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REVIEW ARTICLE

Impact of healthcare-associated infections on mortality of hospitalized patients with COVID-19: a systematic review

Impacto das infecções relacionadas à assistência à saúde na mortalidade de pacientes hospitalizados com COVID-19: uma revisão sistemática

Impacto de las infecciones relacionadas con la salud en la mortalidad de pacientes hospitalizados con COVID-19: una revisión sistemática

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Abstract *Although most cases of COVID-19 are mild cases, severe cases requiring hospitalization and mechanical ventilation were sufficient to overwhelm healthcare systems worldwide, leading to more than 6 million deaths and the increase in healthcare associated infections (HAIs). The incidence of HAIs in COVID-19 hospitalized patients has been addressed in systematic reviews, but in these there was no description of mortality related to these infections. Therefore, the aim of this review was to evaluate the impact of HAIs on mortality of hospitalized patients with COVID-19, specially by multidrug resistant bacteria as Acinetobacter baumannii. A systematic review was carried out in the PubMed database on July 2022 using the keywords "healthcare-associated infection" OR "nosocomial infection" AND "COVID-19" AND "Acinetobacter baumannii". The incidence of HAIs in COVID-19 patients was 18.85%, with 42.17% of mortality rate and relative risk (RR) 2.08 (95%CI 1.61-2.68). Considering that the risk of death was twice greater in co-infection COVID-19/HAI, it is essential the broad vaccination against COVID-19 and the adoption of measures to reduce HAI incidence in hospitalized patients and mortality by superinfections.*
Key words *COVID-19, Healthcare associated infections, Mortality, Acinetobacter baumannii*

Resumo *Apesar de a maioria dos casos de COVID-19 serem leves, os casos graves que necessitam de hospitalização e ventilação mecânica foram suficientes para sobrecarregar os sistemas de saúde no mundo, levando a mais de 6 milhões de mortes e ao aumento das infecções relacionadas à assistência à saúde (IRAS). A incidência de IRAS em pacientes hospitalizados com COVID-19 foi abordada em revisões sistemáticas, mas não houve descrição da mortalidade. Portanto, o objetivo desta revisão foi avaliar o impacto das IRAS na mortalidade de pacientes hospitalizados com COVID-19, especialmente por bactérias multirresistentes como a Acinetobacter baumannii. Uma revisão sistemática foi realizada no banco de dados PubMed em julho de 2022 usando as palavras-chave "infecção associada à saúde" OU "infecção nosocomial" E "COVID-19" E "Acinetobacter baumannii". A incidência de IRAS em pacientes COVID-19 foi de 18,85%, a taxa de mortalidade foi de 42,17% e o risco relativo (RR) foi de 2,08 (IC 95%1,61-2,68). Considerando o risco de morte duas vezes maior na coinfecção COVID-19/IRAS, é fundamental a ampla vacinação contra COVID-19 e a adoção de medidas para reduzir a incidência de IRAS e a mortalidade por superinfecções.*
Palavras-chave *COVID-19, Infecções associadas à assistência à saúde, Mortalidade, Acinetobacter baumannii*

Resumen *Aunque la mayoría de los casos de COVID-19 son leves, los casos graves que requieren hospitalización y ventilación mecánica han sido suficientes para saturar los sistemas de salud en todo el mundo, provocando más de 6 millones de muertes y un aumento de las infecciones relacionadas con la asistencia sanitaria (IRAS). La incidencia de IRAS en pacientes hospitalizados con COVID-19 fue abordada en revisiones sistemáticas, pero no hubo descripción de la mortalidad en estas. Por lo tanto, el objetivo de esta revisión fue evaluar el impacto de las IRAS en la mortalidad de pacientes hospitalizados con COVID-19, especialmente por bacterias multirresistentes como Acinetobacter baumannii. Se realizó una revisión sistemática en la base de datos PubMed en julio de 2022 utilizando las palabras clave "infección asociada a la atención médica" OR "infección nosocomial" AND "COVID-19" AND "Acinetobacter baumannii". La incidencia de IRAS en pacientes con COVID-19 fue del 18,85%, la tasa de mortalidad fue del 42,17% y el riesgo relativo (RR) fue de 2,08 (IC95% 1,61-2,68). Teniendo en cuenta que el riesgo de muerte es dos veces mayor en la coinfección por COVID-19/IRAS, es esencial la vacunación generalizada contra la COVID-19 y la adopción de medidas para reducir la incidencia de las IRAS y la mortalidad por sobreinfecciones.*
Palabras clave *COVID-19, Infecciones relacionadas con la asistencia sanitaria, Mortalidad, Acinetobacter baumannii*

