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Review on the biosafety measures for the prevention and control of SARS-CoV-2 infections in healthcare settings

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REVIEW ARTICLE

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ABSTRACT: **The novel corona virus, Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) is a deadly respiratory disease. The major causes of the rise of new variants of SARS-CoV-2 are genetic mutations and recombination. The club-shaped spike (S) projections of glycoprotein on the virus's envelope has interaction with the host cell's ACE2 (Angiotensin-Converting Enzyme 2) receptors to enable the entrance of infectious virus particles. With-Corona' is possible only when antiviral and vaccination are available. Disease prevention and control is based on new biosafety technologies and guidelines which improve ways to safely handle microbiological material. Corona pandemic is a serious biosafety event. Thus, biosafety is being valued worldwide and applied in medical field. This review presents the current biosafety standards of the COVID-19 pandemic in a comprehensive manner from a fragmented or wide variety of biosafety guidelines and articles available.**

KEYWORDS: **Corona Virus; COVID-19 (Corona Virus Disease 2019); Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) ; Biosafety measures**

INTRODUCTION

Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) is the cause for a deadly respiratory disease called coronavirus disease (COVID-19) [1]. It was confirmed in December 2019 in the City of Wuhan, Hubei Province in china at the first time as β strain [2]. It is an RNA virus, the seventh in corona virus family [3]. Out of these, four relatively 'benign' strains of human corona viruses causing mild respiratory flu like seasonal illnesses are (hCoVs) 229E, NL63, OC43, and HKU1 and three extremely pathogenic strains are (SARS-CoV, MERS-CoV (Middle East Respiratory Syndrome Coronavirus), and SARS-CoV-2) [4]. SARS-CoV-2 is the third corona virus outbreak that has emerged in the past 20 years, after SARS and MERS [5]. It belongs to family Coronaviridae and the order Nidovirales [4]. It is a highly infectious positive-sense, single-stranded RNA virus [6]. It has an envelope, single and positive-stranded RNA virus with a genome comprising 29,891 nucleotides, which encode the 12 putative open reading frames responsible for the synthesis of viral structural and nonstructural proteins [4].

SARS-CoV-2 has alpha, beta, gamma, omicron and delta variants. The Delta variant was the dominant variant in the second wave globally in 2021. The Omicron variants, primarily authenticated in November 2021 in South Africa, has initiated the 5th wave of global pandemics at a significantly higher rate than the Delta variant which had about 32 mutations were found on the spike of Omicron [7], The major causes of the rise of new variants of SARS-CoV-2 are genetic mutations and recombination [8].

The virus is transmitted through the air, through saliva droplets and aerosols originating during coughing and from clinical procedures [9]. There is a more efficient transmission of SARS-CoV-2 than SARS-CoV when symptoms are still minimal and restricted to the upper respiratory tract [10]. The most susceptible human population for corona is pregnant women, aged people, and immune compromised patients [8].

The key structural components of the pathologic strains include the membrane, envelope, nucleocapsid and spike proteins, sharing the core conservative elements across the corona virus family [11]. Corona viruses infect host cells by attaching to their surface and binding to membrane receptors, through the spike (S) proteins of the viral cone [12]. The club shaped spike (S) projections glycoprotein on the virus's envelope has interaction with the host cells ACE2 (Angiotensin-Converting Enzyme 2) receptors to enable the entrance of infectious virus particles [8]. COVID-19 and the renin-angiotensin system (RAS) are linked by angiotensin-converting enzyme 2 (ACE2), a key enzyme in RAS that has been validated as a SARS-CoV-2 receptor [13]. ACE2 receptor is expressed on the mucosa of the oral cavity (especially tongue epithelial cells), esophagus, respiratory tracts (especially alveolar epithelial cells), heart, kidney, intestine and lymphocytes. The virus binds to ACE2 play a central role in Renin-Angiotensin-Aldosterone System (RAAS) [5]. This system facilitates vasoconstrictive effect, ventricular hypertrophy, myocardial infarction, atherosclerosis, reactive oxygen species (ROS) generation, tissue inflammation and aldosterone synthesis results in sodium and water retention [14].

