Review article

COVID-19: Initial synthesis of the epidemiology, pathogenesis, diagnosis, treatment, and public health control approaches

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Abstract

Introduction: The coronavirus disease (abbreviated COVID-19) pandemic caused by SARS-CoV-2 has devastated the world in the space of just a few months. Since it was first reported in December 31, 2019 in the Hubei province of China, at the time of writing, over 2 million people have been infected, with over 127,598 deaths in 202 countries and territories. Records of global distribution show a steady increase, although the USA is leading in its distribution, with Italy reporting close to 20,000 deaths. The purpose of this rapid review is to synthesize available evidence on the epidemiology, pathogenesis, diagnosis and public health control measures to inform policy, programs and research on COVID-19.

Methods: A rapid review method was employed using PubMed and Google Scholar search engines. Journal articles, reports and government documents were included in our search, which is focused on the disease epidemiology, advancements in diagnostics, treatment and vaccines, public health control measures, and psychosocial interventions for health care providers. The contents of the identified articles were examined and abstracted by a team of investigators. The concepts represented by the individual reviews were collated to give a complete picture of COVID-19 based on the evidence we have so far. The search period spanned December 30, 2019 to April 15, 2020.

Findings: The severity of the disease and its fast spread, three times faster than the flu, has challenged the health systems of almost every country in the world. Although, for now, the case burden remains low in Africa, the impact of COVID-19 is anticipated to be severe if it becomes widespread. Efforts to curb the pandemic, involving prevention, disease surveillance, contact tracing, clinical management and the development of new treatments and diagnostics, is ongoing across the globe. While writing this review, more than 73 vaccines are at the exploratory or preclinical stage, while two are in phase I clinical trials. Yet, non-pharmaceutical interventions are critical to stopping the spread of the virus. Africa, in particular, should put extra effort into making preventive public health measures work, because health systems in the continent are too weak to withstand the effect of the pandemic should it hit hard, and the economic implications of extreme control measures following a delayed response would be severe. On the bright side, the lessons drawn from this pandemic are likely to improve the preparedness and response to similar future outbreaks and pandemics. [*Ethiop. J. Health Dev.* 2020; 34(2):129-140]

Key words: Coronavirus, COVID-19, pandemic, SARS-CoV-2

Introduction

A lung disease of an unknown cause was identified among a cluster of patients in Wuhan province, China, on December 31, 2019 (1). On January 07, 2020 the Chinese authorities confirmed that they had isolated a new virus from the coronavirus family (2019 novel coronavirus, 2019-nCoV) (1). Later, the International Committee on Taxonomy of Viruses re-named this virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (2).

SARS-CoV-2 is the third outbreak caused by the coronavirus family in the past two decades. Unlike the previous two, this pandemic has affected the entire world within a short time (3). Severe acute respiratory syndrome (SARS-CoV), which occurred in 2002, claimed the lives of 916 people after infecting nearly 8,422 (4); Middle East respiratory syndrome coronavirus (MERS-CoV), reported in 2012, infected 2,229 and left 791 people dead. The MERS outbreak was relatively localized, with 83% of cases reported by the Kingdom of Saudi Arabia, although sporadic occurrences were reported in Europe, the USA and northern Africa (5). Compared to SARS-CoV and MERS-CoV, the rapid transmission of SARS-CoV-2 has been exceptional, with its spread covering more than 202 countries and territories and affecting over 2 million people across the globe (3). The pandemic has continued to spread and overwhelm the health systems of most of the affected countries. However, it is expected to be more damaging to African countries, as most have under-resourced health facilities and fragile health systems (6). Despite the immense public health and economic impact of the pandemic, we still do not have concrete evidence to guide the direction of research and policy.

Day by day, ever-changing evidence about the disease indicates that the quest for more evidence has grown exponentially. In the past three months, nearly 600 clinical trials have been proposed and over 150 diagnostic tests have been developed (7). This and more evidence in the making has made the information on COVID-19 overwhelming. However, there is still a

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growing interest in acquiring more evidence to guide policy and pandemic response interventions (8). The knowledge management unit of the Centre for Innovative Drug Development and Therapeutic Trials for Africa (CDT-Africa) (9) aims to synthesize the available evidence on the epidemiology, pathogenesis, diagnostics and public health control measures to inform policy, programs and research.

Methods

Design: We employed a rapid review of articles published from December 30, 2019 to April 15, 2020 on SARS-COV-2 and COVID-19 (10). Although numerous researches are underway and considerable number of publications are already available, there is not yet conclusive evidence in relation to all aspects of the disease. This rapid review would help to scope fragmented, opinion-based, large-scale and sometimes contradictory resources for easy use.

Search strategy: We searched the PubMed and Google Scholar databases employing the key terms "COVID-19", "SARS-CoV-2", "coronavirus" and "viral infections". This was supplemented by accessing additional resources from the databases and websites of academic and research institutions, and guidelines of international organizations such as the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC), as we saw fit.

