Systematic Review

Strategies for preventing ventilator-associated pneumonia in adults in the Middle East and North Africa Region: A systematic review and meta-analysis

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ABSTRACT

BACKGROUND: Ventilator-associated pneumonia (VAP) is a common complication in intensive care units (ICUs), particularly in patients undergoing prolonged mechanical ventilation. VAP rates vary significantly across regions, with the Middle East and North Africa (MENA) region experiencing relatively high incidences. This study systematically reviews and analyses the efficacy of various VAP prevention strategies in the adult population of the MENA region.

METHODS: A systematic review and meta-analysis were conducted following PRISMA guidelines. Electronic databases (PubMed, Scopus, and CINAHL) were searched for studies from January 2004 to May 2024 that investigated VAP prevention strategies in adult ICU patients in the MENA region. Data extraction and quality assessment were performed by multiple independent reviewers. Meta-analysis was carried out using the DerSimonian and Laird random effect models.

RESULTS: A total of 10 randomized clinical trials conducted in Iran and Tunisia were included. The studies evaluated various interventions, including respiratory care programs, oral care protocols, and tracheal suction techniques. Significant reductions in VAP incidence were observed with interventions such as aerosolized colistin and comprehensive oral care (e.g., clove mouthwash). However, certain interventions, such as ondansetron and N-acetylcysteine, did not yield significant benefits.

CONCLUSION: This meta-analysis highlights effective VAP prevention strategies in the MENA region, with notable improvements in patient outcomes. These findings can potentially help in developing policies and guidelines to enhance VAP prevention efforts across ICUs in the region. Further research is essential to address existing gaps and refine prevention strategies.

KEYWORDS

Middle East and North Africa, prevention strategies, randomized controlled trials, ventilator-associated pneumonia

Background

Ventilator-associated pneumonia (VAP) is a term used to describe cases of pneumonia that occur more than 48 h following intubation and the initiation of mechanical ventilation.[1,2] The growth of biofilms inside the tracheal/endotracheal tube and the aspiration of oral secretions are the primary pathogenic factors in the development of VAP.[3] Therefore, the chance of getting VAP increases directly with the time spent on ventilation.[4] Due to a variety of factors, including patient demographics, quality of health care, and adherence to preventative practices, its occurrence

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varies greatly between various areas and healthcare settings.[5] A review by Laurent Papazian *et al*. suggested that VAP rates in North American hospitals are as low as 1–2 cases per 1000 ventilator days in adults.[6,7] However, the rates in European centers are significantly higher. For example, the EU-VAP/CAP research reported an incidence density of 18.3 VAP events per 1000 ventilator days.[8] A high risk remains in the Middle East and North Africa (MENA) region, where VAP rates ranged from 7.4 per 1000 ventilator days for surgical cardiothoracic intensive care units (ICUs) to 17.7 per 1000 ventilator days for medical cardiac ICUs.[9] Effective preventive strategies must be put in place since VAP has a large clinical and financial impact.[10] A wide range of therapies have been examined and proposed as part of several efforts aimed at lowering the prevalence of VAP.[1,10] This study aims to examine the efficacy of VAP prevention strategies in the MENA region, evaluate the evidence-based preventive measures currently in use, and optimize patient care protocols by adjusting preventative initiatives based on the gaps identified in the literature.

Material and Methods

Search strategy

We conducted a comprehensive search following PRISMA guidelines [Figure 1]. Electronic databases including PubMed, Scopus, and CINAHL were searched using keywords related to ventilator-associated pneumonia (VAP) in the Middle East and North Africa (MENA) region. The search was restricted to studies published in English from January 2004 to May 2024. In addition, the review protocol was registered and approved in the International Prospective Register of Systematic Reviews (PROSPERO), under registration number CRD42024555002 ensuring that the methodology was predefined and followed rigorously throughout the review process.

Inclusion and exclusion criteria

Inclusion criteria

Studies involving adult ICU patients who developed VAP in the MENA region were included. Eligible study designs encompassed randomized controlled trials (RCTs) that focused on interventions aimed at preventing or managing VAP. Studies were required to provide clear data on VAP incidence, prevention strategies, and outcomes in adult populations, with a focus on ICU settings. Only studies published in peer-reviewed journals and available in English were considered.

