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Global Impact and Implications of Covid-19: Call for Multi-Dimensional Perspectives towards Sustainable Solutions

Teddie O. Rahube*

Department of Biological Sciences and Biotechnology, Botswana International University of Science and Technology, P/Bag 16, Palapye, Botswana.

***Correspondence:**
Teddie O. Rahube, Department of Biological Sciences and Biotechnology, Faculty of Science, Botswana International University of Science and Technology, Palapye, Botswana, E-mail: rahubet@biust.ac.bw.

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ABSTRACT

The COVID-19 pandemic poses an enormous challenge, and it is evidently presenting itself as one of the greatest threats to humanity. The aim of this paper is to review the current state of the COVID-19 pandemic, the global health impact and implications of COVID-19 relative to other recent viral disease outbreaks and antimicrobial resistance (AMR), with the aim to propose the implementation of sustainable solutions.

The magnitude of COVID-19 deaths is incomparable to other coronaviruses (CoVs) disease outbreaks experienced in recent history. The high number of deaths observed in developed countries compared to developing countries may have been triggered by the late response/preparedness to the pandemic rather than by the socio-economic statuses. CoVs will remain a serious health threat to humanity due to absence of vaccines and anti-viral treatments. The absence of specific treatment regimens also lead to heavy reliance on chemical disinfectants and could significantly contribute to the rise in AMR, further raising some important questions surrounding hygiene, microbes, ecosystem health and human diseases.

The CEASE approach, comprising of five key elements; Communication, Education, Advocacy, Socialization, and Experimentation is proposed for implementation at a global level. CEASE approach is critical especially for African countries and can be used to further explore opportunities that can lead to improvements in sanitation, access to clean water, health care, education and infectious disease surveillance systems.

Keywords
COVID-19, Coronaviruses, Pandemic, AMR, Hygiene, CEASE.

Introduction
The world had remained in a state of intermission after the World Health Organization (WHO) officially declared Coronavirus disease 2019 (COVID-19) a global pandemic from the 11th of March, 2020. COVID-19 has emerged and spread rapidly across continents. The disease has been reported to have originated in December 2019 from Wuhan, Hubei Province, China [1] and is caused by a novel virus (SARS-CoV2) that belongs to a family of ribonucleic acid (RNA) viruses known as Coronaviruses (CoVs). Individuals infected with SARS-CoV2 may develop mild to severe symptoms ranging from fever, tiredness, dry cough to pneumonia which ultimately results in breathing difficulties. The elderly and people with underlying health problems like chronic respiratory diseases and cancer are mostly at high risk of dying from COVID-19 (CDC, 2020, WHO). The routes of transmission are human-human contact or through contact with fomites such as contaminated surfaces. Although COVID-19 is not considered airborne, it can spread via aerosols (generated from sneezing, coughing or talking) from one person to another in close proximity (WHO).

The WHO recommends several Infection Prevention Control (IPC) measures to prevent and control the transmission of the COVID-19 virus. The main preventive measures are quarantine of suspected persons and isolation of confirmed symptomatic patients. The IPC measures are very important to ensure that the public is protected especially in relation to water and sanitation, hygiene (WASH) in health care settings, homes and communities. Other measures adopted globally include social distancing, wearing masks to prevent person-person transmission of the virus by contact or aerosols.

The COVID-19 pandemic poses an enormous challenge, and it is evidently presenting itself as a threat to humanity. Another human health threat, currently appearing to be masked by the COVID-19 pandemic is antimicrobial resistance (AMR). During this pandemic, it is relevant to address AMR threat with reference to COVID-19, the anticipated health implications associated with the intensive use of chemical disinfectants (including sanitizers) should not be ignored [2]. Therefore, the current COVID-19 and AMR threats require critical situation analysis, retrospection, formulation of hypotheses and sustainable solutions. In a series of five sub-headings as summarized in Figure 1, this review will discuss the current status of COVID-19 and global deaths distribution, compare COVID-19 to other viral disease outbreaks in recent history, and evaluate the threat of AMR in relation to COVID-19 and the hygiene hypotheses associated with human disease. Ultimately the aim is to propose the implementation of sustainable solutions for combating COVID-19 and future pandemics. Information and data analysed for this paper was extracted electronically from various reliable resources (e.g. WHO, CDC websites), genomics databases (e.g. NCBI), world meter live COVID-19 updates [3] and peer reviewed scientific literature (PubMed) using single or combined keywords ["COVID-19", "coronavirus", "antivirals", "pandemics", "antimicrobial resistance", "hygiene hypothesis"]. Assessment of the COVID-19 global impact was based on the reported death counts irrespective of the total number of cases since confirmation of cases are dependent on the capacity to conduct tests, which varies across developed and developing countries.

