Combined prevention and treatment measures are essential to control nosocomial infections during the COVID-19 pandemic

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Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a highly contagious positive-sense, single-stranded RNA virus that has rapidly spread worldwide. As of December 17, 2023, 772,838,745 confirmed cases including 6,988,679 deaths have been reported globally. This virus primarily spreads through droplets, airborne transmission, and direct contact. Hospitals harbor a substantial number of confirmed coronavirus disease 2019 (COVID-19) patients and asymptomatic carriers, accompanied by high population density and a larger susceptible population. These factors serve as potential triggers for nosocomial infections, posing a threat during the COVID-19 pandemic. Nosocomial infections occur to varying degrees across different countries worldwide, emphasizing the urgent need for a practical approach to prevent and control the intra-hospital spread of COVID-19. This study primarily concentrated on a novel strategy combining preventive measures with treatment for combating COVID-19 nosocomial infections. It suggests preventive methods, such as vaccination, disinfection, and training of healthcare personnel to curb viral infections. Additionally, it explored therapeutic strategies targeting cellular inflammatory factors and certain new medications for COVID-19 patients. These methods hold promise in rapidly and effectively preventing and controlling nosocomial infections during the COVID-19 pandemic and provide a reliable reference for adopting preventive measures in the future pandemic.
INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), a highly contagious single-stranded RNA virus, rapidly spread worldwide, leading to an infection known as coronavirus disease 2019 (COVID-19). This viral infection manifests in various symptoms, including cough, fever, chest discomfort, and, in severe cases, respiratory distress syndrome\textsuperscript{[1]}. As of December 17, 2023, 772,838,745 confirmed cases including 6,988,679 deaths have been reported globally\textsuperscript{[2]}. This directly threatens human life and health and presents new challenges to the healthcare systems. Hospitals, with their dense population and mainly inadequate ventilation, provide an environment conducive to viral transmission\textsuperscript{[3]}, primarily through droplets, airborne particles, and direct contact\textsuperscript{[4]}. Hospitals frequently harbor numerous confirmed COVID-19 cases, including asymptomatic carriers, posing a threat of intra-hospital infections during the COVID-19 pandemic. Since the viral outbreak, multiple hospitals have reported COVID-19 infections. For instance, the University Hospital of Muenster (UHM) witnessed an intra-hospital attack of novel coronavirus infections in its pediatric dialysis unit, involving 48 cases\textsuperscript{[5]}. Nine contacts tested positive for laboratory-confirmed COVID-19 infection, while two cases who tested positive remained asymptomatic. Eleven patients reported flu-like symptoms, while their testing result was negative. Between January 1 and February 9, 2020, 110 out of 9,684 healthcare workers at Wuhan Tongji Hospital tested positive for COVID-19\textsuperscript{[6]}, reflecting an infection rate of 1.1%.

Hence, there is an urgent need to develop effective measures to control intra-hospital transmission of SARS-CoV-2. The initial distribution of vaccines by the end of 2020 significantly reduced the rates of hospitalization, mortality, and infection rates, proving to be the most effective tool against the COVID-19 pandemic. While disinfection methods have played a crucial role, practical implementation is necessary. Implementing disinfection practices not only aids in the current pandemic but also serves as an efficient strategy for the future similar outbreaks.
PREVENTION MEASURES

Vaccination for infection prevention

With the continuous mutation of SARS-CoV-2 and the emergence of variants of concern (VOC), effective and safe vaccines are paramount in controlling the COVID-19 pandemic\(^7\). According to the data released by the World Health Organization (WHO) on March 28, 2022, 153 vaccines have been authorized for clinical trials, while 196 vaccines are undergoing preclinical trials. These COVID-19 vaccines mainly fall into several categories: inactivated vaccines, viral vector vaccines, RNA vaccines, DNA vaccines, protein subunit vaccines, and virus-like particle (VLP) vaccines\(^8\). As of March 28, 2022, a total of 10 vaccines (including 3 Indian vaccines) comprising inactivated, viral vector, mRNA, and protein subunit vaccines have been approved by the WHO for emergency use (Table 1). Pharmaceuticals such as Pfizer-BioNTech's BNT162\(^9\), Oxford-AstraZeneca’s AZD1222, Sinovac’s CoronaVac, Moderna’s mRNA-1273, Johnson & Johnson’s Ad26.COV2.S, Sputnik-V, and adjuvanted recombinant protein nanoparticle Novavax\(^10\), are leading the remarkable research and development efforts against COVID-19\(^11\). At present, 242 vaccines targeting COVID-19 are undergoing clinical research, involving 46 in Phase III and 46 in Phase IV trials\(^12\). Vaccination has been recognized as a crucial preventive measure against exposure to SARS-CoV-2 infection. Improving and optimizing existing vaccines and developing new ones will be highly efficacious against COVID-19, aiding in ending the pandemic.

