Respiratory System-The Port of Entry of SARS-COV-2 with Special Reference to Aerosol Management

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Abstract

The outbreak of novel coronavirus disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has led to a global pandemic of unprecedented proportions. Management of patients infected with COVID-19 has led to a great risk of hospital-based transmission of infection to health-care professionals (HCPs). The HCPs at various levels in a multispecialty health-care setup are at risk of contracting the virus. Those who are involved with performing or assisting in aerosol-generating procedures (AGPs) have a potentially higher risk of developing the infection. The AGPs involve a wide range of procedures such as pulmonary function testing, high-flow oxygen administration, endotracheal intubation, nebulization, application of ventilators, weaning and extubation, bronchoscopy, tracheostomy, and cardiopulmonary resuscitation. Hence, understanding the overall nature of the disease is of vital importance to develop preventive strategies to reduce transmission of the virus through aerosols. This review article intends to elucidate the port of entry associated with SARS-CoV-2 infection and its spread through the AGPs. We also intend to focus on methods to prevent aerosol-related transmission of infection to HCPs by illustrating clinically practiced evidence-based protocol followed in our multispecialty health-care setup.

Keywords: Aerosol-generating procedure, barrier devices in COVID-19, pathophysiology of COVID-19, personal protective equipment, transmission of severe acute respiratory syndrome coronavirus-2

INTRODUCTION

In December 2019, an outbreak of COVID-19 disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred in Wuhan city of China, leading to a global pandemic.^[1] Health-care professionals (HCPs) referred to as “frontliners” or “COVID warriors” include clinicians, nurses, respiratory therapists, laboratory technicians, paramedical staff, and housekeeping personnel. Even with adequate personal protective equipment (PPE), HCPs who care for patients with COVID-19 not only remain at increased risk of hospital-based transmission but also may be responsible for community spread of the virus.^[2]

In this review article, we intend to give a brief summary about the port of entry of SARS-COV-2 and its transmission. We carried out an extensive literature search for a period of 3 months from July 2020 to September 2020. Search engines such as Google Scholar and PUBMED were used to search for relevant articles, using keywords, pathophysiology of

COVID-19, transmission of SARS-CoV-2, aerosol-generating procedures (AGPs), PPEs, and barrier devices in COVID-19. We included original articles, insights from case reports, and review articles in our study. We included only full length studies while the studies with only abstracts were not cited. Our main focus is to understand the AGPs and how they can be performed during this COVID era so as to ensure minimal

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risk to HCPs performing or assisting them. In addition, we highlight the barrier precautions taken for the purpose at our health-care setup.

COVID-19, SYMPTOMS, PORT OF ENTRY, AND TRANSMISSION

Symptoms of COVID-19

COVID-19 disease is principally an illness of the respiratory system, and the main clinical presentation of the disease constitutes pulmonary symptoms. The pulmonary symptoms include fever, dry cough, fatigue, and dyspnea. Other clinical manifestations reported are sore throat, headache, chills, nausea, vomiting, myalgia, nasal congestion, diarrhea, hemoptysis, and conjunctival congestion.^[3] In older patients or those with comorbidities, dyspnea may appear at the onset of symptoms, while those who are young and without any comorbidities, dyspnea might occur at a later stage.^[4] SARS-CoV-2 infection is not only limited to the respiratory system but also may affect other organs. Extrapulmonary symptoms related to neurological, hepatic, renal, and gastrointestinal dysfunction have also been reported.^[5,6]

Port of entry

The main port of entry of SARS-CoV-2 is through the respiratory tract. SARS-CoV-2 is the third coronavirus that is responsible for severe disease in humans to spread globally in the past two decades.^[7] The virus manifests its life cycle in five steps, namely: attachment, penetration, biosynthesis, maturation, and release.^[8]

Angiotensin-converting enzyme 2 (ACE2) was identified as a functional critical receptor for SARS-CoV-2.^[9-11] The viral envelope of corona virus consists of spike protein that binds to specific receptor in the lung; ACE is detectable in the entire alveolar capillary network. ACE2 is primarily produced in club cells of distal bronchioles and type 2 pneumocytes in alveolar epithelium. Both cell types are responsible to prevent acute respiratory distress syndrome. However, when the virus binds to the host's body, it tends to downregulate ACE2 enzyme leading to tissue inflammation and fibrosis.^[12] ACE2 is also highly expressed in other vital organs such as myocardial cells, kidney, brain, adrenals, small intestine, and urinary bladder.^[12-16]

