

Global healthcare-associated respiratory tract infections among inpatients: a systematic review and meta-analysis

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Background: Healthcare-associated respiratory tract infections are common among hospitalized patients. The infections are associated with high mortality, antimicrobial resistance, and health care costs. While there is growing evidence on health care-associated infections (HCAIs) overall, specific evidence for respiratory tract infections (HCA-RTIs) is scarce. Therefore, this study, which estimates the pooled prevalence of HCA-RTIs, provides valuable input for policymakers designing appropriate interventions.

Methods: This review was performed as per the Preferred Reporting Items for Systematic Reviews and Meta-Analysis protocol. Databases such as Scopus, PubMed, Web of Science, DOAJ, and MedNar were used to search published articles from electronic databases from May 27, 2023, to August 25, 2023, with no restriction in year of publication, or study design. Articles were retrieved using Boolean logic operators (AND, OR, and NOT), MeSH terms, and main keywords. The data were analyzed using Comprehensive Meta-Analysis version 4. A random effects model was employed to determine the pooled prevalence of healthcare-associated respiratory tract infections among the inpatients. The Joanna Briggs Institute Critical Assessment Tool for the prevalence and cohort study was employed to assess the quality of the studies. Subgroup analysis and meta-regression were employed to determine the potential sources of heterogeneity. Furthermore, publication bias was evaluated using funnel plots. Sensitivity analysis was employed to examine the influence of extreme values on the overall pooled prevalence.

Results: A total of 33 studies, including cross-sectional and cohort studies conducted on 95,051 inpatients, were used in the analysis. The review revealed that the global pooled prevalence of healthcare-associated respiratory tract infections among inpatients was 2.5% (95% CI: 1.4, 4.2%). The subgroup analysis based on the World Health Organization's region and survey year shows that the highest prevalence was reported in the Southeast Asian Region (16.9%) and the studies performed between 2008 and 2013 (3.4%), respectively.

Conclusion: This study revealed that one out of 40 inpatients had healthcare-associated respiratory tract infections. This finding indicates that there is a need to implement safety measures to reduce healthcare associated respiratory tract infections.

Keywords: Global, Respiratory Tract Infections, Healthcare Associated Infection, Inpatients, Systematic Review, and Meta-Analysis

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Introduction

Healthcare-associated infections (HAIs) are a significant public health concern across the world that threatens patient safety and healthcare provider's well-being (Rosenthal *et al.*, 2014; Allegranzi *et al.*, 2007). Healthcare associated respiratory tract infections (RTIs) are commonly caused by microorganisms, including bacteria, viruses, and fungi (Han *et al.*, 2020). Respiratory tract infections are classified into lower and upper RTIs. Lower RTIs are primarily caused by bacterial infections (Huang *et al.*, 2021).

Annually, it is estimated that hundreds of millions of inpatients are affected by healthcare associated RTIs in the healthcare facilities (Troeger *et al.*, 2019;

Troeger *et al.*, 2017). The lower RTIs are one of the causes for the highest death rates (Singh and Yu, 2016), antimicrobial resistance, healthcare costs (Huang *et al.*, 2021), and result in service losses or puts a significant financial problem for the healthcare systems (Troeger *et al.*, 2019; Troeger *et al.*, 2017). Respiratory tract infections impose a burden on populations in every country (Charani *et al.*, 2022). Additionally, RTIs are projected to be accountable for approximately \$15 billion in costs (direct treatment costs) in the United States alone, and, approximately 1.25 million patients are hospitalized due to community-acquired RTIs. Similarly, the mean cost of emergency department hospitalization alone for RTIs was €3,353

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in Italy (Trucchi *et al.*, 2019). There is little evidence for the combined global prevalence of healthcare-associated respiratory tract infections (RTIs) among inpatients. Despite some studies estimating point prevalence of healthcare-associated RTIs among hospital inpatients, there has not been a systematic review and meta-analysis to provide a global pool prevalence. Such pooled information is required for formulating targeted interventions. Therefore, this meta-analysis and systematic review seek to come up with an estimation of worldwide pooled prevalence of healthcare-associated RTIs in inpatients to allow for improved prevention and management.

This review aimed to address the following questions: (1) what is the global pooled prevalence of health care-associated respiratory tract infection; (2) How does the prevalence of healthcare-associated RTIs vary across different regions? The findings can serve as a valuable resource for relevant agencies and organizations in designing and implementing effective prevention and control measures, ultimately contributing to improved healthcare service delivery. Furthermore, the finding could be a valuable insight for future research, clinical practice, and policy development.

Materials and Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines or protocols was used to conduct this systematic review and meta-analysis (Moher, 2015).

Eligibility Criteria

This systematic review and meta-analysis included a study population consisting of hospitalized patients (inpatients) across the world. It also included studies reported quantitative data (magnitude, frequency, incidence rate, or prevalence of healthcare-associated respiratory tract infections). Only peer-reviewed, full-text, original articles with the study design of cross-sectional, and cohort studies, and published in English were considered. In this study, there is no restriction in terms of publication and survey year, or the study location. It also included the studies regardless of the sources of data and the age group. This systematic review and meta-analysis excluded studies reporting

qualitative outcomes, case report and series, review articles, reports, abstracts, opinions, editorial papers, commentaries, articles with a high risk of bias as well as unpublished articles and articles not available in full text were excluded from this systematic review and meta-analysis.

