

## Hidden aftermath of COVID-19: a structured review of antimicrobial resistance and intensive care unit-associated pathogens

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## Abstract

The coronavirus disease 2019 (COVID-19) pandemic has substantially affected global healthcare systems and accelerated the emergence and dissemination of antimicrobial resistance (AMR). Although COVID-19 is fundamentally a viral illness, widespread empirical antibiotic use, particularly among hospitalized and critically ill patients, created significant selective pressure favoring MDR pathogens. This structured narrative review evaluated the relationship between COVID-19 and AMR through a PRISMA-informed literature search of the PubMed, Scopus, and Web of Science databases covering January 2020 to February 2026. Available evidence demonstrates a marked discrepancy between relatively low confirmed bacterial co-infection rates (approximately 5-10%) and substantially higher empirical antibiotic prescribing rates, which frequently exceeded 60% in hospitalized patients. Intensive care unit (ICU) overcrowding, prolonged hospitalization, invasive procedures, and disruption of antimicrobial stewardship and infection prevention practices further facilitated the emergence and transmission of MDR organisms. Gram-negative bacteria, including *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, were prominently associated with secondary infections in critically ill patients. In addition, fungal superinfections such as COVID-19-associated pulmonary aspergillosis and *Candida auris* infections contributed to adverse clinical outcomes and increased mortality. Strengthening antimicrobial stewardship, infection prevention, surveillance systems, and rapid diagnostic approaches remains essential to mitigate the long-term impact of AMR in the post-pandemic era.

**Keywords:** multidrug-resistant pathogens, antimicrobial resistance, secondary infections, intensive care units, COVID-19

## Introduction

The coronavirus disease 2019 (COVID-19) pandemic placed unprecedented pressure on global healthcare systems and substantially altered infectious disease management worldwide [1]. Beyond its immediate clinical impact, increasing attention has focused on the pandemic's indirect consequences, particularly the acceleration of antimicrobial resistance (AMR) [2].

Even before the pandemic, AMR represented a major global public health threat associated with increased morbidity, mortality, prolonged hospitalization, and escalating healthcare costs. Global estimates indicated that bacterial AMR was associated with approximately 4.95 million deaths in 2019 alone [3]. However, the COVID-19 era created a

unique combination of clinical and organizational conditions that may have further accelerated the emergence and dissemination of multidrug-resistant (MDR) pathogens [4].

One of the principal drivers linking COVID-19 to AMR has been the widespread empirical use of broad-spectrum antibiotics. Although COVID-19 is fundamentally a viral disease, uncertainty regarding bacterial co-infection resulted in extensive antimicrobial prescribing during the early pandemic period. Meta-analyses demonstrated that confirmed bacterial co-infection rates generally remained below 10%, whereas antibiotic prescribing frequently exceeded 60% among hospitalized patients and was even higher in intensive care unit (ICU) settings [5,6]. This discrepancy generated substantial selective pressure favoring resistant organisms.

Simultaneously, the dramatic increase in ICU admissions created highly permissive environments for healthcare-associated infections and MDR pathogen transmission. Critically ill COVID-19 patients frequently required prolonged hospitalization, mechanical ventilation, and invasive supportive interventions, all of which are established risk factors for secondary infections [7]. These conditions contributed to an increased prevalence of opportunistic pathogens, particularly Gram-negative bacteria such as *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* [8].

Disruptions in antimicrobial stewardship programs (ASPs) and infection prevention and control (IPC) practices during periods of healthcare system overload further exacerbated resistance dynamics [9]. In addition, COVID-19-associated immune dysregulation and widespread corticosteroid exposure increased susceptibility to secondary bacterial and fungal infections, including outbreaks involving *Candida auris* in critically ill ICU populations [10].

Collectively, these interconnected factors suggest that COVID-19 substantially reshaped AMR patterns within healthcare systems worldwide. Accordingly, this review provides a structured evaluation of the relationship between COVID-19 and AMR, with particular emphasis on antibiotic prescribing practices, ICU-associated MDR pathogens, secondary bacterial and fungal infections, and post-pandemic resistance trends.

### **Aim of the work**

This review aimed to critically examine the relationship between COVID-19 and AMR by analyzing antibiotic utilization patterns, secondary infections, ICU-associated multidrug-resistant pathogens, and emerging post-pandemic resistance trends. Additionally, the review

aimed to identify key drivers of resistance development and discuss evidence-based strategies to mitigate the long-term consequences of AMR in the post-COVID-19 era.

