EUROPEAN ACADEMIC RESEARCH
Vol. VIII, Issue 2/ May 2020

Impact Factor: 3.4546 (UIF)
DRJI Value: 5.9 (B+)

ISSN 2286-4822
www.euacademic.org

COVID-19: the Prognosis, Mortality, Medications, and Possible Vaccines

AWUCHI, CHINAZA GODSWILL[1]
Department of Physical Sciences
Kampala International University, Kampala, Uganda
Department of Food Science and Technology
Federal University of Technology Owerri, Owerri, Nigeria
AMAGWULA, IKECHUKWU OTUOSOROCHI
Ministry of Health, Imo State, Nigeria
Department of Food Science and Technology
Federal University of Technology Owerri, Owerri, Nigeria
TWINOMUHWEZI, HANNINGTON
Ministry of Health, Imo State, Nigeria
Department of Chemistry
Kyambogo University, Kyambogo, Uganda
ECHETA, CHINELO KATE
Department of Food Science and Technology
Federal University of Technology Owerri, Owerri, Nigeria

Abstract

The systematic review focused on the prognosis, mortality, medications, and promising vaccines for COVID-19. COVID-19 severity varies. Mild cases often recover within two weeks, while people with severe diseases may take 3 – 6 weeks to recover. Among people who died, the time from the onset of symptom to death ranged from 2 – 8 weeks. Children constitute a small percentage of reported cases, with around 1% of cases under 10 years and 4% aged 10 to 19 years. The risk of death is below 0.5% in those younger than 50 years, while more than 8% in those older than 70. Most of the people who die of COVID-19 have pre-existing conditions, including diabetes mellitus, cardiovascular disease, and hypertension. The impact of COVID-19 and its rate of mortality are different for both men and women; mortality rate is higher in men. As of May 2020, it is not

[1] Corresponding author: awuchi.chinaza@kiu.ac.ug and awuchichinaza@gmail.com

known if past infection provides long-term and effective immunity in those who recover from the viral disease. Some of the infected people were reported to develop protective antibodies; the acquired immunity is presumed possible, based on other coronaviruses' behaviour. The total infection fatality rate (IFR) is estimated to be 0.66%. No approved vaccine to treat the disease yet. International research on medicines and vaccines in COVID-19 is underway by academic groups, industry researchers, and government organizations. As of May 2020, there are over 300 active clinical trials underway. Many existing medications are under evaluation for COVID-19 treatment, including remdesivir, chloroquine, lopinavir/ritonavir, hydroxychloroquine, and lopinavir/ritonavir combined with interferon beta; as of May 2020, there is tentative evidence for remdesivir efficacy. Other candidates in trials are vasodilators, immune therapies, lipoic acid, corticosteroids, recombinant angiotensin-converting enzyme 2, bevacizumab, etc. Preliminary evidence suggests hydroxychloroquine might have anti-cytokine storm properties. Transferring concentrated and purified antibodies produced by immune systems of those who recovered from COVID-19 to those who need them is being investigated as non-vaccine method of passive immunization.

Key words: COVID-19, Mortality, Medications, Possible Vaccines

1. INTRODUCTION

The severity of COVID-19 differs. The disease might take a mild course with a few or no symptoms, like other commonly known upper respiratory diseases; e.g., the common cold. Mild cases usually recover within 2 weeks, while those with critical or severe diseases can take 3 to 6 weeks to recover. Among the people who died, the time from the onset of the symptom to death ranged from 2 to 8 weeks (WHO, 2020). Children make up a small percentage of reported cases, with around 1% of cases under the age of 10 years and 4% aged 10 to 19 years. Children are likely to have milder symptoms and lower likelihood of severe disease than adults; the risk of death is below 0.5% in people younger than 50 years, while more than 8% in people

older than 70 (Castagnoli *et al.,* 2020; Lu *et al.,* 2020; Dong *et al.,* 2020). Pregnant women might be at higher risk for severe COVID-19 infection based on the data from other similar viruses, such as SARS and MERS, although data for COVID-19 is lacking (Fang *et al.,* 2020). In China, children got exposed to infections mainly by close contact with their parents (mother or father) or other family members who resided in Wuhan or traveled there (Castagnoli *et al.,* 2020). Some studies have reported that neutrophil to lymphocyte ratio (NLR) could be helpful in the early screening for severe illness (Qin *et al.,* 2020).

Most of the people who die of COVID-19 have pre-existing conditions, including diabetes mellitus, hypertension, and cardiovascular disease (WHO, 2020). The Istituto Superiore di Sanità found that out of 8.8 percent of deaths where the medical charts for review were available, 97.2% of the sampled patients had at least a comorbidity with an average patient having 2.7 diseases (Palmieri *et al.,* 2020). The same report indicated that the median time between the symptoms onset and death was 10 days, with 5 being spent hospitalized. However, the patients transferred to an intensive care unit (ICU) had a median time of 7 days between hospitalization and death (Palmieri *et al.,* 2020). In a study of the early cases, median time from exhibiting the initial symptoms to death was 2 weeks, with a full range of 6 to 41 days (Wang *et al.*, 2020). A study done by the National Health Commission of China reported that men had a mortality rate of 2.8% and 1.7% for women (Worldometers, 2020). Histopathological assessment of the post-mortem lung samples indicate damage of diffuse alveolar with cellular fibromyxoid exudates within both lungs. Changes in viral cytopathic were observed in the pneumocytes. Picture of the lung has a resemblance to acute respiratory distress syndrome (ARDS) (WHO, 2020). In 11.8 percent of the deaths in the report of the National Health Commission of China, damage of heart was noted by elevated troponin levels or cardiac arrest (Zheng *et al.,* 2020). March data from the US reported that 89% of those hospitalized had preexisting conditions (Garg *et al.,* 2020). In Nigeria, the National Centre for Disease Control (NCDC) observed that men are more vulnerable to COVID-19 than women.