Inclusion criteria: Considering the broad scope of the review, we were flexible with our inclusion criteria. Publications ranging from observational to experimental studies, and from grey literature to editorials and perspectives, were included.

Outcomes: The outcomes were those concerning the pathogenesis, descriptive epidemiology, treatments, vaccines, diagnostics, personal protective equipment and public health control measures in relation to COVID-19, and recommendations pertaining to the wellbeing of health care professionals.

Data extraction and analysis: We identified 78 publications on a range of topics concerning COVID-19. The articles were grouped under the following headings: the nature of the virus, epidemiology and pathogenesis of the disease, laboratory diagnosis and developments in diagnostics, drugs in use and under trial, public health control measures, and psychosocial interventions for health care professionals.

The research team was comprised of six academics with different backgrounds in the field of health sciences. Each member rigorously reviewed eight to 10 articles and summarized the content separately. Summaries of the separate reviews were presented and discussed daily at virtual meetings. The discussions were aimed at sharing understanding and to reach consensus on the gist of the publications reviewed by the individual members of the team.

Six consecutive video conferences were held back to back to discuss the findings from the individual reviews. At every meeting, the investigators took turns to present their summary of the findings from their review. The presentations were followed by inputs and further discussions from the rest of the team. These deliberations helped to evaluate the content, reach consensus and, if relevant, expand on the interpretation to be drawn from each article. At the end, the individual reviews were collated, and the seventh video conference was dedicated to discussing and finalizing the draft report.

Results

The virus: Coronavirus disease 2019 (COVID-19) is an illness caused by a novel coronavirus now called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This strain of the coronavirus family was first identified among a cluster of respiratory illness cases in Wuhan City, Hubei province, China (1). Corona is a name given to a large family of respiratory disease-causing viruses under the family *Coronaviridae*, which was first isolated in the1960s. In the past, different strains that belong to this family have crossed over from animals, e.g. bats, birds and warm-blooded flying vertebrates, and infected humans (11).

Based on antigenic relationships of the spike (S), membrane (M), nucleocapsid (N) proteins and viral genetic phylogeny, coronaviruses are classified into four groups: alpha, beta, gamma and delta (4,12). Though coronaviruses mainly infect animals, there are seven strains known to infect humans, called the Human Coronaviruses (HCoVs). The most common of these are HCoV-229E (alpha), HCoV-OC43 (alpha), HCoV-NL63 (beta) and HCoV-HKU1 (beta) (13). These subgroups are associated with a range of respiratory diseases including the common cold, bronchiolitis and pneumonia. The other HCoVs are severe acute respiratory syndrome (SARS)-CoV (beta), Middle East respiratory syndrome (MERS)-CoV (beta) and the newly discovered 2019 novel coronavirus (2019-nCoV). SARS and MERS are known for causing outbreaks in 2002 and 2014 respectively, and they are referred to as agents of great public health threat (14,15). Both are severe and had a high case fatality rate (Table 1), but SARS-COV-2 has covered a significantly wider geographic area.

Pathogenesis: Coronaviruses are enveloped positive-sense RNA viruses, with their size ranging from 60 to 140 nm in diameter. They have spike-like projections on their surface, giving them a crown-like appearance under the electron microscope, which explains the name "corona". Studies reveal that the virus enters the respiratory mucosa using the angiotensin-2 (ACE-2) receptor on the surface of the mucosal cells. This justifies why the virus commonly targets the respiratory system (14,16,17).

Disease symptoms: The incubation period of COVID-19 ranges from two to 14 days (1,18). The clinical manifestations of the mild to moderate disease mimics a regular flu, presenting headache, fever, dry cough and fatigue. In some cases, a productive cough, sore throat, haemoptysis, diarrhoea and lymphopenia may be part of the picture. At later stages (5.2 to 8 days from the time of infection), dyspnoea and acute respiratory distress syndrome (ARDS) can be observed, and multiorgan dysfunction is also reported in some patients (2,16,17,19).

Around 80% of people who are infected either do not exhibit the manifestations or will only have minimal symptoms. Mild to moderate symptoms are observed in 15% of infected people, and 4% to 5% warrant intensive care in hospitals. The median time interval between the onset of the first symptom to hospitalization is 7 days and the median hospital stay, from admission to discharge, is 10 days (19). The median number of days from infection to death is 14 (ranging from 6 to 41 days) (18). Factors such as age and co-morbidity dictate the difference in the duration between the onset of symptoms and death. People older than 70 years and those with comorbidities have a short duration and are prone to develop severe complications (2).

