de risco". Foram identificadas 356 publicações (356 no PubMed, 00 na BVS e 00 no SciELO). Com base nas diretrizes PRISMA, 32 artigos foram incluídos nesta revisão. Estudo recente data de 2021. O manuseio dos cateteres centrais pelos profissionais e a administração de nutrição parenteral foram os principais fatores de risco para infecções por CVC. A implementação de medidas básicas de saúde e higiene é essencial para a prevenção e redução de infecções de corrente sanguínea associadas a cateteres centrais.

Descritores: Cateteres venosos centrais; Infecção cruzada; Fatores de risco.

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INTRODUCTION

Central venous catheters (CVCs) are flexible, radiopaque tubes capable of providing long-term intermittent access for months to years depending on the indication and medical needs of the patient. These invasive devices were first manufactured for medical purposes in the 1980s and have since been used for the administration of chemotherapy, parenteral nutrition, hemodynamic procedures, blood collection, and life-support therapy. Furthermore, CVCs are extremely important in the treatment of malignant neoplasms, as they avoid multiple painful peripheral punctures, which reduces the occurrence of ulcers and tissue necrosis. 5,6

However, the insertion of the CVC may result in injury to the vessel and neighboring structures, allowing microbes at the insertion site to enter the bloodstream. If left unchecked, this invasion may cause severe clinical impairment and progress to life-threatening conditions such as a septic shock.^{2,7} Hence, catheter-related bloodstream infections (CRBSIs) are a critical reality for cancer patients, who are often submitted to increasingly invasive techniques to ensure their survival.^{1,8}

Worldwide, about 20-29% of implanted CVCs may predispose patients with malignant diseases to an increased risk of infection.^{7,9-11} In developed countries such as the United States, the mortality rate related to CVC complications ranges between 10% and 25%. In contrast, with an incidence of 22.72 cases per 1,000 days,^{12,13} in Brazil, the mortality rate reaches up to 40% in catheterized patients.^{9,14}

Approximately 67% of hospitalized patients in cancer centers have CVCs.¹⁵ Therefore, knowledge of evidence-based interventions that can reduce the risk of infection and promote the early diagnosis of pathological conditions associated with the use of venous infusion devices is essential to improve the quality of care in oncology.⁷

Therefore, considering the scarcity of studies in this area^{7,9} and that CRBSI is the most worrisome complication related to CVC use, which can compromise the quality of life of patients,^{7,9,17} the aim of this study, was to identify risk factors for CVC infection in cancer patients. For this purpose, we developed an integrative review identifying, analyzing, and synthesizing results that characterize infectious complications in cancer patients with CVC in a systematic, orderly, and comprehensive manner.¹⁶

MATERIAL AND METHODS

This integrative review was guided by the research question formulated according to the PICO mnemonic, in which P = Population, I = Interest, and Co = Context, which helps describe the focus, scope, and applicability of the literature review. 16 Thus, "P" is represented by cancer patients, "I" by risk factors, and "Co" by infections associated with CVCs, resulting in the research question: "What are the main risk factors for catheter-related bloodstream infections in cancer patients in Brazil and worldwide?".

Integrative reviews (IRs) allow for the synthesis of studies on a specific subject or issue in a systematic way, which contributes to an expansion of knowledge about the investigated theme.¹⁸ In addition, this method has the potential to build knowledge and produce a grounded and uniform understanding while enabling the reader to access a compilation of previous research results in a single study, thereby contributing to more agile dissemination of scientific knowledge.^{16,18,19}

IRs enable the researcher to analyze and synthesize a particular theme, evidencing possible knowledge gaps and encouraging the investigation of new alternatives.²⁰ In this perspective, this review was structured considering the following steps: delimitation of the theme and formulation of the research question, establishment of the inclusion and exclusion criteria, literature search, categorization of the studies, critical evaluation and analysis of the included studies, summarization and interpretation of the results, conclusions based on the findings, and presentation/synthesis of knowledge.^{18,21}

The search strategy followed the PICO framework and was performed in line with the research question, grouping Medical Subject Headings (MeSH) terms and keywords from the Health Sciences Descriptors (DeCS, in Portuguese: *Descritores em Ciências da Saúde*) website. The following databases were selected for the electronic search: Scientific Electronic Library Online (SciELO), Virtual Health Library (VHL), and MEDLINE/PubMed (via National Library of Medicine).