Exclusion criteria

Studies were excluded if they were case reports, narrative or systematic reviews, cross-sectional designs, case–control studies, or cohort studies, as these do not provide the same level of evidence as RCTs. In addition, studies focusing on pediatric or neonatal populations, such as those conducted in pediatric ICUs or neonatal ICUs, were excluded to maintain the focus on adult populations. Studies that did not specifically address the MENA region or lacked sufficient data on VAP prevention and management strategies were also excluded. Non-English language publications were not considered.

Data extraction

Two independent reviewers screened titles and abstracts, followed by full-text review. Discrepancies

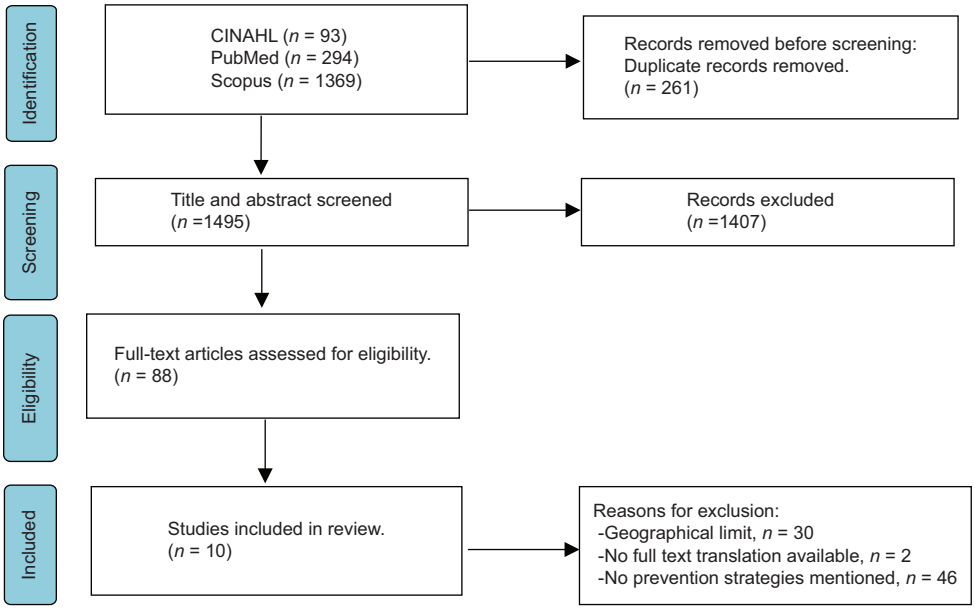

Figure 1: PRISMA flow diagram.

were resolved by a third reviewer. Data extraction includes author details, publication year, study location and design, population, sample size, setting, outcome measures, results for control and intervention groups, and conclusions. This method ensured consistent data collection across all studies for later analysis. Data were recorded in a standardized Excel form and managed using EndNote and Microsoft Excel.

Quality assessment

The Risk of Bias 2 (RoB2) tool was used by four independent reviewers to assess the validity of each included study. Four independent reviewers thoroughly assessed each study across multiple domains, including randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of reported results. Any discrepancies or disagreements in the assessment process were resolved by a fifth reviewer, ensuring consistency and objectivity. This comprehensive evaluation process allowed for the identification of potential biases both at the study level and for specific outcomes, ensuring that only high-quality evidence was considered in the final analysis. The final risk of bias assessment was used to inform the interpretation of study findings and the overall conclusions of the review.

Data synthesis

The included studies were systematically summarized based on the VAP prevention strategies employed and their corresponding recommendations. For each prevention strategy, details such as the recommendation status (e.g., strongly recommended and conditionally recommended), level of evidence (high, moderate, low, or very low), and the quality of the supporting or refuting studies were carefully documented. This process allowed for a clear comparison of the effectiveness and strength of the various interventions across studies. Heterogeneity among the studies was quantified using *I*-squared (I^2) statistics, which measure the percentage of total variation across studies due to heterogeneity rather than chance.

