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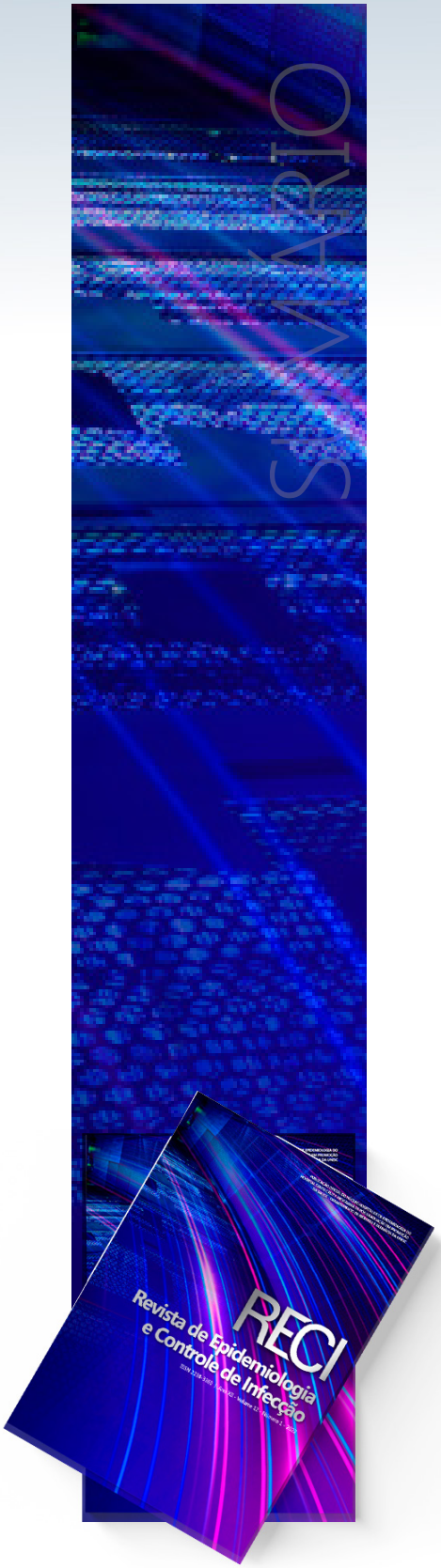
SUMÁRIO



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Hospital Santa Cruz

ORIGINAL ARTICLE

Characterization of healthcare-related infections in an adult intensive care unit

Caracterização das infecções relacionadas a assistência à saúde em unidade de terapia intensiva adulto

Caracterización de las infecciones relacionadas con la asistencia sanitaria en una unidad de cuidados intensivos para adultos

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ABSTRACT

Background and Objectives: Infections related to health care have gradually increased in recent years and occurs more often in intensive care units than in other hospital admissions. The characteristics of the population and infections must be assessed to develop and apply preventive measures. Therefore, we aimed to characterize infections related to health care in patients in an adult intensive care unit in 2019. **Methods**: A quantitative, descriptive and retrospective study, performed in the adult intensive care unit of a reference, regional and tertiary hospital in the countryside of the state of São Paulo. We included data from patients over 18 years old who were in the adult intensive care unit of that hospital and diagnosed with infections officially related to health care in 2019. The data were analyzed by the descriptive statistics, Student's t-test for quantitative variables and Pearson's chi-square test for the categorical ones. The study was approved and excused of the written informed consent form (WICF) by the Human Research Ethics Committee. **Results:** The participants' mean age was 55.6 years old (19.7 standard deviation), affecting mostly men (64%) and with comorbidities (72%), and the systemic arterial hypertension was the most prevalent one (43%). Regarding procedures and devices, most were on mechanical ventilation (87%), sedated (77%), using an indwelling urinary catheter (96%) and with a central venous catheter (94%). The isolated microorganism with the highest incidence was *Klebsiella Pneumoniae* (9%). Vancomycin was the most used antibiotic against microorganisms (66%). As an outcome, 47% of patients were discharged and 53% died. **Conclusion:** *Klebsiella Pneumoniae* was the most prevalent microorganism as well as the respiratory tract infections. The age was the only variable related to the outcome.

Keywords: *Infection control. Nursing. Critical care.*

RESUMO

Justificativa e Objetivos: as infecções relacionadas à assistência à saúde aumentaram gradativamente nos

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últimos anos e sua ocorrência em unidades de terapia intensiva é maior que em outras internações hospitalares. Para desenvolver e aplicar medidas preventivas é necessário primeiramente conhecer as características da população atendida e das infecções; assim o objetivo foi caracterizar as infecções relacionadas à assistência à saúde nos pacientes internados em Unidade de Terapia Intensiva Adulto em 2019. **Métodos:** estudo quantitativo, descritivo, retrospectivo realizado em Unidade de Terapia Intensiva Adulto de um hospital de referência, regional e terciário no interior do estado de São Paulo. Foram incluídos dados de pacientes maiores de 18 anos que estiveram internados nas Unidades de Terapia Intensiva Adulto do referido hospital, com diagnóstico confirmado de infecções relacionadas à assistência à saúde em 2019. Os dados foram analisados por meio de estatística descritiva, teste t de *student* para as variáveis quantitativas e Qui-quadrado de Pearson para as categóricas. O trabalho foi aprovado com dispensa do Termo de Consentimento Livre e Esclarecido (Tcle) pelo Comitê de Ética em Pesquisa com Seres Humanos. **Resultados:** a média de idade dos participantes foi de 55,6 anos (desvio padrão 19,7) com acometimento maior no sexo masculino (64%) e com comorbidades (72%), sendo hipertensão arterial sistêmica a mais prevalente (%). Quanto aos procedimentos e dispositivos, a maioria estava em ventilação mecânica (87%), sedado (77%), em uso de sonda vesical de demora (96%) e com cateter venoso central (94%). O microrganismo isolado com maior incidência foi *Klebsiella Pneumoniae* (9%). O antibiótico mais utilizado para combater os microrganismos foi Vancomicina (66%). Como desfecho, 47% dos pacientes tiveram alta e 53% evoluíram para o óbito. **Conclusão:** Dentre as infecções analisadas, o microrganismo mais prevalente foi a *Klebsiella Pneumoniae* e as infecções do trato respiratório foram as mais prevalentes; a idade foi a única variável relacionada ao desfecho.

Descritores: *Controle de Infecções. Enfermagem. Cuidados Críticos.*

RESUMEN

Justificación y objetivos: las tasas de infecciones relacionadas con la asistencia sanitaria se han incrementado paulatinamente en los últimos años, y su incidencia en unidades de cuidados intensivos es mayor que en las demás unidades. Considerando que para desarrollar y aplicar medidas preventivas, es necesario conocer las características de la población atendida y las infecciones, el objetivo de este estudio fue caracterizar las infecciones relacionadas con la atención de salud en pacientes hospitalizados en una Unidad de Cuidados Intensivos de Adultos en el año 2019. **Métodos:** estudio cuantitativo, descriptivo, retrospectivo realizado en el sector de cuidados intensivos para adultos de un hospital regional de referencia terciario en el interior del estado de São Paulo. Se incluyeron datos de pacientes mayores de 18 años que fueron hospitalizados en las unidades de cuidados intensivos para adultos de ese hospital y que tenían un diagnóstico confirmado de infecciones relacionadas con la asistencia sanitaria en 2019. **Resultados:** La edad media de los pacientes fue de 55,6 años (desviación estándar 19,7) con mayor afectación en varones (64%) y con comorbilidades (72%), de las cuales la hipertensión arterial sistémica fue la más prevalente. En cuanto a los procedimientos y dispositivos, la mayoría fue con ventilación mecánica (87%), sedación (77%), con catéter urinario permanente (96%) y con catéter venoso central (94%). El microorganismo aislado con mayor incidencia fue Klebsiella Pneumoniae (9%). El antibiótico más utilizado para combatir los microorganismos fue la vancomicina (66%). Como resultado, el 47% de los pacientes fueron dados de alta, y el 53% falleció. **Conclusión:** La estadía promedio fue de 16.8 días, la tasa de mortalidad del 53% y el microorganismo más encontrado la Klebsiella Pneumoniae (9%). Las infecciones del tracto respiratorio fueron las más prevalentes, y la edad fue la única variable relacionada con el resultado.

Palabras clave: *Control de Infecciones. Enfermería. Cuidados críticos.*

INTRODUCTION

Intensive Care Units (ICUs) have high technological complexity that receive patients with severe morbidities and dysfunctions, requiring continuous monitoring and complex care. Since it is characterized as a critical area, with unstable patients, There is a high risk of developing infections related to health care (IRHC).[1,2] IRHC, classified as adverse events, are infections acquired during health care and represent one of the largest public health problems, with high morbidity and mortality.[3]

IRHC can start in many foci, such as respiratory, bloodstream, or urinary tract. Among them, the ones in the respiratory tract are the most complicated, such as pneumonia (PNM) and respiratory disorders due to orotracheal intubation, such as ventilator-associated tracheobronchitis (VAT) and ventilator-associated pneumonia (VAP). These infections are defined by their occurrence after 48 hours of intubation and have an incidence of 5 to 15% in ICUs with high mortality.[4-7]

IRHC also includes bloodstream-associated infections that usually occur in two situations, primary bloodstream infections (BSI) and vascular access infections (VAI). In the first case, the infections are associated with the catheter and develop severe consequences, such as bacteremia or sepsis. VAI, in turn, occurs at the catheter insertion place, without systemic repercussion.[8]

Health care in ICUs increases the costs of the hospital, since it uses many high-cost drugs, requires a specialized and numerous team, and uses more frequent and high-tech care tests.[9-11] Prevention is then essential,

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considering the costs of this type of hospitalization, reduced availability of beds and the increase in hospital stay caused by an infection.

The IRHC that affect ICU patients relate to the clinical severity of these patients, the use of many invasive devices and immunosuppressants, long hospital stay and reckless use of antimicrobials. Besides, the environment of these units provides a natural selection of several microorganisms, which causes microbial resistance.[2,12]

The rates of these infections have gradually increased in recent years. They are mainly responsible for the lethality from hospital infections of ICU patients and more prevalent in these sectors. The broad therapeutic care and the peculiarities of care of ICU patients associate with many conditions for the dissemination of resistant pathogens, increasing the possibility of contamination from these infectious agents.[1,2,13]

Due to the severity of IRHC and its high cost, health care providers increased their initiatives to reduce incidence, thus improving the quality of care. Permanent education and teaching strategies for the teams are part of the initiatives.[14]

Therefore, prevention measures are essential for safe and qualified care; however, the characteristics of the population and the infections must be assessed to develop and apply these preventive measures. Thus, our study aims to characterize infections related to health care in patients in an adult ICU in 2019.

METHODS

This is a quantitative, retrospective and descriptive study. The main purpose of a descriptive study is to characterize a phenomenon or population and establish a relationship between the variables. One of its characteristics is the use of the data collection technique, such as the questionnaire and systemic observation. This design portrays facts, indicates their frequency and qualifies the information.[15,16]

The study was developed in the adult ICU of a reference, regional and tertiary hospital in a city in the countryside of the state of São Paulo. The hospital has two adult ICUs, one specific for cardiovascular pathologies and one general ICU, with ten beds for each ICU. The collection was based only on the data from the general ICU. All patients from the database of the Service Control for Infections Related to Health Care (SCIRAS) over 18 years old, who were admitted to the hospital's ICU and diagnosed with IRHC in 2019, were included.

After prior training and under supervision of a researcher, SCIRAS database was explored by two other researchers to find patients who met the established criteria.

This survey was conducted for three days with the aid of an instrument to obtain the following variables: initial focus, treatment, outcome, gender, age, days of ICU stay, associated morbidities, use of mechanical ventilation, sedation, central venous catheter, indwelling urinary catheter, isolated microorganisms, other microorganisms and sensitivity profile.

The recorded data were entered in spreadsheets of the Microsoft Excel program® and then analyzed by descriptive statistics, the Student's *t*-test for quantitative variables and Pearson's chi-square test for categorical ones using IBM SPSS Statistics 22 software®. A 5% significance level (α) was considered.

This study was approved by the Human Research Ethics Committee of the Centro Universitário Central Paulista (CAAE: 32830020.5.0000.5380), according to opinion number 4,125,815, and required no written consent.

RESULTS

In 2019, we identified 47 patients with IRHC admitted to the general adult ICU of the study hospital, in which some were diagnosed with more than one infection. The mean age among patients was 55.6 years old (19.7 standard deviation), mostly men (64%), and the mean length of hospital stay was 16.8 days (13.24 standard deviation). As an outcome, 47% were discharged, and 53% died.

Table 1 shows that the age of the patients relates to the outcome (p = 0.049), based on the relationship between outcome and age, hospital stay and days of sedation. With higher mortality for patients with older age.

Table 1. Description of the relationship between the outcome and age, hospital stay and days of sedation among patients admitted to the adult ICU, São Carlos, SP. 2020.

	Discharge	Death	p value*
Age			
Mean	49.65	60.92	0.049
Standard deviation	20.511	17.715	
Hospital stay			
Mean	15.59	17.96	0.547
Standard deviation	13.968	12.762	
Days of sedation			
Mean	4.09	2.96	0.352
Standard deviation	5.145	2.937	

**Student's t-test*

The patients' main comorbidities were: Systemic arterial hypertension (SAH) (43%), stroke (26%), respiratory disorders (19%), diabetes mellitus (17%), heart diseases (13%), renal insufficiency (11%), and obesity (9%); although 13 patients (28%) did not present this data in medical records.

Most patients were on mechanical ventilation (87%), sedated (77%) — the mean days of sedation was 4.58 (4.12 standard deviation) —, using an indwelling urinary catheter (96%) and a central venous catheter (94%).

Most infections identified were VAT (38%), followed by VAP (28%), pneumonia (PNM) (21%) and bloodstream-associated infections (10%).

The main isolated microorganism was *Klebsiella Pneumoniae* (KPC) (9%), followed by *Pseudomonas Aeruginosa* (6%), *Acinetobacter Baumannii* (4%),

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Streptococcus PNM (4%), *Staphylococcus Aureus S.* (4%), *Pseudomonas Fluorescens S.* (2%), *Staphylococcus Epidermidis* (2%), *Streptococcus Aureus* (2%) and *Serratia Marcescens* (2%). Among the patients, 30 (64%) did not present growth of an isolated microorganism in culture.

Table 2 describes the analysis of the relationship between outcomes and variables of gender, infectious focus, mechanical ventilation, central venous catheter, indwelling urinary catheter and isolated microorganism, without significant association.

Table 2. Description of the relationship between the outcome and age, hospital stay and days of sedation among patients admitted to the adult ICU, São Carlos, SP. 2020.

	Discharge % (n)	Death % (n)	p value*
Gender			
Male	27.65 (13)	36 (17)	0.558
Female	19 (9)	17 (8)	
Main infectious focus			
VAP	9 (4)	19 (9)	0.505
PNM	11 (5)	11 (5)	
VAT	17 (8)	21 (10)	
BSI-C	2 (1)	0	
BSI-Lab	4 (2)	2 (1)	
VAI	2 (1)	0	
Mechanical ventilation			
Yes	40 (19)	45 (21)	0.820
No	6 (3)	9 (4)	
Central venous catheter			
Yes	43 (20)	49 (23)	0.894
No	4 (2)	4 (2)	
Indwelling urinary catheter			
Yes	45 (21)	51 (24)	0.926
No	2 (1)	2 (1)	
Isolated microorganism			
Staphylococcus Aureus S.	2 (1)	2 (1)	0.250
Pseudomonas Fluorescens S.	0	2 (1)	
Pseudomonas Aeruginosa	0	6 (3)	
Streptococcus PNM	0	4 (2)	
Staphylococcus Epidermidis	0	2 (1)	
Acineto Baumannii	0	4 (2)	
Streptococcus Aureus	2 (1)	0	
Klebsiella pneumoniae	4 (2)	4 (2)	
Serratia	2 (1)	0	
Absent	36 (17)	28 (13)	

**Pearson's Chi-square test*
VAP: Ventilator-Associated Pneumonia; PNM: Pneumonia; VAT: Ventilator-Associated Tracheobronchitis; BSI-C: Primary Bloodstream Infection - Clinical; BSI-Lab: Primary Bloodstream Infection - Laboratorial; VAI: Vascular Access Infection.

The main antibiotics were used to treat the infections. Vancomycin (66%), Clindamycin (60%), Meropenem (55%), Gentamycin (40%), Polymyxin (34%), Oxacillin (26%), Clavulin (23%), Rocefin (17%), Cefuroxime (13%) and Amikacin (13%).

DISCUSSION

The high prevalence of these infections often influences an unfavorable outcome for the patients in this unit.[17,18] In our study, the mean hospital stay was 16.8 days. The literature describes that prolonged hospital stay may contribute for the development of new infections or worsening in the clinical condition.[2]

In our study, infections were prevalent in men, contrary to other similar studies, which showed prevalence in women (60%).[18] This data may relate to a regional characteristic of the population assisted in that hospital.

The literature[19] describes that the presence of comorbidities among patients can increase by approximately twice the risk of death.

In the study by Oliveira et al.,[2] they found the microorganisms *Acinetobacter Baumannii* (36.3%), followed by *Klebsiella Pneumoniae* (11%). Compared to another study,[20] the main microorganisms associated with the etiology of hospital infections were *S. Aureus* (12.98%), *A. Baumannii* (9.61%) and *Klebsiella sp* (4.32%). The results of these other studies differ from our study regarding the predominant microorganisms, possibly because of the characteristics of each health service.

The carbapenemases-producing *Klebsiella Pneumoniae* (KPC), is a bacterium restricted to the hospital environment. Its main characteristic is the production of a betalactamase enzyme called carbapenemase, which inhibits carbapenem antibiotics. This bacterium can cause IRHC in immunosuppressed patients and in the ICU patients who have multiple entry routes for contamination that facilitate infection by multidrug-resistant bacteria.[21]

Other similar studies showed data on the antibiotic resistance profile for the treatment of infections, in which the most resistant ones were Imipenem (15.59%), Amikacin (14.65%), Ceftazidime (12.35%), Vancomycin (12.35%) and Ceftriaxone (8.33%).[22]

Regarding invasive devices, only one patient did not use it, while the others used at least one device, such as an indwelling urinary catheter (96%), central venous catheter (94%) and mechanical ventilation (85%). Comparing these data with a similar study, we observed that most patients also used invasive procedures and devices, such as indwelling urinary catheters (70%), mechanical ventilation (49.9%) and central venous catheters (49.6%), which confirm their high rate of use in intensive care.[2]

Most infections in our study occurred due to ventilation-associated tracheobronchitis (VAT), based on the analysis of rates and characteristics. Another study described respiratory tract infections as the most prevalent ones (65.3%), followed by bloodstream infections (17.8%) and urinary tract infections (16.9%),[22] which is similar to our study. Respiratory tract infections are mainly caused by inoculation of the pathogen in the patient's respiratory tract. Intubated patients lose the natural anatomical barrier between the oropharynx and trachea, removing the cough reflex and accumulating secretions, which allows greater colonization and aspiration of contaminated secretions to the lower airways. The long use of mechanical ventilation in patients with orotracheal

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intubation is associated with an increase in morbidity and mortality in the ICU.[2]

The outcome of our study showed that 47% of the patients were discharged and 53% died. Age was the only variable significantly related to the outcome (p = 0.049), with higher mortality in individuals over 60 years old. A similar study found a higher incidence of infections in older adults, but without a significant relationship with the outcome.[18] Another study also showed a higher prevalence of infections in patients over 50 years old and, as in our study, and obtained a significant relationship between outcome and age, which suggests an increase in mortality associated with older adults.[19] Aging is considered a risk factor for infections related to health care, especially respiratory tract infections. The physiological changes in this process may hinder early diagnosis and worsen the infectious condition[23-24].