The descriptors "cancer", "infection", "central venous catheters", and "risk factors" and their equivalents in Portuguese were used. The search entry was (((cancer) AND (infection)) AND (central venous catheters)) AND (risk factors). Regarding additional search settings or filters, in the VHL database, the search filters "title, abstract, subject" were included; in the SciELO database, the item "all indexes" was selected, and "all fields" was added to the query box on PubMed. The electronic search was conducted in October 2021 and revised in August 2022.

The inclusion criteria consisted of studies contemplating the research topic, available in full-text. No restrictions on year of publication, language, and study design were applied. Duplicate publications and investigations that did not address the research question were excluded.

A total of 356 publications were identified, 356 (100%) in PubMed, 00 in the VHL, and 00 in SciELO. After title screening, only 213 articles (59.8%) were selected due to compatibility with the theme, all of which were from the PubMed database. Six articles were excluded due to duplicity, totaling 207 papers (58.1%). After abstract screening, ninety-nine were eliminated due to incompatibility with the research subject. A hundred and eight articles (30.3%) were selected for full-text reading; nevertheless, 76 were eliminated for not answering the research question.



Thus, based on the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA),²² a total of thirty-two articles were selected for this review, as shown in Figure 1.

Some strategies were implemented to facilitate the reading and data extraction structured on the research question. The texts were organized in a Microsoft Excel® 2016 spreadsheet, extracting relevant information for their categorization, description, and interpretation. The systematization, treatment, and analysis of the articles were independently carried out by two researchers. The following information was extracted: title, language, study design, country and year of publication, main results, and conclusions.

Table 1 depicts the title, language, study design, country and year of publication, whereas Table 2 provides a summarized description of the main results and conclusions of each study.

As an integrative review, this research did not require submission to a research ethics committee. Furthermore, the ideas of the authors of the publications used in the development of this study were maintained.^{16,18}

RESULTS AND DISCUSSION

Thirty-two were selected for this integrative review, all of which were extracted from PubMed. A study from 1997 (3.1%) was identified, whereas the others were distributed between 1993 and 2021, and all studies were written in English, as shown in Table 1.

As for the study design, 22 (68.8%) were identified as documentary studies, 05 cohort (16.7%), 02 randomized, 02 literature revision (each representing 6.2%) and 01 study multicenter (3.1%).

These findings evidenced a concern in several countries to develop studies on risk factors for CRBSIs in cancer patients.

It is noteworthy that the studies associated the occurrence of these infections with a significant increase in hospital costs to the health system. 15,23-25 The patient's health can be affected both directly and indirectly by the infection. 7,14 In addition to directly attributable morbidity, CRBSIs may cause critical delays in the treatment of underlying malignancies, resulting in delayed chemotherapy, prolonged hospitalization, and, sometimes, central catheter removal or replacement. 26,27

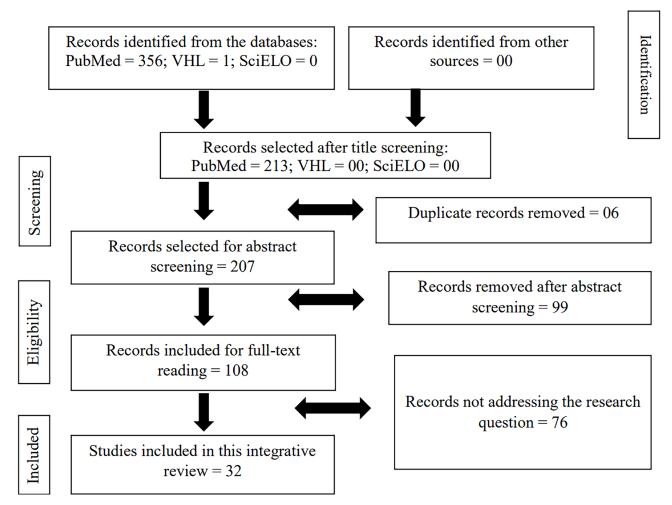


Figure 1. Research flowchart.



