

Review article

Rapid evidence synthesis on COVID-19 pandemic to inform the Ethiopian Ministry of Health

Zelalem Kebede, Sabit Ababor, Firmaye Bogale*, Dagmawit Solomon, Ermias Wolde, Tsegaye Getachew, Samson Mideksa, Desalegn Ararso, Emana Alemu and Yosef Gebreyohannes

Ethiopian Public Health Institute, Addis Ababa, Ethiopia

*Corresponding author: fbbogale93@gmail.com, Cell phone: +251913754332

Abstract

Introduction: At the end of December 2019, Chinese scientists identified a novel coronavirus as the main causative agent for COVID-19, which was declared a pandemic by the WH on March 11, 2020, and had affected more than 1.9 million people. Since this novel infection is overwhelming, the research community has responded promptly to the virus and many preliminary research articles have already been published about different aspects of this pandemic.

Objective: To summarize the best available research evidences on COVID-19 pandemic and to inform the Ethiopian Ministry of Health.

Methods: A rapid evidence review approach was applied to search, appraise and summarize the available evidence on the COVID-19 pandemic. We identified the Population, Concept, and Context with respect to the objective of the review to facilitate searching of relevant articles and unpublished ministry documents. Searching was done on the PubMed database, and Cochrane Library from 01 December 2019 to 07 April 2020. Accordingly, we found a total of 473 studies. By the eligibility criteria, 51 articles are included in this review.

Results: The findings of this review are organized into two major parts. The first part shows the COVID-19 situation in Ethiopia in terms of WHO outbreak scenarios, and readiness of the Ethiopian health system. Though the government of Ethiopia recently adopted different measures, these may not have come in time to prevent the surge of cases. The second part focuses on a review of global research evidence in terms of mode of transmission, pathophysiology and clinical manifestation, risk group, screening and diagnosis, treatment, prognosis, and prevention and control. Current evidence shows COVID-19 is transmitted between people through respiratory droplets and contact routes though the pathophysiologic data is limited. So far there is no known specific, effective, and proved pharmacological treatment for the disease and the only option of case management is infection prevention and supportive care.

Conclusion: Since COVID-19 is a new disease, much is unknown about it. Researchers and scientists around the globe are undertaking many studies to uncover the hidden facts of this pandemic. As of this time, the available evidence shows isolating, testing, treating, and tracing of new cases along with social distancing measures are effective to control the virus spread.

Keywords: COVID-19, SARS-CoV-2, rapid evidence synthesis

Introduction

By the end of December 2019, Chinese public health authorities reported several cases of acute respiratory syndrome in Wuhan City, Hubei province, China. Soon after, Chinese scientists identified a novel coronavirus with the main causative agent named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) where the disease is now referred to as coronavirus disease 2019 (COVID-19). The coronavirus generally belongs to a family of viruses that may cause various symptoms such as pneumonia, fever, breathing difficulty, and lung infection (Wuhan Municipal Health Commission, 2019). These viruses are common in animals worldwide, but very few cases have been known to affect humans (CDC 2020a). This respiratory illness

caused by a new coronavirus (COVID-19) is believed to arise from animal markets in Wuhan city and came into health care workers attention for the first time on December 8, 2019. This illness was declared a pandemic by the world health organization (WHO) on March 11, 2020. By the time this report was being written the virus had affected more than 1.9 million people causing more than 120,400 deaths in over 210 countries and territories around the world and two international conveyances where confirmed COVID-19 cases in Africa were more than 10,000 (CDC 2020; Worldometer 2020). Since this novel infection is spreading rapidly and is overwhelming the most advanced and toughest medical science and technology, everyone is curious about what is there to know and what to contemplate with this pandemic.

Consequently, the research community has responded promptly to the virus and many preliminary research articles have already been published about this pandemic. The amount of evidence produced in this short period is overwhelming and needs to be filtered for any decision to be made on the best available evidence.