Epidemiology – Global: The first five cases were reported from China in mid-December 2019; they were hospitalized for ARDS and one of them died after admission. On December 31, 2019, a cluster of cases of pneumonia of unknown cause were detected in Wuhan City, the capital of Hubei province. By January 02, 2020, 41 hospital-admitted patients were diagnosed for COVID-19 infection and 10 days later the WHO declared the advent of an outbreak caused by a novel coronavirus, 2019 (2019-nCoV) (1). By January 22, 2020, a total of 571 cases and 17 COVID-19 related deaths had been reported from 25 provinces (districts and cities) of China (20). Following this, a report on January 30 indicated the emergence of 90 new cases in 16 nations from five out of the seven continents (only sparing Africa and Antarctica). At this point, the number of confirmed cases in China had reached 7,734. As a result, the WHO declared the COVID-19 outbreak as a global public health emergency and officially renamed it as severe acute respiratory syndrome coronavirus-2 (SARS- CoV-2) (13,21). On March 11, 2020 it was declared a global pandemic (22).

When we prepared this report (April 15, 2020), the pandemic had affected more than 202 countries and boundaries, infecting 2 million people and causing 127,000 deaths (23,24). The United States of America reported the highest number of cases (614,246), followed by Spain (174,060), Italy (164,488) and France (143,303). The other most affected countries were Germany, United Kingdom, China and Iran. Of the confirmed COVID-19 patients, 95% had mild to moderate illness and 5% were seriously sick needing critical care (25). Taking the total number of infected people as a denominator (485,362), 24.2% have recovered from the disease so far (23,24). However, this proportion would be significantly higher (i.e. 79%) if we take cases with the reported outcome as a denominator.

Epidemiology – Africa: In Africa, the first COVID-19 case was reported from Egypt on February 14, 2020. Since then, 52 African countries have been affected, reporting 16,302 cases, 880 deaths, and 340 recoveries in the continent. South Africa has the largest number of cases in the continent (2,415), followed by Egypt, with a total of 2,350 cases. Morocco (1,888), Algeria (2,070), Tunisia (747) and Burkina Faso (528) are the other African countries with a high number of cases. Even though South Africa has a high number of cases, only 27 deaths have been reported, while 164 deaths have been reported in Egypt, 326 in Algeria and 126 in Morocco (18,26,27).

Epidemiology – Ethiopia: In Ethiopia, the first coronavirus case was reported in Addis Ababa on March 12, 2020. The index case was a 48-year-old Japanese man who came to Ethiopia from Burkina Faso on March 04, 2020. According to the Ethiopian Public Health Institute, by April 15, 2020, a total of 85 confirmed cases, three deaths and two recoveries have been reported. The two initial cases were transferred back to their home countries and there were 19 active cases under medical treatment in a designated treatment centre (27,28).

Disease transmission: COVID-19 is transmitted through droplets produced when coughing or sneezing. After leaving the infected person, the droplets can travel up to 2 meters and stay suspended in the air or get deposited on surfaces or the ground for varying periods. The virus can remain viable on surfaces for days if the atmospheric conditions are favourable. But common disinfectants such as ethyl alcohol (70%), sodium hypochlorite and hydrogen peroxide can effectively disinfect materials in less than a minute following application (29).

Both symptomatic and asymptomatic people can be sources of infection. Even though conclusive findings are not yet available, experts believe that people can stay infectious for as long as the symptoms last and even on clinical recovery. The portal of entry for the virus is either the respiratory system, when the droplets are inhaled, or touching the eyes, buccal or nasal cavity with a contaminated hand (17,23,30). The portal of exit is the same, and a person does not need to be symptomatic to transmit the infection, as long as they contaminate their hands with discharge from the buccal or nasal cavity.

Table 1: **Comparison of COVID-19 with the previous HCoV global outbreaks**

	SARS	MERS	COVID-19
Year, origin	November 2002, Guangdong province of China	2012, Saudi Arabia and many countries in the Arabian Peninsula	Dec 31, 2019, Hubei province of China
Incubation period	2-14 days	5-6 days after exposure, but can range from 2-14 days	2-14 days
Symptoms	Fever, chills, and body aches, progressing to pneumonia	Fever, chills, headache, cough, shortness of breath, diarrhea and nausea/vomiting	Fever, cough, shortness of breath, headache, fatigue and sore throat
Reservoir	Bats and intermediate host civets	Bats and intermediate host camels	Bats; the intermediate animal has not yet been identified
Total cases	8,422	2,229	2,014,554
Deaths	916	791	127,598
CFR	10.8%	34.3%	3-5%
Transmission rate (R_o)	R_o - 2	R_o - (2.5 - 8.09)	R_o - (3.6 - 4)

Note: Reprinted from "COVID-19:Lessons from SARS and MERS" by Park.M, Thwaites R.S, Openshaw P.J, 2020, European Journal of Immunology,50,308-316; Worldometer 2020. COVID-19 coronavirus pandemic.

