Review

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Increase in SARS-CoV-2 infected biomedical waste among low middle-income countries: environmental sustainability and impact with health implications

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Abstract: Studies have shown that severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) is a highly infectious disease, with global deaths rising to about 360,438 as of 28 May 2020. Different countries have used various approaches such as lockdown, social distancing, maintenance of personal hygiene, and increased establishment of testing and isolation centers to manage the pandemic. Poor biomedical waste (BMW) management, treatment, and disposal techniques, especially SARS-CoV-2 infected BMW, may threaten the environmental and public health in most developing countries and, by extension, impact the economic status of individuals and the nation at large. This may increase the potential for the transmission of air/blood body fluid-borne pathogens, increase the growth of microorganisms, risk of mutagenesis, and upsurge of more virulent strain. In contrast, uncontrolled substandard burning could increase the potential spread of nosocomial infection and environmental exposure to toxic organic compounds, heavy metals, radioactive, and genotoxic bio-aerosols which might be present in the gaseous, liquid, and solid by-products. The paucity of understanding of pathophysiology and management of the SARS-CoV-2 pandemic has also necessitated the need to put in place appropriate disposal techniques to cater for the sudden increase in the global demand for personal protective equipment (PPE) and pharmaceutical drugs to manage the pandemic and to reduce the risk of preventable infection by the waste. Therefore, there is a need for adequate sensitization, awareness, and environmental monitoring of the impacts of improper handling of SARS-CoV-2 infected BMWs. Hence, this review aimed to address the issues relating to the improper management of increased SARS-CoV-2 infected BMW in low middle-income countries (LMICs).

Keywords: biomedical waste; environmental impact; low middle-income countries; public health; SARS-CoV-2.

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Introduction

The current pandemic of a novel infectious disease caused by severe acute respiratory syndrome corona virus-2 (SARS-CoV-2), officially named coronavirus disease-19 (COVID-19) by the World Health Organization (WHO) [1], has become a global burden and caused major setbacks worldwide [2]. This disease originated in Wuhan, China, in 2019 and has spread to over 213 countries worldwide as of 28 May 2020. Several factors, including age, sex, and underlying health abnormalities, predispose to this disease and promote exponential spread and mortality, making COVID-19 a public health emergency of global concern [3, 4].

While many cases of this disease resolve spontaneously, some patients develop mild symptoms like sore throat, dry cough, fever, dizziness, and septic shock requiring intensive care. Other patients with comorbidity progress to severe illness, including multiple organ failure, severe pneumonia, acute respiratory distress syndrome (ARDS), dyspnea, and death [5, 6]. Among the recommendations made by the WHO toward reducing the spread of this disease include early detection, isolation, immediate treatment, and effective strategies to identify contacts. Thus, reducing the health burden of the virus on the economy and promoting unified response worldwide [7].

Though the causative virus is not air-borne and most contagious in symptomatic people, the easiest mode of transmission of the disease is not clear in its entirety [8]. However, studies have shown that this disease spreads in different ways, including direct contact with infected persons, close contact with the respiratory droplets produced by an infected individual during coughing, sneezing, or talking, and through aerosols, especially during medical procedures like intubation. There is also an increased risk of transmission when a person touches the eyes, nose, or mouth after touching a contaminated surface, i.e., fomite transmission [9, 10]. Accumulating evidence shows that direct interhuman transmission majorly occurs during the asymptomatic incubation period, usually 2–14 days [11, 12].

