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ORIGINAL ARTICLE

Healthcare-associated infections and mechanisms of microorganism resistance: a scoping review

Infecções relacionadas à assistência à saúde e os mecanismos de resistência de microrganismos: revisão de escopo

Infecciones asociadas a la atención sanitaria y los mecanismos de resistencia de los microorganismos: revisión del alcance

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ABSTRACT

Background and Objectives: healthcare-associated infections are preventable adverse events that contribute to microbial resistance and constitute a public health problem. Thus, this study aims to evaluate the profile of healthcare-associated infections and resistance mechanisms of microorganisms from 2019 to 2024. **Methods:** this scoping review was prepared according to the PRISMA Extension for Scoping Reviews checklist. The acronym "participants, concept, and context" was used as the search strategy. The participants in this study were patients with nosocomial healthcare-associated infections who were aged 18 years or older. The concept included studies on nosocomial infections, epidemiology, and mechanisms of microorganism resistance. Randomized and non-randomized clinical trials, observational studies, and reviews with and without meta-analysis that were published in English, Portuguese, and Spanish and carried out from January 2019 to August 2024, were considered. The sources of evidence used were the Virtual Health Library, the National Library of Medicine, Scopus, and Google Scholar. **Results:** the incidence of healthcare-associated infections in Brazil and worldwide has increased, with the main sites of infection referring to the bloodstream, urinary tract, and respiratory tract. The predominant microorganisms were Gram-negative, with the following main resistance mechanisms: oxacillinases, carbapenemase-producing *Klebsiella*, New Delhi metallo-β-lactamases, and Verona integron. **Conclusion:** knowledge about the epidemiology of healthcare infections can help promote health actions and control and prevent infections.

Keywords: *Cross Infection. Health care. Health care delivery. Anti-infectives. Microbial drug resistance.*

RESUMO

Justificativa e Objetivos: as infecções relacionadas à assistência à saúde são eventos adversos evitáveis, que contribuem para a resistência microbiana, constituindo-se um problema de saúde pública. Assim, o estudo objetiva avaliar o perfil de infecções relacionadas à assistência à saúde e os mecanismos de resistência dos microrganismos no período de 2019 a 2024. **Métodos:** trata-se de uma revisão de escopo, elaborada de acordo com o checklist PRISMA Extension for Scoping Reviews. Foi empregado como estratégia de busca o acrônimo *participants*, *concept* e *context*. Os participantes desse estudo foram pacientes com infecções relacionadas à assistência à saúde nosocomiais com 18 anos ou mais. Foram incluídos como conceito estudos sobre infecções nosocomiais, epidemiologia e mecanismo de resistências de microrganismos. Foram considerados como base deste artigo ensaio clínico randomizado e não randomizado, estudos observacionais e revisão com e sem metanálise publicados em inglês, português e espanhol, realizadas entre janeiro de 2019 a agosto de 2024. As fontes de evidências utilizadas foram a Biblioteca Virtual em Saúde (BVS - Lilacs), National Library of Medicine, Scopus e Google acadêmico. **Resultados:** destaca-se o aumento da incidência de infecções relacionadas à assistência à saúde no Brasil e no mundo, tendo como principais sítios de infecção a corrente sanguínea, o trato urinário e o trato respiratório. Os microrganismos predominantes foram os Gram-negativos, e como principais mecanismos de resistências: as oxacilinases, *Klebsiella* Produtora de Carbapenemase, metalo-β-lactamases de Nova Délhi e Intergron de Verona. **Conclusão:** o conhecimento acerca da epidemiologia das infecções em saúde pode auxiliar na promoção de ações em saúde e no controle e prevenção de infecções.

Descritores: *Infecção Hospitalar. Assistência em saúde. Prestação de cuidados de saúde. Anti-infecciosos. Resistência microbiana a medicamentos.*

RESUMEN

Justificación y Objetivos: las infecciones relacionadas con la atención sanitaria son eventos adversos prevenibles y contribuyen a la resistencia microbiana, lo cual es un problema de salud pública. Así, este estudio tiene como objetivo evaluar el perfil de las infecciones relacionadas con la atención sanitaria y los mecanismos de resistencia de los microorganismos de 2019 a 2024. **Métodos:** esta es una revisión del alcance, preparada de acuerdo con la lista de verificación de PRISMA *Extension for Scoping Reviews*. Se utilizó como estrategia de búsqueda los términos *participants, concept* y *context*. Los participantes en este estudio fueron pacientes con infecciones nosocomiales asociadas a la atención médica, con edades de 18 años o más. El concepto incluía estudios sobre infecciones nosocomiales, epidemiología y mecanismos de resistencia de los microorganismos. Se consideraron ensayos clínicos aleatorios y no aleatorios, estudios observacionales y revisiones con y sin metaanálisis publicados en inglés, portugués y español, realizados entre enero de 2019 y agosto de 2024. Las fuentes de evidencia utilizadas fueron la Biblioteca Virtual en Salud (BVS - Lilacs), Biblioteca Nacional de Medicina, Scopus y Google Scholar. **Resultados:** se destaca el aumento de la incidencia de infecciones relacionadas con la atención sanitaria en Brasil y en el mundo, y los principales sitios de infección son el torrente sanguíneo, las vías urinarias y las vías respiratorias. Los microorganismos predominantes fueron gran-negativos; y los principales mecanismos de resistencia, oxacilinasas, *Klebsiella* productora de carbapenemasas, metalo-β-lactamasas de Nueva Delhi e Intergron de Verona. **Conclusión:** el conocimiento sobre la epidemiología de las infecciones sanitarias puede ayudar a promover acciones sanitarias y a controlar y prevenir infecciones.