As a limitation of our study, we cite the absence of some data in the records of some patients, such as comorbidities and isolated microorganism in the initial focus, resulting in gaps of information.

As implications for the practice, we emphasize that this type of study allows the identification of the hospital's profile of infections and to direct prevention actions for quality care, with an efficient and effective multidisciplinary team.

We aimed to characterize infections related to health care in patients admitted to an adult ICU in 2019, which contributes to support other studies on infection control, by demonstrating the importance and value of an efficient SCIRAS in hospitals, with the participation of health care providers to avoid major care-related problems and possible infectious complications.

The mean length of hospital stay was 16.8 days for patients with hospital infections. Mortality was 53% among patients, and discharge, 47%. The most common resistant microorganisms responsible for infections were *Klebsiella Pneumoniae* (KPC) (9%), followed by *Pseudomonas Aeruginosa* (6%). VAT was the most prevalent infection, affecting 38% of patients, followed by VAP (28%) and pneumonia (21%). We concluded that the mean age was the only prevalent variable to the outcome of the patients' clinical condition. Therefore, we note the importance of preventive actions toward patients aged ≤ 60 years of age, and those intubated and tracheostomized in ICUs.

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ORIGINAL ARTICLE

The consequences Sars-CoV-2 pandemic on medical education in the combat leprosy

As consequências da pandemia de Sars-CoV-2 sobre a educação médica no combate à hanseníase

Las consecuencias de la pandemia de Sars-CoV-2 en educación médica en combate à lepra

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ABSTRACT

Background and objectives: Leprosy is an infectious disease in which early diagnosis is a decisive factor to prevent disability and disabilities. This study sought to analyze the panorama of leprosy between 2016 and 2021 in the state of Rio Grande do Sul and unveil the importance of medical education in the context of Neglected Tropical Diseases during the Sars-CoV-2 pandemic. **Methods:** Cross-sectional study using the State Center database of Health Surveillance of Rio Grande do Sul. In the data collection, were included leprosy data of individuals residents in the state of Rio Grande do Sul (RS), in the 2016 period 2021. The variables analyzed were confirmed leprosy cases, notified cases, the number of cases in terms of operational classifications of leprosy, the therapeutic scheme, and the number of cases according to the degrees of physical disability. **Results:** Over this period, 725 cases were confirmed as leprosy, 70% in the years 2016, 2017 and 2018. Of the total number of cases, 88% were Multibacillary form of the disease, 50% had some degree of disability at diagnosis time and 80% underwent the standard treatment regimen. **Conclusion:** There is a delay in leprosy diagnosis, and there is underdiagnosis of the disease in the state of Rio Grande do Sul: which highlights the need to reaffirm educational practices on mycobacteriosis.

Keywords*: Neglected Diseases. Leprosy. Diagnostic Errors. Education, Medical. Health Services Research.*

RESUMO

Justificativa e objetivos: A hanseníase é uma doença infectocontagiosa na qual o diagnóstico precoce é fator decisivo para prevenir incapacidade e deficiências. O presente estudo buscou analisar o panorama da hanseníase entre os anos de 2016 e 2021 no estado do Rio Grande do Sul, desvelando a importância da educação médica no contexto das Doenças Tropicais Negligenciadas durante a pandemia da Sars-CoV-2. **Métodos:** Estudo transversal por meio da base de dados do Centro Estadual de Vigilância em Saúde do Rio Grande do Sul. Na coleta de dados, foram incluídos os dados de hanseníase em indivíduos residentes do estado do Rio Grande do Sul (RS), no período de 2016 a 2021.

As variáveis analisadas foram os casos confirmados de hanseníase, os casos notificados, o número de casos quanto às classificações operacionais de hanseníase, o esquema terapêutico e o número de casos de acordo com os graus de incapacidade física. **Resultados:** No período analisado, foram confirmados 725 casos de hanseníase, sendo 70% nos anos de 2016, 2017 e 2018. Do número total de casos, 88% eram a forma multibacilar da doença, 50% apresentaram algum grau de incapacidade física no momento do diagnóstico e 80% realizaram o esquema terapêutico padrão. **Conclusão:** Existe atraso no diagnóstico de hanseníase e há subdiagnóstico da doença no estado do Rio Grande do Sul, o que evidencia a necessidade de reafirmação das práticas educacionais sobre a micobacteriose.

Descritores: *Doenças Tropicais Negligenciadas. Hanseníase. Erros de Diagnóstico. Educação Médica. Pesquisa sobre Prestação de Cuidados de Saúde.*

RESUMEN

Justificación y objetivos: La lepra es una enfermedad infecciosa en la que el diagnóstico precoz es un factor decisivo para prevenir la incapacidad y las discapacidades. Este estudio buscó analizar el panorama de la lepra entre 2016 y 2021 en el estado de Rio Grande do Sul y develar la importancia de la educación médica en el contexto de las Enfermedades Tropicales Desatendidas durante la pandemia Sars-CoV-2. **Métodos**: Estudio transversal con datos del Centro Estatal de Vigilancia en Salud de Rio Grande do Sul. La recolección de datos incluyó datos sobre lepra en individuos residentes en el estado de Rio Grande do Sul (RS), de 2016 a 2021. Las variables analizadas fueron casos confirmados de lepra, casos notificados, el número de casos en términos de clasificaciones operativas de lepra, el esquema terapéutico y el número de casos según los grados de discapacidad física. **Resultados:** En el período analizado se confirmaron 725 casos de lepra, 70% en los años 2016, 2017 y 2018. Del total de casos, 88% fueron la forma multibacilar de la enfermedad, 50% tenían algún grado de discapacidad física en el momento del diagnóstico y el 80% realizó el régimen terapéutico padrón. **Conclusiones:** Hay un retraso en el diagnóstico de la lepra y hay un infradiagnóstico de la enfermedad en el estado de Rio Grande do Sul: lo que pone de relieve la necesidad de reafirmar las prácticas educativas sobre micobacteriosis.

Palabras clave: *Enfermedades Desatendidas. Lepra. Errores Diagnósticos. Educación Médica. Investigación sobre Servicios de Salud.*

INTRODUÇÃO

Hanseníase é uma doença infectocontagiosa, granulomatosa e crônica, causada pelo bacilo *Mycobacterium leprae*, agente etiológico intracitoplasmático que afeta macrófagos e células de Schwann.[1] De forma predominante, apresenta manifestações cutâneas, nos nervos periféricos, na mucosa do trato respiratório superior, podendo resultar em neuropatia e consequências associadas a longo prazo. É transmitida através de gotículas respiratórias no ar durante o contato com doentes não tratados. São classificados, a depender do número de lesões na pele, como paucibacilares (PB) ou multibacilares (MB) - classificação operacional utilizada no território nacional.[2] A classificação pode variar conforme outros critérios empregados, tais como o número de lesões cutâneas, a presença de neuropatia e a presença de bacilos na biópsia de pele.[2,3] Por ser uma doença curável, o tratamento em estágios iniciais pode prevenir deformidades, incapacidades e estigma causado pela morbidade.

A redução da carga da doença é promovida através do diagnóstico precoce e tratamento completo com poliquimioterapia (PQT). O padrão terapêutico envolve os medicamentos Rifampicina, Clofazimina e Dapsona, sendo que a duração do tratamento depende do tipo de hanseníase e a dose depende da idade do paciente. As medidas mais eficazes no combate à hanseníase englobam a vacinação e/ou o uso de antibióticos profiláticos entre pessoas em exposição como forma preventiva de cuidado,[2,3] embora a quimioprofilaxia ainda não esteja em vigor no Brasil.

Artigos recentes demonstram a persistência da incidência da infecção: novos casos continuam a ocorrer, em especial nos cuidadores de pessoas institucionalizadas, os quais persistem apesar da eliminação da hanseníase como um problema de saúde pública – meta definida pela OMS de alcançar uma prevalência pontual abaixo de 1 caso por 10 mil habitantes.[4-9] Em 2016, mais de 200 mil novos casos de hanseníase foram relatados. Anualmente, 210 mil novos casos são reportados em todo o mundo, dos quais 15 mil são em crianças.[2] Com base nos 178.371 casos do final de 2019, a prevalência corresponde a 22.9 por milhão de pessoas.[10] Cerca de 3 a 4 milhões de pessoas já foram curadas, mas apresentam algum grau de desabilidade. Índia, Brasil e Indonésia apresentam, entre os países populosos, as maiores incidências,[11] representando 81% dos novos casos confirmados a nível global. Nesse cenário, 8,8% das notificações (18.869 pacientes) eram, em 2014, de crianças detectadas.[3] Mais de 2 mil pacientes diagnosticados naquele ano apresentavam deformidades visíveis causadas pela hanseníase.

Nota-se, assim, que o diagnóstico precoce e o tratamento são cruciais para mitigar o *Global Burden* da hanseníase. Doenças Tropicais Negligenciadas

(DTNs) são um conjunto de 20 enfermidades, incluindo a hanseníase, que afetam mais de 1 bilhão de pessoas, com consequências socioeconômicas devastadoras e impactos na saúde.[10,12] DTNs são importantes causas de morbidade, incapacidade e mortalidade em populações pobres e vulneráveis em diversos países ao redor do mundo, incluindo o Brasil.[3,8,9]

Ademais, no contexto da pandemia de Sars-CoV-2, a qualidade da educação foi negativamente afetada, com implicações na educação médica e reflexos sobre as habilidades necessárias para manejo adequado frente a um quadro de suspeita clínica da condição.[13] No Rio Grande do Sul, são esperados resultados similares no que se refere ao ensino médico. Diante disso, o presente estudo buscou analisar o panorama atual da doença entre os anos de 2016 e 2021 no Rio Grande do Sul a fim de desvelar a importância da educação médica no contexto das DTNs durante a pandemia de Sars-CoV-2, mediante análise fundamentada em base de dados secundários em face à epidemiologia da hanseníase nesse estado brasileiro.

MÉTODOS

Trata-se de um estudo observacional, retrospectivo, de abordagem quantitativa. Para o presente trabalho, utilizaram-se dados públicos, de livre acesso, coletados no sítio eletrônico do Centro Estadual de Vigilância em Saúde do Rio Grande do Sul (RS), na área de tabulações da vigilância epidemiológica. No que se refere à atualização de dados do Sistema de Informação de Agravos de Notificação (SinanNet), as últimas modificações foram inseridas no dia oito de julho de 2021, correspondendo, então, aos números parciais do ano em questão, com a análise feita a partir da ponderação desse adendo.

Dessa feita, foram analisados os casos confirmados de hanseníase em indivíduos residentes do estado do Rio Grande do Sul (RS), no período de 2016 a 2021. Ademais, analisaram-se as notificações dos casos de hanseníase (confirmados e descartados) em residentes do RS, de 2016 a 2021. Posteriormente, fez-se a comparação quantitativa entre os casos confirmados e descartados, a fim de mensurar possíveis erros de diagnóstico. Conforme os mesmos critérios, estendeu-se a análise à prevalência das classificações operacionais de hanseníase em paucibacilar e multibacilar e à prevalência dos graus de incapacidade física, com intuito de explorar a precocidade do diagnóstico e a efetividade das atividades de controle epidemiológico da patologia. Este escrito não necessitou passar por apreciação do comitê de ética em pesquisa, uma vez que utiliza dados de acesso público, conforme consta na resolução Nº 510 de 07 de abril de 2016 realizada pelo plenário do conselho nacional de saúde em sua quinquagésima nona reunião extraordinária.

RESULTADOS

A partir da análise do número de casos notificados em residentes no estado do Rio Grande do Sul, que incluem os confirmados e os descartados, observa-se que, dos 768 casos notificados, 725 foram confirmados, o que representa uma proporção de 94% da amostra de casos notificados como sendo confirmados para hanseníase (Tabela 1). Em números totais de casos notificados, 153 ocorreram no ano de 2016, 170 no ano de 2017, 184 no ano de 2018, 147 no ano de 2019, 82 no ano de 2020 e 32 até o mês de julho de 2021. Do total de casos confirmados, 70% ocorreram nos três primeiros anos analisados. O número de diagnósticos confirmados iniciou seu decréscimo no ano de 2018, o qual apresentou 185 confirmações, enquanto 2019, 2020 e 2021 apresentaram, respectivamente, 112, 78 e 27 casos diagnosticados como hanseníase.

Tabela 1. Casos Novos de Hanseníase notificados e confirmados (frequência de diagnóstico) segundo o ano de notificação no SinanNet no estado do Rio Grande do Sul, de 2016 a 2021.

Ano notificação	Notificações/frequência de diagnóstico
TOTAL	768/725
2016	153/150
2017	170/173
2018	184/185
2019	147/112
2020	82/78
2021	32/27

Quanto à classificação do tipo de hanseníase, a MB apresentou-se como a mais frequente, totalizando 639 casos, o que corresponde a cerca de 88% da amostra de casos confirmados, enquanto a PB foi responsável pelos

Tabela 2. Casos confirmados notificados conforme classificação operacional atual no SinanNet no estado do Rio Grande do Sul, de 2016 a 2021.

Ano diagnóstico	Paucibacilar	Multibacilar	Total
TOTAL	84	639	723
2016	12	137	149
2017	17	156	173
2018	17	168	185
2019	20	91	111
2020	12	66	78
2021	6	21	27

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Tabela 3. Casos confirmados notificados conforme terapia atual segundo o ano de diagnóstico no SinanNet no estado do Rio Grande do Sul, de 2016 a 2021.

Ano diagnóstico	Branco/Ign	Grau zero	Grau I	Grau II	Não avaliado	Total
TOTAL	45	274	207	156	43	725
2016	7	52	58	24	9	150
2017	7	68	51	37	10	173
2018	6	80	43	45	11	185
2019	10	42	29	25	6	112
2020	10	25	18	19	6	78
2021	5	7	8	6	1	27

Tabela 4. Casos confirmados notificados conforme avaliação da incapacidade segundo o ano de notificação no SinanNet no estado do Rio Grande do Sul, de 2016 a 2021.

Ano diagnóstico	Branco/Ign	PQT/PB 6 doses	PQT/MB 12 doses	Esquemas substitutivos	Total
TOTAL	15	68	514	128	725
2016	1	12	110	27	150
2017	5	10	125	33	173
2018	1	15	131	38	185
2019	4	19	74	15	112
2020	3	7	57	11	78
2021	1	5	17	4	27

12% restantes (Tabela 2). Sobre o esquema terapêutico utilizado nesse período, a PQT foi empregada em cerca de 80% dos casos diagnosticados com hanseníase MB e PB, com duração de 12 meses e 6 meses, respectivamente. Outros esquemas substitutivos para o tratamento foram empregados em 128 casos, correspondendo a 17,6% dos casos diagnosticados. A porcentagem restante corresponde aos casos classificados pelo SinanNet como não informados, ignorados ou em branco (Tabela 3).

Na classificação quanto ao Grau de Incapacidade Física (GIF), que pode ser utilizado como indicador epidemiológico da precocidade dos diagnósticos, do total de 725 casos novos de hanseníase diagnosticados, notificados no Sinan e confirmados, 637 foram avaliados quanto ao GIF, no momento do diagnóstico, significando 87,9%. Dos 637 avaliados, 274 (43%) eram Grau Zero, 207 pacientes (32,5%) eram Grau 1 e 156 (24,5%) eram Grau 2. Logo, 57% dos casos avaliados já apresentavam incapacidade ou deformidade no momento do diagnóstico. Dos pacientes, 88 (12,1%) constam como não avaliados (Tabela 4).

DISCUSSÃO

O presente estudo encontrou que, no estado do Rio Grande do Sul, há evidências de subdiagnóstico e atraso no diagnóstico de hanseníase, assim como evidenciado em outros estudos similares.[4,14,15] Indicativo disso é o predomínio das formas multibacilares e com GIF em uma unidade federativa com baixa prevalência, em comparação com os níveis nacionais.[14,16] Tais indicadores possibilitam o entendimento de que a educação médica sobre o conhecimento da hanseníase, uma doença em que a avaliação clínica é determinante, é fundamental para o controle epidemiológico na região abordada, permitindo ponderar que na pandemia de Sars-CoV-2 o ensino foi negativamente afetado, com repercussões na formação médica e reflexos sobre as habilidades necessárias para manejo adequado frente a um quadro de suspeita. É necessário, então, entender as consequências da pandemia na manutenção do caráter negligenciado da doença.

O diagnóstico de hanseníase é feito quando o paciente apresenta pelo menos um dos três sinais cardinais: perda definitiva de sensibilidade em uma área de pele esbranquiçada (hipopigmentada) ou avermelhada, nervo periférico espessado/aumentado com perda de sensibilidade ou presença de bacilos álcool-ácido resistentes em esfregaço de raspado intradérmico.[3] Nesse sentido, o exame clínico qualificado, consequência de uma boa educação médica, é determinante para um diagnóstico preciso e precoce.

A região Sul do Brasil abriga grande concentração de erros no diagnóstico da hanseníase.[14] Tal fato pode ser explicado devido ao baixo número de casos e à alta proporção de pacientes com incapacidades, relacionados também ao diagnóstico tardio. Ainda sobre essa análise, convém frisar que o estado acompanha a redução do coeficiente de detecção de casos novos na região Sul, com diminuição de 59,74%, entre os anos 2005 e 2015.[16] Ademais, o decréscimo de diagnósticos no Rio Grande do Sul, desde o ano de 2018, torna a hanseníase pouco prevalente no estado, o que demanda limitada quantidade de profissionais especializados e centralização dos serviços, favorecendo, assim, mais erros de diagnóstico.

Nessa perspectiva, um estudo realizado em três grandes centros de tratamento de hanseníase, no Brasil,

demonstrou que 42,6% dos pacientes reportaram erro no diagnóstico, reforçando, novamente, a importância da abordagem do presente tema durante a formação médica. Ainda que a incidência de casos diminua, deve haver atenção e preparo, principalmente em regiões endêmicas, uma vez que há uma tendência dos profissionais a negligenciar patologias de baixa prevalência.[17]

A análise dos dados sobre a classificação do GIF dos pacientes diagnosticados apresenta que 57% apresentaram grau 1 ou grau 2 de incapacidade motora/neurológica, isto é, metade dos pacientes diagnosticados manifestaram perda de sensibilidade protetora e/ou deformidade visível em consequência de lesão neural e/ou cegueira. Isso indica, pois, que esses diagnósticos foram realizados em fases mais avançadas, apontando falha das práticas que preconizam a interrupção na cadeia de transmissão.[6,9]

O presente estudo encontrou que 94% da amostra de casos notificados foram confirmados para hanseníase – dos 768 casos notificados, 725 foram confirmados –, fato que revela grande acurácia dos diagnósticos frente à suspeita. Ou seja, o perfil de paciente multibacilar e incapacitado facilita a confirmação diagnóstica, porém, indica falha no diagnóstico precoce.

Uma limitação deste estudo foi a utilização de base de dados secundária, sendo coletados através do Sistema de Informação de Agravos de Notificação (Sinan). A ferramenta possibilita uma análise ampla dos dados epidemiológicos da doença, entretanto, restringe a análise individual dos pacientes, limitando a análise sobre os diagnósticos diferenciais e as causas de erro de diagnóstico,[18] que possibilitaria ampliar o entendimento do problema enfrentado. Além disso, os dados correspondentes ao ano de 2021 são parciais e não revelam a exata situação do ano em questão. Entretanto, as informações analisadas não alteraram o objetivo do trabalho, sendo possível, mesmo assim, entender as repercussões da pandemia na educação médica no combate à hanseníase de maneira adequada.

