Review Article

COVID -19: Literature review and learning from UK Experience

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Keywords: COVID 19; Corona virus; Pandemic.

Abstract

COVID19 (Corona virus disease 2019) is an illness caused by novel corona virus, first reported from Wuhan in China in December 2019. This pandemic has spread to most of the countries of the world and has already taken a huge human toll. Transmission is mostly by the respiratory droplets and also by fomites. While most infected individuals have mild symptoms, a small but significant proportion of individuals develop severe bronchopneumonia, sometimes leading to multiorgan dysfunction. Common symptoms are fever, cough, myalgia, fatigue, nausea, vomiting, diarrhoea, breathlessness etc. Diagnosis is made by clinical features in the right epidemiological setting, blood tests and usually confirmed by a PCR test with a nasopharyngeal and oropharyngeal swab. Management is mainly supportive as currently there is no proven antiviral treatment.

Reconfiguration of services was necessary to manage a large number of patients admitted to a UK hospital with COVID 19 disease as elective admissions were cancelled and hospital admissions due to due to other diseases significantly declined. Staff were reallocated to cope with the surge in hospital admissions. A system of training was put in place to upskill the staff. All but absolutely necessary outpatient consultations were done by telephone or videoconferencing.

COVID 19 patients were cared for in dedicated areas of the hospital and strict infection control procedures were followed. Intensive care unit facilities with ventilators were rapidly expanded with involvement of operation theatre areas. Non-invasive respiratory support was provided in respiratory wards.

Introduction

Coronavirus disease 2019 (COVID -19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS- COV2) continues to grow at an alarming rate since it was first detected in Dec 2019 Wuhan, China. As of 1 May 2020, there have been 3.58 million confirmed cases of COVID-19 worldwide with 238,937 deaths reported.1 COVID -19 has brought a tsunami of sufferings for families and communities and immense losses for the economy. It has created unprecedented health and social challenges. Here we would like to discuss the presentation and management of COVID-19 and share our UK experiences.

Transmission:

COVID-19 is a highly transmissible disease and the average infected person spreads the disease to two or three other people. There is a strong evidence to suggest that it can be transmitted by people who are mildly ill or asymptomatic.[2,3] A key factor in the transmissibility of COVD-19 is the high level of SARS- COV2 in the upper respiratory tract even among asymptomatic patients. The effective reproduction number (Rt) for SARS- COV2 has been estimated to be 2-4 compared to Rt of 1.4 to 1.7 for influenza.[4,5] An Rt greater than 1 indicates spread and Rt less than 1 indicates control.

SARS- COV2 is primarily spread from person to person through

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respiratory droplets. With droplet transmission, virus is released in respiratory secretions when a person with infection coughs, sneezes or talks and can infect other person if it makes direct contact with the mucous membrane. Infection can also occur if a person touches an infected surface and then touches his or her eyes, nose or mouth. Though transmission is not considered to occur through inhalation of virus suspended in air, the virus may be aerosolised during certain procedures like intubation or use of nebulisers. [3] Droplets normally do not travel more than 2 metres and do not linger in air.

Incubation period

The estimated incubation period for COVID-19 is up to 14 days from the time of exposure with a median incubation period of 4 to 5 days. [6-7]

Clinical manifestation

The spectrum of illness can range from asymptomatic infection to severe pneumonia with Acute Respiratory Distress Syndrome (ARDS) and death. According to initial data from China, around 80% of the reported cases had mild to moderate disease , 14% had severe disease and 6% had critical illness. 7-9 The overall case fatality rate (CFR) is estimated to be 2.3%.[9] A major challenge with accurate calculation of CFR is the denominator – the number of people infected with the virus. Asymptomatic COVID-19 patients or patients with mild symptoms are unlikely to be included in the denominator leading to overestimation of CFR.

