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COVID-19 and Co-Infections: A Review of Clinical Implications and Management Challenges

Riaz Ahmed

ABSTRACT

Bacteria, viruses, and fungi often play a major but ignored role in infections associated with coronavirus disease 2019 (COVID-19). With the progress of the pandemic, studies have found that being infected with multiple viruses simultaneously can have a strong effect on SARS-CoV-2-infected patients' health care, treatment plans, and recovery. The epidemiology, impact on patients, challenges in identifying coinfections, and management approaches are all examined during this review of COVID-19 patients. Common issues in this field are infections from *Streptococcus pneumoniae*, *Staphylococcus aureus*, influenza, respiratory syncytial virus, *Aspergillus* spp., and Mucorales—most of which affect immunocompromised or critically ill people. Having coinfections increases the chances of acute respiratory distress syndrome, sepsis, blood clots, longer stays in the intensive care units, and a higher risk of death. Despite efforts, similar symptoms in different patients and a lack of proper tests often cause health care professionals to prescribe antibiotics early on, leading to more cases of antimicrobial resistance. Biomarkers such as procalcitonin and multiplex tests for several pathogens play a bigger role in leading antimicrobial stewardship. Since the risk of infections is high and their clinical settings are intricate for tuberculosis- or HIV-coinfected cancer patients, transplant recipients, and the elderly, these individuals need special approaches. The review stresses that using coordinated approaches, advanced rapid diagnostic methods, and strong surveillance can greatly reduce problems from coinfections and improve the readiness for pandemics.

Keywords: COVID-19 co-infections, Antimicrobial resistance, Diagnostic challenges, Immunosuppression, Fungal co-infections

Introduction

When SARS-CoV-2, responsible for coronavirus disease 2019 (COVID-19), appeared late last year, it triggered a crisis like none other in the field of public health. The COVID-19 pandemic, which has confirmed cases numbering over 700 million and has caused millions of deaths globally, has placed a burden on health systems, made it clear that more can be done to prepare for infectious diseases, and motivated high-intensity research into the characteristics and control of the coronavirus.¹ Most people with COVID-19 are infected by a virus, but evidence indicates that other microbial infections at the same time change severity, success of treatments, and risk of death (Figure 1).²

Several viral pandemics have shown that coinfections are a major issue. In both the 1918 and the 2009 influenza pandemics, there were many cases of people dying because of bacterial infections that developed

after influenza. Besides, some of the most commonly found bacteria in the lungs of critically ill or immunocompromised COVID-19 patients are *Streptococcus pneumoniae* and *Staphylococcus aureus*, together with viral copathogens such as influenza and respiratory syncytial virus (RSV), while opportunistic fungi such as *Candida* spp., *Aspergillus* spp.,³ and Mucorales have been noticed as well. When coinfections happen, the illness becomes more severe and treatment is often delayed, more difficult to diagnose, and may lead to unnecessary use of antibiotics.⁴

Since the symptoms of coinfections and COVID-19 are often very similar at first, telling them apart can be tough. Moreover, applying therapies that weaken the immune system, like corticosteroids and biologics, in COVID-19 care may leave patients at increased risk for secondary infections, bringing thoughts of whether the advantages of the treatment outweigh the hazards and the value of strong antimicrobial stewardship.⁵

This review synthesizes evidence from 2020 to 2025 with a unique focus on antimicrobial stewardship metrics (e.g., Antimicrobial Stewardship Programs [ASPs] efficacy, Table 4) and integrates emerging data on multiplex diagnostics and resource-limited settings, filling gaps left by prior reviews.

Hence, the main goals of this study are:

1. To review the prevalence and types of coinfections (bacterial, viral, fungal) observed in COVID-19 patients
2. To analyze how coinfections affect clinical outcomes, disease severity, and mortality in COVID-19 cases
3. To evaluate diagnostic challenges in differentiating COVID-19 from overlapping infectious syndromes
4. To assess current treatment strategies and antimicrobial stewardship practices in coinfecting patients

Methodology

Study Design and Scope

The present review was conducted as a systematic review since the sampling populations were heterogeneous, there is no consistent reporting of the coinfection percentage, and there have been clinical guidelines that have changed throughout the pandemic. Nevertheless, fundamental postulates of methodological transparency have been used to enhance the quality and reproducibility of evidence.

Search Strategy

In the literature, a structured search was done in PubMed, Scopus, and Google Scholar, and relevant research on COVID-19-related coinfections from January

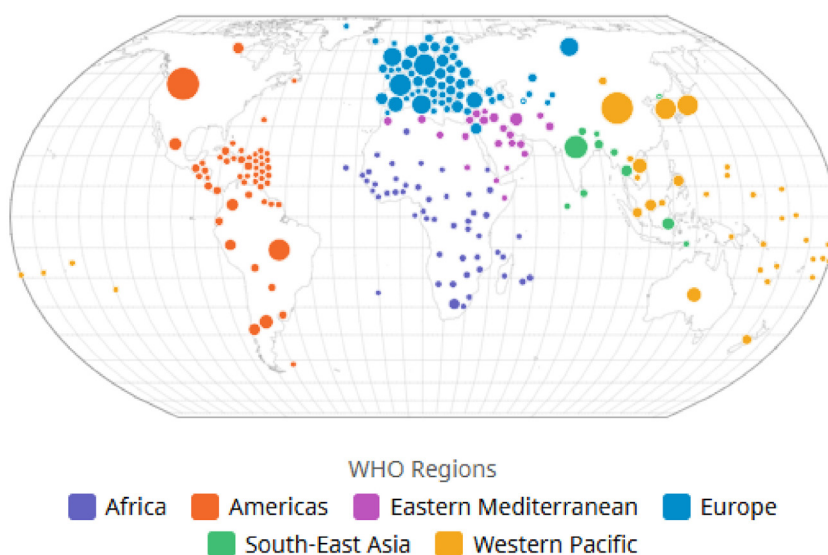


Fig 1 | Global map of COVID-19 burden overlaid with the incidence of coinfections by region²

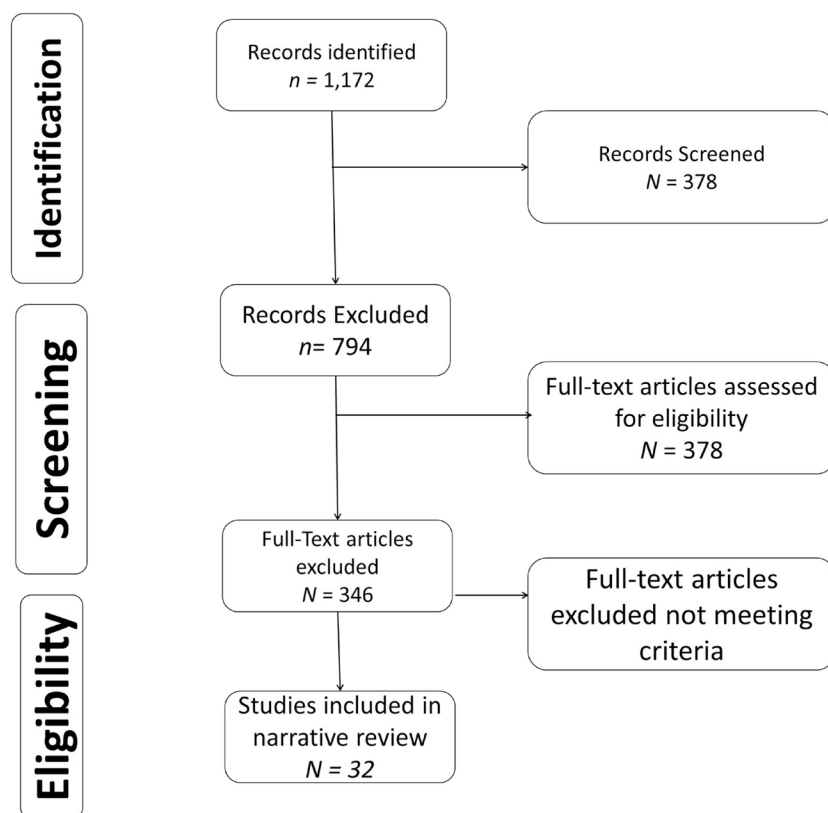


Fig 2 | PRISMA flow diagram

2020 to February 2025 was identified. Search terms were a combination of:

1. COVID-19 and ("bacterial coinfection" OR "viral coinfection" OR "fungal coinfection")
2. SARS-CoV-2" OR ("secondary infection" OR "ICU infection" OR "superinfection")
3. COVID-19 antimicrobial stewardship OR Diagnostic issues facing COVID-19

All significant review articles referenced and World Health Organization (WHO)/CDC/Infectious Diseases Society of America (IDSA) recommendations were sifted manually to be included.

Inclusion Criteria

1. Peer-reviewed work in the English language
2. Meta-analyses, systematic reviews, cohort studies, as well as case series
3. Research reporting on the prevalence, diagnostic, or therapeutic information connected to bacterial, viral, or fungal coinfections of COVID-19 patients

Exclusion Criteria

1. Non-peer-reviewed preprints, opinion pieces, and editorials
2. Monoinfection with SARS-CoV-2 only, i.e., studies concentrating on a single infection with SARS-CoV-2
3. Articles not related to clinical outcome, diagnostics, and coinfection management

Data Synthesis and Extraction

Data based on copathogen type, intensive care units (ICU) vs. non-ICU setting, diagnostic tools, treatment strategies, and clinical outcome were of key interest and were extracted. Thematic synthesis was applied to find the common patterns, challenges, and stewardship implications regarding specific pathogens.

Given heterogeneous sampling populations, inconsistent coinfection reporting, and evolving clinical guidelines during the pandemic, a narrative synthesis was deemed most appropriate to capture broad clinical insights.

As indicated in Figure 2, which is a PRISMA-type flow diagram applied in the present narrative review, a total of 1,172 records were found, followed by the screening of 378 entries, with 32 studies being included in the current narrative review according to predetermined inclusionary and exclusionary criteria.

Epidemiology and Prevalence of Coinfections in COVID-19

The level of coinfections experienced by people with COVID-19 varies significantly based on where they receive care, their demographics, the equipment available to clinicians, and the local environment. Initially, it appeared that COVID-19 had fewer coinfections than influenza; however, further analysis revealed a much wider range, particularly among patients requiring hospital care (Figure 3).⁶

Bacterial Coinfections

Most cases of secondary infection in COVID-19 are associated with bacteria, and these are most common for patients who are in intensive care. Pathogens often found in pneumonia are *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. More than 30,000 COVID-19 patients were studied in a recent systematic review and meta-analysis, which found that about 8.6% had a coexisting bacterial in-

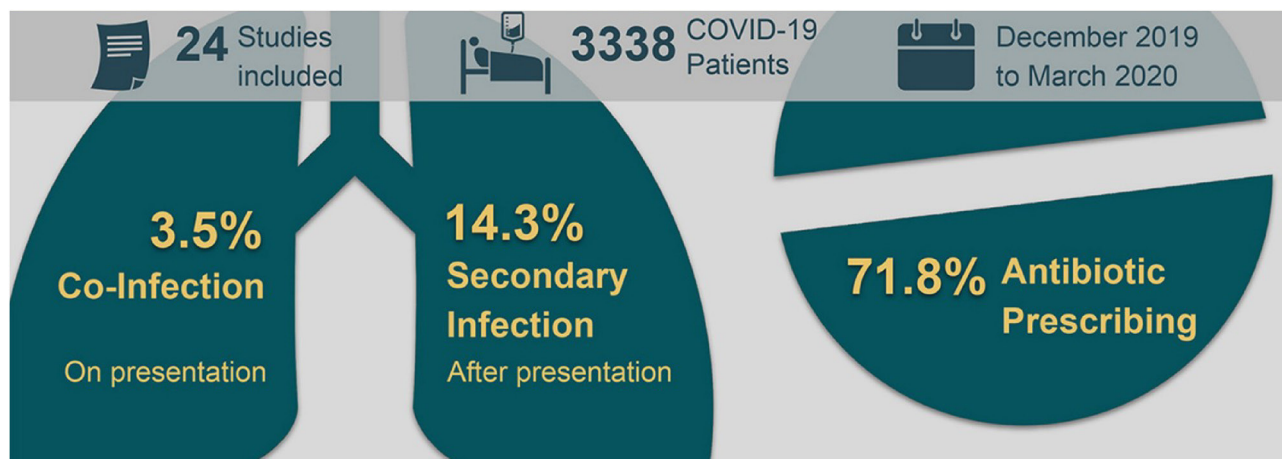


Fig 3 | Acute bacterial coinfection in COVID-19⁷

Table 1 Comparative outcomes: CAPA vs. CAM		
Feature	CAPA	CAM
Incidence in ICU patients	5–10%	<1% (higher in India)
Main risk factors	Corticosteroids, ventilation	Uncontrolled diabetes, steroids
Diagnostic challenges	Requires bronchoscopy, galactomannan	Low sensitivity in PCR, histopathology needed
Mortality rate	40–60%	50–80%
Typical timing	Early ICU stay (days 3–7)	Later, often postdischarge
Common pathogen	<i>Aspergillus fumigatus</i>	<i>Rhizopus</i> , <i>Mucor</i> spp.

fection. Among ICU patients and those receiving ventilation, the infection rates were 14–17%.⁸ On the same note, fungal coinfections in the ICU have been documented with incidence ranging between 5–10% of patients, especially mycotic species like *Aspergillus* spp., using aggregated data on more than 30,000 patients with COVID-19. Many times, people get these infections from equipment in the hospital, such as VAP, problems related to catheters, or remaining in the hospital for a long period.⁷ Particularly, noticing when an infection occurs allows us to see whether it was present at arrival (primary) or acquired in the hospital (secondary), as both are important for clinical care (Figure 3).

Viral Coinfections

Coinfections with SARS-CoV-2 are noticed less often in studies, which may be due to a lack of multiplex testing in overloaded health care centers. Cases of infections caused by both influenza A and B viruses, together with RSV, adenovirus, cytomegalovirus (CMV), and human metapneumovirus have been reported.⁹ Viral coinfection is more common in pediatric patients, notably with RSV and rhinovirus, which is difficult to diagnose since both have similar symptoms and appear together during seasons.¹⁰ Several investigations in the Northern Hemisphere winter months found that about 3–7% of patients were infected with two viruses, and those coinfecting patients were often hospitalized and required oxygen (Figure 4).