It is not known, as of May 2020, if past infection provides long-term and effective immunity in those who recover from COVID-19 (Schraer, 2020). Some of the infected people have been indicated to develop protective antibodies; acquired immunity is presumed possible, based on behaviour of other coronaviruses (The Independent, 2020). However, the cases in which COVID-19 recovery was followed by positive tests for the coronavirus at a later date have also been reported (Politi, 2020; Omer *et al.,* 2020). These cases are thought to be lingering infection instead of reinfection (Omer *et al.,* 2020), or false positives because of the remaining fragments of the viral RNA (Parry, 2020). Some other coronaviruses in circulation among people are capable of reinfection after approximately a year (Columbia University, 2020).

In the United States, a greater percentage of deaths due to COVID-19 occurred among African Americans (Dorn *et al.,* 2020). Structural factors which prevent African Americans from observing social distancing include their "essential" occupations such as health-care workers, public transit employees, among others, and their concentration in crowded substandard housing. The greater prevalence in lack of health insurance and care, as well as of underlying health conditions such as hypertension, heart disease, diabetes, also increase their risks of death (WHO, 2020). Similar issues affect Native American and Latino communities (Dorn *et al.,* 2020). When people with preexisting respiratory problems are infected with or exposed to COVID-19, they are at higher risk for severe symptoms (DeRobertis, 2020). COVID-19 also poses a higher risk to those who misuse methamphetamines and opioids, as far as their drug use might have caused lung damage (DeRobertis, 2020).

Humans seem to be capable of spreading the coronavirus to some other animals. In Liège, Belgium, a domestic cat tested positive for the virus after it started showing symptoms including vomiting, shortness of breath, diarrhoea, a week later after its owner tested positive. In New York, the United States, Tigers at the Bronx Zoo tested positive for the coronavirus and showed COVID-19 symptoms, including a loss of appetite and dry cough (Goldstein, 2020). In the Netherlands, Minks at two farms also tested positive for COVID-19 (Fox News, 2020). A study done on domesticated animals inoculated with the coronavirus found that ferrets and cats appear to

be greatly susceptible to COVID-19, while dogs seem less susceptible, with lesser levels of viral replication. In the study, no evidence of viral replication in chickens, pigs, and ducks was found (Shi *et al.,* 2020).

During the initial outbreak of the virus in Wuhan, China, the virus and its disease were commonly referred to as the coronavirus and the Wuhan coronavirus (McNeil Jr, 2020), with the disease sometimes referred to as the Wuhan pneumonia (Jiang *et al.,* 2020). Previously, many diseases were named after the geographical locations, such as the Middle East Respiratory Syndrome, the Spanish flu, and Zika virus (Shablovsky, 2017). In January 2020, the WHO recommended 2019-nCov and also 2019-nCoV acute respiratory disease as the provisional names for the cornavirus and the disease per 2015 guidance as well as international guidelines against using the geographical locations (for example, Wuhan, China), groups of people or animal species in virus and disease names to prevent social stigma (WHO, 2020). The official names SARS-CoV-2 and COVID-19 were issued by the on February 11, 2020 (WHO, 2020). WHO chief Tedros A. Ghebreyesus explained that CO stands for *corona*, VI stands for *virus*, D stands for *disease,* and 19 stands for the first time (year) the outbreak was identified (31 December 20*19*) (WHO, 2020). Additionally, the World Health Organization uses the "virus responsible for COVID-19" and the "COVID-19 virus" in public communications (WHO, 2020). In the media and in public discourse, both the disease and virus are often referred to as "COVID-19" or "coronavirus".

2. PROGNOSIS, MORTALITY, TREATMENT, AND POSSIBLE VACCINES

2.1. COVID-19 Prognosis

The socioeconomics and the availability of medical resources of a region may affect the mortality rate. The estimations of the mortality vary due to regional differences (Li *et al.*, 2020), but also due to methodological constraints. The under-counting of mild cases may cause overestimation of the mortality rate. Nonetheless, as deaths are the result of the cases contracted in the past, it may mean the recent mortality rate is underestimated (Chughtai and Malik, 2020). Smokers were reported to be 1.4 times more likely to have

severe COVID-19 symptoms and roughly 2.4 times more likely to need intensive care or die, as compared to the non-smokers (Vardavas and Nikitara, 2020).