The most commonly reported clinical symptoms include fever, cough, malaise, dyspnoea, sore throat and myalgia. Less common symptoms include diarrhoea and vomiting. [11,12] Anosmia and ageusia have been reported. [13]

Risk factors for severe COVID 19 include old age greater than 65, cardiovascular disease, chronic lung disease, hypertension, diabetes and obesity.[6,8] Certain other conditions such as chronic kidney disease, immunosuppression and malignancy may be associated with worse prognosis. Studies from China and Italy have shown a disproportionately high number of deaths in males.[9,10]

Laboratory findings

Lymphopenia is especially common and other common laboratory findings in hospitalised COVID-19 patients include elevated inflammatory markers such a C-reactive protein and ferritin, elevated aminotransaminase and elevated lactic dehydrogenase levels.[6,11,14] The procalcitonin is typically normal at presentation. Particular laboratory features have been associated with poor prognosis. These include an increasing white cell count with lymphopenia, a prolonged prothrombin time, elevated levels of D-dimer, troponin, interlukin-6, liver enzymes, lactic dehydrogenase, liver enzymes, C-reactive protein and procalcitonin.[8,11,15]

Imaging studies

Chest X-ray may be normal in early or mild disease.[16] Although CT scan of the chest may be more sensitive than chest X-ray, it should be reserved only for those patients where there are specific indications.[17] Common abnormal radiograph findings include consolidation and ground glass opacities with bilateral and lower lung distributions.

Complications

Adult respiratory distress syndrome is a major complication in patients with severe disease. The other complications include arrhythmias, acute myocardial injury, shock, and acute kidney injury.[9,11,18,19] Thromboembolic complications including pulmonary emboli and acute stroke have been described. [20,21,22, 23]

A subgroup of patients with severe COVID-19 have evidence of a virally driven hyperinflammatory response similar to cytokine release syndrome with persistent fevers, elevated inflammatory markers such as D-dimer, ferritin and elevated proinflammatory cytokines and these laboratory abnormalities have been associated with poor prognosis.[24]

Microbiological diagnosis

The diagnosis of COVID-19 is made by detection of SARS- COV2 RNA by reverse transcription polymerase chain reaction (RT-PCR) from upper respiratory samples (nasophrangeal or oropharyngeal swabs). However false negative tests have been reported. [25] The false negative tests can be due to faulty technique in specimen collection or transport, wrong timing of the collection of the specimen or the level of viral RNA below the level of detection by the test. If the initial test is negative but the clinical suspicion is high, we suggest repeating the test. In such cases, WHO recommends testing from lower respiratory tract specimen. The likelihood of a positive upper respiratory RT-PCR may be higher earlier in the course of illness especially from day 1 to day 5 of illness.[26] The viral loads may be higher in lower respiratory tract specimens and more likely to give positive tests than upper respiratory tract specimens. [27,28] The duration of viral shedding is variable which may depend on severity of illness.[28- 31] Though a positive test for SARS-COV2 by PCR generally confirms the diagnosis of COVID-19, it does not always correlate with viral transmissibility .The inability to differentiate between infective and non-infective virus remains a major limitation of RT-PCR.[29] There may be a threshold of viral RNA level below which infectivity is unlikely . The study carried out by Wolfel and colleagues showed virus was not detected from respiratory secretions in COVID-19 patients when the viral RNA was less than 106 copies/ml. [29]

Serological tests

In response to the growing COVID-19 pandemic and shortage of laboratory based molecular testing capacity and reagents, multiple diagnostic test manufactures have developed rapid easy-to-use test kits. These test kits are based on either detection of proteins from the COVID-19 virus in respiratory samples (sputum or throat swab) or detection in blood or serum of human antibodies generated in response to infection. Though these tests are available at the point of care and the results available within minutes, they have not been validated in the appropriate populations and settings. At present, based on current evidence, WHO recommends the use of these tests only in research settings.[32] Nevertheless, they can play an important role in control of COVID-19 pandemics.

Population serological testing (specifically measuring SARS-CoV-2-specific IgG antibody titres) can estimate the total number of infections by assessing the number of individuals who have shown an immune response whether the infection was subclinical or occurred in the recent past. This information can be used to determine epidemiological variable such as case-fatality rate more accurately and to assess the effect of interventions at population level and to formulate policy changes to release such measures. Population serological testing can identify immune health workers so they can be deployed at appropriate settings. They can help to separate individuals showing a strong immunological response to the virus whose antibody can be used to treat patients with plasma therapy. Nevertheless, there are

several challenges assessing the sensitivity, specificity and validity of these serology tests. The serology tests can be false positive as they can cross-react with other viral pathogens belonging to Coronavirus family. The immunocompromised patients may not elicit an immune response and we still do not know how long the immunity to this virus might last. Despite these challenges, the data obtained from population serological testing will be helpful in control of COVID-19 pandemics.[33]

Management

The mainstay of management is supportive care. So far none of the antiviral treatment has had any significant effect on the ultimate outcome although several trials are still ongoing.