## **Methods**

### *Study design*

This study was conducted as a structured narrative review to comprehensively evaluate the relationship between COVID-19 and AMR, with particular emphasis on ICU-associated infections, secondary bacterial and fungal infections, and MDR pathogens. The review was not designed as a formal systematic review or meta-analysis. However, the literature search, screening, and study selection processes were performed using PRISMA-informed methodological principles to improve transparency, reproducibility, and methodological rigor.

### *Literature search strategy*

A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science. The search covered publications from January 2020 to February 2026 and was updated in February 2026 to include recent post-pandemic evidence and surveillance data.

The search strategy included combinations of Medical Subject Headings (MeSH) terms and free-text keywords related to COVID-19, AMR, antibiotic prescribing, secondary infections, and ICU-associated pathogens. The following terms were used in different combinations: “COVID-19”, “SARS-CoV-2”, “antimicrobial resistance”, “antibiotic use”, “antibiotic prescribing”, “co-infection”, “secondary infection”, “intensive care unit”, “ICU”, “multidrug-resistant pathogens”, “ventilator-associated pneumonia”, and “*Candida auris*”. Boolean operators AND and OR were applied to refine the search strategy.

In addition, the reference lists of eligible studies and relevant review articles were manually screened to identify further publications not captured through the initial database search.

### *Eligibility criteria*

Studies were considered eligible if they investigated antimicrobial use, AMR patterns, bacterial or fungal co-infections, secondary infections, or healthcare-associated infections in

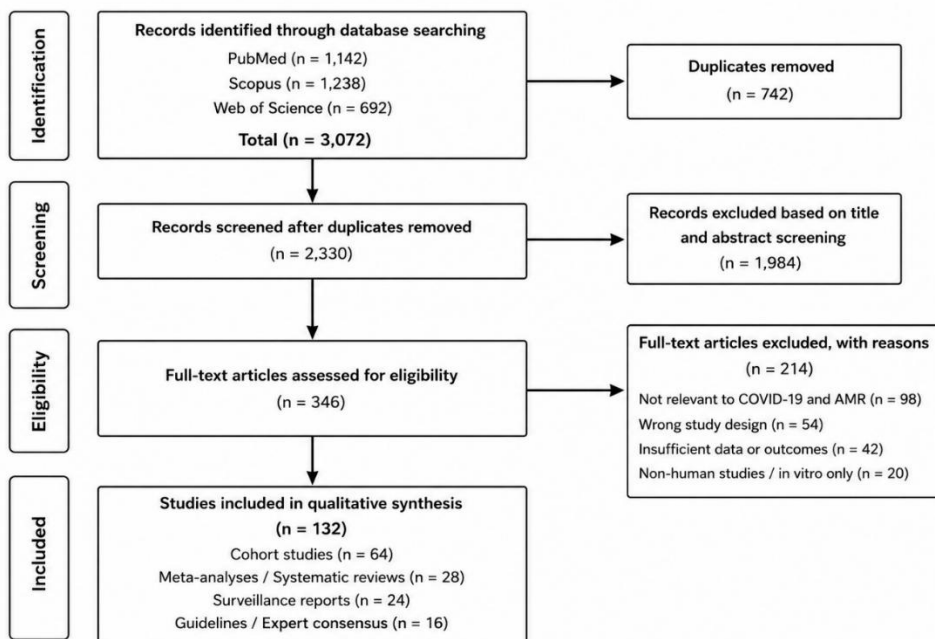
the context of COVID-19. Eligible studies included hospitalized or critically ill adult patient populations, particularly ICU patients. Original research articles, observational studies, cohort studies, systematic reviews, meta-analyses, surveillance studies, and surveillance reports from recognized international public health organizations were considered for inclusion.

Studies were excluded if they were not published in English, consisted solely of editorials, commentaries, letters, expert opinions, or conference abstracts without sufficient primary or synthesized data, or lacked direct clinical, microbiological, epidemiological, or AMR-related relevance to the review topic.

### *Study selection process*

The study selection process was conducted in a structured, multistep manner. Following database searching, duplicate records were removed prior to screening. Titles and abstracts were subsequently assessed for relevance according to the predefined eligibility criteria. Full-text articles considered potentially eligible were then evaluated in detail.

The literature screening and study selection process were independently conducted by two reviewers. Discrepancies regarding study eligibility were resolved through discussion and consensus. A PRISMA flow diagram illustrating the identification, screening, eligibility assessment, and inclusion process is presented in Figure 1.