Concerns have been raised regarding the long-term sequelae of COVID-19. The Hong Kong Hospital Authority reported a drop of 20 to 30 percent in lung capacity in many people who recovered from COVID-19, and lung scans have suggested organ damage (Cheung, 2020). This may also result in post-intensive care syndrome following recovery.

2.2. **Epidemiology of COVID-19**

Several measures are frequently used to quantify mortality. The numbers vary over time, by region, and influenced by the volume of testing, time since the initial outbreak, treatment options, healthcare system quality, and population characteristics such as sex, overall health, and age (Ritchie and Roser, 2020). The death-to-case ratio shows the number of deaths per (divided by) number of diagnosed cases in a given interval of time. Based on the statistics from Johns Hopkins University, the global death-to-case ratio stands at 6.8% (total deaths/total confirmed cases) as of 15 May 2020 (Johns Hopkins University, 2020). The number varies by regions/countries. Other measures include the infection fatality rate (IFR) that reflects the percentage of infected individuals (undiagnosed and diagnosed) who die from a disease, and the case fatality rate (CFR) that reflects the percentage of diagnosed individuals that die from a disease. The statistics are not time-bound and observe a specific population from the infection through the case resolution. Many researchers and academics have made attempts to calculate these numbers for different specific populations. Outbreaks have been reported in prisons due to crowding and inability to enforce proper social distancing (Hawks *et al.,* 2020). In the US, with aging prisoner population, many of them are at great risk for poor COVID-19 outcomes due to high rates of coexisting lung and heart disease, and inadequate access to high-quality healthcare (Hawks *et al.,* 2020). Some countries such as Uganda have released some inmates, as a means reducing the risk of spreading of the disease in prisons.

Table 1: Case fatality rates (%) by age and country

Age	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89	90+
Germany as of 9 May	0.0	0.0	0.1			1.7		18.2		28.5
South Korea as of 9 May	0.0	0.0	0.0	0.2	0.2	0.8	2.7	10.8	25.0	
Finland as of 8 May	0.0	0.0	0.0	<0.5	<0.5	0.5	2.6	13.4	32.9	
Netherlands as of 8 May	0.0	0.2	0.1	0.2	0.5	1.6	8.0	25.2	32.2	32.7
Norway as of 8 May	0.0	0.0	0.0	0.0	0.2	0.4	1.7	8.5	21.3	50.4
Canada as of 5 May	0.0		0.1		0.6		6.4		21.5	
Denmark as of 5 May	0.2						4.4	16.7	26.4	44.3
Portugal as of 5 May	0.0	0.0	0.0	0.0	0.2	0.8	3.1	9.5	17.8	
Spain as of 5 May	0.3	0.4	0.2	0.3	0.6	1.5	4.8	13.9	20.9	21.9
Sweden as of 5 May	0.9	0.0	0.4	0.4	0.9	2.3	7.4	22.8	32.0	36.1
Switzerland as of 5 May	0.0	0.0	0.0	0.1	0.1	0.5	2.9	10.9	25.9	
Israel as of 3 May	0.0	0.0	0.0	0.9	0.9	3.1	9.7	22.9	30.8	31.3
Italy as of 28 April	0.1	0.0	0.1	0.3	0.9	2.6	9.8	24.2	29.0	24.7
China as of 11 February	0.0	0.2	0.2	0.2	0.4	1.3	3.6	8.0	14.8	
United States										
Connecticut as of 5 May	0.4	0.1	0.1	0.4	0.8	2.1	7.3	19.7	36.2	
Idaho as of 9 May	0.0	0.0	0.0	0.0	0.0	0.5	3.2	8.2	28.9	
Kentucky as of 5 May	0.0	0.0	0.0	0.2	0.6	2.3	6.8	13.3	27.9	
Maryland as of 9 May	0.0	0.0	0.3	0.3	0.7	1.8	5.6	13.3	26.5	
Massachusetts as of 5 May	0.0	0.0	0.0	0.1	0.4	1.3	4.5	14.2	24.7	
Mississippi as of 7 May	0.1			0.6	0.9	1.8	7.3	15.3	17.8	23.8
N. Hampshire as of 5 May	0.0	0.0	0.3	0.0	1.1	0.0	2.1	7.7	18.4	
Texas as of 8 May	0.0	0.5	0.5	0.4	0.8	2.0	13.5	25.8	30.0	
Washington as of 3 May	0.0		0.2		1.3		9.1		29.8	

2.2.1. Infection fatality rate (IFR)

Our World in Data reported that as of March the 25th, 2020, the IFR cannot be calculated accurately. In February, the World Health Organization (WHO) estimated the Infection fatality rate at 0.94%, with a confidence interval range of 0.37 to 2.9 percent. The Centre for Evidence-Based Medicine (CEBM) of the University of Oxford estimated a global case fatality rate of 0.72% and IFR of 0.1 to 0.36% (Haake, 2020). According to the CEBM, the random antibody testing in Germany suggests an IFR of 0.37 percent (0.12 to 0.87 percent) there, but there are concerns about false positives (Haake, 2020; Vogel, 2020; Lassaunière *et al.,* 2020). Firm lower limits of IFR have been established in some locations. In the City of New York, with 8.4 million population, as of May 7, 2020, 14,162 (0.17 percent of the total population) have died from COVID-19 (New York City, 2020). In Bergamo province, 0.57% of the population has died (Modi, 2020; Modi *et al.,* 2020). To get a better understanding of the number of infected people, initial testing of antibody have been carried out, however there is no valid scientific report based on any of them currently (Mole, 2020).