COVID-19 Global Death Distribution

COVID-19 has spread rapidly across the world in an unprecedented fashion, partly as a result of increased globalisation, and therefore remains a serious global health threat. The numbers of COVID-19 cases and deaths continue to grow tremendously in many countries across the world despite the WHO's IPC measures and travel restrictions from lockdowns imposed in many countries. As of 15th December 2020, the total global death toll reported was 1,630,581 from over 73 million confirmed total cases. America recorded the highest number of COVID-19 deaths (795,042), followed by Europe (463,415) and Asia (314,322). Africa (56,768) and Oceania (1,039) currently have the least confirmed deaths. The U.S recorded 308,091 deaths, which is 67.8% of the total deaths recorded in North America and by far the highest death toll in the world, followed by Brazil (181,945). Most of the death counts in Europe were from Italy (65,011), U.K (64,402), France (58,282), and Spain (48,013). India recorded the highest (143,746) in Asia, while China recorded only (4,634). In Africa, South Africa tops the rest with 23,451 deaths followed by Egypt (6,943) and Oceania records 1,039, with 908 (87.4%) deaths from Australia (Figure 1.1).

The COVID-19 impact and implications cannot be underestimated, as witnessed by the currently high death counts in many developed countries such as USA, UK, Italy, France, and Spain. The number of COVID-19 new cases continues to grow and threatens to cripple the healthcare infrastructures in the affected countries across the world, and this may be triggered by the late response/preparedness to the pandemic rather than the socio-economic statuses. China despite being the most populated (>1,4 billion people), used experience from the previous SARS epidemic and have relatively responded swiftly to contain and control COVID-19 spread. Some of the strategies used by China involved going into immediate lockdown, deploying thousands of military and health care workers, increased key infrastructures that include construction of more than 100 fever clinics across the country, supply of large quantities of personal protective clothing (PPE), fast training of the use of PPE, disease management and hygiene approaches [4].

From the socio-economic standpoint, many developing countries especially in Africa could suffer the worst fatalities due to lack of resources in health care systems that would enable maximum individual testing efficient contact tracing, strict isolation and quarantine measures, as well as management of COVID-19 patients. Given the conditions of poverty in many developing countries, important factors including access to clean water, poor nutrition, lack of sanitation and poor hygiene practices, together with the high prevalence of infectious diseases (such as Tuberculosis, HIV/AIDS, Diarrhoea, Malaria), COVID-19 remains a serious threat to the elderly, the immunocompromised and vulnerable children under the age of five. Researchers around the world are racing to develop treatment protocols for COVID-19 as the number of deaths continue to increase. The current situation has since forced many countries in both developing and developed worlds to remain within closed borders and lockdowns introduced as desperate measures.

Recent Viral Disease Outbreaks

Viral diseases in recent history have proved to be difficult to control with some eventually becoming pandemics, examples of previously experienced coronaviruses (CoVs) disease outbreaks include Severe Acute Respiratory Syndrome (SARS) originating from Guangdong Province, China in 2003 and the Middle East Respiratory Syndrome (MERS) that emerged from the Kingdom of Saudi Arabia in 2012 [5,6]. Adding to SARS, MERS, and COVID-19 are other recent viral but non CoVs disease outbreaks; H1N1 Swine flu that emerged from Mexico and USA in 2009 [7] and Ebola from West Africa in 2014 [8] are also worth mentioning based on their ability to re-emerge and affect large populations (Figure 1.2).

