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Tracheal tube infections in critical care: A narrative review of influencing factors, microbial agents, and mitigation strategies in intensive care unit settings

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Abstract

Tracheal tube infections pose significant challenges in the management of mechanically ventilated patients in intensive care units. These infections contribute to prolonged intensive care unit stays, increased healthcare costs, the spread of antibiotic resistance, and poor patient outcomes. This study aims to elucidate the complex relationship between environmental factors, hospital practices, and the incidence of tracheal tube infections. Our comprehensive review explores the impact of factors such as air quality, water sources, equipment contamination, ventilation strategies, infection control protocols, and microbial reservoirs within hospital settings on tracheal tube infection rates. Additionally, it investigates global variations in tracheal tube infection prevalence, which are influenced by differences in healthcare infrastructure, infection control adherence, antibiotic resistance profiles, and patient demographics. Our findings highlight the importance of targeted interventions and collaborative approaches to reduce the burden of tracheal tube infections and improve patient care in intensive care units. By fully understanding the interplay between environmental conditions and hospital practices, effective prevention and management strategies can be developed to reduce the impact of tracheal tube infections on patient outcomes and healthcare resources, ultimately enhancing the quality of care in critical care settings.

Keywords

Tracheal tube infection, intensive care units, environmental factors, nosocomial infection, microbial reservoirs, antibiotic resistance

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Introduction

Tracheal tube infection (TTI) refers to the colonization or infiltration of microorganisms within the airway, facilitated by the use of endotracheal or tracheostomy tubes. This infiltration can lead to various respiratory complications, including pneumonia, tracheobronchitis, and potential systemic infections. Tracheal tube infections encompass both ventilator-associated pneumonia (VAP) and ventilator-associated tracheobronchitis (VAT), though these conditions are distinct. VAP is a type of pneumonia that occurs in mechanically ventilated patients after more than 48 h, characterized by new or progressive pulmonary infiltrates on imaging and clinical signs such as fever, purulent secretions, and

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abnormal white blood cell counts. In contrast, VAT is limited to the trachea and bronchi without lung involvement, presenting with symptoms like purulent tracheal secretions, fever, and increased airway resistance, but lacking the infiltrates seen in VAP. VAT can act as a precursor to VAP, though not all patients with VAT develop pneumonia.[1]

The sources of such infections can be endogenous microbial flora or cross-contamination from environmental sources within the hospital setting. TTIs present a significant challenge in managing mechanically ventilated patients in intensive care units (ICUs). These infections, which range from localized respiratory tract issues to severe systemic complications, have a profound impact on patient morbidity and mortality. Despite advancements in medical care and infection control practices, TTIs continue to impose a substantial burden on healthcare systems globally.[2]

TTIs in ventilated ICU patients are underscored by their multifaceted implications. First, these infections lead to prolonged ICU stays, heightened healthcare resource utilization, and increased treatment costs. Moreover, they contribute to the emergence of antibiotic resistance, exacerbating the challenge of managing infectious diseases in hospital settings. Additionally, TTI can compromise patient outcomes, resulting in prolonged mechanical ventilation, VAP, and sepsis.[3] Therefore, understanding the underlying factors contributing to TTI is paramount for developing targeted preventive strategies and optimizing patient care in ICUs. Patient-related characteristics, environmental conditions, healthcare practices, and microbial colonization dynamics all play intricate roles in the pathogenesis of these infections. Investigating these factors can provide invaluable insights into risk assessment, early detection, and effective management strategies.[4]

In light of the increasing prevalence of multidrug-resistant pathogens and the persistent threat posed by healthcare-associated infections, implementing robust infection control measures in ICU settings is more crucial than ever. *Pseudomonas aeruginosa* and *Acinetobacter baumannii* are among the most concerning pathogens associated with nosocomial infections, particularly in ICUs, where their incidence has risen over time. These bacteria are frequently resistant to antibiotics and pose a significant risk of severe outcomes, especially in cases of bloodstream infections and pneumonia. Both pathogens contribute to increased morbidity and mortality, highlighting the urgent need for effective infection control protocols and innovative therapeutic strategies to address these resilient organisms in high-risk healthcare environments.[5,6]

By elucidating the relationship between environmental factors, hospital practices, and TTIs, the purpose of this comprehensive review is to explore the complex relationship between environmental factors, hospital practices, and the incidence of TTIs in ICU settings. Specifically, the review focuses on the role of air quality, water sources, equipment contamination, ventilation strategies, infection control protocols, and microbial reservoirs in influencing TTI rates. Additionally, this review seeks to investigate global variations in TTI prevalence and their relationship with healthcare infrastructure, infection control measures, and antibiotic resistance patterns. By providing a thorough analysis of these factors, we aim to identify key areas for intervention and propose evidence-based strategies to reduce the burden of TTIs, improve patient outcomes, and optimize healthcare resource utilization in critical care settings.

Methods

This review was conducted as a comprehensive analysis of the available literature on TTIs in ICU settings. We performed a systematic literature search across databases, including PubMed, Scopus, and Web of Science, focusing on articles published within the past 5 years. The following keywords were used: "environmental factors," "hospital factors," "TTI," "VAP," "ICU," "infection transmission routes," "infectious agents," "risk factors," and "control and prevention."

Studies included in the review met the following criteria: Published within the last 5 years; focused on TTIs, ICU patients, or related hospital-acquired infections (HAIs); original research articles, clinical trials, or relevant review articles. Exclusion criteria included: Studies focusing on non-ICU patient populations; non-peer-reviewed publications or papers in languages other than English.

Two independent reviewers screened the titles and abstracts of identified studies for relevance. Disagreements between reviewers were resolved through discussion, with a third reviewer available to mediate unresolved cases. Full texts of selected articles were then reviewed for inclusion based on the predefined criteria. The quality of the included studies was assessed using the Newcastle-Ottawa Scale for observational studies and the Cochrane Risk of Bias Tool for randomized trials. These tools helped to evaluate the potential for bias, methodological rigor, and the applicability of the findings to the study objectives. We also implemented a grading system to assess the strength of the evidence supporting each preventive strategy discussed. The Grading of Recommendations, Assessment, Development, and Evaluations framework was used to classify the level of evidence into four categories.[7]