Palabras Clave: *Infección hospitalaria. Asistencia sanitaria. Prestación de asistencia sanitaria. Antiinfecciosos. Farmacorresistencia microbiana.*

INTRODUCTION

Healthcare-associated infections (HAIs) are considered avoidable adverse events, as correctly adopting prevention and control measures nullify the emergence of these diseases.[1,2] For health services, HAIs configure a public health problem as their prevalence is related to high rates of morbidity and mortality, longer hospitalization stays, and increased health costs that negatively affect quality of care and favor the selection and dissemination of multidrug-resistant microorganisms.[3,4]

Epidemiology estimates a 10% global prevalence of HAIs cases (developed countries show a 15% incidence).[5] The United States diagnoses about 1.7 million patients a year (of whom almost

100,000 die) and averages US$ 35 to 45 billion dollars in hospitalizations a year.[3,6] On the other hand, Brazil shows a 15.5%, incidence; daily hospitalization costs 55% more in patients with HAIs.[3,4]

HAIs can be defined as a clinical nosocomial condition patients acquire after 48 hours of hospitalization that were absent or in incubation at the time of admission.[7,8] The main risk factors include invasive devices, prolonged hospitalizations, antibiotics and immunosuppressants, age > 60 years, multiple comorbidities, and previous surgical history.[9] Urinary tract (UTI), primary bloodstream (PBSI), surgical site (SSI), and lower respiratory tract infections (lRTI) stand out among the most common conditions.[4] However, it is of paramount importance to know the origin, the focus, and the main involved microorganisms of these infections to guide the choice of appropriate antibiotic therapy.

This perspective considers antimicrobial resistance as a global threat since it restricts the available therapeutic options and increases the risk of in-hospital mortality due to lack of treatment.[10,11] However, the indiscriminate use of empirical antibiotics and the low rate of de-escalation are associated with multidrug-resistant microorganisms,[12] as per a study in Serbia, which found a 12.8% pan-drug resistant profile, i.e., no susceptibility to the tested antimicrobials.[13]

In line with this, the World Health Organization updated, in May 2024, the list of bacteria with a multidrug-resistant profile in need of research into new antimicrobials to reduce morbidity and mortality. The list classifies these bacteria into three groups: critical, medium, and high. The carbapenem-resistant *Acinetobacter baumannii*, third-generation cephalosporin-resistant *Enterobacteriaceae*, and carbapenem-resistant *Enterobacteriaceae* deserve critical priority.[14] This scenario further evinces the need to strengthen evidence-based practices to prevent and control HAIs by implementing hospital infection control programs that emphasize adherence to standardized protocols, multiprofessional teams' continuous training, and care indicator monitoring.[7]

Thus, this study aims to evaluate the profile of HAIs and the resistance mechanisms of microorganisms from 2019 to 2024.

METHODS

This scoping review was prepared in accordance with the recommendations of the international checklist Preferred Reporting Items for Systematic Reviews and Meta-analyses for Scoping Review. to retrieve, investigate, and synthesize information on the subject from databases and portals.[15] The protocol of this review was registered on the Open Science Framework according to DOI 10.17605/OSF. IO/P6AXG under public disclosure. The following guiding question was used: What is the scientific evidence about the profile of HAIs and the mechanisms of resistance of their related microorganisms from 2019 to 2024?

The acronym "participants, concept, and context" was used as the search strategy. Hospitalized patients with HAIs who were aged 18 years or older were included in this study. Studies on nosocomial infections, epidemiology, and mechanisms of microbial resistance were included as the concept. Quantitative and experimental studies, randomized and non-randomized clinical trials, observational studies, and reviews with and without meta-analysis that were published in English, Portuguese, and Spanish from January 2019 to August 2024 were considered as context. Animal studies, letter to the author, reviews, and articles unavailable in full were excluded.

The literature was evaluated in August 2024 on the following portals: Virtual Health Library (VHL – Lilacs), National Library of Medicine (PubMed), Scopus, and Google scholar (gray literature). Medical subject headings the Boolean operators "AND" and "OR" were used to find the area terms and subjects. The concepts "infecção hospitalar" and "assistência à saúde" were translated as "cross infection" and "delivery of health care," respectively. Note the use of entry terms (synonymous with the terms in question) for the search strategy.

In this context, the following general search strategy was used: ("*Cross Infection*" *OR* "*cross infections*" *OR* "*Healthcare Associated Infections*" *OR* "*Healthcare Associated Infection*" *OR* "*Health Care Associated Infection*" *OR* "*Health Care Associated Infections*" *OR* "*Hospital Infection*" *OR* "*Nosocomial Infection*" *OR* "*Nosocomial Infections*" *OR* "*Hospital Infections*"*) AND (*"*Delivery of Health Care*" *OR* "*Delivery of Healthcare*" *OR* "*Healthcare Deliveries*" *OR* "*Healthcare Delivery*" *OR* "*Health Care Delivery*" *OR* "*Delivery, Health Care*" *OR* "*Health Care*" *OR* "*Care, Health*" *OR* "*Healthcare*" *OR* "*Health Care Systems*" *OR* "*Health Care System*"). However, some adaptations were made to the PubMed database. The term MESH followed only the keywords cross infection and delivery of health care, whereas "text word" succeeded all entry terms. However, these words were removed from the explicit strategy, which preserved the remaining terms.

To select articles, the Rayyan-Intelligent Systematic Review was used*,* a software to assist the identification, selection, and organization of publications to be included in literature reviews. The articles were evaluated in pairs by independent reviewers. Any conflict was solved by consensus without the need for a third author in the following order: I – titles and the respective abstracts of the retrieved studies by the search strategy, II – complete reading of the articles after the first phase.

The following data were extracted from the eligible articles: journal, authors, country, study design, year of publication, participants, and sample. From the results of the articles, information was extracted on the prevalence and incidence of HAIs, the main involved microorganisms, the site of infections, and antimicrobial resistance profiles. This research performed a pilot study to evaluate its chosen tool in 10 articles to standardize result extraction. These articles were included in this review.