Sources of Information

To retrieve the studies required for this review, the authors (FAM, DAM, MD, MT, AT, and TG) used SCOPUS, PubMed/MEDLINE, Web of Science, the Directory of Open Access Journals (DOAJ), and MedNar databases. The articles were retrieved from May 27, 2023, to August 25, 2023. A structured search strategy using Boolean logic (AND, OR, NOT) and MeSH terms were employed across multiple databases with a relevant keyword, such as “incidence,” “prevalence,” healthcare associated infections “respiratory tract infections,” and “patients,” to retrieve relevant articles required for this systematic review and meta-analysis. Furthermore, the reference lists of eligible studies were reviewed for additional studies not initially captured in the database used to retrieve the studies.

Search Strategy

To retrieve articles required for this systematic review and meta-analysis, particularly from PubMed databases, the search terms included were “Prevalence” [Mesh Terms] OR “Prevalence” [All Fields] OR “Incidence” [Mesh Terms] OR “Incidence” [All Fields] OR “Proportion” [Mesh Terms] OR “Proportion” [All Fields] AND “Nosocomial” [Mesh Terms] OR “All Fields] OR “Hospital Acquired” AND “Infection” [Mesh Terms] OR “Respiratory disease” OR “pulmonary infection” [Mesh Terms] OR “Hazards” [Mesh] AND “Patient” [All Fields] OR “Patients” [All Fields] OR “Service Users” [All Fields]. The authors (FAM, DAM, TG, and DD) used the same terms to retrieve the studies from other included databases with a minor modification in search strategies.

Study Selection Process

The PRISMA flow chart, which indicates the number of studies included in, and excluded from this systematic review and meta-analysis with the reasons of exclusion, was used in the selection process. Duplicated articles were removed by using ENDNOTE software

version X5 (Thomson Reuters, USA). The eligibility of the studies was independently screened by all authors based on their title and abstract. To determine the current systematic review and meta-analysis, all authors subsequently evaluated the full texts of the eligible articles. Disagreements between the authors for the inclusion and exclusion of the studies were resolved through discussion. Finally, the studies that met the inclusion criteria were included in this systematic review and meta-analysis.

Data Extraction and Quality Appraisal

The data extraction was done independently. A predetermined Microsoft Excel sheet developed by the authors was used to systematically capture key study characteristics, including publication year, survey year(s), country or region, sample size, and reported outcomes such as the incidence or prevalence of healthcare-associated RTIs. Disagreements encountered among the authors regarding data extraction were resolved through discussion. The authors evaluated the quality of each study using the Joanna Briggs Institute Critical Assessment Tools (JBI) for prevalence/cross-sectional and cohort studies (JBI, 2019). Then, the studies were evaluated by the authors (FAM, DAM, MD, MT, AT, DD, EMA, and TG) independently to determine their eligibility. For all types of the study designs, each criterion of the appraisal tool was scored as “Yes” (1) or “No” (0). Based on the cumulative score, studies were graded into three quality categories: high quality (85% or above), moderate quality (60–84%), and low quality (below 60%). Only studies with a moderate quality (moderate risk of bias) or high quality (low risk of bias) were included in this systematic review and meta-analysis.

Statistical Procedures and Data Analysis

The analysis was carried out by DAM FAM, DD, and EMA. Statistical software called Comprehensive

Meta-Analysis (CMA) version 4.0 was used to determine the pooled overall prevalence of RTIs linked to healthcare among inpatients. The extracted data were analyzed using a random-effects model and visualized using a forest plot. The percentage of the total variability in a set of effect sizes due to true heterogeneity (I^2 statistics) was employed to assess the heterogeneity between the included articles. The level of heterogeneity was then classified as no heterogeneity (0%-25%), low heterogeneity (25%-50%), moderate heterogeneity (50%-75%), and high heterogeneity (>75%) (Ades *et al.*, 2005). The publication bias was assessed using funnel plots.

The authors employed a subgroup analysis to assess the variations in prevalence of healthcare associated RTIs based on the survey periods, publication years, and study regions, where the studies were conducted. Additionally, the authors employed a sensitivity analysis to assess the effects of extreme outcomes or values on the overall pooled prevalence of healthcare associated RTIs among the inpatients by excluding outcomes expected to influence the overall pooled prevalence.

Ethical Consideration

No applicable

Results

Study Selection

A total of 2081 studies were retrieved from the databases and another search engine (Google Scholar). A total of 859 duplicate studies were excluded. Furthermore, 233 studies were excluded based on their title and abstracts. In addition, 989 full-text articles were further assessed to determine their eligibility, of which 525 articles were excluded. Similarly, 464 articles were assessed based on their objective, methods, and outcome, of which 431 were excluded. Finally, 33 studies were included in the current study (Figure 1).