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Introduction

The outbreak of coronavirus disease (COVID-19) has created a global health crisis and has become the largest pandemic in human history[1]. From December 31, 2019, until July 27, 2022, a total of 572,638,253 COVID-19 cases were reported, including 6,389,559 COVID-19-associated deaths[2].

Usually, the clinical manifestations of COVID-19 are less severe, typically manifested as a mild upper respiratory tract disease or even asymptomatic "sub-clinical" infection[3]. However, it can also lead to severe and critical respiratory failure requiring mechanical ventilation, resulting in septic shock or other organ dysfunction requiring intensive care treatment[4-6]. Moreover, studies suggest that coinfections and secondary infections can play an important role in higher mortality risk among hospitalized COVID-19 patients[5,6].

The World Health Organization (WHO) defines a healthcare-associated infection (HAI) as an infection occurring in a patient during the process of care in a hospital or other healthcare facility, which was not present or incubating at the time of admission[7].

COVID-19 infection increased the number of hospitalizations and the need for Intensive Care Units (ICUs) and mechanical ventilation, which are recognized risk factors associated with the development of HAIs. In addition, longer hospital stays, selective pressure exerted by the previous use of antimicrobials and, as highlighted by Shinohara *et al.*[8], inadequate training in infection prevention and control by health professionals hired on an emergency basis to respond to the COVID-19 pandemic situation, contributed to high rates of HAIs.

Zhou *et al.*[6], analyzed 191 hospitalized adult COVID-19 patients in Wuhan and observed sepsis as a common complication in both non-survivors and survivors of the disease. They suggested that sepsis could have resulted from viral infection in these patients and hence, specific data confirming bacterial involvement in COVID-19 were still needed.

Zhang *et al.*[9] analyzed 221 patients admitted in a hospital in Wuhan, China, and they observed that severely affected patients who required ICU admission and mechanical ventilation therapy showed a significant higher rate of bacterial co-infection ($p < 0.001$) compared with patients with non-severe COVID-19 disease (25.5% versus 1.8%).

Li *et al.*[5], in a retrospective study, observed a considerable proportion of hospitalized COVID-19 patients acquiring secondary bacterial infections, correlated with illness severity on admission and featuring gram-negative bacteria with high resistance rates like *Acinetobacter baumannii* and *Klebsiella pneumoniae* in Wuhan, China.

Acinetobacter baumannii (*A. baumannii*) is a ubiquitous, Gram-negative, non-flagellated coccobacillus bacterium commonly isolated from the environment. In human medicine, this opportunistic pathogen is responsible for hospital and community-acquired infections. Resistance to last-resort antibiotics, such as colistin, tigecycline, and carbapenems, underscores its significance as a nosocomial ESKAPE pathogen (*E. faecium, S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa* and *Enterobacter* species). According to the World Health Organization (WHO) this species is classified as a bacterium for which research and development of new antibiotics is critically needed and it is also considered an urgent threat to public health by the Centers for Disease Control and Prevention (CDC)[10].

Shinohara *et al.*[8] reported an outbreak of Carbapenem-resistant *Acinetobacter baumannii* (CRAb) in a tertiary teaching hospital in southern Brazil. A total of 19 CRAb isolates were recovered from blood, endotracheal aspirates, and/or rectal swabs of 14 patients. A total of 9 deaths was observed, two (2/4) of CRAb colonized patients and seven (7/10) of infected patients. According to the authors, colonization or infection with CRAb can lead to worse outcomes by extended hospital stays, escalated medical expenses, and amplified ICU mortality rates.