Preventive measures to curtail the spread of coronavirus

Sequel to the continued increase in the incidence of COVID-19 infections, the high transmission efficiency of the SARS-CoV-2, and unavailability of vaccine, adequate preventive measures are urgently needed to curtail the global spread of this virus as well as damage associated with COVID-19 [13, 14]. In line with this objective, various health organizations around the world have recommended several measures to prevent the further spread of the disease. These recommendations include but not limited to: restrictions to highly contagious areas and maintaining social distancing to reduce contact with disease patients; practice good respiratory hygiene involving covering of mouth and nose with bent elbow or tissue when coughing or sneezing as well as prompt disposal of the used tissue; regular and thorough cleaning of hands with an alcohol-based hand rub or soap and water to kill the virus; early medical attention to sick persons and strict adherence to the information given by health authorities [15, 16]. Also, the use of medical mask or face covering when physical distancing is not possible. This measure protects people around even if asymptomatic [17].

Furthermore, additional measures must be implemented by the healthcare provider caring for COVID-19 patients. The most important measure by this personnel is the use of personal protective equipment (PPE), including selecting the appropriate PPE with adequate training on wearing, removal and disposal after use. The use of PPEs has been a vital means of preventing the spread of SARS-CoV-2 [18].

PPE

PPE is a protective gadget including clothing, helmet, gloves, gown, goggles, face shields/masks, and other apparatus designed to protect the wearer from injury or spread of infection [19]. Healthcare providers commonly use this equipment, majorly in hospitals and laboratories, to form a protective barrier preventing the transmission of contaminants in body fluids and respiratory gases. The choice of appropriate PPE is determined by the type of hazards, e.g., biohazards, air-borne infections, or chemicals the healthcare provider is exposed to. It is worthy to note that PPE does not eliminate the infection source but protects the wearer. Hence, there may be a transmission of infection if not properly used. Also, PPEs can create additional stress and slight discomfort on the wearer, thereby discouraging the wearer and placing them at risk of infection. In light of these, appropriate training on the proper use of PPE by healthcare providers will enhance the effectiveness of this equipment in the prevention of disease [20]. Also, implementations of various guidelines underlining proper use of PPEs with other control measures such as good respiratory hygiene and thorough hand-washing could effectively reduce human-to-human transmission of SARS-CoV-2 infection [21]. For effective use of PPE, the following basic principles must be carefully observed;

- Always clean the hands thoroughly before using the equipment.
- Remove or replace damaged PPE promptly once noticed that it is not in its optimal working condition.
- Quickly remove PPE as soon as possible after completing the task and avoid transferring contaminants to other people around.
- Promptly discard all PPE appropriately and ensure hand hygiene immediately.

Regulation of PPE use

To ensure the safe and effective use of PPE, the Food and Drug Administration (FDA) in the United States have set-up adequate regulations and ensure that all PPE meet

applicable voluntary consensus standard for protection [22]. However, the proposed standard and regulations differ with the specific type of PPE. The producer must prove that this equipment fulfills specific criteria and obtain approval declaring that the equipment is 'substantially equivalent' (SE) before selling legally. A new device granted SE approval means that it is safe and effective as the predicate. These criteria include, but are not limited to, performance, labeling, and intended use to demonstrate substantial equivalence. Among the consensus standard used to validate the acceptance of PPE to be used as a medical device is its ability to function as a barrier, resistance to tear, sterility, biocompatibility, resistance to fluid, and flammability. Also, the manufacturers must present test procedures used to validate conformance to standards and provide supporting data for each test [23].

Use of PPEs in COVID-19 prevention

The use of PPE during the present outbreak of SARS-CoV-2 has become an essential discussion by the healthcare providers working toward curtailing the pandemic. The major PPE used to manage the spread of this virus is air-borne equipment such as the closely fitted high-filtration masks and N95 respirator that can prevent respiratory gases that may contain the virus [24, 25]. Masks (surgical/face): This is a loose-fitting, disposable device that provides a physical barrier between the mouth and nose of the wearer and potential contaminants in the immediate environment. These masks are of different thicknesses and strength; if used correctly, they can provide adequate restriction to contaminants from reaching the mouth and nose as well as reducing saliva and respiratory droplets to others [26]. However, the surgical mask does not always provide complete protection from small contaminants transmitted during sneezing and coughing due to the loose fit between the face and the mask. Also, the use of masks should be discontinued after a single-use, damage, or if it makes breathing uneasy. This should be done safely by dropping it in a plastic bag, trashed and discarded appropriately. Afterward, the hands should be washed thoroughly. N95 Respirators: It is a high-performance filtering mask intended for use in the healthcare setting. It closely fits the face to provide an effective barrier and filtration of gaseous contaminants. N95 respirators filter efficiently when adequately used than face masks, blocking more than 95% of tiny particles. However, due to their close-fitting on the face, people with respiratory and cardiac disorders must observe extra precautions when using it [27].