Table 2: Estimate of infection fatality rates (IFR) and probability of the severe disease course (%) by age based on the cases from China

Age	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80+
Death	0.0016 (0.00016–0.025)	0.0070 (0.0015–0.050)	0.031 (0.014–0.092)	0.084 (0.041–0.19)	0.16 (0.076–0.32)	0.60 (0.34–1.3)	1.9 (1.1–3.9)	4.3 (2.5–8.4)	7.8 (3.8–13)
Severe disease	0.0 (0.0–0.0)	0.04 (0.02–0.08)	1.0 (0.62–2.1)	3.4 (2.0–7.0)	4.3 (2.5–8.7)	8.2 (4.9–17)	11 (7.0–24)	17 (9.9–34)	18 (11–38)

The total infection fatality rate (IFR) is estimated to be 0.66 percent (0.39–1.3). Infection fatality rate (IFR) is the fatality per all the infected individuals, irrespective of whether they had any symptoms or were diagnosed. Numbers in parentheses are 95 percent credible intervals for the estimates.

2.2.2. Sex differences due to COVID-19

The impact of the COVID-19 pandemic and its rate of mortality are different for men and women (Wenham *et al.,* 2020). Mortality rate is higher in men in the studies conducted in China, Italy (Rabin, 2020), the US, Nigeria, and some other countries. For men, the higher risk appears in their 50s, and starts to taper off only at 90 (Rabin, 2020). The death rate in China was 2.8% for men and 1.7% for women (Rabin, 2020). The exact reasons behind this sex differences are unknown, but behavioural and genetic factors may be a reason (Wenham *et al.,* 2020). Lower smoking prevalence in women, sex-based immunological differences, and men developing co-morbid health conditions, e.g. hypertension, at younger age than women may have contributed to the higher rate of mortality in men (Rabin, 2020). In Europe, of people infected with COVID-19, 57 percent were men; of people infected with COVID-19 and died, 72% were men (Gupta, 2020). Research has indicated that viral illnesses such as HIV, influenza, SARS, and Ebola affect men and women differently (Gupta, 2020). A greater percentage of health workers, especially nurses, are women, and they also have a higher chance of getting exposed to the virus (WHO, 2020). Lockdowns, school closures, and reduced access to the healthcare following this 2019–20 coronavirus pandemic might differentially affect genders and likely exaggerate existing gender disparity (Wenham *et al.,* 2020).

2.3. COVID-19 Research

No approved medication or vaccine to treat the disease yet. Experts suggest that the earliest possible time for vaccine approval is 2021; although there is no guarantee for vaccine development. International research on the vaccines and the medicines in COVID-19 is currently underway by government organizations, industry researchers, and academic groups (Dhama *et al.,* 2020). In March 2020, the "SOLIDARITY Trial" was initiated by the WHO to assess the treatment effectiveness of four already existing antiviral compounds with most efficacy promise (Kupferschmidt and Cohen, 2020). There has been a huge deal of COVID-19 research which involve accelerated research processes as well as publishing shortcuts to meet global demand. To minimize the impacts of misinformation, the public and medical professionals are advised to expect rapid and sudden changes to available information, and to pay attention to retractions and other updates (Bradley-Ridout *et al.,* 2020).

2.3.1. Vaccine for COVID-19

There is no available or approved vaccine, however many agencies are actively developing likely vaccines or vaccine candidates. The previous works on SARS-CoV are being used as both SARS-CoV-2 and SARS-CoV use the ACE2 receptor as means to enter human cells (Cascella *et al.,* 2020). Three vaccination strategies are under investigation. First, the researchers aim to make a whole virus vaccine. Using such a virus, dead or inactive, aims to elicit prompt the human body's immune response to a new COVID-19 infection. The second strategy, referred to as subunit vaccines, aims to make a vaccine that sensitizes the immune system of the human body to certain subunits of the coronavirus. For SARS-CoV-2, such research put more emphasis on the S-spike protein which helps the coronavirus intrude ACE2 enzyme receptor. The third strategy is focused on the nucleic acid (DNA or RNA) vaccines, a novel technique for making a vaccination. Any experimental vaccines from any of the three strategies would be tested for efficacy and safety (Chen *et al.,* 2020). On March 16, 2020, the first clinical trial for a vaccine started in Seattle, United States, with four volunteers. The vaccine contains harmless genetic code copied from the coronavirus that causes the disease (Roberts, 2020). Antibody-dependent enhancement has been controversially suggested

as potential challenge for the vaccine development for SARS-COV-2 (Peeples, April 2020).