Table 1. Title, language, study design, country, and year of publication.

	TITLE	LANGUAGE	KIND OF STUDY	YEAR/COUNTRY
P1	Comparison of outcomes of central venouscatheters in patients with solid and hematologic neoplasms: an Italian realworldanalysis	English	Cohort study	ltaly/2020
P2	Risk factors for peripherally inserted central catheter (PICC)-associated infections in patients receiving chemotherapy and the preventive effect of a self-efficacy intervention program: a randomized controlled trial	English	Randomized clinical trial	China/2021
Р3	Risk factors for central line-associated bloodstream infection in pediatric oncology patients with a totally implantable venous access port: A cohort study	English	Cohort study	USA/2017
P4	Risk factors for infectious and noninfectious complications of totally implantable venous catheters in cancer patients	English	Documentary study	Brazil/2016
P5	Long-Term Central Venous Catheter Use andRisk of Infection in Older Adults With Cancer	English	Documentary study	USA/2014
P6	Risk factors for infection of adult patients withcancer who have tunnelled central venous catheters	English	Cohort study	USA/1995
P7	Incidence and risk factor for infection oftotally implantable venous access port	English	Documentary study	China/2021
P8	Bloodstream infection in paediatric cancercentres- leukaemia and relapsed malignancies are independent risk factors	English	Documentary study	Switzerland 2015
P9	Candida tropicalis bloodstream infection: Incidence, risk factors and outcome in a population-based surveillance	English	Documentary study	Spain/2015
P10	Late complications of totally implantablevenous access ports in patients with cancer: Risk factors and related nursing strategies	English	Documentary study	USA/2018
P11	Catheter-associated bloodstream infectionincidence and risk factors in adults with cancer: a prospective cohort study	English	Cohort study	England/2011
P12	Risk of thrombosis and infections of central venous catheters and totally implanted accessports in patients treated for cancer	English	Documentary study	USA/2010
P13	Central Line–Associated Bloodstream Infection in Hospitalized Children with Peripherally Inserted Central Venous Catheters: Extending Risk Analyses Outside the Intensive Care Unit	English	Documentary study	USA/2011
P14	Risk Factors for Early Port Infections in Adult Oncologic Patients	English	Documentary study	USA/2020
P15	The pathogenesis and prevention of central venous catheter-related infections	English	Documentary study	USA/1994
P16	Propensity score analysis confirms the independent effect of parenteral nutrition on the risk of central venous catheter-related bloodstream infection in oncological patients	English	Documentary study	USA/2012

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	TITLE	LANGUAGE	KIND OF STUDY	YEAR/COUNTRY
P17	Total parenteral nutrition is a major risk factor for central venous catheter-related bloodstream infection in colorectal cancer patients receiving postoperative chemotherapy	English	Documentary study	Japan/2008
P18	Impact of chest subcutaneous fat on the occurrence of central venous port-related infectious complications in cancer patients	English	Documentary study	Japan/2021
P19	A Model to Predict Central-Line–Associated Bloodstream Infection Among Patients With Peripherally Inserted Central Catheters: The MPC Score	English	Documentary study	USA/2017
P20	Risk factors for early catheter-related infections in cancer patients	English	Documentary study	USA/2007
P21	Clinical Predictors of Port Infections in Adult Patients with Hematologic Malignancies	English	Literature revision	USA/2018
P22	Low infection rate and long durability of nontunneled silastic catheters. A safe and costeffective alternative for long-term venous access	English	Literature revision	USA/1993
P23	Late complications associated with totally implantable venous access port implantation via the internal jugular vein	English	Documentary study	Japan/2020
P24	Risk determinants for catheter-associated blood stream infections in children and young adults with cancer	English	Documentary study	USA/2008
P25	Catheter-Related Complications in Children With Cancer Receiving Parenteral Nutrition: Change in Risk Is Moderated by Catheter Type	English	Cohort study	USA/2017
P26	Central venous catheter-related sepsis in a cohort of 366 hospitalised patients	English	Documentary study	Italy/1997
P27	Factors influencing central line infections in children with acute lymphoblastic leukemia: results of a single institutional study	English	Randomized clinical trial	Saudi Arabia/2004
P28	Conditions associated with infections of indwelling central venous catheters in cancer patients: a summary	English	Documentary study	Italy/2003
P29	Evaluation of infectious complications of the implantable venous access system in a general oncologic population	English	Documentary study	China/2003
P30	Bloodstream infection in paediatric cancer centres - leukaemia and relapsed malignancies are independent risk factors	English	Multicenter study	Germany/2015
P31	Mechanical and infective central venous catheter- related complications: a prospective non-randomized study using Hickman and Groshong catheters in children with hematological malignancies	English	Documentary study	ltaly/1997
P32	Surveillance with successful reduction of central line-associated bloodstream infections among neutropenic patients with hematologic or oncologic malignancies	English	Documentary study	Germany/2009