Overview of TTIs

Global perspectives on TTI

Despite advancements in medical care and infection control practices, there is considerable global variability in TTI incidence, particularly between high-income countries (HICs) and low- and middle-income countries (LMICs).[8] Empirical data shows that the incidence of TTIs is generally higher in LMICs due to disparities in healthcare resources, infection control protocols, and access to advanced medical equipment. For instance, a study from a Bangladeshi hospital

reported a TTI incidence of 15%, which was significantly higher than the 5%–8% typically reported in HICs. This higher rate was attributed to overcrowded ICUs, poor ventilation systems, and inconsistent adherence to infection control protocols.[9] Similarly, in Sub-Saharan Africa, research indicated that lack of access to disposable medical equipment and suboptimal sterilization practices contributed to an increased risk of ventilator-associated infections, including TTIs.[10] In contrast, HICs have lower TTI rates due to standardized infection control measures, advanced ventilation systems, and comprehensive surveillance protocols. For example, in the United States, the National Healthcare Safety Network reported a 30% reduction in TTI-related complications over the last decade, thanks to the widespread adoption of care bundles and improved hand hygiene practices.[11]

Moreover, variability in adherence to infection control practices plays a crucial role. Facilities with robust infection control protocols typically experience lower TTI rates, emphasizing the importance of standardized practices such as hand hygiene, sterilization procedures, and environmental cleaning.[12] Antibiotic resistance patterns also contribute to TTI variability. Regions with higher rates of antibiotic resistance may face increased TTI incidence due to limited treatment options and prolonged infections, highlighting the necessity of antibiotic stewardship programs. Patient demographics, including age, comorbidities, and severity of illness, further influence TTI rates. Elderly patients and those with underlying health conditions are more susceptible to infections, contributing to variability in TTI rates among different populations. Furthermore, variability in surveillance systems and reporting practices complicates the assessment of TTI rates. Standardized surveillance protocols and reporting systems can enhance accuracy and facilitate benchmarking between healthcare facilities, thus enabling better-informed decision-making.[9]

In addressing these factors, targeted interventions tailored to specific challenges can effectively reduce TTI rates. Collaborative efforts involving international organizations and sharing best practices in infection control are essential for mitigating TTI variability globally, ensuring optimal patient care and resource allocation. In total, understanding and addressing the factors contributing to variability in TTI rates worldwide are paramount. By implementing comprehensive strategies and collaborative initiatives, healthcare systems can alleviate the burden of TTIs, improve patient outcomes, and optimize resource utilization on a global scale.

Sources of TTIs

Environmental sources of TTI infections. Airborne pathogens in ICU environments: ICU environments can harbor various airborne pathogens, including bacteria, viruses, and fungi. These pathogens can originate from various sources within the ICU setting and can contaminate tracheal tubes directly or indirectly through aerosolized particles in the air. Factors such as poor ventilation, overcrowding, and inadequate air filtration can increase the concentration of airborne pathogens in ICUs. Examples of airborne pathogens in ICU environments are viruses such as influenza and respiratory syncytial virus (RSV) which can spread through respiratory droplets expelled when infected individuals cough, sneeze, or talk, and also bacteria such as *S. aureus* and *P. aeruginosa* which colonized on surfaces, medical equipment, and even within ventilation systems which can transmitted through the air in ICU environments. Improper cleaning and disinfection practices, as well as inadequate ventilation, can contribute to the dissemination of these bacterial pathogens in the air.[13]

Contaminated surfaces and medical equipment: Surfaces and medical equipment in ICUs can serve as reservoirs for pathogenic microorganisms that can contaminate medical equipment, including tracheal tubes. Contamination can occur on various surfaces and equipment within hospitals and medical facilities, leading to the spread of pathogens and subsequent infections among patients. Improper cleaning and disinfection practices can lead to the persistence of pathogens on surfaces and medical devices, including tracheal tubes. Healthcare workers' (HCWs) hands and gloves can also transfer pathogens to tracheal tubes during handling and care procedures. Examples of contaminated surfaces in healthcare settings are hospital room surfaces, such as bed rails, doorknobs, countertops, and medical devices. These surfaces can harbor pathogens such as bacteria, viruses, and fungi, which can survive for extended periods and pose a risk of transmission to patients, HCWs, and visitors.[14]

Water sources in infection transmission: Water sources can serve as reservoirs for various pathogens, including bacteria, fungi, and amoeba, which can lead to infections when they come into contact with patients or are used in medical procedures. Water reservoirs and sources within healthcare facilities, such as water tanks, pipes, faucets, humidifiers, and water systems connected to ventilators, can harbor microbial contaminants. Contaminated water can lead to biofilm formation and the growth of pathogenic bacteria that may colonize tracheal tubes. Improper maintenance of water systems and humidification equipment can contribute to the transmission of infections to patients via tracheal tubes. *P. aeruginosa*, *L. pneumophila*, *A. baumannii*, *M. tuberculosis*,and *Aspergillus species* are examples of pathogens that can be transmitted to patients through water sources in the ICU. This issue highlights the importance of water quality management and infection control measures to prevent the transmission of pathogens from water sources to patients in the ICU.[15]

Hospital factors and infection transmission routes of TTIs. Patient-to-patient transmission: Patient-to-patient transmission through direct or indirect contact is a common route for TTIs within the ICU. Several factors contribute to this mode of transmission, including the proximity of patients in shared

spaces such as wards or ICUs. Respiratory droplets containing pathogens, such as bacteria or viruses, can easily spread between patients, especially in settings where ventilation may be inadequate or compromised. Studies have shown instances of VAP being transmitted from one patient to another via respiratory droplets in ICU environments. The most important pathogens that can transmitted through this ware are Methicillin-resistant *S. aureus* (MRSA), *C. difficile, Influenza* Virus, Norovirus, Vancomycin-resistant *Enterococcus* (VRE), *A. baumannii*: these issues highlight the diverse range of pathogens involved in patient-to-patient transmission within healthcare facilities. Preventive measures such as proper hand hygiene, isolation protocols, and environmental cleaning are crucial in reducing the spread of these pathogens and preventing nosocomial infections.[16]

Healthcare worker transmission: HCWs play a crucial role in patient care but can also serve as potential vectors for TTIs if proper infection control practices are not followed. HCWs may inadvertently carry pathogens on their hands, clothing, or medical equipment from one patient to another. This can occur during direct patient contact, procedures, or when handling contaminated materials. For instance, studies have identified cases where HCWs unknowingly transmit multi-drug resistant organisms (MDROs) to patients due to inadequate hand hygiene practices or improper use of personal protective equipment (PPE).[17] Factors contributing to HCWs as potential vectors of pathogens which cause TTIs are[18,19]:

1. *Asymptomatic carriage*: HCWs can carry and transmit pathogens even when they do not exhibit symptoms of infection. For example, a HCW may carry MRSA on their skin or clothing without showing signs of illness.
2. *Contaminated hands*: Improper hand hygiene practices or inadequate hand washing techniques can lead to the contamination of HCWs' hands with pathogens. This can occur during patient care activities, such as touching patients, handling medical equipment, or coming into contact with contaminated surfaces.
3. *PPE compliance*: Inadequate use or improper donning and doffing of PPE can increase the risk of HCWs becoming contaminated with infectious agents. For instance, failure to wear gloves or masks when indicated can result in pathogen transmission.
4. *Movement between patients*: HCWs frequently move between different patients and care areas within healthcare facilities. This movement increases the potential for cross-contamination if proper infection control practices, such as hand hygiene and equipment cleaning, are not followed diligently.
5. *Environmental contamination*: HCWs may inadvertently contaminate the environment with pathogens through activities such as touching surfaces, handling medical devices, or disposing of infectious waste. Contaminated environmental surfaces can serve as reservoirs for pathogen transmission.
6. *Lack of awareness or training*: Insufficient knowledge or training regarding infection control practices can contribute to HCWs unintentionally becoming vectors for infections. Regular education and training on infection prevention protocols are essential to mitigate this risk.
7. *Contaminated hands and contact surfaces in TTIs*: Contaminated hands and contact surfaces serve as reservoirs for TTIs within hospitals. Patients, visitors, and HCWs can unknowingly transfer pathogens to surfaces such as bed rails, doorknobs, and medical devices. Without proper disinfection protocols, these surfaces can harbor infectious agents and contribute to cross-contamination between individuals. For example, studies have demonstrated the role of contaminated environmental surfaces in transmitting pathogens like Clostridium difficile and methicillin-resistant MRSA among hospitalized patients.[20]

Infection transmission routes

Direct transmission routes. In healthcare settings, particularly in ICUs, direct transmission routes play a significant role in the transmission of infectious agents, including those causing TTIs in ventilated patients.[21] Methods of direct transmission of infection in the ICU are[22]:

- *Droplet transmission*: This mode of transmission occurs when infectious respiratory droplets, generated through coughing, sneezing, or talking, are propelled into the air and subsequently inhaled by individuals within proximity. TTIs can be transmitted via respiratory droplets containing pathogens such as bacteria or viruses.
- *Contact transmission*: Direct contact with infected respiratory secretions, contaminated surfaces, or infected individuals can lead to the transmission of TTIs. This includes physical contact with tracheal tubes, ventilator equipment, or contaminated hands of healthcare personnel.
- *Airborne transmission*: Airborne transmission of infections can occur in ICU settings, particularly with aerosol-generating procedures. Airborne pathogens can contaminate the environment and be inhaled by individuals, contributing to TTIs in ventilated patients.

To minimize the risk of direct transmission of TTIs in ventilated patients, a comprehensive approach to infection control is essential. This includes the implementation of isolation precautions, which involve isolating infected patients to prevent the spread of pathogens to others. Additionally, HCWs must use suitable PPE such as masks,

gloves, gowns, and eye protection to reduce exposure to infectious agents during patient care. Proper hand hygiene practices, including regular handwashing with soap and water or using alcohol-based hand sanitizers, are critical in preventing the transmission of pathogens from contaminated surfaces to patients or HCWs. Moreover, promoting respiratory hygiene practices among patients, such as cough etiquette and wearing masks, can further minimize the dissemination of respiratory droplets containing infectious agents.[23]

Indirect transmission routes. Common vehicles of indirect transmission of infectious agents in ICU include[21,24]:

- *Contaminated surfaces*: Surfaces and objects in healthcare environments can become contaminated with pathogens, serving as reservoirs for transmission when individuals come into contact with these surfaces.
- *Medical equipment*: Improperly cleaned or inadequately sterilized medical equipment, including tracheal tubes and ventilator accessories, can act as vehicles for indirect transmission of infections.
- *Healthcare personnel*: HCWs who come into contact with infected patients or contaminated materials can inadvertently transmit infections to other patients if proper infection control practices are not followed.

Infectious agents associated with TTIs

TTIs are associated with a range of infectious agents, including bacteria, viruses, and fungi, which can lead to serious complications and increased morbidity and mortality rates. In the following, the most important pathogen factors causing TTIs are explained (Table 1).[25]

Bacterial pathogens. The most common bacterial agent associated with TTIs can vary depending on the specific clinical setting, patient population, and prevailing antibiotic resistance patterns. However, some of the most frequently encountered bacterial pathogens in TTIs include:

1. *S. aureus*: Both methicillin-sensitive *S. aureus* (MSSA) and MRSA strains can cause TTIs. MRSA, in particular, poses a significant challenge due to its resistance to multiple antibiotics, making treatment more complicated.[29]
2. *P. aeruginosa*: This bacterium is a leading cause of TTIs, especially in critically ill patients in ICUs. *P. aeruginosa* is known for its ability to form biofilms on medical devices like tracheal tubes, making it difficult to eradicate and treat.[25,30]
3. *E. coli*: A Gram-negative bacterium commonly found in the gastrointestinal tract, can also cause TTIs. In certain cases, *E. coli* may ascend from the lower respiratory tract or enter the tracheal tube through contamination during intubation or suctioning procedures.[25,30]
4. *A. baumannii*: Is another Gram-negative bacterium commonly associated with TTIs, especially in healthcare settings with high antibiotic resistance rates. It can survive on environmental surfaces and medical devices, contributing to nosocomial infections.[25,30]
5. *K. pneumoniae*: This bacterium is known for causing respiratory infections, including TTIs such as VAP. Its ability to develop resistance to antibiotics, including carbapenems, can complicate treatment.[25,30]
6. *Enterococcus species*: Various species of *Enterococcus*, including *E. faecalis* and *E*. faecium, are recognized as causative agents in TTIs. These bacteria are often found in healthcare environments and can contribute to device-related infections.[25,30]
7. *S. pneumoniae*: This is a Gram-positive bacterium, which can also be involved in TTIs, particularly in patients with underlying chronic respiratory conditions.[25,30]
8. *M. catarrhalis*: This is a Gram-negative bacterium, which is recognized as a potential pathogen in TTIs, particularly in patients with chronic respiratory diseases.[25,30]
9. *H. influenzae*: This bacterium can also contribute to TTIs, especially in patients with underlying chronic respiratory conditions.[25,30]
10. Enterobacter species: Enterobacter species, including E. cloacae and E. aerogenes, are mentioned as additional bacterial agents that can be associated with TTIs.[25,30]
11. *Non-tuberculous mycobacteria (NTM) infections*: NTM, such as *Mycobacterium avium* complex (MAC) and *M. abscessus*, can cause respiratory tract infections, including tracheal tube-associated infections, in immunocompromised individuals and those with pre-existing lung conditions. NTM infections are often challenging to treat due to intrinsic resistance to many antibiotics.[15,31]
12. *Anaerobic infections*: *Anaerobic* bacteria, including species like *Bacteroides* and *Prevotella*, can cause infections in the respiratory tract, including tracheal tube-associated infections in ventilated patients. Anaerobic infections are often associated with aspiration events, chronic lung diseases, and compromised airway defenses.