RESULTS AND DISCUSSION

This research found 457 results in the searched databases. Its first phase, after reading the titles and abstracts of the chosen studies, excluded 379 articles following its inclusion/exclusion criteria and one duplicate. Its second phase excluded 39 articles according to its eligibility criteria after reading them in full text, rendering 38 studies and one dissertation as its final sample (Figure 1).

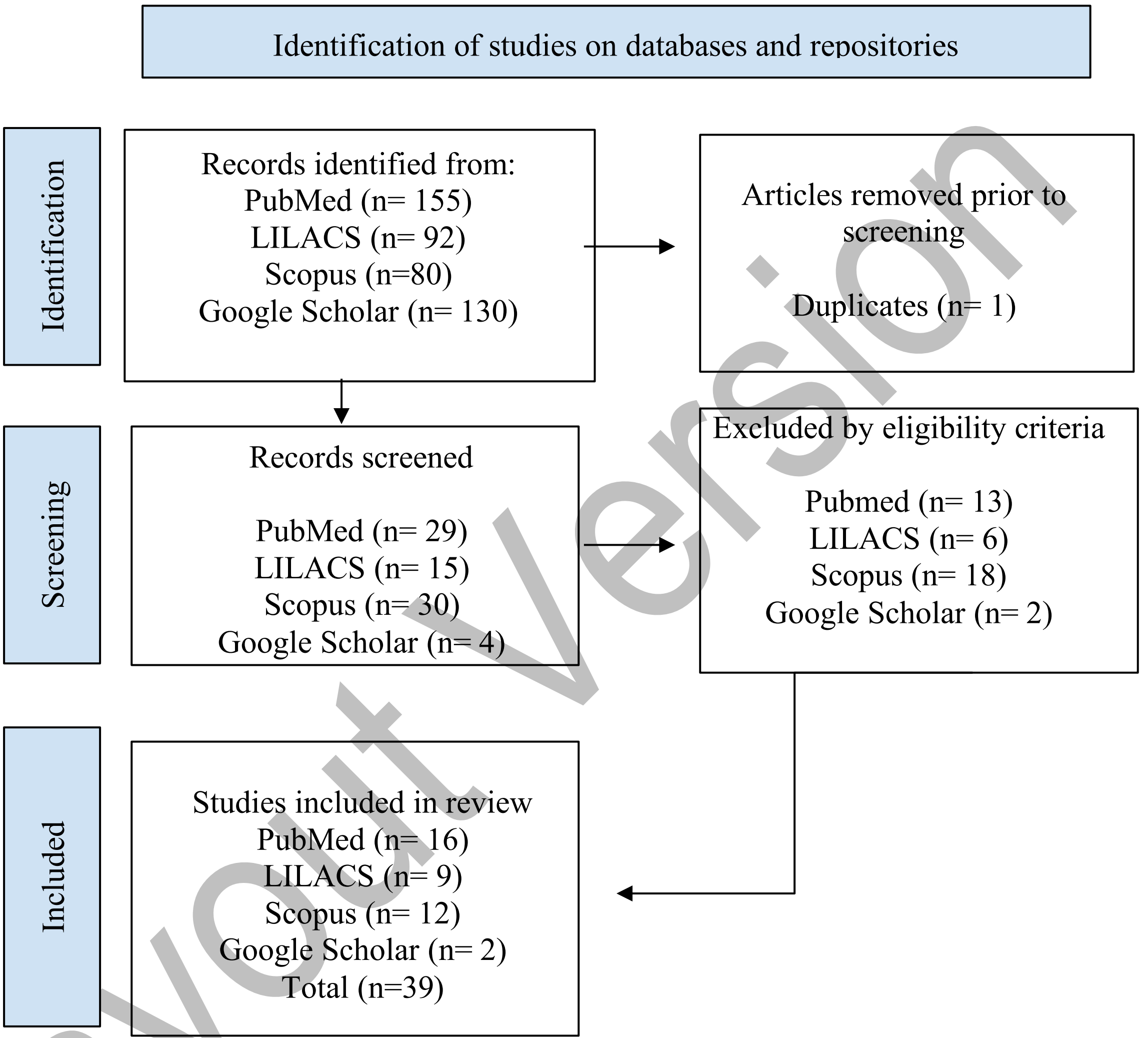

Figure 1. Flowchart referring to the selection process of the studies in this scoping review, adapted from Systematic Reviews and Meta-analyses for Scoping Review, Bahia, Brazil, 2024.

The 39 eligible articles included six studies that had been conducted in Brazil and 33 in other countries. Regarding study design, the sample included two systematic reviews with meta-analysis, two narrative revisions, and 34 cross-sectional and one cohort observational studies (Chart 1).

The eligible studies found the following the risk factors for the development of HAIs: age > 60 years, the male gender, length of hospital stay > 7 days, previous use of antibiotics, surgical procedures, and invasive devices such as mechanical ventilation (MV), probes, orotracheal tubes, central venous catheters (CVC), and hemodialysis.[8,9,12,21,27,29,32,34,46]

The most mentioned microorganisms referred to Gram-negative bacilli, especially *Pseudomonas aeruginosa*, *A. baumanni*, *Klebsiella pneumoniae*, *Escherichia coli*, *Proteus mirabilis*, *Serratia marcescens*, and *Stenotrophomonas. Malthophilia.*[1,2,13,18,19,2,23,24,25,26,27,29,30,31,32,33,34,36,37,39,42,44,45,46,49] Some species of Gram-positive bacteria received fewer mentions, such as *Staphylococcus aureus*, *Enterorococus faecalis*, and *Enterococcus faecium.*[12,13,17,18,19,24,25,27,33,35,39,49] Class B metallo-β-lactamases (MβLS) configured the most frequent resistance mechanisms: *K. pneumoniae* carbapenemase (KPC), imipenemase (IMP), New Delhi metallo-β-lactamase (NDM), Verona integron-encoded metallo-β-lactamase (VIM), followed by class D oxacillinase-23 (OXA-23), oxacillinase-48 (OXA-48), oxacillinase-51 (OXA-51), oxacillinase-58 (OXA-58) oxacillinases and class A extended-spectrum β-lactamase (ESBL).[16,20,21,23,28,29,36]