É primordial que profissionais da Atenção Primária à Saúde sejam capacitados, a fim de possibilitar um manejo adequado e rápido dos pacientes sintomáticos e, quando necessário, realizar o encaminhamento correto para especialista. Nesse sentido, a educação médica entra como forte aliada no combate à negligência da hanseníase, visto que proporciona entendimento e segurança na confirmação do diagnóstico, principalmente em casos de sintomatologia complexa ou pouco elucidativa.[14,19]

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ORIGINAL ARTICLE

Profile and costs of dengue hospitalizations in Southeast Pará from the SUS perspective (2000-2015)

Perfil e custos das internações por dengue no Sudeste do Pará na perspectiva do SUS (2000-2015)

Perfil y costos de las hospitalizaciones por dengue en el Sudeste de Pará en la perspectiva del SUS (2000-2015)

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ABSTRACT

Background and objectives: Considering the little evidence associated with dengue hospitalizations, their public expenditures in Southeast Pará and its relevance to the public health in Brazil, this study aims to demonstrate the records of hospitalizations and expenses associated with this arbovirus between 2000 and 2015 from the perspective of the Unified Health System (SUS). **Methods:** This is a descriptive research that sought to assess the records and expenses (USD) of hospitalization caused by dengue (SUS code: 74500457, 74300440, 0303010010) and severe dengue (SUS code: 74300628, 74500627, 0303010029), as well as their associated deaths (CID: A90 and A91), respectively, from the SIH/SUS and SIM/SUS from 2000 to 2015 for all 39 municipalities in the southeast of Pará. **Results:** A total of 1206 deaths, 22,860 individuals with dengue and 306 with severe dengue underwent services in the SUS between 2000 and 2015, representing 23,166 hospitalizations (23,613: dengue and 313: severe dengue), in which Bom Jesus do Tocantins and Goianésia do Pará represent the municipalities with the highest number of hospitalizations associated with dengue. **Conclusion:** It is possible to verify the relevance of continuing efforts to combat and fight dengue in southeastern Pará. It reinforces the need to conduct studies that contribute to a better understanding of the distribution of hospitalizations and deaths in the different municipalities of the state of Pará, as well as reflections on the epidemiological and economic scenario for the implementation of a rational and efficient decision-making process.

Keywords*: Dengue. Hospitalizations. Unified Health System. Pará.*

RESUMO

Justificativa e objetivos: Considerando as poucas evidências associadas às internações por dengue, seus gastos públicos no Sudeste do Pará e sua relevância para a saúde pública no Brasil, este estudo tem como objetivo

demonstrar os registros de internações e gastos associados a esta arbovirose entre 2000 e 2015 a partir da perspectiva do Sistema Único de Saúde (SUS). **Métodos:** Trata-se de uma pesquisa descritiva que buscou avaliar os registros e gastos (USD) de internação por dengue (código SUS: 74500457, 74300440, 0303010010) e dengue grave (código SUS: 74300628, 74500627, 0303010029), bem como seus óbitos associados (CID: A90 e A91), respectivamente, do SIH/SUS e SIM/SUS de 2000 a 2015 para todos os 39 municípios do sudeste paraense. **Resultados:** Um total de 1.206 óbitos, 22.860 indivíduos com dengue e 306 com dengue grave foram atendidos no SUS entre 2000 e 2015, representando 23.166 internações (23.613: dengue e 313: dengue grave), nas quais Bom Jesus do Tocantins e Goianésia do O Pará representa os municípios com maior número de internações associadas à dengue. **Conclusão:** É possível verificar a relevância da continuidade dos esforços de combate e combate à dengue no sudeste paraense. Reforça a necessidade da realização de estudos que contribuam para um melhor entendimento da distribuição das internações e óbitos nos diferentes municípios do estado do Pará, bem como reflexões sobre o cenário epidemiológico e econômico para a implementação de um processo decisório racional e eficiente. Fazendo processo.

Palavras-chave: *Dengue. Hospitalizações. Sistema Único de Saúde. Pára.*

RESUMEN

Justificación y objetivos: Considerando la poca evidencia asociada a las hospitalizaciones por dengue, sus gastos públicos en el Sudeste de Pará y su relevancia para la salud pública en Brasil, este estudio tiene como objetivo demostrar los registros de hospitalizaciones y gastos asociados a este arbovirus entre 2000 y 2015 a partir de la perspectiva del Sistema Único de Salud (SUS). **Métodos:** Se trata de una investigación descriptiva que buscó evaluar los registros y gastos (USD) de hospitalización por dengue (código SUS: 74500457, 74300440, 0303010010) y dengue grave (código SUS: 74300628, 74500627, 0303010029), así como sus muertes asociadas (CID: A90 y A91), respectivamente, del SIH/SUS y SIM/SUS de 2000 a 2015 para los 39 municipios del sureste de Pará. **Resultados:** Un total de 1206 muertes, 22.860 personas con dengue y 306 con dengue grave fueron atendidos en el SUS entre 2000 y 2015, lo que representa 23.166 hospitalizaciones (23.613: dengue y 313: dengue grave), en las que Bom Jesus do Tocantins y Goianésia hacen Pará representan los municipios con mayor número de hospitalizaciones asociadas al dengue. **Conclusión:** Es posible verificar la relevancia de continuar los esfuerzos para combatir y luchar contra el dengue en el sureste de Pará. Refuerza la necesidad de realizar estudios que contribuyan a una mejor comprensión de la distribución de hospitalizaciones y muertes en los diferentes municipios del estado de Pará, así como reflexiones sobre el escenario epidemiológico y económico para la implementación de una decisión racional y eficiente. proceso de fabricación.

Palabras clave: *Dengue. Hospitalizaciones. Sistema Único de Salud. Paraca.*

INTRODUCTION

According to the World Health Organization (WHO), dengue is a viral infection commonly recorded in tropical and subtropical regions caused by the Dengue virus (DENV) and transmitted to humans by the bite of female mosquitoes of the Aedes genus.[1] It is a disease of compulsory notification. According to the Resolution No. 204 of 2016, all diseases associated with this infection registered in Brazil might be notified and communicated to the epidemiological surveillance of the municipality to facilitate better control.[2]

DENV belongs to the Flavivirus genus and has five serotypes (DENV1-5), four of which (DENV1-4) have been associated with human infections. An individual can be infected by different serotypes, and a specific immune response can be generated for each of them. The detection of the fifth serotype, isolated in Malaysia, is considerably recent. A study by Mustafa et al. (2015) showed that DENV-5 is associated with mild infection and has been circulating among primates from the Southeast Asian forest.[3]

The individual infected by DENV may be asymptomatic or present more severe symptoms. In dengue cases, individuals may have a high fever (39° to 40°C), headaches or eye pain, muscle and bone pain, tiredness, nausea, lack of appetite, presence of red spots on the skin, feeling of dizziness, and vomiting. On the other hand, in severe dengue, clinical events such as hemorrhage, circulatory collapse, abdominal pain and shock stand out.[4]

According to the Pan American Health Organization (PAHO), the incidence of dengue in some endemic countries has increased in recent years. Between January and May 2020, about 1.6 million infected people were registered in the Americas. In 2019, Brazil alone was responsible for 2,241,974 occurrences of this infection, ranking first in the total number of cases, with 70% of the records from Latin America and more than half of the deaths that year.[5]

In this scenario, the State of Pará stood out regarding the records of this arbovirus in the North region of Brazil between 2010 and 2016, with about 83,371 cases. This state presents a vast diversity and territorial extension and is popularly known for its climatic variability. Furthermore, it has a hot, humid equatorial tropical climate and high rainfall levels, with average temperatures of 27°C, especially in the mesoregion of Southeast Pará[6], which is important for the proliferation of the vector and,

consequently, a high number of infected individuals.

Dengue represents a significant public health challenge in the country. To date, there is no evidence available on the records of hospitalizations, expenses, and deaths associated with DENV in Southeast Pará. Therefore, it is relevant to carry out this study to demonstrate the records of hospitalizations, as well as the expenses associated with the treatment of dengue and severe dengue, together with the deaths caused by this arbovirus involving 39 municipalities, which comprise the mesoregion of Southeast Pará, from 2000 to 2015, from the perspective of the Unified Health System (SUS).

METHODS

This is a descriptive study that aims to evaluate the epidemiological and economic impact of dengue and severe dengue in the SUS hospitalization services over 16 years (2000-2015) in the southeastern mesoregion of Pará based on the records available in the Hospital Information System (SIH/SUS) and Mortality Information System (SIM/SUS) databases. The southeast of Pará is composed by 39 municipalities: Abel Figueiredo, Água Azul do Norte, Bannach, Bom Jesus do Tocantins, Brejo Grande do Araguaia, Breu Branco, Canãa dos Carajás, Conceição do Araguaia, Cumaru do Norte, Curionópolis, Dom Eliseu , Eldorado dos Carajás, Araguaia Forest, Goianésia do Pará, Itupiranga, Jacundá, Marabá, Nova Ipixuna, Novo Repartimento, Ourilândia do Norte, Palestina do Pará, Paragominas, Parauapebas, Pau D`Arco, Piçarra, Redenção, Rio Maria, Rondon do Pará, Santa Maria das Barreiras, Santana do Araguaia, São Domingos do Araguaia, São Félix do Xingu, São Geraldo do Araguaia, São João do Araguaia, Sapucaia, Tucumã, Tucuruí, Ulianópolis, and Xinguara. These municipalities were included in our collection and analysis of data.

In 2014, the most severe denomination of dengue infection, previously denominated as dengue/hemorrhagic fever, changed to severe dengue. Furthermore, the terms dengue and severe dengue were used to represent the mildest and most severe conditions associated with DENV infection, respectively.[7]

The analyses followed the following steps: an annual and global assessment of the number of hospitalization records caused by dengue and severe dengue in the SUS, as well as the number of individuals hospitalized with this arbovirus, considering the procedure codes made available by the SUS for dengue (74300440, 74500457, 0303010010) and severe dengue (74300628, 74500627, 0303010029) and analysis of expenditures (USD) recorded with the treatment of hospitalized individuals and the global assessment of deaths associated with DENV in southeastern Pará between 2000 and 2015. The database used for the analyses was previously obtained from the probabilistic matching strategy involving the databases offered by the SUS, namely the Hospital Information System (SIH/SUS) and the Mortality Information System (SIM/SUS). The data obtained by the SIH and SIM platforms were used to acquire data on hospitalizations, expenses, and deaths involving this arbovirus in the mesoregion of southeastern Pará between January 2000 and December 2015. All costs for the treatment of dengue and severe dengue were obtained in US dollars (USD), and the database used was evaluated for previously published studies involving different scenarios, such as the northern region of Brazil,[8] the State of Minas Gerais,[9] as well as Brazil.[10]

This study was approved by the Ethics Committee of the Federal University of Minas Gerais (COEP) under CAEE Registry: 57219816.0.0000.5149 (Approval Report No: 1,619,654).

RESULTS

A total of 22,860 individuals with dengue and 306 with severe dengue were hospitalized and used SUS services between 2000 and 2015, representing 23,926 hospitalizations (23,613: dengue and 313: severe dengue). It was found that most cases were registered for male individuals, of which 50.8% were dengue cases. Individuals between 05 and 44 years old accounted for 72.9% and 62.4% of dengue and severe dengue cases, respectively. Moreover, 3.2% of the individuals had more than one hospitalization caused by DENV in the same year and/or complications resulting from the infection in the study period.

Table 1. Population characteristics: profile of dengue and severe dengue in the Southeast region of Pará (2000-2015).

Variables	Dengue	Severe Dengue
Number of individuals (n)	22.860	306
Gender (%)		
Men	50.8	47.4
Women	48.6	52.0
NA*	0.6	0.6
Frequency by age group (years old) (%)		
< 1	1	5.9
01 – 04	3.7	9.2
05 – 14	14.9	22.5
15 – 24	24.1	14.5
25 – 34	20.2	13.4
35 – 44	13.7	12
45 – 54	10.1	8.8
55 – 64	6.4	7.2
65 – 74	3.9	4.2
75 – 84	1.6	2.0
> 84	0.4	0.3
Number of hospitalizations (n)	23.613	313
Hospitalizations for Dengue more than once a year (%)	3,2	0,3
Deaths (CIDA90 e A91)	1206	0

**Note: NA = Not available*

In addition, 2003, 2007, 2008, and 2011 stood out regarding the number of hospitalizations associated with dengue (Table 2).

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Table 2. Summary of infected individuals and hospitalizations associated with dengue and severe dengue in the Southeast region of the Pará State 2000-2015.

Year	Population	Infected Individuals	Hospitalization	Infected/100 thousand inhabitants	Hospitalizations/100 thousand inhabitants
2000	6.192.307	847	876	13.7	14.1
2001	6.341.711	1483	1549	23.4	24.4
2002	6.453.699	1905	2006	29.5	31.1
2003	6.574.990	2724	2830	41.4	43
2004	6.695.940	1203	1239	17.9	18.5
2005	6.970.591	1005	1039	14.4	14.9
2006	7.110.462	775	798	10.9	11.2
2007	7.249.184	2247	2310	31	31.8
2008	7.321.493	2969	3077	40.5	42
2009	7.431.041	1495	1549	20.1	20.8
2010	7.581.051	1454	1495	19.2	19.7
2011	7.688.593	2115	2163	27.5	28.1
2012	7.822.205	1255	1285	16.0	16.4
2013	7.999.720	974	991	12.2	12.4
2014	8.104.880	456	459	5.6	5.6
2015	8.206.923	259	260	3.1	3.1
Total		23166	23926	-	-

Note: Data referring to the number of inhabitants were extracted from DataSUS and Statistical Yearbook of Pará 2019.[11,12]

The municipalities that stood out regarding the highest number of hospitalizations associated with dengue in southeastern Pará were Jacundá (2,294), Goianésia do Pará (1,225), Bom Jesus do Tocantins (1144), São João do Araguaia (1043), Xinguara (1,116), São Domingos do Araguaia (1007), Rondón do Pará (1,007), and Marabá (1,000). For hospitalizations caused by severe dengue, Redenção (94), Conceição do Araguaia (32), Parauapebas (29), and Xinguara (21) presented the highest incidence of hospitalization.

Global costs associated with dengue and severe dengue in terms of hospitalization, from the perspective of the SUS, totaled USD 5,051,272.82 and USD 122,542.97, respectively, from 2000 to 2015 in Southeast Pará. A considerable consumption of public resources for treating DENV infection can be highlighted for 2003 and 2008. In 2003, dengue cost USD 662,228.45; in 2008, USD 45,272.07 were spent on severe dengue hospitalizations. Expenses with dengue represent 98% of total costs with this arbovirus, and the average expense with hospitalization for treating dengue and severe dengue in southeastern Pará was USD 213 and USD 391, respectively (Table 3).

Table 3. Summarization of records and expenses (USD) with hospitalization associated with dengue in each of the municipalities in the Southeast region of the Pará State 2000-2015.

Municipality	Individuals	Hospitalizations (n)	Expenses (USD)	Deaths
Abel Figueiredo	160	161	32,037.05	8
Água Azul do Norte	613	653	129,163.08	27
Bannach	97	101	18,330.81	7
Bom Jesus do Tocantins	1144	1182	258,574.31	49
Brejo Grande do Araguaia	372	394	82,379,82	20
Breu Branco	111	111	25,741.03	1
Canaã dos Carajás	446	453	104,093.52	18
Conceição do Araguaia	754	776	164,638.4	30
Cumaru do Norte	47	48	9,617.33	1
Curionópolis	687	708	158,146.16	50
Dom Eliseu	553	563	114,561,13	19
Eldorado dos Carajás	596	614	139,373.09	43
Floresta do Araguaia	210	213	43,892.38	19
Goianésia do Pará	1225	1264	295,069,27	64
Itupiranga	553	566	116,611,67	25
Jacundá	2296	2400	519,306.25	130
Marabá	1012	1075	254,472.72	94

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Nova Ipixuna	16	16	3977,03	1
Novo Repartimento	223	228	47.279,84	21
Ourilândia do Norte	394	399	80,156.13	12
Palestina do Pará	453	461	96,214.75	15
Paragominas	233	235	52,571.51	13
Parauapebas	863	881	205.903,12	55
Pau D, Arco	124	131	25,521.05	4
Piçarra	237	246	48,598.03	7
Redenção	871	882	209,466.78	45
Rio Maria	636	668	140,046,58	36
Rondon do Pará	1908	1962	430,194.7	96
Santa Maria das Barreiras	89	90	19,049.62	3
Santana do Araguaia	354	365	74,782.46	10
São Domingos do Araguaia	1011	1048	234,725.52	56
São Félix do Xingu	687	702	140,426.18	27
São Geraldo do Araguaia	1047	1098	214,900.1	50
São João do Araguaia	269	271	57,450.76	13
Sapucaia	82	83	15,152.2	5
Tucumã	853	886	181,529.93	26
Tucuruí	234	237	59,428.34	19
Ulianópolis	569	576	124,329.71	17
Xinguara	1137	1179	246,103.43	70
Total	23166	23926	5,173.815.79	1206

It is noteworthy that the municipalities of Bom Jesus do Tocantins, São Domingos do Araguaia, Marabá, São Geraldo do Araguaia, Parauapebas, Xinguara, Tucumã, and Redenção presented between 801 and 1200 hospitalization records, followed by Goianésia do Pará, Jacundá, and Rondón do Pará, with 1,201 to 2,500 cases of hospitalizations during 2000 and 2015 (Figure 1). Figure 2 shows the age profile of cases and deaths due to DENV infections in Southeast Pará.

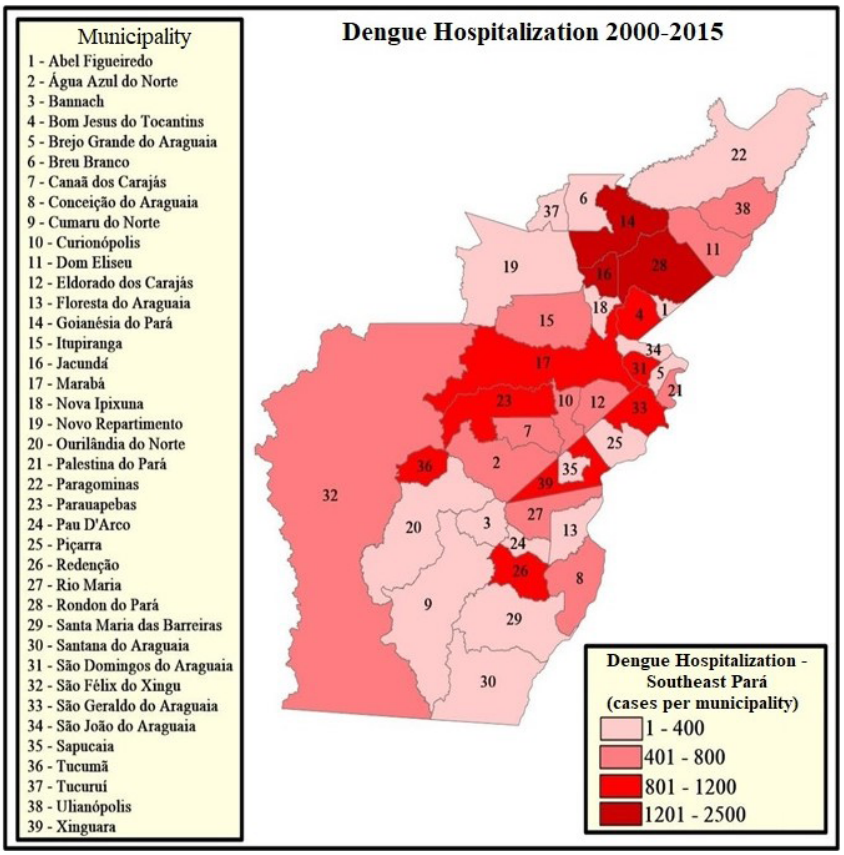

Figure 1. Dengue cases by municipality in the Southeast Pará (2000-2015).