Disinfection as a preventive measure

Dynamic disinfection

Researchers have discovered the presence of SARS-CoV-2 on surfaces particularly in hospitals where COVID-19 patients were admitted, indicating the need for surface disinfection\(^13\). Adequate ventilation and air purification systems can reduce the risk of COVID-19 transmission. Ultraviolet (UV) light is a traditional method for air disinfection, which is simple to be used as an effective method against airborne bacteria.
However, its prolonged exposure can irritate human eyes, skin, and respiratory mucosa, leading to the decreased white blood cell count and the increased risk of skin cancer\cite{14}. Therefore, UV disinfection should be applied only in unoccupied areas. When inhaled, ozone competes with hemoglobin for oxygen in the bloodstream and harms human health, making it inappropriate for air disinfection in occupied spaces. Disinfectant sprays provide temporary effects on contaminated environments. Cleanrooms and central air conditioning systems with filtration are expensive and challenging to implement widely. Air disinfection machines utilize low-ozone, high-intensity UV lamps, electrostatic adsorption, negative ion generators, and air filtration systems to eliminate bacteria collectively in the air. Dynamic air disinfection, conducted without disrupting regular operations, helps maintain air cleanliness and reduces airborne microbial content\cite{15}. This method has been proved more effective than static UV disinfection. Air disinfection machines are harmless to humans, can operate in occupied spaces, are user-friendly, and are proper for utilization in grassroots-level hospitals, contributing to preventing and controlling COVID-19 infections\cite{16}.

*Precise disinfection*

Disinfection can promptly cut off the transmission routes of infectious diseases, while it should be conducted with scientific precision. If disinfection is not standardized and methods are incorrect, it may not control the epidemic and may even lead to additional health safety issues. Different disinfection methods are employed for various contaminants of the novel coronavirus, targeting indoor air, pollutants, surfaces of floors and walls, object surfaces, clothing and textiles, dining utensils, skin mucous membranes, and transportation tools. To date, numerous studies have concentrated on disinfection techniques. These studies mainly included assessment through air sampling before and after disinfection, as well as surface sampling of objects, to verify the effectiveness of the disinfection process\cite{17}. Excessive disinfection poses risks to personal safety. Spraying disinfectants on individuals without protective gear can lead to several diseases. There are potential risks if individuals inhale disinfectants or are
repeatedly spread with them all over their bodies\textsuperscript{[18]}, which can also result in environmental pollution\textsuperscript{[19]}. Microorganisms may develop drug resistance, diminishing the sterilization effect, and the chemical residues left in the environment are new sources of pollution, disrupting ecological balance if excessive disinfection is used.

\textit{Cold sterilization}

Cold chain systems play a vital role in maintaining food quality, extending shelf life, and reducing food waste. During the pandemic, the food cold chain systems could potentially serve as a medium for the transmission and infection of SARS-CoV-2. Despite the likelihood of foodborne transmission being lower than other transmission pathways, considering the substantial quantity of refrigerated foods transported across different countries and regions, cold chain transportation remains a significant risk factor that should not be overlooked. SARS-CoV-2 may persist on the surfaces of packaged food under cold processing and refrigeration temperatures for up to 60 days\textsuperscript{[20]}. Several imported cold chain products were tested positive for COVID-19 at Chinese customs. In June 2020, sealed packaging containing salmon in a cold storage area outside the Xinfadi Market in Beijing, China, was tested positive for SARS-CoV-2 RNA\textsuperscript{[21]}. Since the initial discovery of COVID-19 related to cold chain incidents in 2020, Guangzhou has reported a total of 283 COVID-19-positive cases related to the cold chain\textsuperscript{[22]}. Therefore, there is a need for virus sterilization methods specific to the cold chain environment to maintain its safety\textsuperscript{[23]}. At present, customs primarily use chemical disinfection as a sterilization method. Additionally, high-intensity ultraviolet-C irradiation has proven effective in deactivating SARS-CoV-2 at typical cold chain temperatures\textsuperscript{[24]}. Analyzing the resistance data of coronaviruses in the environment revealed the importance of disinfecting the patient’s living environment, potentially contaminated items, as well as waste, sewage, and excreta.