Statistical analysis

Meta-analyses were conducted in R software (version 4.0.2; R Foundation for Statistical Computing, Vienna, Austria) using the Metafor package.[11] Relative risk (RR) with 95% confidence interval (CI) was used to measure the VAP prevention strategies. To take account for both within- and between-study variability, DerSimonian and Laird random effect model was used to produce summary treatment effects in terms (RR) and 95% CI. Cochrane's Q test was used to assess the heterogeneity (I^2 <25%: weak heterogeneity; I^2 = 25%–50%: moderate heterogeneity; I^2 >50%: large or extreme heterogeneity) across included studies with the level of significance set at 0.1 (10%).[12] Begg's test and Egger's test were used to assess the potential publication bias with funnel plots.

Results

Characteristics of the included studies

This review summarizes 10 randomized clinical trials conducted in Iran and Tunisia, focusing on various interventions to prevent VAP in ICU patients [Table 1]. The studies explored diverse strategies including respiratory care programs, different medications for stress ulcer prophylaxis, oral care interventions (such as Miswak, clove mouthwash, and chlorhexidine), nasal care, tracheal suction techniques, and positioning protocols. Sample sizes ranged from 60 to 200 participants, with intervention durations typically lasting 5–14 days. Most studies reported positive outcomes, with several showing significant reductions in VAP incidence in intervention groups. Notable findings include the superiority of aerosolized colistin over intravenous administration, the effectiveness of clove mouthwash compared to chlorhexidine, and the success of comprehensive oral healthcare protocols. However, some interventions, such as ondansetron injection and N-acetylcysteine for tracheal suction, did not show significant benefits in VAP prevention. The studies used various assessment tools, including the Modified Pulmonary Infection Clinical Scale and Clinical Pulmonary Infection Score, to measure outcomes.

The risk of bias assessment reveals a mixed profile across different domains [Figure 2]. While the study demonstrates low risk in areas such as randomization, adherence to intended interventions, and selection of reported results, there are some concerns regarding missing outcome data. The most significant issue lies in the measurement of outcomes, where a substantial portion is deemed high risk. The majority of studies show a low risk of bias in the randomization process, deviations from intended interventions, and selection of reported results [Figure 3]. However, bias in the measurement of outcome emerges as the most problematic domain, with 5 studies rated as high risk and 2 as some concerns. Missing outcome data also show some variability. Overall, 5 studies are rated as low risk of bias, 7 as some concerns, and one study[11] presents a mixed profile with mostly low-risk domains but high risk of bias in the measurement of outcome. This variability results in an overall risk of bias that is split between low risk and some concerns, indicating that while the study has several methodological strengths, there are important limitations to consider.

This meta-analysis examined the effectiveness of VAP prevention strategies in adult populations across the MENA region. The analysis included 10 studies with a

Table 1: Summary of randomized clinical trials on ventilator-associated pneumonia prevention strategies in intensive care unit patients

