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Review Study

Medical and Pharmacological Evaluation of Infection Control in Covid-19 Patients

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ABSTRACT

Unfortunately, many medical staff in hospitals and referral centers became ill, and some died due to frequent encounters with patients and severe cases of the disease. In the meantime, the issue of the spread of nosocomial infections should never be overlooked, and it should be thought that all attention should be focused on coronavirus, as the interaction between the virus and other strains of nosocomial infections is completely unknown. These measures are especially important in intensive care units for the care of Covid-19 patients, because the spread of this infection in these wards is strongly and exponentially associated with high mortality due to the disease. The outbreak of Covid-19 disease affected almost every country in the world, leading to more than 44 million cases and 1.2 million deaths by the end of October 2020. Another important point is the application of special and intensive protocols in the referral centers of patients in such a way as not only to prevent the spread of infection from disease to another patient but also to minimize the chances of infection of care and treatment personnel.

GRAPHICAL ABSTRACT
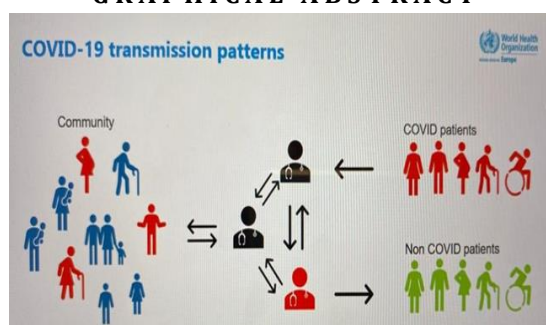
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Introduction

Unfortunately, a significant part of the medical staff in hospitals and referral centers became ill, and some died due to frequent encounters with patients and severe cases of the disease. These measures are especially important in intensive care units for the care of Covid-19 patients, because the spread of this infection in these wards is strongly and exponentially associated with high mortality due to the disease (Figure 1 and 2) [1-3].
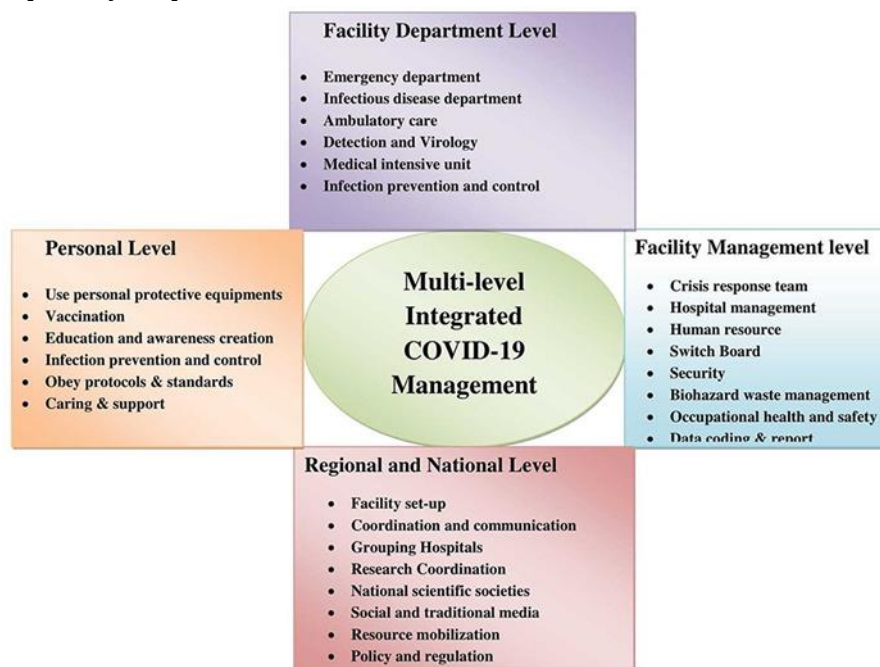

Figure 1: Multidisciplinary effort and integrative preparedness [4]
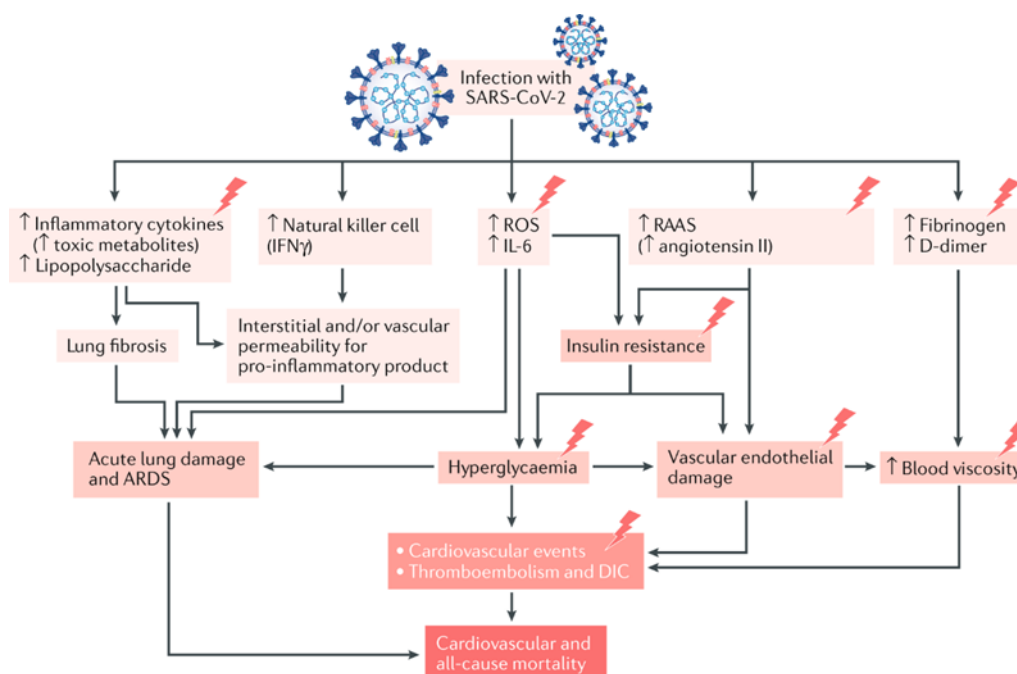