\textit{Management of talent development}
Monitoring and controlling nosocomial infections are crucial tasks for hospitals; individuals must implement effective surveillance and control plans tailored to their circumstances. Typically, epidemiologists, supervisors, and infection control personnel should collaborate to implement scientific monitoring and control measures. The current pandemic has revealed the persistent vulnerability of public health systems, particularly due to insufficient public health professionals, especially at senior levels. The imbalance in the development between medical and public health systems has resulted from the emphasis on medical treatment over prevention. This has led to a weakening of professional value, declining recognition, rapidly diminishing awareness, inadequate attractiveness of the profession, and a significant talent drain. These issues underscore the severe deficiency in the training and retention of public health professionals. Therefore, cultivating and managing public health talent in hospitals are exceedingly critical. To enhance the effectiveness of public health talent’s cultivation and management, we should emphasize the principle of prevention as the primary focus, combined with treatment. Allocating substantial resources and investments in preventive medicine education is crucial for fostering public health professionals[^23]. Establishing a comprehensive research system across the entire spectrum, including health assessment and exposure evaluation, rapid disease diagnosis and forecasting, standardized clinical research and trials, vaccine development and evaluation, population control strategies, health management, and regulatory formulation, is crucial. Additionally, building an emergency response mechanism and promptly assembling specialized public health emergency teams comprising epidemiologists, infection control specialists, and public health managers are essential[^26]. Given the analysis of the pathogenic mechanisms, transmission routes, and resistance characteristics of the novel coronavirus, prompt disinfection of places before viral transmission is imperative to sever the transmission pathway. Additionally, routine disinfection of air and items in contact with infected individuals by staff members is essential. Environmental areas where cases have been isolated, living quarters, transportation, and objects touched by the infected should undergo specific disinfection.
Professional disinfection personnel must disinfect and handle the contracted areas after thorough isolation. The disinfected regions and contact points must be entirely free of viruses.

Furthermore, encouraging interdisciplinary collaboration and exchanges among professionals from diverse disciplines, such as medicine, public health, and psychology is critical\textsuperscript{[27]}. Engaging in co-designed and executed training programs, along with regular multidisciplinary seminars and case analysis sessions for senior management and potential leaders, are essential components of leadership and crisis management training\textsuperscript{[28]}. Periodically evaluating the performance of management personnel and providing feedback and advice may assist in enhancing their decision-making and team management skills. Providing scholarships, research opportunities, and domestic as well as international exchange programs for public health workers may encourage innovative thinking and the application of new technologies. This fosters their enthusiasm for learning and innovation. Moreover, prioritizing management of mental health and professional burnout is also essential. Providing psychological support and stress management training for frontline medical and public health workers, devising rational work schedules, and implementing rotation systems may prevent professional burnout\textsuperscript{[29]}. Additionally, ensuring adequate and equitable resource allocation, judicious distribution of human resources, and ensuring sufficient professional personnel in critical positions are vital. Adapting training content and methods flexibly based on changes in the epidemic and new characteristics of public health challenges may enhance the adaptability and efficiency of public health personnel. These strategies enable effective training and management of hospital public health personnel to confront the challenges posed by the novel coronavirus and prepare for the future public health crises.

\textbf{TREATMENT MEASURES}

\textit{Therapies targeting inflammatory cytokines}
During SARS-CoV-2 infection, some cases with chronic illnesses may experience 'cytokine storm'. This severe immune response involves releasing numerous cytokines in the body, resulting in intense inflammation, which can lead to multi-organ failure even death\[^{30}\]. Therefore, managing the cytokine storm is a crucial aspect of COVID-19 treatment. There are several treatment measures for addressing cytokine storm and inflammatory response in COVID-19 patients. Corticosteroids, such as dexamethasone, can suppress the inflammatory response, reducing the mortality rate in patients requiring mechanical ventilation, and they are utilized to treat severe and critical COVID-19 cases\[^{31}\]. Some cytokine inhibitors (e.g., tocilizumab and sarilumab), which are interleukin-6 (IL-6) receptor antagonists, can be used to treat critically ill COVID-19 patients, improving survival rates\[^{32}\]. These medications can inhibit the IL-6 signaling, thereby alleviating inflammation. Baricitinib, a JAK inhibitor, can block inflammatory signal transduction and is used in the treatment of early-stage COVID-19 patients\[^{33}\]. Studies demonstrated that mesenchymal stem cell therapy might be beneficial for treating severe COVID-19 patients, particularly in suppressing inflammation and promoting tissue repair. However, the application of mesenchymal stem cell therapy is still under investigation, and its safety and efficacy require further clinical validation\[^{34}\]. Additionally, healthcare professionals need to consider specific factors, including the severity of patients' condition and existing underlying diseases. A recent article published in *World Journal of Virology* by Shanmugavel Geetha *et al* studied and demonstrated a positive correlation between elevated inflammatory markers, including C-reactive protein, ferritin, and D-dimer, and the rate of invasive and non-invasive mechanical ventilation among COVID-19 patients with chronic kidney disease (CKD), suggesting that these inflammatory biomarkers may be used as clinical tools to guide the diagnosis and management amongst stage IIIb-V CKD patients with COVID-19 disease\[^{35}\]. Their specific treatment measures should be conducted based on clinical guidelines and professional medical advice to ensure safety and efficacy of treatment.