Year	Journal	Authors	Country	Study design	Number of particip ants	Epidemiology/Risk factors/HAI sites of infection	Prevalence of microorganisms	Microorganism resistance mechanisms
2022	CAMbios Rev Med	Trujillo T, et al.[16]	Ecuador	Review	-	-	-	*K. pneumoniae*: KPC, IMP, NDM, VIM, OXA-48; *E. coli*: KPC, NDM, OXA-48; *E. cloacea*: KPC, NDM, IMP, OXA-48; *S. marcensens*: KPC, NDM, OXA-48; *E. Aerogens:* KPC, NDM, OXA-48; *P. mirabilis*: KPC, NDM; *P. aeruginosa*: KPC, NDM, IMP, VIM; *A. baumannii*: IMP, OXA-48, OXA-51, OXA-24, OXA-24, OXA-143, OXA-58; *Enterobactereacea:* ESBL
2022	Repert Med Cir	Sendoya Vargas JD, et al.[17]	Colombia	Observational Cross-sectional	100	TI%: (57%) HAIs P: 0.154%	GP: *E. faecalis* (72%), *E. faecium* (28%)	-
2021	Rev Cuba Angiol Cir Vasc	Rodríguez Álvarez V, Hernández Seara A[18]	Cuba	Observational Cross-sectional	89	TI%: (49.4%) SI: (43%) SSI, (25%) PNM, (1%) UTI, (18%) skin and mucous membranes, (2%) associated with device	GN: *P. aeruginosa* (13.5%), *A. baumanni* (9%). GP: *S. aureus*	-
2021	Rev Soc Bras MedTrop	Gaspar G, et al.[19]	Brazil	Observational Cross-sectional	466	-	GN: *K. pneumoniae* (53%), *A. baumanni* (37%). GP: *S. aureus* (10%)	-
2020	Cuban Med Trop Review	Pérez DQ, et al.[59]	Cuba	Cross-sectional observational	119	-	-	*E. coli*: ESBL (43.7%), cAMP (92.4%), MβL (99.2%)

2020	Braz J Cardiovasc Surg	Ferreira GB, et al.[8]	Brazil	Observational Cross-sectional	195	TI%: (22.6%) SI: SSI (45.5%), pulmonary (45.5%), UTI (11.4%), and others (11.4%). FR: female gender (56.8%), (p=0.015); LHS>9 days: (15%), (p= <0.001)	-	-
2020	Rev Soc Bras MedTrop	Kurihara M, et al.[21]	-	Literature Review	-	RF for Infection *A. baumanni* in the ICU: CVC use, MV use, previous ATB use, previous hospitalization, ICU stay >3 days, surgical procedures	-	blaOXA-23, blaOXA-51, blaOXA-58, blaOXA-65
2019	HU Rev	Dias V, *et al.,* [22]	Brazil	Observational Cross-sectional	39,547	SI: Pulmonary (70.6%), BSI (15.5%), tissue (3.5%), other (10.4%)	GN: 14% isolated *S. maltophilia*	
2019	Rev Esc Enferm USP	Alvim A, et al.[2]	Brazil	Observational Cross-sectional	82	SI: PBSI 30%, CAUTI 22%, lRTI except pneumonia 20%, SSI 17%, VAP 7%, other: 4	GN: *K. pneumoniae* 68% *S. marcescens* 2% *E. Cloacea* 9%	blaKPC gene 100% of the samples.
2022	Int J Infect Dis	Ergonul O, et al.[23]	Türkiye	Observational Cross-sectional	59	TI%: (49%) HAIs	GN: *A. baumanni* (49%)	(76%) of the isolates produced OXA-23 carbapenemase
2023	J Hosp Infect	Liu X, et al.[9]	China	Systematic review with meta-analysis	-	RF: age > 60 years, the male gender, arteriovenous cannula, catheterization, IUC, intravenous infusion, MV, Surgery, TCT, ventilator, Coma, DM, bed restriction, chemotherapy, HD, hormonal therapy, use of immunosuppressants, use of ATB, and LHS>15 days. All FR with (p-value=<0.001)	-	-
2023	J Hosp Infect	Gajic I, et al.[13]	Serbia	Observational Cross-sectional	6,478	TI%: (12.5%) HAIs SI: PNM (n: 240), BSI (n: 268), UTI (n: 169), gastroenteritis (n: 103), skin and soft tissues (n: 29).	GN: (69.3%); *K. pneumoniae* (24.9%), *A. baumanni* (24.5%), *C. difficile* (9%) *P. aeruginosas* (5%), *P. mirabilis* (3.7%), *E. coli* (1.2%) GP: 30.7 *S. aureus* (1.2%)	-
2023	BMC	Aiesh BM, et	Palestine	Observational	157	TI%: (61%) HAIs	GN:	