Accordingly, we conducted a rapid evidence synthesis to summarize and critically analyze the published scientific articles regarding the new coronavirus. This review aims to provide the evidence of early findings on the mode of transmission, pathophysiology and clinical manifestations, screening and diagnostic methods, treatment, prognosis, prevention, and control and risk groups. This review can provide meaningful information for decision-making on strategies to handle this public health emergency at the community or national levels.

Materials and Methods

Rapid evidence review approach was applied to search, appraise and summarize the available evidence on COVID-19 pandemic. We identified the Population, Concept and Context (PCC) on which studies on human population with a concept focus on the mode of transmission, pathophysiology, clinical manifestation, diagnosis, treatment Prognosis, prevention and Control, and risk groups of COVID-19 are included without restriction to any geographical context, with respect to the objective of the review to facilitate searching of relevant articles and unpublished ministry documents. All human studies conducted starting from December 1, 2020, with the last search made on April 07, 2020 on COVID-19 with regard to mode of transmission, pathophysiology and clinical manifestations, screening and diagnostic methods, treatment, prognosis, prevention and control, risk groups were included while reviews that are not systematic and transparent (e.g. literature reviews, news, letters, editorials, reports, communications, comments, and correspondence) with the exception of the Ethiopian Ministry of Health document; studies published other than the English language, and studies conducted before December 1st, 2019 were excluded from this rapid synthesis. Unpublished literature were retrieved from WHO website and Ministry's documents and reports were accessed via personal contacts and retrieval. This review was due on April 8, 2020. PubMed database, the Cochrane Library, Ethiopian Public Health Emergency Operation Center (PHEOC), MoH documents and reports, and WHO website were used as data sources. "COVID-19" OR COVID OR coronavirus OR Corona OR "SARS-CoV-2" OR Coronaviridae OR "novel corona" OR

"coronavirus" (limited to human and English) were used for Search strategy.

Results

The findings in this review are organized into two major parts. The first part addresses the COVID-19 situation in Ethiopia in terms of WHO outbreak scenarios, and readiness of the Ethiopian health system in terms of human and material resources. The second part focuses on a review of global research evidence in terms of mode of transmission, pathophysiology and clinical manifestation, risk group, screening and diagnosis, treatment, prognosis, and prevention and control.

Part I: COVID-19 situation in Ethiopia

Timeline of Ethiopia's COVID-19 Situation and measures taken so far: Ethiopia confirmed the first case of COVID-19 on March 13, 2020. The first confirmed case of COVID-19 in Ethiopia was a 48 years old Japanese citizen who was tested positive on March 12, 2020, by the Ethiopian Public Health Institute after coming from Burkina Faso eight days prior to being identified as a case. Ethiopia recorded the first death of COVID-19 as of March 29, 2020 (Figure 1).

The WHO has defined four transmission scenarios for COVID-19 where Scenario 1 indicates countries with no cases (No Cases); scenario 2 shows countries with 1 or more cases, imported or locally detected (Sporadic Cases); scenario 3 indicates countries experiencing cases clusters in time, geographic location and/or common exposure (Clusters of cases); and scenario 4 indicates countries experiencing larger outbreaks of local transmission or community transmission (World Health Organization 2020).

Countries could experience one or more of these scenarios at the national and sub-national levels. Accordingly, estimation was done for Ethiopia based on the currently available epidemiological data in the globe and literature (Ferguson et al. 2020; Han and Yang 2020; Khalid et al. 2020; Krupp 2020; Ministry of Public Health 2020). Consequently, considering WHO transmission scenario four for a population of 110,000,000 million populations, approximately 11,000,000 persons (10%) might contract the symptomatic infection, over a period of the next few months. Of these cases; 1,650,000 (15%) might seek healthcare, out of which 330,000 (20%) would require hospital admission and 33,000 (2%) would be admitted to the intensive care unit (ICU) with an estimated death toll of 24,750 (1.5% of those seeking healthcare) considering that Ethiopia has a relatively young population compared to those high-income countries with high comorbidities. If the outbreak is

not contained in a timely manner, the Ethiopian health system will be overwhelmed; patients with coronavirus or other urgent medical conditions will

not receive their needed care, and a substantial number of unnecessary deaths will become inevitable (Fisher and Heymann 2020).