Several studies have reported the incidence of HAIs in hospitalized COVID-19 patients, including the profile and risk factors of these patients as well as the profile of bacterial isolates[11], the impact of HAIs on mortality of COVID-19 patients[12,13] and some studies have also compared the occurrence of HAIs before and during the pandemic period[14,15]. In addition, various researchers have assessed the mortality rate of COVID-19 patients with and without HAIs[16-21].

Lansbury *et al.*[22] conducted a systematic review and meta-analysis to evaluate co-infections in patients with COVID-19. The authors systematically searched Embase, Medline, Cochrane Library, LILACS and CINAHL for eligible studies published from January 1, 2020 to April 17, 2020. Thirty studies totaling 3,834 patients were included. Overall, 7% of hospitalized COVID-19 patients had a bacterial co-infection

Ciência & Saúde Coletiva, 30(2):1-11, 2025

(95%CI 3-12%, n = 2183, I^2 = 92·2%), with this proportion rising to 14% in studies focusing exclusively on ICU patients. It is worth noting that these studies did not provide data on the outcomes of these co-infected patients.

Another systematic review and meta-analysis performed by Langford *et al.*[23], observed that of 24 studies eligible and included in the review, a population of 3,338 patients with COVID-19 was evaluated for acute bacterial infection. In the meta-analysis, secondary bacterial infection was identified in 14.3% of patients (95%CI 9.6-18.9%), although this analysis did not include an evaluation of mortality rates.

Recognizing the importance of understanding the influence of healthcare-associated infections on patient outcome and acknowledging the absence of systematic reviews specifically addressing mortality, the objective of this study was to carry out a systematic review and meta-analysis to evaluate the impact of HAIs on the mortality of hospitalized COVID-19 patients with later emphasis on infections caused specifically by *A. baumannii.*

Methods

Search strategy and article selection criteria

For this systematic review, a search was conducted in the PubMed database on July 4, 2022, using the following keywords in Advanced Search: "(healthcare-associated infection) OR (nosocomial infection) AND (COVID-19) AND (Acinetobacter baumannii)". The primary aim was to identify articles presenting numerical data on co-infections among patients simultaneously affected by COVID-19 and healthcare-associated infections (HAI + COVID-19). Specifically, articles that provided information on both the mortality rate within the HAI+ COVID-19 and the COVID-19 groups were selected for inclusion in the subsequent meta-analysis. Studies published before 2020 and those with limited access to their full text were excluded from consideration.

Inclusion of additional studies occurred subsequent to the assessment of bibliographic references derived from the studies initially screened within databases. The flow of the systematic review design is presented in Figure 1.

Data extraction

The gathered data from the articles encompassed the following elements: authorship, publication year, country, study period, number of patients and number of deaths of patients with COVID-19 without co-infection (Control), number of patients and number of deaths of patients with COVID-19 and HAI (Experimental) and the prevailing bacteria associated with HAIs.

Statistical analysis

A meta-analysis of the collected data was performed using a random effect model, presented as Relative Risk (RR), with a 95% confidence interval (CI). The statistical analysis was performed using R software version 4.2.1 for Microsoft Windows, employing meta package version 5.5-0. Heterogeneity was assessed through the I^2 statistic, where an I^2 value approximating 0% indicates non-heterogeneity between studies, around 25% indicates low heterogeneity, around 50% moderate heterogeneity and close to 75% indicates high heterogeneity among studies. Concerning the analyzes presented as Relative Risk, the following methods were used: the Mantel-Haenzel method, Restricted-maximum-likelihood estimator for tau^2 and Q-profile method for interval confidence of tau^2 and tau.

A "leave-one-out" analysis was conducted to evaluate the impact of each study on the RR value. Given the presence of substantial heterogeneity among the studies, the Random effect model was employed. This analysis involved calculating RR and 95%CI (confidence interval) after excluding one study at a time.