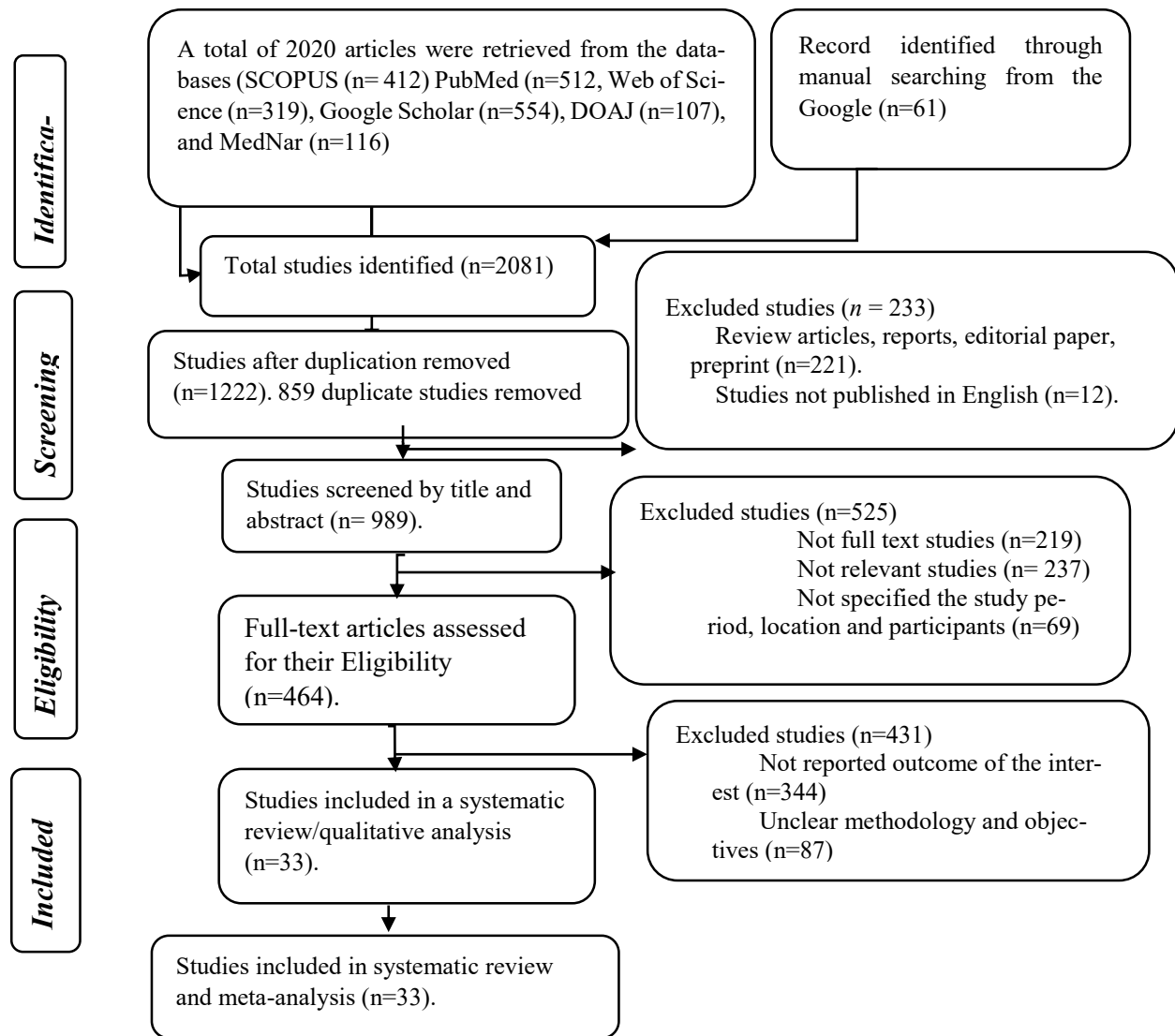


Figure 1: Study selection process of included articles for Systematic Review and Meta-analysis, 2023

Study characteristics

This study included a total of 33 articles involving 95,051 inpatients from 26 countries worldwide, with the number of study participants ranging from 86 (Knutsen *et al.*, 2012) to 9,865 (Danchaivijitr *et al.*

2007).The studies were conducted from January 1, 1996 to December 31, 2022. Twenty-one out of 33 studies have low risk of bias and the remaining have a moderate bias (Table 1).

Table 1: General characteristics of the studies included in the systematic review and meta-analysis, 2023.