	Infect Dis	al.[24]		Cross-sectional		SI: Skin and soft tissue infections (35.8%), UTI (33.7%), pneumonia (36.8%), intra-abdominal infection (20%), BSI (27.4%)	*P. aeruginosa* (26.3%), *A. baumanni* (25.3%), *E. coli* ESBL (23.2%), *K. pneumoniae* ESBL (15.8%). GP: *S. epidemidis* (17.9%), *E. facium* (17.7%), *E. faecalis* (7.4%). Fungi: *C. albicans* (17.9%)	-
2021	J Hosp Infect	Stewart S, et al.[25]	Scotland	Observational Cross-sectional	99,018	SI: UTI, BSI, lRTI, SSI, and PNM	GN: (40.7%), *E. coli* (18.4%), *K. pneumoniae* (4.34%), *P. mirabilis* (2.74%), *S. marcescens* (1.67) GP: (36%) *S. aureus* (10.8%), *E. faecalis* (5%), *E. faecium* (4.3%), *C. difficile* (2.8%) Fungi (7.31%) *C. albicans* (1.98%)	-
2021	Crit Care	He Q, et al.[26]	China	Observational Cross-sectional	22,343	SI (2.9%) VAP	GN: *A. baumanni* (42%), *K. pneumoniae* (18%), *P. aeruginosa* (15%), *Enterobacteria spp.* (9%), *S. maltophilia* (7%), *B. cepecia* (7%) GP: *A. aureus* (5%)	-
2023	Ann Ig	Damico V, et al.[27]	Italy	Observational Cross-sectional	118	TI%: 33.1% SI: UTI (36.8%), BSI (20.6%), PNM (13.2%), skin (5.9%), associated device (2.9%), CNSI (1.5%) RF: length of stay > 7 days (OR: 2.6, 95% CI: 1.19-3.54, p=0.002), type II DM (OR: 1.8, 95% CI: 1.07-2.29, p=0.019), cardiovascular disease use, MV, surgery,	GN: *Klebsiella spp.* (15.9%), *A. baumanni* (13.8%), *Enterococcus spp*. (13.8%), *P. aeruginosa* (10.6%), *P. mirabilis* (5.3%), *S. maltophilia* (1.1%), *E. coli* (1.1%)	

						prolonged hospitalization, tracheostomy wound and devices. (OR: 1.4; 95%CI: 1.05-2.29, p=0.021), CVC (OR: 4.9; 95%CI: 1.56-11.52 p=0.014, MV >48h (OR: 4.2; 95%CI: 1.49-11.51, p=0.003.	GP: *C. difficile* (14.9%), *S. aureus* (2.1%), *S. epidermidis* (1.1%) Fungus: *Candida* spp. (10.6%)	
2019	Acta Med Port	Costa RD, et al.[12]	Portugal	Observational Cross-sectional	60	TI%: (58.3%) HAP acquired in the ICU; (41.7%) HAP acquired outside the ICU. SI: (58.3%) VAP RR: use of ATB in the last 30 days (75%) and immunosuppression (16.7%)	GN: *P. aeruginosa* (20%)**,** *A. baumanni* (9.2%), *K. pneumoniae* (7.7%), *S. marcescens* (3.1%) GP: *S. aureus* (26.2%). Fungi: *C. albicans* (6.1%)	-
2020	Antimicrob Resist Infect Control	Saharman YR, et al.[28]	Indonesia	Observational Cross-sectional	412	TI%: (32.1 %) HAIs	GN: *K. pneumoniae* (32.1%)	96% of the isolates produced the blaNDM MDL-resisting gene.
2020	Rev Esp Quimioter	Pintos-Pascual I, et al.[29]	Spain	Observational Cross-sectional	272	TI%: (63.2%) HAIs SI: UTI (58.7%), lRTI (14.8%), skin and soft tissues (11.7%), intra-abdominal (10.5%) FR: male gender, transplants, immunosuppressive use, ICU and SC admission, and previous antibiotic treatment	GN: *K. pneumoniae* (62.7), *E. cloacea* (10.1%), *K. oxytoca* (8.9%), *E. coli* (6.6%)	OXA-48 (53.8%) VIM (43%), KPC (2.8%), NDM (0.4%)
2021	Scientific Rep	Lakbar I, et al.[30]	France	Cohort	18,497	TI%: (8.6%) HAIs SI: VAP	*S. aureus, P. aeruginosa, A. baumanni, Enterobacteriaceae,*	-
2020	J Infect Dev Ctries	Salehi M, et al.[31]	Iran	Observational Cross-sectional	152	SI: VAP	*A. baumanni* (56.6%) *K. pneumoniae ESBL.* (55.1%)	-
2020	Eur J Clin Microbiol Infect Dis.	Massart N, et al.[32]	France	Observational Cross-sectional	3,861	RF: age >65 years (p=0.07), colonization by BGN-ESBL (p<0.001).	*Enterobactereacea* (32.4%), *P. aeruginosa* (17.8%),	-
2022	Euro	Glasner C, et	Netherland	Observational	3,365	-	GN: *E. coli* (92.2%), *K.*	-

	Surveill.	al.[33]	s Germany	Cross-sectional			*pneumoniae* (6.8%) GP: *E. faecium* (1.8%)	
2019	Crit Care	Zhu S, et al.[34]	China	Observational Cross-sectional	5,046	TI%: NCRBSI - 2013 (70.2%), 2014 (68.4%), 2015 (66%), 2016 (74.4%), 2017 (78.3). RF: NCRBSI (OR: 2.30; 95%CI: 1.38-3.82, p=0.001), Trauma (OR: 3.45, 95%CI 2.24–5.30, p < 0.001), Surgery (OR 1.82, 95%CI 1.19–2.78, p = 0.006), Catheter (OR 2.93, 95%CI 1.65–5.22, p <0.001), Sepsis (OR 1.69, 95%CI 1.09– 2.63, p = 0.02), Pneumonia (OR 1.53, 95% CI 1.03–2.28, p = 0.038)	NCRBSI-associated microorganisms *A. baumanni* (53%), *K. pneumoniae* (41%), *Enterobacteriaceae* (33%), *P. aeruginosa* (7%), and *B. cepacia* (5%)	-
2020	Euro Surveill.	Piezzi V, et al.[35]	Switzerlan d	Observational Cross-sectional	5,369	-	*E. faecium* (40.5%) *E. faecalis* (59.5%)	-
2020	Rev Prev Infec Saúde	Alencar DL de, et al.[1]	Brazil	Observational Cross-sectional	181	TI%: (28.7%) HAIs SI: pulmonary and UTI	*A. baumanni* (56.25%) *K. pneumoniae* (2.25%) *P. aeruginosa* (4.41%)	-
2019	Dissertatio n	Ribeiro, Edlainny Araújo[36]	Brazil	Cross-sectional observational	18	-	*A. baumanni*	60% of isolates carrying the bla-OXA 23 resistance gene
2021	Int J Microbiol	Karimi K, et al.[37]	Iran	Observational Cross-sectional	83	SI: (58.9%) Pulmonary, (21.6%) UTI, (7.25%) BSI, others (12.25%)	*K. pneumoniae*	-
2021	Med J Islam Republic Iran	Khammarnia M, et al.[38]	Iran	Systematic review with meta-analysis		Overall prevalence: 0.111; 95%CI: 0.0.105 – 0.116) SI: UTI and respiratory	*E. coli* *Klebsiella* spp. *S. aureus*	-
2024	Pak Armed Forces Med J	Tariq A, et al.[39]	Pakistan	Cross-sectional observational	196	SI: PAV, UTI, SSI, PBSI	*K. pneumoniae* (33%); *E. Coli* (26%); *A. baumanni* (22%); *Pseudomonas* spp (11%), *Enterococcus* (2%) *S. aureus* (6%)	-