Mode of transmission

SARS-CoV-2 virus is reported to survive in aerosols for >3 h,^[17] leading to a greater need to identify and categorize the areas which are high risk for spread. HCPs are at risk of contracting the virus, especially while performing AGPs. High-risk AGPs are those clinical events that have the potential to generate aerosols that consists of high viral loads, and they pose an elevated risk for acquiring SARS-CoV-2 infection by HCPs.^[18] Procedures such as suctioning the airway, intubation, nebulization, noninvasive ventilation (NIV), invasive ventilation, cardiopulmonary resuscitation (CPR), tracheostomy, and bronchoscopy are identified as high-risk AGPs.^[18,19]

Factors that may lead to an increased risk of transmission during AGPs include duration of exposure, proximity of provider to aerosol, manipulation of high viral load tissue, and aerosolization through the use of energy devices. The ability to limit the transmission of COVID-19, in the health-care setup, involves practicing evidence-based prevention and control measures, of which PPE is a fundamental element. Practicing the use of barrier devices during AGPs also should be considered to prevent transmission.

Aerosols from cough, sneeze, exhalation, and speech

Respiratory viruses are transmitted by droplets generated during coughing, sneezing, exhalation, and speech.^[20] SARS-CoV-2 virus spreads through tiny droplets released from the nose and mouth of an infected patient's cough or sneeze. A single cough is said to produce up to 3000 droplets.^[21,22] COVID-19 may spread in four ways. The proposed direct transmission ways are by (i) infectious droplets expelled by coughing or sneezing onto a mucous membrane (mouth, nose, and eyes); (ii) from AGPs; (iii) by direct contact; and (iv) indirect transmission by contact with contaminated surfaces (fomites).^[23]

The formation of aerosols can be categorized based on diameter. Large droplets are >100 µm, medium droplets are 5–10 µm, and small droplets or droplet nuclei (aerosols) are <5 µm. Large droplets tend to get deposited due to gravity and are responsible for direct transmission and indirect contact transmission. Small droplets (aerosols) are responsible for short and long-range airborne route and also indirect contact transmission.^[24]

A recent insight by Bourouiba^[25] highlighted that the mucosal droplets expelled through exhalation, coughs, and sneezes are made of multiphase turbulent gas “cloud” that entrains the ambient air and carries it in the form of clusters. The gas cloud loaded with pathogen-bearing droplets may travel up to 7–8 m. Furthermore, the lifetime of the droplets may extend by a factor of up to 1000 as compared to isolated droplets.

A study by Tang *et al.*^[26] used the schlieren optical method to visualize the speed (flow rate) of a single cough in an indoor setting. The technique involves optical phase gradient encompassing temperature differences. The character of the expelled cough is turbulent jet flow. They reported that without application of mask, the exhaled airflow can be more than 0.5 m vertically and at initial phase of cough (until 0.1 s), the airflow can be 8 L/s. Speech might also generate a trajectory flow of aerosol responsible for transmission. An experiment conducted by Anfinrud *et al.*^[27] using laser light scattering technique showed that aerosol transmission during speech can traverse a distance of 50–75 mm. The recommended social distancing given by Center for Disease Control and Prevention (CDC) is 2 m. However, some studies observed that the recommendation of 2 m or 6 feet distance may not be sufficient as droplet transmission can happen beyond 2 m.^[28,29]

Aerosol-generating procedures

Procedures such as CPR, tracheostomy, bronchoscopy, suctioning, intubation, nebulization, NIV, and invasive ventilation are identified as high-risk AGPs.^[30,31] Selection and utilization of appropriate respiratory PPEs are of utmost priority in this current COVID-19 pandemic. How significant is the role of transmission related to the AGPs as compared to other modes of transmission in the spread of SARS-COV-2 remains unclear. HCPs pose a high risk of acquiring preventable

infections during various AGPs attributing to the lack of clarity of risks associated with various procedures.^[32,33]