Fungal Coinfections

Especially during the COVID-19 pandemic, fungal infections have become more common in patients

who get corticosteroids or other immunosuppressive medications. *Aspergillus* spp. is linked to a condition known as COVID-19-associated pulmonary aspergillosis (CAPA), affecting 5–10% of ICU patients, depending on how and if fungi are cultured.⁷ Many *Candida* infections happen in the blood, and these cases often involve patients who are using ventilators or have a device implanted.⁸ A big concern was the rise of COVID-19-associated mucormycosis (CAM), mainly in India, during the second wave (Figure 4). There was a major increase in CAM among individuals with uncontrollable diabetes, those exposed to fungal spores, and those taking systemic corticosteroids, proving that risk depends on local and personal factors (Table 1).⁹

Geographic and Clinical Setting Variability

The trends in epidemiology differ greatly by region, how serious the disease is, and the quality of medical facilities available. Countries that can offer extensive diagnostic testing tended to see bacterial, viral, and fungal coinfections balanced, though in poorer settings, many fungal cases are missed. Inside the ICU, the number of coinfections tends to be highest, mainly because invasive devices, lowered immunity, and prolonged hospital time can lead to more infections.¹⁰ Antimicrobial policies, ways to control infections, and the number of diseases affected by pathogens differ widely across the globe (Figure 4).⁹

A comparison analysis of possible copathogens, bacteria, viral, and fungal agents of COVID-19 infection depicts different but similar disease patterns. The most common types of bacterial coinfections (in the ICU environment and with the use of the ventilator), viral coinfections (in pediatric and winter-season infections), and fungal coinfections (mainly *Aspergillus* and *Mucorales*) are underpinned by immunocompromised regimes. These observations support the importance of combined diagnostics plans and effective antimicrobial stewardship because every class of pathogen demands careful, yet integrated treatment applications.

Clinical Implications of Coinfections

It has become very important to pay attention to coinfections in patients with COVID-19 because these infections

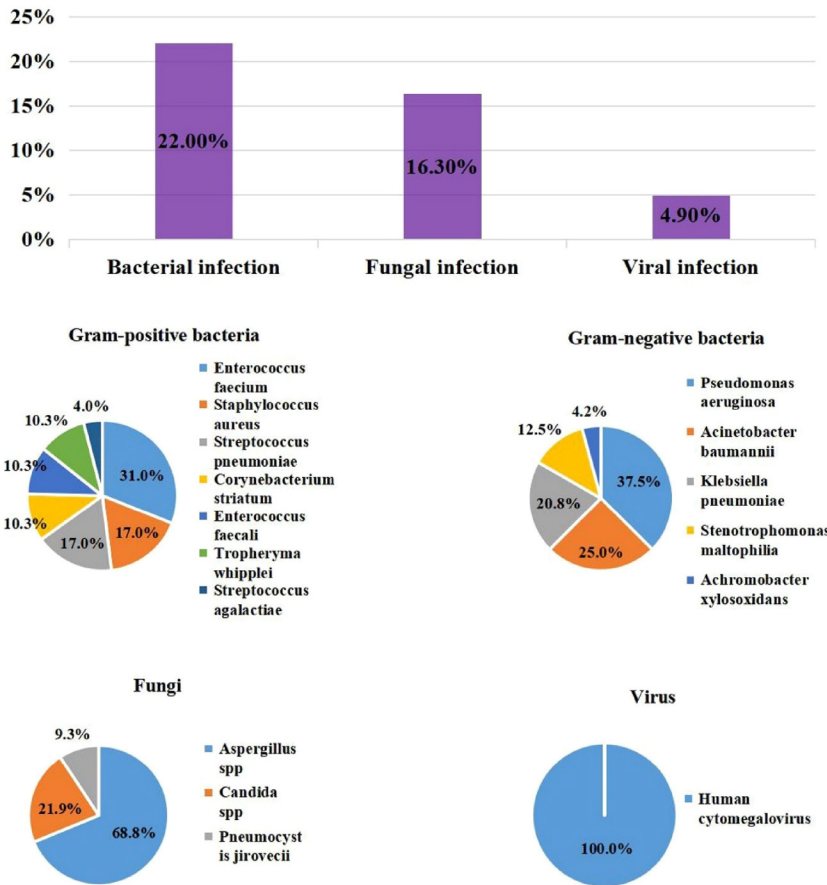


Fig 4 | Bar chart comparing bacterial, viral, and fungal coinfection rates in ICU vs. non-ICU settings⁹

often affect the course of the disease, treatment options, and patient outcomes. Having SARS-CoV-2 combined with other microbes—bacteria, various viruses, and fungi—boosts inflammation, hurts lung function, and makes it more likely for systemic complications to develop.¹¹ Scientists now see coinfections as an important predictor of outcomes, mainly in people who are hospitalized and seriously ill (Figure 5).¹²

Impact on Disease Progression and Clinical Complications

Coinfected patients with COVID-19 have a much different disease course than those with a single infection. Superinfections by bacteria like *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* promote rapid decline of the lungs, make gas exchange difficult, and raise the body's inflammatory level.¹² They can result in the development of acute respiratory distress syndrome (ARDS), septic shock, and multiorgan dysfunction syndrome. As infection multiplies, there are increased amounts of cytokines and endothelial damage, which results in a severe and fast deterioration of symptoms.¹³

Furthermore, when there are influenza or RSV coinfections, immunity is more difficult to control in people with COVID-19.¹⁴ The respiratory epithelium is a usual target for these viruses, and they can team up with SARS-CoV-2 to boost too much immune system activity and blood vessel inflammation. Lymphopenia, raised D-dimer levels, and problems with coagulation may happen in coinfecting patients, which increases the likelihood of deep vein thrombosis and pulmonary embolism.¹⁰