Author (year)	Country	Type of study	Sample characterization	Sample size	Duration of intervention	VAP prevention strategy	Outcome measurement tools	Key findings
Abbasinia *et al*., 2016[13]	Iran	Randomized clinical trial	Patients undergoing mechanical ventilation in ICU	T: 64 (I: 32, C: 32)	5 days	Upper respiratory care program (oral and subglottic suctioning, cuff pressure regulation, backrest elevation)	MPICS	Reduced VAP incidence in intervention group by day 5
Abdellatif *et al*., 2016[11]	Tunisia	Single-Blind Randomized Clinical Trial	Critically ill adults with gram negative VAP in ICU	T: 149 (I: 73, C: 76)	14 days	AS colistin versus IV colistin	Incidence of VAP	AS colistin was non-inferior to IV colistin for clinical cure, lower incidence of ARF in AS group, faster bacterial eradication, earlier ventilator weaning
Bashar *et al*., 2013[12]	Iran	Randomized double blind clinical trial	ICU patients with trauma	T: 120 (I: 60, C: 60)	1 year	Ranitidine versus pantoprazole for stress ulcer prophylaxis	Incidence of VAP, duration of tracheal intubation, length of ICU stay	Incidence of VAP: 10% with ranitidine, 30% with pantoprazole (P=0.006); Hospital stay longer with pantoprazole
Halili *et al*., 2024[14]	Iran	Single-blind randomized clinical trial	Patients hospitalized in ICU	T: 62 (I: 31, C: 31)	5 days	Nasal care program combining with oral care	Incidence of VAP using MPICS	No significant difference in VAP incidence between intervention and control groups on the 3rd day after intervention; significant reduction on the 6th day
Irani *et al*., 2019[15]	Iran	Single-blind randomized clinical trial	ICU patients undergoing mechanical ventilation	T: 70 (I: 35, C: 35)	5 days	Oral care with Miswak versus chlorhexidine mouthwash	Incidence of VAP, BOAS, MCPIS	No VAP in Miswak group; 17.1% VAP incidence in chlorhexidine group; significant difference in VAP incidence between groups
Jahanshir *et al*., 2023[16]	Iran	Randomized triple-blind clinical trial	ICU patients undergoing mechanical ventilation	T: 168 (I: 84, C: 84)	5 days	Clove mouthwash versus chlorhexidine mouthwash	Incidence of VAP, BOAS, MCPIS	VAP incidence: 20.2% (clove) versus 41.7% (chlorhexidine); Risk of VAP 2.06 times higher in control group
Karimi *et al*., 2023[17]	Iran	Double-Blind Multicentre Randomized Controlled Trial	ICU patients with neurological conditions, intubated and mechanically ventilated	T: 200 (I: 100, C: 100)	7 days	Supervised oral health care protocol (hand hygiene, oral examination, subglottic suctioning, tooth brushing with baby toothbrush, rinsing with normal saline, chlorhexidine 0.2% mouthwash, moisturizing gel) versus routine oral care	CPIS	VAP incidence: 5% (intervention) versus 64% (control); Risk of VAP reduced by 97%; Higher VAP risk in patients with lower consciousness
Madineh *et al*., 2017[18]	Iran	Randomized clinical trial	ICU patients aged 15–65, mechanically ventilated	T: 80 (I: 40, C: 40)	5 days	Ondansetron injection versus placebo (distilled water)	Incidence of VAP, CDC diagnostic criteria	No significant difference in VAP incidence between ondansetron group (12.5%) and control group (15%) (P=0.74); comorbidity was significantly associated with VAP

Contd...

Table 1: Contd...

Author (year)	Country	Type of study	Sample characterization	Sample size	Duration of intervention	VAP prevention strategy	Outcome measurement tools	Key findings
Mir *et al*., 2022[19]	Iran	Single-blind randomized clinical trial	ICU patients with trauma, intubated and mechanically ventilated	T: 60 (I: 30, C: 30)	5 days	Tracheal suction with NAC versus tracheal suction with normal saline	MCPIS	No significant difference in VAP incidence between intervention (13.3%) and control (23.3%) groups; NAC can be used safely for tracheal suction without specific complications
Yaghoubinia *et al*., 2017[20]	Iran	Single-blind randomized clinical trial	Intubated patients under mechanical ventilation in ICUs	T: 70 (I: 35, C: 30)	3 days	Head-of-bed elevation, daily gastric residual volume management, abdominal massage, oral care with chlorhexidine	MCPIS	VAP incidence: 0% (intervention) versus 54% (control); significant reduction in VAP with the care program

CPIS=Clinical pulmonary infection score, MCPIS=Modified CPIS, BOAS=Beck Oral Assessment Scale, MPICS=Modified Pulmonary Infection Clinical Scale, ICUs=Intensive care units, VAP=Ventilator-associated pneumonia, AS=Aerosolized, IV=Intravenous, NAC=N-acetylcysteine, ARF=Acute Respiratory Failure.

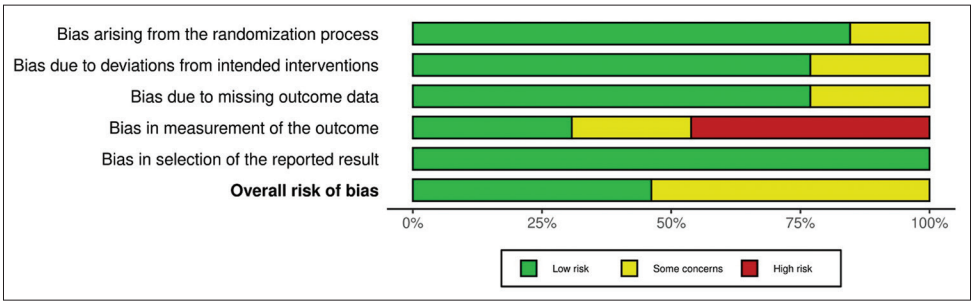

Figure 2: Overall risk of bias.