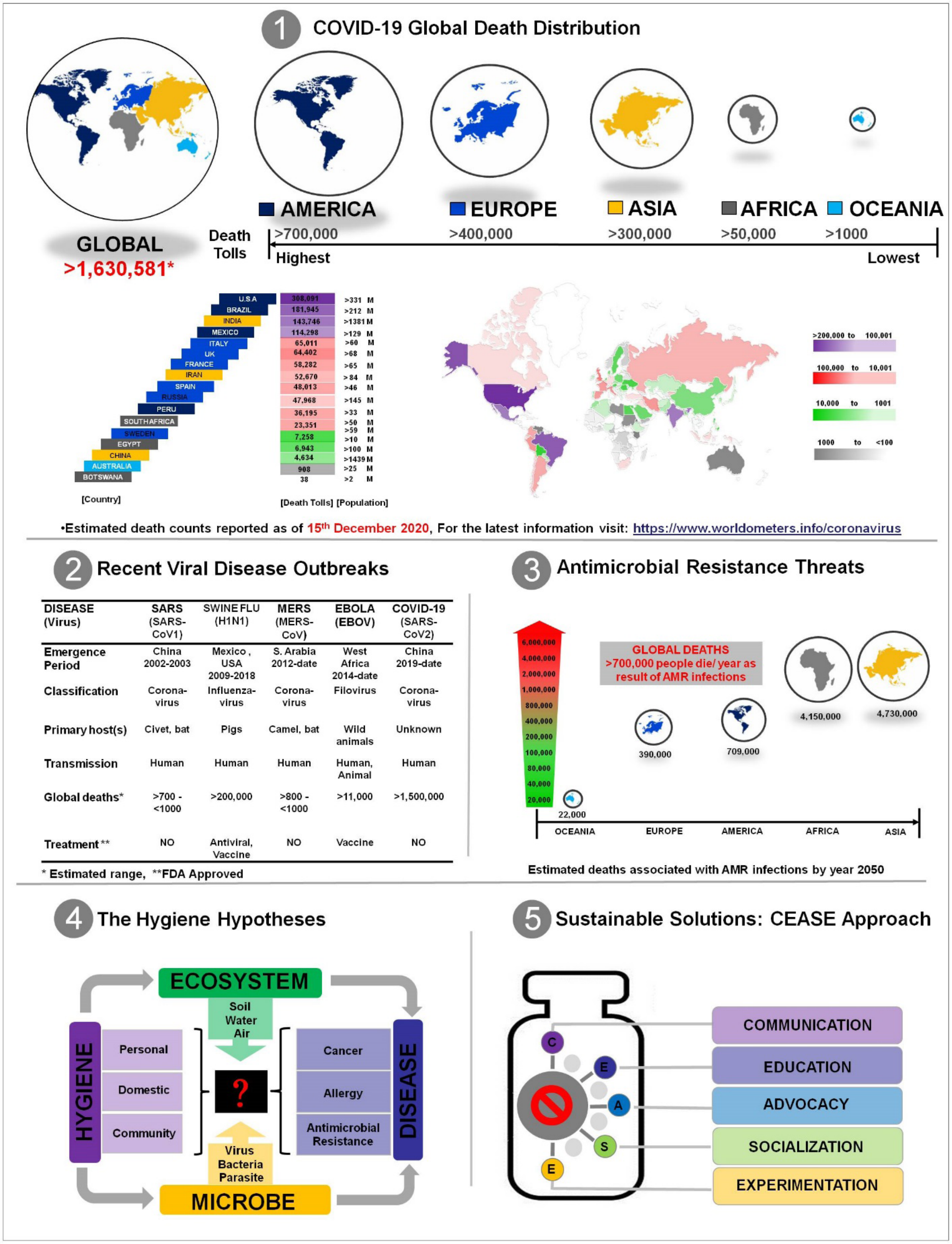

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Figure 1: A Summary diagram of the 5 key topics addressed to reveal (1) COVID-19 global death distribution, (2) COVID-19 comparison to other recent viral disease outbreaks, (3) the rising threat of antimicrobial resistance (AMR), (4) the hygiene hypotheses linked to ecosystem, microbes and human disease, and (5) implementation of CEASE approach as the most sustainable solution towards combating COVID-19, AMR and other human infectious disease threats.