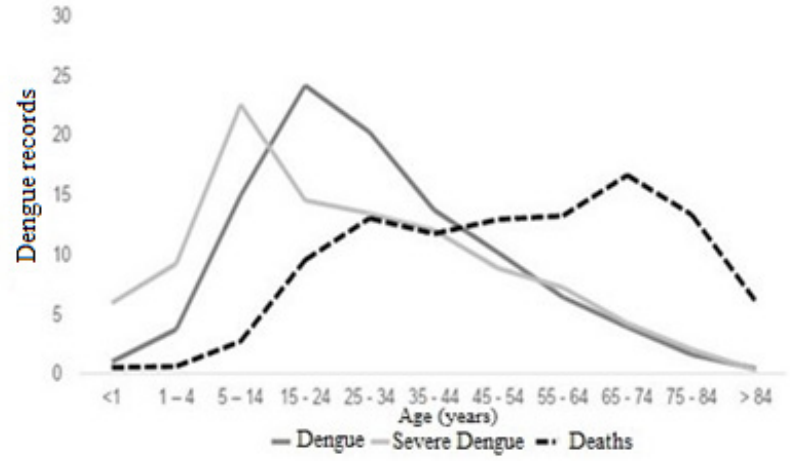

Figure 2. Distribution of dengue, severe dengue and deaths, by age, in the Southeast of Pará State from 2000 to 2015.

DISCUSSION

This study was the first to assess hospitalization records and costs from the perspective of the SUS caused by dengue and severe dengue, as well as the deaths associated with the disease in Southeast Pará over 16 years (2000-2015). A total of 23,166 individuals infected with DENV and 23,926 hospitalizations in the 39 municipalities of this mesoregion were reported, representing an impact on public coffers of USD 5,173,815.79. In this context, the importance of encouraging and directing efforts to prevent this disease is highlighted.

Dengue is a serious public health problem in Brazil. It is endemic in all regions of the country, with a considerable epidemiological burden[13] mainly in the Northeast (336,222), Southeast (137,035) and North (128,471) regions, as demonstrated in a previous study that also considered the same period of the present work.[10] It is relevant to note that from 2000 to 2015, 1,621,797 notifications associated with DENV infection were verified in the North of Brazil, which was higher than the number of hospitalizations (128,471) since for this arbovirus, in most cases, hospitalizations are not necessary.[10,14] Considering the North region of Brazil, the State of Pará was highlighted from 2010 to 2016 regarding the number of notifications of DENV infection, with a total of 83,371 records.[14] In this scenario, the municipalities of Jacundá (10.2%), Goianésia do Pará (5.84%), Bom Jesus do Tocantins (5.11%), Marabá (4.90%), Xinguara (4.74%), São Domingos do Araguaia (4.61%), and São Geraldo do Araguaia (4.2%) presented the highest incidence of dengue hospitalizations in southeastern Pará, corresponding to 39.6%.

Among the states of the North Region, Pará was the most affected by this arbovirus, with 82,211 notifications, 84,693 hospitalizations, 18,340,822.3 (USD) in expenses, and 491 deaths caused by dengue between 2000 and 2015.[8] Based on the results of this study, approximately 23,166 new cases were associated with this infection, with 22,860 dengue cases and 306 severe dengue reports. The southeast of Pará presents conditions that favor the cases of this and other arboviruses, considering its high rainfall, high temperatures, precarious sanitation, and inadequate housing conditions, education and income distribution, which contribute to the increase in the incidence of dengue.[15-17]

Furthermore, it was observed that most of the female population was hospitalized with severe dengue (52%), as found in a study that evaluated the epidemiological profile of this arbovirus in Brazil from 2000 to 2015 and in another study that evaluated in the same period in the North region of Brazil.[8,] In our study, most dengue hospitalizations were reported to the male public (50.8%), differently from what was found in previous studies.[8,10] It is noteworthy that individuals between 5 and 44 years old were the most hospitalized due to DENV infection, representing 72.9% of the dengue cases and 62.4% of severe dengue, a result similar to that found in a published article conducted with individuals within this age group.[8]

Arboviruses are responsible for a high economic and social impact in Brazil. A previous publication showed that the costs related to the management of these infections, including the control and combat of the vector, and direct and indirect medical costs, represented about 2% of the country's health budget for 2016.[18] In this context, it is noteworthy that approximately R$ 1.5 billion in investments to combat the vector were estimated in Brazil in 2016, in which approximately R$ 78.6 million were allocated by the federal government for acquiring larvicides and insecticides. It is estimated that the country spends

approximately R$ 374 million on arbovirus treatment, of which about R$ 175,876,163 is directed only to dengue and R$ 1,684,053 to the State of Pará. Regarding the indirect costs with arboviruses, approximately R$ 431 million were spent with loss of productivity.[18] In this study, 23,926 hospitalizations associated with DENV in the southeastern mesoregion of Pará were reported. It represented an economic impact of USD 5,173,815.79 to public coffers in Brazil and included only medical services and medicines to treat hospitalized individuals for 16 years (2000-2015). Finally, this infection still represents a considerable challenge for the health public in this region of Pará state, as well as for the entire state and country.

To combat dengue, efforts and strategies are carried out by the Brazilian government, emphasizing investments in public policies. Among the measures adopted by the government are the creation of the Aedes aegypti Eradication Program (PEAa) in 1996 and the Aedes aegypti Eradication Program in 2002. National Dengue Control Program (PNCD) was also created, and later, in 2015, the National Program to Combat Aedes and Microcephaly (PNEAM) was created.[15] However, many epidemics and high numbers of cases were reported, indicating the need to improve and review the strategies and adopt them at the national level to combat arboviruses since the vector is present throughout the Brazilian territory, as well as facilitate their implementation and development, especially in the North region of the country. In addition, the importance of carrying out studies that better demonstrate the clinical, epidemiological, and economic panorama of each of these diseases in different locations is also crucial to provide subsidies for the rational decision-making process to face these diseases. This process should involve the population, health professionals, and managers.[10]

It reinforces the need to intensify campaigns to combat the dengue vector, which is also responsible for spreading other arboviruses, such as chikungunya and zika virus. Some strategies can help fight the vector, such as using larvicides in mosquito breeding sites, cleaning and emptying wastewater reservoirs, and using insecticides in homes. Moreover, vaccines are one of the main strategies used to control infections, and so far, new studies have demonstrated the evidence on the first dengue vaccine approved in Brazil so that it can be made available by the SUS.[19-21,24,25]

So far, Brazil has licensed a vaccine called Dengvaxia® to prevent dengue. This vaccine is available only for commercialization in the private market and is not yet available in the National Immunization Program by the SUS.[21]A study evaluated the consumer willingness to pay for a dengue vaccine in Brazil, showing a maximum value of USD 36.04 (120.00BRL) for the three-dose regimen or USD 12.01 (40.00 BRL) per dose.[22] A study developed in Brazil estimated the potential impact of vaccination against dengue. The results show a 22% reduction in dengue records.[23] Furthermore, the decision to incorporate or not a new vaccine or drug in the SUS is made by the National Commission for the Incorporation of Technologies in the SUS (CONITEC). In 2016, Dengvaxia® was not recommended for the National Vaccination Calendar, as the results of clinical studies showed limitations and/or questions about its incorporation in the SUS.[25]

This study sought to contribute and highlight the context associated with direct medical costs, the distribution profile, and the number of hospitalizations due to DENV infections in southeastern Pará. Some limitations can be listed: (i) the availability of only the data applied to direct costs with hospitalizations by the SUS, having adopted the perspective of the Brazilian public health system, and (ii) non-availability and identification of the type of DENV serotype associated with each hospitalization, considering the unavailability of this type of information in the systems (SIH/SIM/SUS) consulted from the SUS. Despite these limitations, it is believed that this study can provide reliable and relevant information to promote discussions and reflections on the epidemiological and economic scenario of dengue in this mesoregion and its municipalities, highlighting the little evidence and publications on the topic.

Dengue remains an important public health problem in southeastern Pará. The present study revealed some of the expenses with hospitalizations due to dengue and severe dengue by the SUS, as well as the epidemiological context of this infection and its deaths for this mesoregion of Pará over 16 years. In this context, the municipalities of Jacundá, Goianésia do Pará, Bom Jesus do Tocantins, Marabá, Xinguara, São Domingos do Araguaia, and São Geraldo do Araguaia presented the highest records of hospitalizations, costs and deaths associated with this arbovirus.

Thus, even with the initiatives to combat this arbovirus adopted so far, the continued efforts and strengthen campaigns, joint efforts and training of Endemic Combat Agents (ACE) to promote actions focused on health education to better monitor and promote awareness of the risks and precautions to be adopted to combat arboviruses are urgently needed. Considering the budgetary limitations experienced in Brazil, the need for the search for prevention strategies that allow a significant reduction of cases and expenses caused by this problem by the SUS is reinforced. Finally, we emphasize the importance of carrying out more studies and disseminating evidence on dengue in different locations of Brazil so that they can contribute to a better perception of the epidemiological and economic situation regarding this arbovirus, which is essential for planning rational and efficient measures in the face of the many scenarios to be discussed and rethought about this.

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CONFLICT DE INTEREST

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PUBLICAÇÃO OFICIAL DO NÚCLEO HOSPITALAR DE EPIDEMIOLOGIA DO HOSPITAL SANTA CRUZ E PROGRAMA DE PÓS GRADUAÇÃO EM PROMOÇÃO DA SAÚDE - DEPARTAMENTO DE BIOLOGIA E FARMÁCIA DA UNISC

Revista de Epidemiologia e Controle de Infecção

Hospital Santa Cruz

REVIEW ARTICLE

Risk factors and spatial distribution associated with deaths due to COVID-19: an integrative review

Fatores de risco e distribuição espacial associados aos óbitos por COVID-19: uma revisão integrative

Factores de riesgo y distribución espacial asociados a las muertes por COVID-19: una revisión integradora

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ABSTRACT

Background and objectives: understanding the clinical-epidemiological and environmental factors related to deaths due to COVID-19 and their distribution in space can serve as subsidies to direct and implement more effective health actions for vulnerable populations. Thus, the objective was to synthesize the scientific evidence related to risk factors and spatial distribution of deaths due to COVID-19 in the world. **Content:** this is an integrative literature review, and the following guiding question emerged: what is the scientific evidence related to risk factors and spatial distribution of deaths due to COVID-19 in the world? Searches were carried out in the Scientific Electronic Library Online (SciELO) and the Scopus, Web of Science and National Library of Medicine (PubMed) databases in June 2021. Original studies in Portuguese, English or Spanish, without time frame, excluding studies with a specific age group or with an audience with specific comorbidity, were used. A total of 25 studies were included, with findings in different scenarios around the world. Factors such as age, sex, pre-existing diseases were associated with deaths due to COVID-19, which had a heterogeneous spatial distribution and occurred in environmental, socioeconomic and geographic conditions peculiar to these territories. **Conclusion:** age equal to or greater than 60 years, males, cardiovascular diseases, diabetes mellitus and geographic areas with greater environmental pollution, greater population density and precarious sanitary conditions influenced the mortality of COVID-19.

Keywords*: COVID-19; Mortality; Risk Factors; Spatial Analysis; Global Health.*

RESUMO

Justificativa e objetivos: compreender os fatores clínico-epidemiológicos e ambientais relacionados aos óbitos por COVID-19 e sua distribuição no espaço pode servir de subsídio para direcionar e implementar ações de

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saúde mais efetivas para populações vulneráveis. Assim, o objetivo foi sintetizar as evidências científicas relacionadas aos fatores de risco e distribuição espacial dos óbitos por COVID-19 no mundo. **Conteúdo:** trata-se de uma revisão integrativa da literatura, e emergiu a seguinte questão norteadora: quais são as evidências científicas relacionadas aos fatores de risco e distribuição espacial dos óbitos por COVID-19 no mundo? As buscas foram realizadas nas bases de dados Scientific Electronic Library Online (SciELO) e Scopus, Web of Science e National Library of Medicine (PubMed) em junho de 2021. Estudos originais em português, inglês ou espanhol, sem recorte temporal, excluindo estudos com faixa etária específica ou com um público com comorbidade específica. Um total de 25 estudos foram incluídos, com achados em diferentes cenários ao redor do mundo. Fatores como idade, sexo, doenças pré-existentes foram associados aos óbitos por COVID-19, que tiveram distribuição espacial heterogênea e ocorreram em condições ambientais, socioeconômicas e geográficas peculiares a esses territórios. **Conclusão:** idade igual ou superior a 60 anos, sexo masculino, doenças cardiovasculares, diabetes mellitus e áreas geográficas com maior poluição ambiental, maior densidade populacional e condições sanitárias precárias influenciaram na mortalidade por COVID-19.

Palavras-chave: *COVID-19; Mortalidade; Fatores de risco; Análise espacial; Saúde global.*

RESUMEN

Justificación y objetivos: comprender los factores clínico-epidemiológicos y ambientales relacionados con las muertes por COVID-19 y su distribución en el espacio puede servir como subsidio para orientar e implementar acciones de salud más efectivas para poblaciones vulnerables. Así, el objetivo fue sintetizar la evidencia científica relacionada con los factores de riesgo y la distribución espacial de las muertes por COVID-19 en el mundo. **Contenido:** se trata de una revisión integrativa de la literatura, y surgió la siguiente pregunta orientadora: ¿cuál es la evidencia científica relacionada con los factores de riesgo y la distribución espacial de las muertes por COVID-19 en el mundo? Las búsquedas se realizaron en las bases de datos Scientific Electronic Library Online (SciELO) y Scopus, Web of Science y National Library of Medicine (PubMed) en junio de 2021. Estudios originales en portugués, inglés o español, sin marco de tiempo, excluyendo estudios con se utilizó un grupo de edad específico o con un público con comorbilidad específica. Se incluyeron un total de 25 estudios, con hallazgos en diferentes escenarios alrededor del mundo. Factores como la edad, el sexo, las enfermedades preexistentes se asociaron a las muertes por COVID-19, que tuvo una distribución espacial heterogénea y se produjo en condiciones ambientales, socioeconómicas y geográficas propias de estos territorios. **Conclusión:** la edad igual o mayor a 60 años, la maldad, las enfermedades cardiovasculares, la diabetes mellitus y las áreas geográficas con mayor contaminación ambiental, mayor densidad poblacional y precarias condiciones sanitarias influyeron en la mortalidad por COVID-19.

Palabras clave: *COVID-19; Mortalidad; Factores de riesgo; Análisis espacial; Salud global.*

INTRODUCTION

COVID-19 is a disease that presents rapid spread, mainly affects the respiratory system[1], but can affect other organs and systems of the human body.[2] Since it demonstrates high contagion, accelerated transmission between humans[3] and dissemination in many countries on several continents, the World Health Organization (WHO) declared, on March 11, 2020, a pandemic state.[4]

It is a viral, infectious disease with respiratory symptoms, whose etiological agent is SARS-CoV-2, a type of beta coronavirus. The predominant symptoms are fever, malaise and cough, with mild course in most infected[5]. However, some patients develop the most severe form, and when the organism cannot recover, they evolve to death.[6]

It is in this context and pandemic scenario that many cases and deaths related to the disease worldwide have been and continue to be recorded. Assessing the overview of COVID-19 deaths worldwide, until October 24, 2021, there were a total of 4,927,723 deaths. To date, the United States had the highest cumulative number of deaths, with 726,846, followed by Brazil, with 604,228, India, with 453,042, Mexico, with 285,347, and Russia, with 228,453.[4]

As for the global mortality rate, until October 23, 2021, a rate of 627.8 deaths/1 million inhabitants was recorded. Among countries with a population of more than 1 million, Peru had the highest rate, with 5,995.9 deaths/1 million inhabitants, followed by Bosnia, with 3,469.3/1 million inhabitants.[7] It is believed that individual and collective factors can interfere with these rates and influence the outcome of discharge or death, such as socioeconomic factors and vulnerabilities related to housing, population income conditions, aging and level of social exclusion.[8] Moreover, the approach, clinical guidance and previous identification of comorbidities are equally important, as these are significant points in the course of a disease.

The clinical management of SARS-CoV-2 infection still requires further clarification to obtain better control over the disease, and, as in other pathologies, it is inferred that early diagnosis and follow-up act positively and can prevent the most serious manifestations of COVID-19. The virus causes an acute respiratory syndrome that ranges from mild to very severe cases, with evolution to severe respiratory failure, and its lethality differs ac-

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cording to associated comorbidities and age.[9]

With regard to comorbidities, the most severe cases have been recorded in older adults who have some associated disease, especially hypertension and diabetes mellitus, but this association was also verified in cardiac and respiratory diseases.[10] Regarding age, it is verified that over 50 years old is positively associated with cases of deaths.[11,12]

It is also noteworthy that knowledge of how diseases are distributed and disseminated in time and space is a central point of spatial epidemiology and health geography. Spatial analysis is essential to understand the spatial spread of an infection and its association with the community and the environment,[13] and can thus be used in the field of health research, as it brings a significant contribution to the observation of diseases and injuries in an area or region, making it possible to verify how each territory's particularities influence the dissemination of a given disease.

Understanding the clinical-epidemiological and environmental factors and their distribution in space can serve as an instrument for directing more effective health actions to vulnerable populations. Considering that conducting literature review studies related to risk factors and their associations with COVID-19 mortality can collaborate with professionals, managers and health services in promoting a more efficient clinical and epidemiological management, the objective was to synthesize the scientific evidence related to risk factors and spatial distribution of COVID-19 deaths worldwide.

METHODS

This is an integrative literature review, which aims to synthesize the knowledge about a given subject, making use of a systematic process and with scientific rigor.[14] The construction of this review consisted of the following phases: research question formulation; database search and primary study selection; study screening; analysis and synthesis of selected studies; and presentation of results.

For data collection, the PICo strategy (Population or problem, Phenomenon of Interest and Context) was used.[15] Problem (P) covered the deaths due to COVID-19, Interest (I), risk factors and spatial analysis, and Context (Co), studies published worldwide. Thus, the following guiding question was formulated: what is the scientific evidence related to risk factors and spatial distribution of COVID-19 deaths in the world?

The searches for the studies took place in June 2021, in the Web of Science, Scopus, National Library of Medicine (PubMed) and in the Scientific Electronic Library Online (SciELO) databases, using the Descriptors in Health Sciences (DesC) in Portuguese: "COVID-19", "*Mortalidade*", "*Fatores de Risco*", "*Análise Espacial*" e "*Saúde Global*". The corresponding terms in English of the Medical Subject Headings (MeSH) of the National Library were used in the databases: "COVID-19", "Mortality", "Risk Factors", "Spatial Analysis" e "Global Health". The descriptors were combined with Boolean operators AND and OR. The crosses were performed as follows: (COVID-19) AND (mortality) AND ((Risk Factors) OR (Spatial Analysis)) AND (Global Health).