Respiratory gases from an infected patient can be spread while talking, sneezing, or coughing with varying viral load and infective capacity [28]. A large cluster of particles of different sizes is usually expelled during sneezing and coughing; therefore, the degree of spread by the infected person can significantly be reduced by wearing a fluid-resistant surgical face mask [29]. It is important to note that PPE is only a part of the more extensive protective system to manage contamination of healthcare providers to COVID-19 patients as they stand at higher risk. Thus, other strategies to reduce the spread of infection should also be implemented. However, several pieces of literature have questioned the air-borne transmission of coronaviruses. However, various healthcare regulatory bodies (including the WHO, European Centers for Disease Control, Public Health England) comply with most countries' directives have recommended appropriate precautions against air-borne transmission and contact with infected patients [30]. Thus, there has been an increasing demand for air-borne precaution PPEs to fight against the spread of COVID-19 [29].

Increase in PPE demands across the globe

PPE helps to protect healthcare providers against infectious materials, toxins, and other contaminants frequently produced during healthcare delivery. Currently, there is a significant shortage of PPE due to excessive demand following the outbreak of highly-infectious SARS-CoV-2 that causes COVID-19. This equipment (PPE) is witnessing high demand globally due to its accessibility, affordability, and effectiveness against the transmission of this ravaging disease. Thus, adequate strategies to optimize PPE include identifying alternative measures to prevent the spread of the virus, nonsupply of PPE to public area, using PPE (e.g., mask) for a longer period where possible, and an increase in their production. This will help to reduce shortage and ensure that PPE is available to health care workers when needed.

Disruption in the global supply chain or increase demand of PPE across the globe

The inappropriate use and excess demand for PPE during this pandemic have disrupted the global supply of PPE [31]. While only a few countries like the United Kingdom and China have a substantial stock of PPE, adequate supply to the healthcare provider, and maintenance of the supply chain,

several countries have limited stocks, and supply is uncertain. This disruption in the global supply could, if not corrected promptly, cause a significant setback to the fight against SARS-CoV-2 globally. Currently, the global stock of medical masks, respirators, gowns, and goggles is limited due to increased COVID-19 cases globally, misinformation, panic buying, multiple inconsistency, and inappropriate use [32]. Also, the possibility of increasing production to meet the demand for PPE is limited due to national lockdown strategies implemented in several countries with resultant reduction in the workforce even though there has been an increase in substandard production by local manufacturers. Thus, it is vital to ensure that PPEs are used adequately to avoid transmission and waste [33, 34]. Transmission-based precautions such as social distancing, avoiding high-risk areas, and touching the face with dirty hands should be strongly implemented to minimize PPE usage.

Strategies for optimizing the supply of PPE

To optimize PPE availability globally, drastic measures need to be put in place to limit the disruption in the distribution chain of PPE. Some of these measures are discussed.

Minimize the need for PPE

To achieve this aim, telemedicine could be considered as a means to diagnose suspected cases of the disease, thereby reducing physical contact between healthcare providers and the suspected patient. Physical barriers such as transparent glasses, windows, and doors other than PPE could be used at the front-desk offices where patients first present to register or at the dispensary. Also, there should be a strict restriction (especially to non health care providers) to movement in/or around the isolation and treatment centers for SARS-CoV-2 patients [35].