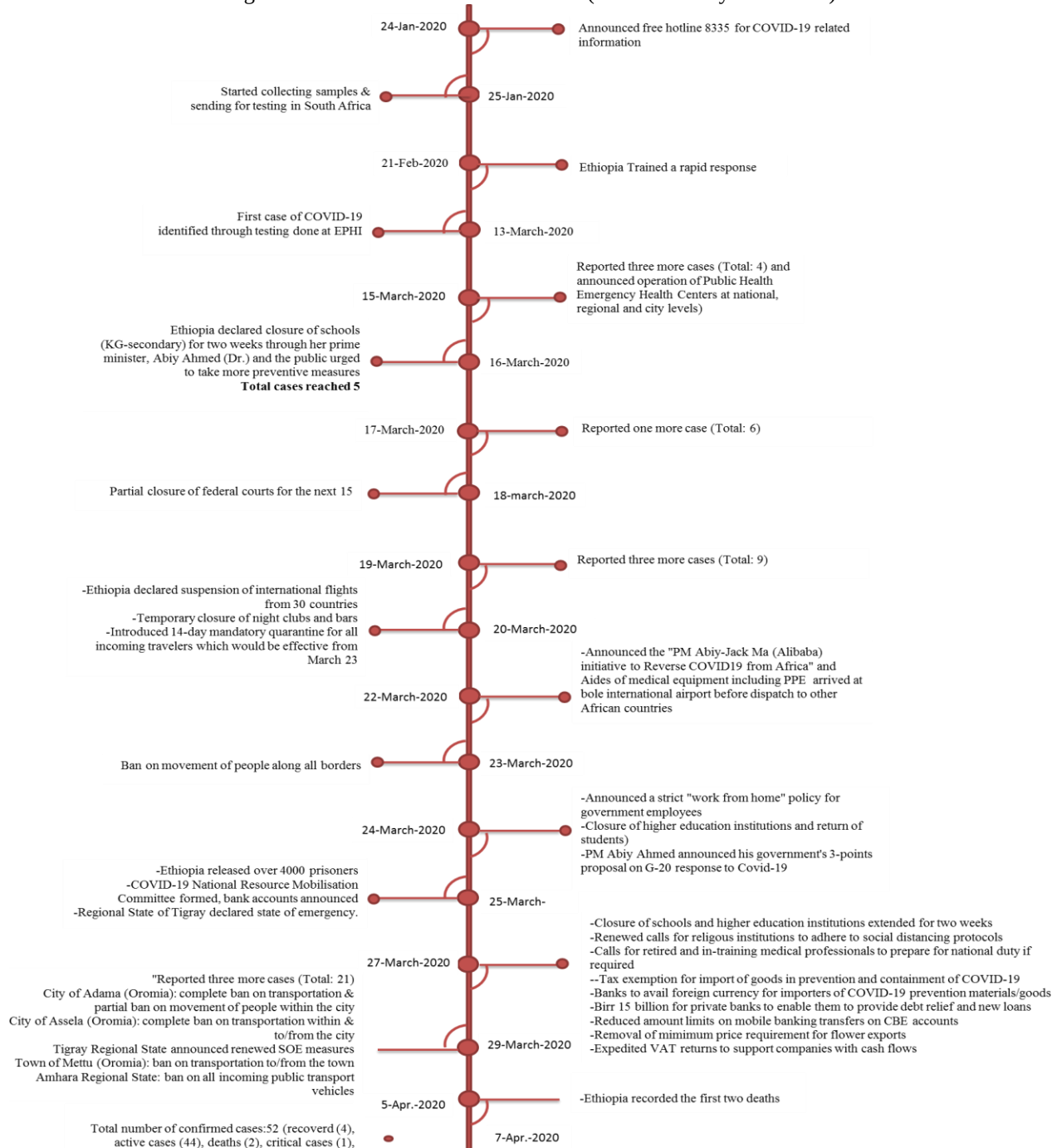


Figure 1: Ethiopia's timeline of COVID-19 situation, April 7, 2020

Ethiopia's Readiness: To tackle the possible consequences of COVID-19, the Ethiopian government has enacted a range of measures to control the epidemic, starting with temperature screening at the airport and testing of suspected cases