In study selection, we included original studies, made available free of charge, in Portuguese, English or Spanish, and without time frame. Editorials, letters to the editor, expert opinions, reviews (literary, integrative and systematic), theses, dissertations, studies that did not answer the guiding research question and studies in which research was conducted with groups of patients with specific age and/or comorbidity were excluded.

For the initial analysis of pre-selected articles, the Rayyan Systems Inc instrument was used, a free technological application web version, which presents in its interface the studies' main information, collaborating with the initial screening of the articles through a semi-automated process.[16] At this stage, a thorough reading of titles and abstracts was carried out in order to verify which were related to the research question and the inclusion and exclusion criteria adopted.

The strategy adopted in article search and selection was based on the Preferred Reporting Items for Systematic reviews and Meta-Analyzes (PRISMA) model.[17] The studies selected for the application of eligibility criteria were read and analyzed in full, in order to identify which met the objective of this review and thus select those that composed the final sample.

Thus, study characterization was carried out through an instrument designed to present the data related to the objective of this review. The data for descriptive analysis of this instrument are authorship, year of publication, country where the study was conducted, population, data source, objective(s), main findings and study limitations.

RESULTS AND DISCUSSION

Based on the criteria established for review, 25 articles were selected, published between 2020 and 2021. Figure 1, adapted from PRISMA[17], synthetizes the steps for sample selection.

As for the setting of the studies, five were carried out in the United States of America (USA), three in Brazil, two in Mexico, one in Africa, China, Spain, France, India, Indonesia, England, Italy and Iran. Continent-wise, one assessed the European continent and five studies made the analysis at the world level. Most studies were published in English (96.00%), and only 4.00% of them were available in Portuguese.

Among the included studies, more than half investigated the association of COVID-19 mortality with sociodemographic characteristics such as age and sex,[10,12,18-28] pointing out that age from 65 years and being male are risk factors for deaths.[10,18,20,22,26] It was also noted that comorbidities were associated with the outcome of death and constituted important risk factors,[1,11,18,20,23,27-32] especially those resulting from cardiovascular complications, especially hypertension and diabetes mellitus (DM).[18,20,23,29-31]

As for the spatial analysis, ten studies were selected, which investigated which risk factors were associated with deaths in the studied areas and in certain populations. [1,19,24,29,30,33-37] In these investigations, different

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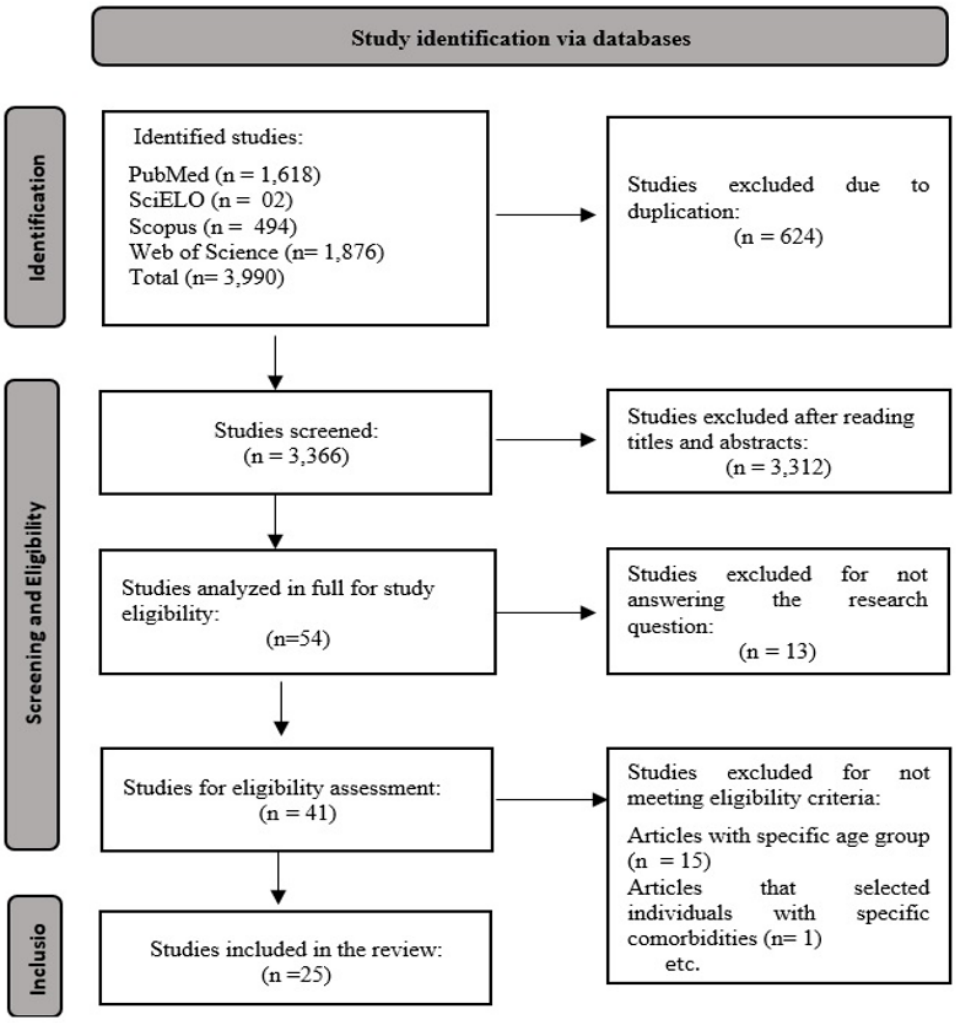

Source: own elaboration, 2021.

Figure 1. Adapted PRISMA flowchart.[17]

techniques were used, among them: empirical Bayesian estimate (EBE);[37] geographically-weighted random forest (GW-RF);[1] geographically-weighted regression (GWR);[33] spatial Durbin model;[30] Least Absolute Shrinkage and Selection Operator (LASSO);[24] space-time scanning techniques (discrete Poisson model);[34-36] spatial correlation (Moran's Index);[29,30,33,37] and Pearson's correlation.[29,34,37] With the use of such tools, a heterogeneous distribution of deaths and/or mortality rates was evidenced, with socioeconomic and environmental conditions[1,19,29,30,33] and population density [24,29,30,35,37] being explanatory factors for the occurrence of events in these territories in space and space-time.

Regarding selected studies' limitations, incomplete feeding of some variables in consulted databases, possibility of underreporting and ecological fallacy stood out.

Chart 1 shows the synthesis of studies included in this review.

It was identified in the global context that several factors appeared as potentiators or associated with deaths due to COVID-19. Some of these factors were distinct or had significant differences depending on the region, country, or continent. Variables such as advanced age and male gender were associated with the risk of death due to the disease in almost all studies.

COVID-19 mortality rates in the world were heterogeneous and varied between 2% and 4.2% of those affected by the disease.[11,19,29] Among patients with worsening conditions and hospitalized in the Intensive Care Unit (ICU), these rates were much more expressive and changed from one health institution to another. Regarding mortality rates among hospitalized patients, there was a variation between 20.3% and 21.7% in the USA,[12,38] 24% in Europe and 25% in Africa.[22,23] In Spain and Italy, these rates were higher, respectively 42.4% and 44.3%.[21,26]

It was noted that, in outpatients, the mortality rate was 13% in the USA,[12,38] significantly lower than in patients in hospital. This discrepancy between the rates can be justified due to age. Outpatients were mostly younger than hospitalized patients. Furthermore, in the hospitalized group, there were people more likely to have pre-existing diseases (asthma, chronic obstructive pulmonary disease, hypertension, obesity, DM), changes

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Chart 1. Articles included in the integrative review (n=25).

Author / place / year	Population and data source	Objective	Main findings
Donamou et al, Guinea, 2021.[22]	140 patients hospitalized with COVID-19 in the ICU. Secondary data extracted from medical records between March and July 2020.	Identify COVID-19-related mortality factors in ICUs in Guinea.	MR of 25% in intensive care. Mean age of patients who died was 65 years, prevalence of death among people with occupation in the informal sector (77%). There was a predominance of males in both subgroups.
Albitar O, et al, World, 2020.[10]	828 cases and 219 deaths due to COVID-19. Data collected at https:github.com/beoutbreakprepared/nCoV2019 until April 21, 2020.	Assess the risk factors for COVID-19 mortality in the world.	Male, advanced age, hypertension, DM and the region of America were the independent risk factors for death.
Baqui et al, Brazil, 2020.[20]	11,321 hospitalized patients positive for SARS-CoV-2 by May 4, 2020. Secondary data extracted from SIVEP-Grip.	Characterize the COVID-19 pandemic in Brazil and assess variations in mortality according to region, ethnicity, comorbidities and symptoms.	Brown ethnicity is more prone to death due to COVID-19 than other ethnicities, it appeared as the second variable more associated with mortality, being the first age. As for comorbidities, CVD was the most associated with death (77.4%). Pattern of increased deaths at a median age of 65.3 years and higher percentages of death in males (67.2%).
Sorci, Faivre, Morand. World, 2020.[11]	3,778 COVID-19 patients from 72 countries. Secondary Data by 11 June 2020 from the European Centre for Disease Prevention and Control (ECDC).	Analyze the factors that may cause variability in COVID-19 MR between countries.	Worldwide lethality rate due to COVID-19 was around 4%. Countries with the lowest CVD MR had the lowest fatality rate, and countries with the highest MR from smoking and people over the age of 70 years had the highest mortality.
Garcia et al, Europe, 2020.[23]	398 patients who completed their ICU stay for SARS-CoV-2 as of April 22, 2020. Data were collected in the RISC-19-ICU record.	Analyze the progression of COVID-19 in the first 7 days in the ICU and the prognostic factors of mortality in patients.	It showed moderate mortality in the ICU of 24%. It suggests that creatinine, d-dimer, lactate, potassium, and ischemic heart disease are predictors of mortality in these patients. Thus, 58 of mechanically ventilated patients died, with a predominance of males and ages ranging from 70 to 81 years.
Cao Y., Hiyoshi A., Montgomery S., World, 2020.[29]	10, 445,656 confirmed COVID-19 cases and 511,130 deaths due to two hundred and nine countries and territories worldwide. Secondary data from the Our World in Data website.	Investigate the influence of demographic and socioeconomic factors on COVID-19 case fatality rate (CFR) globally.	The mean COVID-19 MR of countries and territories is about 2% to 3% worldwide. Risk factors associated with deaths were CVD and DM. SA: used spatial autocorrelation (Moran's Index), Pearson's correlation and multivariate linear regression. There were spatial clusters of deaths in Yemen (Asia), Western and Northern Europe and North America.
Kranjac AW; Karanjac D, World, 2021.[31]	4,098 deaths due to SARS-CoV-2 in 17 nations worldwide. Secondary data extracted from the ECDC between 13 January and 1 November 2020.	Examine the structural, sociodemographic and environmental factors of estimated MR in 17 nations affected by the COVID-19 pandemic.	The lethality rate of COVID-19 was higher in European and North American countries than that observed in Asia. The USA and the United Kingdom had high mortality (7.84%) compared to Japan and Singapore (1.54%). Obesity, DM and age are positively associated with MR. Ambient air pollution was a risk factor for higher lethality rates due to COVID-19.
Middya AI; Roy S; India, 2021.[33]	156,742 cumulative deaths related to COVID-19 until February 24, 2021. Data obtained from a public domain website: https:covidindia.org.br.	Explore the socioeconomic and demographic potential and environmental factors determining COVID-19 deaths.	The highest number of deaths due to COVID-19 was mainly in the western part of India. Associated factors were socioeconomic level and age greater than 50 years. SA: used the OLS (ordinary least square) and GWR (geographically-weighted regression) models and spatial correlation (Moran's Index) to verify associations of deaths. Significant clusters of deaths due to the disease were identified in the state of West Bengal.
Castro et al, Brazil, 2021.[34]	5,082,637 confirmed cases and 150,198 deaths in the period from February 23, 2020 to October 10, 2020. Secondary data from state health departments.	Understand, measure and compare the pattern of spread of COVID-19 cases and deaths in Brazil at thin spatial and temporal scales.	The first cluster of COVID-19 deaths was in May 2020 in Recife. Afterwards, five others emerged until June 2020. The clusters were around Fortaleza, Rio de Janeiro, Amazonas, Pará and Amapá. In January 2021, Manaus (the capital of Amazonas) had a cluster with significant cases and deaths, with collapse of the hospital network and death rates 39.8% higher than in 2020. SA: used spatiotemporal scanning and spatial correlation techniques (Moran's Index), presenting thematic maps with clusters of cases and deaths in Brazilian states by epidemiological weeks.

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Mallipattu et al, USA (New York), 2020.[24]	1,325 patients with COVID-19, hospitalized between March 2 and May 11, 2020. Data were extracted from electronic medical records of patients at the Renaissance School of Medicine at Stony Brook University.	Identify predictors of length of stay and death in hospitalized patients with COVID-19.	Mean age 62 years, most were male (57%) with a history of hypertension (60%), obesity (41%), and diabetes (42%). SA: LASSO. The geospatial distribution of patients' homes in relation to population density was mapped by USA regions, and the analysis showed that geographic residences of patients hospitalized with COVID-19 were associated with greater population housing or were located in regions with clusters.
Mikami T et al., USA, 2021.[12]	6,493 COVID-19 patients between March 13 and April 17, 2020. Secondary data extracted from the medical records of Mount Sinai Health System.	Describe the clinical characteristics and risk factors associated with mortality in a large population of patients in the USA.	858 patients died (13.2%), of which 52 were on an outpatient basis and 806 were hospitalized. There was an increased risk of in-hospital mortality over 50 years old, male, hypotension, tachypnea, hypoxia, impaired renal function, elevated D-dimer and elevated troponin. Asians had a higher MR than other ethnic groups.
Rosenthal, et al., USA, 2020.[38]	64,781 COVID-19 patients treated at 592 US hospitals between April 1 and May 31, 2020. Data extracted from the Premier Healthcare database.	Characterize COVID-19 patients in US hospitals and examine risk factors associated with in-hospital mortality.	The in-hospital MR was 20.3%. The use of hydroxychloroquine and azithromycin was associated with a higher chance of mortality. Common acute complications included acute respiratory failure, acute renal failure, and sepsis.
Grasselli et al, Italy, 2020.[26]	3,988 individuals with COVID-19 in the ICU. Data collected from records of the Ca Granda Coordination Center of COVID -19 between February 20 and April 22, 2020.	Assess risk factors associated with mortality among COVID-19 patients in ICUs in Lombardy, Italy.	60.5% of patients had at least one comorbidity. At ICU admission, 2,929 patients required invasive mechanical ventilation (IMV). Some independent factors associated with MR included advanced age (mean 63 years), male gender, history of COPD, type 2 DM, and hypercholesterolemia.
Berenguer et al., Spain, 2020. [21]	4,035 patients with COVID-19 hospitalized in 127 Spanish centers. Data extracted from electronic medical records, until March 17, 2020.	Analyze the characteristics and predictors of death in hospitalized patients with COVID-19 in Spain.	High mortality in patients aged ≥80, who presented three or more comorbidities (47.7%) and in ICU patients (42.4%). Some factors independently associated with mortality were hypertension, CVD, DM, obesity and active cancer. Males accounted for 68% of deaths.
Harris R, England (London), 2021.[36]	20,283 deaths due to COVID-19 in the period from March 1 to April 17. Secondary data collected from the Office of National Statistics (ONS).	Explore neighborhood-level correlations of COVID-19 deaths in London, England.	Mortality was associated with Asian ethnic groups, blacks, socioeconomic disadvantages, and large families. SA: Poisson spatial regression and Spearman spatial correlation. Neighborhoods with higher mortality were Faling, Merton and Croydon.
Kathe NJ, Wani RJ, USA, 2021.[30]	Cumulative confirmed cases (11,025,775) and deaths (199,170) due to COVID-19 in 3,011 US cities. Data extracted from The New York Times repository on February 27, 2021.	Assess ecological factors and clinical care associated with the United States COVID-19 lethality rate.	DM, age 65 years or older, reason for income inequality, social issues, were positively associated in some US cities with higher mortality. SA: Durbin spatial regression model and Moran's index were used, and clusters of high COVID-19 mortality in the border counties of the Phoenix area in Arizona were found.
Sousa, GJB et al. Brazil, 2020.[32]	2,070 cases and 131 deaths of people with COVID-19. Secondary data obtained from IntegraSUS until April 14, 2020.	Identify the risk factors associated with mortality and survival due to COVID-19 in a state in northeastern Brazil.	6.3% died. Variables that potentiated MR were elderly, CVD, DM, neurological diseases and lung diseases. The difference between the sexes was not significant, but the male had a higher death (relative risk of 1.1, while for females, 1.0).
Contreras-Manzano, et al., Mexico, 2020.[35]	175,148 cases with 20,773 deaths due to COVID-19. Secondary data extracted from the General Directorate of Epidemiology of the Mexican Ministry of Health on June 20, 2020.	Analyze the factors at the municipal level associated with a high MR due to COVID-19 in Mexico.	At the municipal level, the prevalence of DM, obesity, population density and others influenced mortality. In 82 municipalities, MR was higher than expected, with 13.8 deaths/100,000 inhabitants. SA: the Poisson regression model was used to assess the binary outcome of death by COVID-19 and in the independent variables analyzed other characteristics and comorbidities.
Alamdari NM et al, Iran, 2020.[18]	It included 459 hospitalizations due to COVID-19 with 63 deaths. Data extracted from forms validated from electronic health records between January 30 and April 5, 2020.	Determine prognostic factors associated with COVID-19 mortality in patients admitted to a hospital in Tehran, Iran.	Older age, higher BMI, presence of lymphopenia, hypomagnesemia and elevated creatinine on admission have a higher risk of mortality. Predominance of male patients in hospitalizations 69.7% and deaths 77.8%. The MR was higher in patients with comorbidities of DM, malignancy, CKD and obesity.