The impact of antibiotic-resistant bacteria on TTI infections. The emergence of antibiotic-resistant bacteria has become a critical concern in healthcare, particularly in the context of TTIs. Antibiotic resistance strains such as ESBL produced, MRSA, and MDR strains among bacterial pathogens such as *P.*

Table 1. Most common bacterial infection associated with TTIs and their features.

Bacterial agent	Source of infection	Mode of transmission	Antibiotic resistance	Type of infection	Ref
S. aureus	Endogenous (from patient's own flora)	Direct contact, droplets	Methicillin-resistant strains (MRSA)	Ventilator-associated pneumonia, tracheobronchitis	19
P. aeruginosa	Exogenous (environmental sources)	Direct contact, contaminated equipment	Multidrug-resistant, including carbapenem-resistant strains	Ventilator-associated pneumonia, tracheobronchitis	21
E. coli	Endogenous (from patient's own flora)	Ascending from lower respiratory tract, contamination during intubation/suctioning	Variable resistance patterns (including extended-spectrum β-lactamase (ESBL) production)	Ventilator-associated pneumonia, tracheobronchitis	22
K. pneumoniae	Endogenous (from patient's own flora)	Direct contact, contaminated equipment	Multidrug-resistant, including carbapenem-resistant strains	Ventilator-associated pneumonia, tracheobronchitis	19
Enterococcus species	Endogenous (from patient's own flora), exogenous (healthcare environment)	Contaminated equipment, healthcare-associated transmission	Vancomycin-resistant strains (VRE), multidrug-resistant	Device-related infections, pneumonia	26
S. pneumoniae	Endogenous (from patient's own flora)	Respiratory droplets	Variable resistance patterns	Ventilator-associated pneumonia, tracheobronchitis	22
Acinetobacter species	Exogenous (healthcare environment)	Direct contact, contaminated equipment	Multidrug-resistant, including carbapenem-resistant strains	Ventilator-associated pneumonia, tracheobronchitis	21
M. catarrhalis	Endogenous (from patient's own flora)	Respiratory droplets	Variable resistance patterns	Ventilator-associated pneumonia, tracheobronchitis	27
H. influenzae	Endogenous (from patient's own flora)	Respiratory droplets	Variable resistance patterns	Ventilator-associated pneumonia, tracheobronchitis	28
Enterobacter species	Endogenous (from patient's own flora)	Direct contact, contaminated equipment	Multidrug-resistant, including extended-spectrum β-lactamase (ESBL) producing strains	Ventilator-associated pneumonia, tracheobronchitis	22

aeruginosa, *A. baumannii*, *K. pneumoniae*, and *S. aureus* have significantly complicated the management of TTIs. These bacteria have developed various mechanisms of resistance, including the production of beta-lactamases, efflux pumps, and alterations in cell wall permeability, rendering many commonly used antibiotics ineffective. The presence of antibiotic-resistant bacteria in TTIs not only prolongs the duration of treatment but also increases the risk of treatment failure, disease progression, and adverse patient outcomes. Moreover, the limited availability of effective antibiotics against these resistant strains highlights the urgent need for judicious antibiotic use, antimicrobial stewardship programs, and the development of novel antimicrobial agents to combat these infections effectively.[11]

The role of biofilm formation in TTIs. A biofilm is a complex and structured community of microorganisms, including bacteria, fungi, and algae, which adhere to surfaces and are embedded in a self-produced extracellular matrix composed of polysaccharides, proteins, and DNA. Biofilms can form on various biotic and abiotic surfaces, such as medical devices, tissues, rocks, and water pipes. The formation of biofilms is a dynamic process involving initial attachment, microcolony formation, maturation, and detachment or dispersal of cells. Moreover, biofilms play a critical role in the development and persistence of infections, particularly those resistant to antibiotics. The protective nature of biofilms provides several advantages to microorganisms: resistance to antibiotics, protection against disinfectants and drugs, enhanced horizontal resistant gene transfer, and persistence in hospital environments.[25]

Biofilm formation on medical devices, including tracheal tubes, plays a significant role in the development and persistence of infections. Biofilms are complex microbial communities encased in a self-produced extracellular matrix, providing protection and resilience against antimicrobial agents and host immune responses.[32] Bacterial species such as *P. aeruginosa*, *A. baumannii*, and *S. aureus* are well-known for their ability to form robust biofilms on medical surfaces. The presence of biofilms on tracheal tubes promotes bacterial

adhesion, colonization, and subsequent infection of the respiratory tract in ventilated patients. Biofilm-associated infections are often challenging to treat due to the reduced susceptibility of biofilm-embedded bacteria to antibiotics and disinfectants. Additionally, biofilms can serve as reservoirs for recurrent infections and contribute to the spread of antibiotic-resistant strains within healthcare settings.[33]

Fungal infections

The most common fungal infections associated with TTIs include (Table 2):