Results

A total of 45 records were obtained through a search in the PubMed database using the keywords described in the methodology. Twenty-six studies were chosen for the systematic review and 15 of these met the criteria for meta-analysis, which presented the number of deaths in both the experimental (HAI+ COVID-19) and control group (COVID-19). Meta-analysis was used to calculate the impact of HAIs on the mortality of hospitalized patients with COVID-19. A summary of the characteristics from the 15 studies included in this meta-analysis is presented in Table 1.

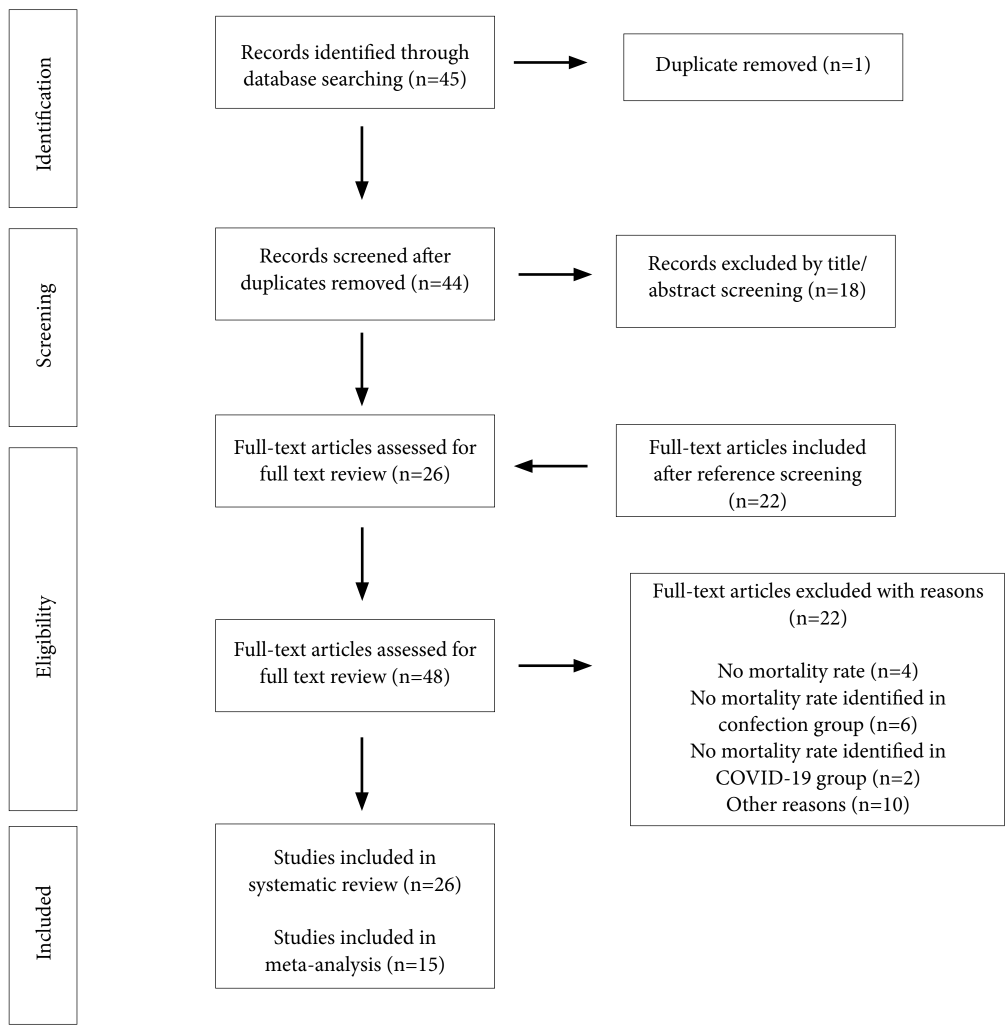

Figure 1. Flowchart for article selection.

Source: Authors.