Mortality rates: The overall case fatality rate (CFR) among those initially infected was calculated as 1.6%, but recent estimates (around the beginning of March) from the WHO indicated an increase in the CFR to 3.4% (23). Mortality from COVID-19 differs based on background characteristics, such as age, with different countries reported varying CFRs. Age-specific CFR indicates a significantly higher mortality among the elderly than the general population. So far, Italy has reported the highest CFR (10.8%), which is substantially higher than China (2.3%). The difference in demographics and culture of the people in the two countries is argued to explain the difference in CFR. Italy has a large proportion of elderly population and young people have close social ties with their parents and grandparents. These frequent social encounters between family members might have exposed the vulnerable elderly population to the disease. The second argument is that patients in Italy were taking ibuprofen as a symptomatic therapy, but latterly clinicians advised against its use, assuming the drug to exacerbate the proliferation of the virus (31,32). In contrast, Germany has had the lowest death rate from COVID-19 (0.6%), with the second lowest rate reported in USA and Switzerland (1.4%) (23).

Risk factors – Age: According to a WHO report and related studies, older age is strongly associated with higher mortality from COVID-19. The mortality rate among patients older than 80 years is reported to be 15%, but under 1% for those younger than 40 years. So far, no death has been reported among children in the age range of 0 to 9 years (19,23,33).

Risk factors – Sex: COVID-19 is reported to have a significant male preponderance, in terms of both morbidity and mortality. Thus far, 63.1% of patients have been males and the mortality among this group is 4.7%, which is more than twice the rate among females (1.7%). Higher smoking rates and lower personal hygiene practices among men compared to women are believed to explain the skewed distribution (13,19).

Risk factors – Cigarette smoking: The association between cigarette smoking and COVID-19 remains controversial. A recent update from the WHO suggests that using tobacco products increases the risk of infection (34). Bringing the hand close to the mouth while smoking may allow entry of the virus into the body and sharing cigarettes can facilitate the transmission. In general, cigarette smoking predisposes the respiratory system to infection, although two systematic reviews found no association between smoking and either developing COVID-19 or mortality from the disease (35-37).

Risk factors – Comorbidities: According to the Worldometer data, the death rate among patients with pre-existing cardiovascular disease, diabetes, hypertension and chronic respiratory diseases is 10.5 %, 7.3%, 6.3% and 6.0%, respectively (23). However, among patients with no underlying conditions, the number drops to 0.9%. Related epidemiological studies also support this finding (16,19,32). In establishing the association between sociodemographic characteristics and the risk of infection, it is worth noting the effect of such underlying health conditions in the causal pathway.

Diagnostics: The reverse real-time polymerase chain reaction assay (rRT-PCR) remains the primary diagnostic approach for SARS-CoV-2 (38-40). The test can run on a variety of clinical specimens, including bronchoalveolar lavage fluid, fibro bronchoscopy brush biopsies, sputum, nasal swabs, pharyngeal swabs, feces, or blood (40).

This current diagnostic approach is high maintenance, requiring well-equipped laboratories and highly trained staff. In addition, the multiple procedures involved between specimen collection and producing the result makes it difficult to use and time-consuming (40,41). A short turnaround time from giving a sample to obtaining the result increases the effectiveness of the control measures, since the subsequent public health interventions hinge on the test result and how fast it is obtained. Furthermore, going to and staying around testing facilities can increase the risk of transmission, not to mention the strain on the limited health care resources (40).

The rapid spread and non-specific presentation of the infection warrants an accurate, cheap and easy-to-use diagnostic tool for point of care (POC) testing (38,40-42). Because of this, the WHO made it a priority to assist and lead research projects in the area of low tech and rapid POC diagnostics for use at the community level (43). As part of this initiative, diagnostic companies such as FIND are working closely with the WHO and providing technical support to partners, building their capacity through staff training to ensure access to accurate and high-quality diagnostic test kits, particularly for low- and middle-income countries (44).

Aiming to expedite the approval process for new tests, the U.S. Food and Drug Administration (FDA) announced a new guideline which shortens the previous lengthy procedures (45). As of March 28, 2020, the FDA has approved two coronavirus tests that can be used at POC (46,47). The first test was granted emergency use authorization (EUA) on March 20, 2020. This test is intended for use in patient care settings and can produce the result in less than 45 minutes. A nasal swab or a saline wash using a small catheter can be used to collect a specimen for the test. Patients reported that neither approaches are comfortable, but the wash avoids the use of a swab, which is already in short supply (46). The second test was granted approval on March 27, 2020 for the fastest molecular POC developed so far to test COVID-19. The test delivers positive results in no more than five minutes and negative results in 13 minutes. The test is fit for use in a wide range of health care settings such as physicians' offices, emergency care clinics and hospital emergency departments (47).