Transmission of the viruses is quite possible between humans, animals and the environment (water, soil, air, plants and inanimate objects). Animal workers, health care staff and people working in hotels are among the high risk groups of contracting these viral diseases based on reports from previous SARS and MERS outbreaks [6,9,10]. Nevertheless, the overall combined deaths reported for SARS (774 deaths between 2003 and 2004) and MERS (866 deaths between 2012 and 2020) are not comparable to the high numbers (>1 million) currently being reported for COVID-19 between December 2019 to present.

Before SARS and MERS epidemics, CoVs were formerly regarded as relatively harmless with only a few known to be circulating in humans (Song *et al.,* 2019). The change in the CoVs dynamics from causing mild illnesses such as common cold to emerging as cause of acute respiratory distress syndrome (ARDS) is not surprising from an evolutionary perspective. The reality is that if the disease causing agent is not completely cured, it remains in the hosts (human and/ animal reservoirs) giving time to mutate and re-emerge later more deadly than before. To date, there is no approved vaccine or anti-viral therapeutics specific for CoVs causing SARS, MERS, COVID-19 [11-13] and therefore, these CoVs diseases will remain a serious health threat to humanity.

Antimicrobial Resistance Threats

Antimicrobial resistance is a multifaceted condition that results when a microbe (such as bacteria, fungi, protozoa, and viruses) counteracts the effects of specific antimicrobial drugs (antibiotics, antifungals, anti-parasites, antivirals) meant for therapeutic purposes [14]. The common mechanism for development of resistance in microbes is through genetic mutations (either spontaneous or induced by selective pressures) which occur in specific genes encoding proteins that are targeted by antimicrobials. The evolving threat of AMR is caused by extensive use of antimicrobials in agricultural food production, human and veterinary medicine [11]. Antiviral resistance is inevitable especially for RNA viruses such CoVs; COVID-19 virus has a relatively small genome of about 29, 903 bp [REF Seq Accession Number: NC_045512.2] and therefore prone to genetic mutations. High mutation rates are also caused by lack of proof-reading capabilities during genome replication [15,16]. Antiviral resistance remains a challenge due to the rapid development and global spread of antiviral resistant strains even in the absence of selective pressure [17].

Antibiotic resistance in bacteria is the most widely studied and recognized by WHO among the human health threats of 21st century (WHO, 2013). According to the 2019 Antibiotic/ Antimicrobial Resistance (AR/AMR) report by United States CDC, more than 35,000 people (over 2,8 million infections) die as a result of antibiotic resistance (CDC, 2019). Research from the European CDC has also estimated a death toll over 33,000 caused by antibiotic resistant bacteria in Europe [18]. Based on population and literature review, the Asian region is regarded as one of the epicentres of AMR globally [19]. Although data is limited in other regions such as Africa due to lack of AMR surveillance systems, WHO predicts deaths associated with AMR to increase significantly, with Africa and Asia expected to reach over 4.1 billion and over 4,7 billion deaths by year 2050 [2] (Figure 1.3).

Stuart Levy described in the book, “The antibiotic paradox” how the indiscriminate use of antibiotics destroyed the effectiveness of antibiotic therapy, ultimately leading to the current global problem of AMR [21]. The use of antibiotics such as azithromycin for COVID-19 treatment should be avoided as this could contribute to the rise of AMR [2].

The Hygiene Hypotheses

During this time of the COVID-19 pandemic, the use of chemical disinfectants such as hand sanitizers and antimicrobial soaps has increased significantly. The WHO recommends alcohol-based sanitizers (comprising of either ethanol or isopropanol) due to their fast-acting, broad-spectrum microbicidal activities with minimal risk of promoting AMR (WHO). A guide for local production of alcohol based sanitizers has been made globally available following extensive use which leads to shortages of commercial hand sanitizer during this period of COVID-19 pandemic.