Authors	Sample size (N)	Survey year	Publication year category	Respiratory tract infection prevalence	Country	WHO region	Risk of bias
Pittet <i>et al.</i> , 1999	1,349	1996	1996 -2001	0.02	Switzerland	EuR	Moderate
Ahoyo <i>et al.</i> , 2014	3130	2012	2008-2013	0.0363	Benin	AfR	Moderate
Girard <i>et al.</i> , 2006	286	2001	1996 -2001	0.007	France	EuR	Moderate
Esen <i>et al.</i> , 2004a	236	2004	2002-2007	0.2797	Turkey	EuR	Moderate
Izquierdo-Cubas <i>et al.</i> , 2008	4240	2004	2002-2007	0.016	Cuba	AmR	Moderate
Danchaivijitr <i>et al.</i> , 2007	9,865	2006	2002-2007	0.234	Thailand	SeAR	Moderate
Knutsen <i>et al.</i> , 2012	86	2012-2014	2008-2013	0.384	India	SeAR	Moderate
Faria <i>et al.</i> , 2007	968	2003	2002-2007	0.009	Albania	EuR	Low
Huang <i>et al.</i> , 2020	6717	2014-2018	2014-2018	0.007	China	WpR	Low
Labi <i>et al.</i> , 2019	2107	2016	2014-2018	0.0142	Ghana	AfR	Low
Askarian <i>et al.</i> , 2012	3450	2008-2009	2008-2013	0.013	Iran	EmR	Low
Abubakar, 2020	321	2019	2019-2023	0.019	Nigeria	AfR	Moderate
Zotti <i>et al.</i> , 2004	9467	2000	1996 -2001	0.016	Italy	EuR	Low
Gentili <i>et al.</i> , 2020	6263	2013-2018	2014-2018	0.0148	Italy	EuR	Low
Durlach <i>et al.</i> , 2012	4249	2008	2008-2013	0.034	Argentina	AmR	Low
Miihleemann <i>et al.</i> , 2011	520	2000	1996 -2001	0.01	Switzerland	EuR	Moderate
Ott and Wiersma, 2013	1047	2010	2008-2013	0.0229	Germany	EuR	Moderate
Lee <i>et al.</i> , 2007	1021	2005	2002-2007	0.014	Hong kong	WpR	Low
Patil and Moirangthem, 2025	267	2011-2012	2008-2013	0.2771	India	SeAR	Low
Shirani <i>et al.</i> , 2020	7,703	2019	2019-2023	0.00211	Saudi Arabia	EmR	Low
Kolpa <i>et al.</i> , 2018	1849	2016-2017	2014-2018	0.099	Poland	EuR	Low
Ghali <i>et al.</i> , 2021	2729	2012-2020	2014-2018	0.026	Tunisia	EmR	Low
Shrestha <i>et al.</i> , 2022	300	2016	2014-2018	0.19	Nepal	SeAR	Low
Alfouzan <i>et al.</i> , 2021	1408	2018-2019	2019-2023	0.018	Kuwait	EmR	Low
Magill <i>et al.</i> , 2012	851	2009	2008-2013	0.0106	USA	AmR	Moderate
Russo <i>et al.</i> , 2019	2767	2018	2014-2018	0.024	Australia	WpR	Low
Zhang <i>et al.</i> , 2016	4,029	2012-2014	2008-2013	0.0268	China	WpR	Low
Custovic <i>et al.</i> , 2014	834	2010	2008-2013	0.0671	Herzegovina	EuR	Moderate
Wang <i>et al.</i> , 2019	1347	2013-2015	2014-2018	0.0327	China	WpR	Low
Heydarpour <i>et al.</i> , 2017	6,000	2011-2014	2008-2013	0.0083	Iran	EmR	Low
Sahu <i>et al.</i> , 2016	6,864	2013-2014	2008-2013	0.0205	India	SeAR	Low
Nouetchognou <i>et al.</i> , 2016	307	2013-2014	2008-2013	0.003	Cameroon	AfR	Low
Tomczyk-Warunek <i>et al.</i> , 2021	2474	2018-2020	2019-2023	0.0016	Poland	EuR	Low

N: Sample size; *RTIs*: Respiratory tract infections; *EuR*: European Region; *AfR*: African Region; *EmR*: Eastern Mediterranean Region; *AmR*: American Region; *SeAR*: South-East Asia Region; *USA*: United State of America; *WpR*: Western Pacific Region; *WHO*: World Health Organization.

Prevalence of healthcare associated respiratory tract infections among inpatients

This study revealed that the global pooled prevalence of healthcare-associated RTIs among inpatients was

2.5% (95% CI: 1.4, 4.2%), with a p value of < 0.001; $I^2 = 79.02$ (Figure 2).