Figure 2: COVID-19 and diabetes mellitus: from pathophysiology to clinical management [5]

Unfortunately, in developing countries, the arrangements available in the intensive care units have been few and far between and did not meet the high volume of referral patients [5-7]. This issue, along with the lack of proper management of infection control in these sectors, has led to high human casualties due to the disease, which point reports from some of these countries fully support the claim [8-10] (Figure 3 and 4). What we are dealing with in the present systematic review is, first of all, addressing the challenges related to infection control in the intensive care

units, and then the instructions and guidelines related to solving these challenges that have been presented so far will be reviewed and summarized [11-13].
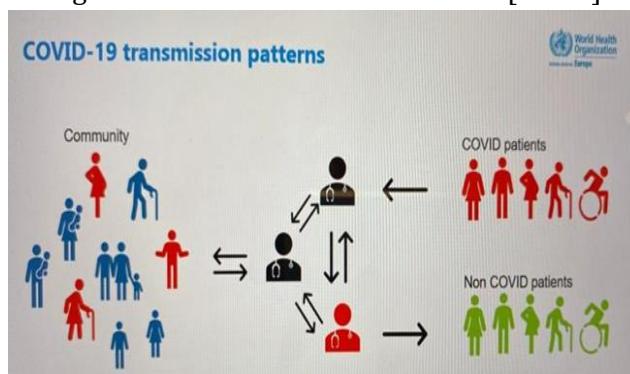

Figure 3: CEI-WHO from guidance to action: stepping up infection prevention and control in healthcare [12]
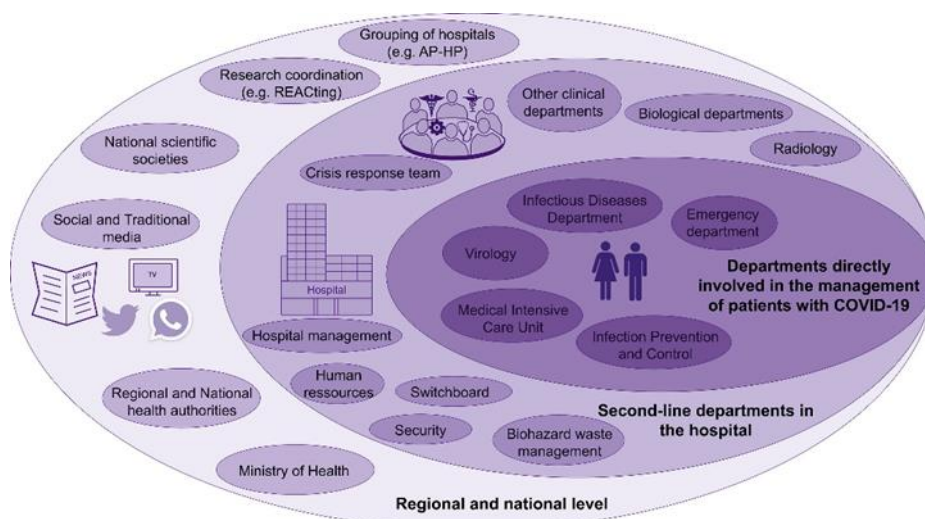

Figure 4: Challenges and issues about organizing a hospital to respond to the COVID-19 outbreak [13]

Bloodstream infection, or 'sepsis', sometimes called blood poisoning, is a dangerous and serious immune reaction caused by the release of immune chemicals into the bloodstream to fight infection and can lead to death. Inflammation caused by a blood infection causes the arteries to become perforated and clots to form, resulting in insufficient blood flow to the body's organs and the organs to be disrupted by a lack of oxygen and nutrients. In acute cases, blood pressure drops to such an extent that the heart becomes weak and suffers from septic shock (Figure 5 and 6). In this case, the liver, kidneys, lungs and other vital organs fail. Studies show low levels of vitamin C in patients with sepsis; Therefore, these patients are advised to take vitamin C supplements to strengthen the immune system. Vitamin C also improves capillary function in patients [14].
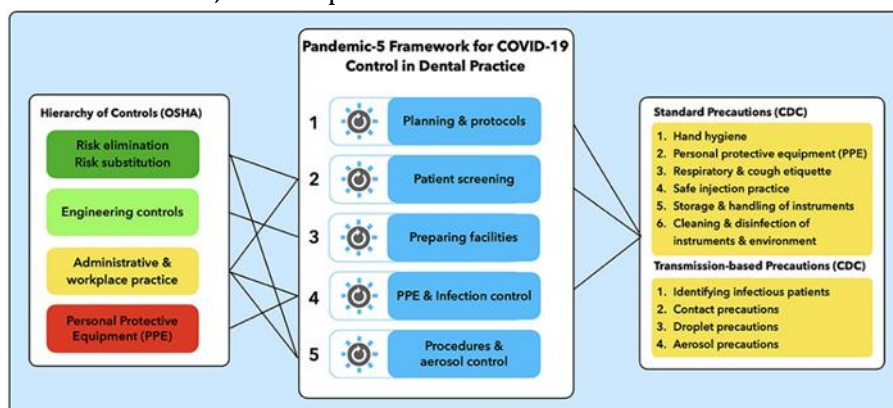