Complication of SARS-CoV-2 infection includes acute lung failure, acute liver failure, acute kidney damage, and cardiovascular illness, in addition to a wide spectrum of hematological abnormalities and neurological problems ([8]. SARSCoV-2 infection of the pancreas may promote acute and especially chronic pancreatic dysfunction that could potentially lead to new-onset diabetes [15]. The disease is not limited to the respiratory system but has widespread involvement including the gastrointestinal (GI) tract and liver [16].

"*Coronavirus disease-19 will never ever say goodbye to us*". 'With-Corona' is possible only when antiviral and vaccination are available [17]. Given the emerging nature of the virus, several repurposed agents were considered as potential antiviral agents for COVID-19 [18].

The disease prevention and control is based on new biosafety measures and guidelines which improve ways to safely handle microbiological material. In addition, a better understanding of the risks associated with manipulations of agents helps to apply appropriate biosafety practice [19]. Corona pandemic is a serious biosafety event. Thus, biosafety is being valued worldwide and applied in medical field [20]. The aim of this review is to present the current COVID-19 pandemic biosafety standards in an all-inclusive manner, drawing from a diverse range of biosafety guidelines and papers.

BIOSAFETY MEASURES FOR COVID-19 IN CLINICAL SETTING

1. Leadership and Administrative controls

Leadership should formulate proper standard operating procedures (SOPs) for the workers. Arrange training to aware the risk and safe handling of COVID-19 samples and the proper use of PPE (personal protective equipment) [1]. Deal with scarcity, who gets what, when, how, and who gets to decide on these matters [21]. Some administrative controls include obtain applicable approvals from biosafety committee to conduct research. When possible, use less hazardous materials in experiments, especially when unfamiliar methods are used. Procedures must be documented and record keeping is vital [19].

2. Personal Protective Equipment (PPE)

PPE is critical to protect healthcare workers (HCWs) from highly infectious diseases such as COVID-19 [22]. Eye protection can be done by wearing goggles, facial shields, or full-face elastomeric respirators. Mouth and nasal protection are conferred by N95/KN95/FFP2 (filtering face piece) or higher respirators. The protection offered by masks and respirators against particles larger than 0.3 μm is a surgical mask: 80%, FFP2: 94%, N95: 95%, FFP3: 99.9%, N100: 99.9% [3]. The indicated PPE respirators are N95, PFF2, PFF3, N99 or N100 a minimum efficiency of 98% of filtration of particles up to 0.3μm and bacteriological filtration efficiency greater than 95% [23]. Wear closed work shoes with non-slip soles and surgical boots for clinical use. Put on respirators or high-performance filtering masks (NF95, PFF2, PFF3, or equivalent). Put on clinical PPE such as a cap, a face mask that resists liquids, gloves, goggles, and shoe covers [9].

3. Reorganization of flows and routines

It should be necessary to make structural adjustments, such as enlarging the surroundings, rearranging traffic to accommodate patients, separating those who exhibit respiratory symptoms, and stepping up hand and environmental hygiene. Negative pressure air conditioning with at least 12 air changes per hour is required for intensive care unit (ICU) rooms. Diagrams, flowcharts, and photographs simulating the PPE donning and doffing procedures should be posted in the procedure places to make viewing easier. Posters on the PPE procedure could also be used [23].

4. Surface disinfection

The SARS-CoV-2 susceptibility on surfaces of different materials approximately at 4–5°C for > 28 days, 20– 22 °C (room temperature) for 3–9 days, and 30–40 °C for a few hours. It can survive in respiratory specimens at 20 °C for 5 days. It can survive at 4 °C for 21 days and able to survive in diarrheal stool samples for 4 days. It remains infectious for several days and few hours in suspensions and after drying respectively. The viruses were more stable on plastic and stainless steel (72 h) than on copper and cardboard (4– 8 h), in aerosols (3 h) [24].