Souris, Gonzales, France, 2020.[37]	94,238 hospitalizations with 16,380 deaths due to COVID-19. Secondary data taken on the Santé Publique France website between March 19 and May 8, 2020.	Analyze the effectiveness of France's health system against COVID-19 and discuss differences in France's lethality rates with other countries.	The hospital MR in the period was 0.174. SA: spatial correlation (Moran's Index) at the district level showed no correlation between hospital capacity (number of beds per 100,000/inhab.) and the standardized lethality rate COVID-19 in France. High MR affect rural districts with low population density.
Yu C et al., China, 2020.[28]	1,464 patients hospitalized with COVID-19, with 212 deaths. Data extracted from electronic medical records between January 14 and February 28, 2020.	Examine the risk factors for mortality due to COVID-19 and establish a mortality risk prediction model.	Older age, males, hypertension, history of diabetes, lymphopenia and increased procalcitonin on admission were the variables associated with increased mortality.
Luo Y; Yan J; Clure S; USA, 2021.[1]	All daily COVID-19 deaths in 3,108 US counties between January 22 and June 26, 2020. Data collected on the USA FACTS and US Census Bureau websites.	Explore the variation in nonlinear relationships between multiple risk factors and the COVID-19 MR in different locations.	Risk factors related to socioeconomic levels were the ones that most correlated with COVID-19 mortality, other aspects highlighted were moving towards work, the environment, health status and climate. SA: GW-RF was used to estimate the nonlinear relationship between the COVID-19 MR and associated risk factors.
Surendra H et al., Indonesia, 2021. [27]	4,265 patients with COVID-19, hospitalized between March 2 and July 31, 2020, in 55 hospitals. Data collected from medical records extracted by the epidemiological investigation instrument.	Assess clinical characteristics and factors associated with in-hospital mortality of COVID-19 patients in Jakarta, Indonesia.	Higher MR due to COVID-19 was associated with age, male gender, pre-existence of hypertension, DM or CKD and immediate admission to the ICU or intubation. At all ages, the risk of death was higher for patients with more than one comorbidity.
Najera H; Ortega-Avila Ag, Mexico, 2020.[25]	515,090 cases with 55,963 deaths due to COVID-19. Secondary data extracted from the general direction of epidemiology data of the Government of Mexico until August 15, 2020.	Analyze how the interaction effects of noncommunicable diseases affect the mortality risk of patients with COVID-19 and estimate the risk variation between institutions with different comorbidity profiles.	Males, indigenous (speakers of the indigenous language) and older were more likely to die. Those with DM, obesity, CKD, hypertension and use of immunosuppressants had a higher risk of death. CVD were not associated with higher mortality. The interaction of DM with other comorbidities such as CKD and hypertension doubles the risk of COVID-19 mortality.
Alshogran OY et al, World, 2021.[19]	Confirmed cases and deaths due to COVID-19 in 113 countries that had more than 100 positive cases by April 13, 2020. Secondary data collected from the Johns Hopkins University coronavirus resource center.	Check the association of social, demographic, non-communicable diseases and health care factors with deaths due to COVID-19 worldwide.	The MR of COVID-19 varies between countries by 4.2 ± 3.8%, about half of the countries had a MR > 3.2%. There was no significant positive association at the country level between comorbidities hypertension and DM and deaths. SA: multivariate logistic regression and Spearman correlation. The analyses showed that the proportion of people over 60 years of age was positively correlated with fatal cases.

Source: own authorship. Caption: SA= spatial analysis; DM= diabetes mellitus; CVD = cardiovascular diseases; COPD = chronic obstructive pulmonary disease; CKD= chronic kidney disease; MR= mortality rates; ICU= Intensive Care Unit.

in vital signs [12] and more severe conditions, such as severe acute respiratory syndrome, requiring the use of mechanical ventilation.[23,38]

Specifically, regarding age, all studies that evaluated this variable demonstrated the association of higher death rates among older patients. A study that analyzed several countries found that 80% of deaths caused by COVID-19 occurred among adults aged ≥ 65 years.[10] Other studies showed similar results, thus showing that older adults aged 60 years and over had a higher risk of death.[18-20,22-24,26,28,31]

The greater vulnerability to COVID-19 in this age group may be associated with the weakening of the immune system in the fight against infections,[39,40] when the functions of T and B cells become potentially more defective with high production of type 2 cytokines, thus causing a deficiency in the control of viral replication, which is possibly related to the worse clinical prognosis in this age group.[28,41]

Gender was another factor that was associated with higher mortality due to COVID-19, with the male being the most prevalent.[10,12,18,21,22,24-28,38] In China, a retrospective study analyzing factors associated with mortality due to COVID-19 demonstrated, through multivariate logistic regression analysis, 2.75 more chances of mortality in men than in women.[28] Approximate value was verified in a survey conducted in a hospital unit in Iran, in which the odds ratio of mortality was three times higher in men.[18]

This higher mortality in men can be analyzed from some factors, such as higher prevalence of pre-existing

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diseases in this group (coronary, chronic lung diseases and DM), more frequent risk behaviors such as smoking and alcohol habits, occupational exposure and sexual, genetic and hormonal differences.[42] Additionally, women generally produce a more effective and adaptive immune response to viruses, which favors a less severe evolution of COVID-19.[43]

Regarding the clinical manifestations of patients who progressed to death, the most frequent were dyspnea, fever, cough,[22,28] severe acute respiratory syndrome and consequent need for mechanical ventilation support.[18,23,26] This is justified due to the disease predominantly affecting the respiratory system, causing upper and/or lower airway infection.[44,45]

Among the comorbidities associated with deaths due to COVID-19, cardiovascular diseases (CVD) and DM stood out.[18,20,23,29-31] Patients with CVD have increased serum levels of angiotensin-converting enzyme 2, which binds to the Spike protein of SARS-CoV-2, which may contribute to more severe manifestations.[46] In diabetics, the higher concentration of glucose in monocytes can result in greater viral replication and production of pro-inflammatory cytokines, so they present a late hyperinflammatory response and a decrease in adaptive immunity.[47] Other studies have also shown other health conditions associated with deaths, such as neurological,[20,32] respiratory, kidney diseases[12,27,38] and obesity.[20,21,35]

In addition to biological and clinical factors, other factors that influenced mortality due to COVID-19 were socioeconomic, environmental and spatial distribution of the disease in the area of residence. Research conducted in 209 countries around the world,[29] in which spatial analysis techniques were used, such as global and local Moran's Index, in addition to multivariate logistic regression, identified the association of economic factors and population density related to mortality from the disease, establishing that mortality rates were associated with low economic level and higher population density in low- and middle-income countries. These data corroborate a study conducted in the United States, where it was found that income inequality and precarious housing conditions influenced the increase in mortality rates from the disease.[30]

Still in this perspective, in research that covered countries on the American, European and Asian continents, researchers reported that socioeconomic status can affect mortality due to COVID-19, because, as the number of severe cases increases and the public health system is overloaded, patients who need intensive care may not be able to receive care and do not have financially resources to provide another source of care.[11]

Socioeconomic and demographic risk factors, commuting route to work, environment, health status, and climate-related factors in the United States were associated with the COVID-19 mortality rate. It is also noteworthy that the concentration of benzene in the air showed a high correlation with death due to COVID-19, appearing as the main risk factor in 24% of the municipalities analyzed in this study.[1]

These findings are possibly related to the fact that SARS-CoV-2 spreads through the air; thus, walking to work reduces social distancing, which increases the risk of infection and dissemination. As for the influence of benzene concentration on increased mortality, it occurs due to the possible bonds of suspended particles that spread in the air, so an air with more pollutant particles is more favorable in viral propagation.[1]

Regarding the spatial distribution of COVID-19 deaths worldwide, until July 2, 2020, it was found that the highest concentration of deaths occurred in Yemen (27%), Western and Northern Europe (14% – 19%) and North America (9% – 12%). When employing Moran's analysis, a statistically significant spatial dependence relationship was found around countries/territories with high lethality due to the disease; thus, the areas considered to be at greatest spatial risk were North America and Western Europe.[29]

A study that investigated the association of multiple factors, including demographic, social, economic, health care, child health and non-communicable diseases with COVID-19 lethality worldwide, employed multivariate logistic regression and Spearman's correlation, revealed that, in April 2020, the three countries with the highest mortality rates from the disease were Zimbabwe, with a rate of 21.4% (Africa), Algeria with a rate of 17.6% (Africa) and Italy, with a rate of 15.6% (Europe).[19] In addition to this, it was also observed that the polio vaccine immunization coverage was related to a lower mortality due to COVID-19.

Research carried out in India using GWR techniques showed that the geographical distribution of deaths reported by COVID-19 did not occur randomly and was related to underlying factors, including demographics, socioeconomic and environmental variations related to pollution between different territories, with emphasis on regions with higher mortality rates linked to environmental pollution by $PM_{2.5}$ particles in the east of the country.[33]

It is also noteworthy that, through spatial scan statistic, significant clusters of high relative risk were detected statistically significant for the occurrence of deaths, and priority locations for health interventions were indicated by management and health services and systems, namely the city of Manaus, in the state of Amazonas (Brazil)[34], and in the states of Oaxaca, Yucatán and Sonora (Mexico).[35] This technique has been routinely used in several ecological studies carried out around the world dealing with communicable diseases, as it allows the identification of clusters, whether of low or high relative risk, of a given event in space and space, calculating radii in which values maximize the likelihood function related to the total number of cases observed.[49]

Other significant clusters for mortality were identified through spatial analysis of the global and local Moran's Indexes in border counties in the Phoenix area of Arizona (USA),[30] state of West Bengal (India).[33] Clusters with high lethality values were found in regions of high morbidity, especially in the state of Grand-Est (France).[37]

It is noteworthy that the global and local Moran methods incorporate information about the meaning of spatial patterns and identify spatial autocorrelation between ecological units of analysis.[50] In the case of the studies of this review that used them, it was possible to

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identify and visualize, through LISA Maps, areas with higher mortality and lethality due to COVID-19, considered as priority areas for interventions aimed at monitoring the disease. This index provides a unique value as a measure of spatial association for the entire data set. This general measure of spatial association in the data set ranges from –1 to +1, in which values close to zero are related to the lack of spatial autocorrelation considering the values of the objects and their neighbors. Values close to 1 indicate positive autocorrelation, and negative values indicate negative autocorrelation.[50]

Thus, the use of geography in health through spatial analysis techniques in diseases is substantial, as it shows geographic patterns, detects spatial or spatial-temporal clusters of diseases and verifies their significance, pointing out which spatial correlations occur in the studied areas, as well as to make maps that allow visualizing disease mortality. Thus, in relation to COVID-19, in which spatial dissemination is an important factor, it assists in surveillance and control, by pointing out priority areas for necessary health and socio-spatial interventions.[29]

Among the limitations identified in the studies analyzed, the fact that they were carried out from secondary data (collections in databases, public domain websites or electronic patient records) stands out initially. Thus, the possibility of underreporting of pre-existing cases, deaths and comorbidities stands out, which interferes with the reliable determination of the disease's morbidity and mortality indicators, in addition to making it difficult to verify other variables of the clinical and epidemiological context associated with deaths due to the disease. Another limitation cited in studies on the spatial distribution of deaths was the so-called ecological fallacy, emphasizing that these findings should not have their results reproduced at the individual level, since they are population studies with interpretation at the group level of the regions analyzed.[48]

CONCLUSION

The studies analyzed demonstrated how some risk factors and geographic distribution affected COVID-19 mortality worldwide. Clinical, social and epidemiological conditions are crucial points in the outcome of the disease. Variables, such as age over 60 years, males and presence of comorbidities resulting from cardiovascular complications and DM, were predominantly associated with deaths due to COVID-19 and were listed as the main risk factors.

As for the spatial distribution of deaths, a heterogeneous distribution was observed in the different settings investigated. The use of different analysis techniques helped to identify geographic areas with higher population density, lower income, lower presence of sanitary sewage, higher environmental pollution and lower hospital capacity, associated with increased mortality.

These data indicate disparities in health, environmental and socioeconomic conditions that exist in different parts of the world. From this, the need to intervene on the identified risk factors emerges and to investigate, through additional studies, other factors associated with death in infected patients, as well as to know the spatial distribution of the disease in vulnerable territories, in order to contribute to the fight against the pandemic and to the elaboration of health strategies and policies that minimize mortality due to COVID-19.

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REVIEW ARTICLE

Prevention of COVID-19 aerosol exposure during orotracheal intubation

Prevenção da exposição ao aerossol COVID-19 durante a intubação orotraqueal

Prevención de la exposición a aerosoles de COVID-19 durante la intubación orotraqueal

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ABSTRACT

Background and objectives: during orotracheal intubation (OTI), it occurs the exposure to COVID-19 aerosols and consequent contamination of the professionals involved, observing the need to apply preventive measures. The objective is to know, in the scientific literature, which are the main preventive measures for health professionals to aerosols generated during OTI of patients suspected or confirmed for COVID-19. **Contents:** this is an integrative review, with search in the LILACS, SciELO, BDENF, MEDLINE, PubMed and Cochrane Wiley databases. Primary articles, with full text in Portuguese, Spanish and English, which contemplated the research objective, were selected. Of the 335 articles found, 22 were selected according to the inclusion criteria. In 18 (82%) of articles, they highlighted the use of barrier methods when performing the intubation procedure, such as acrylic box and plastic tarpaulin. In other studies (3; 14%), it was observed the need to include qualified intubation teams in hospital institutions to reduce the contamination of professionals, in addition to the application of checklists that guide the procedure. A single article brought the use of an orthopedic protective cover adapted to protect the intubator. **Conclusion:** the measures are defended to reduce exposure to aerosols and allow the safety of health professionals. The use of an intubation box must be used with caution, weighing the risks and benefits against the possibility of aerosolization during its use in orotracheal intubation.

Descriptors: *COVID-19. Aerosols. Health Personnel. Intratracheal Intubation.*

ABSTRATO

Justificativa e objetivos: durante a intubação orotraqueal (IOT), ocorre a exposição a aerossóis de COVID-19 e consequente contaminação dos profissionais envolvidos, observando a necessidade de aplicação de medidas preventivas. O objetivo é conhecer, na literatura científica, quais são as principais medidas preventivas dos profissionais de saúde aos aerossóis gerados durante a IOT de pacientes suspeitos ou confirmados para COVID-19. **Conteúdo:** trata-se de uma revisão

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integrativa, com busca nas bases de dados LILACS, SciELO, BDENF, MEDLINE, PubMed e Cochrane Wiley. Foram selecionados artigos primários, com texto completo em português, espanhol e inglês, que contemplassem o objetivo da pesquisa. Dos 335 artigos encontrados, 22 foram selecionados de acordo com os critérios de inclusão. Em 18 (82%) dos artigos, destacaram o uso de métodos de barreira na realização do procedimento de intubação, como caixa de acrílico e lona plástica. Em outros estudos (3; 14%), observou-se a necessidade de incluir equipes de intubação qualificadas nas instituições hospitalares para reduzir a contaminação dos profissionais, além da aplicação de checklists que orientam o procedimento. Um único artigo trouxe o uso de uma capa protetora ortopédica adaptada para proteger o intubador. **Conclusão:** defendem-se as medidas para reduzir a exposição aos aerossóis e permitir a segurança dos profissionais de saúde. O uso da caixa de intubação deve ser feito com cautela, ponderando os riscos e benefícios em relação à possibilidade de aerossolização durante seu uso na intubação orotraqueal.

Palavras-chave: *COVID-19. Aerossóis. Pessoal de Saúde. Intubação Intraqueal.*

RESUMEN

Justificación y objetivos: durante la intubación orotraqueal (OTI), ocurre la exposición a los aerosoles de COVID-19 y la consecuente contaminación de los profesionales involucrados, observándose la necesidad de aplicar medidas preventivas. El objetivo es conocer, en la literatura científica, cuáles son las principales medidas preventivas de los profesionales de la salud ante los aerosoles generados durante las IOT de pacientes sospechosos o confirmados de COVID-19. **Contenido:** se trata de una revisión integradora, con búsqueda en las bases de datos LILACS, SciELO, BDENF, MEDLINE, PubMed y Cochrane Wiley. Fueron seleccionados artículos primarios, con texto completo en portugués, español e inglés, que contemplaran el objetivo de la investigación. De los 335 artículos encontrados, 22 fueron seleccionados según los criterios de inclusión. En 18 (82%) de los artículos, destacaron el uso de métodos de barrera al realizar el procedimiento de intubación, como caja de acrílico y lona plástica. En otros estudios (3; 14%), se observó la necesidad de incluir equipos de intubación calificados en las instituciones hospitalarias para reducir la contaminación de los profesionales, además de la aplicación de listas de verificación que orientan el procedimiento. Un solo artículo trajo el uso de una cubierta protectora ortopédica adaptada para proteger al intubador. **Conclusión:** se defienden las medidas para reducir la exposición a los aerosoles y permitir la seguridad de los profesionales de la salud. El uso de una caja de intubación debe hacerse con precaución, sopesando los riesgos y beneficios frente a la posibilidad de aerosolización durante su uso en la intubación orotraqueal.

Descriptores: *COVID-19. aerosoles Personal sanitario. Intubación Intraqueal.*

INTRODUCTION

In December 2019, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2) was responsible for the first cases of pneumonia of unknown etiology in the city of Wuhan, China.[1] It is an RNA virus of family *Coronaviridae*, widely distributed among humans and other animals.[2] The exponential growth of cases in China, reaching hundreds of countries, led the World Health Organization (WHO) to declare the disease called Coronavirus Disease 2019 (COVID-19) as a pandemic.

The disease can occur as flu-like syndrome (FLS), through fever, simultaneously with the onset of dry cough, tiredness, nasal congestion or sore throat.[3] However, the clinical manifestation can present as Severe Acute Respiratory Syndrome (SARS) and pneumonia, ranging from low to high criticality in patients.[1] Severity is related to age and the presence of comorbidities, such as diabetes, obesity and cardiovascular diseases, with mortality of 14.8% in older adults over 80 years and with an association of fatal outcome for the presence of comorbidities for all ages.[3,4]

The number of patients admitted for hospital care without progression to criticality is higher when compared to those who need beds in the Intensive Care Unit (ICU).[5] However, when assessing patients who evolve to the ICU, between 33% and 75% of critically ill patients require artificial respiratory support by invasive mechanical ventilation (IMV), with mortality of 10.2% for all those affected by COVID-19 and 14.6% for mechanically ventilated patients.[5,6] Mortality occurs in 61.5% of critically affected patients, in 28 days of ICU admission.[1]

Thus, health professionals should be prepared for the assistance of those who evolve to ventilatory failure, with the imminent need for orotracheal intubation (OTI). However, during the assistance for definitive airway management, the team is exposed to aerosols resulting from the procedures, with risk of contamination associated with the different routes of transmission, contact with patients for a longer period of time, intense working hours and greater complexity of care tasks.[7]

The National Health Commission of China reported that 3,300 health professionals were infected during care until March 2020, with 22 deaths.[8] For the care of these patients, it is imperative to use all personal protective equipment for standard precaution, droplets and aerosols, especially for aerosol-generating procedures (AGP).[9]

Health professionals who participate in critical AGP, such as OTI, cardiopulmonary resuscitation and airway aspiration, must be equipped with personal protective equipment (PPE), such as gloves, caps, face shield or goggles, N95 mask and waterproof apron.[10] Furthermore, it

is advised to perform these procedures in isolation rooms of respiratory infection with negative pressure and the use of special filters of the high-efficiency particulate air (HEPA) type in mechanical ventilators.[10]

New guidelines for the use of PPE constantly emerge, as well as aerosol prevention measures are updated to the knowledge of professionals and health establishments. Considering the cases of critically ill patients who require OTI and permanence in IMV, associated with the risk of exposure during PGE by the care team and the need to constantly update the guidelines for infection control, we see the need to compile the main guidelines to facilitate the reading, access and understanding of these professionals who are on the front line. Thus, this research aims to know in scientific literature what are the main prevention measures for health professionals to aerosols generated during OTI of patients suspected or confirmed for COVID-19.

METHODS

This is an integrative review, in which the six methodological steps necessary for its development were followed, namely: 1) guiding question elaboration; 2) search or sampling in literature; 3) critical analysis of included studies; 4) data collection; 5) discussion of results; and 6) integrative review presentation.[11] Through the strategy PICo, the research question to be investigated was elaborated: what are the aerosol exposure prevention measures during OTI by health professionals in patients suspected or confirmed for COVID-19? Population would be health professionals, Intervention, measures to prevent contamination of health professionals by the virus, and Context, exposure to aerosols during OTI.

The inclusion criteria were articles from primary studies published in Portuguese, English or Spanish, available as full texts for reading in full. This integrative review excluded studies that did not answer the research question or did not contemplate the objective, in addition to articles in the format of letters, consensus and guidelines, in addition to review articles (narrative, integrative and scoping review).