Figure 5: Systemic Management of Pandemic Risks in Dental Practice [14]

Figure 6: Visual guide to safe PPE according to guidance on infection prevention [15]

Material and Methods

The main issues focused in our systematic review were:

1. The main issues and challenges of infection controls in intensive care unit's referral for Covid-19 patients,

2. Nosocomial infections associated with COVID-19 in the intensive care units,

3. Severe COVID-19 and healthcare-associated infections on the ICU

4. The strategies and considerations for preparing the intensive care units for admitting Covid-19 patients, and

5. Physical interventions to interrupt or reduce the spread of the coronavirus in intensive care units. The current systematic review followed the principles of the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" guideline. First, all manuscripts related to Covid-19 were deeply searched by the two reviewers using the related keywords including "Covid-19", "infection control", "intensive care unit", "guideline", "strategy" and "management" in the international manuscript databases such as Web of Knowledge, SCOPUS, Web of knowledge (ISI), PubMed, Google Scholar, and Cochrane database. Any disagreement across our reviewers was rechecked by the third reviewer as the final arbitrator. The details of eligibility and the reasons for excluding the papers were shown schematically (Figure 7).

The primary criterion for selecting articles was their relationship with infection control (related to both coronavirus and other nosocomial infections) in intensive care units and the presence of one of the keywords in the title of the article. In the inclusion criteria for selecting the articles were:

1- English language papers,

2- The articles with complete structure and contents,

3- Access to the full text of the article. Thus, the manuscripts with only abstract availability or with incomplete information were not included into our review. The retrieved articles were placed in Endnote software and then duplicate

and shared articles were removed in the foreword databases.

Finally, the obtained information was categorized and analyzed by descriptive statistics and content analysis [15]. Of the 132 articles available, a total of 97 full-text articles were retrieved and placed at Endnote. After considering the inclusion and exclusion criteria and eliminating duplicate and

common articles in the foreword databases (82 articles), 50 articles were obtained and finally assessed. At this stage, all obtained articles were studied separately and the type of article and the main axis of the article were reviewed and extracted [16].
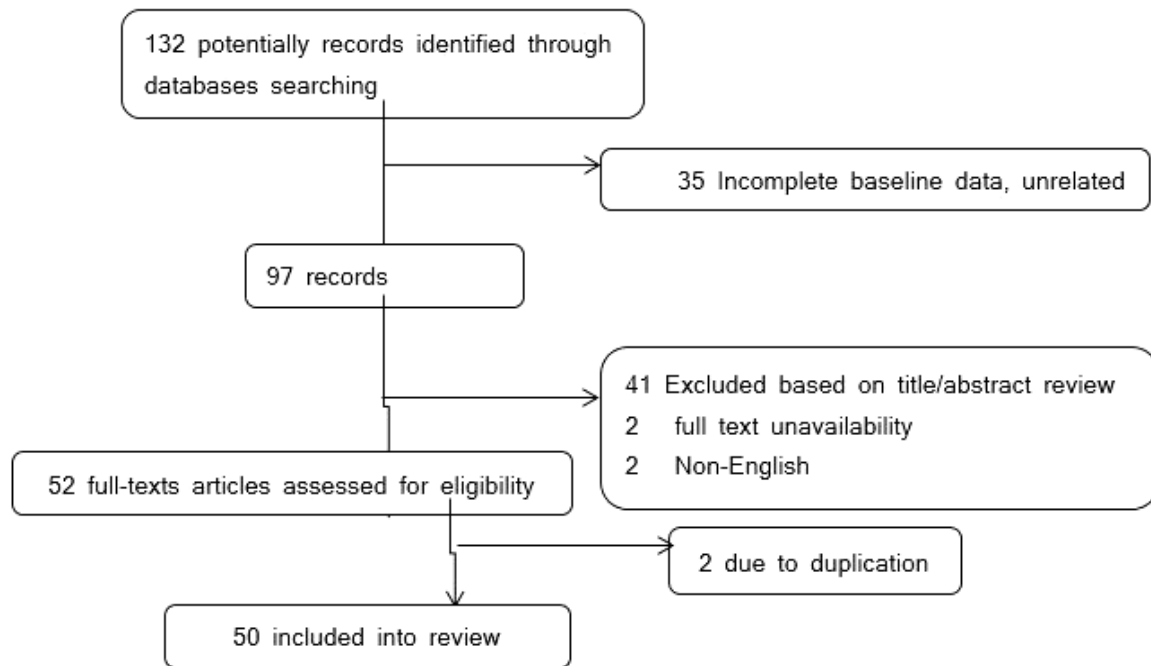