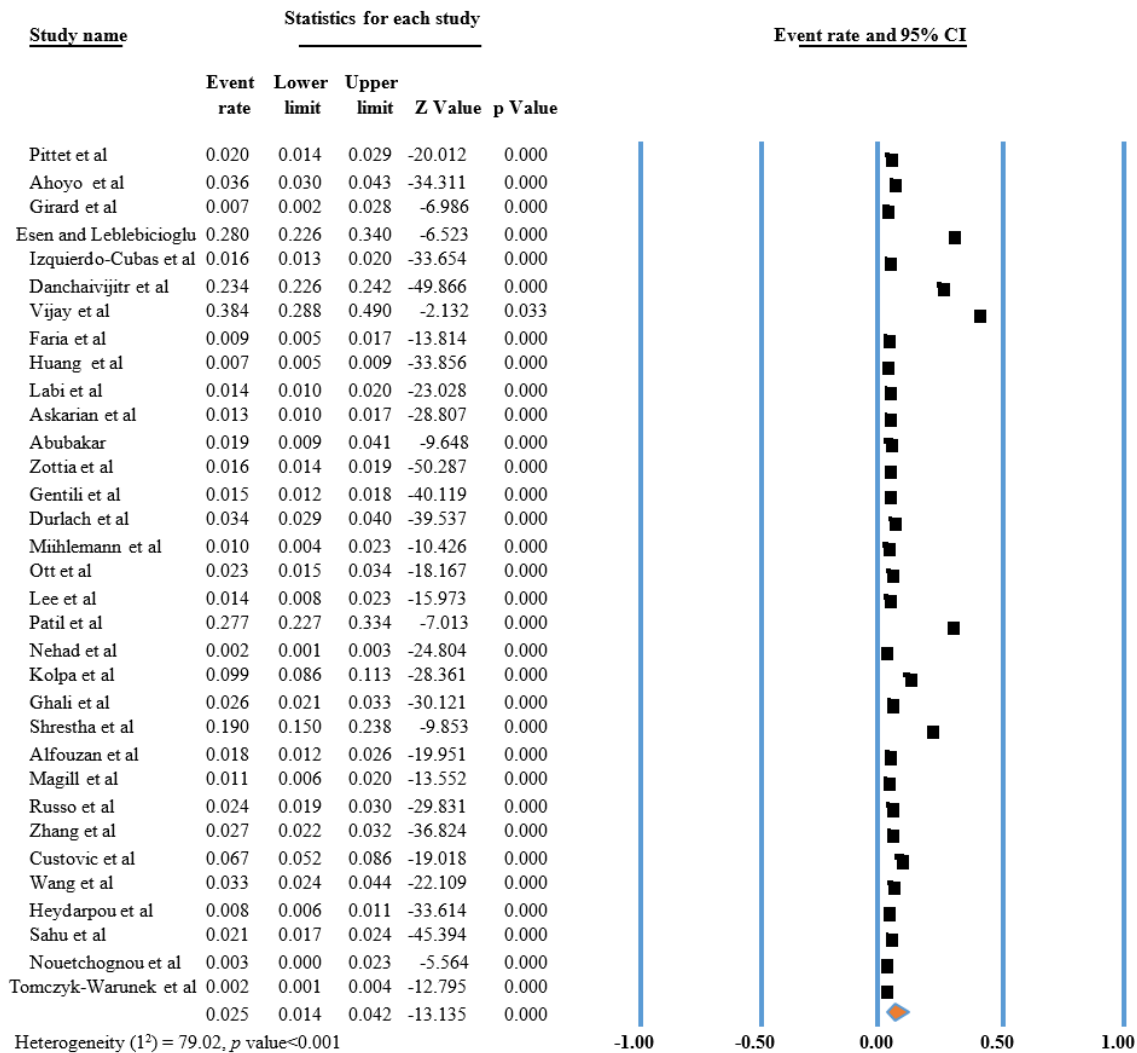


Figure 2: Overall global pooled prevalence of healthcare-associated respiratory tract infections among inpatients, 2023.

The subgroup analysis shows that the lowest pooled prevalence of RTIs among inpatients is 0.6% (95% CI: 0.2, 2.3%) in the studies conducted between 2019 and 2023, and the highest pooled prevalence is 4.6%

(95% CI: 1.0%, 18.2%) in the studies conducted between 2002 and 2007. The analysis revealed a declining trend of RTIs from 2007 to 2023 (Figure 3).