It is now acknowledged that the indiscriminate and intensive use of chemical disinfectants contributes to AMR, and during the COVID-19 pandemic this has raised some questions surrounding hygiene, microbes, ecosystem health, and diseases (Figure 1.4.). Personal, domestic and community hygiene is essential in the prevention of viral transmission and control of disease outbreaks such SARS and Ebola [22,6]. Understanding of microbes in relation to the use of chemical disinfectants and their implication to the ecosystem (soil, water, air) health and development of human diseases is vital. Extensive use of chemical disinfectants and antimicrobials remains a health concern due to persistence of some chemicals in the environment [2]. The human body also contain essential microbes (microbiome) known to play a significant role in early development of the human immune system, and subsequently preventing conditions such as allergies, cancer, inflammatory and autoimmune diseases as explained in previously formulated hypotheses [24,25]. Sehrawat and Rouse in their recent commentary argue that “the hygiene hypothesis may apply to COVID-19 susceptibility and also that residence in low hygienic conditions acts to train innate immune defenses to minimize the severity of infection” [26]. The hygiene hypotheses linked to microbes, ecosystem, and human diseases including AMR need to be addressed using strict scientific methods that are supported by AMR stewardships to ensure that antimicrobials/ chemical disinfectants are used prudently and do not contribute the next pandemic.

Sustainable Solutions-CEASE Approach

Failing to control emerging and re-emerging infectious diseases will periodically lead to pandemics, and because of AMR there is challenge in the development of new antimicrobials such as antivirals for treatment of COVID-19. For most microbial diseases, the development of vaccines is the most favourable treatment option since vaccines are created to enhance human's natural immunity against infectious microbes and therefore microbes cannot develop resistance [27]. However, creating vaccines has also proven to be difficult particularly for viral infections based on the time and cost associated with vaccine development.

The question of how do we survive COVID-19 now and begin to deal with future pandemics or similar situations that are a threat to humankind need to be addressed immediately. The world is consequently getting informed and coming up innovative ideas, effective and sustainable approaches such as 'targeted hygiene" that was used previously during the SARS outbreak [22], and 'one health', multi-disciplinary approach targeting human, animal and environment [28]. The CEASE idea was proposed recently as a multi-dimensional approach for combating COVID-19, AMR and future microbial threats is recommended for implementation at a global level [2]. The framework in the CEASE approach comprises of five key elements viz. *Communication, Education, Advocacy, Socialization, and Experimentation* (Figure 1.5), and is re-enforced by efforts from individuals and organizations including political leaders, health officials, researchers, policymakers, journalists and members of the general public working together [2].

The governments however, have a huge responsibility in the successful implementation of the CEASE approach, and this should begin with establishing robust multi-disciplinary teams of experts that deal strictly with microbial threats to help in prediction, generating scientific evidence and dissemination of relevant information for early response, prevention and control spread of microbial infectious diseases. To ensure that the citizens are well informed and protected from COVID-19 and other microbial threats, governments are also expected to provide infrastructures for public health education, establish proper health care systems including testing, quarantine and isolation facilities. Health care workers and auxiliaries should also be well trained and equipped with proper PPE. Government funding of experimental research is mandatory, and should be made a priority to support government decision making and inform health policies. Hygiene policies should be implemented and constantly communicated to members of the general public to maintain good targeted hygiene practices that do not compromise human, animal and environmental health. Furthermore, laws should be made to change all norms/cultural practices that undermine IPC measures.

Conclusion

Global health issues such COVID-19 and AMR remain complex and difficult to tackle due to the socio-economic, geographical, and climatic differences; hence these issues require innovative thinking, multi-dimensional and sustainable strategies to overcome them. The CEASE approach is especially critical for African countries, and can be used to further explore opportunities that can lead to improvements in sanitation, access to clean water, health care, education and infectious disease surveillance systems.

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