Chemical and physical inactivation methods such as UV radiation, heat inactivation and detergents are assumed to be effective inactivation methods against SARS-CoV-2 [25]. The surface disinfection process should start with soap and water or neutral detergents to remove dirt and reduce the load of pathogens. Second, the use of disinfectants, the WHO recommends hydrogen peroxide, chlorine-based solutions & alcohol. Alcohols inactivate microorganisms by denaturation of proteins acting on the cell membrane [26].

WHO recommended two alcohol-based hand rub formulations (ethanol 70– 95% and 2-propanol 70–100%) had an efficient virucidal activity in less than 60 second (S) by more and equal 4 log10 (≥ 99.99) approximately and could be used for disinfection in public health and health-care facilities [24]. Ethanol 70–90% requires 30s–1 minute to be effective. Chlorine-based products (e.g., hypochlorite) at 0.1% (1000 ppm) for general environmental disinfection or 0.5% (5000 ppm) for blood and large body fluid spills require 1 min. Hydrogen peroxide > 0.5% at least 1 min. Objects of everyday use (door handles, keyboards & tables must be cleaned with higher frequency [3]. Infection prevention measures should include: disinfecting footwear, bags, and phones at the entrance using a mat; providing patients with a disinfectant nebulizer for shoe treatment; cleaning and sanitizing reusable protective equipment; disinfecting incoming and outgoing items; sterilizing essential tools; and using commercial disinfectants like Lysol and Roccal for general decontamination [19].

5. Monitoring of healthcare professionals

When screening suspected instances, take into account symptoms like cough and dyspnea in addition to taking a body temperature reading. Perform serological assays for IgM, IgA, and IgG antibodies. While positive IgG tests show prior viral exposure, positive IgM or IgA tests indicate an acute infection. Reverse transcriptase poly chain reaction (RT-PCR) molecular testing is the gold standard test for detecting the illness in medical experts. For COVI-19, contact screening ought to be conducted [23].

6. Scheduling recommendation

Appointment management should involve strict scheduling to minimize patient overlap, with aerosol-generating procedures booked as the last appointment. Patient interaction should be limited. Individuals with fever or potential contamination should have their appointments rescheduled or postponed. Utilize technology for initial patient screening, such as phone calls, video conferences, or messaging [9].

7. Instructions on behavior and preventive measures

It is highly advised to do debriefings and briefings before and after every shift in order to modify behavior. There have been reports of anxiety, sleeplessness, sadness, and cognitive strain in healthcare workers. They fear spreading illness, contaminating their family, failing, and passing away. It takes a lot of effort and time to put on and take off PPE, and carrying out procedures is getting harder. The goggles get hazy; it takes more effort to breathe while wearing disposable or elastomeric respirators; cuts appear on the skin; and headaches, fever, thirst, and dizziness are experienced. Increased cognitive load raises the likelihood of failing and getting contaminated and sick [3].

The training aimed at altering behavior ought to encompass subjects such as hand cleanliness, medical waste disposal, and performing high-risk contamination procedures. Training procedures and activities like donning and doffing, along with non-technical abilities like leadership, communication, and situational awareness—all crucial components of safety—may be the most effective strategy to reduce cognitive load and improve behavior [23].

Avoiding handshakes, donning masks over N95 respirators, allowing them to be reused, disposing of personal protective equipment (PPE) in the proper location, not touching one's mask, washing work clothes every day at a temperature of at least 60°C/140°F, providing a place to put on the work uniform, maintaining natural, short, and clean nails without the use of artificial ones, avoiding having a beard, adhering to cough/sneeze etiquette (protocol), maintaining up-to-date inventories of available biosafety supplies, using PPE to perform cleaning and disinfection, keeping track of professionals' health to detect respiratory infections, providing information and training on the protocols, providing the recommended immunization for healthcare professionals [9].

8. Organization and biosafety of the physical facility environment

Keeping patient belongings in plastic containers, separating patients with suspected or confirmed COVID-19 from other patients in private rooms with closed doors and private bathrooms, offering a sink and soap so that patients can wash their hands and faces, erecting a physical barrier (made of glass, acrylic, or another material) in any area where patients and staff are in close proximity, avoiding companions, preventing patients from staying in the waiting room, removing items that can spread the virus (such as business cards, toys, magazines, etc.) and maintaining a safe distance (1-2 meters) [9].