Figure 7: The flowchart of screening the eligible studies

Results and Discussion

The main challenges of infection controls in ICU s referral for Covid-19

Challenges related to the management of Covid-19 in hospital referral centers, especially intensive care units, can be discussed in several ways, including initial distinguishing the cases candidate for admitting to ICUs, the suitable capacity of the wards, the triage of patients, the ICU staffing, the infrastructure of the ICUs, and proper background for education and research on Covid-19. The first challenge related to the management of infection control in ICUs is first the definitive diagnosis of patients admitted to these wards. In other words, turning suspicion to definitive level of disease is the initial issue in Covid-19 specific ICUs (Figure 8 and 9, Table 1).

In fact, distinguishing severe Covid-19 cases requiring ICUs admission and other community-acquired pneumonia seems to be now very difficult due to the commonalities between their

demonstrations [17]. According to recent guideline of the World Health Organization, the suspected patients for Covid-19 include "the evidence of fever or acute respiratory illness along with traveling to or residing in a location reporting community transmission, or contact with a confirmed or probable COVID-19 case in the 14 days before symptom onset" [18-20]. In this regard, the diagnosis of patients with severe condition requiring ICUs admission has been already remained as a major challenge. In this regard, it has been presented some scoring systems and criteria based on clinical, laboratory and imaging evidences to predict those who need to admit to ICUs [19]. However, none of these recommendations provides a basis for distinguishing between Covid-19 and other severe infectious diseases that are not sometimes differentiated from Covid-19 disease, so we may still see many patients being admitted with a true diagnosis of other respiratory infections [20]. In

this regard, the sensitivity of molecular and imaging modalities such as RT-PCR and CT scanning to diagnose critically ill patients are now questioned. Additionally, some technologies especially RT-PCR assays may not be available in many ICUs, and where available still take time to run [21]. It is clear that the optimal triage of patients to ICUs depends directly on the definitive diagnosis of really serious patients. Due to the limited capacity of ICUs and the high bed occupancy rate in countries with high rates of disease and most importantly, and in total ICU infrastructure, accurate identification of patients with the aim of minimizing the possibility of infection transmission between patients and from the patient to the treatment staff is very necessary and vital [22] (Figure 10).
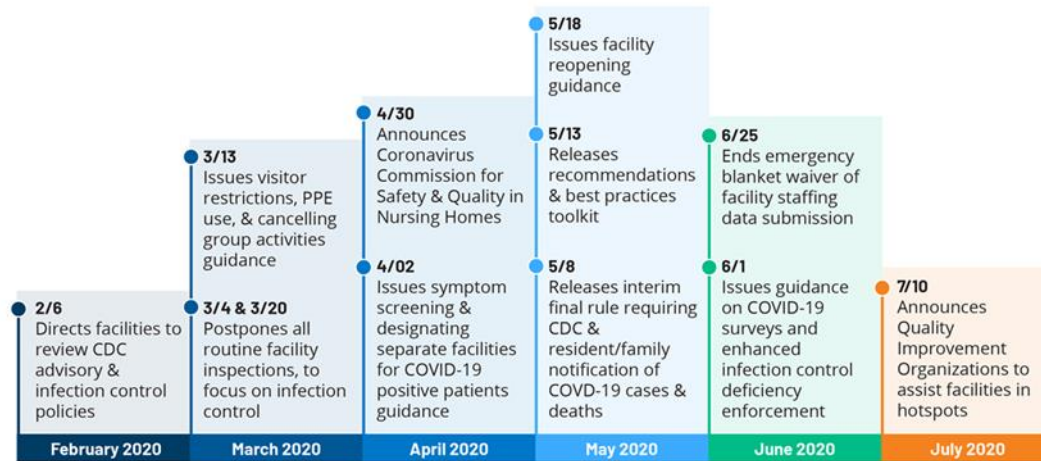