**Figure 1.** PRISMA flow diagram illustrating the study identification, screening, eligibility assessment, and inclusion process

A total of 3,072 records were initially identified through database searching. After removal of duplicate records, studies were screened based on title and abstract evaluation. Following full-text eligibility assessment, studies meeting the predefined inclusion criteria were included in the final narrative synthesis.

#### *Data extraction and narrative synthesis*

Relevant data were extracted and synthesized narratively. The primary focus areas included antibiotic prescribing patterns during the COVID-19 pandemic, prevalence of bacterial and fungal co-infections, healthcare-associated infections in ICU settings, emergence and dissemination of MDR pathogens, fungal resistance including *Candida auris*, clinical outcomes and mortality associated with AMR, and post-pandemic AMR surveillance trends.

Given the substantial heterogeneity among the included studies in terms of study design, patient populations, clinical settings, microbiological methods, reported outcomes, and surveillance systems, quantitative meta-analysis was not performed. Instead, findings were interpreted using a qualitative narrative synthesis approach, with emphasis on clinically meaningful trends, consistency across studies, ICU-specific resistance patterns, and emerging post-pandemic AMR dynamics.

#### **Literature review results**

##### *Pathophysiological mechanisms linking COVID-19 to secondary infections and AMR*

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is associated with immune dysregulation, epithelial barrier disruption, prolonged hospitalization, invasive interventions, and extensive therapeutic exposure, all of which predispose critically ill patients to secondary bacterial and fungal infections. These mechanisms constitute one of the principal biological links between COVID-19 and accelerated AMR.

A hallmark of severe COVID-19 is profound immune dysfunction characterized by lymphopenia, impaired adaptive immune responses, and dysregulated inflammatory activity [11,12]. Reduced CD4<sup>+</sup> and CD8<sup>+</sup> T-cell counts, together with immune cell exhaustion, compromise host defense against opportunistic pathogens and increase susceptibility to secondary infections [12]. In parallel, SARS-CoV-2 directly damages the respiratory

epithelium, impairing mucociliary clearance and facilitating bacterial adhesion and invasion [13].

Therapeutic interventions such as corticosteroids and immunomodulatory therapies may further increase susceptibility to bacterial and fungal superinfections because of their immunosuppressive effects [14,15]. Critically ill patients are also frequently exposed to invasive procedures, including mechanical ventilation, endotracheal intubation, and central venous catheterization, all of which substantially increase the risk of healthcare-associated infections, particularly ventilator-associated pneumonia (VAP) and bloodstream infections [16].

Prolonged ICU stay, extensive antimicrobial exposure, and increased opportunities for healthcare-associated transmission additionally promote the emergence and dissemination of MDR pathogens [17]. Gram-negative bacteria such as *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* emerged as dominant causes of secondary infections in critically ill COVID-19 patients. In addition, fungal superinfections, including COVID-19-associated pulmonary aspergillosis (CAPA), invasive candidiasis, and *Candida auris* outbreaks, became increasingly important during and after the pandemic period .

Collectively, these interconnected mechanisms created a highly permissive environment for the emergence, persistence, and dissemination of AMR within healthcare systems.