1. *Candida* spp: *Candida* species, particularly *C. albicans*, are commonly implicated in fungal TTIs. These fungi are opportunistic pathogens that can colonize and infect the respiratory tract, especially in immunocompromised patients or those receiving prolonged mechanical ventilation. *Candida* infections can lead to tracheobronchitis, pneumonia, and systemic *candidiasis*, posing challenges in clinical management due to antifungal resistance and biofilm formation.[34,35]
2. *Aspergillus spp*: *Aspergillus* species, such as *A. fumigatus*, can cause invasive fungal infections in ventilated patients, particularly those with underlying lung diseases or immunosuppression. *Aspergillus* infections may manifest as tracheobronchitis, invasive pulmonary aspergillosis, or tracheal tube-associated *aspergillosis*, leading to significant morbidity and mortality, especially in critically ill individuals.[34,35]
3. *Cryptococcus neoformans*: This is an opportunistic fungal pathogen known to cause cryptococcal infections, including cryptococcal pneumonia and meningitis. In ventilated patients, *Cryptococcus* infections can occur as a result of inhalation of fungal spores, leading to tracheal tube-associated infections and dissemination to other organs, particularly in individuals with compromised immune functions.[34,35]
4. *Mucorales*: Members of the Mucorales order, such as *Rhizopus, Mucor*, and *Rhizomucor* species, can cause invasive fungal infections known as mucormycosis. These fungi are often encountered in immunocompromised patients, including those with diabetes mellitus, hematologic malignancies, or solid organ transplants. Mucormycosis can involve the respiratory tract, leading to tracheal tube-associated infections, sinusitis, and invasive pulmonary disease.[34,35]
5. *Candida auris*: This is an emerging multidrug-resistant fungal pathogen associated with healthcare-associated infections, including TTIs. *C. auris* infections are challenging to treat due to their resistance to multiple antifungal agents, leading to high mortality rates, particularly in critically ill patients.[34,35]

Viral infections

The most common viral infections associated with TTIs include (Table 2):

1. *Respiratory syncytial virus*: RSV is a common cause of viral respiratory infections, particularly in infants, young children, and immunocompromised individuals. In ventilated patients, RSV infections can lead to tracheal tube-associated bronchiolitis and pneumonia, causing respiratory distress and exacerbating underlying lung conditions.[36,37]
2. *Influenza virus*: including influenza A and B strains, can cause severe respiratory tract infections, especially in high-risk populations such as the elderly, immunocompromised individuals, and patients with chronic medical conditions. In ventilated patients, influenza infections can lead to tracheal tube-associated pneumonia and exacerbate respiratory failure.[36,37]
3. *Adenovirus*: Adenoviruses are common respiratory pathogens associated with upper and lower respiratory tract infections. In ventilated patients, adenovirus infections can manifest as tracheobronchitis, pneumonia, and tracheal tube-associated infections, particularly in immunocompromised individuals and military recruits.[36,37]
4. *Herpes simplex virus (HSV)*: Herpes simplex viruses, including HSV-1 and HSV-2, can cause respiratory infections, especially in immunocompromised individuals and neonates. In ventilated patients, HSV infections can lead to tracheal tube-associated esophagitis, tracheitis, and pneumonia, particularly in those with underlying conditions such as HIV/AIDS or organ transplantation.[36,37]
5. *Varicella-zoster virus (VZV)*: VZV, which causes chickenpox and herpes zoster (shingles), can lead to respiratory tract infections and pneumonia, especially in susceptible populations. In ventilated patients, VZV infections can contribute to tracheal tube-associated pneumonia and respiratory complications, particularly in individuals with impaired immune function.[36,37]
6. *Cytomegalovirus (CMV)*: CMV is an opportunistic viral pathogen that can cause severe respiratory infections, especially in immunocompromised patients, transplant recipients, and those with HIV/AIDS. CMV infections in ventilated patients can lead to tracheal tube-associated pneumonia and exacerbate respiratory failure, particularly in critically ill individuals.[36,37]

Table 2. Most common fungal and viral infection associated with TTIs and their features.

Pathogen	Source of infection	Mode of transmission	Antibiotic resistance (for fungi)	Type of Infection	Ref
Candida species	Endogenous (from patient's own flora)	Contaminated equipment, healthcare-associated transmission	Variable antifungal resistance patterns	Ventilator-associated pneumonia, tracheobronchitis	34–37
Aspergillus species	Exogenous (environmental sources)	Inhalation of spores	Variable antifungal resistance patterns	Invasive pulmonary aspergillosis	26
Pneumocystis jirovecii	Exogenous (environmental sources)	Inhalation of cysts	Susceptible to specific antimicrobial agents (e.g., trimethoprim-sulfamethoxazole)	Pneumocystis pneumonia	27
Influenza virus	Exogenous (respiratory droplets)	Respiratory droplets, direct contact	Antiviral resistance can emerge (e.g., oseltamivir-resistant strains)	Influenza-associated pneumonia, tracheobronchitis	11
Respiratory syncytial virus (RSV)	Exogenous (respiratory droplets)	Respiratory droplets, direct contact	No specific antiviral resistance reported	RSV-associated pneumonia, tracheobronchitis	38
Human metapneumovirus (hMPV)	Exogenous (respiratory droplets)	Respiratory droplets, direct contact	No specific antiviral resistance reported	hMPV-associated pneumonia, tracheobronchitis	38
Parainfluenza virus	Exogenous (respiratory droplets)	Respiratory droplets, direct contact	No specific antiviral resistance reported	Parainfluenza-associated pneumonia, tracheobronchitis	39
Adenovirus	Exogenous (respiratory droplets)	Respiratory droplets, direct contact	No specific antiviral resistance reported	Adenovirus-associated pneumonia, tracheobronchitis	39
Coronavirus (including SARS-CoV-2)	Exogenous (respiratory droplets)	Respiratory droplets, direct contact	Antiviral resistance can emerge (e.g., remdesivir-resistant strains)	COVID-19-associated pneumonia, tracheobronchitis	15
Rhinovirus	Exogenous (respiratory droplets)	Respiratory droplets, direct contact	No specific antiviral resistance reported	Rhinovirus-associated pneumonia, tracheobronchitis	15

Diseases associated with TTIs

Ventilator-associated pneumonia: TTIs are predominantly linked to VAP, which is one of the most frequent and severe complications in mechanically ventilated patients in the ICU. VAP occurs when pathogens bypass the tracheal tube cuff and enter the lower respiratory tract, leading to lung infection. The presence of the tracheal tube disrupts normal respiratory defense mechanisms, such as mucociliary clearance and cough reflex, providing a direct route for bacterial colonization and infection. VAP significantly increases patient morbidity and mortality rates, prolongs ICU stays, and escalates healthcare costs. Effective prevention and early identification of VAP are critical in improving patient outcomes and reducing the burden on healthcare systems.[40]

Bacteremia and sepsis: Bacteremia is another serious condition associated with TTIs. The infection can spread from the trachea to the bloodstream, leading to systemic inflammatory response syndrome and sepsis. Sepsis is a life-threatening condition characterized by widespread inflammation, tissue damage, and organ dysfunction. Patients with sepsis require immediate and aggressive treatment to manage the infection and prevent septic shock, which can be fatal. The management of bacteremia and sepsis in patients with TTIs involves prompt antibiotic therapy, supportive care, and in severe cases, intensive monitoring and intervention.[41]