1. Hydration: Patients can be dehydrated because of diarrhoea, vomiting and insensible fluid loss because of high body temperature. We would recommend assessing hydration status for each patient and maintain adequate hydration by either oral or intravenous supplement as necessary.

2. Oxygen: We would recommend setting target oxygen saturation for each patient depending on whether they had chronic lung disease and chronic hypoxia. This would usually be 92-96% in people with no chronic lung disease[34] and 88-92% in people with chronic lung disease[35]. Subjects should then have whatever supplemental oxygen necessary to maintain oxygenation. Sometimes non-invasive respiratory support in the form of continuous positive airways pressure (CPAP) or invasive ventilatory support may be necessary depending on the condition of patient. Extracorporeal membrane oxygenation (ECMO) has also been used in severe cases.

3. Anticoagulation: We would recommend thromboprophylaxis in all patients as thromboembolic events have been reported in many severe cases. Some patients may need full anticoagulation, but this will need to be decided on case by case basis[36.]

4. Antibiotics: There is no role for antibiotics in definite viral disease. However, when the diagnosis is not very clear or when secondary infection is suspected, antibiotics could be used until the situation is clear[37].

5. Corticosteroids: There is no evidence base for routine use of Corticosteroids. High dose steroids have been used in certain clinical settings to manage immune hyperreaction or organising pneumonia particularly after the first week (after the viral replicative phase). This will need to be decided on cases by case basis until more evidence is available.

Currently trials are ongoing for Chloroquine/Hydroxychloroquine, Azithromycin, Remdesivir, interleukin 6 pathway inhibitors (Toclizumab), Lopinavir-Ritonavir, Interferon beta, Dexamethasone and convalescent plasma.

Recently American FDA (Food and drug Administration) has provided an emergency authorization for Remdesivir as it was shown to reduce the time to recovery in a trial (yet unpublished). Patients with multiorgan dysfunction i.e. cardiac, liver, renal etc should be managed in intensive therapy unit with appropriate organ support/ supportive care as necessary.

For management of fever and body pains we would recommend using Paracetamol as first line. Although some earlier reports raised concern regarding use of nonsteroidal anti-inflammatory agents, there is no large-scale data to suggest adverse outcome in COVID 19 disease. The world health organisation (WHO) advisory agrees with the above statement.[38]

A UK Hospital Response to the COVID-19 Pandemic

The UK government has described its policy response to COVID-19 in four parts: contain, delay, research and mitigate. The UK Government reported the first 2 cases of COVID 19 on 31 January 2020. The number of confirmed cases jumped to about 10,000 on 25 March, almost 50,000 on 5 April and 100,000 on 16 April.[39] Due to the increasing number of positive COVID-19 cases and rapid transmission, the UK Government introduced various measures such as physical distancing, self-isolation for those with possible symptoms of COVID-19, regular handwashing etc. Coronavirus Act 2020 was introduced which gave the Government discretionary power in the areas of NHS (National Health Service) and social care. Nevertheless, there has been some criticism aimed at the UK Government because of an initially slow response to COVID-19 compared to other European countries, lack of testing for COVID-19 and inadequate PPE (personal protective equipment) provisions.

Planning for admission surge:

In early March 2020, it was expected that there would be a surge of COVID 19 patients with serious illness when the pandemic started to affect the local population. Hospitals could be potential hotbeds for spread of infections if not managed properly. Planning for overall management and infection control was done at a high level with the involvement of the hospital's chief executive. All the NHS organisations were asked to establish a COVID-19 Incident Management Team.

Elective activities:

All elective surgeries were cancelled. Outpatient face to face consultation was significantly reduced, mainly reserved for cancer patients and other urgent cases who needed to be seen face to face. Many outpatient consultations were done through video conferencing or over the phone.

Infection control:

The whole hospital was divided into green (COVID19 free) and purple zones (patients with COVID 19). The purple zone was in the middle of the hospital, next to the emergency department with green zones at either end. Each zone had a separate entrance and exit. Admission procedure for patients with COVID 19 was streamlined from ambulance onwards to dedicated clinical areas looking after COVID 19 patients. Maintaining strict infection control was challenging but we did what was possible. The whole idea was to avoid cross infection between non COVID 19 and COVID 19 patients. All involved staff would have to use appropriate personal protective equipment (PPE) as per guidance.