A total of 8,438 hospitalized COVID-19 patients were analyzed in the 15 studies, of which 1,591 had HAI (18.85%). The present study also evaluated the number of deaths within the group called Experimental (COVID-19 + HAI) and the Control group (COVID-19), a mortality rate of 42.17% (671/1,591) and 16.6% (1,136/ 6,847) was observed, respectively (Table 1).

Considering the high heterogeneity of the studies (I^2 = 91%), a meta-analysis was performed using a random effect model (Figure 2). This analysis showed a relative risk (RR) of 2.08 (95%CI 1.61-2.68), that indicates that the risk of death in the COVID-19 + HAI group is approximately twice that observed in the COVID-19 group (Figure 2). Values below 1.0 would indicate a "protective effect" of HAIs on the risk of death, while values above 1.0 means an increase of mortality risk in the experimental group when compared to control.

The "leave-one-out" analysis yielded a range of RR values (95%CI) from 1.93 (1.52-2.46), with the exclusion of the study by Protonotariou *et al.*[24] to 2.20 (1.72- 2.81) excluding study by Falcone *et al.*[19]. After this analysis on the sensitivity of the statistical test, the authors decided to maintain the 15 studies in the meta-analysis. It is also possible to observe in this complementary analysis that the removal of the studies by Kumar *et al.*[20] and Protonotariou *et al.*[24] led to RR values below 2.0 (RR 1.99 and 1.93, respectively). Conversely, excluding the

Table 1. Characteristics of studies included in meta-analysis (n = 15).

			COVID-19 + HAI		COVID-19			
Study	**Country**	**Study period**	**Number of deaths**	**Number of co-infected**	**Number of deaths**	**Number of infected**	**Total study population**	**Most prevalent bacteria**
Ramanan *et al*., 2021[38]	Australia	Feb20-Sept20	16	60	46	430	490	*S. aureus, Enterococcus (faecium/faecalis); Enterobacter; Pseudomonas*
Nebreda-Mayoral, 2020[27]	Espanha	Mar20-May20	43	113	135	599	712	*Enterococcus (faecium/ faecalis), E. coli, A. baumannii, Staphylococcus* coagulase negative
Garcia-Vidal *et al*., 2020[39]	Espanha	Feb20-April20	8	43	86	917	960	*Pseudomonas and E. coli, S. pneumoniae, S. aureus*
Bardi *et al*., 2021[16]	Espanha	Mar20-May20	31	57	20	83	140	*Enterococcus (faecium/ faecalis), Pseudomonas, MRSA, Staphylococcus coagulase negative*
Cohen *et al*., 2021[17]	Israel	Mar20-Mar21	34	74	2	19	93	*P. aeruginosa, S. aureus*
Grasselli et. al, 2021[25]	Italia	Feb20-May20	114	359	120	415	774	*Enterobacterales, S. aureus*
Falcone *et al*., 2021[19]	Italia	Mar20-April20	13	69	57	246	315	*Klebsiella, Pseudomonas, Enterococcus*
Kumar *et al*., 2021[20]	USA	Mar20-Aug20	24	59	178	1,514	1,573	*Pseudomonas, E. coli, Klebsiella, MRSA, C. difficile*
Said *et al*., 2022[21]	Saudi Arabia	mid-quarter 21	34	109	19	192	301	*K. pneumoniae, A. baumannii* (XDR), *E. coli* (MDR); *P. aeruginosa* (XDR)
Khurana *et al*, 2021[40]	India	April20-July20	50	151	159	1,028	1,179	*K. pneumoniae; A. baumannnii*
Samantaray *et al*, 2022[41]	India	May20-Oct20	62	103	56	190	293	*K. pneumoniae* (MDR), *A. baumannii; Candida sp*
Copaja-Corzo *et al*., 2021[28]	Peru	Mar20-Mar21	29	50	12	74	124	*A. baumannii, P. aeruginosa*
Sang *et al*., 2021[42]	China	Jan20-April20	83	165	12	25	190	*K. pneumoniae, A. baumanni, S. maltophilia, C. albicans, Pseudomonas spp*
Da Costa *et al*., 2021[43]	Brazil	Mar20-May20	27	57	41	134	191	*A. baumannii* (96% MDR), *P. aeruginosa, K. pneumoniae* (57% MDR)
Protonotariou *et al*., 2021[24]	Greece	Sept20-Dec20	103	122	193	981	1,103	*A. baumannii, K. pneumoniae, E. faecium*
Total			671	1,591	1,136	6847	**8,438**	