In the early days of the outbreak in Wuhan, the standard laboratory nucleic acid sequencing analysis was used to test for the infection. But it was labour-intensive and costly, and there was a severe shortage of test kits. Hence, the National Medical Products Administration of China took immediate action to speed up the work of biotech companies to develop detection kits. As a result, the first kit was introduced on January 13, 2020, with enough supply made available after two weeks. From China's experience, it is apparent that having specific, reliable, accurate and fast detection methods to screen infected and non-infected people plays a major role in limiting the spread of the virus (48). In Africa, there were only two countries with some diagnostic capacity at the start of the pandemic. Initially, Ethiopia did not have test facilities, and samples were sent to South Africa for analysis, which required complex coordination activities and continuous communication. Ethiopia started in-country testing for the virus on February 7, 2020, and the results are reportedly produced on the same day (49).

Advancements in drug and vaccine development: To date, there are no approved drugs and vaccines in the market to prevent or treat COVID-19 (39). The WHO's working recommendation (Table 2) for suspected and actual cases of COVID-19 is health facility-based triage employing symptom severity and risk markers (40).

Table 2: **Levels of severity and corresponding treatment recommendations for COVID-19 (adopted from WHO, 2020)**[40]

Level of severity	Manifestation of COVID-19	Recommendation
Mild	Mild clinical symptoms. No pneumonia manifestation in imaging.	No hospital interventions required. Isolation of patients to contain virus transmission. Patients can be given symptomatic treatment, such as antipyretics. Counsel patients about signs and symptoms of complicated disease so that they will seek urgent care.
Moderate	Symptoms such as fever and respiratory tract symptoms, and manifestations of pneumonia can be seen in imaging.	Symptomatic treatment, and treatment of pneumonia with antibiotics.
Severe	Respiratory rate ≥ 30 breaths/min; oxygen saturation ≤ 93% at a rest state; arterial partial pressure of oxygen (PaO2)/oxygen concentration (FiO2) ≤ 300 mmHg. Patients with > 50% lesions progression within 24 to 48 hours in lung imaging.	Oxygen therapy: recommended for patients with respiratory distress and severe acute respiratory infection. Oxygen supplementation treatment can correct hypoxemia, relieving secondary organ damage caused by respiratory distress and hypoxemia. Closely monitor patients for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and respond immediately with supportive care interventions.
Critical	Occurrence of respiratory failure requiring mechanical ventilation; presence of shock; other organ failure that requires monitoring and treatment in the intensive care unit.	Artificial liver support system and blood purification can effectively diminish inflammatory mediators and cytokine cascade, and prevent the incidence of shock, hypoxemia and respiratory distress syndrome. They can also improve multiple organ functions, including of the liver and kidney. Thus, they can increase treatment success and reduce mortality from severe disease. Mechanical ventilation (could be non-invasive or invasive).

Despite the lack of approved drugs and vaccines for COVID-19, the scientific community has been looking into repurposing drugs approved for other diseases to treat COVID-19. As of March 29, 2020, there were 209 clinical trials registered at *clinicaltrials.gov* (50). However, the actual number of clinical trials is estimated to be over 500. The trials include drugs, dietary supplements, vaccines, surgical procedures, and a wide range of products (43). The drugs under investigation include anti-viral hydroxychloroquine and chloroquine, protective monoclonal antibodies, and human convalescent serum.

Lopinavir–ritonavir

Lopinavir is an HIV-1 protease inhibitor, often combined with ritonavir to increase its half-life. The drug has shown promise to inhibit coronavirus replication *in vitro*, and in previous studies it has improved the clinical outcome of patients with MERS-CoV when used in combination with interferon.

Currently, a clinical trial is under way to study the safety and efficacy of the drug for SARS-CoV-2 (44,45). According to an experience from designated hospital for COVID-19 patients, in China, the administration of lopinavir–ritonavir (two capsules, orally, every 12 hours) with Arbidol (umifenovir) (200mg, orally, every 12 hours) for 49 patients resulted in a negative nucleic acid test result, however it was reported that these results lasted for an average duration of 13.5 days (42).

Remdesivir

Remdesivir is an RNA polymerase inhibitor. Both *in vitro* and *in vivo* experiments have shown promising results against coronavirus. Currently, a randomized controlled trial is under way to test the efficacy of the drug in patients with mild to moderate and severe COVID-19. This drug has been used in the USA, China and Italy on a compassionate basis to treat small numbers of patients with severe COVID-19 (39,44,46,47).