The selection of articles took place through the Virtual Health Library (VHL), in the Latin American and Caribbean Literature in Health Sciences (LILACS), Medical Literature Analysis and Retrieval System Online (MEDLINE) and Database in Nursing (BDENF) databases. Likewise, the search was carried out in the Scientific Electronic Library Online (SciELO), and, for the selection of randomized clinical studies, a search was carried out in Cochrane Wiley. To expand the selection of international studies not included in the VHL, the search was carried out through the National Library of Medicine (PubMed). During the selection in virtual libraries, the international indexed Medical Subject Headings (MeSH) descriptors were used: "COVID-19", "aerosols", "intubation", "protect". With the help of the Boolean operator AND, sets of descriptors were applied to the following databases: BDENF, LILACS, MEDLINE and Cochrane Wiley, "(COVID-19) AND (aerosols) AND (intubation)"; SciELO, "(COVID-19) AND (aerosols)"; and PubMed, "(((COVID-19) AND (aerosols)) AND (intubation)) AND (protect)".

After the identification of primary articles, the selection process was carried out from the exclusion of duplicates, subsequent reading of titles and abstracts to exclude those that did not contemplate the research topic. The steps of identification, selection and inclusion of articles were carried out between May and June 2021 and followed the PRISMA method (Figure 1).[12]

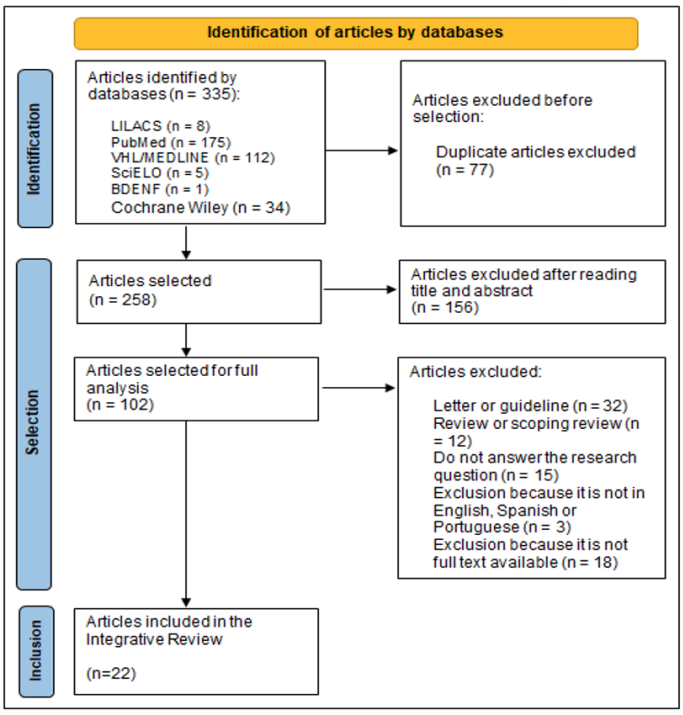

Figure 1. Updated PRISMA flowchart 2021, including database searches.

The 22 selected primary studies were assessed for methodological scientific rigor, classified according to the level of evidence (LoE).[13] Articles with LE I were considered to be systematic reviews or meta-analyses; LoE II, randomized controlled trials; LoE III, controlled studies without randomization; LoE IV, case-control or cohort studies; LoE V, systematic reviews of qualitative or descriptive studies; LoE VI, qualitative or descriptive studies; and LoE VII, opinions or consensus.[13] Subsequently, the information contained in the studies was summarized, according to author, year and place of publication, objective, design and LoE, and measures to prevent aerosols from COVID-19 during OTI.

RESULTS AND DISCUSSION

A total of 22 primary studies were selected to make up this integrative review. Almost all studies were found in PubMed (20; 92%), followed by MEDLINE (1; 4%) selected through VHL and Cochrane Wiley (1; 4%). The United States published 12 (55%) articles, Canada, four (19%), Australia, two (10%), Israel, one (4%), Turkey, one (4%), England, one (4%), and Malaysia, one (4%). No studies published in Brazil or other countries in Latin and South America were identified.

Regarding the methodology, no meta-analysis studies were identified, considered the best scientific evidence among scientific studies. Randomized clinical trial-type studies made up most of the sample, with 11 (50%) whose LoE is II; non-randomized or quasi-experimental studies comprised eight (36%) of LoE III; cohort studies comprised one (5%) of LoE IV; while descriptive studies, of the case study type, totaled two (9%), of LoE VI.

Article synthesis was carried out regarding author, year and country, objective, design and level of evidence, and the main protection measures highlighted in the scientific articles, as shown in Chart 1.

Of the studies analyzed, it was found that 18 (82%) highlighted the use of barrier methods during the

Chart 1. Synthesis and level of evidence of selected articles.

Main author / year / place	Objective	Design and LoE	COVID-19 aerosol prevention measures during OTI
Rose P, 2020, Canada.[14]	Assess the risk of droplet and contact contamination for healthcare professionals using 3 intubation techniques as part of a quality assurance study.	Double-blind randomized quality assurance study LoE II	Intubation was assessed simulating droplet dispersion with: a) no protective barrier between manikin and intubator; b) use of transparent plastic; and c) acrylic box, covering the dummy's head. The use of plastic barrier did not add any benefit when compared to the other techniques. When using plastic, the risk of droplet dispersion and subsequent contamination to the intubator increased when compared to the acrylic box.
Azhar MN, et al., 2021, Malaysia.[15]	Investigate the relationship between the use of a protective aerosol box and contamination of health professionals before and after personal protective equipment (PPE) donning and doffing.	Randomized double-blind controlled study LoE II	Simulation of intubation with and without plastic box, through videolaryngoscopy in dummy. The use of a box for intubation reduces droplets and aerosols contaminants in PPE of health professionals involved in the procedure. There was an increase in mobility and visualization during intubation, in addition to the decrease in success in the first attempt.
Turner JS, et al., 2020, United States.[16]	Measure the effects of a box to contain aerosols on intubation in different simulation scenarios in the Emergency Department.	Randomized double-blind controlled study LoE II	Five intubation scenarios were used, with the participation of 48 medical residents, performing 96 intubations. OTI time was significantly longer with the use of a protective box, compared with no use. There was greater difficulty in intubating in difficult-to-manage emergency airways. The box use can increase intubation time and hinder the procedure (17 versus 10 seconds, respectively).
Derrick J et al., 2020, Australia.[17]	Investigate whether the use of a plastic casing could reduce aerosol exposure during laryngoscopy.	Randomized double-blind controlled study LoE II	Simulation of 90 intubations on a dummy, with saline nebulization to simulate aerosols. The measured mean aerosol count was significantly reduced when the wrap was worn over the patients' head. Thus, casings during intubation can avoid the chance of increased levels of dispersed aerosol particles. There was no difference in OTI time compared to the conventional technique.
Feldman O et al., 2021, Israel.[18]	Assess the time to OTI of paramedics wearing personal protective equipment with and without an aerosol protection box.	Randomized double-blind controlled simulation study LoE II	A total of 18 paramedics simulated intubation by laryngoscopy with and without an aerosol protection box. The results suggest that professionals wearing adequate PPE (N95, face shield, apron and gloves) and adequately trained can successfully intubate using the box, however, the procedure time can be prolonged compared to non-use (27 versus 37 seconds, respectively).

Fong S, et al., 2021, Canada.[19]	Explore the impact of using a protection box for aerosols during normal and difficult-to-handle OTI.	Randomized double-blind controlled simulation study LoE II	The performance of 296 intubations with and without the protection box was verified in 4 difficult airway scenarios. The mean intubation time with and without the box was 31 versus 25 seconds, respectively. With the protection box, there were more OTI attempts, damage to the PPE entirety and optimization of maneuvers to achieve intubation.
Burnett GW, et al., 2020, United States.[20]	Assess intraoperative contamination and decontamination of an aerosol protection box and the impact of a preoperative educational visual aid.	Randomized double-blind study LoE II	It was divided into groups that could previously see contamination points in the box and without access. Those who could see contaminated themselves less and the box was completely cleaned. It should be considered to educate professionals for correct use. There is a potential risk of contamination when removing the box after intubation for both professionals and the environment.
Ozbek AE, et al., 2021, Turkey.[21]	Compare the use of conventional PPE, protective box and transparent plastic, and its impacts on intubation time by experienced emergency workers.	Randomized, prospective, double-blind LoE II study	OTI was assessed in different scenarios: a) only with the use of PPE; b) use of PPE and transparent plastic; and c) PPE and box. The use of box increased the time required to intubate compared to other scenarios, but without statistical significance. Although participants were successful in the first OTI, there was greater difficulty in mobility and visualization using the barriers compared to just wearing PPE.
Querney J, et al., 2020, Canada.[22]	Assess the acceptance of the use and airway management of two modalities of protective aerosol barrier.	Double-blind randomized simulation study LoE II	In an intubation scenario with a) only PPE and b) PPE added to protective box and plastic barrier, there was no significant difference between intubation times. For participants, adding protection barriers does not affect visibility, mobility, and communication in OTI.
Begley JL, et al., Australia.[23]	Assess the impact of two aerosol protection boxes on the OTI of patients with COVID-19.	Randomized study without blinding LoE III	When assessing two acrylic box formats for OTI, both showed an increase in the time required to intubate, compared to non-use. There was also a violation of PPE integrity when using both barrier box formats. It was concluded that barrier box increases OTI time, putting patients at risk of hypoxemia.
Madabhushi P, et al., 2020, United States.[24]	Determine whether the use of a barrier box with videolaryngoscope delays intubation time to acceptable parameters.	Double-blind randomized clinical trial LoE II	After allocating 76 patients in a group (without barrier and with barrier to intubation), it was observed that. with the use of videolaryngoscope, there is no delay in intubation time in patients with normal airway conditions, when professionals are well trained previously.
Ben-Yakov M, et al., 2020, Canada.[25]	Determine the degree of protection offered by barrier methods and explore the usage factors by two popular barrier systems.	Randomized clinical trial LoE II	Comparing three methods of OTI using PPE (without barrier, box and frame with plastic tarpaulin), there was greater contamination of the environment with the box, without statistical significance. Barrier systems increase OTI time (no barrier 24 seconds, frame 54 seconds, and box 34 seconds), $p<0.001$. Tarpaulin and frame reduce contamination, but at the expense of mobility and visibility.
Fidler RL, et al., 2021, United States.[26]	Describe the behavior of aerosols using 7 protection models during OTI, for how long each barrier limits aerosols and protection outside barriers.	Near-experimental study* LoE III	After assessing 7 barrier methods, the fully or partially closed ones reduce the particle count directly to the intubator, which does not include the acrylic protective box in the group, as it contains holes for the entry of the intubator's arms. Thus, methods that are not fully closed, allow aerosol dispersion. Barrier methods should be used in conjunction with PPEs, as there was aerosol in the environment.
Bryant J, et al., 2020, United States.[27]	Verify the effectiveness of a barrier method in reducing the risk of exposure to aerosolized pathogens in airway management, including OTI.	Near-experimental study* LoE III	In the operating room of a surgical center, when using a transparent plastic barrier and air flow outlet (suction), there was a decrease in the exposure of aerosols to the environment. The use of this barrier method in association with airflow through suction methods can reduce the contamination of professionals.

Gore RK, et al., 2020, United States.[28]	Assess the effectiveness of aerosol containment in a new protective barrier system, compared to the protective box, and without the use of a barrier.	Near-experimental study* LoE III	The new barrier system consists of protectors that prevent the exposure of the intubator's arms, in addition to a plastic cover that covers the patients' chest. Compared to the traditional acrylic box, the new method exposed the intubator less to aerosols, but both are more effective when no barrier method was used.
Patel GP, et al., 2020, United States.[29]	Describe the Emory Healthcare Hospital intubation team during the COVID-19 pandemic.	Descriptive study, case study LoE VI	About 16 OTI teams formed, performing 253 intubations in the hospital. Protocols were created with the use of devices for clamping the OTT (orotracheal tube), use of HEPA filters, minimal participation of people in the OTI, and proper use of PPE (cap, gloves, gown and N95). Only one limb was contaminated by SARS-CoV-2. The use of skilled OTI teams allows the safety of professionals.
Wills TT, et al., 2020, United States.[30]	Describe the integration of an orthopedic cover as an item for COVID-19 protection.	Descriptive study, case study type LoE VI	It is an additional protective equipment that can be used in health professionals during the performance of procedures such as OTI. The disadvantage is the lack of a ventilation system for those who use this PPE.
Ahmad I, et al., 2020, England.[31]	Report the experience of a Rapid Endotracheal Mobile Intubation Team and the outcomes in patients in a seven-week observation period.	Observational, prospective cohort study. LoE IV	About 150 OTI were analyzed. Videolaryngoscopy was used in 91.3%, with single pass success in 80%. In all, 11 of the 63 professionals were contaminated and only one incident of PPE violation. Trained intubation teams followed by protocolized rapid sequence OTI are beneficial in promoting patient and staff protection.
Brant-Zawadzki GM, et al., 2021, United States.[32]	Create an alternative design of protection of the patients' head during aerosol-generating procedures.	Near-experimental study* LoE III	A transparent plastic barrier fixed on an iron support was used. When simulating aerosol scattering with an aspiration system connected to the HEPA filter, there was little concentration of aerosols within the barrier system and in the arms of the intubator, and minimal concentration in the environment.
Fried EA, et al., 2020, United States.[33]	Test two commonly used protection barriers (intubation box and transparent plastic) and observe the impact on containing aerosol spread.	Near-experimental study* LoE III	Comparing the effectiveness between the protective box and a plastic barrier, it was found that both retain the aerosols, but can redirect the dispersion to the head, neck, chest and intubator's arms. Reverse trendelenburg position can avoid direct contact. The use of barriers is ineffective and removal allows contamination of professionals.
Tronnier A, et al., 2020, United States.[34]	Create a quality improvement framework to ensure safe practices for intubation providers and describe a multidisciplinary model to track adherence to OTI protocols.	Near-experimental study* LoE III	A model was created to assess adherence to the safe intubation checklist and a multidisciplinary group that reassessed procedures to program improvements. The authors emphasize that the creation of intubation teams and protocols can be used to guarantee a safe procedure among professionals during the COVID-19 pandemic.
Turer DM, et al., 2021, United States.[35]	Quantify the ability of protective barriers to contain aerosols using industrial assessment protocols.	Near-experimental study* LoE III	The use of a commonly used protective barrier was compared, and another associated with a vacuum and air filtration system. Barriers without vacuum system allow aerosol exhaust in open areas for intubator handling. In OTI simulation, there was high concentration in the environment. When using barriers, associate vacuum and air filtration systems to contain particles.

**Articles whose methodology was not described, classified according to the authors' understanding.*

orotracheal intubation procedure, such as transparent plastic and acrylic box. It was observed in 3 (14%) the need for previously trained multidisciplinary intubation teams, as well as structured checklists to perform the definitive airway management procedure. According to the authors, trained intubation teams and protocols would make it possible to reduce the risks of exposure of professionals, as well as minimize unfavorable outcomes for patients infected by COVID-19. Still, 1 (5%) reported the use of an adapted orthopedic covering, which would cover the head of the intubator as a new PPE, but the disadvantage refers to mobility and diffi-

culty in ventilation for professionals.

The need for OTI occurs in up to 75% of critically ill patients affected by COVID-19 who require direct ICU care.[5,6] However, the performance of this procedure by health professionals puts them at risk of exposure to the virus. Intubation, along with orotracheal extubation procedures, non-invasive manual ventilation, tracheostomy, oxygen support by high-flow cannula, bronchoscopy and suction of secretions by suction, are among the critical assistance supports that generate aerosols.[36]

In an example of OTI, doctors and nurses are the professionals who are most contaminated, as they handle the upper and lower airways with very close contact, as a result of the high risk of exposure.[37] During the collapse in public health seen in Italy in early 2020, where the country reached the highest number of contaminations and deaths by COVID-19, about 9% of those infected were health professionals.[37] Thus, it is crucial to know measures that prevent exposure to the virus and the contagion of those who work in critical sectors such as emergency and ICU.

Among the articles assessed, the mandatory use of PPE is unanimous to those involved in intubation. Considering the public health emergency and the high risks of contamination of professionals during aerosol--generating procedures, it is recommended to use a N95 mask, aprons, face shield and gloves, because these devices protect professionals from direct exposure to SARS-CoV-2 viruses.[9,10] We emphasize the need for correct donning and doffing of PPE used during service, as well as the correct disposal after the OTI procedure. Carrying out the correct processes for both times of use and disuse of PPE avoids both inadvertent exposure and the risk of contamination with aerosols accumulated on professionals' mask, gloves, face shields or apron.[38]

When dealing with preventive measures during OTI, studies mostly bring the use of protective barriers in association with the use of PPE: devices in acrylic box format, protective plastic and cover that cover the patients' headboard.[14-28,32,33,35] The hypothesis raised is that only the use of PPE does not adequately protect, requiring the association of protective barriers to ensure safety.[36] Intubation boxes are acrylic boxes containing two holes, where the intubator allocates the arms for access to the airway, and an opening in its lower portion to attach the patients' head.[19] The application of barriers such as an acrylic box makes it possible to concentrate the aerosols inside and prevent dispersion to the environment during the procedure.[15,22,28] However, there was an increase in intubation time compared to non-use, difficulty in mobilizing the intubator and access to the airway, as well as the risk of error in the first attempt to intubate.[15,16,18,19,21,25]

In emergencies, the delay and difficulty of access to intubate inadvertently expose patients to hypoxemia and worsening of their clinical condition.[16,23] When trying to handle the airway, there was a violation of the apron and glove due to the holes in the acrylic box, exposing to risk of contamination.[19,23] The two openings designed to accommodate the intubator's arms allow for the redirection of aerosols to the environment, with evidence of accommodation on professionals' arms, chest and head.[14,20,26,33]

Some articles highlighted the need to associate airflows with negative suction systems inside the acrylic box, coupled in HEPA filters, showing less contamination of the intubator, as well as the almost minimal dispersion to the environment.[29,32,35] The post-procedure risk was also evidenced: at the end of intubation, the removal of the acrylic box allows the dispersion of aerosols concentrated inside it directly to the bedside, procedure materials, as well as the team involved.[26,28,30] If the association of barrier protectors with OTI is chosen, teams must be trained in the decontamination of boxes and plastic barriers, with additional risk of exposure during removal after completion of the procedure.[20,33]

The use of protective acrylic boxes should be based on team familiarization and training of those involved in handling, in order to reduce exposure to aerosols.[20,24] The use of a video laryngoscope facilitates the visualization of the airway and avoids the increase in intubation time, providing greater safety for both professionals and patients.[24] Thus, teams should analyze care routines on the benefit and risk of adding barrier protectors to intubation, and the possibility of increasing the videolaryngoscope in daily life. The training of professionals to perform OTI in emergency and ICU, as well as the use of checklists that guide the methodology of the procedure, show safety for both teams and patients.[29,31,34]

In a study developed in the United States, after the creation of a protocol containing guidelines on intubation (number of professionals present in the room to reduce exposure, use of tube clamps and HEPA filter, training in airway management and rapid OTI sequence), it was observed that, after 253 intubations, only 1 professional was contaminated and there was success in the first attempts, demonstrating that the application of protocols and the constant training of teams enable safety.[29]

On the contrary, in another study, despite the complete use of PPE and training for intubation skills, of the 63 professionals, 11 were infected. First-attempt OTI success occurred in 80% of procedures.[31] The creation of intubation teams, similar to the rapid response teams, can benefit from the guarantee of safety in performing high--risk care for teams.[34] Only one study addressed the use of tube clamps when passing the airway and the application of a HEPA filter to the expiratory circuit of the mechanical ventilator, as they were part of the OTI protocol.[29]

During the assessment of articles obtained in research, it was observed that the vast majority of published studies were guidelines and experts' recommendation letters. Recommendations regarding the association of certain OTI devices and methods in suspected or confirmed COVID-19 patients come from experts in the field to guide professionals during intubation.[10,36,37,39,40] Among the guidelines, the following stand out: performing OTI preferably in negative pressure rooms; minimum permanence of professionals (in a negative pressure room, the permanence of a doctor, a nurse and an assistant physician in a critical room, and in an auxiliary circula-

ting anteroom with a cardiopulmonary resuscitation cart; drugs and complete airway material); HEPA filters in the mechanical ventilator's expiratory circuit; avoid bag-valve-mask inflation, clamps to clamp the OTT when disconnecting the ventilation system.[10,36,37,39,40]

Although the guidelines are sources of experts in the area, there is a lack of original primary studies highlighting the efficiency of these recommendations in protecting professionals from exposure to COVID-19 aerosols. As this is a very recent topic, considering the emergence of guidelines for professionals regarding the care of critically ill patients who need a definitive airway, it is believed that there was not enough time to assess all these guidelines in methodology studies with a high level of evidence.