2.3.2. COVID-19 Medications

Over 29 phase II–IV efficacy trials in the COVID-19 were finalized in March 2020 or at least scheduled to give results in April 2020 from hospitals in China (Koch and Pong, 2020). There are over 300 active clinical trials underway (Sanders *et al.,* 2020) as of May 2020. Among these trials, seven were evaluating treatments already approved, including four studies on chloroquine or hydroxychloroquine (Koch and Pong, 2020). Repurposed antiviral drugs constitute most of the Chinese research, with 9 phase III trials on remdesivir across many countries as a result of report in April (Koch and Pong, 2020). Other candidates in trials include immune therapies, corticosteroids, bevacizumab, recombinant angiotensin-converting enzyme 2, vasodilators, and lipoic acid (Koch and Pong, 2020).

The goals of the COVID-19 Clinical Research Coalition include to (a) facilitate fast reviews of clinical trial proposals by the ethics committees and the national regulatory agencies, (b) fast-track the approvals for candidate therapeutic compounds, (c) ensure standardized and quick analysis of the emerging efficacy and safety data, and (d) facilitate sharing of the clinical trial outcomes before publication (Maguire and Guérin, 2020; COVID-19 Clinical Research Coalition, 2020). Several existing medications are evaluated for COVID-19 treatment, including remdesivir, hydroxychloroquine, chloroquine, lopinavir / ritonavir, and lopinavir / ritonavir in combination with interferon beta (Kupferschmidt and Cohen, 2020; UN News, 2020). Tentative evidence for efficacy by remdesivir was reported, as of March 2020 (Feuerstein *et al.,* 2020). Clinical improvement was observed in the patients treated with the compassionate-use remdesivir (Grein *et al.,* 2020). Remdesivir was reported to inhibit SARS-CoV-2 *in vitro* (Wang *et al.,* 2020). Phase III clinical trials are in progress in the U.S., Italy, and China (Beeching *et al.,* 2020). A trial in 2020 found that lopinavir/ritonavir was not effective in treating the severe illness (Cao *et al,* 2020). Nitazoxanide was recommended for additional *in vivo* study after demonstrating a low concentration inhibition of SARS-CoV-2 (Wang *et al.,* 2020).

As of April 2020 there are mixed results as to the efficacy of hydroxychloroquine as a COVID-19 treatment, with some study groups showing little or no improvement (Seley-Radtke, 2020). The studies involving hydroxychloroquine and chloroquine with or without azithromycin have been reported to have major limitations which prevented the medical community from accepting these therapies without additional study (Sanders *et al.,* 2020). Oseltamivir does not inhibit the SARS-CoV-2 *in vitro* and does not have any known role in treatment of COVID-19 (Sanders *et al.,* 2020).

2.3.3. Anti-cytokine storm in COVID-19

Cytokine release syndrome (CRS) may be a complication during the later stages of a severe COVID-19. Preliminary evidence suggests hydroxychloroquine might have anti-cytokine storm properties (Yao *et al.,* 2020). After the completion of a small study, tocilizumab was included in the treatment guidelines given by China's National Health Commission (Liu and Miller, 2020). It is under a phase 2 non-randomized trial at national level in Italy after demonstrating positive results in those with severe disease (Ovadia and Agenzia, 2020). In combination with serum ferritin blood test to identify the cytokine storms, it is intended to counter such developments that are believed to be responsible for the death in some affected individuals (Ruan *et al.,* 2020). The interleukin-6 receptor antagonist got approval from the US FDA to undergo phase III clinical trial to assess the impact of the medication on COVID-19 based on the retrospective case studies for treatment of steroid-refractory cytokine release syndrome which is induced by CAR T cell therapy, a different cause, in 2017 (Slater, 2020). So far, there is no randomized, controlled evidence supporting tocilizumab as an efficacious CRS treatment. Prophylactic tocilizumab has been reported to increase the levels of serum IL-6 by saturating IL-6R, driving IL-6 across blood-brain barrier, and aggravating neurotoxicity while, at the same time, having no impact on the CRS incidence (Locke *et al.,* 2020).

An anti-GM-CSF monoclonal antibody, known as lenzilumab, is protective in murine models for the CAR T cell-induced cytokine release syndrome and neurotoxicity and is a possible therapeutic option because of the observed increase in pathogenic GM-CSF

secreting T-cells in the hospitalized patients with COVID-19 (Sterner *et al.,* 2020). The Feinstein Institute of Northwell Health reported in March 2020 study on a human antibody which may prevent activity of IL-6 (WHO, 2020).

2.3.4. Passive antibodies

Transferring concentrated and purified antibodies produced by immune systems of people who recovered from COVID-19 to those who need them is undergoing investigation as non-vaccine method of passive immunization (Casadevall and Pirofski, 2020). This strategy was tried for the SARS with inconclusive results (Casadevall and Pirofski, 2020). Viral neutralization is an anticipated mechanism of action through which passive antibody therapy mediate defense against the SARS-CoV-2. However, other mechanisms such as the antibody-dependent cellular cytotoxicity or/and phagocytosis, can be possible (Casadevall and Pirofski, 2020). Other kinds of passive antibody therapy, e.g., using manufactured monoclonal antibodies, are under development (Casadevall and Pirofski, 2020). Production of convalescent serum, consisting of liquid parts of the blood from COVID-19 recovered patients and has antibodies specific to this coronavirus, may be increased for rapid deployment (Pearce, 2020).