Source: Authors.

studies by Grasseli *et al*.[25] and Falcone *et al*.[19] resulted in RR values near to 2.20 (RR 2.19 and 2.20, respectively). It is important to point that the country of study, the analysis period and the most prevalent bacteria in HAI cases could influence in the clinical outcomes of the patients (death or discharge). These aspects can be assessed in Table 1.

Despite of the importance of *A. baumannii* as a causative agent of HAIs in critical patients in ICUs, there are few studies that explore this aspect. The number of deaths and the respective studied population are presented in Table 2. Evidently, there is a wide range (from 30 to 70%) in the mortality rates and this variability can be explained considering the country of study and the adoption of precaution measures by the hospitals analyzed.

Discussion

As previously reported, in the present study, the incidence of HAIs observed in hospitalized COVID-19 patients was 18.85% with a mortality rate of 42.17% in patients with HAIs, 16.6% in "no-HAIs" patients with 2.08 of RR. This value of HAI incidence is close to those reported by Lansbury *et al.*[22] and Langford *et al.*[23] in their systematic reviews, which obtained values of 14% (considering ICU patients) and 14.3%, respectively. However, HAIs incidence differs from those observed by Lansbury *et al.*[22] (7% considering overall patients) and less than 4% of bacterial infections described by Westblade *et al.*[26].

The HAIs incidence of our study is also similar to 16% reported by Nebreda-Mayoral *et al.*[27] in Spain, and differs from the values obtained by Nori *et al.*[12] and Kumar *et al.*[20], both in the USA, with values of 3.6% and 3.7%, respectively. It is important to point out that the studies that analyzed patients in ICU, HAIs prevalence was significantly higher, as observed in studies by Bardi *et al.*[16] in Spain and Copaja-Corzo *et al.*[28] in Peru that obtained 40.7% and 40.32% of prevalence, respectively, confirming the impact of disease severity at admission on patient outcome.

Among the main causes for the occurrence of HAIs are the length of hospital stay, which tends to be higher according to the patient's level of care, APACHE II score[16]; previous empirical antibacterial therapy[26]; CRE intestinal colonization, mechanical ventilation, use of immunomodulators and elevated CRP on admission[19].

Table 2. Number of deaths and respective number of COVID-19 patients infected with *A. baumannii.*

	COVID-19 + Acinetobacter baumannii infection		
	Deaths	**Infected population**	**%**
Gottesman et al., 2021[44]	2	5	40
Shinohara et al., 2022[8]	7	10	70
Said et al., 2022[21]	11	34	32
Thoma et al., 2022[45]	4	7	57

Source: Authors.

Study	Experimental Events	Experimental Total	Contol Events	Contol Total	RR	95%-CI	Weight
RAMANAN et al., 2021	16	60	46	430	2.49	[1.51; 4.11]	6.4%
NEBREDA-MAYORAL, 2020	43	113	135	599	1.69	[1.28; 2.23]	7.7%
GARCIA-VIDAL et al., 2020	8	43	86	917	1.98	[1.03; 3.83]	5.4%
BARDI et al., 2021	31	57	20	83	2.26	[1.44; 3.54]	6.7%
COHEN et al., 2021	34	74	2	19	4.36	[1.15; 16.57]	2.6%
GRASSELLI et. al, 2021	114	359	120	415	1.10	[0.89; 1.36]	8.0%
FALCONE et al., 2021	13	69	57	246	0.81	[0.47; 0.47]	6.1%
KUMAR et al., 2021	24	59	178	1514	3.46	[2.47; 4.85]	7.4%
SAID et al., 2022	34	109	19	192	3.15	[1.89; 5.25]	6.3%
KHURANA et al., 2021	50	151	159	1028	2.14	[1.64; 2.80]	7.7%
SAMANTARAY et al., 2022	62	103	56	190	2.04	[1.56; 2.68]	7.7%
COPAJA-CORZO et al., 2021	29	50	12	74	3.58	[2.02; 6.32]	6.0%
SANG et al., 2021	83	165	12	25	1.05	[0.68; 1.62]	6.8%
DA COSTA et al., 2021	27	57	41	134	1.55	[1.07; 2.25]	7.1%
PROTONTARIOU et al., 2021	103	122	193	981	4.29	[3.70; 4.97]	8.2%
Random effects model		**1591**		**6847**	**2.08**	**[1.61; 2.68]**	**100.0%**