2021	J Infect Prev	Behera B, et al.[40]	India	Observational Cross-sectional	116	TI%: CAUTI - 9.08 per 1,000 catheter-days in 24 months	*Candida* spp.; *E. coli; Enterococcus* spp.	-
2023	Microb Infect Dis	Abdel-Salam SA, et al.[42]	Egypt	Observational Cross-sectional	60	SI: UTI (43.3%), Sputum (23.3%), CNSI (6.7%), PBSI (3.3%), others (3.3%)	*P. aeruginosa*	MexA genes (56.7%) MexB (46.7%)
2021	Infect Prev Pract	Morioka H, et al.[43]	Japan	Observational Cross-sectional	4,339	P: (9%) HAIs SI: SSI, PNM, PBSI, CRBSI, and UTI	Enterobacteria, *S. aureus, Enterococcus, Streptococcus* spp., *P. aeruginosa, A. baumanni.*	metallo-β-lactamase-producing *E. cloacea* and KPC-producing *K. pneumoniae*
2022	J Antibiotics	Papanikolopoulou A, et al.[44]	Greece	Observational Cross-sectional	4,754	I: VAP ranged from 10.1-10.9/1,000 ventilated patients	*A. baumanni* *K. pneumoniae*	-
2019	Egypt J Med Micro	Sultan AM, et al.[45]	Egypt	Observational Cross-sectional	240	SI: UTI (35.4%), VAP (32.5%), PBSI (23.3%), and SSI (8.8%).	*P. aeruginosa* (31.3%), *E. coli* (25.8%), *K. pneumoniae* (19.2%), *A. baumanni* (18.8%), *P. mirabilis* (5%)	Production in cAMP (40.9%)
2022	Microb Infect Dis	Thabet A, et al.[46]	Egypt	Observational Cross-sectional	225	SI: SSI (24%), UTI (16%), VAP (8%), fabrics (12%) RF: DM, debilitating chronic disease, anemia, broad-spectrum ATB use, MV, surgery, prolonged hospitalization, tracheostomy wound and devices.	*P. aeruginosa* (33.3%)	-
2022	J Infect Prev	Shrestha SK, Shrestha S, Ingnam S[47]	Nepal	Observational Cross-sectional	160	P: 11.25% HAIs SI: UTI 72.2%, PAV (16.6%), SSI (11.2%)	-	-
2024	J Health Popul Nutr	Bai HJ, et al.[48]	China	Cross-sectional observational	-	SI: PBSI, PNM, and UTI	GP: *S. aureus, E. faecalis, S. epidermidis,* and *S. haemolyticus.* GN: *E. coli, K. pneumoniae, A. baumanni,* and *P. aeruginosas.*	-

2022	J Renal Inj Prev	Khaleel RA, et al.[49]	Iraq	Observational Cross-sectional	710	SI: UTI	*S. aureus* (7.7%)	tetK (85.4%), gyrA (63.3%), msrA (45.4%), blaZ (100%)

Chart 1. Selected articles for this scoping review and main results, Bahia, Brazil, 2019–2024.
Caption: No.: number; I: incidence; TI%: HAI rate; P: prevalence; HAIs: healthcare-related infections; RF: risk factor; SI: site of infection; GN: Gram-negative; GP: Gram-positive; SSI: surgical site infection; BSI: bloodstream infection; PBSI: primary bloodstream infection; lRTI: lower respiratory tract infection; VAP: ventilator-associated pneumonia; PMN: pneumonia; HAP: hospital-acquired pneumonia; NCRBSI: non-catheter-related bloodstream infection; CNSI: central nervous system infection; CAUTI: catheter-associated urinary tract infection; UTI: urinary tract infection; CRBSI: central venous catheter-related bloodstream infection; ATB: antimicrobials; LHS: length of hospital stay; HD: hemodialysis; ICU: intensive care unit; DM: diabetes mellitus; SC: surgical center; MV: mechanical ventilation; CVC: central venous catheter; IUC: indwelling urinary catheter; TCT: tracheostomy; OXA: oxacillinases; GNB: Gram-negative bacillus; β-lactamases: beta-lactamases; EBSL: extended-spectrum beta-lactamase; VIM: Verona integron-encoded metallo-β-lactamase; KPC: carbapenemase-producing *K. pneumoniae*; NDM: New Delhi metallo-β-lactamases; MβL: metallo-β-lactamases; cAMP: cyclic adenosine monophosphate; tetK: tetracycline-encoding gene, gyrA: quinolone-encoding gene, msrA: macrolide-specific resistance gene, blaZ: penicillin-resistance encoding gene.