*Other new drug treatments*
Remarkably, with the ongoing development of new research findings and clinical practices, an increasing number of novel methods and medications for treating COVID-19 have emerged (Table 2). Consequently, healthcare professionals need to stay updated with the latest research advancements and guidance from health authorities to promptly adjust their treatment protocols. Remdesivir, a broad-spectrum antiviral drug initially used for treating Ebola virus infection, has exhibited to inhibit SARS-CoV-2 replication and reduce viral load when administered preventively or in the early stages\(^{[36]}\). Oral antiviral drugs, such as Molnupiravir and Paxlovid, significantly reduce the rates of hospitalization and mortality, and they can be utilized for treating mild-to-moderate COVID-19 cases, particularly for treating patients who are at the high-risk of severe illness\(^{[37]}\). Monoclonal antibodies (e.g., Bamlanivimab and Etesevimab) used in early infection prevent virus binding to host cells, impeding viral replication\(^{[38]}\). Another combination, Casirivimab plus Imdevimab (REGN-COV2), is used for treating mild-to-moderate COVID-19 cases. Immunosuppressants, such as cyclosporine and other immunomodulators, may assist in tempering an overactive immune system, while their usage requires careful consideration and guidance by healthcare professional\(^{[39]}\). Convalescent plasma therapy, using the plasma from recovered individuals containing antibodies capable of neutralizing the virus, is also noteworthy, which may alleviate the cytokine storm by removing inflammatory mediators and cytokines from the patient’s blood\(^{[40]}\).

When using these medications, individual patient differences, drug tolerability, potential complications, and drug interactions must be thoroughly considered. Importantly, all new therapeutic interventions should be employed in appropriate clinical trials and in accordance with recommendations from national health authorities, following the latest guidelines from international organizations, involving the WHO. As the situation evolves and research progresses, treatments for COVID-19 will continue to be updated and refined.

CONCLUSION
During the COVID-19 pandemic, healthcare-associated infections posed a significant challenge in the hospital. COVID-19 could spread through direct contact with the patient’s blood, body fluids, respiratory droplets, and virus-contaminated surfaces. However, the combination of high population density and a large susceptible population has led to hospitals frequently encountering a significant number of diagnosed COVID-19 cases and asymptomatic carriers. This poses a serious threat of nosocomial infections during the pandemic. Therefore, reducing infections in healthcare facilities remains an urgent and formidable task for healthcare providers.

This study explored some primary strategies for preventing and controlling hospital-acquired COVID-19 infections (Figure 1). Firstly, vaccination plays a crucial role in preventing and controlling COVID-19, reducing the rates of hospitalization, mortality, and infection. Secondly, effective disinfection methods also play a vital role, interrupting the transmission chain through dynamic, targeted, and low-temperature disinfection approaches. Thirdly, nosocomial infection management is a also critical component of healthcare quality control. Particularly in high-risk populations with inadequate preventive measures, early detection of mild and asymptomatic cases is paramount in the current stage of epidemic prevention and control. Adherence to safety distances, isolation measures, adequate supplies, and a well-functioning healthcare system are crucial preventive measures for hospital-acquired infections. When treating infected patients, healthcare workers must consider patients’ specific conditions, including illness severity, potential complications, and underlying health conditions. These treatment measures should be guided by clinical guidelines and professional medical advice to guarantee patient safety and treatment effectiveness. As scientific technologies advance, strategies for COVID-19 prevention and control, as well as novel public health interventions, will continue to evolve and enhance. Integrated prevention and treatment approaches will be instrumental in managing nosocomial infections during the ongoing COVID-19 pandemic.
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