Hydroxychloroquine/Chloroquine

Chloroquine is an anti-malarial drug sometimes used to treat certain inflammatory conditions, such as rheumatoid arthritis and systemic lupus erythematosus. Hydroxy chloroquine is a prodrug for chloroquine. These drugs are currently under investigation for prophylaxis, as well as treatment, of patients with mild, moderate or severe COVID-19 (51). In China, chloroquine phosphate was given to adults aged 18-65 years of age (weight ≥ 50 kg: 500 mg twice a day for seven days; weight ≤50 kg: 500 mg twice a day for the first two days, 500 mg once a day for the following five days) (52). It is important to note that the drug has a narrow safety margin between the therapeutic and toxic dose. Therefore, self-treatment using these drugs is not advised, as inappropriate use may cause fatal complications (53).

Convalescent plasma treatment

This involves the administration of antibodies extracted from the blood plasma of a recovered COVID-19 patient into an individual in the hope of treating the patient or preventing future transmission. If deemed successful, this approach promises a great potential due to the availability of recovered COVID-19 patients in great numbers who can provide immunoglobulin-containing serum. However, it requires caution and use of the right technology not to risk inadvertently transmitting other pathogens or trigger immunologic reaction in the recipient (54).

Vaccines: Most of the vaccines under trial are S-protein based and are intended to induce an immunoreaction. The S-protein act in the SARS-CoV by producing neutralizing antibodies and T-cell responses (55). Among those under investigation is mRNA1273 vaccine, which has been expedited from the design stage straight to phase I clinical trial for its effect on SARS-CoV-2 (56).

Public health control measures

How it all started

The fast dynamics of Wuhan, a bustling city of 11 million residents with high population density, favoured the rapid transmission of COVID-19 at its earliest stage (53). A banquet in Wuhan for 400,000 guests that was held immediately before the lockdown is also believed to have fuelled the transmission (53). By the time the outbreak was detected, community transmission was imminent, forcing the lockdown of Hubei province. Countries subsequently affected by the outbreak have employed different levels of control measures depending on the epidemiologic pattern of the outbreak and the local socioeconomic circumstances.

Epidemiologic parameters and control measures

More than two thirds of countries in the world are taking serious measures to control the COVID-19 pandemic following the surge in disease transmission and the loss of tens of thousands of lives. Designing effective outbreak control measures requires a good understanding of the course of the disease and accurate estimates of the epidemiologic parameters. The conventional isolation and contact tracing approach is recommended for a localized outbreak with minimal community transmission (54). This approach will be effective if two epidemiologic parameters are optimal: the basic reproductive number and the time to infectiousness (54).

The basic reproductive number (R_0)

Basic reproductive number (R_0) stands for the number of secondary cases developed following contact with the infectious patient. It is estimated from mathematical models, taking into account the varying environmental- and patient-related factors that can modify transmission. An R_0 value of 1 indicates steady transmission. An R_0 value of less than 1 indicates a decline in transmission. A R_0 value >1 is consistent with an outbreak or indicative of a highly likely outbreak. An accurate estimate of R_0, especially for a new disease, will be obtained if the estimation is done once the outbreak is through its course. This way we can account for the total number of cases that occurred during the outbreak (54).

We have found few publications on basic reproductive number for COVID-19 from studies conducted 1-2 months after the outbreak. The studies have provided varying estimates of R_0 values for the outbreak. The first study involved 24 provinces in China with a minimum of 100 confirmed cases (55). In this study, the final R_0 estimate obtained after updating the model a few times was <1 (55). The basic assumption when calculating R_0 is a complete absence of control interventions and the whole population is susceptible to the infection (54). Nonetheless, when the above study was conducted, aggressive control measures were under way. Therefore, it is safe to assume that the R_0 value could have been higher if those measures had not been in place. But this drawback was addressed in another study, where the investigators modelled the transmission based on data from the passengers of the *Diamond Princess* cruise ship. There were 3,711 people on board when the outbreak was detected among the passengers (56). This study has estimated a median R_0 value of 2.28, which is significantly higher than the previous study, but lower than estimates from other studies (R_0=3.58) (57). The estimate from the *Diamond Princess* cruise ship study is likely to be more accurate because it was conducted in a close to ideal setting to estimate R_0. The complete control over the movement of people on and off the ship, the ability to avoid potential animal to human transmission, and being able to account for the level of control measures taken, are important to maximize the accuracy of the estimate (56).

The generation time

The second important parameter is the generation time. This is the time interval between the infection of the source and the generation of secondary cases (54). The isolation and contact tracing approach works best in diseases where the generation time overlaps with or exceeds the incubation period. In this scenario, people will have time to isolate themselves and health personnel can screen patients before the disease transmits (58).

Epidemiologists attribute the effective control of the 2002 SARS outbreak to the nature of the infection where the infectiousness hits peak after the onset of disease symptoms. This made the isolation and contact tracing interventions effective, leading to control before it had impacted on more nations (59). However, evidence on the generation time of COVID-19 is lacking and this undermines the effectiveness of the control interventions (60).