(including contact tracing) before moving to closure of schools, universities and international travel ban to and from 80 countries and quarantining any remaining international travelers coming to the country for a mandatory of 14 days in dedicated

centers for this purpose. A national structure and functional relationship of the COVID-19 response at the higher level and the structural arrangements of the Public Health Emergency Operation Center (PHEOC) at Ethiopian Public Health Institute is also created where the technical leadership responsibility is under the Ethiopian Public Health Institutes through its Public Health Emergency Management (PHEM). According to the 2020 data from the Ministry of Health Ethiopia, there are a total of 7,198 medical doctors, 0.7 per 10,000 ratio, which is well below the WHO recommendation of 2.3 per 10,000 (WHO 2016). Across the ten regions and two

administrative cities of Ethiopia, there are about 410 public and private hospitals of different categories with only 29,748 beds in total (MoH 2019).

Part II: Summary of global research evidence for COVID-19

Based on the search strategy we found a total of 473 studies from PubMed and Cochrane library. Using the eligibility criteria 51 articles were reviewed and summarized (See PRISMA diagram). The table indicating the characteristics of the included study is not annexed in this document and can be obtained upon request to the authors at any time.

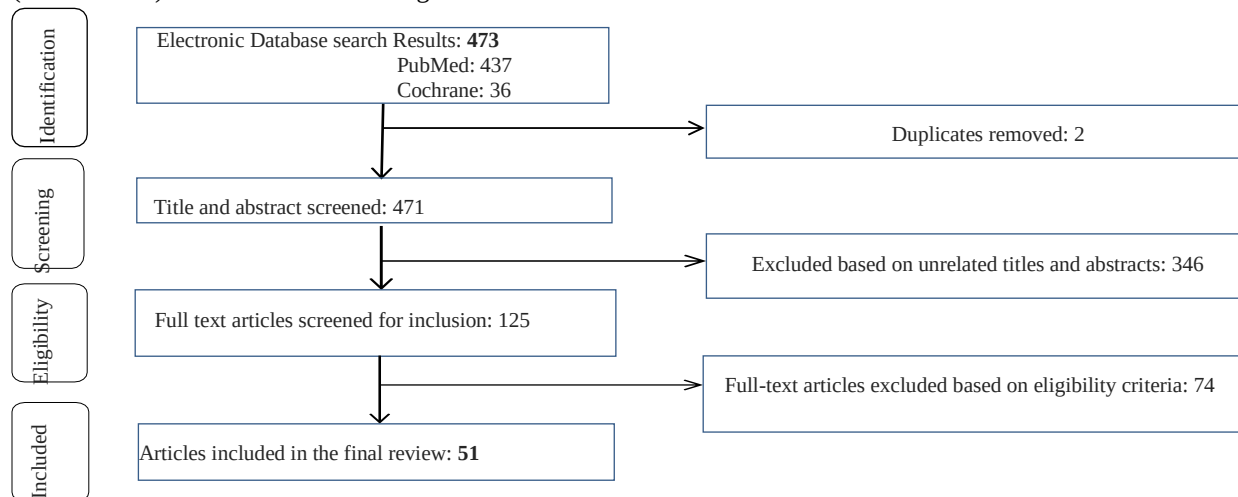


Figure 2: PRISMA diagram

The included articles in this review are summarized into different thematic areas: mode of transmission, pathophysiology and clinical manifestation, risk group, screening and diagnosis, treatment, prognosis, and prevention and control. The summary of the findings of each theme is presented below.

Mode of Transmission: As per different research evidence, the COVID-19 virus is primarily transmitted between people through respiratory droplets and contact with infected individual, even asymptomatic ones (Ceccarelli et al. 2020; Zou et al. 2020). Droplet transmission occurs when a person is in close contact (within 1 meter) with someone who has respiratory symptoms.