This scoping review shows that HAI incidence has progressively increased in Brazil and worldwide, representing a serious public health problem as its development prolongs hospitalization and increases morbidity and mortality rates and hospitalization costs.[4] However, some research in France, Serbia, and Switzerland from 2013 to 2020 pointed to a decrease in the overall prevalence rate of HAIs: 6.1, 11.5, and 2%, respectively.[13,32,35]

Brazil showed study variability. Research from 2012 to 2018 in the state of Paraná found a 22.6% HAI incidence.[8] On the other hand, a study in an ICU the state of Minas Gerais showed a lower incidence of HAI over the years: 3.4% in 2014, 2.4% in 2015, and 1.8% in 2016.[4] The care profile of the institution and the incorporation of HAI prevention and control actions may explain these findings. Health education practices configure an effective tool to control HAIs, in which the adherence of health professionals to hand hygiene constitutes one of the essential measures.[1]

UTI stands out as the first cause of nosocomial infection in the selected studies.[25,27,29] It can be defined as the presence of one or more pathogens in a urine sample in patients with clinical manifestations. Its main predictor refers to IUC use.[50] A study in the United Kingdom indicated an incidence rate for UTI of 52.2/100,000 days of occupied beds and associated IUC use with infections in 37.8% of cases, the onset of symptoms of which began seven days after admission.[25]

Observational studies in Italy, Scotland, and Brazil have pointed to PBSI as the second leading cause of hospital infections.[22,25,27] The research'' in Scotland showed that 95.1% of the cases were related to vascular catheters, reinforcing that device use has increased the development of HAIs, necessitating prevention and control measures and the reassessment of institutional protocols in units.[22,25]

The development of pneumonia in patients undergoing MV worsens prognoses and increases length of hospital stays. A study in Rio de Janeiro showed that 92.31% of individuals suffered from VAP,[1] which may have stemmed to the lack of adherence to protocols such as bundles (sets of standardized and evidence-based interventions to be applied simultaneously by care teams) to prevent pneumonia (contributing to reducing cases and increasing therapy success).[8] As in a Chinese study on ICU patients, about 93% of hospitalized individuals received MV, only 2.9% of whom developed MV-associated pneumonia, a result attributed to adherence to institutional prevention protocols.[26]

Regarding predictive factors, older adults show a high risk for infections, the main cause of death in individuals aged > 65 years.[52] Its associated factors include a decline in immune function due to multiple comorbidities and metabolic and hormonal changes related to the physiological process of senility, which hinders recovery and can increase the length of hospital stay.[8,52]

Males constitute the gender most affected by HAIs, corroborating the findings of studies across Brazil. In total, three cross-sectional studies with ICU patients showed a predominance of nosocomial infections in men (from 47.5 to 71.9%).[4,53,54] However, no analyzed study discussed the possible biological, behavioral, or care mechanisms that could justify this greater susceptibility of men to HAIs.

Invasive devices have also been linked to HAIs. Thus, care professionals must daily assess the need for these devices, adhere to standard institutional operating procedures to properly handle catheters and probes, and replace them after any sign of infection.[27] Measures such as hand hygiene and aseptic techniques are essential in care plans.[1]

The prolonged and indiscriminate use of antimicrobials increases microbial resistance and causes the emergence of HAIs, such as those by *Clostridioides difficile.*[55] Irrational use unbalances the gut microbiota due to competition between commensal bacteria.[55] Thus, antimicrobial stewardship programs are essential to evaluate, control, and monitor the rational use of antimicrobials. Awareness and sensitization practices also belong to this proposal.[52]

The chosen articles evince the prevalence of Gram-negative microorganisms, especially: *A. baumanni, K. pneumoniae*, *P. aeruginosa*, and *E. coli*. Other microorganisms stand out, but in a smaller proportion, such as: *S. maltophilia*, *P. mirabilis,* and *S. marcescens.* The most frequent Gram-positive bacteria were *S. aureus*, *E. faecalis, E. faceium*, and *C. difficile*. *Candida albicans* constituted the main pathogen in fungal infections.

Gram-negative microorganisms are widely disseminated in the environment and are directly associated with HAIs, especially in immunocompromised patients.[56] They can resist many available antibiotics due to their ability to acquire resistance genes and to adhere to surfaces and remain for long periods in health environments.[51]

A. baumanni, a microorganism that belongs to the *Moraxellaceae* family, commonly occurs in HAIs, most often in VAP, UTI, PBSI, intra-abdominal infections, among others.[21,36] In 2022, the World Health Organization reported the surveillance of antibiotic resistance and consumption, monitoring eight microorganisms that represent public health problems, the genus *Acinetobacter* spp. occupied the top of the list, highlighting *A. baumanni* as the most prevalent in PBSI and as having a higher multidrug resistance profile.[57]

The enterobacteria *K. pneumoniae* and *E. coli* stand among the most prevalent species in hospital units, affecting critically ill patients. Alvim et al., evaluating the epidemiological profile of enterobacteria, found *K. pneumoniae* to be the most prevalent topography in enterobacterial infections: BSI (30%), UTI (25%), and lRTI (20%).[2] Observational research in Brazil, Serbia, and Indonesia has pointed to *K. pneumoniae* as the first cause of HAIs, totaling 53, 69.3, and 32.1% of the cases, respectively.[13,19,28]

P. aeruginosa has been described as the main pathogen of infections in ICUs.[18,24] A survey in a Palestinian hospital showed a 26.3% prevalence of infections caused by *P. aeruginosa*, with the following main sites of infection: soft tissues, urinary tract, and ventilator entry.[24]

Studies in China[26] and Italy[27] found an association of infections with *S. aureus* and prolonged hospitalization. The former also found an association with hospital deaths, highlighting the importance of measures to prevent Gram-positive bacterial infections, the pathogenicity of which occurs from local or systemic multiplication and the subsequent production of exotoxins and enzymes, which can induce microbial resistance.[58]