3. CONCLUSION

There are variations in the severity of COVID-19. Mild cases often recover in two weeks, while people with critical or severe diseases may take 3 to 6 weeks to recover. Among the people who died, the duration from the onset of symptom to death ranged from 2 to 8 weeks. Children make up a small percentage of the reported cases, with around 1 percent of cases under 10 years and 4 percent aged 10 to 19 years. In people younger than 50 years the risks of dying is below 0.5%, while in people older than 70 it is over 8%. Most of the people who die of COVID-19 have pre-existing conditions, including diabetes mellitus, cardiovascular disease, and hypertension. The impact of this pandemic and its mortality are different for sex (men and women). Mortality is higher in men. As of May 2020, it is not known if past infection provides long-term and effective immunity in those who recover from COVID-19. Some of the infected people have

been reported to develop the protective antibodies, as a result acquired immunity is assumed likely, based on behaviour of other coronaviruses. The infection fatality rate cannot be calculated accurately as at May 2020; the total infection fatality rate is roughly 0.66% (0.39–1.3). Based on the statistics from Johns Hopkins University, the global death-to-case ratio stands at 6.8% (total deaths/total confirmed cases) as of 15 May 2020. No medication or vaccine is approved for the treatment of COVID-19. International research on medicines and vaccines in COVID-19 is ongoing by government organizations, industry researchers, and academic groups. As of May 2020, there are over 300 active clinical trials underway. Many existing medications are evaluated for the COVID-19 treatment, including remdesivir, hydroxychloroquine, chloroquine, lopinavir/ritonavir, and lopinavir/ritonavir in combination with interferon beta; as of May 2020, there is tentative evidence for the efficacy by remdesivir. Other candidates in trials are vasodilators, immune therapies, lipoic acid, corticosteroids, recombinant angiotensin-converting enzyme 2, bevacizumab, etc. Preliminary evidence suggests that hydroxychloroquine might have anti-cytokine storm properties. Transferring concentrated and purified antibodies produced by immune systems of people who have recovered from COVID-19 to those who need them is under investigation as non-vaccine method of passive immunization.

REFERENCES

1. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, *et al.* (2020). "Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents: A Systematic Review". *JAMA Pediatrics*. doi:10.1001/jamapediatrics.2020.1467.
2. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, *et al.* (2020). "SARS-CoV-2 Infection in Children". *The New England Journal of Medicine.* Massachusetts Medical Society. **382** (17): 1663–1665. doi:10.1056/nejmc2005073.
3. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, Tong S (2020). "Epidemiology of COVID-19 Among Children in China". *Pediatrics*: e20200702. doi:10.1542/peds.2020-0702.
4. Fang L, Karakiulakis G, and Roth M (2020). "Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?". *The Lancet. Respiratory Medicine*. **8** (4): e21. doi:10.1016/S0140-6736(20)30311-1.

5. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, *et al.* (2020). "Dysregulation of immune response in patients with COVID-19 in Wuhan, China". *Clinical Infectious Diseases*. doi:10.1093/cid/ciaa248.
6. Palmieri L, Andrianou X, Barbariol P, Bella A, Bellino S, Benelli E, *et al.* (2020). Characteristics of COVID-19 patients dying in Italy Report based on available data on April 2th, 2020 (Report). Istituto Superiore di Sanità.
7. Worldometers (2020) "Coronavirus Age, Sex, Demographics (COVID-19)". www.worldometers.info.
8. Garg S, Kim L, Whitaker M, O'Halloran A, Cummings C, Holstein R, *et al.* (2020). "Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 - COVID-NET, 14 States, March 1-30, 2020". *MMWR. Morbidity and Mortality Weekly Report*. **69** (15): 458–464. doi:10.15585/mmwr.mm6915e3.
9. Chughtai A and Malik A (2020). "Is Coronavirus disease (COVID-19) case fatality ratio underestimated?". *Global Biosecurity*. **1** (3). doi:10.31646/gbio.56(inactive 26 April 2020).
10. Vardavas CI and Nikitara K (2020). "COVID-19 and smoking: A systematic review of the evidence". *Tobacco Induced Diseases*. **18** (March): 20. doi:10.18332/tid/119324.
11. Cheung E (2020). *"Some recovered COVID-19 patients may have lung damage, doctors say"*. South China Morning Post.
12. Schraer, R (2020). *"Coronavirus: Immunity passports 'could increase virus spread"*.
13. Centers for Disease Control and Prevention (2020). *"Coronavirus Disease 2019 (COVID-19)"*. Centers for Disease Control and Prevention. 11 February 2020.
14. Wang K, Zhao W, Li J, Shu W, and Duan J (2020). "The experience of high-flow nasal cannula in hospitalized patients with 2019 novel coronavirus-infected pneumonia in two hospitals of Chongqing, China". *Annals of Intensive Care*. **10**(1): 37. doi:10.1186/s13613-020-00653-z.
15. The Independent (2020). *"Can you get coronavirus twice or does it cause immunity?"*. The Independent. 13 March 2020.
16. Politi D (2020). *"WHO Investigating Reports of Coronavirus Patients Testing Positive Again After Recovery"*. Slate.
17. Omer SB, Malani P, and Del Rio C (2020). "The COVID-19 Pandemic in the US: A Clinical Update". *Jama*. doi:10.1001/jama.2020.5788.
18. Parry RL (2020), "Coronavirus patients can't relapse, South Korean scientists believe", The Times
19. Columbia University (2020). "Direct observation of repeated infections with endemic coronaviruses". Columbia University in the City of New York. Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University. 15 April 2020.
20. WHO Q&A on coronaviruses (COVID-19) (2020). World Health Organization (WHO).
21. Ritchie H and Roser M (2020). Chivers T (ed.). "What do we know about the risk of dying from COVID-19?". Our World in Data. Archived from the original on 28 March 2020. Retrieved 28 March 2020.