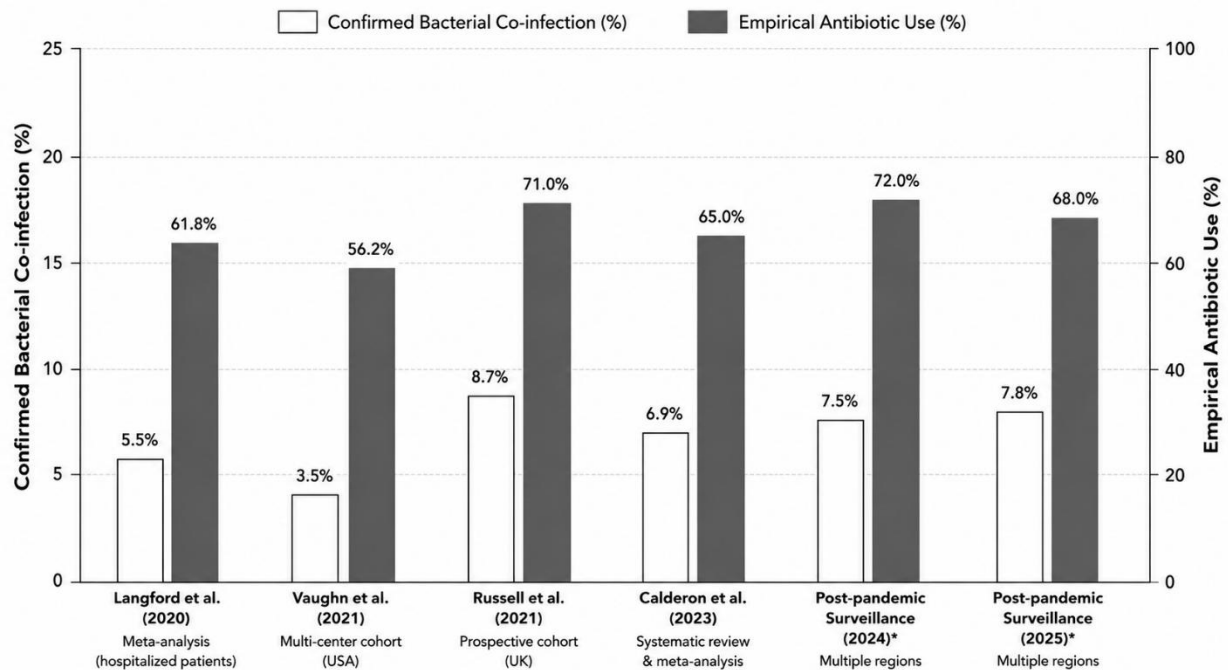
#### *Antibiotic overuse and disruption of antimicrobial stewardship*

The COVID-19 pandemic profoundly altered global antibiotic prescribing practices, frequently resulting in widespread empirical antimicrobial use despite relatively low rates of confirmed bacterial infection. This imbalance has emerged as one of the principal drivers linking the pandemic to the accelerated emergence and dissemination of AMR.

During the early phases of the pandemic, substantial uncertainty regarding disease progression and the possibility of bacterial co-infection prompted the extensive use of broad-spectrum antibiotics in hospitalized patients. However, accumulating evidence consistently demonstrated that bacterial co-infection at hospital admission remained relatively uncommon, generally ranging between 5% and 10% [5,18]. In contrast, antibiotic prescribing rates frequently exceeded 60% among hospitalized patients and were even higher in critically ill ICU populations [6,19].

Several cohort studies and meta-analyses have consistently demonstrated a substantial discrepancy between confirmed bacterial co-infection rates and empirical antibiotic prescribing

in hospitalized COVID-19 patients (Figure 2). Despite relatively low rates of microbiologically confirmed bacterial infection, antibiotic exposure remained disproportionately high across diverse healthcare settings, particularly among mechanically ventilated and critically ill patients.



**Figure 2.** Discrepancy between confirmed bacterial co-infection rates and empirical antibiotic prescribing among hospitalized COVID-19 patients based on selected cohort studies, meta-analyses, and post-pandemic surveillance data

Notes: Adapted from Langford et al. [5], Vaughn et al. [6], Russell et al. [10], and the WHO surveillance data [19].

This discrepancy highlights a major divergence between evidence-based antimicrobial stewardship principles and real-world clinical practice during periods of healthcare system strain. Excessive use of broad-spectrum antibiotics, particularly agents targeting Gram-negative organisms, exerts substantial selective pressure that promotes the emergence and dissemination of MDR pathogens [20]. In ICU settings, where baseline antibiotic exposure and invasive procedures are already common, this selective pressure becomes even more pronounced.

Concurrently, the pandemic substantially disrupted established ASPs, which are critical for optimizing antibiotic prescribing practices. Healthcare systems overwhelmed by COVID-19 surges frequently redirected personnel and institutional resources away from stewardship activities toward acute pandemic management. Core ASP components, including prospective

audit, antimicrobial de-escalation, feedback interventions, and routine microbiological reassessment, were often inconsistently implemented during peak pandemic periods [21].

Diagnostic uncertainty further complicated antimicrobial decision-making. Biomarkers such as procalcitonin and C-reactive protein were widely used to support clinical management; however, their limited specificity in distinguishing viral inflammation from bacterial superinfection in severe COVID-19 reduced their reliability for antimicrobial stewardship purposes [22]. Consequently, prolonged empirical therapy and delayed antibiotic discontinuation became increasingly common.