A study of 17 symptomatic COVID-19 patients indicated higher viral load in the nasal and throat swab specimens right after the onset of symptoms. This indicates the possibility of transmission earlier in the course of the infection, even before the onset of the symptoms (61,62). Viral load in the asymptomatic patients was comparable to viral load in the symptomatic patients (61). This finding is crucial, mainly because 30% of the people who are positive for COVID-19 infection are asymptomatic (57). These important epidemiologic characteristics make it clear that employing isolation and contact tracing solely are not enough to control the outbreak. A mathematical model showed that if we employ isolation and contact tracing as the only control strategy, one should trace and isolate 80% of contacts of each patient to achieve a probability of 90% control in three months' time, assuming a 2.5 basic reproductive number (58).

These findings unequivocally indicate that using only one conventional outbreak control approach is simply inadequate to control the COVID-19 pandemic. Countries need a combination of various interventions implemented with the utmost efficiency and central coordination (63). Extensive physical and social distancing interventions with increased and regular hand washing practices, coupled with isolation and contact tracing, can improve the likelihood of control in the foreseeable future. Social distancing (if done correctly) alone can reduce transmission by 60% given the outbreak is at its early stage (62). But at later stages, after community transmission is witnessed, the intervention should progressively scale to community containment.

This recommendation holds true for Ethiopia as well. In the past three weeks (counting from April 15, 2020), 85 confirmed cases have been reported. All except a few came from abroad or had contact with people who had recently arrived from overseas (28). Considering the short doubling time (4-5 days) of the outbreak, 85 cases over a week's period is encouraging (62). On the other hand, it could be suggestive of inadequate testing. Up until we prepared this report, only 700 people who were deemed to have a close contact with confirmed cases had been tested. The limited testing and the unclear course of the disease portend a rapid increase in the number of cases any time soon. Therefore, the number of tests should increase to aid the effectiveness in the implementation of isolation and contact tracing, social distancing and related public health interventions.

The use of face masks as a preventive measure

When we prepared this report, the WHO maintains that there is no evidence showing the effectiveness of wearing masks in reducing the transmission of the virus (30,43,58), although there is a separate WHO recommendation that states wearing a medical mask is one of the preventive measures to limit the spread of certain respiratory diseases, including COVID-19 (43). Despite recommendations that the use of face masks should be restricted to health professionals only, the absence of evidence regarding their effectiveness among the general public does not prove their ineffectiveness, especially when facing an outbreak with limited control alternatives (59). Moreover, viruses can also transmit through the eyes and tiny viral particles, known as aerosols, which can penetrate masks, although some argue that masks are effective at capturing droplets, which is a main transmission route of coronavirus (60). Furthermore, since there is asymptomatic and pre-symptomatic transmission, the universal use of masks contributes to a decrease in the transmission (59,61). Though the WHO's stance on the universal use of face mask is unclear at the time, it has called for a 40% increase in the production of protective equipment (62).

The Ethiopian Ministry of Health has been recommending symptomatic individuals and health care providers should wear masks. But the latest directive also encourages the use of cotton masks by the rest of the population, especially in public places.

The use of alcohol hand sanitizers

Hand hygiene is one of the main preventive measures in response to COVID-19 (63,64). Washing hands often with soap and water for at least 20 seconds is essential. If soap and water are not readily available, the CDC recommends consumers use an alcohol-based hand sanitizer that contains *at least* 70% alcohol (also referred to as ethanol or ethyl alcohol). Since health care professionals are having problems accessing alcohol-based sanitizers, the CDC has provided a policy guide for compounding them. As the COVID-19 outbreak is a public health emergency, the FDA announced it does not intend to take action against compounders who prepare alcohol-based hand sanitizers for consumers and hand rubs for health care personnel for the duration of the public health emergency, as long as the requirements are met (65).

With hand sanitizers in short supply and the increasing number of COVID-19 cases, it is essential to locally produce alcohol-based hand rub formulations with guidelines available in local settings (66).

Psychosocial interventions for health care providers

The WHO has developed key recommendations on mental health considerations for the general population, health workers, including team leaders and health facility managers, care providers, and people with underlying health conditions (67).

In relation to health workers, the recommendations focus on normalizing the experience of stress, the need for employing healthy coping strategies (adequate sleep, healthy eating, exercise and staying in touch with loved ones), equipping oneself with the required knowledge, and managing possible stigma. Team leaders are encouraged to protect their staff from chronic stress, clearly communicate with staff, encourage staff to provide mutual support, and ensure the availability of essential, generic psychotropic medications at all levels of health care.

Mindfulness-based stress reduction is one of the recommended techniques to cope with stress (68). There is evidence that mindfulness has a great potential to reduce stress, anxiety and burnout (69).