Exacerbation of chronic respiratory conditions: Patients with underlying chronic respiratory conditions, such as chronic obstructive pulmonary disease (COPD) and asthma, are particularly vulnerable to complications arising from TTIs. The presence of a tracheal tube and subsequent infection can trigger acute exacerbations of these chronic conditions. Exacerbations are characterized by a sudden worsening of respiratory symptoms, such as increased breathlessness, cough, and sputum production, which can be life-threatening and require urgent medical attention. Managing TTIs in patients with chronic respiratory diseases involves not only treating the infection but also optimizing the management of the underlying condition to prevent further exacerbations.[19]

Colonization by MDROs: Prolonged use of tracheal tubes can lead to the colonization of the airway by MDROs, complicating the treatment of infections. MDROs, such as methicillin-resistant MRSA and multi-drug-resistant *P. aeruginosa*, are resistant to multiple classes of antibiotics, making infections difficult to treat and increasing the risk

of treatment failure. The colonization by MDROs necessitates the use of more potent and often more toxic antibiotics, increasing the potential for adverse effects and limiting therapeutic options. Preventing the colonization and subsequent infection by MDROs requires strict adherence to infection control practices, judicious use of antibiotics, and regular surveillance of microbial resistance patterns in the ICU.[11,12]

Urinary tract infections (UTIs): While less direct, TTIs can also predispose ventilator patients to UTIs. The systemic inflammation and immunosuppression associated with severe respiratory infections can weaken the body's defense mechanisms, making it easier for pathogens to colonize the urinary tract. Catheter-associated UTIs are particularly common in this patient population. *Escherichia coli*, *Klebsiella* species, and *Enterococcus faecalis* are frequent culprits.[42]

Gastrointestinal infections (GI): GI infections in ventilator patients can arise from several factors, including antibiotic therapy, which disrupts normal gut flora, and the use of enteral feeding tubes. *C. difficile*-associated diarrhea is a notable example, often resulting from broad-spectrum antibiotic use. The translocation of pathogens from the gut to other body sites is another potential risk, exacerbating the overall infection burden.[21,43] In addition to antibiotic exposure, prolonged hospitalization is another critical risk factor, as extended stays in healthcare settings increase patient exposure to this pathogen through surfaces, equipment, and healthcare personnel. For example, patients in ICUs who require long-term antibiotic therapy are particularly vulnerable to *C. difficile* infections. Studies have shown that patients hospitalized for more than a week, especially in high-risk areas like the ICU, face significantly higher rates of *C. difficile* infection compared to those with shorter stays. Together, these factors contribute to the high incidence of *C. difficile* infections in healthcare settings, highlighting the need for targeted infection control measures, routine disinfection protocols, and judicious use of antibiotics to reduce infection risks and protect vulnerable patients.[44]

Soft tissue infections: Soft tissue infections, such as surgical site infections or decubitus ulcers, can occur in patients with TTIs. These infections often arise due to prolonged immobility, poor nutritional status, and the presence of invasive devices. The bacteria responsible for TTIs can spread to these areas, complicating the clinical picture. Managing soft tissue infections requires a multidisciplinary approach, including wound care, antibiotic therapy, and, in some cases, surgical intervention.[45]

CNS infections: Though rare, TTIs can lead to CNS infections, particularly in patients with compromised immune systems. Meningitis and brain abscesses can develop if pathogens spread from the bloodstream to the central nervous system. Common organisms include *Streptococcus pneumoniae* and *Neisseria meningitidis*. Early recognition and treatment are crucial to prevent long-term CNS sequelae.[46]

Risk factors associated with TTIs

Patient-related factors

Age and comorbidities: Elderly patients and those with underlying chronic diseases such as diabetes, COPD, and cardiovascular diseases are at higher risk of developing TTIs. Their weakened immune systems make it more difficult to fight off infections.

Immunosuppression: Patients who are immunocompromised, whether due to medical conditions (HIV/AIDS, cancer) or treatments (chemotherapy, corticosteroids), are more susceptible to infections, including TTIs.

Nutritional status: Malnutrition can impair immune function, making patients more vulnerable to infections. Adequate nutritional support is essential in critically ill patients to enhance their ability to combat infections.

Length of mechanical ventilation: Prolonged use of mechanical ventilation increases the risk of TTIs. The longer the duration of intubation, the higher the likelihood of bacterial colonization and infection.

Prior antibiotic use: Previous or ongoing antibiotic treatment can disrupt normal flora and promote the growth of resistant bacteria, which can contribute to TTIs.

Underlying respiratory conditions: Conditions such as COPD, asthma, and previous respiratory infections can predispose patients to TTIs due to the already compromised state of their respiratory systems.[47,48]

Hospital-related factors

Ventilator care practices: Inadequate hand hygiene, improper cleaning and disinfection of ventilator equipment, and suboptimal care of the ventilated patient can increase the risk of TTIs. Adherence to strict infection control protocols is essential.

Intubation and reintubation: Traumatic intubation, multiple attempts at intubation, and the need for reintubation can increase the risk of TTIs. These procedures can cause damage to the tracheal mucosa and provide an entry point for pathogens.

Hospital environment: The presence of MDROs in the ICU environment poses a significant risk. Contaminated surfaces, medical devices, and HCWs can serve as reservoirs and vectors for transmission.

Staffing levels and training: Inadequate staffing and insufficient training of healthcare personnel in infection control practices can contribute to higher rates of TTIs. Continuous education and training are necessary to maintain high standards of care.

Use of sedation and paralytics: The use of sedatives and paralytics can impair the patient's ability to clear secretions effectively, leading to an increased risk of TTIs. Careful management and regular assessment of sedation levels are important.