9. Hand washing

It is essential to wash your hands for at least 20 seconds with plenty of soap, water, and antibacterial gel. Washing hands can cut the chance of transmission by 6–14%. Fecal-oral transmission of COVID-19, underscoring the practical necessity of hand washing [27].

10. Disposal of Biohazards

Biological waste must be treated before disposal. It should be categorized into liquids, solids, and sharps. Liquid waste can be disinfected or sterilized. Solid and sharp waste should be disposed of according to specific guidelines. Swabs for testing should be transported in a viral transport medium at either room or cold temperature [19].

11. Vaccination

The devastating health, economic, and social consequences of the COVID-19 pandemic have united researchers globally in their efforts to develop safe and effective COVID-19 vaccines including three WHO licensed inactivated vaccines [28]. Vaccines licensed by WHO and have been deployed globally include, three inactivated vaccines (Sinovac CoronaVac, Sinopharm BBIBPCorV, and Bharat Biotech BBV152), two mRNA COVID19 vaccines (PfizerBioNTech BNT162b2 and Moderna mRNA1273 CX024414) as well as two versions of adenovirus vectored vaccines (AstraZenecaOxford ChAdOx1 nCoV19 and Janssen Ad26.COV2.S) [28]. Vaccination is a pivotal means to prevent the spread of SARSCoV-2 and ultimately quell the pandemic [6]. The most commonly reported side effects of corona vaccine were injection site pain, headache, fever, muscle pain, fatigue, tenderness at the site and joint pain [29]. Other symptoms like shivering, sleepiness, nausea, dysphagia, and cold were also reported [30]. While most side effects from the vaccine are mild, some individuals have experienced severe autoimmune reactions such as blood clotting issues, liver inflammation, heart inflammation, and an overactive thyroid [31]. COVID-19 vaccine components can deplete crucial substances in the body, leading to damage to blood vessel linings. This damage contributes to an overactive immune response, inflammation, and oxidative stress [32]. Myositis is one of the uncommon adverse events following COVID- 19 vaccination, and its mechanism is still unclear [33]. Gillian-Barr´e-Syndrome (GBS) can follow COVID-19 vaccination [34].

12. Other preventive measures

It involves recording the phone number and email address of everyone who enters the clinic, replacing door handles with ones that are simple to push or pull open, designating a designated area where staff can change into their regular clothes and put on personal protective equipment, refraining from eating and drinking, painting floor markings that are easily seen to assist patients in maintaining social distance, giving hand washing instructions, avoiding crowds, and providing information on how to prevent the spread of cough and sneeze etiquette [9].

BIOSAFETY MEASURES FOR COVID-19 IN LABORATORY SETTING

1. Generic (basic) biosafety measures

Many countries have adopted behavioral interventions, of which physical distancing is one of the most widely adopted, persistent, pragmatic, and effective policies [35]. Approximately 2 m social distancing is recommended. Potential air propagation is possible 1m, 2m and 6m while breath, talk, cough and sneeze respectively. The potential exposure and health status of the laboratory personnel is monitored daily [5].

2. Personal hygiene and personal protective equipment (PPE)

Always use the required personal protective equipment (PPE) in the lab, such as masks, gloves, a coat or gown, and eye protection. When performing aerosol-generating techniques on any non-centrifuged sample that may include essential SARS-CoV-2 particles, it is recommended to use a N95 mask [5].

3. Handling of routine patient specimens

Use automated devices and analyzers with closed pre analytical robots for routine testing of bodily fluids such as blood, urine, and samples. Processing of aerosol-generating non-centrifuged samples is done in a cabinet while working with non-respiratory specimens. Upon testing, the specimens ought to be sealed right away. Specimens at high risk should be autoclaved or disinfected right away [5].