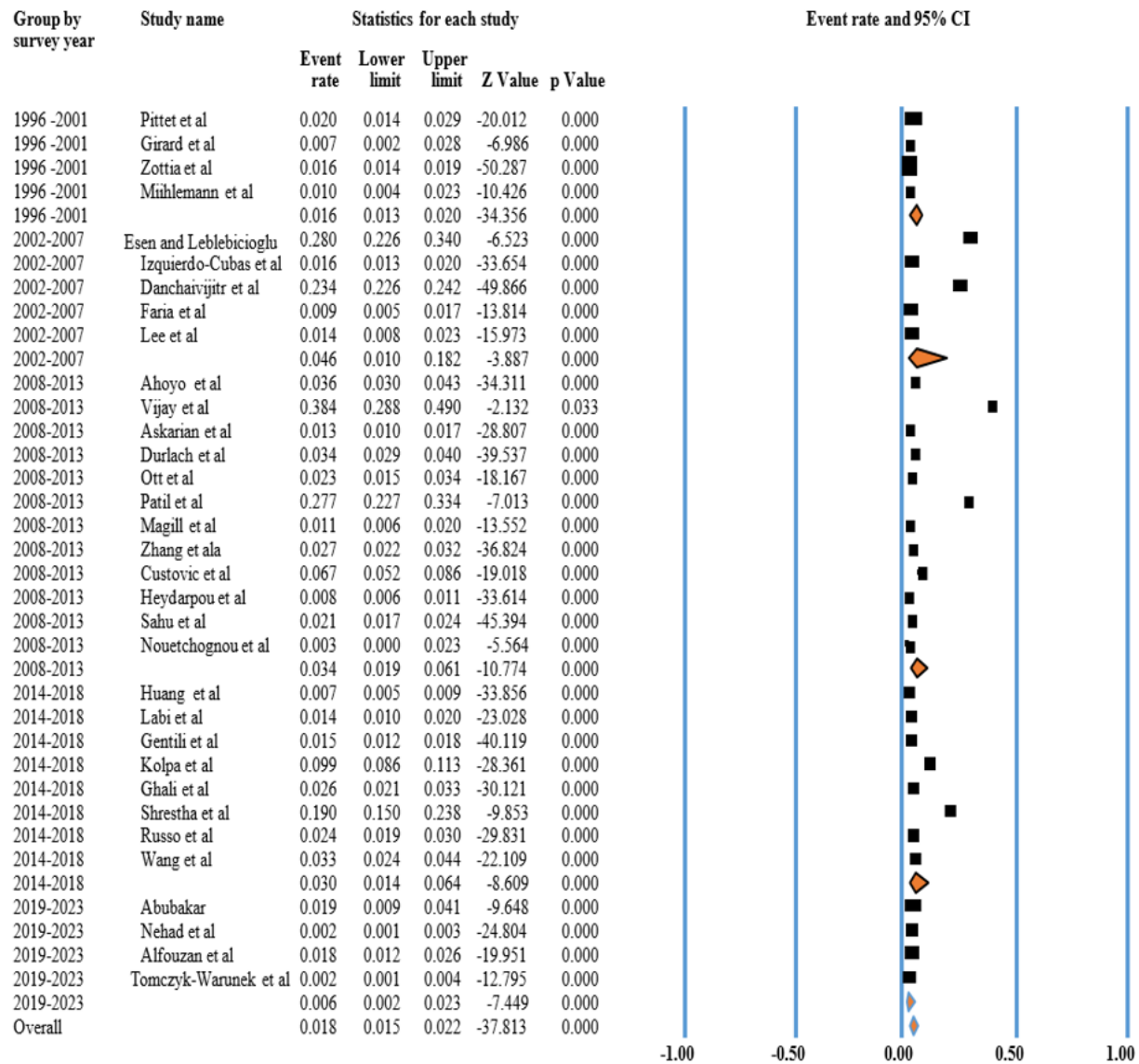


Figure 3: The pooled prevalence of healthcare-associated respiratory tract infections among inpatients based on the survey period, 2023.

This systematic review and meta-analysis revealed that the overall pooled prevalence of healthcare associated RTIs is highest in the Southeast Asian Region [16.9% (95% CI: 5.5, 41.4%)], whereas the lowest pooled prevalence of healthcare associated is reported

in the Eastern Mediterranean Region accounted for 1.0% (95% CI: 0.5, 2.1%), followed by 1.8% (95% CI: 0.9, 3.8%) and 1.9% (95% CI: 1.0, 3.6%) in African and American Region, respectively (Figure 4).