The consequences of excessive antimicrobial exposure extend beyond individual patient management and significantly affect microbial ecology within healthcare systems. Several post-pandemic surveillance studies have reported increasing rates of carbapenem-resistant *Acinetobacter baumannii*, extended-spectrum beta-lactamase-producing Enterobacterales, and other resistant Gram-negative organisms during and after the pandemic period [4]. Emerging surveillance data from 2024-2025 additionally suggest that elevated antimicrobial consumption and resistance trends have persisted beyond the acute pandemic phase in several regions worldwide.

In parallel, IPC practices were variably affected throughout the pandemic. Although heightened awareness initially improved adherence to protective measures in some institutions, prolonged healthcare system strain, workforce shortages, ICU overcrowding, and staff fatigue ultimately contributed to lapses in standard IPC precautions [9]. These disruptions facilitated the persistence and transmission of resistant organisms within healthcare facilities.

Collectively, these findings suggest that the COVID-19 pandemic created a highly permissive environment for AMR through the combined effects of excessive antibiotic consumption, disruption of stewardship activities, prolonged ICU burden, diagnostic uncertainty, and compromised infection control practices. Addressing these long-term consequences requires resilient antimicrobial stewardship systems, integrated AMR surveillance programs, rapid diagnostic strategies, and sustainable infection prevention measures capable of functioning effectively during future healthcare crises.

#### *ICU-associated MDR pathogens in the COVID-19 era*

The ICU has long been recognized as a high-risk environment for the emergence, persistence, and transmission of MDR pathogens. However, the COVID-19 pandemic substantially amplified these risks, transforming many ICUs into major reservoirs of

antimicrobial resistance. The convergence of prolonged hospitalization, high patient density, extensive antimicrobial exposure, invasive supportive interventions, and healthcare system strain created a highly permissive ecological environment for the selection and dissemination of resistant organisms.

Among ICU-associated pathogens during the COVID-19 era, Gram-negative bacteria have predominated. In particular, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* have consistently been reported as major causes of VAP, bloodstream infections, catheter-associated infections, and secondary healthcare-associated infections in critically ill COVID-19 patients [23,24]. Several studies additionally reported increased incidence of carbapenem-resistant *A. baumannii* and carbapenem-resistant Enterobacterales during periods of peak ICU burden, particularly in regions with high baseline AMR prevalence [4,20].

Among these organisms, *A. baumannii* emerged as one of the most problematic pathogens during the pandemic because of its remarkable environmental persistence, ability to survive on hospital surfaces, resistance to desiccation, and extensive multidrug resistance profiles. Multiple outbreak investigations demonstrated rapid transmission of carbapenem-resistant *A. baumannii* within overwhelmed ICUs, particularly in mechanically ventilated COVID-19 patients requiring prolonged hospitalization [23]. The increased use of broad-spectrum antibiotics, combined with compromised IPC measures during healthcare system surges, likely contributed substantially to these outbreaks.

Similarly, *K. pneumoniae* became increasingly important because of the emergence and dissemination of carbapenemase-producing strains, including isolates harboring KPC, NDM, and OXA-type resistance mechanisms. Several post-pandemic surveillance studies reported increasing rates of carbapenem-resistant *K. pneumoniae* in ICU settings, raising major concerns regarding limited therapeutic options and increased mortality [24]. The widespread empirical use of carbapenems during severe COVID-19 management may have further accelerated selective pressure favoring these resistant organisms.

*P. aeruginosa* has also remained a significant cause of ICU-associated infections during the pandemic period. Its intrinsic resistance mechanisms, biofilm-forming capacity, and ability to rapidly acquire additional resistance determinants make this pathogen particularly difficult to eradicate in mechanically ventilated patients. An increased incidence of MDR and extensively drug-resistant *P. aeruginosa* strains has been reported in several COVID-19 ICUs worldwide [25].

In addition to Gram-negative bacteria, Gram-positive organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* spp. continued to contribute to healthcare-associated infections during the pandemic, although their relative prevalence varied across regions and institutions [26]. Persistent device utilization and prolonged ICU stay remained important risk factors for these infections.

Fungal pathogens also emerged as an increasingly important component of ICU-associated infections during and after the pandemic period. CAPA, invasive candidiasis, and outbreaks of *Candida auris* were increasingly reported among critically ill patients receiving prolonged corticosteroid therapy, immunomodulatory treatment, and mechanical ventilation. Of particular concern, MDR *C. auris* has become a major healthcare-associated pathogen because of its environmental persistence, resistance to multiple antifungal agents, ability to colonize healthcare settings, and propensity to cause nosocomial outbreaks associated with elevated mortality rates.