Table 2. Summarized description of the main results and conclusions of each study.

	RESULT	SUMMARY OF CONCLUSIONS
P1	130 peripherally inserted central venous catheters - PICC (73%) and 48 implanted central venous	Peripherally inserted central venous catheters were associated with a higher risk of infectious
	catheters (27%) were analyzed. The overall rate of infectious complications was significantly increased in the PICC compared to as an implanted catheter	complications compared to central venous catheters. The choice of catheter in cancer patients should be guided by the type and duration of treatment, risk-benefit assessment, patient preferences and adherence
P2	Among the 159 chemotherapy patients, 26 (16.35%) had infections associated with PICC (peripherally inserted central catheter). PICC length of stay, diabetes history, and immunity were significantly related asrisk factorsfor PICC - associated infections	PICC length of stay, history of diabetes, and immunity are risk factors for PICCassociated infections.
P3	Overall, 188 children were evaluated over 77,541 catheter days, 50% diagnosed with central lineassociated bloodstream infection in pediatric cancer patients.	Risk factors for line-associated bloodstream infection in cancer patients with can be related to malnutrition and bone marrow aplasia, which can increase the risk of line-associated bloodstream infection
P4	We studied 1,255 implanted central catheters inserted in 1,230 patients, for a combined total of 469,882 catheter-days of use. Regarding the site of introduction, patientsin which the femoral vein was the access site had more infections than the others (28.6% vs 9.4%)	Central venous catheter implantation in hospitalized patients and the use of femoral access are risk factors for infection
P5	Exposure to central venous catheters was associated with a significantly increased risk of infection. For elderly patients, the risk of infections during the exposure period was three times greater	associated with an increased risk of infections for older adults with cancer
P6	Neutropenia was significantly associated with the risk of catheter-related infection	Neutropenia was the only risk factor for infection related to central venous catheters
P7	A total of 3,001 central venous accesses were implanted in 2,897 patients, and the mean followup time was 424 days, reaching a combined total of 1,648,731 catheter days. 198 had infection	The implantation of central venous accesses in hospitalized patients combined with the performance of surgeries are associated with high rates of infections
P8	Included 770 paediatric cancer patients. One The study included 770 patients. One hundred and forty-two patients had at least one bloodstream infection (179 bloodstream infections. In 57%, bloodstream infection occurred in hospitalized patients, in 79% after chemotherapy	This study confirmed recurrence of malignancy as a risk factor for bloodstream infection in cancer patients using central venous catheters
P9	Fifty-nine out of 752 bloodstream infections. Early removal of the central venous catheter exerted a protective effect against bloodstream infection	Infection was associated with advanced age, hematologic malignancy, and respiratory comorbidity
P10	This study included 500 patients. The cumulative maintenance period for fully implanted central venous access devices was 159,605 days	Risk factors for infection included age and certain types of cancer, such as breast cancer, lung cancer, and gastric cancer
P11	Among the 473 central venous catheters placed, infections developed in 53 patients (12%)	Neutropenia and non-administration of prophylactic antibiotics were risk factors for the development of central venous catheter infection in cancer patients
P12	Device characteristics, device management aspects, administration of therapies, and clinical conditions of selected patients represented the main risk factors for long-term catheter-related infection in cancer patients	Identifying risk rate factors is pivotal to support evidence-grounded preventive strategies and maximize cancer patient safety
P13	Long catheter length of stay, ICU exposure, and administration of parenteral nutrition were important risk factors for bloodstream infection associated with central venous catheters in hospitalized patients	patients hospitalized with central venous catheters
P14	A total of 20 patients (1.2%) had infections and the mean infection time was 20 days	Hematologic malignancy, hypoalbuminemia, leukopenia, and diabetes mellitus at the time of catheter placement were factors for infections