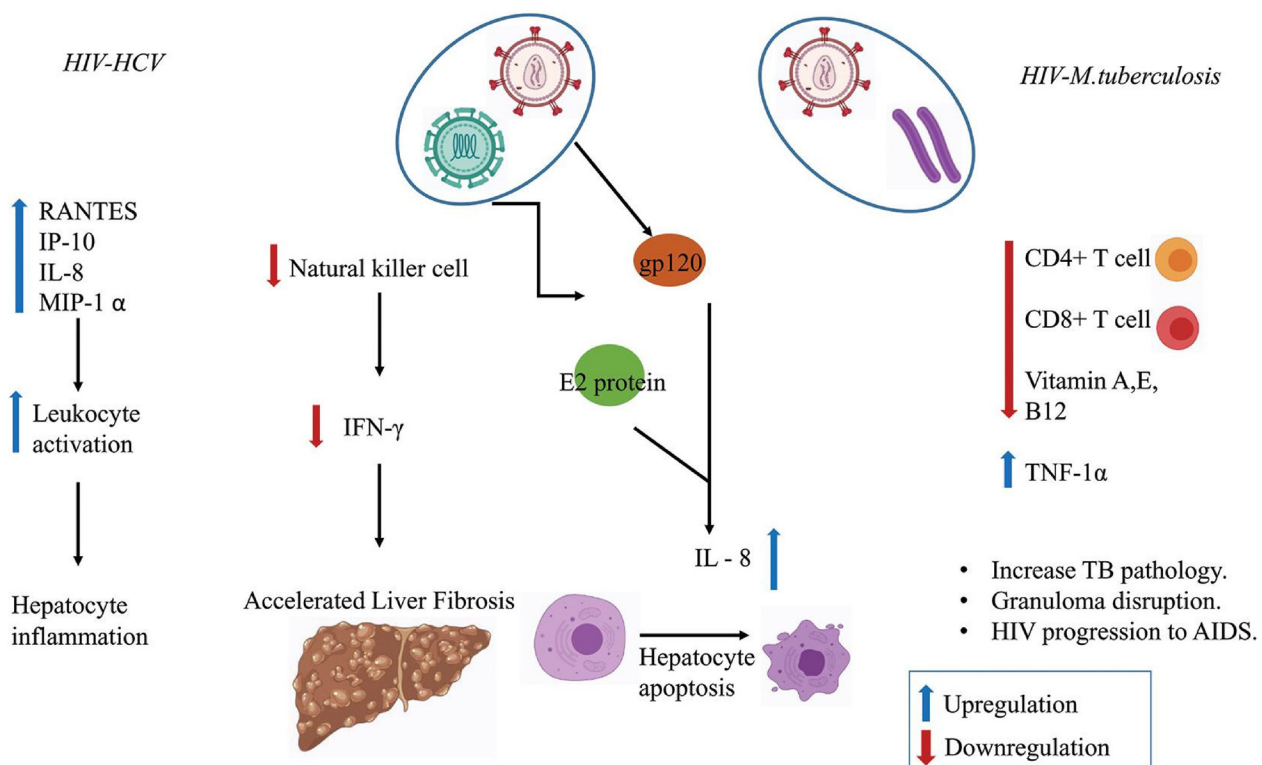


Fig 5 | Coinfection in regulating the immune response¹²

Increased ICU Admission and Mechanical Ventilation

Some retrospective cohort studies have found that patients with COVID-19 and other infections often need intensive care and mechanical ventilation. The research of 1,000 hospitalized COVID-19 cases uncovered that people with bacterial coinfection were twice as likely to develop ARDS and had over 2.3-fold higher chances of being admitted to the ICU. Most cases of superimposed fungal infections, especially those linked to COVID-19, are marked by tough-to-treat low oxygen levels, which leads to prolonged use of ventilators and vasopressors.¹⁵

The bad effects get worse in people with conditions such as a weak immune system, uncontrolled diabetes, or prolonged steroid consumption. Such patients end up in the ICU more often and stay longer in hospitals, plus they find themselves with more neurological infections during their stay.¹⁶

Mortality Outcomes in Coinfected vs. Monoinfected Patients

Patients who have COVID-19 and another illness usually have a higher risk of death than those with only COVID-19. Having CAPA or CAM in addition to SARS-CoV-2 infection has been found to increase the likelihood of poor outcomes.¹⁷ CAPA reportedly leads to death in 40–60% of patients if the diagnosis is delayed or if antifungal treatment is not used until later.¹⁸ Likewise, in several regions, CAM has caused death in over 50% of patients, which underlines the seriousness of the disease and how hard it is to diagnose in the beginning (Table 2).¹⁹

Even though bacterial coinfections are usually addressed with antibiotics, they may still increase mortality because they can cause septic complications and affect multiple organs.²⁰ Viral coinfections, though they are not very common, make the outcome worse if they are present, especially for people who are elderly or have other health problems. An analysis covering ICU patients discovered that people with coinfections had a 1.7 times higher risk of dying for any reason than people who had single infections.²¹

Clinical Significance and Need for Vigilance

They highlight how important it is to spot and treat coinfections in patients with COVID-19 quickly and strongly. A slower diagnosis of pathogens results in more severe infections for patients and uses more of the hospital's resources and ICU space. Being more alert to infections, timely microbiology, and use-of-antibiotics principles reduce coinfections in people with COVID-19.²²

Diagnostic Challenges and Overlapping Syndromes

It is still very difficult to accurately and promptly spot coinfections in patients with COVID-19.²³ Many

infectious agents in the lungs, whether bacterial, viral, or fungal, share similar symptoms and spread, which makes it hard to know if a person has more than one infection during SARS-CoV-2. Because of diagnostic uncertainty, some patients receive treatment too late or may not be given proper medications which also makes it hard to manage infection control and the wise use of medicines.²⁰

Overlapping Respiratory Symptoms and Clinical Mimicry

Many symptoms of COVID-19 are like those of other respiratory infections, with examples being fever, a dry cough, breathlessness, muscle pain, and imaging showing bilateral areas of shadows or ground-glass opacity.¹⁸ They are just like the signs and symptoms of bacterial pneumonia, influenza, and such fungal infections as pneumocystis or invasive aspergillosis. Therefore, depending on clinical signs alone does not give clear answers, especially for patients who lack immunity or during flu season, because many illnesses show similar symptoms.¹⁷

Limitations of RT-PCR, Serological Testing, and Imaging

RT-PCR is still the main method used for finding SARS-CoV-2 infections. But there are some problems with COVID-19 tests, such as missed infections in those with lower viral load, different outcomes from one test to another, or delayed recognition in those with advanced disease.²¹ RT-PCR is unable to tell if the virus present is still active, and it does not detect coinfecting illnesses unless designed for that purpose. If a patient has both coronavirus infection and RSV or influenza, only multiplex panels can detect all three; singleplex assays are not reliable for this.¹⁵

They do not work very well for the initial detection of infections and cannot point out other harmful pathogens. While techniques such as chest radiography and CT scans easily find lung involvement, they do not always determine what the involvement is due to.²² Observing ground-glass opacities and opacities in the lungs is common in bacterial pneumonia, certain fungal infections, and even diseases not caused by infection, which makes it challenging to tell COVID-19 apart.¹⁸

Need for Multiplex Panels and Rapid Diagnostics

To solve the confusion in diagnosis, more multiplex panels are required that can identify SARS-CoV-2 as well as other respiratory infections simultaneously. Using BioFire® FilmArray, TaqPath™, and Allplex™ respiratory panels can bring a big increase in the accuracy of testing, mostly for those in the ICU and other high-risk groups.²⁴ As an example, the BioFire 2.1 FilmArray respiratory panel has a sensitivity of ~97% and specificity of ~99% toward some of the major respiratory pathogens, whereas the Allplex™ panel has a sensitivity of ~95% and specificity of ~98%. Multiplex testing is \$120–\$150 per patient/cost per diagnosis, depending upon platform and regional pricing.²⁵ They save time for labs and let clinicians see many different

Table 2 | Comparative outcomes in monoinfected vs. coinfecting COVID-19 patients¹⁹

Clinical Outcome	Monoinfected Patients	Coinfected Patients
ICU Admission Rate	17% (mdpi.com)	48% (mdpi.com)
Mechanical Ventilation	Data not specified	Data not specified
Mortality Rate	3.4% (mdpi.com)	32% (mdpi.com)

bacteria, which allows them to choose the best treatment. On the other hand, many countries with fewer resources find that it is difficult to get hold of, afford, or have approved the new medicines.²⁶

Tests such as serum galactomannan, 1,3-β-D-glucan, and DNA PCR for *Aspergillus* and Mucorales are appropriate, but they are not very sensitive in people who are not immunosuppressed. Using bronchoalveolar lavage remains a useful tool to diagnose invasive fungal infections, but it may not work well with unstable patients or when pandemic precautions against aerosolized material are in place (Table 3).²⁷