Antibiotic stewardship: Poor antibiotic stewardship practices, such as overuse or misuse of antibiotics, can lead to the development of resistant organisms, complicating the management of TTIs. Implementing robust antibiotic stewardship programs is critical.[49,50]

The role of microbiome in TTIs

The human microbiome plays a critical role in health and disease, including in the context of TTIs in patients with mechanical ventilation. Understanding the interactions between microbial communities and their host is essential for devising strategies to prevent and manage these infections. Key areas of focus include microbial diversity in the respiratory tract, the gut-lung axis, and the impact of dysbiosis on infection susceptibility.[51]

Microbial diversity in the respiratory tract: The respiratory tract is home to a diverse array of microorganisms, including bacteria, viruses, and fungi, which coexist in a balanced state. This microbial community plays a protective role by competing with potential pathogens, modulating the host immune response, and maintaining mucosal integrity. Mechanical ventilation can disrupt the normal respiratory microbiome, leading to a shift in microbial composition. This alteration often results in decreased microbial diversity and the overgrowth of pathogenic organisms, such as *S. aureus*, *P. aeruginosa*, and *Acinetobacter* species. These changes can increase the risk of TTIs. The endotracheal tube can serve as a conduit for the introduction and colonization of pathogens. Biofilm formation on the surface of the tube further complicates the issue, providing a reservoir for persistent infection and resistance to antimicrobial treatment.[52]

Gut-lung axis and its influence: The gut and lungs are interconnected through the gut-lung axis, where microbial communities in the gut can influence respiratory health and vice versa. This bidirectional relationship is mediated by immune system interactions, microbial metabolites, and inflammatory responses. Alterations in the gut microbiota, such as those caused by antibiotic use, diet, or illness, can impact lung immunity and susceptibility to infections. A healthy gut microbiome supports a robust immune response, whereas dysbiosis can lead to increased inflammation and impaired immune function in the lungs. Microbial metabolites, such as short-chain fatty acids produced by gut bacteria, have systemic effects and can modulate immune responses in the respiratory tract. These metabolites play a role in maintaining epithelial barrier function and regulating inflammation.[53]

Dysbiosis and infection susceptibility: Dysbiosis refers to the imbalance in microbial communities, where beneficial microbes are reduced, and pathogenic microbes are increased. This imbalance can compromise the host's defense mechanisms, making it more susceptible to infections. Critically ill patients, particularly those on mechanical ventilation, are prone to dysbiosis due to factors like antibiotic use, reduced mobility, and changes in diet. Dysbiosis in these patients is associated with an increased risk of TTIs and other healthcare-associated infections. Probiotic supplementation, prebiotic intake, and careful antibiotic stewardship are potential strategies to maintain or restore a healthy microbiome in critically ill patients. These approaches aim to enhance microbial diversity, support immune function, and reduce the incidence of TTIs.[51]

Relationship between environmental sources and infection

The hospital environment significantly influences the risk of TTIs in patients on mechanical ventilation. Environmental sources, such as air and water, surfaces and hospital equipment, and hospital staff, can serve as reservoirs and vectors for pathogenic microorganisms, thereby contributing to the incidence and severity of infections.[30]

Air quality: Hospital air quality plays a crucial role in preventing TTIs. Airborne pathogens can be transmitted through ventilation systems, especially in ICUs where patients are at higher risk. The presence of airborne bacteria, fungi, and viruses can increase the likelihood of respiratory tract colonization and subsequent infection. High-efficiency particulate air (HEPA) filters and regular maintenance of ventilation systems are essential measures to mitigate this risk.[54]

Water systems: Water systems within hospitals, including sinks, showers, and humidifiers, can harbor pathogens such as *P. aeruginosa* and *L. pneumophila*. These microorganisms can contaminate respiratory therapy equipment, leading to TTIs. Regular monitoring and disinfection of hospital water systems are critical to prevent waterborne infections.[55]

Surfaces and hospital equipment: Hospital surfaces, including bed rails, doorknobs, and medical instruments, can act as fomites for the transmission of infectious agents. Pathogens such as MRSA and *C. difficile* can survive on surfaces for extended periods. Strict adherence to cleaning protocols and the use of effective disinfectants are necessary to minimize surface contamination.[56] Medical equipment, particularly respiratory therapy devices like ventilators and nebulizers, can be sources of infection if not properly sterilized. The formation of biofilms on equipment surfaces can shield pathogens from disinfection efforts, leading to persistent contamination. Implementing rigorous sterilization procedures and regular maintenance of medical devices are vital for infection control.[57]

Hospital staff: Hospital staff, including doctors, nurses, and support personnel, can inadvertently transmit pathogens to patients. Poor hand hygiene practices are a significant contributor to HAIs. Comprehensive hand hygiene programs, including the use of alcohol-based hand sanitizers and regular handwashing, are fundamental to reducing this risk. Training hospital staff in infection control practices is essential for preventing TTIs. This includes the proper use of PPE, adherence to isolation protocols, and awareness of the

importance of aseptic techniques during medical procedures. Continuous education and monitoring of staff compliance with infection control measures are crucial components of a successful infection prevention strategy.[58]

Control and prevention of TTIs

Regular cleaning and disinfection: Routine cleaning and disinfection of all surfaces in the ICU, including bed rails, doorknobs, and medical equipment, are critical. The use of hospital-grade disinfectants that are effective against a broad spectrum of pathogens is recommended.

Air quality management: Ensuring good air quality through proper ventilation and the use of HEPA filters helps reduce the presence of airborne pathogens. Regular maintenance and monitoring of HVAC systems are necessary to ensure they function optimally.

Water system management: Regular testing and disinfection of hospital water systems help prevent the growth and spread of waterborne pathogens. Implementing protocols to manage and monitor water quality in sinks, showers, and humidifiers is essential.

Implementation of infection control protocols includes hand hygiene: Hand hygiene is the single most important measure to prevent the spread of infections. All healthcare personnel must adhere to strict hand hygiene practices, including using alcohol-based hand sanitizers or washing hands with soap and water before and after patient contact.

Use of disposable equipment: Wherever possible, disposable equipment should be used to minimize the risk of cross-contamination. Items such as suction catheters, respiratory tubing, and other single-use devices can significantly reduce infection risk.

Surface disinfection: Regular disinfection of high-touch surfaces in patient care areas is crucial. This includes the use of effective disinfectants on surfaces such as bed rails, medical instruments, and bedside tables. Ensuring that cleaning protocols are rigorously followed is essential.[59,60]

Advances in medical equipment sterilization: Automated systems that use hydrogen peroxide vapor or ultraviolet (UV) light to sterilize medical equipment and patient rooms offer an efficient and effective method for eliminating pathogens. These systems can reach all surfaces and are particularly useful for disinfecting complex medical devices. The development of materials resistant to biofilm formation helps prevent persistent contamination of medical equipment. Incorporating such materials into the design of tracheal tubes and other respiratory devices can reduce the risk of TTIs. Technologies that continuously monitor the sterilization process ensure that equipment is properly disinfected. These systems provide real-time feedback and can alert staff to any deviations from standard sterilization protocols, ensuring high levels of hygiene.[61]