4. Decontamination of laboratory equipment and surfaces

In the event that a sample tests positive for CoV-2 and contaminates the bench and biosafety cabinet, use a disinfectant with a chlorine content of 5500 mg/L for a minimum of 30 minutes. If the lab area is polluted, seal the lab area and cover the contaminated area for more than 30 minutes with a towel that has a chlorine concentration of 5500 mg/L. A disinfectant aerosol can be sprayed for one to two hours, or the lab can be fumigated overnight. Examples of such aerosols are acetic acid (2 g/m3), H2 O2 (3%), and chlorine dioxide (100 mg/L) [5].

5. Biosafety concerns during transport

If the specimen is being transported a short distance, it should be sealed in a biohazard zip-lock bag or container within a leak-proof cryobox. The outer layer of the box should be disinfected, the labeling of samples should be clear, and a biohazard symbol should be present on the box. If the specimens are being transported to another city or country for further processing, triple-layered packaging should be used. Triple-layered packaging consists of a primary leak-proof receptacle holding the specimen, which is wrapped with a material that can absorb the fluids in case of damage to the receptacle [36].

6. General Biosafety guidelines routine precautions when working with biohazards

Laboratory safety protocols include restricted access, daily decontamination of surfaces, proper waste disposal, and personal hygiene measures such as handwashing and avoiding mouth pipetting. Protective equipment, including lab coats, gloves, and eye/face protection, should be worn as necessary. Aerosol generation should be minimized. Sharps should be used sparingly. Laboratory materials must be transported and transferred safely. Emergency procedures and waste disposal protocols must be followed. The laboratory environment should be clean, pest-free, and equipped with proper ventilation [19].

CONCLUSION

Healthcare personnel may come into contact with a novel corona (COVID-19), a highly transmissible disease. The general population, medical and laboratory personnel are in a state of panic as a result. There has been a lot of work done to stop the sickness from spreading because the virus is airborne and spreads by droplets. Additionally, the virus can infect workers when they sample, transport, process, and dispose of tested samples. Biosafety protocols and possible safety measures should be followed throughout these processes to prevent virus infection. The likelihood of transmission is influenced by the pathogen's properties, the accessibility of high-quality personal protective equipment, and human variables related to healthcare personnel' performance. Understanding the virus is essential. Improved biosafety protection measures and optimized work flow should be taken into consideration to ensure the safety and smooth development of daily work in strict accordance with the applicable laws and regulations, technical specifications, and expert consensus, combined with their own conditions. Better biosafety measures should be implemented to perfect the working process, effectively prevent exposure to the working environment, maintain strict working conditions for a long time, and continue to improve. Vaccination as a special biosafety measures offer significant benefits such as preventing severe illness and death from COVID-19, reducing spread of the virus, and protecting those who cannot be vaccinated. Vaccine can also cause mild side effects for some individuals such as pain, redness, or swelling at the injection site, fatigue, headache, muscle pain, chills and fever. Most side effects are mild, but serious reactions can occur in rare cases such as allergic reactions and blood clots (in specific cases with certain vaccines). It's important to note that the benefits of vaccination far outweigh the risks for most people. In general, biosafety protection methods have an excellent preventive and control effect on preventing medical staff infections, which will significantly lower the risk of medical staff infections and establish effective biosafety protection working habits.

DECLARATIONS

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We authors declare that

- We agree to its publication after any amendments arising from the peer review;
- We agree to the posting of the full text of this work on the web page of the journal and to the inclusions of references in databases available on the internet;
- no results of other researchers were used in the submitted manuscript without their consent, proper citation or acknowledgement of their cooperation or material provided;
- the results (or any part of them) used in the manuscript have not been sent for publication to any other journal nor have they already been published (or if so, that the relevant works are cited in this manuscript);
- submission of the manuscript for publication was completed in accordance with the publishing regulations pertaining to their workplace.

Data availability

Data is available upon the request to the corresponding author.

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Authors' contributions

Marew Alemnew designed and wrote the review; Birhanu Andualem critically read and modified the review; Eyuel Kassa and Addis Getu performed literature revision and took care of the editing of the review; Aschalew Gelaw performed final revision.

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Competing interests

The authors have no conflict of interest to disclose.

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