Heterogeneity: I^2=91%, τ^2 = 0.2036, $p < 0.01$
Test for overall effect: z = 5.57 ($p < 0.01$)

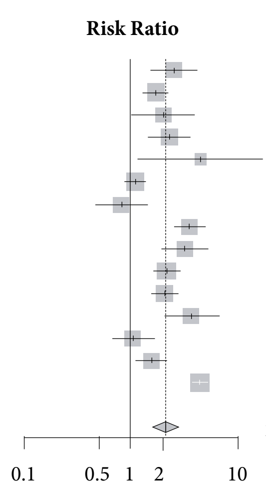

Figure 2. Forest plot of the number of deaths in the experimental group (COVID-19 + HAI) and the control group (COVID-19) reported in the 15 studies included in the meta-analysis.

Source: Authors.

Considering the impact of these HAIs on mortality, the rates obtained are similar to Kumar *et al.*[20] that, despite a 3.7% of HAIs occurrence, observed 40.7% of mortality rate in patients with HAIs when compared to 11.8% in "no-HAI" patients.

The studies conducted by Nori *et al.*[12], Giacobbe *et al.*[13] and Copaja-Corzo *et al.*[28] yielded mortality rates of 57%, 46% and 33%, respectively. Copaja-Corzo *et al.*[28] analyzed 124 patients admitted to ICUs at a hospital in Southern Peru from March 28, 2020, to March 1, 2021 and they observed a strong association between HAIs and mortality risk, revealing an adjusted hazard ratio (aHR) of 2.7 (95%CI: 1.33-5.60).

In an investigation by Jeong *et al.*[29], a total of 436 samples collected between August 2020 and October 2021 in Korea were analyzed, revealing a bacteria detection rate of 52.6%. Through multivariate analysis, several risk factors were identified, including coinfection (odds ratio [OR] = 6.095), advanced age (OR = 1.089), and elevated levels of lactate dehydrogenase (OR = 1.006). Moreover, coinfection with bacteria (OR = 11.250), resistant pathogens (OR = 11.667), and infection with multiple pathogens (OR = 10.667) were significantly related to death. Notably, the study highlighted several frequently isolated bacteria, including *Staphylococcus aureus, Haemophilus influenzae, Acinetobacter* species, *Escherichia coli, Klebsiella pneumoniae, Streptococcus pneumoniae,* and *Pseudomonas* species. It is important to highlight that among the isolated *A. baumannii* strains, a substantial 90% demonstrated a non-susceptibility to carbapenem antibiotics.

Westblade *et al.*[26] concluded that empirical antibacterial therapy and diagnostic testing for bacterial pathogens in hospitalized COVID-19 patients are indicated only for critical patients, those with severe immunosuppression, radiographic findings suggestive of bacterial pneumonia, or multiple laboratory parameters indicative of bacterial infection. The authors also showed that *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Haemophilus influenzae* were the most isolated bacteria, even though carbapenem-resistant Gram-negative infections are being increasingly reported in intensive care COVID-19 patients.