Figure 8: Key Questions About Nursing Home Regulation and Oversight in the Wake of COVID-19 [15]
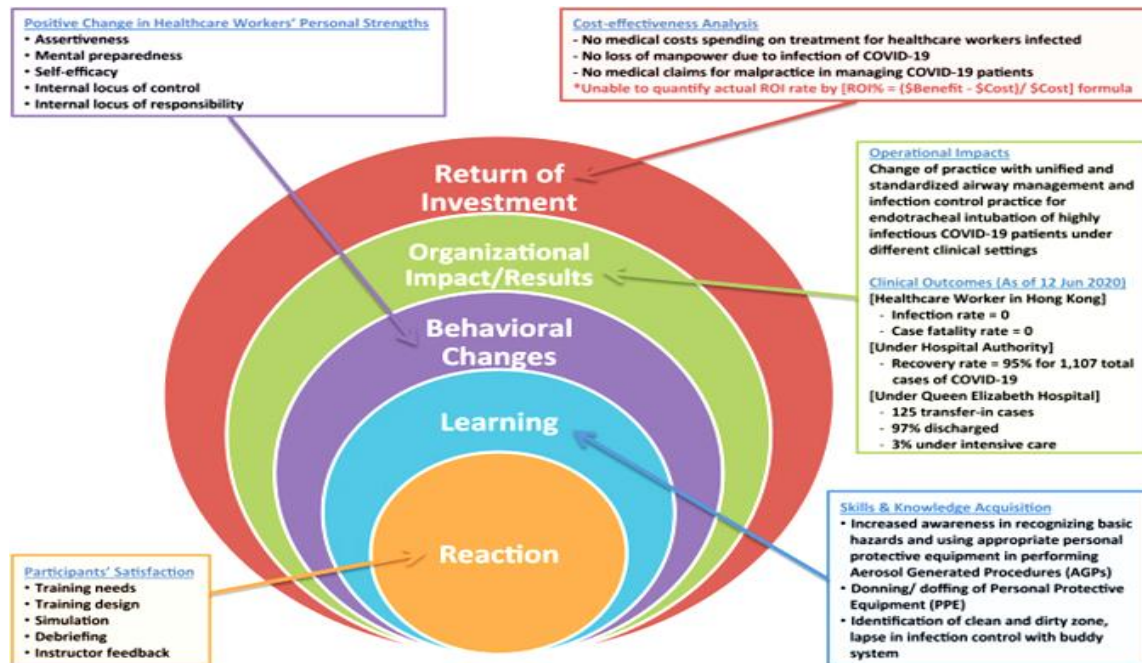

Figure 9: Investigating effects of healthcare simulation on personal strengths and organizational impacts [20]

Table 1: Results of search strategy in selected databases between 2011-2011 and identification of final articles

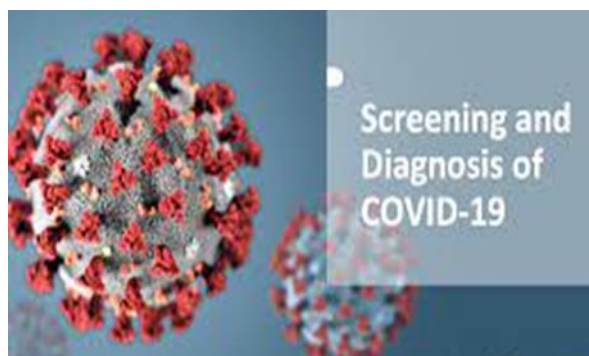| Database	Number of papers	Abstracts	Letters	Guidelines	Research papers
PubMed	26	6	1	1	18
Google Scholar	5	1	---	2	2
Web of Knowledge	12	2	1	2	7
SCOPUS	2	---	---	---	2
Cochrane database	5	---	---	4	1

Figure 10: Screening and Diagnosis of COVID-19 [1]

Another important issue in management of Covid-19 patients admitted to ICUs is the lack of specific recommendations on supportive ICU cares for such patients to minimize viral transmission [23]. One of the main concerns is high likelihood of aerosol generation by ICU supportive devices such as high-flow nasal cannula and non-invasive ventilation that are commonly used for ICUs patients [24]. In previous experiences on SARS infections, the use of such devices had led to high risk of nosocomial transmission of infection [25]. Although applying these supportive arms can effectively reduce tracheal intubation and thus mortality, due to their probable role in transmitting the infection in ICUs environment, the death rate especially in moderate to severe cases may be considerably raised [26]. Therefore, it is now believed that the use of this tool is safe for patients with mild disease severity [27]. In addition, due to high rates of viral transmission through intubation particularly to healthcare workers, thresholds for intubation in the event of deterioration and the absence of single rooms should be kept low [28]. Another important challenge related to infection control in ICUs is to divide the number of healthcare staff based on the capacity of the ICUs, the daily load of patients requiring admission, the mortality rate registered in the community and the facilities and equipment's available in the ICUs especially personal protective equipment's. As a main rule, the number of assistants and interns should be limited to reduce exposure. All indicators related to the ward, including bed occupancy rate, daily admission rate of patients, the ratio of ward capacity to the total hospital space, the possibility of expanding the space of the ICUs in the hospital environment, the

possibility of relocating staff and hiring and employing surplus staff should be considered [25].

Another challenge in the discussion of infection control in the wards is the indiscriminate use of various drugs, especially antibiotics in the management of Covid-19 disease due to the unavailability of an approved and definitive protocol for the treatment of the disease. This will be especially critical in countries and centers with high antibiotic resistance and high rates of immunocompromised patients admitted [29].

According to the reports released by some countries such as China and Iran, most of the Covid-19 patients admitted to ICUs were given empirical broad-spectrum antibiotics due to taking a long time between admission and laboratory diagnosis of COVID-19, a lack of proper and effective treatment protocol for disease control, and also the lack of distinguishing the disease from other viral and bacterial pneumonias [30].

Another important dilemma is the co-infection of Covid-19 with other microbial agents which may not be definitive at all. The rate of such co-infections has been reported in the range of 0.4% to 6.0%. In this regard, it has been strongly recommended to de-escalate such empirical antibiotic and anti-viral therapies based on microbiology test results and clinical response. Along with antibacterial and antiviral therapies exclusively used, the use of systemic corticosteroids in ICUs in most patients with Covid-19 is also a major challenge for infection control [31-33].