Nanotechnology applications: Nanotechnology holds significant promise for preventing TTIs by offering novel approaches to combat microbial colonization and enhance device biocompatibility. Nanomaterials, such as silver nanoparticles and antimicrobial coatings, can be applied to tracheal tubes to inhibit biofilm formation and reduce bacterial adherence. Furthermore, nanotechnology-enabled drug delivery systems facilitate localized and sustained release of antimicrobial agents directly at the infection site, improving therapeutic outcomes and minimizing systemic side effects.[62]

Surveillance systems for early detection: Advanced surveillance systems are essential for the early detection of TTIs in ICUs, where prompt intervention is critical to prevent complications. These systems integrate continuous monitoring of patient parameters, such as vital signs and biomarkers, with automated alerts for abnormal trends indicative of infection. Real-time data analytics and predictive algorithms enhance surveillance capabilities, enabling healthcare providers to initiate timely diagnostic testing and targeted antimicrobial therapy, thereby reducing the risk of infection progression and associated morbidity.[4,63]

Innovative ventilation strategies: Innovative ventilation strategies play a pivotal role in minimizing the risk of TTIs by optimizing air quality and reducing airborne pathogen transmission in ICU settings. Technologies such as HEPA filtration systems and ultraviolet germicidal irradiation (UVGI) devices effectively remove or inactivate airborne pathogens, including those associated with respiratory infections. Additionally, advanced ventilation designs incorporate airflow management techniques to control microbial dispersion and maintain clean air environments around ventilated patients, thereby enhancing infection prevention measures.[64]

Molecular diagnostics: Advancements in molecular diagnostics and biomarkers offer precise and rapid identification of microbial pathogens associated with TTIs. PCR assays, next-generation sequencing, and biomarker panels allow for early detection of specific pathogens and their antimicrobial resistance profiles. Integration of these technologies into clinical practice enables targeted antimicrobial therapy, personalized treatment strategies, and improved infection control measures tailored to individual patient needs.[65]

Limitations and challenges of TTI in ICUs

Antibiotic resistance: Antibiotic resistance presents a significant challenge in the context of TTIs in ventilated patients within ICUs. The overuse and misuse of antibiotics contribute to the emergence of multidrug-resistant pathogens, complicating treatment strategies and potentially leading to treatment failures. Moreover, the diversity of bacterial strains and their varying resistance profiles necessitate tailored antibiotic regimens, which may not always be effective due to resistance mechanisms such as biofilm formation on tracheal tubes.[66]

Variability in ICU settings: ICUs exhibit considerable variability in their infrastructure, patient demographics,

and clinical practices, which can influence the risk and management of TTIs. Variability in ventilation protocols, environmental conditions, and staff practices may impact infection rates and outcomes. Standardizing protocols across diverse ICU settings is challenging, potentially affecting the consistency and efficacy of infection prevention and control measures.[63]

Compliance with infection control measures: Effective infection control measures, including hand hygiene, proper disinfection practices, and sterilization of equipment, are pivotal in reducing TTIs. However, ensuring consistent compliance with these measures among healthcare personnel remains a persistent challenge. Factors such as workload, staff turnover, and adherence to protocols can affect the implementation and sustainability of infection control practices, potentially compromising patient safety and exacerbating infection risks.[67]

Diagnostic challenges: Accurately diagnosing TTIs poses diagnostic challenges in ICU settings. Clinical manifestations of infection may overlap with other respiratory complications common in ventilated patients, leading to delays in diagnosis and initiation of appropriate treatment. The reliance on traditional culture-based methods for microbial identification may be insufficient in detecting fastidious or biofilm-forming pathogens, necessitating the integration of molecular diagnostics and biomarkers to improve diagnostic accuracy and timely intervention.[11]

Resource limitations: Resource constraints, including financial limitations and availability of trained personnel, pose significant barriers to effective infection prevention and control in ICU settings. Adequate staffing levels, access to advanced diagnostic technologies, and availability of infection control resources are crucial for implementing comprehensive strategies to mitigate TTIs. Addressing resource disparities among healthcare facilities is essential to enhancing patient outcomes and reducing healthcare-associated infections.[4,63]

Limitations of the study. This review is subject to several limitations. First, it relies primarily on published literature, which may not fully represent unpublished or recent studies in this rapidly evolving field. Additionally, variations in study designs, patient populations, and definitions of TTIs across studies may limit the generalizability of the findings. Finally, the scope of this review is limited to current diagnostic, prevention, and management strategies, which may overlook emerging technologies and novel treatment approaches that are still in early research phases.

Future directions and research opportunities

Future research in infection prevention for TTIs should explore several promising areas. Understanding host-microbiome interactions is crucial, as it can reveal how immune responses and microbiome composition influence infection susceptibility. Developing effective biofilm disruption strategies, such as nanotechnology-based antimicrobial coatings, is essential to prevent biofilm formation on tracheal tubes. Personalized infection prevention approaches tailored to individual patient factors, including genetic predisposition and immune status, could enhance treatment efficacy.

Environmental factors, like ICU design and ventilation systems, play a significant role in infection rates and should be studied further. Breakthroughs in immunomodulatory therapies and targeted antimicrobial delivery systems offer the potential to enhance host defenses and improve treatment outcomes. Precision medicine approaches integrating genomics and proteomics could optimize infection prevention strategies.

Research gaps include understanding the long-term effects of biocompatible materials used in tracheal tubes and assessing the economic impact of novel ventilation strategies. Additionally, studying patient-centered outcomes and quality-of-life assessments is crucial to improving holistic patient care approaches in ICU settings. These efforts will advance infection prevention in TTIs, fostering interdisciplinary collaboration and innovative technologies to optimize clinical outcomes.

Conclusion

This review highlights the critical factors contributing to the incidence of TTIs in mechanically ventilated ICU patients, focusing on environmental conditions, hospital practices, and global disparities in healthcare infrastructure. Key elements such as air quality, water contamination, equipment handling, and infection control protocols play a pivotal role in the prevention and management of TTIs. Additionally, the global variability in TTI rates is influenced by healthcare resources and adherence to infection control measures, especially in LMICs. To reduce the burden of TTIs, targeted interventions must be developed based on the unique needs of healthcare settings. Preventive strategies, including the implementation of care bundles, the improvement of ventilation systems, and the promotion of antimicrobial stewardship, have shown varying levels of effectiveness based on the strength of available evidence. Future research should focus on closing gaps in the literature, particularly in the areas of environmental controls and long-term outcomes of infection prevention strategies. Collaborative efforts between healthcare providers and policymakers are essential to reduce TTI rates and improve patient care in ICU settings worldwide.

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Data availability

The data that support the findings in this study are available from the corresponding author upon reasonable request.

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