Importantly, the pandemic not only increased the incidence of MDR pathogens but also disrupted routine infection prevention and antimicrobial stewardship practices that are essential for controlling pathogen transmission in ICUs. Staff shortages, increased patient turnover, ICU overcrowding, and prolonged use of personal protective equipment frequently complicated adherence to standard IPC measures. In several institutions, temporary ICU expansion areas and altered staffing patterns may have further facilitated transmission of resistant organisms.

Emerging post-pandemic surveillance data from 2024-2025 suggest that many of these resistance trends have persisted beyond the acute phase of the pandemic. Increasing rates of carbapenem-resistant Gram-negative bacteria, MDR fungal pathogens, and healthcare-associated outbreaks continue to be reported in several regions worldwide, indicating that the long-term consequences of pandemic-related antimicrobial pressure may extend well beyond the immediate COVID-19 era [19].

Collectively, these findings demonstrate that COVID-19 ICUs represented uniquely favorable environments for the emergence and dissemination of MDR pathogens. The combined effects of antimicrobial overuse, prolonged invasive support, disrupted infection control, and healthcare system overload substantially accelerated AMR dynamics during the pandemic and may continue to influence ICU microbiology in the post-pandemic period.

### *Acinetobacter baumannii: a dominant ICU pathogen*

Among ICU-associated MDR organisms during the COVID-19 pandemic, *Acinetobacter baumannii* emerged as one of the most clinically significant and difficult-to-control pathogens. Its ability to persist on abiotic surfaces, tolerate environmental stress, and rapidly acquire AMR determinants facilitated extensive transmission within overwhelmed healthcare systems, particularly in COVID-19 ICUs [25].

The pathogenic success of *A. baumannii* is closely associated with biofilm formation, environmental persistence, and resistance to routine disinfection procedures. These characteristics enable prolonged colonization of ventilators, medical equipment, and ICU surfaces, thereby increasing opportunities for cross-transmission among critically ill patients [26]. In addition, the organism readily acquires resistance mechanisms, including OXA-type carbapenemases that play a major role in carbapenem resistance.

Several outbreak investigations conducted during the pandemic documented increased incidence of carbapenem-resistant *A. baumannii* (CRAB) in mechanically ventilated COVID-19 patients requiring prolonged hospitalization and extensive antimicrobial exposure [23,25]. Pandemic-related healthcare disruptions, including ICU overcrowding, staffing shortages, and compromised IPC practices, likely contributed to the persistence and transmission of CRAB within healthcare facilities.

From a clinical perspective, CRAB infections are associated with limited therapeutic options, prolonged hospitalization, increased healthcare costs, and elevated mortality. Treatment frequently depends on last-line agents such as colistin, tigecycline, or combination-based regimens; however, increasing reports of colistin resistance have further complicated management strategies [27].

### *Other key gram-negative pathogens*

In addition to *A. baumannii*, *Klebsiella pneumoniae* has remained a major ICU-associated pathogen during and after the pandemic period. Extended-spectrum beta-lactamase-producing and carbapenem-resistant *K. pneumoniae* strains have been frequently associated with bloodstream infections, ventilator-associated pneumonia, and catheter-related infections in critically ill COVID-19 patients [28]. The emergence of carbapenemase-producing isolates harboring resistance mechanisms such as KPC, NDM, and OXA-type enzymes has significantly limited available therapeutic options and contributed to increased mortality.

Similarly, *Pseudomonas aeruginosa* continues to represent an important opportunistic pathogen in ICU populations. Its intrinsic resistance mechanisms, biofilm-forming ability, metabolic adaptability, and capacity to rapidly acquire additional resistance determinants during antimicrobial therapy make eradication particularly challenging [29]. Increased rates of MDR and extensively drug-resistant *P. aeruginosa* have been reported among COVID-19 patients requiring prolonged mechanical ventilation, repeated invasive procedures, and prior broad-spectrum antibiotic exposure.

Emerging post-pandemic surveillance studies from 2024-2025 suggest that resistance trends involving CRAB, carbapenem-resistant *K. pneumoniae*, and MDR *P. aeruginosa* have persisted beyond the acute pandemic phase in many healthcare systems worldwide [19]. These findings indicate that the antimicrobial pressure and infection control disruptions experienced during the COVID-19 era may continue to influence ICU microbiology and resistance epidemiology in the coming years.