The limitation of this study is the research method, because it is an integrative review, and not systematic literature. Due to the very recent emergence of COVID-19, robust studies on the safety of devices such as clamps, HEPA filters, the separation of procedure rooms to avoid contamination of professionals, as well as oxygen therapy devices for the pre-oxygenation stage prior to OTI have not been identified.

Thus, with the acquisition of experience in the care of infected patients who need OTI, there is a need for original research on aerosol prevention measures for professionals involved in the procedure. The exclusion of 3 articles in other languages and 18 articles not available in full are limitations regarding the research method, inclusion and exclusion criteria.

Knowledge about methods of preventing dispersed aerosols during definitive airway management is crucial for the protection of professionals.[36] In this way, constant updates from studies with a high level of evidence allow teams to be confident in the implementation of these measures in the daily care of patients suspected or confirmed for COVID-19.

CONCLUSION

The use of barrier protectors such as the intubation box in everyday care should be analyzed with caution. Despite concentrating the aerosols in its interior, the risk of escape in its openings directly to the intubator is evident. There is difficulty in mobility and visualization, requiring previous training and experience from professionals so that there is no harm to patients with its use. Likewise, without familiarity with the device, there is an increase in procedure time, exposing patients to hypoxemia.

On the other hand, the intubation teams, the use of protocols and the training of teams demonstrate effectiveness in reducing contamination to professionals. It is necessary to observe the need for more clinical studies on safety and guarantee of protection, using other recommendations described in guidelines and expert guidance.

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AUTHORS' CONTRIBUTIONS

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Hospital Santa Cruz

EXPERIENCE REPORT

Rhodotorula fungemia in a patient with acute lymphoblastic leukemia

Fungemia de Rhodotorula em paciente com leucemia linfoblástica aguda

Fungemia por Rhodotorula en un paciente con leucemia linfoblástica aguda

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ABSTRACT

Objectives: *Rhodotorula* is an environmental yeast that belongs to *Basidiomycota* Phylum. *Rhodotorula* species are ubiquitous in nature, can be found in soil and freshwater. Immunocompromised patients can develop Rhodotorulosis due to wide-ranging exposure to *Rhodotorula* in the hospital environment. **Case Discussion:** The patient was a 3-year-old male with a diagnosis of Pro B-Acute Lymphoblastic Leukemia (ALL). He was admitted to the hospital with complaints of malaise, fatigue, weight loss, and diarrhea between courses of chemotherapy. *Rhodotorula* was isolated from the patient's blood culture obtained during the elevation of temperature. After 14 days of amphotericin B treatment, clinical situation of the patient was improved and he was discharged. **Conclusion:** *Rhodotorula* spp. as a rare yet emerging pathogen, often presents as fever of unknown etiology resistant to antibacterial treatment and can be associated with fungemia and other severe complications.

Keywords*: Rhodotorula. Amphotericin B. Precursor Cell Acute Lymphoblastic Leukemia-Lymphoma.*

RESUMO

Objetivos: *Rhodotorula* é uma levedura ambiental que pertence ao filo *Basidiomycota*. As espécies de *Rhodotorula* são onipresentes na natureza, podem ser encontradas no solo e na água doce. Pacientes imunocomprometidos podem desenvolver rodotorulose devido à ampla exposição a *Rhodotorula* no ambiente hospitalar. **Descrição do caso:** O paciente era uma criança de 3 anos de idade com diagnóstico de Leucemia Linfoblástica Aguda Pro B (LLA). O paciente deu entrada no hospital com queixas de mal-estar, cansaço, perda de peso e diarreia entre os ciclos de quimioterapia. A *Rhodotorula* foi isolada da hemocultura do paciente obtida durante a elevação da temperatura. Após 14 dias de tratamento com anfotericina B, a situação clínica do paciente melhorou e o paciente recebeu alta. **Conclusão:** *Rhodotorula* spp. como um patógeno raro, porém emergente, frequentemente se apresenta como febre de etiologia desconhecida resistente ao tratamento antibacteriano e pode estar associada a fungemia e outras complicações graves.

Palavras-chave: *Rhodotorula, Anfotericina B. Leucemia-Linfoma Linfoblástico de Células Precursoras*

RESUMEN

Objetivos: *Rhodotorula* es una levadura ambiental que pertenece al filo *Basidiomycota*. Las especies de *Rhodotorula* son ubicuas en la naturaleza, se pueden encontrar en el suelo y en agua dulce. Los pacientes inmunodeprimidos pueden desarrollar Rhodotorulosis debido a una amplia exposición a *Rhodotorula* en el entorno hospitalario. **Descripción del caso:** El paciente era un niño de 3 años con diagnóstico de leucemia linfoblástica aguda Pro B (LLA). El paciente ingresó en el hospital con quejas de malestar, fatiga, pérdida de peso y diarrea entre ciclos de quimioterapia. Se aisló *Rhodotorula* del hemocultivo del paciente que se obtuvo durante la elevación de la temperatura. Después de 14 días de tratamiento con anfotericina B, la situación clínica del paciente mejoró y fue dado de alta. **Conclusión:** *Rhodotorula* spp. como patógeno poco común pero emergente, a menudo se presenta como fiebre de etiología desconocida resistente al tratamiento antibacteriano y puede asociarse con fungemia y otras complicaciones graves.

Palabras clave: *Rhodotorula. Anfotericina B. Leucemia-Linfoma Linfoblástica de Células Precursoras.*

INTRODUCTION

Rhodotorula is an environmental yeast that belongs to *Basidiomycota* Phylum. *Rhodotorula* species produce carotenoid pigments usually causing pink or coral mucoid colonies, multilateral budding cells, undistinguished pseudohyphae and infrequently, an indistinct capsule [1]. *Rhodotorula* species are ubiquitous in nature, can be found in soil and freshwater.[1] *Rhodotorula* isolation from food such as fruit juice and milk, several medical equipments, such as dialysis equipment, fiber-optic bronchoscopes, and other environmental sources, such as shower curtains, bathtubs, and toothbrushes due to strong affinity with plastic, was also reported.[2]

In the last three decades, *Rhodotorula* species have become an increasing challenge, especially in immunocompromised patients as an opportunistic yeast.[3] Extensive use of central venous catheters (CVC) and intensive treatments may be the potential explanation for the greater number of *Rhodotorula* infection cases after the first reports in late 1980s.[4]

Immunocompromised patients can develop Rhodotorulosis that is usually associated with endocarditis, peritonitis, meningitis, and endophthalmitis due to a wide-ranging exposure to *Rhodotorula* in the hospital environment.[4]

CASE DESCRIPTION

The patient was a 3-year-old male with a diagnosis of Pro B-Acute Lymphoblastic Leukemia (ALL). He was admitted to hospital with complaints of malaise, fatigue, weight loss, and diarrhea between courses of chemotherapy. At hospital admission, the cardiac examination was normal, lymphadenopathy, hepatomegaly, and splenomegaly were not found. At admission, c-reactive protein (CRP) was found 35.44 mg/L (normal range: 0-5 mg/L), white blood cell count was 4.02 10^3/µL (normal range : 3.8-8.76 10^3/µL) and hemoglobin was 8.4 g/dL. Rapid immunochromatographic test from stool sample for Rotavirus, *Giardia intestinalis*, *Entamoeba histolityca*, and Adenovirus antigens and *Clostridium difficile* Toxin A was negative. Direct microscopic examination of stool and stool sample culture were also negative. Teicoplanin and amikacin therapy were prescribed as empiric antibiotics. Although antibacterial therapy was administered, the patient had fever episodes. Tuberculosis was excluded with acid-fast stain and PCR tests. Fungal infection was suspected but anti-mannan antibody and galactomannan antigen tests were negative.

After eight days of hospital stay, *Rhodotorula* was isolated from the patient's blood culture obtained during the elevation of temperature. Standard procedure for blood cultures was followed. When the patient had a fever, two sets of blood cultures were collected from different peripheral veins. Blood culture sample from the CVC was also collected simultaneously in order to find differential time to positivity. Blood samples were inoculated into aerobic blood culture bottles and administered to the BACTEC FX-400 system (Becton Dickinson, USA). Bottles with the positive signal in BACTEC FX-400 system were inoculated onto Columbia Agar (with 5% Sheep Blood) and Eosin Methylene Blue Agar (BD, USA). The inoculated plates were incubated at 36°C in 5% CO2. After 24h incubation, colonies were identified with BD Phoenix automated system (BD, USA). After the first isolation of *Rhodotorula*, eight subsequent blood cultures were *Rhodotorula* positive in ten-day periods, but CVC culture was negative. After the isolation of *Rhodotorula* spp, amphotericin B was added to the prescription of the patient. After 14 days of amphotericin B treatment, the clinical situation of the patient was improved and he was discharged. The c-reactive protein remained high for a very long time and was high even at patient's discharge.

DISCUSSION

Rhodotorula species are an increasing health problem with their ability to colonise and infect patients with depressed immunity, and account for 0.5%-2.3% of fungemia in the USA.[5] Approximately 90% of patients with *Rhodotorula* infections have immunodepressant clinical conditions such as AIDS, solid or hematologic malignancy, organ/bone marrow transplant, or immunosuppression due to corticosteroid use, neutropenia, or malnutrition.[6] *Rhodotorula* infections in patients with hematologic

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malignancies are usually associated with CVC and result in fungemia, whereas *Rhodotorula* infections in patients with AIDS usually result in central nervous system infections.[7] In our case, having the negative culture of CVC indicates the difficulty of finding a source for contamination. Therefore, detailed environmental surveillance may be necessary especially in case of outbreaks.

Intestinal colonization is found in up to 5% of healthy children and in up to 12% of young adults.[8] Although one of the patient's complaint at admittance was diarrhea, to our knowledge there is no report for *Rhodotorula* species causing diarrhea. However, it may be responsible for unsettling gut flora in immunocompromised patients. Furthermore, they often colonise hands of medical staff.[9] Control interventions, including training to reemphasize hand washing for reducing nosocomial transmission risk, were applied in our hospital for the prevention of an outbreak infection.

The isolation of *Rhodotorula* species from sterile site samples, such as blood, peritoneal fluid or cephalo spinal fluid, is generally suggestive of the infection, especially in patients without indicative symptoms of infection. Morphological and biochemical confirmation of the diagnosis is usually necessary, as yeast cells can usually be seen on microscopic examination.[6] Overall, mortality from *Rhodotorula* fungemia is 17.3%.[7] Expected mortality may be higher in immunocompromised pediatric patients.

Rhodotorula species are susceptible to amphotericin B and flucytosine *in vitro*, resistant to fluconazole and caspofungin, and have varying susceptibility to voriconazole.[7] Amphotericin B is the first choice drug for *Rhodotorula* infections.[10] In our case, Amphotericin B was effective as a treatment.

In conclusion, *Rhodotorula* spp. as a rare yet emerging pathogen, often presents as fever of unknown etiology resistant to antibacterial treatment and can be associated with fungemia and other severe complications, especially in immunocompromised patients.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

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Hospital Santa Cruz

LETTER TO THE EDITOR

Serviços e movimentos sociais apontam caminhos para o cuidado de pessoas com tuberculose e coinfecção TB/HIV

Health care and social services, social movements point out ways to care for tuberculosis and HIV/Aids patients

Servicios y movimientos sociales apuntan formas de cuidar a personas con tuberculosis y coinfección tuberculosis/VIH

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Caro editor:

Em setembro de 2021 dezenas de pesquisadores, trabalhadoras/es do Sistema Único de Saúde (SUS) e de outras políticas sociais, gestoras/es, conselheiras/os de saúde e representantes de movimentos sociais participaram de uma jornada de cinco encontros virtuais semanais, promovida pelo Comitê Estadual de Enfrentamento da Tuberculose do RS (CEETB/RS), intitulada *Tuberculose em debate: perspectivas para proteção e cuidado de populações vulneráveis à tuberculose e coinfecção tuberculose-HIV/Aids*. Buscou-se, nesses encontros, situar a epidemia de tuberculose no contexto das crises sanitária, econômica e social vivenciadas no Brasil nos últimos anos e debater alternativas para ampliar o cuidado e a proteção social das populações com maior risco de adoecimento.

A tuberculose é a segunda doença infecciosa que mais mata no mundo e, atualmente, perde apenas para a Covid-19.[1] Tem íntima relação com a desigualdade social, pois sua disseminação é facilitada pela precariedade das condições de vida de importante parcela da população. Nesse sentido, determinados grupos apresentam maior risco de adoecimento. São eles: pessoas em situação de rua, população privada de liberdade, pessoas vivendo com HIV/Aids e indígenas. Estas populações sofrem com estigmas e barreiras de acesso às políticas sociais de longa data, o que afeta diretamente o cuidado em saúde. Sistemas de saúde públicos devem ter como objetivo principal a busca da equidade, o que representa que aqueles que têm maior vulnerabilidade devem ser tratados de maneira diferente de modo que as desvantagens resultantes da posição social possam ser reduzidas ou anuladas.[2]

A pandemia de Covid-19 provocou diversas alterações no modo de se produzir saúde e ações programáticas tiveram que ser colocadas em segundo plano a fim de dar conta da emergência em saúde pública. Passados dois anos desde os primeiros casos, o SUS urge por uma reorganização de modo que possa fortalecer as ações em áreas que sempre foram negligenciadas, como o enfrentamento da Tuberculose.

O cenário atual expressa o aprofundamento da desigualdade social, a qual se manifesta através do aumento do desemprego e da informalidade, do aumento sem precedentes da fome e da desnutrição e do crescimento

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do contingente de pessoas em situação de rua, para citar alguns exemplos. Soma-se a este cenário os retrocessos no financiamento da Atenção Primária à Saúde e o desmonte do Sistema Único de Assistência Social (SUAS). Todos esses fatores contribuem para a degradação das condições de vida da população e abrem o flanco para o aumento da prevalência de doenças socialmente determinadas.

A fim de sintetizar e dar visibilidade aos debates e proposições da jornada, foi elaborado o presente documento. Os temas abaixo elencados expressam demandas e propostas históricas dos movimentos sociais, atualizadas pelos retrocessos no campo dos direitos sociais em curso no Brasil.

Revogação da Emenda Constitucional 95/2016:[3] também conhecida como emenda do Teto de Gastos, a medida congela por 20 anos os investimentos do governo em serviços públicos, possibilitando apenas a reposição da inflação. Levantamento do Conselho Nacional de Saúde aponta que a emenda retirou do Sistema Único de Saúde cerca de R$42,5 bilhões nos anos pré-pandemia (2018 e 2019) e em 2022.[4]

Defesa da Atenção Básica: reverter imediatamente o desmonte da Atenção Básica do SUS e ampliar sua capacidade assistencial (com o aumento, por exemplo, do número de agentes comunitários de saúde). Ademais, incentivar a implantação das linhas de cuidado para o HIV/Aids e tuberculose e facilitar o acesso ao Tratamento Diretamente Observado para todos que necessitarem, com apoio matricial de qualidade e fortalecimento das redes de saúde e socioassistenciais existentes.

Combate ao preconceito às pessoas com tuberculose e/ou HIV-Aids: preconceito, estigma e discriminação em relação às pessoas com HIV/Aids e/ou tuberculose ainda fazem parte do dia a dia da nossa sociedade e precisam ser superados com ações mais efetivas em educação e comunicação em saúde que superem abordagens moralistas e de culpabilização dos indivíduos.

Uso problemático de álcool e outras drogas: é necessário repensar os processos de trabalho buscando novas formas de intervenção e a necessidade de reconhecer o alcoolismo e a dependência química como fatores que influenciam o tratamento da tuberculose, buscando estratégias de cuidado não excludentes, na perspectiva da redução de danos, dando importância ao trabalho dos Centros de Atenção Psicossocial (CAPS), dos Agentes Comunitários de Saúde (ACS), dos Centros de Referência da Assistência Social (CRAS), grupos de ajuda mútua, entre outros recursos existentes.

População Privada de Liberdade (PPL): é preciso superar a histórica submissão da saúde à segurança, o que dificulta o acesso dessa população ao cuidado integral e em tempo oportuno. Ademais, é de amplo conhecimento as precárias condições das instalações prisionais, o que exige uma reforma estrutural, que garanta a redução dos fatores de risco para a tuberculose nestes ambientes. Por fim, é necessário ampliar políticas de acesso à saúde das pessoas privadas de liberdade, especialmente em relação à prevenção de agravos, bem como facilitar o fluxo de informações para a comunidade prisional, respeitando o papel dos conselhos de comunidade enquanto instâncias de controle social junto às prisões. Para além dessas medidas, em longo prazo é importante que se debata com a sociedade civil e com os estudiosos da área de segurança pública uma agenda de desencarceramento, tendo em vista a superpopulação carcerária brasileira, seus marcadores sociais (em especial, de raça e classe) e as péssimas condições de saúde vividas nas prisões do país.

Populações indígenas, migrantes e refugiados, quilombolas e LGBTTQIA+: deve-se garantir equipes de saúde em quantidade suficiente e capacitadas para interagir com estas populações, respeitando questões culturais e crenças, valorizando seus conhecimentos e promovendo momentos de informação, projetos, ações, oficinas, com materiais gráficos, cartilhas e outros recursos que permitam compreensão e inclusão.

População em Situação de Rua: é imprescindível estabelecer compromisso para instituir políticas sociais estruturantes, como habitação, educação, trabalho e renda, enquanto garantia de construção de autonomia e emancipação dos sujeitos. Além disso, os esforços devem incluir a ampliação e o fortalecimento dos Centros de Referência Especializado para População em Situação de Rua (Centro POP), albergues, abrigos e outros equipamentos ou espaços de descanso e higiene que acolham esta população, assim como ampliar também a atuação dos Consultórios na Rua.

Acesso a políticas sociais públicas é fundamental para garantir a cura da tuberculose: ampliar políticas públicas que garantam acesso aos serviços de saúde, alimentação, vale transporte e distribuição de renda. Estudo publicado recentemente por pesquisadores brasileiros demonstra que o Bolsa Família trouxe impacto positivo em relação à adesão ao tratamento da tuberculose, reduzindo mortalidade e taxas de abandono.[5]

Não obstante a conjuntura desfavorável, com o advento de uma crise sanitária que afetou o Brasil em um período de recessão econômica e fragilidade do sistema democrático, o CEETB/RS não tem medido esforços para mobilizar a sociedade civil organizada e articular iniciativas que denunciem os retrocessos no combate à tuberculose.

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