22. Hawks L, Woolhandler S, and McCormick D (2020). "COVID-19 in Prisons and Jails in the United States". *JAMA Internal Medicine*. doi:10.1001/jamainternmed.2020.1856.
23. Haake D (2020). *"Gangelt — A representative study on the lethality of COVID-19*". Medium.
24. Vogel G (2020). "Antibody surveys suggesting vast undercount of coronavirus infections may be unreliable". *Science* | AAAS.
25. Lassaunière, Ria; Frische, A; Harboe, ZB.; Nielsen, A CY; Fomsgaard, Anders; Krogfelt, KA; Jørgensen, Charlotte S. (2020). "Evaluation of nine commercial SARS-CoV-2 immunoassays". *medRxiv*: 2020.04.09.20056325. doi:10.1101/2020.04.09.20056325.
26. New York City (2020). *"COVID-19: Data*". City of New York.
27. Modi C (2020). *"How deadly is COVID-19? Data Science offers answers from Italy mortality data"*. Medium.
28. Modi C, Boehm V, Ferraro S, Stein G, and Seljak U (2020). "Total COVID-19 Mortality in Italy: Excess Mortality and Age Dependence through Time-Series Analysis". *MedRxiv*: 2020.04.15.20067074. doi:10.1101/2020.04.15.20067074.
29. Mole B (2020). "*Experts demolish studies suggesting COVID-19 is no worse than flu*". Ars Technica.
30. Wenham C, Smith J, and Morgan R (2020). "COVID-19: the gendered impacts of the outbreak". *Lancet*. **395** (10227): 846–848. doi:10.1016/S0140-6736(20)30526-2.
31. Rabin RC (2020). "*In Italy, Coronavirus Takes a Higher Toll on Men"*. The New York Times.
32. Gupta AH (2020). *"Does COVID-19 Hit Women and Men Differently? U.S. Isn't Keeping Track*". The New York Times.
33. Dorn AV, Cooney RE, and Sabin ML (2020). "COVID-19 exacerbating inequalities in the US". *Lancet*. **395** (10232): 1243–1244. doi:10.1016/S0140-6736(20)30893-X.
34. DeRobertis J (2020). *"People who use drugs are more vulnerable to coronavirus. Here's what clinics are doing to help"*. The Advocate (Louisiana).
35. McNeil Jr DG (2020). *"Wuhan Coronavirus Looks Increasingly Like a Pandemic, Experts Say*". The New York Times. ISSN 0362-4331.
36. Jiang S, Xia S, Ying T, and Lu L (2020). "A novel coronavirus (2019-nCoV) causing pneumonia-associated respiratory syndrome". *Cellular & Molecular Immunology*. **17** (5): 554. doi:10.1038/s41423-020-0372-4.
37. Shablovsky S (2017). "The legacy of the Spanish flu". *Science*. **357** (6357): 1245. Bibcode:2017Sci...357.1245S. doi:10.1126/science.aao4093. ISSN 0036-8075.
38. Goldstein J (2020). "*Bronx Zoo Tiger Is Sick With the Coronavirus"*. The New York Times.
39. Fox News (2020)."*Coronavirus hits Netherlands farm animals as minks test positive for virus"*. Fox News. 26 April 2020.
40. Shi J, Wen Z, Zhong G, Yang H, Wang C, Huang B, *et al.* (2020). "Susceptibility of ferrets, cats, dogs, & other domesticated animals to SARS-coronavirus 2". *Science*: eabb7015. doi:10.1126/science.abb7015.