Transmission may also occur through fomites in the immediate environment around the infected person (Wu et al. 2020). In an analysis of 75,465 COVID-19 cases in China, airborne transmission was not reported but may be possible in specific circumstances and settings in which procedures or support treatments that generate aerosols like endotracheal intubation and bronchoscopy are performed (Xu 2020). The study recalled that the

early evidence was most consistent with limited human-to-human transmissibility (Wu et al. 2020). Another study showed that stool samples were positive until the 17th day since symptom onset (Park et al. 2020). However, there have been no reports of faeco-oral transmission of the COVID-19 virus to date (WHO 2020b). Regarding the potential risk of mother to newborn vertical transmission, we only found one study that included nine women with confirmed COVID-19 pneumonia. This study did not find any evidence of the presence of SARS-CoV-2 viral particles in the products of conception or in neonates (Qiao 2020). Regarding transmission of the virus with animal food, there is only one study conducted on 99 patients with 2019-nCoV pneumonia of which 49% had a history of exposure to the Huanan seafood market (Chen et al. 2020). However, we could not find a study that confirms animal foods to transmit the virus.

Pathophysiology and clinical manifestation: Though there is limited pathophysiologic data on COVID-19, studies indicate that the entry receptor for COVID-19 in humans is Angiotensin-converting enzyme2 (ACE2). The virus replicates efficiently in

the upper respiratory tract and infected people produce a large quantity of the virus at the beginning of the infection. As the body gets infected a cytokine response is triggered whereby immune cells attack the virus. In some cases and for reasons unknown, the virus may trigger an over-reactive response from the immune system, which can further diminish recovery efforts (Fung et al. 2020; IFLScience 2020).

The lung appears to be the most vulnerable target organ of this virus and one reason is that the vast surface area of the lung makes it highly susceptible to inhaled viruses. This is coupled with another biological factor where 83% of ACE2-expressing cells are alveolar epithelial type II cells (AECII) that can serve as a reservoir for viral invasion. The expression of the ACE2 receptor is found in many extrapulmonary tissues including heart, kidney, endothelium, and intestine. Consequently, a study has predicted the intestine might be a major entry site for SARS-CoV-2 which has an important implication for fecal–oral transmission and containment of viral spread (Zhang et al. 2020). Patients with this infection could also be asymptomatic carriers or could experience different complications including ARDS, RNAemia, acute cardiac injury, gastrointestinal infection, secondary (super) infections, and multiple organ failure.

The incubation period for COVID-19 is thought to be within 14 days following exposure, with most cases occurring approximately 4-5 days after exposure (Xu et al. 2020). A study suggests that individuals with compromised immune status might be subjected to a longer incubation period (Jin et al. 2020). Major clinical presentations of this infection include fever, dry cough, myalgia, fatigue, dyspnea, diarrhea, muscle ache, confusion, headache, sore throat, rhinorrhea, chest pain, nausea, and vomiting. In addition to the above symptoms, chest radiology findings showed changes in the lung and thorax. These include chest X-ray presentation of bilateral, multi-lobar ground-glass opacities; chest CT showing patchy or nodular consolidations with peripheral ground-glass opacities in sub-pleural areas of the right lower lobe; and CT scan of thorax displaying diffuse ground-glass opacities and consolidation on both lungs consistent with ARDS. Laboratory abnormalities of lymphopenia or elevated LDH could potentially serve as early surrogate markers in the absence of clear dysregulated host response to infection (Li et al. 2020; Park et al. 2020; Wei et al. 2020; Yoon et al. 2020).

Risk group: Based on articles reviewed, the virus that causes COVID-19 infects people of all ages. However, evidence to date suggests that older people

(that is people over 60 years old) and those with underlying medical conditions (such as cardiovascular disease like hypertension, diabetes, chronic respiratory disease, and cancer) are at a higher risk of getting severe COVID-19 disease. The risk of severe disease gradually increases with age starting from around 40 years (Chen et al. 2020; Liu et al. 2020; Shi et al. 2020; WHO 2020c). Although we could not find a published primary study relating smoking and COVID-10, the limited available data show that smoking is most likely associated with the negative progression and adverse outcomes of COVID-19. So, being a smoker makes it more likely to fall into one of the main risk groups (Vardavas and Nikitara 2020).