Provision of Personal protective equipment (PPEs):

Staff needed to be protected and maintaining adequate supply of right PPEs was a huge challenge. Our hospital followed guidance from Public Health England who recommended full PPE in areas where aerosols are generated. Public Health England recommended surgical masks, plastic aprons and gloves while seeing patients in areas where aerosols are not generated. Many of the staff felt that the latter was inadequate, but the trust stuck to the guidance which remains the same even now.

Working pattern in the wards and addressing the shortage of manpower

Available staff from the cancellation of elective activities were redeployed in the wards looking after COVID patients. Junior

doctors/trainees from Surgery, Gynaecology, Paediatrics. Ophthalmology, ENT (Ear, Nose and Throat) etc and the Specialists were deployed in Medical wards. Final year medical students were allowed to graduate before their final exams and were given provisional license to practice. Several training sessions were organised by the respiratory physicians to upskill the staff. They were advised to maintain management at basic level and keep it very simple with supportive care. Any patient needing significant respiratory or other organ support would be cared for in the dedicated respiratory ward or intensive care unit. Ward areas were grouped into nests of two wards to provide Consultant, and round the clock cover by trainees and junior doctors.

Staff Communication:

As the situation evolved, it became very clear that the plans needed to change rapidly. The lead management team met at least twice a day. A WhatsApp group of the involved clinicians was made for effective communication. A separate group was made to share the learning and learn about guidelines issued by relevant clinical groups nationally and internationally. The hospital email system was also used but WhatsApp became the main modality of communication.

Clinical advisory group:

A clinical advisory group was formed which comprised of a Respiratory Physician, intensivists and a senior General Physician. The main role was to advise on patient management as the situation and learning evolved. The group tried to learn from evidence from other countries who were ahead of the UK in the timeline for the pandemic and tried to learn from their experience and limited evidence. This helped standardise patient management in the hospital.

Provisions for patients needing intensive respiratory/ multiorgan support:

The rapidly evolving situation needed rapid expansion of capacity for ventilators and also for non-invasive respiratory support. Continuous positive airway pressure (CPAP) was provided in the respiratory ward. Ventilator capacity was expanded while involving operation theatres and the theatre recovery area. All the anaesthetists involved in routine surgeries were now looking after ventilated patients. Finances were made available to purchase whatever equipment was necessary.

This required extra nurses and other clinicians to support expanding bed bases. Several of the surgeons volunteered to work as assistants in the intensive care unit.

Strain on Oxygen supply:

Most patients admitted to hospital had severe bronchopneumonia and needed oxygen. Oxygen demand surged significantly and there was a severe strain on the supply system. Extra provisions had to be made to cope with the demand.

Individuals coping with COVID19:

Staff involved in looking after these patients were seeing a large number of rapidly deteriorating patients with a significant number of deaths. There was also a feeling of helplessness as a significant proportion of patients deteriorated irrespective of the treatment provided to patients. Many staff feared getting the sickness themselves while caring for patients and also worried that they could potentially infect their families.

We have already seen suicides amongst professionals providing care in the current pandemic. There are reports of anxiety, depression and distress in the staff managing these patients. It is likely that there would be 'post-traumatic stress disorder' and the workforce would be affected in the future.

Provisions have been made to provide psychological and mental health support to the staff, but more specialist provisions will be needed as the situation evolves.

Conclusion

The current COVID 19 pandemic has spread to most of the countries of the world and has already taken a huge human toll. COVID-19 is here to stay until a safe and effective vaccine is developed and becomes widely available. As this is a new disease, there will be genuine uncertainty and differences in relation to how we mange COVID-19 in different settings. This pandemic has prompted us to revisit how we deliver health services. We have seen the adoption of video and telephone consultations and this may be a new "normal" in the near future. This pandemic is a long-term event requiring constant proactive strategy development and we have to learn lessons from diverse experiences. COVID-19 is a highly transmissible disease and therefore a timely introduction of public health measures is crucial to contain the spread and save lives. Over a span of last 20 years , we have seen outbreaks of SARS (severe acute respiratory syndrome), H1N1 flu, Ebola etc . Human behaviour is difficult to change and we are likely to see at least one or two pandemics during our lifetime. It is not a question of "if" but a question of "when". Our health system needs to be prepared to face the challenges posed by the future pandemics.

Publication History:

EIC: Umid Kumar Shrestha, Nepal Mediciti, Lalitpur, Nepal

Date of submission: May 5, 2020
Date of acceptance: May 22, 2020

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