Use PPE appropriately

The availability of PPE can be influenced by its overall usage as its overuse can directly translate to limited availability when needed. Therefore, to ensure that PPE is used efficiently, adequate training should be provided for clarity of purpose and actions when using PPE because the choice of PPE is determined by the risk of exposure and mode of transmission of the disease pathogen. This training will enable the proper selection of appropriate PPE suitable for the types of transmission, how to put on and discard PPE after use, and hand hygiene to prevent self-contamination [36]. In addition to this, a healthcare provider can wear a single respirator when attending to several patients with similar diagnoses because respirators maintain their protection when used for longer hours [37, 38]. Use of PPE when not needed should be prohibited (for example, an asymptomatic person wearing a mask of any type) as this can increase cost and indirectly exert financial burden during procurement as well as creating a false sense of security for the person with negligence to other essential preventive strategies [39].

Coordinate PPE supply chain

This is another essential measure to ensure the optimal availability of PPE. Effective coordination of the PPE supply chain should be implemented by the concerned national and international stakeholders via different mechanisms, including; the use centralized request management system to avoid multiple stock and ensuring that there is adherence to stock management rules to reduce waste and damage, request for PPE supply should be rationalized using appropriate quantification models and proper monitoring of PPE distribution to each COVID-19 infected country to ensure adequate provision of PPEs when necessary. Also, requests for PPE from each country, significant responders, and medical facilities and their distribution should be adequately monitored and controlled [40, 41].

BMW

BMW can be solid or liquid substances generated when providing healthcare services to humans or animals or in the course of research relating to production or testing biological samples. These substances contain potentially infectious components and are broadly classified into 10 different categories as follows [42]. Human anatomical wastes (e.g., body parts, tissues, or organs); animal waste (e.g., research animals and waste from veterinary hospitals and animal houses); microbiological and biotechnological waste (e.g., waste from laboratory cultures, live or attenuated vaccines, microbial cultures, and stocks); waste sharps (e.g., needles, syringe. Lancet); discarded medicines and cytotoxic drugs (expired drugs); soiled wastes (e.g., plaster casts, bedding, and other items contaminated with blood and body fluids); solid wastes (e.g., bandages, discarded gloves, catheters); liquid wastes (e.g., discarded

blood, saliva, and urine samples as well as waste generated from disinfection and laboratory cleaning); incineration ash (include all wastes obtained during the incineration of BMW) and chemical waste (all chemicals and reagents used in the production of biological and disinfection). BMW generated by various healthcare establishments, research facilities, and laboratories is a potential reservoir of pathogenic microorganisms and requires appropriate, safe, and reliable elimination from society because they can create various health risks [43]. To ensure adequate handling and treatment of these wastes, their physicochemical properties should be evaluated, and management strategies should be implemented accordingly. Amongst the properties to be evaluated are combustibility, total suspended solids, biological oxygen demand (BOD), chemical oxygen demand (COD), heating value, density (physical and chemical properties), pH, aggregate stability, biodegradability, composition (heavy metals, radioactive substances), bioavailability, total hardness, bioconcentration, and moisture content [44] (Figure 1).

BMW management practice and challenges among low-middle income countries (LMICs)

Recently, the management of BMW has attracted laudable attention especially given the rapid transmission of coronavirus (SARs-CoV-2) infection present in several countries in the world. This results from the fact that improper management of this waste could enhance the transmission of viruses and other vectors with a significant outbreak of disease. While some developed countries have implemented adequate guidelines to handle effectively and dispose of their BMWs, LMICs have suffered significant setbacks in this regard due to poor infrastructure and inadequate waste management practices [45–47]. Despite these setbacks, the type and amount of BMW generated in these countries, if not correctly managed, could be a source of future outbreaks and pandemics, ravaging the African continent with several LMICs.