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contir	RESULT	SUMMARY OF CONCLUSIONS
P15	The skin and the catheter hub were the two main sources of introduction of colonizing organisms. Both microbial and host factors contributed to the formation of the biofilm that was essential for adherence and maintenance of colonization. Staphylococcus and Candida were the main causative agents	for infections
P16	Patients with parenteral nutrition were at a higher risk for central venous catheter related bloodstream infection	This study confirmed that parenteral nutrition was a risk factor for central venous catheter-related bloodstream infection in cancer patients
P17	One hundred nine patients received 542 central venous cathetersfor a total of 5,558 catheter-days. Administration of parenteral nutrition was the only risk factor for central venous catheter-related bloodstream infection	Parenteral nutrition was an important risk factor for central venous catheter-related bloodstream infection in cancer patients receiving postoperative chemotherapy
P18	Within a median follow-up of 306 days, patients had significantly longer infection-free survival than those with low and high amounts of subcutaneous tissue	Low amount of subcutaneous fat in the midclavicular line was a risk factor for infectious complications in the chemotherapy setting
P19	Significant risk factors associated with central catheter-associated bloodstream infections included hematologic cancer, multilumen peripherally inserted central catheters (PICC), receiving total parenteral nutrition through the PICC, and the presence of another central venous catheter at the time of PICC placement	Future studies are needed so that appropriate interventions aimed at preventing these infections are carried out.
P20	Over 10,392 days of catheterization, 14 of 371 patients had catheter-related infections	Were identified 2 variables that were associated with a high risk of developing an early catheter-related infection: young age and difficulties during insertion
P21	The total duration of the segment was 83,722 catheterdays. Catheter infections were identified in 34 patients	Hypoalbuminemia at the time of catheter placement and steroid use were a predictor of infections
P22	The mean in-place duration of the catheter for the 359 nontunneled central venous catheter studied was 109 days, and the infection rate was 0.13 per 100 catheter days	
P23	The analysis revealed that age over 65 years was a significant unfavorable factor for complications related to fully implantable venous accesses.	Patients older than 65 years had a significantly high risk of infectious complications related to fully implantable venous access ports.
P24	Fifty-eight catheter-associated bloodstream infections were identified in 139 patients over a 35,935-day period of central venous catheterization	Hospitalized cancer patients are at increased risk of developing catheterassociated bloodstream infections
P25	The risk of central catheter-associated bloodstream infection was higher during parenteral nutrition for patients with a central venous catheter	Cancer patients receiving parenteral nutrition are at increased risk of central catheter-associated bloodstream infection
P26	Over a total of 6,428 days of catheter use, the infection rate was 0.8 cases of sepsis per 100 catheter days	Neutropenia and administration of parenteral nutrition are risk factors for catheter-related infection
P27	The overall rate of infectious episodes (infections/1000 catheter days) was 3.43	Age was the risk factor
P28	Infections in indwelling central venous catheters have been determined by many different factors	The number of central venous catheter manipulations represented the most important risk factor for the development of central venous catheter related infections
P29	The average duration for ports after placement in patients was 358 days (range, 1-1742 days), and the median duration was 242 days	The administration of parenteral nutrition and central venous catheter manipulations were a relevant risk factor for developing infection
P30	This study included 770 cancer patients. Comprising 153,193 individual surveillance days. One hundred and forty-two patients (18%; suffered at least one nosocomial bloodstream infection	This study confirms relapsed malignancy as an factor for bloodstream infection
P31	At the end of the observation period, 54 central venous catheter patients were analyzed. No patients died from device-related complications	The neutropenia was the most important risk factor for the outbreak of infections
P32	A total of 268 patients were followed up. During the entire study period, there were no changes in the treatment protocol for infection prevention	The duration of neutropenic phases caused by chemotherapy represented an important risk factor for acquiring nosocomial