Screening and diagnosis for COVID-19: Tests that are currently under consideration and already being used in the COVID-19 pandemic include screening tests (mainly thermal) and various forms of laboratory diagnostic tests among which serology, molecular and viral strain sequencing are included (Li et al. 2020).

The WHO recommends a combination of measures of rapid diagnosis and immediate isolation of cases, rigorous tracking, and precautionary self-isolation of close contacts. Thermal screening is currently considered as the primary tool for screening. With thermal screening, there are likely many people who would be missed during the screening processes at the airports as well in clinical settings, because of the poor sensitivity nature of the thermal screening, as the majority of COVID-19 are asymptomatic. According to a report, the effectiveness of thermal passenger screening for 2019-nCoV infection at airport exit and entry is only about 56% (Han et al. 2020). Serological tests for diagnosis of COVID-19 are also entering the market and used for diagnosis in some countries (Johns Hopkins Center for Health 2020). WHO has made available some molecular diagnostic protocols for testing coronavirus-19 in suspected human cases. Accordingly, real-time-PCR (the gold standard method) is the diagnostic tool in place at the global level and throat, or a nasal swab is used as a sample (Corman et al. 2020; Zou et al. 2020; WHO 2020a). However, we found one study that indicated the real-time PCR test showed false-negative results where the authors call for the use of real-time PCR combined with clinical manifestations, and chest CT to diagnose SARS-CoV-2 infection (Li et al. 2020; Wu et al. 2020).

Treatment: Apart from studies showing promising results, there is no known specific, effective, and proven pharmacological treatment for COVID-19 as of this time. Current clinical management includes

infection prevention and control measures and supportive care, including supplemental oxygen and mechanical ventilator support when indicated (CDC 2020b). Several clinical trials of pre-exposure prophylaxis, post-exposure prophylaxis, or treatment of COVID-19 are currently underway. In-vitro studies have indicated that chloroquine is effective in reducing viral replication in infections, including the SARS-associated coronavirus and MERS-CoV. Although chloroquine has been used worldwide for more than 70 years the efficacy and safety of chloroquine for the treatment of COVID-19 pneumonia remains unclear (Cortegiani et al. 2020; Gao et al. 2020).

A combination of antiviral treatments, such as lopinavir/ritonavir, litonavir, Fabiravir, ribavirin, Baricitinib, and interferon- β are newly identified treatments of COVID-19 at an in-vitro level (Lim et al. 2020; Wang et al. 2020). Beside in-vitro level testing, a combination of lopinavir/ritonavir was tested in a single patient in South Korea, the result indicates the decrease in viral level after the first dose administration of the medication (Lim et al. 2020). Remdesivir has been recently recognized as a promising antiviral drug against a wide array of RNA viruses (including SARS/MERS-CoV) infection in cultured cells, mice and nonhuman primate (NHP) models (Wang et al. 2020).

Prognosis: WHO estimates the case fatality rate of COVID-19 at an average of 3.4%. Compared to other viruses, the case fatality rate for COVID-19 is less (SARS: 9.6%, MERS: 34%) (Worldometer 2020).

From the previous experiences, coronavirus infections (SARS/MERS-CoV) in pregnancy indicate that these agents are capable of causing adverse clinical outcomes including life-threatening maternal disease that in some cases requires hospitalization, intensive care, and ventilator support. Both of these coronaviruses can result in maternal death in a small but significant number of cases, but the specific risk factors for a fatal outcome during pregnancy have not been clarified (Schwartz and Graham 2020).

A small proportion of recovered patients may test positive after discharge, calling for post-discharge surveillances thus the need for post-discharge surveillance and isolation strengthening. A study on post-discharge surveillance after clinical recovery indicated that swabs were positive in two asymptomatic cases (3.23%). One of the two cases was presented with typical clinical and radiological manifestations on admission, while manifestation in the remaining was very mild (Xing et al. 2020).