Poor waste management practices in LMICs

The concept and management practice of BMW is receiving significant attention, primarily because of the rapid increase of COVID-19 disease. The impact of BMWs (both solid and liquid waste) on the increasing rate of disease outbreaks in the society is a global health concern as it significantly affects the economic stability of the country and exerts a significant burden on the well-being of the populace. Literature has reported significant health effects concerning individuals residing near waste sites [48]. The primary poor waste management practice in LMICs includes.

– Disposal of large amounts of these wastes in illegal places [49].

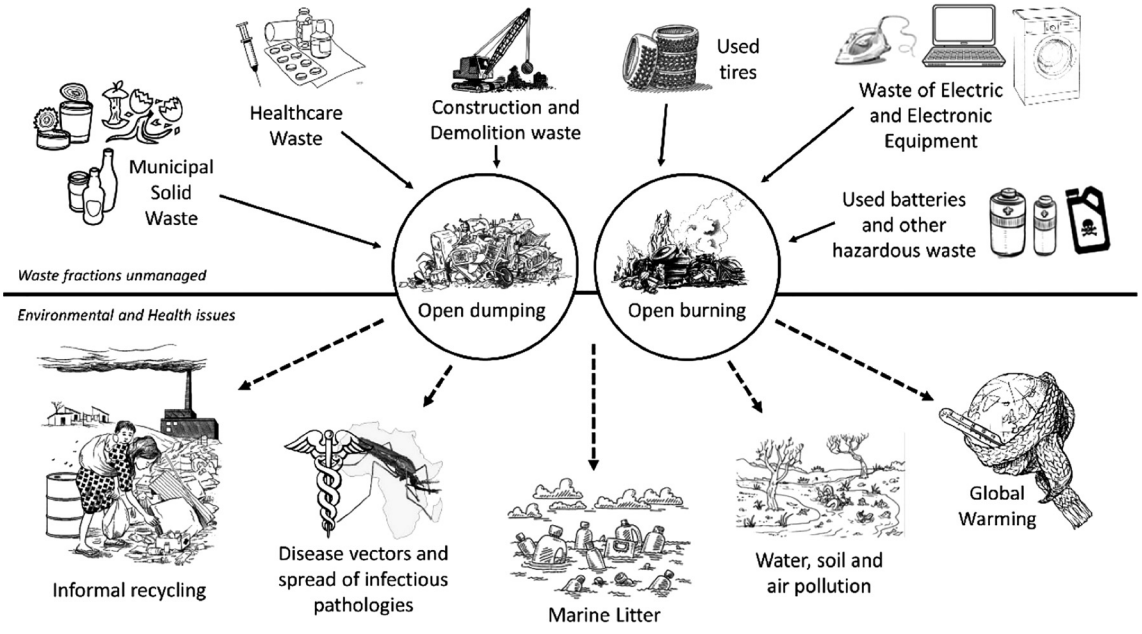


Figure 1: Waste management in developing countries [45].

- Uncontrolled burnt without following appropriate guidelines generate pollutants that contaminate the atmosphere and impose a severe health threat to lives around such premises [50, 51].
- Improper disposal of these BMWs without treatment into water bodies. This is worrying for both toxicological and esthetical reasons as it tends to damage the quality of the receiving streams and also significantly pathogenic to the marine food chain [52].

Thus, drastic interventions are required to properly manage these BMWs, especially in LMIC with unsustainable management policies to prevent further transmission and outbreak of the disease in these countries [53, 54]. These interventions should be geared towards reducing the generation of BMWs, comprehensive assessment of the environmental impact, and implementation of proper management practices for effective solutions [45] (Figure 2).