Risk of Misdiagnosis and Delayed Treatment

Because they often use broad-spectrum antimicrobials without testing, misdiagnosis, or late detection of coinfections is more likely in less-resourced areas. Practicing this way can make people resistant to antibiotics and result in incorrect treatment, which might worsen health outcomes for patients. Simple and rapid methods for diagnosing COVID-19 are very important for reducing risks and supporting accurate care decisions (Figures 6 and 7).^{28,29}

Management Strategies and Antimicrobial Stewardship

Handling the presence of different infections in a COVID-19 patient is very challenging, as both the disease and the infections have similar symptoms. At the start of the pandemic, it was common for clinicians to give antibiotics without a definitive diagnosis because of concerns about bacterial infections and empty labs.²⁷ Although the use of antibiotics and antifungals seemed acceptable at the beginning, using them for a long and indiscriminate time has brought about major concerns about antimicrobial resistance (AMR), how effective they remain, and safety for patients.³⁰

Figure 7 shows an implemented clinical decision tree to help clinicians deal with suspected coinfections in COVID-19 patients. Depending on the clinical phenotype of the patient at the time of query—e.g., immunocompromised state, ICU admission, or comorbidities—the multiplex diagnostic panel of choice is selected (bacterial/viral/fungal) leading to targeted antimicrobial, antiviral, or antifungal therapy. This systematic process aids antimicrobial stewardship in a way that makes diagnosis coincide with the phenotype-related danger (Figure 8).

Table 3 | Diagnostic accuracy and turnaround time of common multiplex panels

Panel Name	Sensitivity (%)	Specificity (%)	Pathogens Detected	Turnaround Time	Cost/Test (USD)
BioFire® FilmArray	~97	~99	20+ (viral/bacterial)	~45 min	\$120–150
Allplex™	~95	~98	18+ (viral only)	~2–3 h	\$100–130
TaqPath™ Combo Kit	~93	~98	SARS-CoV-2, Flu A/B, RSV	~2 h	\$80–100

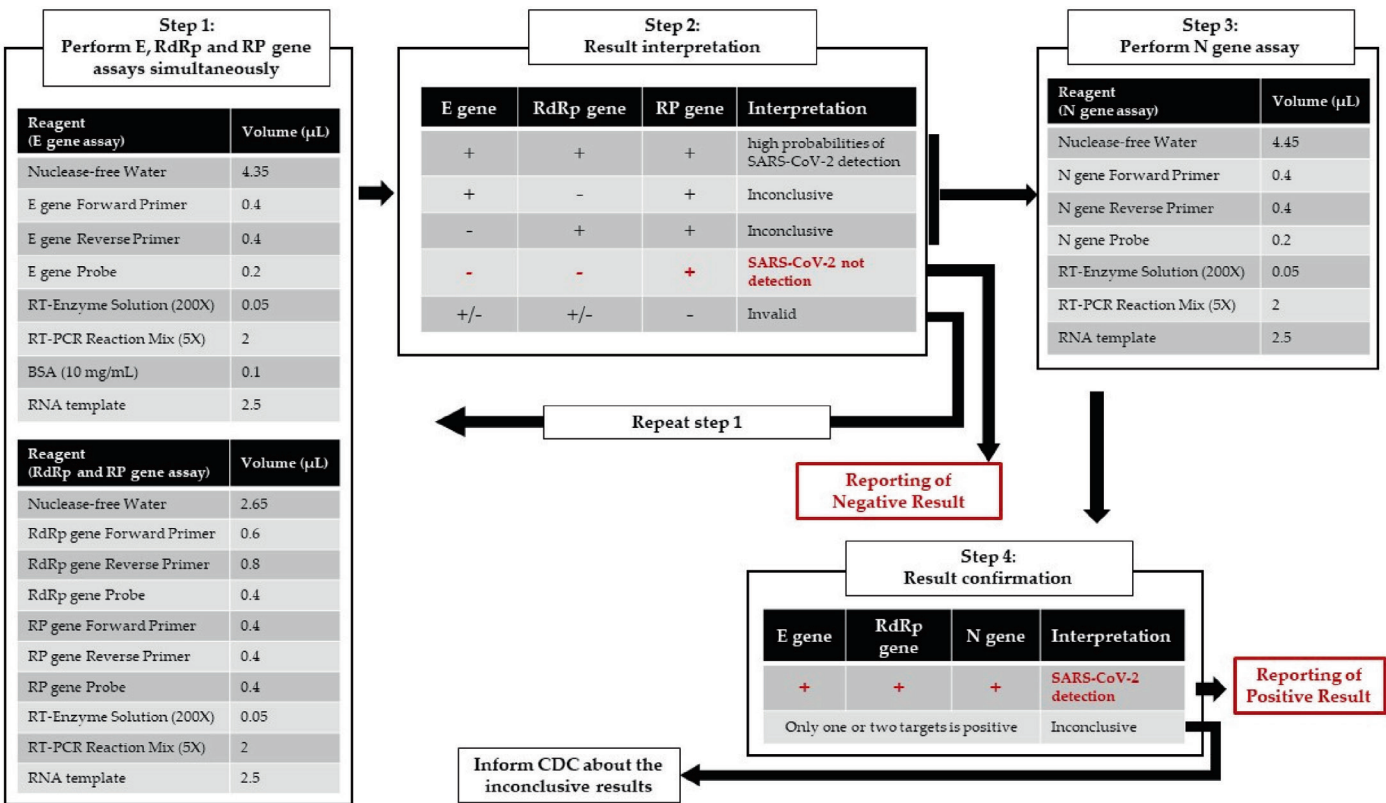


Fig 6 | Flowchart of the optimized COVID-19 molecular diagnostic workflow protocol²⁸