Discussion

The epidemiology and nature of COVID-19 are changing. In this rapid review, we have tried to synthesize what is known about the disease, the causative pathogen and treatment, and prevention strategies employed at the time this review was conducted (April 15, 2020). The pandemic has affected both developed and developing countries, overwhelming health systems and challenging economies, and it is now threatening to engulf Africa. Gender, cigarette smoking and underlying disease conditions are associated with unfavourable outcomes. A reverse real-time polymerase chain reaction assay is used for diagnosis, but no vaccine or treatment has been discovered to treat the infection. Most countries have taken progressively stringent measures of control with the hope of averting the impending calamity. This review, by summarizing the key evidence regarding the seriousness of the threat, the resources for treatment, diagnosis, prevention, and control, hopes to assist in the effort to avert the pandemic.

Although the symptoms are consistent with atypical upper respiratory tract infection and atypical pneumonia, the information is based on the experience of China and developed countries. There is a need to systematically describe the clinical features and course of COVID-19 in Ethiopia and other countries in Africa. There may be variations in presentation because of host and pathogen factors. In relation to host factors, people in Africa have a somewhat different co-morbidity profile, age distribution, economic and nutritional factors and service use practices that may affect the presentation and course of the illness.

Age and co-morbidities may be of particular interest because they predict disease severity and death (70). COVID-19-related risk of deaths is 1.4% and it increases with age (23). Communities with a high proportion of aging population have suffered the wrath of the pandemic. This has been particularly demonstrated in Germany and Italy. Germany, with a significantly low number of deaths has two thirds of the patients in the age range of 35 to 50, with only 19% older than 60 years (71), while in Italy there have been much higher numbers of older people affected and the death toll was also higher. For Africa, the much lower proportion of people older than 60 may translate into fewer deaths, although Africa's weak health systems may increase vulnerability. Therefore, strong control interventions should be directed towards protecting the elderly (72).

Though we still do not have concrete evidence, chronic infectious diseases such as tuberculosis (TB) and HIV/AIDS, as well as chronic undernutrition, may increase the risk of death secondary to COVID-19. As these conditions are prevalent in the developing world, COVID-19 control measures should consider the increased risk among these groups of people (73). Strategies to carry out the follow-up of patients with chronic diseases and TB remotely may reduce the risk of exposure at medical facilities.

The reverse real-time polymerase chain reaction is a test currently in use to diagnose SARS-CoV-2 infection. Though this test has a high diagnostic accuracy, it requires well-trained technologists, sound laboratory facilities and multiple reagents (74). This makes the test ill fit to deal with a pandemic of this scale and nature. Currently, simpler POC antibody tests are under development (75). Such simple tests will make large-scale community-based screening feasible, even in the under-developed and under-resourced parts of the world. The number of available tests (assuming it is conducted at the right time) determines nations' ability to control the pandemic (74). Therefore, developing countries should be encouraged and supported to locally produce such less expensive and easier-to-use antibody tests.

The world is uncertain about what the future holds (76). Vaccinating a significant proportion of the population creates herd immunity, breaking the chain of transmission (77). The large number of vaccine trials under way (78) encourages the hope that vaccine development will be completed in the coming 12 to 18 months. The challenge seems, given the need to produce the vaccine in large amounts at one time, how the vaccine can be allocated in a fair way. The experience from previous flu-like pandemics suggests that the developing world needs to be vigilant. Cautious steps should be taken not to widen the already existing rift between high-income and low-income countries in relation to access to vaccines (79).

So far there is no robust evidence for effective treatment against SARS-CoV-19. While the need for a rapid development of treatment cannot be disputed, caution must be exercised in providing compassionate treatments or conducting clinical trials to avoid additional risks to patients. In the absence of clear evidence, the trade-off in shifting drugs which were originally intended to treat other diseases to COVID-19 patients should also be considered. Therefore, clinical trials should be conducted to account for the safety and efficacy of repurposed drugs.

Health care personnel are invaluable resources in the fight against the pandemic. As first responders, they face an exceptional risk of contracting the infection. Thus, protecting their wellbeing is paramount. This extends from making the needed personal protective equipment and testing available to ensuring their psychosocial and physical wellbeing. For the general public, although directives on face mask use are fluid, we strongly recommend that the universal use of face masks will help control the outbreak by reducing escape of the virus from infected people. To avoid stockout of medical masks restricting the general public (non-health care providers) to using cotton face masks only can be considered.

While we believe that this review offers important information on a broad range of issues relevant to understanding the pathogen, the magnitude of illness and the status of knowledge about treatment and control, the primary data collected is mostly anecdotal, and report- and opinion-based. Additionally, knowledge about COVID-19 is extremely fluid. For example, the data on the magnitude of the disease provides the overall trend and level of threat; this will have changed substantially by the time this paper is published. The recommendations on treatment and diagnosis are unlikely to change, although better POC diagnostics might be, if produced by the time this paper is published. The possible methodologic drawbacks with such publications and the ever-changing science surrounding the disease warrants readers to keep pace with the updates.

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