The most common species of *Enterococcus* spp. Gram-positive bacilli in the human gastrointestinal flora refer to *E. faecalis* and *E. faecium*. Europe considers this genus the fourth most prevalent in PBSI causes.[35] A study on prevalence in Colombia showed that about 57.0% of HAIs were due to *Enterococcus* spp. since the most prevalent species is the *E. faecalis* (72.0%), followed by *E. faecium* (28%), which mainly caused UTI (31.0%) and BSI (29.0%).[17] The factors in infections by this genus include previous use of vancomycin, third-generation cephalosporin, prolonged hospitalization, neutropenia, diabetes, use of MV, and gastrointestinal colonization.[17,25]

Regarding resistance mechanisms, 11 studies [2,16,21,23,28,29,42,43,45,49,59] (in which the main carbapenemase-producing bacteria referred to enterobacteria, followed by *A. baumanni* and *P. aeruginosa)* treated this problem. Phenotypic tests mentioned the following carbapenemases the most: VIM, NDM, KPC, and the OXA-48, OXA-23, OXA-58 oxacillinases.

Bacteria can develop resistance to antibiotics by several mechanisms that decrease their susceptibility, including changes in outer membrane permeability, the production of enzymes that can inactivate antimicrobials or altering their binding site, and the activation of the efflux pump system.[11,21]

The association of several resistance mechanisms by bacteria generates multidrug resistance. On the other hand, the alteration of the site of action of penicillin-binding proteins prevents the binding of the antibiotic to the protein, limiting its function,[4] whereas the modifications that alter membrane permeability comprise the loss or reduction of the expression of the genes responsible for the expression of porins since this reduces the entry of the antibiotic into the cell, reducing its plasma concentration. Moreover, the efflux pump mechanism prevents toxic compounds from accumulating at the intracellular level, causing bacterial resistance.[36]

The most discussed resistance mechanism in the eligible studies refer to the production of β-lactamases, i.e., enzymes that can hydrolyze antibiotics. This may stem from the prevalence of Gram-negative bacteria in the articles as these microorganisms use this mechanism most often.[36]

A. baumanni produces metallo-β-lactamases and oxacillinases.[36] However, the latter show the greatest prevalence and variety, as studies have found more than 490 types of genes for them.

This enzyme can hydrolyze most forms of penicillin (and carbapenems at a lower proportion).[21,36] A cross-sectional study in Türkiye isolated *A. baumanni* in 50.0% of the HAIs and found oxacillinase production in 76.0% of its culture samples, the most common of which referring to the OXA-23 gene.[23]

Research in Spain investigated the prevalence of carbapenemase production in Enterobacteria, pointing out the main species involved: *K. pneumoniae*, *Enterobacter* spp., and *E. coli*, the most common carbapenemase referring to OXA-48 (53.8%), followed by VIM (43%), KPC (2.8%), and NDM (0.4%).[29] On the other hand, a study in Indonesia found *K. pneumoniae* as the main producer of the bla-NDM gene, occurring in 96% of microbiological isolates.[28] The NDM and VIM genes participate in the MβLs group, which confer resistance to all beta-lactams and carbapenems.[4]

Enterobacteria that produce the bla-KPC gene emerged in a study of the prevalence of HAI in Brazil. It belongs to penicillinases, enzymes that can hydrolyze carbapenems at the site of serine action. *K. pneumoniae* produce these enzymes the most.[2]

This scoping review showed that carbapenem-resistant *A. baumannii*, third-generation cephalosporin-resistant *Enterobacteriaceae*, and carbapenem-resistant *Enterobacteriaceae* constitute a reality in health institutions across geographic regions. Hospitals should improve their surveillance of infections by these bacteria the World Health Organization classified as critical by implementing sanitary measures to prevent and control them to minimize their spread (multidisciplinary actions that permeate management and care in which all play a role for the benefit and care of patients).[59]

The limitations of this review include its exclusive assessment of articles published in English, Portuguese, and Spanish and its publication period (2019-2024). Also, each territory has different rules, practices, and realities regarding the identification, prevention measures, and control of HAIs, which can influence finding comparability. Added to this are the variation in the number of participants in the included studies (some with expressive samples and others with reduced numbers) and the heterogeneity of methodological designs, which can hinder result synthesis and interpretation. Its strengths refer to the produced knowledge about the main microorganisms and the profile of resistance that cause nosocomial infections in hospital units, a measure to guide health institutions and encourage the implementation of control and prevention programs against the dissemination of multidrug-resistant microorganisms and toward the rational use of antimicrobials.

CONCLUSION

The results showed the relevance of continuous monitoring and the implementation of preventive measures to cope with HAIs. The increase in incidence, associated with the use of invasive devices, senility, previous use of antimicrobials, and prolonged hospitalization reinforce the need for safe care practices and the strengthening of prevention protocols.

The predominant microorganisms, mostly multidrug-resistant Gram-negatives, highlight the seriousness of the situation since their resistance mechanisms limit therapeutic options and increase hospital mortality and health costs. This scenario must effectively implement hospital infection control programs focusing on the proper management of antimicrobial use, continuous training of healthcare providers, and systematic epidemiological surveillance.

Thus, these results reinforce that the fight against HAIs should go beyond treatment, aiming, above all, at prevention by robust and integrated institutional policies that can reduce the spread of multidrug resistance, ensuring the rational use of antimicrobials and greater patient safety.

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AUTHORS' CONTRIBUTION

Karla Neco Rodrigues contributed to the bibliographic research, drafting of the abstract, introduction, methodology, discussion, and interpretation, description of the results, and the elaboration of tables, conclusions, and references. **Adriano Max Moreira Reis** contributed to the review and correction of the bibliographic research, analysis of the results, and discussion. **Tuany Santos Souza** contributed to the review of the abstract, methodology, interpretation of results, conclusions, review, and statistics. **Gisele da Silveira Lemos** contributed to the review and correction of the bibliographic research, analysis of the results, and discussion.

All authors have approved the final version of this manuscript and are responsible for all its aspects, including ensuring its accuracy and completeness.