total of 1049 participants (523 in experimental groups and 526 in control groups) and 272 VAP events. The random effects model yielded a risk ratio of 0.36 (95% CI: 0.20–0.65), indicating a significant reduction in VAP risk with the implemented prevention strategies ($P = 0.003$) [Figure 4]. However, substantial heterogeneity was observed among the studies ($I^2 = 65.4\%$, $Q = 26.02$, $P = 0.002$), suggesting variability in the effectiveness of different interventions or study populations. The wide prediction interval (95% CI: 0.08–1.54) further reflects this heterogeneity and indicates that future studies might find varying results. Despite this variability, the overall findings support the use of VAP prevention strategies in this region, though further research may be needed to identify the most effective interventions across different settings.

Publication bias

To address potential publication bias, Begg's test was conducted, yielding a Z score of −0.45 and a P value of 0.65. This result suggests no significant evidence of publication bias in the meta-analysis. The bias estimate of −5.00 (standard error = 11.18) indicates a small, nonsignificant negative bias. These findings suggest that the results of the meta-analysis are likely not substantially influenced by publication bias, enhancing the reliability of the conclusions drawn about the effectiveness of VAP prevention strategies in the studied population. The funnel plot [Figure 5] appears symmetrical and roughly inverted funnel-shaped, suggesting no clear evidence of publication bias in the studies included.

Discussion

This systematic review and meta-analysis of VAP prevention strategies in the MENA region reveals significant insights with broad implications for critical care practice and research. Our analysis demonstrates a substantial reduction in VAP risk with implemented prevention strategies (RR: 0.36, 95% CI: 0.20–0.65, $P = 0.003$), aligning with global trends but providing specific context for the MENA region.

This finding is consistent with previous global studies, such as the one by Martinez-Reviejo *et al*., which reported significant reductions in VAP episodes (odds ratio = 0.42, 95% CI: 0.33, 0.54) and mechanical ventilation duration with ventilator care bundles.[21] However, our study offers unique insights into region-specific interventions, such as the noninferiority of aerosolized colistin to