Although using corticosteroids can be very beneficial for patients suffering Covid-19 because of the inflammatory basis of the disease, the

administration of such medications may be also harmful. First, in patients with the fundament immuno suppressive state such diabetes mellitus or cancer patients. Second, it has been shown that the use of systemic corticosteroids may lead to delay viral clearance [34-36]. Third, such medication may even increase the risk for death due to other bacterial and viral infections such as bacterial pneumonia and influenza. As of this writing, corticosteroids have not been approved as a routine treatment regimen. This risk along with needing the use of mechanical ventilation (leading ventilator-associated pneumonia), needing to prolonged ICU stay, and also requiring repeated intubation in some cases can result in high nosocomial infection rates [37].

Another important issue is the need for continuous transfer of patients with Covid-19 between the ICUs and other hospital wards, especially imaging centers. Unfortunately, the use of portable imaging techniques such as ultrasound has been associated with little accuracy in assessing the presence or extent of involvement in the disease. There is a need for a chest CT scanning to assess the severity of pulmonary involvement of the disease with relatively acceptable sensitivity in almost all patients, as well as to screen people suspected of having the disease. This issue becomes more complicated when in some limited medical centers in underdeveloped countries, even transferring the patient for further evaluations to other centers is considered due to limited facilities. Such transfers can increase the risk of infection spreading from other departments to the ICUs and vice versa, which will be a major challenge in managing the infection control of patients.

Infrastructure ICUs especially in developing countries is another problem issue in controlling infection in ICUs. According to the literature, about one-third of ICUs in Asian countries had no proper airborne infection isolation room (with negative pressure relative to surrounding areas), the most important space for preventing the infection spreading. It is obvious that in the absence of such room, the patients had to be placed in adequately ventilated single rooms, but according to another reports, about 13% of ICUs in Asia had no such proper single rooms. As a cohort alternative, caring the patients in shared rooms with beds spaced apart can be considered, however such last alternative can be accompanied with high airborne transmission of coronavirus.

Another problem that is faced in countries with high morbidity and mortality, as well as frequent waves of disease, is burnout, chronic fatigue, and the development of anxiety disorders and depression among the medical staff of patients who admitted to ICUs. The risk of transmitting coronavirus to such personnel with high exposing the virus has been reported to be high. Long shifts, constant stress from the severe form of the disease, stress due to the possibility of transmitting the disease to family members, lack of adequate and complementary financial support for staff performance [31]. In the long run, such a problem will reduce the adherence and adherence of medical staff to infection control protocols in these wards and will not only increase the possibility of leaving these staff to continue to serve these patients, but also the possibility of transmitting the infection to patients and other staff. It will also increase treatment over time [32].

The final challenge from the perspective of the authors of this article regarding infection control is the lack of necessary and specialized training of assistants and other medical staff in the wards. Despite providing comprehensive and desirable instructions on how to manage infection control in these centers, methods to protect personnel against the risk of disease transmission to them, how to implement the best treatment protocols for patients and minimize the excessive and inappropriate use of antibiotics and also, instructions for the optimal use of the facilities available in the centers, as well as the necessary training to use the basics in many centers are not given. This has led to the spread of nosocomial infections along with severe coronavirus infection, causing high morbidity and mortality among staff and treatment staff (Figure 11) [33].
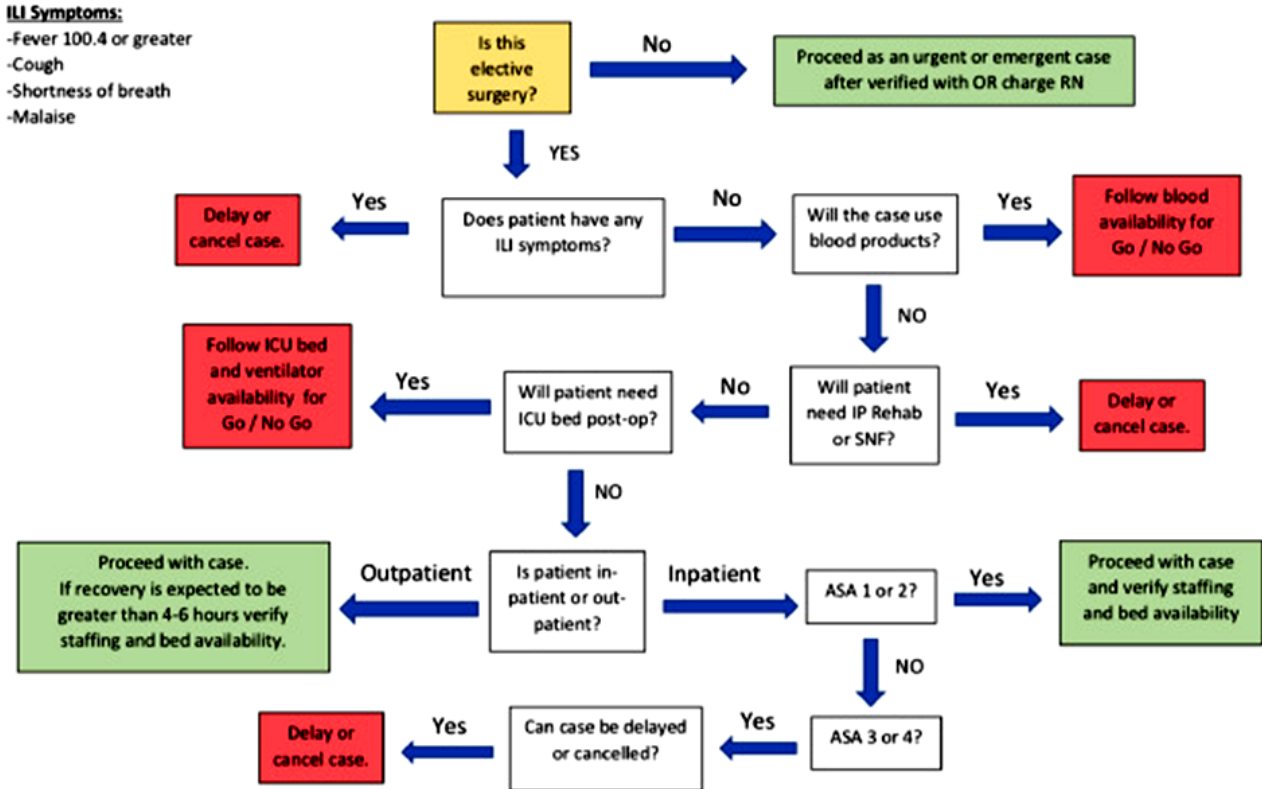
Elective Surgery Algorithm