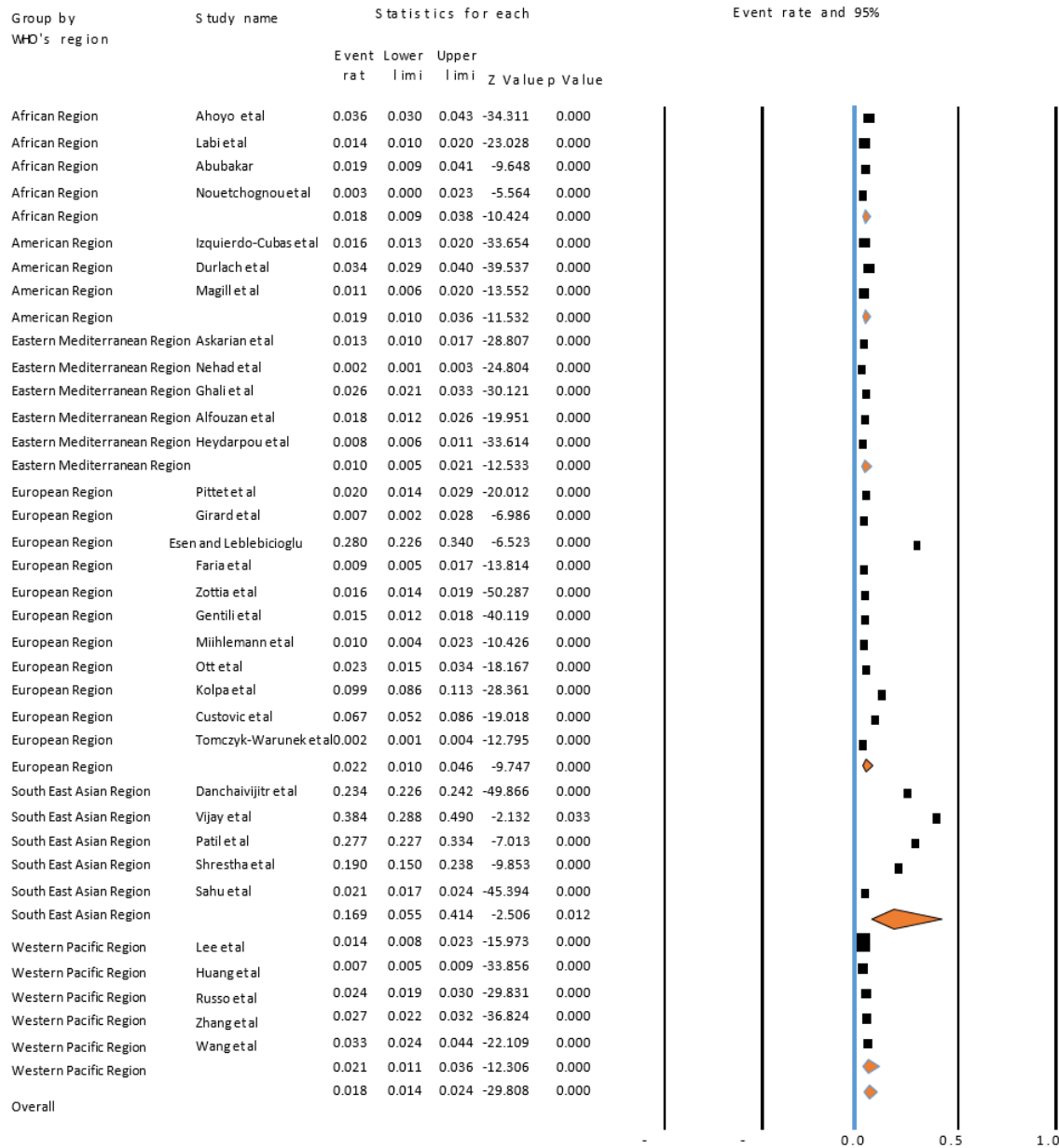


Figure 4: Forest plot showing the pooled prevalence of healthcare-associated respiratory tract infections among inpatients based on WHO's Region, 2023.

Publication Bias

The authors used a funnel plot to evaluate the publication bias, which visually represents the distribution of study findings. Accordingly, almost all findings are symmetrically distributed around the total effect size, with a minor publication bias. To address these few outliers and to assess their impact on the overall pooled prevalence, a sensitivity analysis was carried out (Figure 5).

Meta Regression

The meta-regression result based on a random-effects model displays a coefficient of $-3.8355 + 0.22$ (SE) with a 95% confidence range (-4.268, -3.402, Z-value of -17.36, and p-value < 0.001), with little variation.

Sensitivity Analysis Results

Furthermore, the authors employed sensitivity analysis by excluding extreme outcomes, and the sample size expected to influence the overall pooled prevalence of healthcare-associated RTIs among inpatients.

However, the exclusion of these extreme outcomes has no significant effect on the variation of the overall global pooled prevalence of healthcare associated RTIs among inpatients (Table 2).

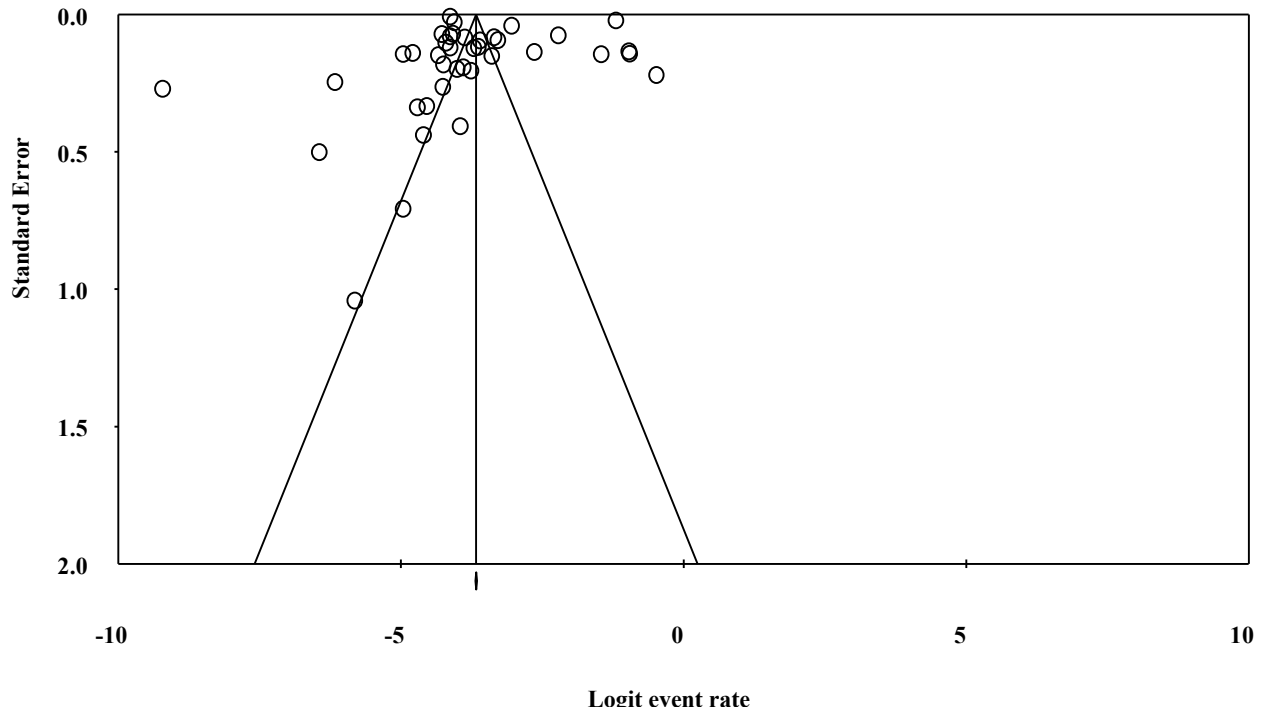


Figure 5: Funnel plot of standard error by logit event rate of healthcare-associated respiratory tract infections among inpatients in WHO’s Region, 2023

Table 2: Sensitivity analysis results based on extreme sample size and outcomes expected to affect the overall pooled prevalence of healthcare-associated RTIs.