#### *Fungal co-infections in the ICU setting*

In addition to bacterial pathogens, fungal infections emerged as important complications among critically ill COVID-19 patients, particularly in ICU settings. CAPA, invasive candidiasis, candidemia, and outbreaks of *Candida auris* were increasingly reported during and after the pandemic period, especially among patients receiving prolonged corticosteroid therapy, immunomodulatory treatment, broad-spectrum antibiotics, and mechanical ventilation [30].

Severe SARS-CoV-2 infection is associated with immune dysregulation, epithelial barrier disruption, prolonged ICU exposure, and extensive antimicrobial use, all of which facilitate fungal colonization and opportunistic infection. CAPA has attracted particular attention because of its association with severe respiratory failure and elevated mortality rates in mechanically ventilated patients. Delayed diagnosis remains a major challenge because clinical and radiological findings frequently overlap with severe COVID-19 pneumonia.

Invasive candidiasis and candidemia have also been increasingly recognized in ICU populations during the pandemic. Major predisposing factors include central venous catheterization, prolonged hospitalization, broad-spectrum antibiotic exposure, and immunosuppressive therapies. Importantly, candidemia in critically ill COVID-19 patients has been associated with prolonged ICU stay and increased mortality.

Of particular concern, MDR *Candida auris* emerged as a major healthcare-associated fungal pathogen because of its environmental persistence, antifungal resistance, and ability to cause nosocomial outbreaks. Collectively, these findings highlight the growing importance of fungal superinfections, antifungal stewardship, and early diagnostic strategies in critically ill patient populations.

#### *Drivers of MDR pathogen emergence in COVID-19 ICUs*

The emergence and dissemination of MDR pathogens in intensive care units (ICUs) during the COVID-19 pandemic resulted from the interaction of multiple clinical and organizational factors. Widespread empirical use of broad-spectrum antibiotics, particularly carbapenems and anti-pseudomonal agents, generated substantial selective pressure favoring resistant organisms within ICU environments [20].

Prolonged mechanical ventilation, invasive supportive interventions, and extended ICU hospitalization further increased susceptibility to healthcare-associated infections. Biofilm formation on endotracheal tubes and medical devices additionally promoted microbial persistence and reduced antimicrobial susceptibility. Critically ill patients exposed to central venous catheterization, urinary catheterization, extracorporeal membrane oxygenation, and renal replacement therapy were particularly vulnerable to secondary infections caused by resistant pathogens.

Healthcare system overload during pandemic surges also substantially contributed to MDR pathogen transmission. ICU overcrowding, increased patient turnover, staffing shortages, and disruption of routine IPC practices frequently compromised adherence to standard precautions and facilitated healthcare-associated spread of resistant organisms.

Environmental persistence of pathogens such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Candida auris* further complicated infection control efforts because of their ability to survive on abiotic surfaces and resist routine disinfection procedures. In addition, diagnostic uncertainty and limited access to rapid microbiological testing frequently contributed to prolonged empirical antimicrobial exposure and delayed de-escalation strategies.

Collectively, these interconnected factors created highly favorable conditions for the emergence, persistence, and dissemination of MDR pathogens in COVID-19 ICU settings.

### *Clinical implications and outcomes*

The increasing burden of MDR pathogens during the COVID-19 pandemic has been strongly associated with adverse clinical outcomes, particularly among critically ill ICU patients. Secondary bacterial and fungal infections contribute to prolonged mechanical ventilation, extended ICU stay, delayed recovery, increased healthcare utilization, elevated mortality, and substantially increased healthcare costs [31,32].

A major clinical challenge is the difficulty in distinguishing severe viral disease progression from secondary bacterial or fungal superinfection. Overlap in clinical manifestations, radiological findings, and inflammatory biomarkers frequently contributes to diagnostic uncertainty, potentially resulting in delayed targeted therapy or prolonged unnecessary empirical antimicrobial exposure.

VAP, frequently caused by MDR Gram-negative organisms, represents a major contributor to respiratory deterioration in mechanically ventilated patients. Infections caused by carbapenem-resistant pathogens, particularly *Acinetobacter baumannii* and *Klebsiella pneumoniae*, are associated with especially poor prognosis because of limited therapeutic options and delayed effective treatment [33]. Mortality rates in critically ill patients with carbapenem-resistant infections have frequently exceeded 40–50% in severe cases. Management often depends on last-line agents such as colistin, tigecycline, or ceftiderocol, while emerging resistance to these reserve antimicrobials further complicates treatment strategies [27].

Fungal superinfections, including CAPA, candidemia, and MDR *Candida auris* infections, have also been increasingly associated with poor clinical outcomes and increased mortality in ICU populations [30,31].