Workup and Radiology Imaging in COVID-19

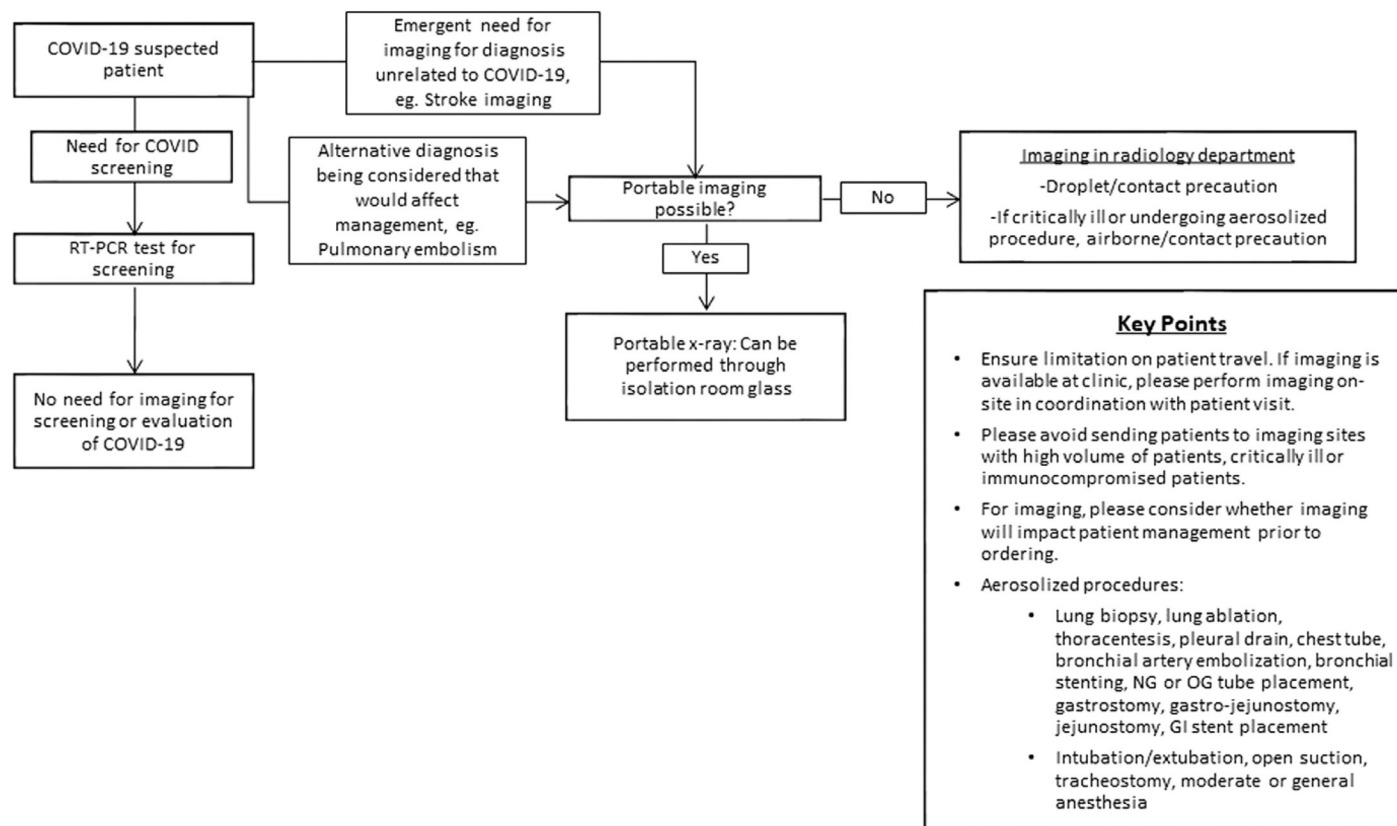


Fig 7 | This chart outlines the process of checking and imaging patients thought to have COVID-19²⁹

Empirical Use of Antimicrobials in COVID-19 Care

Bacteria were not the main cause of disease in COVID-19. However, there was a big increase in antibiotic prescriptions during the first stage. Research shows that even when bacterial coinfection was rare, 60–70% of the patients in the hospital with COVID-19 received antibiotics.²⁹ Because prescribing does not match scientific research, global use of antibiotics is now much too high. Because COVID-19 was linked to more cases of CAPA and mucormycosis, antifungals such as voriconazole and amphotericin B were given to many patients.³¹

Guideline Recommendations: WHO and IDSA Positions

Following these issues, the WHO and the IDSA advised that antibiotics are not needed for minor to moderate COVID-19 cases without solid evidence or suspicion of a bacterial infection.³⁰ They point out that antimicrobial therapy should be guided by lab results and a doctor's decision, instead of being given automatically. Such recommendations underline that the choice of treatment should be based on local findings regarding the resistance of microbes in severe or ICU cases.³²

Antibiotic Resistance: An Escalating Threat

Using lots of antibiotics during the pandemic has been linked to seeing more multidrug-resistant (MDR) organisms like extended-spectrum β -lactamase-producing Enterobacteriaceae, carbapenem-resistant *Acinetobacter baumannii*, and *Candida auris*.³³ There is an increase in hospital-acquired resistance cases reported in Asia, Europe, and Latin America, which is caused by extended stays in hospitals, specific treatments, and poor infection control. The rise in AMR might reduce how effective standard treatments work in the period after the pandemic ends.³⁴ In the aftermath of stewardship program implementation, researchers have recorded a decrease in unnecessary antibiotic utilization of 20–30% and a perceptible decrease in the incidence of MDR organisms up to 15% more, especially in ICUs (Table 4).

Role of Biomarkers in Therapeutic Decision-Making

Examining procalcitonin (PCT), C-reactive protein, ferritin, and the neutrophil-to-lymphocyte ratio is now important to differentiate viral infection from any bacterial or fungal superinfection. Also, PCT has often shown useful results.³³ When PCT levels are this low (<0.1 ng/mL), there is a low possibility of infection

with bacteria, so antibiotics may be stopped safely.³⁴ Similarly, increasing PCT may suggest the presence of secondary bacterial infection, prompting action to increase treatment. Biomarker-based algorithms added to antimicrobial stewardship measures may stop unnecessary treatment options yet maintain strong treatment results.³⁵

Immunosuppressive Therapies and Secondary Infection Risks

Because corticosteroids (for example, dexamethasone) and tocilizumab (a treatment targeting IL-6 receptors) are used in severe COVID-19, the risk of infection has changed. By lowering the cytokine storm and the death rate in hypoxemic patients, these drugs also lessen the

innate immune system, which makes patients more vulnerable to infectious diseases.²⁸ We have noticed new cases of aspergillosis, mucormycosis, and CMV virus activation among patients taking medication such as steroids—mainly those with diabetes, cancer, or long-term immunosuppression.³¹

The Future of Antimicrobial Stewardship in COVID-19 and Beyond

To meet these new challenges, ASPs should focus on immediate diagnostics, monitoring infections, and helping health care professionals. Ensuring proper use of diagnostic tests also means making sure that antibiotics are correctly chosen, given, and used for the proper length.³⁴ To improve stewardship frameworks, teamwork should be practiced among infectious disease specialists, microbiologists, pharmacists, and intensivists in pandemic and endemic respiratory care contexts.³³

Case Studies and Special Populations

There are extra difficulties in finding and treating COVID-19 when it is present with other diseases in people at high risk. Such complexities are being illuminated more by case reports and cohort studies, mainly where there are a lot of chronic infections or where the immune system is compromised. Getting to know these groups well supports precision medication use and enhanced outcomes for patients.³⁵

COVID-19 and Tuberculosis (TB) Coinfection

In places where TB is common, being infected with SARS-CoV-2 as well is a difficult problem to manage. Respiratory issues can occur because of both lung TB and COVID-19, and difficulties in diagnosis arise from the common symptoms and X-ray appearances these illnesses share.³⁶ Also, getting infected with SARS-CoV-2 and undergoing immunosuppressive treatments, mainly with corticosteroids, can rekindle previously hidden TB. In many cases, patients who get better from moderate to severe COVID-19 can develop active TB afterwards, which means they need to use two types of medications and their liver function must be monitored closely (Figure 9).³⁷

HIV and COVID-19 Coinfection

HIV's effect on COVID-19 cases seems to be different for different people. Individuals with HIV who have it under control are likely to cope the same as others, but those with severely decreased immunity risk severe sickness and infections and continue to shed the virus for a longer period.⁴ For some participants in observational studies, living with HIV was linked to higher hospitalization rates and increased risk of death, but this was not always true in all regions or for those taking antiretroviral drugs. Because HIV can mess with the immune system, interpreting inflammatory signs and the course of COVID-19 becomes difficult.¹⁵

Immunocompromised Patients

Chemotherapy patients, those who receive solid organ or hematopoietic stem cell transplants, and people