ILI Symptoms:
-Fever 100.4 or greater
-Cough
-Shortness of breath
-Malaise

Figure 11: Addressing a national crisis: the spine hospital and department's response to the COVID-19 [7]

An overview of the proposed solutions to the infection control problem

To solve each of the mentioned challenges, solutions and instructions can be provided, some of which are presented in the guidelines and some in the articles. Based on each of the challenges presented, we will review some of these solutions [28].

1. Modification of patients' identification roots: It is obvious that due to the limited ability of admitting patients to ICUs and with the aim of minimizing the possibility of spreading the virus and other infections among hospitalized patients as well as the medical staff, accurate identification of patients based on risk level stratification is essential. In this regard, paying attention to some scoring systems for patients in need of hospitalization in the ICUs can be very helpful. Many logistic regression models have been employed to determine and weight the main determinants for requiring ICU admission of Covid-19 patients. Summarizing such scoring systems led to identify some clinical, laboratory, and imaging predicting indicators (Figure 12).

Aiding these scoring systems can differentiate the real patients need to intensive care and to ICU admission and therefore creating a better balance between the available facilities and the load of patients referred to the hospital. This balance is very effective in preventing the spread of infection in the relevant centers.

2. Modification of triage policy: recent triage strategies have been developed considering both patients' conditions and available clinical settings. In this regard, to achieving the best triaging Covid-19 patients especially those who needing intensive cares, some principles must be followed. First, trained and experienced ICU practitioners should be employed in the first line of patients' admission to ICUs and second, the most appropriate clinical decision support systems should be applied to select the best candidates for admitting to ICUs.

3. Modification of ICU staffing support strategies: As mentioned earlier, occupational, financial, and even psychological support for ICUs staff can reduce the risk of burnout by reducing the risk of burnout and their psychological consequences

can reduce the risk for infection transmitting. Maintaining a sense of responsibility for staff by encouraging them, sharing the right work and exercising reasonable shifts as well as holding psychological counseling sessions with them will be the supporting factors in achieving better

feedback and greater efficiency. Overall, minimizing the risk of infection is essential, not only because of the direct loss of manpower but because of the potentially devastating effect of staff infection on morale, which might result in absenteeism.
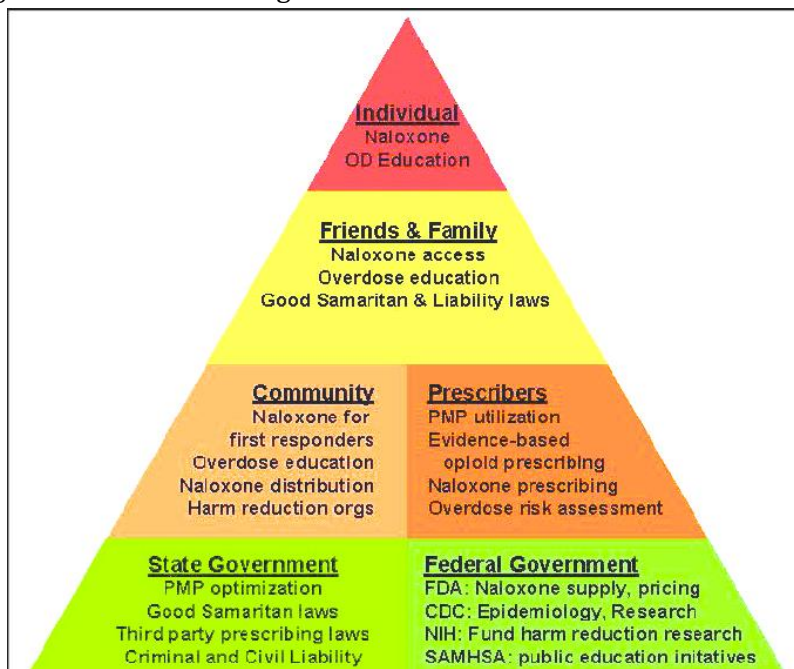

Figure 12: Harnessing implementation science to optimize harm prevention in critically ill children [26]

4. Modification of ICUs capacity: expanding and preserving the capacity of the ward, both in terms of physical space and in terms of sharing the available facilities, is necessary in order to reduce the risk of transmission of infections between people. Providing adequate beds for the ward, creating appropriate distances between the beds and in fact the optimal design of beds based on the area of the ward, providing proper ventilation, providing adequate isolated rooms, minimizing the connection between ICU wards and other hospital wards along with improvement of intensive care equipments are all desirable strategies for improving ICUs capacity. However, such strategies could not be applied in most developing countries and thus this issue has turned to a serious concern in Covid-19 patients' management and infection control [34].