Therefore, a reduction in the infection rate could contribute to not only an improvement in the patient's general health condition but also a decrease in the need for medications and wound dressings, allowing professionals to spend more time in other patient-focused activities.^{23,28}

Among the risk factors for CRBSI, the malignancy of the cancer,⁷ the time between catheter implantation and removal,³⁰ were cited. However, the most prevalent mentioned (25%) risk factor were the care and handling of the central catheters (21.9%) and the administration of parenteral nutrition.^{23,26,31-33}

Parenteral nutrition is known as a high-risk factor for central venous catheter-related bloodstream infection.^{11,15} A significantly greater chance of developing an infection occurs when a central catheter is used for the administration of parenteral nutrition.^{10,42}

Rosado et al. (2011)⁷ stated that shorter catheterization time accounts for a reduction in the risk of infection. When the catheter is inserted and removed within less than 10 days, microbial biofilm formation is normally observed only on the external surface of the tube; however, at longer catheterization periods, these microorganisms may reach and colonize the inner lumen of the catheter.34 Considering that catheters usually need to be kept for long periods,35 preventive measures must be taken to avoid the formation of biofilm, such as the use of aseptic technique for the insertion of the CVC, its immediate removal when the device is no longer needed and even the use of catheters impregnated with antimicrobials.³⁶ Inadequate insertion and handling techniques have been identified as the main causes of CRBSI, which may reflect the lack of institutional training of the multidisciplinary team regarding aseptic care related to the catheter.^{37,38} In addition, low adherence to hand hygiene has been associated with high rates of CRBSI, also highlighting the importance of adequate team training.^{39,40}

Some studies also investigated the microbial composition of the biofilms in CVCs, revealing a predominant presence of gram-positive microorganisms, such as *Staphylococcus aureus* and coagulase-negative staphylococci (bacteria) and *Candida albicans* (yeast), especially in immunocompromised patients with prolonged catheterization.⁹ It is important to highlight that *Candida* spp. has been increasingly identified in bloodstream infections, especially in more recent studies, thereby warranting further in-depth investigations.⁴¹

CRBSIs are commonly associated with high mortality (estimated at around 25%), longer hospital stay (seven days longer, on average), and increased health care costs for cancer patients.^{3,7,42} Therefore, the practice of evidence-based interventions that can contribute to reducing the risk of infection combined with further research on the pathogenesis of CVC-related infections is essential to improve the quality of care in oncology.⁷

CONCLUSION

The analysis of the current scientific data available on risk factors for central venous catheter infection in cancer patients enabled the identification and discussion of the main characteristics associated with this topic.

Hence, in this integrative review, the main factors identified as directly or indirectly favoring the onset of infections associated with CVCs in cancer patients were the handling of the central catheters by professionals and the administration of parenteral nutrition were the main risk factors for CVC infections.

The current literature has presented extended discussions on nosocomial infections, which constitute a serious and recurrent public health problem, and growing concernregarding this subject was demonstrated in the included studies. This process motivates health professionals to discover new methods of prevention and control of cross infections to ensure the quality of care provided to the patients, thereby favoring a reduction in hospitalization time and hospital costs.

Research followed by scientific production is essential to understand and intervene in the health-disease process and successfully modify the reality of the hospitals, contributing to patient safety. On that account, more research and studies related to this subject, at regional and worldwide levels, are necessary to disseminate knowledge and awareness among health professionals during CVC-related procedures.

AUTHORS' CONTRIBUTIONS

ECBB: Conception and design, Manuscript writing.

FSC: Data analysis and interpretation, Final approval of manuscript.

FNC: Data analysis and interpretation, Final approval of manuscript.

FWGC: Data analysis and interpretation, Final approval of manuscript.

ANBC: Data analysis and interpretation, Final approval of manuscript.

CMM: Data analysis and interpretation, Final approval of manuscript.

MRRRC: Data analysis and interpretation, Final approval of manuscript.

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