Nebreda-Mayoral *et al.*[27] reported 11% superinfections (80/712) and 54% of these were gram-negative bacillus (BGN) with *A. baumannii* being one of the main isolated bacteria. The term superinfections is used to describe infections caused by multidrug resistant (MDR) bacteria. Additionally, all MDR isolates were only susceptible to colistin. Among the mortality predictors, coinfection with *A. baumannii* showed an Odds Ratio (OR) of 9.329 (95%CI 2.289-38.020), p = 0.002.

Copaja-Corzo *et al.*[28] reported that 80% of isolated bacteria were classified as XDR (extensively resistant) to antibiotics, and the most common species were *Acinetobacter baumannii* (54%) and *Pseudomonas aeruginosa* (22%).

The worsening incidence of HAI by *A. baumannii* – typically important bacteria in the hospital environment – during the pandemic period was mostly due to the greater use of mechanical ventilation and inappropriate antimicrobial use. Rawson *et al.*[30] found that 72% of COVID-19 patients had received antibacterial therapy and that recorded agents tended to be broad-spectrum antibiotics prescribed empirically in both critical and non-critical settings. In the meta-analysis performed by Langford *et al.*[23], of 3338 hospitalized and critical COVID-19 patients across 24 studies, it was observed that most COVID-19 patients received antibiotics (71.9%, 95%CI 56.1%-87.7%). Rickman *et al.*[31] also noted that patient-to-patient transmission was involved in 55% of hospital-acquired COVID-19 cases, and shared-use facilities and equipment, or staff movement potentially contributed to a further 14% of cases.

The adoption of Contact Precaution Measures is indicated to control outbreaks and prevent the dissemination of MDR pathogens. These measures include placement of patients in a private room, single and disposable gowns and cohort of patients and professionals[32]. These measures, when combined with Standard Precaution Measures, like proper hand hygiene, glove usage and aprons are part of a multifaceted strategy that improves the effectiveness of these actions. It is also worth noting, the importance of cleaning and disinfecting environments, as well as antimicrobial optimization programs as strategies to reduce HAIs.

Regarding disinfection of mechanical ventilators, Cureño-Díaz *et al.*[33] conducted a study involving 338 mechanical ventilators, concluded that implementing a cleaning and disinfection protocol with enzymatic detergents/isopropyl alcohol for mechanical ventilators used by patients with SARS-CoV-2 and ESKAPE bacteria (including *A. baumanii*) had a positive impact on post disinfection microbial contamination rates.

Langford *et al.*[23] have recommended for patients with suspected bacterial infections that antibiotic selection be based on local epidemiology and patient factors, with early discontinuation when there is no evidence of bacterial infection.

These measures are strongly recommended, considering the high empirical use of broad-spectrum antibiotics observed for COVID-19 patients. There is heightening concern that antibiotic overuse during the COVID-19 pandemic will exacerbate the problem of antimicrobial resistance in clinically relevant microorganisms in the future[34-36]. In order to minimize this problem, it is recommended the adoption of Antibiotic Stewardship Programs (ASPs), these programs include various interventions, ranging from Hospital Leadership Commitment to activities, such as prospective audit and feedback, which aim to monitor antibiotic prescriptions and regularly provide data on antibiotic resistance[37].

It is important to acknowledge that this study has certain limitations. The high heterogeneity (I^2 91%); the diversity of infections included in the survey (ventilation-associated pneumonia (VAP), blood stream infections (BSI) and urinary tract infections (UTI), in contrast to some studies that included only BSI. Another limitation is the inclusion of co-infections (≤ 48 h after admission) and superinfections/secondary infections (> 48h after admission) while others included only superinfections. All these factors can interfere in the isolated bacteria and consequently in the clinical outcome.

Considering that HAIs acquired by hospitalized COVID-19 patients increased nearly twofold the risk of death, especially if caused by MDR bacteria, such as *Acinetobacter baumannii*. It is of paramount importance the broad vaccination against COVID-19 and the adoption of measures to reduce HAI among hospitalized patients, consequently mitigating mortality due to superinfections.

Contributions

Conception, planning, analysis, interpretation and writing of the work: TF Petroni. Review and final approval of the manuscript: MA Ono.

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