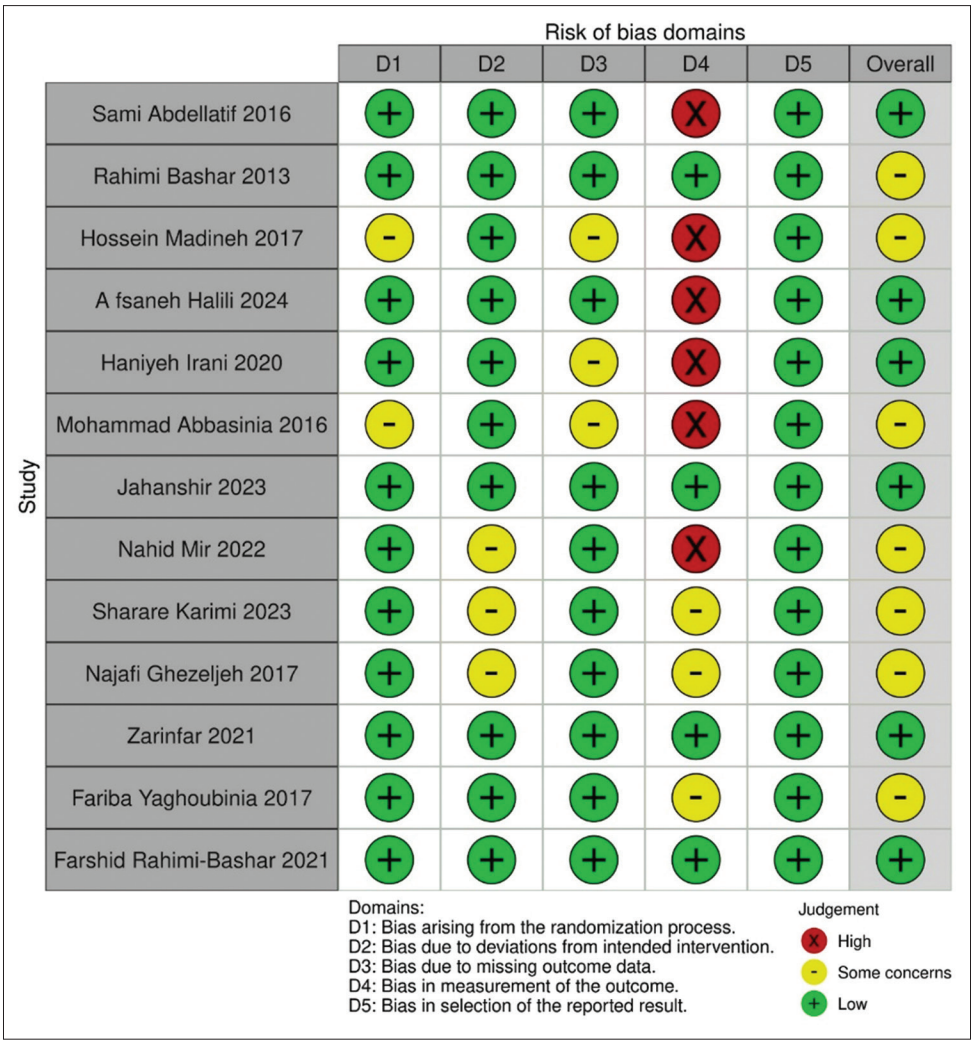

Figure 3: Risk of bias for the included studies.

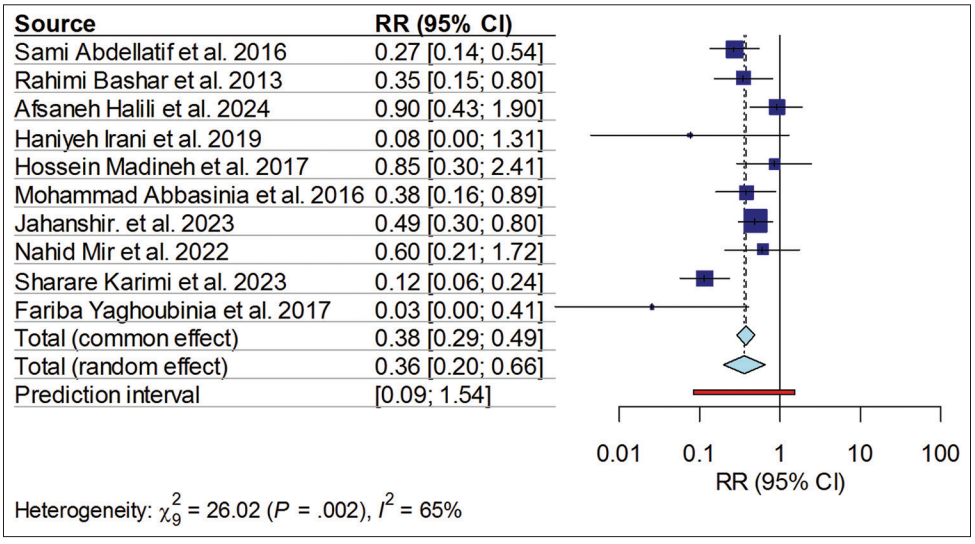

Figure 4: Forest plot for ventilator-associated pneumonia. RR: Relative risk, CI: Confidence interval.

intravenous administration and the superior efficacy of local practices such as Miswak and clove mouthwash compared to chlorhexidine. These findings highlight the potential of incorporating cultural practices into

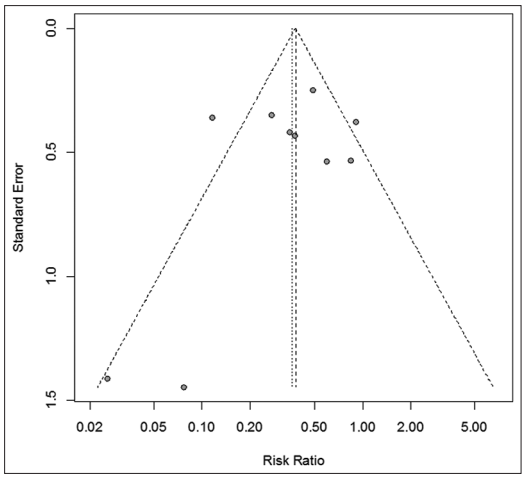

Figure 5: Funnel plot for the publication bias.