Criteria	Pooled prevalence	<i>p</i> -value
After dropping one lowest outcome	2.2 (95% CI: 1.3, 3.9%)	<0.001
After dropping one smallest sample size	2.2 (95% CI: 1.3, 3.9%)	<0.001
After dropping two largest sample size	2.4 (95% CI: 1.6, 3.5%)	<0.001

Discussion

This review aimed to determine the global prevalence of healthcare-associated respiratory tract infections. The systematic review and meta-analysis included 33 studies, encompassing a total of 95,051 inpatients, with individual study sample sizes ranging from 86 to 9,865 participants. The finding revealed that the global pooled prevalence of healthcare-associated RTIs among patients was 2.5% which is lower than another study that reported a prevalence rate of 22.4% (Wu *et al.*, 2015). However, in the present report, the pooled prevalence of healthcare associated respiratory tract infection was higher than the global hospital infection rate of 0.14% (Raofi *et al.*, 2023). Variations in healthcare

associated RTI prevalence across studies may be attributed to the differences in participant demographics (age, health status, underlying conditions), differences in the types of healthcare-associated RTIs studied, the geographical or institutional context, disparities in healthcare infrastructure, and infection control practices (Abubakar *et al.*,2022; Alemu *et al.*, 2020)..

The findings of the present study revealed that the pooled prevalence of healthcare associated RTIs declined from 4.6% (2002 to 2007) to 0.6% (2019 to 2023). However, it increased from 1.6% (1996 to 2001) to 4.6% (2002 to 2007). The variation in healthcare-associated RTI prevalence might be attributed to the

variation in the number of studies analyzed, participant characteristics, such as health conditions and immunity, and variations in the implementation of infection prevention and control. Furthermore, based on the WHO's Regions, the highest pooled prevalence of healthcare associated RTIs was reported in the Southeast Asia Region accounted for 16.9%. This high rate may be due to the region is prone to issues such as limited healthcare resources, overcrowded hospital settings, and poor infection prevention and control structures, all of which increase the risk of transmission of infection within healthcare facilities. Further, lack of consistency in the implementation and adherence to standard hygiene practices and antimicrobial stewardship may result in high rates of infection (Feddemba *et al.*, 2021).

The lowest pooled prevalence of healthcare associated RTIs among inpatients was reported in the Eastern Mediterranean Region accounted for 1%, followed by 1.8% and 1.9% for African Region and American Region, respectively. These variations may be due to differences in study scope, RTIs surveillance and reporting systems, and infection control practices across regions. Standardizing these practices and reporting methods globally could improve monitoring and prevention efforts for healthcare-associated infections. There is variation in the pooled prevalence of healthcare associated with RTIs worldwide, with the highest prevalence of healthcare associated RTIs reported in the Southeast Asia Region. The findings underscore the urgent need to implement robust infection prevention and control strategies to increase patient health and safety (Brude and White, 2018). Effective measures, including reinforcing health system capacities, improving infection prevention protocols, and ensuring that healthcare providers receive adequate training to strengthen their skills and knowledge in infection control is needed (Nakahara *et al.*, 2019).

Due to the high heterogeneity in the current systematic review and meta-analysis, the authors employed subgroup analysis, however, there were no significant variations in the overall pooled prevalence. In addition, publication bias was evaluated using a funnel plot, which found no substantial bias, with almost all data being symmetrically distributed. Furthermore, sensitivity analysis was conducted to assess the impacts of extreme outcomes on the pooled. However, no substantial variation was observed after the extreme values were excluded from the analysis

Strength and Limitation

The global distribution of articles was uneven due to the limited number of studies available. Consequently, the

prevalence of healthcare-associated respiratory tract infections (RTIs) in many countries was not included, as only a few studies met the eligibility criteria for this review. Additionally, differences in national surveillance, recording, and reporting systems may have contributed to variations in reported prevalence rates. Furthermore, due to the scarcity of relevant studies, existing systematic reviews and meta-analyses on the prevalence of healthcare-associated RTIs remain insufficient for a comprehensive comparison with the findings of this review.

Conclusion

The current study revealed that the overall prevalence of RTIs among inpatients was 2.5%. However, the prevalence of RTIs varies among the WHO's region of the world and during the survey period. Healthcare-associated respiratory tract infections were most prevalent in Southeast Asia (16.9%). There is a need to implement interventions or infection prevention and control practices for RTIs management in hospitals to minimize the health effects posed by RTIs and to improve treatment outcomes.

Author Contributions

FAM and DAM conceived the idea and had a major role in the review, extraction, and analysis of the data and writing, drafting, and editing of the manuscript. FAM, DAM, MD, MT, AT, DD, EMA, and TG contributed to data extraction, analysis, and editing. Finally, all the authors (FAM, DAM, MD, MT, AT, DD, EMA, and TG) read and approved the final version of the manuscript to be published and agreed on all aspects of this work.

Competing Interests

The author declare that they have no competing interests.

Funding Statement

The authors did not receive funding for this work.

List of Abbreviations

RTIs: Respiratory tract infections; CMA: Comprehensive Meta-Analysis; JBI: Joanna Briggs Institute; Preferred Reporting Items for Systematic Review and Meta-Analysis; WHO: World Health Organization; MeSH: Medical Subject Heading.

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