Prevention and Control: The research findings summarized here suggest combination measures to help the prevention and control of the COVID-19. After initial assessment for symptoms and epidemiological risk factors, including travel to affected areas and exposure to confirmed 2019-nCoV patients within 14 days, patients are classified in a risk-stratified system. Upon confirmation of a suspected 2019-nCoV case, affected persons must immediately be placed in airborne infection isolation and the appropriate public health agencies notified. The modified 3I's tool could assist emergency and primary care clinicians, as well as out-of-hospital providers, in effectively managing persons with suspected or confirmed 2019-nCoV. The concise nature of the 2019-nCoV 3I's tool allows for the rapid and effective management of a novel COVID-19 disease by healthcare providers (Zou et al. 2020). With regard to contact tracing and isolation of cases, a mathematical model which bases on 2.5 reproduction number scenarios, suggests the need for tracing and isolating 80% of contacts to achieve control of 90% of outbreak (Zhan et al. 2020). The probability of control decreases with long delays from symptom onset to isolation, fewer cases ascertained by contact tracing, and increasing transmission before symptoms (Hellewell et al. 2020).

The WHO guideline recommends frequent, regular, and thorough hand washing, practicing respiratory hygiene, and maintaining physical distancing (UCRG 2020). A study by (Ceccarelli et al. 2020), also shows that one way of preventing COVID-19 pandemic is through hand hygiene. Front line health workers should also take appropriate measures to protect themselves and their other patients from COVID-19 (Razai et al. 2020).

In general, the available public health tools to control person-to-person transmittable diseases are isolation and quarantine, social distancing, and community containment measures (Wilder-Smith and Freedman 2020). Specific up-to-date and accurate health information and precautionary measures (e.g., hand hygiene, wearing a mask) were associated with a lower psychological impact of the outbreak and lower levels of stress, anxiety, and depression. This same study found, about 36.3% of subjects who would wear masks can not wear it correctly, with common mistakes of nose exposure to the air and long-time mask wear without replacement (Zhan et al. 2020).

Conclusion

To tackle the possible consequences of COVID-19, the Ethiopian government has enacted a range of measures to control the epidemic. However, with the

current progression of the disease, the outbreak needs to be contained to prevent the Ethiopian health system from becoming overwhelmed. Though evidences on COVID-19 are still developing this review shows that COVID-19 is transmitted between humans through respiratory droplets and contact routes. The virus replicates efficiently in the upper respiratory tract and the lung appears to be the most vulnerable target organ. The incubation period for COVID-19 is thought to be within 14 days following exposure, with most cases occurring approximately 4-5 days after exposure. We have seen in this review that COVID-19 presents with major clinical symptoms including fever, dry cough, myalgia, fatigue, dyspnea, diarrhea, muscle ache, confusion, headache, sore throat, rhinorrhea, chest pain, nausea and vomiting where older adults and people who have chronic underlying conditions might be at higher risk for severe illness from COVID-19. There is limited evidence regarding risk factors for severe disease. However, based on currently available evidence, older adults and people of any age who have chronic underlying conditions might be at higher risk for severe illness from COVID-19. Thermal screening is currently considered as the primary tool to screen patients though its effectiveness is under question as the majority of COVID-19 are asymptomatic. Real-time-PCR is the diagnostic tool in place at the global level and the use of integrated criteria to diagnose SARS-CoV-2 infection should be considered as well.

As for management, infection prevention and control measures and supportive care, including supplemental oxygen and mechanical ventilator support, when indicated, are the currently practiced interventions. In addition to the available public health tools such as proper handwashing, respiratory hygiene, quarantine, social distancing, and containment measures the backbone to effectively suppress and control this infection in every country includes isolating, testing, treating, and tracing of new cases. As of this time, there is no treatment developed for COVID-19 and the available evidence shows isolating, testing, treating, and tracing of new cases to effectively suppress and control the virus spread are the backbone of the response in every country. In general, the public health measures to control the spread of COVID-19 includes social distancing measures (schools and workplace closures, isolation of sick and quarantine of exposed, and stay at home); protective measures (hygiene and surface cleaning); and travel-related measures. Supportive care, including oxygen supplementation and mechanical ventilator support

for severely ill patients, is practicing when indicated.

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Competing interest: No competing interest.

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