evidence-based protocols, a perspective often overlooked in global studies. The effectiveness of comprehensive oral healthcare protocols, particularly the dramatic reduction in VAP incidence from 64% to 5% in one study, underscores the critical role of meticulous oral hygiene in VAP prevention, echoing the findings of Mitchell *et al*. on nonventilator-associated healthcare-associated pneumonia prevention.[4]

Interestingly, our review challenges some conventional practices, such as the use of ondansetron injection and N-acetylcysteine for tracheal suction, which showed limited efficacy. This emphasizes the need for continuous re-evaluation of ICU protocols based on emerging evidence. The considerable heterogeneity observed in our analysis (I^2 = 65.4%, Q = 26.02, P = 0.002) warrants careful interpretation of results and suggests variability in intervention effectiveness across different settings, a limitation also noted in previous global reviews. Our findings should be interpreted in the context of global VAP epidemiology, considering the higher incidence of VAP in lower- and middle-income countries and the predominance of Gram-negative bacteria, as reported in Asian studies.

The review of VAP diagnostics reveals a heavy reliance on microbiological confirmation, particularly bronchoalveolar lavage culture, aligning with the findings of previous diagnostic studies. However, the lack of consensus on diagnostic criteria and the limited use of histopathological criteria highlight the need for standardized, comprehensive reference standards in VAP research. A key strength of our study is its focus on the MENA region, providing context-specific evidence that can inform tailored prevention strategies in resource-limited settings.

However, limitations include the heterogeneity in study designs and the potential for bias in outcome measurement, as revealed by our risk of bias assessment. Future research should address these methodological limitations through large-scale, multicenter trials within the MENA region and incorporate cost-effectiveness analyses to guide resource allocation.

Future directions

To advance VAP prevention in the MENA region, researchers and policymakers should focus on integrating culturally relevant practices like Miswak and clove mouthwash into region-specific guidelines, while addressing diagnostic standardization and resource allocation challenges unique to lower- and middle-income countries. Future efforts should prioritize large-scale, multicenter trials, cost-effectiveness studies, and the development of consensus on diagnostic criteria. Policymakers should enhance ICU resources, promote meticulous oral hygiene, and reevaluate existing protocols based on emerging evidence. Capacity building through education, faculty development workshops, and regional collaboration is essential, along with leveraging technology and innovation for tailored solutions. Establishing regional registries and monitoring intervention outcomes will further guide effective policy-making and improve ICU patient outcomes.

Conclusion

This meta-analysis provides compelling evidence for the efficacy of VAP prevention strategies in the MENA region while also highlighting areas for improvement in both clinical practice and research methodology. These insights can inform policy-making and clinical guidelines, ultimately contributing to improved patient outcomes in ICUs across the MENA.

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Authors' contributions

OA and JS conceptualized the study, designed the systematic review protocol, and outlined the research objectives. OA, AA, and NA conducted the comprehensive literature search, screened the identified studies, and extracted the relevant data. JS and NA developed the methodology for the meta-analysis, conducted the statistical analysis, and interpreted the results. OA and JS wrote the initial draft of the manuscript. AJ, NA, and AA critically revised the manuscript for intellectual content, provided feedback on the analysis, and contributed to revisions. JS supervised the overall project, ensuring alignment with the study protocol and research goals.

Ethics statement

This systematic review and meta-analysis utilized data from previously published studies. As it involved the analysis of secondary, publicly available data, no approval from an Institutional Review Board or Ethics Committee was required. All original studies included in this analysis had obtained the appropriate ethical approvals during their respective data collection processes.

Data availability statement

The data supporting the findings of this study, "*Strategies for Preventing Ventilator-Associated Pneumonia in Adults in the Middle East and North Africa Region: A Systematic Review and Meta-Analysis*," are derived from publicly available sources and published literature included in the systematic review. All relevant data have been cited within the manuscript and its references. Any additional data or supporting materials can be made available upon reasonable request from the corresponding author.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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