41. Dhama K, Sharun K, Tiwari R, Dadar M, Malik YS, Singh KP, and Chaicumpa W (2020). "COVID-19, an emerging coronavirus infection: advances and prospects in designing and developing vaccines, immunotherapeutics, and therapeutics". *Human Vaccines & Immunotherapeutics*: 1–7. doi:10.1080/21645515.2020.1735227.
42. Kupferschmidt K and Cohen J (2020). "WHO launches global megatrial of the four most promising coronavirus treatments". *Science Magazine*. doi:10.1126/science.abb8497.
43. Bradley-Ridout G, Fuller K, Gray M, and Nekolaichuk E (2020). *"Navigating the COVID-19 Evidence Landscape"*. University of Toronto Libraries - Gerstein Science Information Centre.
44. Chen WH, Strych U, Hotez PJ, and Bottazzi ME (2020). "The SARS-CoV-2 Vaccine Pipeline: an Overview". *Current Tropical Medicine Reports*: 1–4. doi:10.1007/s40475-020-00201-6.
45. Roberts M (2020). *"Coronavirus: US volunteers test first vaccine"*. BBC News.
46. Peeples L (2020). "News Feature: Avoiding pitfalls in the pursuit of a COVID-19 vaccine". Proceedings of the National Academy of Sciences of the United States of America. *Proceedings of the National Academy of Sciences*. **117** (15): 8218–8221. doi:10.1073/pnas.2005456117.
47. Koch S and Pong W (2020). *"First up for COVID-19: nearly 30 clinical readouts before end of April"*. BioCentury Inc.
48. COVID-19 Clinical Research Coalition (April 2020). "Global coalition to accelerate COVID-19 clinical research in resource-limited settings". *Lancet*. **395** (10233): 1322–1325. doi:10.1016/s0140-6736(20)30798-4.
49. Maguire BJ and Guérin PJ (2020). "A living systematic review protocol for COVID-19 clinical trial registrations". *Wellcome Open Research*. **5**: 60. doi:10.12688/wellcomeopenres.15821.1.
50. UN News (2020). "UN health chief announces global 'solidarity trial' to jumpstart search for COVID-19 treatment". UN News. 18 March 2020. Archived from the original on 23 March 2020.
51. Feuerstein A, Garde D, Robbins R (2020). "Gilead data suggests coronavirus patients are responding to treatment". STAT.
52. Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A, *et al.* (2020). "Compassionate Use of Remdesivir for Patients with Severe COVID-19". *The New England Journal of Medicine*. doi:10.1056/NEJMoa2007016.
53. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, *et al.* (2020). "Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro". *Cell Research*. **30** (3): 269–271. doi:10.1038/s41422-020-0282-0.
54. Beeching NJ, Fletcher TE, Fowler R (2020). *"BMJ Best Practices: COVID-19"*. BMJ.
55. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, *et al.* (2020). "A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe COVID-19". *The New England Journal of Medicine*. **382** (19): 1787–1799. doi:10.1056/NEJMoa2001282.

56. Seley-Radtke K (2020). *"Professor of Chemistry and Biochemistry and President-Elect of the International Society for Antiviral Research, University of Maryland, Baltimore County"*. The Conversation.
57. Murthy S, Gomersall CD, and Fowler RA (March 2020). "Care for Critically Ill Patients with COVID-19". *Jama*. **323** (15): 1499. doi:10.1001/jama.2020.3633.
58. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, and Di Napoli R (2020). *"Features, Evaluation and Treatment Coronavirus (COVID-19)"*. StatPearls. Treasure Island (FL): StatPearls Publishing.
59. WHO (2020). *Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)*. World Health Organization. 16–24 February 2020.
60. Zheng YY, Ma YT, Zhang JY, and Xie X (2020). "COVID-19 and the cardiovascular system". *Nature Reviews. Cardiology*. **17** (5): 259–260. doi:10.1038/s41569-020-0360-5.
61. Centers for Disease Control (2020). *"Coronavirus Disease 2019 (COVID-19)*: Prevention & Treatment".
62. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB (2020). "Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19): A Review". *Jama*. doi:10.1001/jama.2020.6019.
63. Yao X, Ye F, Zhang M, Cui C, Huang B, Niu P, *et al.* (March 2020). "In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)". *Clinical Infectious Diseases*. doi:10.1093/cid/ciaa237.
64. Liu R and Miller J (2020). "China approves use of Roche drug in battle against coronavirus complications". Reuters.
65. Ovadia D and Agenzia Z (2020). *"COVID-19—Italy launches an independent trial on tocilizumab"*. Univadis from Medscape. Aptus Health.
66. Ruan Q, Yang K, Wang W, Jiang L, and Song J (2020). "Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China". *Intensive Care Medicine*. doi:10.1007/s00134-020-05991-x.
67. Slater H (2020). "FDA Approves Phase III Clinical Trial of Tocilizumab for COVID-19 Pneumonia". www.cancernetwork.com. Cancer Network.
68. Locke FL, Neelapu SS, Bartlett NL, Lekakis LJ, Jacobson CA, Braunschweig I, *et al.* (2017). "Preliminary Results of Prophylactic Tocilizumab after Axicabtageneciloleucel (axi-cel; KTE-C19) Treatment for Patients with Refractory,Aggressive Non-Hodgkin Lymphoma (NHL)". *Blood*. **130** (Supplement 1): 1547. doi:10.1182/blood.V130.Suppl_1.1547.1547 (inactive 11 April 2020).
69. Sterner RM, Sakemura R, Cox MJ, Yang N, Khadka RH, Forsman CL, *et al.* (2019). "GM-CSF inhibition reduces cytokine release syndrome and neuroinflammation but enhances CAR-T cell function in xenografts". *Blood*. **133**(7): 697–709. doi:10.1182/blood-2018-10-881722.
70. Casadevall A and Pirofski LA (April 2020). "The convalescent sera option for containing COVID-19". The *Journal of Clinical Investigation*. **130** (4): 1545–1548. doi:10.1172/JCI138003.

71. Pearce K (2020). "Antibodies from COVID-19 survivors could be used to treat patients, …, including the SARS epidemic and the 1918 flu pandemic". The Hub at Johns Hopkins University.