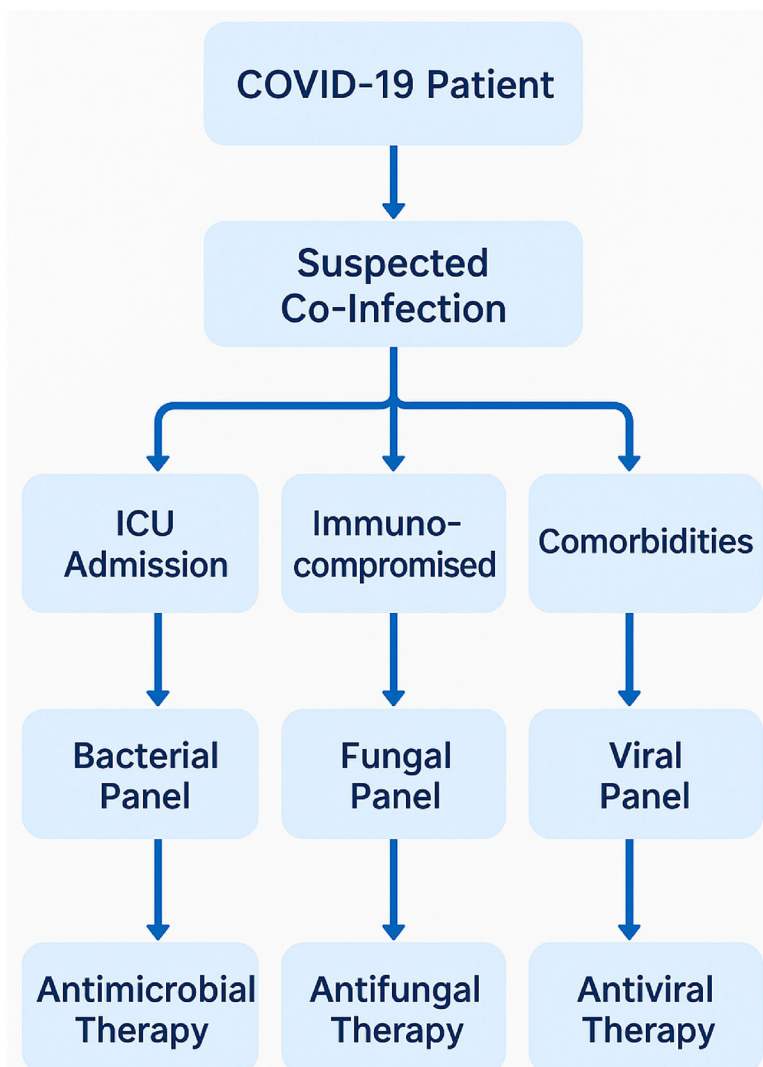


Fig 8 | A decision tree outlining diagnostic and treatment pathways based on patient phenotype

Table 4 | Impact of ASPs on resistance and antibiotic use

Metric	Before ASP (%)	After ASP (%)	Relative Change
Broad-spectrum antibiotic use	68	42	↓ 38%
MDR organism incidence (ICU)	22	17	↓ 23%
Unnecessary antibiotic prescriptions	44	25	↓ 43%
The mean length of hospital stays	12.4 days	10.2 days	↓ ~18%

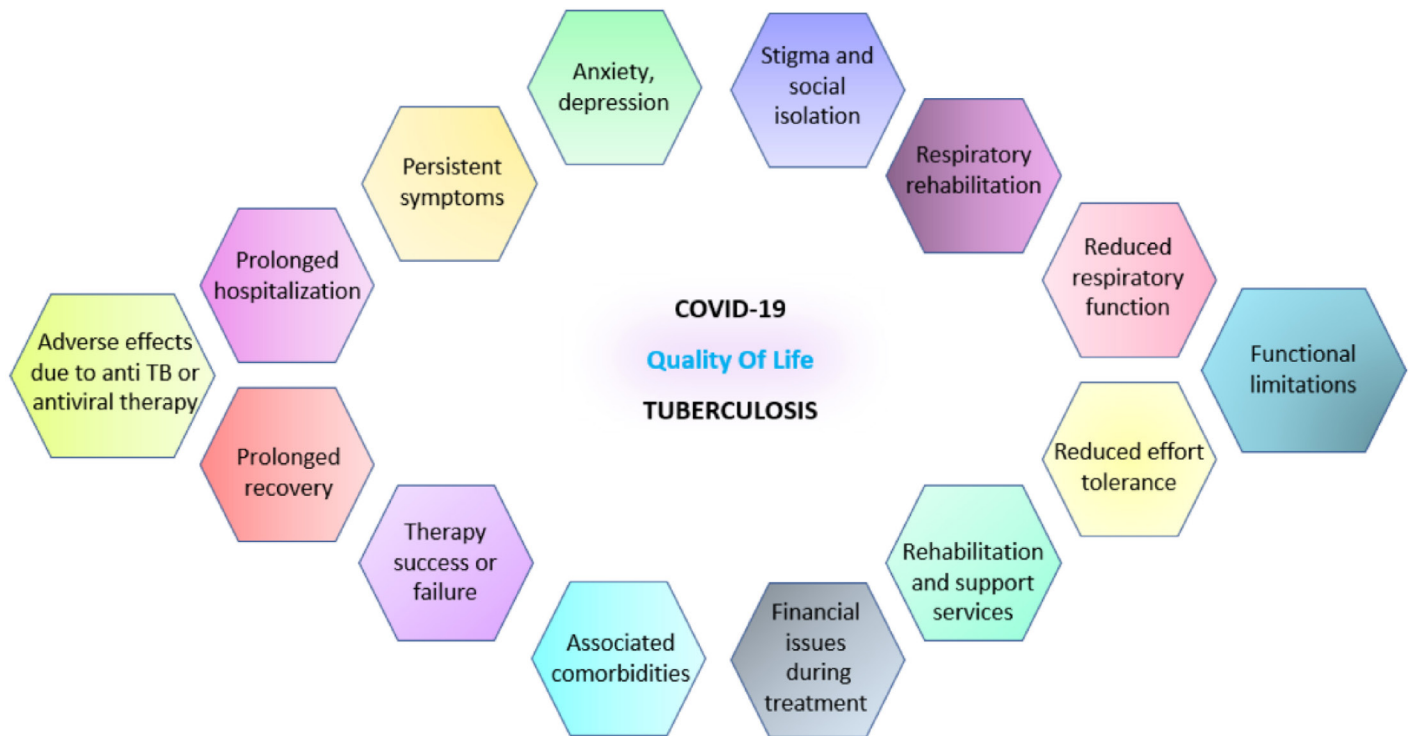


Fig 9 | COVID-19 and TB coinfection³⁷

using chronic medicine for autoimmune conditions are at an increased risk of infection.¹² For these individuals, COVID-19 symptoms can be different because not all start right away, and they tend to get secondary infections like invasive fungal diseases (aspergillosis or Candida).⁴ Taking immunosuppressive medicines like rituximab helps the virus to stay longer in the body and weakens the body's defenses, which calls for extended isolation and regular viral load tests.¹⁵

Pediatric and Geriatric Considerations

Respiratory infections often occur in children together with viruses such as RSV, adenovirus, and rhinovirus. Bronchiolitis and pneumonia, which are common in infants, are more likely to occur among infants who have pediatric COVID-19 but also suffer from another infection at the same time.²⁸ Unlike younger people, elderly patients can show atypical symptoms such as delirium or lack of appetite, and they are more likely to suffer from bacterial infections, often resulting in hospital admission (Figure 10). Students often have many conditions and take several drugs, which can complicate the right choice of an antimicrobial and how well it is tolerated by their bodies.³⁸