5. Modification of oxygenation support: the protocols for oxygenation should be specialized for Covid-19 patients. It should be achieved by prolonged pre-oxygenation by minimization of bag-mask ventilation, rapid sequence induction

with muscle relaxants to reduce the likelihood of coughing, the application of closed suctioning systems after intubation to minimize aerosol spreading, using lung-protective ventilation supportive systems to reduce ventilator-related lung injuries, positioning the patients in prone situation, and using veno-venous extracorporeal membrane oxygenation.

6. Modification of antimicrobial prophylactic regimens: within the pandemics of Covid-19, more than 70% of infected patients received a wide range of antibiotics while only a few numbers of patients (about 8%) faced with superimposed bacterial or fungal co-infections. Such wrong protocols led to higher risk for transmitting multidrug-resistant microorganisms in ICUs. According to the latest WHO guideline, antibiotic prophylaxis should not be indicated for those who suffering mild or moderate COVID-19 unless the appearance of the symptoms or signs of bacterial infection. In severe cases of Covid-19 requiring ICU admission, the antibiotics use should be considered according to the host

immunity condition, the appearance of bacterial signs, in the elderly receiving long-term care facilities or in the children aged less than 5 years with moderate to severe disease state.

7. Modification in education and research plans: In order to raise the level of knowledge and attitude of medical staff about the risk of infection distribution and the importance of infection control in ICUs wards, informing through specialized workshops in this regard,

continuous publication of educational pamphlets and monitoring their performance in the wards should be considered by ICU managers. It is also important to focus clinical and laboratory researches on disease-related nosocomial infections, routes and strains associated with infection transmission, and ways to prevent the spread of infection in ICUs admitting Covid-19 patients (Figure 13).
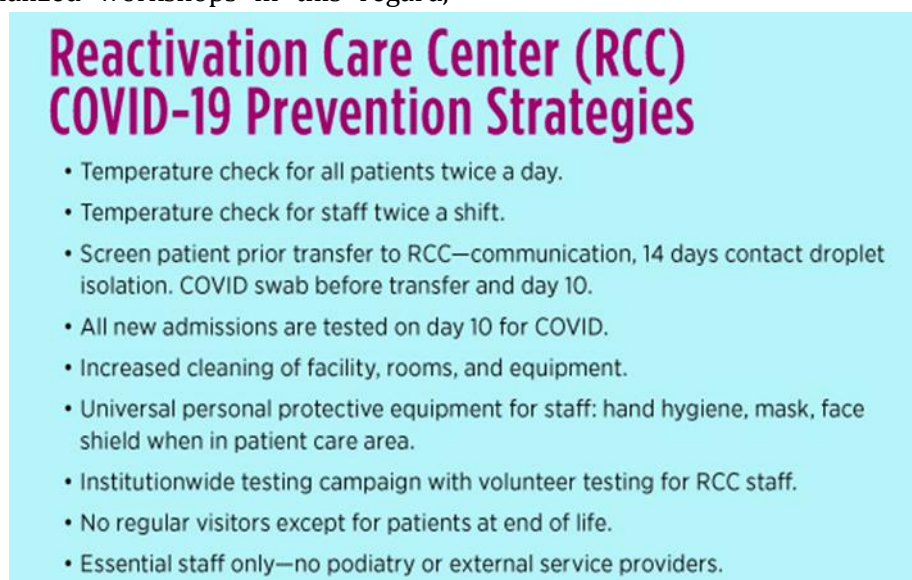

Figure 13: The Impact of COVID-19 in Long Term Care - Today's Geriatric Medicine [6]

Conclusion

High rates of nosocomial infections and the spread of Covid-19 infection in ICU wards have been reported during the disease pandemic. Regarding such a high risk of infection distribution in the relevant wards, various factors have been identified, including insufficient knowledge of staff about infection control methods, inappropriate and unprincipled triage of candidates for hospitalization in the special ward, insufficient access to isolated rooms, lack of optimal design of ICU wards in terms of connection with other wards, failure to use the necessary facilities to control infection in the ward and, most importantly, indiscriminate and unprincipled administration of antibacterial prophylactic drugs. Therefore, it seems necessary to develop comprehensive guidelines to prevent the spread of infection, whether it is the Covid 19 virus or nosocomial infections, as well as how to

screen and control related infections with emphasis on the items mentioned in this article.

Authors' contributions

All authors have contributed significantly and met criteria for authorship. All the authors read and approved the final copy of the manuscript.

Conflict of Interest

We have no conflicts of interest to disclose.

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