Oxygen delivery devices

In normal spontaneously breathing patients, application of a simple face mask may generate aerosols that may spread up to 0.2 m.^[34] Maximum exhaled air distance using a simple face mask at a flow of 4 L/min is 0.20 m. When flow is increased from 4 L/min to 6 L/min and then to >10 L/min, the exhaled air distance was 0.22 m, 0.40 m, respectively.^[35]

Figure 1: Donning of personal protective equipment (wearing the PPE)

Nebulizers

The delivery of medications through nebulization can also cause dispersion of aerosolized particles in the proximity. The maximum exhaled air distance while using a jet nebulizer which is driven by air at 6 L/min in healthy lung is 0.45 m, while in severe lung injury, it can be beyond 0.8 m.^[35,36] A review by Roy *et al.*^[34] recommends that open nebulizers might be avoided rather manual in-line nebulization be considered. At present, there do not exist sufficient evidences either on the safety or on the risk of transmissibility of SARS-CoV-2 during nebulization in COVID-19 patients.^[36]

Noninvasive ventilation

The evidence suggesting that NIV increases risk of acute respiratory infections is not strong.^[37] However, some studies show a significant association of NIV and risk of aerosolization.^[38]

Raboud *et al.*^[39] in his study surveyed 624 HCWs who were exposed to 45 intubated patients diagnosed with SARS. Twenty-six HCWs contracted SARS from a single patient. 38% of HCWs developed SARS exposed to NIV compared with 17% of those who did not, which was a statistically significant association.

Simonds *et al.*^[40] mentioned in their study that NIV application using vented masks is a droplet-generating procedure and not aerosol generating as produced droplets are >10 µm. They compared the droplet generation using NIV and NIV with circuit modification done by inclusion of an exhalation filter. It was noted that the droplet count reduced by 1 m with NIV circuit modification.

Suctioning

Suctioning an intubated patient infected with SARS-COV-2 is a high-risk AGP.^[41] Open suctioning of intubated patients' airways

Figure 2: Doffing of personal protective equipment (removing the PPE)

involves disconnecting the tracheal tube from the ventilator, and this, or the suction itself, may lead to dispersal of aerosols from within the airway. Increased number of airborne particles near patients has been detected in association with airway suctioning.^[42] Close suctioning is recommended to reduce transmission of aerosols generated from patient's end.^[43,44]

Endotracheal intubation, extubation, tracheostomy

The process of intubation for a COVID-19 patient is considered a high-risk procedure attributed to the high viral load due owing to the proximity of the HCPs to airway secretions.^[45,46] After tracheal intubation, exhaled normal cough could generate a plume that can disperse a distance of around 460 mm.^[47] The use of aerosol box to reduce the risk of transmission during intubation is recommended.^[48]

Videolaryngoscopy is ideally recommended during intubation of COVID-19 patients, as it not only provides a better view of the glottis entrance but also increases the proximity

of the clinician and the patient's face, reducing risk of contamination.^[49]

Bronchoscopy

In a study conducted by O'Neil *et al.*,^[50] it was concluded that two procedures showed a significant increase in aerosol particle concentrations: nebulized medication administration and bronchoscopy; these undoubtedly pose a distinct risk of infection transmission to health-care personnel. Similar findings were reported by a study conducted by Doggett *et al.*,^[51] wherein particle generation during and immediately following bronchoscope removal was compared to a preprocedure baseline. It was found that there is an increased aerosol production in 0.3 mm size particles. Similar findings were also reported by Lavoie *et al.*^[52]

Bag mask ventilation

BMV may also lead to dispersion of the exhaled plume for a distance of 220 mm transversely, while leakage at the patients' interface during the bag mask process may increase the dispersion distance by 340 mm. However, the use of a filter and ensuring nonleakage at the interface reduces dispersion distance.^[47]

Cardiopulmonary resuscitation

There is contrasting consensus whether CPR can be categorized under "AGP." The WHO has categorized it as AGP in the year 2007. However, it was delisted later. Since CPR not only consists of chest compressions, it can be considered as an AGP. In the study by Liu *et al.*, chest compressions were found to be associated with infection risk.^[53] In an experimental study by Ott *et al.*, they evaluated the spread of aerosol spread during CPR using dummy and cadaver models.^[54] In the dummy model, they nebulized disinfection detergents which could be