Research Gaps and Future Directions

Need for Enhanced Surveillance and Microbiological Data

Research related to other illnesses associated with COVID-19 is expanding, though major gaps persist in tracking and reporting cases. Strong systems for tracking infections and pathogens together in many health care facilities are missing in many low- and middle-income countries.¹⁵ Because there are no

standard ways to define cases or make diagnoses, it is difficult to compare data across countries, which limits the general usefulness of study findings.²²

Development of Integrated Management Protocols

Nowadays, doctors usually treat COVID-19 along with other infections separately, without considering what other infections may be present. We need integrated guidelines to manage polymicrobial infections by considering how to combine antiviral, antibacterial, and antifungal medications. Risk assessment, decisions based on biomarkers, and coordination between experts are valuable for these protocols to improve patients' results and lower the chance of negative outcomes.³⁰

Investment in Rapid Diagnostics and Resistance Monitoring

Future studies need to focus on inventing and applying tests that can pinpoint SARS-CoV-2, plus common bacteria, viruses, and fungi found within infections, quickly and at clinics. They would lower the risk of misdiagnosis and make it possible to start the right treatment earlier.³² Continued monitoring of AMR patterns during the pandemic is needed to help with drug stewardship and hinder further quickening of resistance.¹⁸

Preparing for Future Pandemics with Coinfection Awareness

Because of the COVID-19 pandemic, it is crucial to include cases involving several diseases in approaches to pandemic readiness. Planning in public health needs to support continuous supplies of antimicrobials,

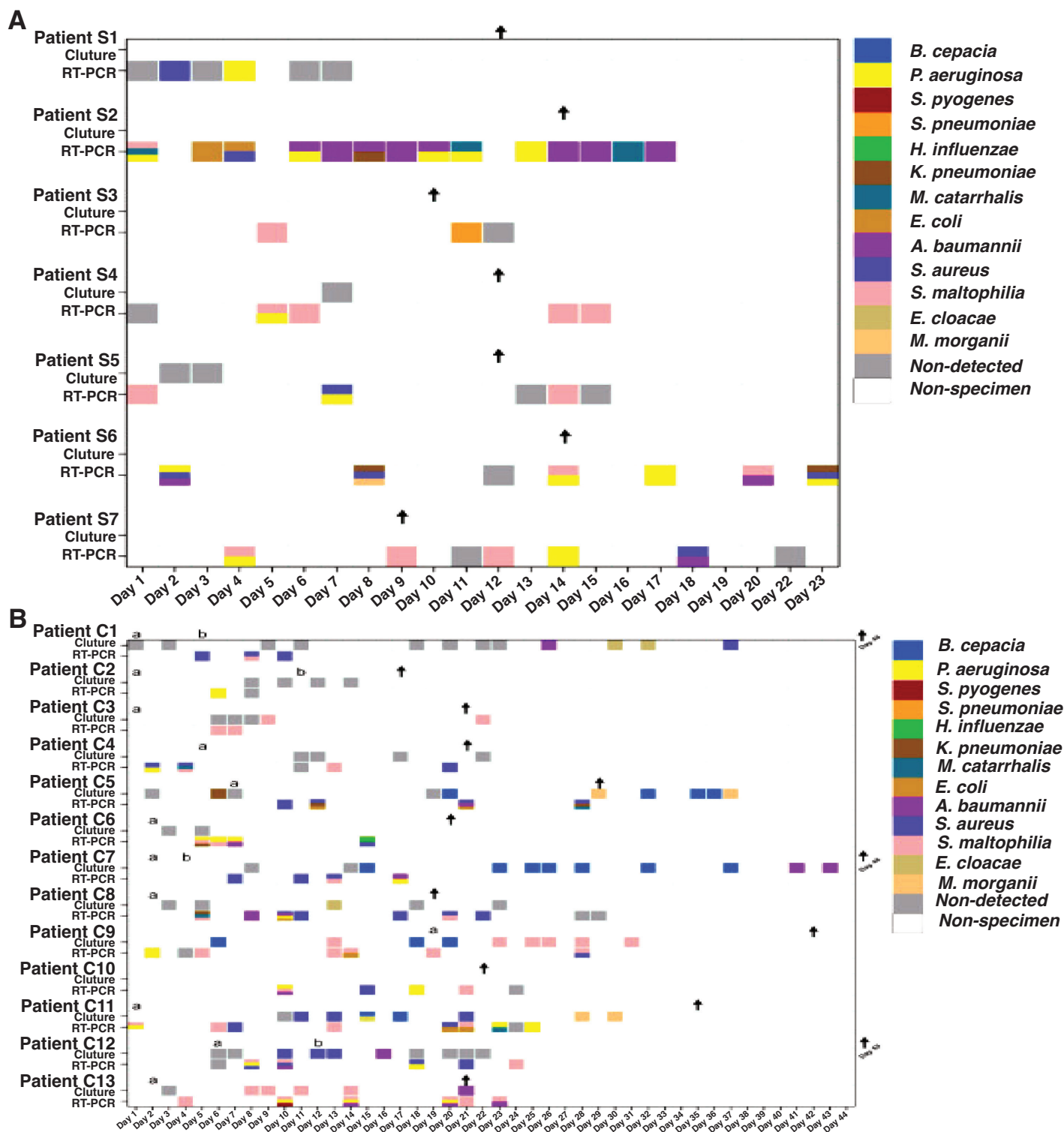


Fig 10 | Comparative bar graph of ICU admission, mechanical ventilation, and mortality rates in monoinfected vs. coinfecting COVID-19 patients³⁸

increase vaccination rates for respiratory infections (e.g., influenza and pneumococcus), and train health care workers how to recognize and deal with patients who have more than one infection at a time.²⁶ Adding these elements to current plans will better prepare us for upcoming respiratory virus outbreaks that might greatly affect treatment outcomes due to coinfections.⁵

Conclusion

Summary of Key Findings

The presence of multiple infections in COVID-19 patients affects how serious the disease is, its outcome, and the amount of hospital resources required. Regardless of where people are treated, coinfections with bacteria, viruses, and fungi have been linked with higher

chances of serious complications, respiratory distress, sepsis, and death. Patients who have two different viruses are more likely to need intensive care and remain on loud ventilation devices, which shows why medical staff must monitor these cases closely.

Importance of Early Detection and Rational Therapeutics

Identifying coinfections early and accurately is important for caring for patients, but this is difficult because of similar symptoms and challenges in getting diagnoses. Use of antimicrobials, monitored by biomarkers like PCT and your judgment as a clinician, is important to stop using antibiotics when they are not needed. Treating these patients well depends on joining knowledge from infectious disease, critical care, and microbiology.

Call for Sustained Research and Clinical Guideline Updates

Because the pandemic and its coinfections are changing, keeping research going allows us to refine methods and continue validating approaches to manage cases. Regular updates to clinical guidelines, using new information and real-world experiences, can aid health care providers in giving correct and up-to-date care to patients. Collaborating with other countries worldwide and sharing data will be essential to get ready for future cases of pandemics with coinfections.

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