Collectively, these findings demonstrate that AMR represents not only a microbiological challenge but also a major determinant of clinical prognosis and healthcare burden in the post-pandemic era. Rapid diagnostics, antimicrobial stewardship, and sustained infection prevention strategies remain essential for improving patient outcomes in critically ill populations.

### *Future perspectives and strategies*

The COVID-19 pandemic exposed major vulnerabilities in global healthcare systems, particularly regarding antimicrobial stewardship, IPC, ICU capacity, and AMR surveillance.

The widespread empirical use of broad-spectrum antimicrobials, prolonged ICU burden, invasive supportive interventions, and disruption of routine healthcare practices collectively accelerated the emergence and dissemination of MDR pathogens during the pandemic period.

Strengthening ASPs remains one of the highest priorities moving forward. Stewardship activities should remain functional even during healthcare crises and pandemic surges to reduce unnecessary antimicrobial exposure and support timely de-escalation practices. In parallel, expansion of rapid diagnostic capacity, including molecular diagnostic platforms and rapid antimicrobial susceptibility testing, may improve differentiation between viral disease progression and secondary bacterial or fungal infections, thereby facilitating earlier targeted therapy and more appropriate antimicrobial use.

Enhanced surveillance systems and resilient IPC infrastructure are also essential for monitoring resistance trends and limiting healthcare-associated transmission of resistant organisms. Environmental persistence of pathogens such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Candida auris* further emphasizes the importance of rigorous infection control measures, real-time surveillance, and sustained outbreak monitoring in ICU settings.

Emerging technologies, including artificial intelligence-supported clinical decision systems, may additionally contribute to improved antimicrobial stewardship and earlier detection of healthcare-associated outbreaks through integration of microbiological, clinical, and epidemiological data. However, successful implementation of these approaches requires adequate infrastructure, multidisciplinary collaboration, and integration into routine clinical workflows.

Importantly, future pandemic preparedness planning should incorporate AMR mitigation as a central component of healthcare response strategies. Continued global collaboration, integrated surveillance systems, rapid diagnostics, sustainable stewardship frameworks, and resilient healthcare infrastructure will remain essential for reducing the long-term impact of AMR in the post-pandemic era.

## Conclusions

Although COVID-19 is fundamentally a viral illness, its indirect consequences on AMR have been profound, multifactorial, and likely long-lasting. The convergence of excessive empirical antimicrobial use, prolonged ICU burden, invasive supportive interventions, healthcare system overload, and disruption of infection prevention and antimicrobial

stewardship practices created highly favorable conditions for the emergence and dissemination of MDR pathogens during the pandemic.

Critically ill COVID-19 patients became particularly vulnerable to secondary bacterial and fungal infections, especially in ICU environments characterized by prolonged mechanical ventilation, extensive antimicrobial exposure, and sustained healthcare system strain. Pathogens such as *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and MDR *Candida auris* emerged as major contributors to healthcare-associated infections associated with limited therapeutic options, increased mortality, and prolonged hospitalization.

Importantly, the pandemic highlighted the fragile balance between urgent infectious disease management and the unintended ecological consequences of widespread antimicrobial exposure. Diagnostic uncertainty, delayed microbiological confirmation, and pandemic-related disruption of ASPs substantially contributed to inappropriate antimicrobial prescribing practices and accelerated resistance dynamics within healthcare systems worldwide.

Emerging post-pandemic surveillance data further suggest that many resistance trends observed during the acute pandemic phase have persisted beyond the initial COVID-19 waves, indicating that the long-term consequences of pandemic-associated antimicrobial pressure may continue to influence ICU microbiology and resistance epidemiology for years to come.

Addressing this complex challenge requires an integrated and multidisciplinary approach that combines resilient ASPs, rapid and advanced diagnostic technologies, robust IPC strategies, real-time surveillance systems, and continued investment in healthcare system preparedness. In addition, emerging approaches, including artificial intelligence-supported clinical decision systems and precision medicine strategies, may offer promising future opportunities for optimizing infection management and mitigating antimicrobial resistance.

Ultimately, the COVID-19 pandemic has demonstrated that AMR must be regarded not only as a microbiological problem but also as a critical component of pandemic preparedness and healthcare system resilience. Sustained global collaboration, integrated surveillance, and evidence-based antimicrobial management will remain essential for limiting the long-term impact of AMR in the post-pandemic era.

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