Figure 3: Illustration of aerosol box (reproduced with permission from ref.^[57]) The top panel shows bronchoscopy being done in pulmonology lab using intubation box and personal protective equipment level 3. The lower panel shows the use of aerosol hood demonstrating use of a high flow nasal cannula. (a). Rear-view (caudal) image of the aerosol hood, showing all iris port and the HEPA filter. (b) Images 30–40 s after igniting a smoke candle within the hood; left: no active suction. (c); right: active suction at > 10,000 L/min (d). The active suction directs smoke particles towards the HEPA filter and releases clean air into the room (Courtesy: Dr. Balani)

Figure 4: (a) Intubation box on a patient prior to endotracheal intubation. (b) Use of videolaryngoscope for endotracheal intubation. (c) View of glottis with a videolaryngoscope. (d) pre-oxygenation, bag mask ventilation is either avoided or done extremely gently with low flow of oxygen

Figure 5: (1) In-line nebulization. (2) Noninvasive ventilation application with health-care professionals wearing level-3 personal protective equipment. (3) Closed suctioning. (4) Use of bacterial filters. (5) Disconnection of endotracheal tube must be done beyond HME or clamping endotracheal tube if disconnected before HME (6)

detected through ultraviolet rays. The nebulizer operated with a flow of 8 L/min. Chest compression was done and the aerosol plume was detected in compression-only CPR. However, addition of a face mask followed by application of oxygen reservoir mask reduced the aerosol spread. Similar findings were also reported in the cadaver model.^[55]

Infection control to minimize risk of hospital-based transmission

Infection control practices during the management of COVID-19 are of prime importance to break the chain and reduce the risk of transmission of COVID-19 to the HCPs who are involved in the management of patients at various health-care settings.

Infection control practices in our tertiary care multispecialty institution

Levels of PPE and application in COVID-19

The levels of PPE to be used by HCPs at various departments whether direct or indirect contact with suspected/confirmed cases of patients is a major determinant that would help to contain the spread of the virus. At our health-care setup, three levels of PPE have been formulated along with the

donning and doffing sequence. The sequences are on the basis of guidelines given by CDC.^[56] The PPE required has been divided into three levels – 1, 2, and 3, according to the risk of exposure. Level 3 is recommended for the highest risk procedures. The entire setup is divided into the following categories, depending on which, correct and judicious use of PPE is carried out.

1. “High COVID risk” areas – patients in these areas have been admitted from the community
2. “Low COVID risk” areas – patients in these areas are of low risk for COVID based on history and a negative COVID polymerase chain reaction (PCR) result. Although the COVID PCR is negative, PPE based on the type of exposure is required.

Level 3 PPE: Steps for donning (putting on) the PPE [Figure 1]. This should be done outside the patient care area.

Level 3 PPE: Doffing (removing) of PPE [Figure 2] reproduced with permission from Dr. Vijay Richard.

The use of aerosol box, intubation box, and respiratory care procedures is illustrated in Figures 3-5. Figure 6 shows the Code Blue protocol in COVID-19 patients at our hospital.

Figure 6: Code blue protocol during COVID-19 pandemic for in-hospital cardiac arrest

Surgical smoke evacuator

Surgical smoke evacuators (SSE) consist of a high flow negative pressure pump that provides negative airflow rates that are 25–40 times greater than the standard suction used in hospitals. It also consists of an ultra-low particulate air filter and a disposable plastic suction hose. An SSE may be used as a mechanical barrier during intubation and extubation. The aerosolized viral load which is generated during airway management is captured and diverted from the HCPs. A SSE can be thought of as a “vacuum cleaner” and it follows the well-accepted infection control principles of “source control” and “negative pressure respiratory isolation.”^[58]

CONCLUSION

Coronavirus is contagious and spreads through respiratory tract. Hence, the knowledge of various AGPs and measures that must be taken to prevent spread is of utmost importance to prevent its spread to the HCPs.

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Conflicts of interest

There are no conflicts of interest.

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