Challenges facing BMW management in LMICs

In the developed countries (such as China), there are policies from the national to the regional and local levels guiding all stakeholders in the proper management of BMW. However, most LMICs cannot effectively manage their waste, accounting for increased incidences of disease outbreaks and a higher financial burden on the health sector. Some of the challenges facing LMICs in the management of BMW are:

Insufficient infrastructures: To deal with the ever-increasing burden of BMW has resulted in the dumping of a large quantity of the waste in illegal sites and sometimes burning within the premises of the health facilities [50]. In most of these countries, incineration is the most common method to dispose of toxic medical waste; however, incinerators pollute the air by releasing toxic metals to the atmosphere, polluting soil and surface water [56].

Insufficient funding: Many of these countries are not financially buoyant to procure sufficient and state-of-the-art facilities as well as employ expatriates in all their health facilities, therefore, relying on the traditional method of waste disposal such as open burning, sewage disposal, and employing casual workers to manage the country's wastes. Arguably, most cleaners and waste handlers in these countries are the worst victims of inadequate occupational safety procedures. A larger number of these workers are casual laborers with no training on the appropriate response to occupational risks to which they are exposed.

Inadequate waste management practices: Excessive production, inability to recycle, poor recording, separation, transportation, and disposal of these wastes resulting in environmental pollution and toxic emissions, which are harmful to workers and society. Regardless of the significant challenges, guidelines, expertise, and policies needed for efficient waste management, many countries, especially in LMIC, are poor, therefore, requiring appropriate interventions to salvage the potential danger.

Poor training: In LMIC, health care staffs are not adequately trained about occupational safety education and are not aware of the proper handling of hazardous substances. Also, there is a paucity of information on the use of PPE and a casual attitude to emergency procedures like spillages and accidents [57].

Nontransparent administration: There is usually instability and non-ransparency in government administration in most of these countries, causing significant limitations on the effectiveness of the national waste



Figure 2: BMW management in developing countries by open dumping [55].

management agencies. In this regard, public agencies and other stakeholders involved in waste management find it difficult to fulfill their obligations, limiting professionalism.

Research: Lack of adequate research and research funding on waste management and the vast potential benefits in adopting and utilizing beneficial microorganisms capable of generating biomolecules such as biosurfactants for bioremediation and treatment of water wastes and landfills.

BMWs differ from general waste and are usually hazardous because they can promote the spread of infectious diseases and serve as a potential threat to human health. It was reported that a significant percentage of healthcare providers sustain injury from sharp waste when discharging their duties, while improper handling of cytotoxic and chemical waste can be mutagenic [58]. Thus, proper disposal is highly required as continuous exposure to BMW could cause the accumulation of microbes (microorganism causing disease) in the body. Adequate implementation of good management practices is vital to promote sustainable development goals in public health among LMIC. Also, adequate waste management and treatment is among the primary goals for improving sustainability and designed to ensure access to good, safe, and reasonable waste removal services; eliminate uncontrolled dumping and open burning; to achieve viable and environmentally sound management of all wastes, particularly hazardous ones [59]. Some of the possible interventions reported in the literature to improve BMW management practice in LMIC include but not limited to implementation of waste-to-energy plans and technologies, waste recycling, energy production from the disposed wastes, and providing adequate incentives to waste pickers as well as the implementation of organic waste buyback program [60–62].

BMW and environmental health

Recently, an increasing trend in BMW production has been observed, resulting from the increased number of health organizations providing healthcare services to the growing human population and the increased usage of medical-related products during disease outbreak [63–65]. Excess BMW generation increases the cost of waste treatment and disposal, rendering the available management practice ineffective [66]. Therefore, waste management agencies advocate for reducing and possibly reusing bio-medical waste [67]. However, COVID-19 infected BMWs should not be recycled due to the viability of the virus and the severity of the accompanying diseases. The improper disposal of BMW can negatively affect water quality because of different contaminants (such as cadmium, lead, aluminum, vanadium, and iron) that may leach out from the waste dumping sites into the groundwater [68]. Studies have shown that incineration of BMW contains a high concentration of toxic chemicals (mercury, dioxin, and lead) that may increase the amounts of contaminants polluting the atmosphere and groundwater. These toxicants increase the risk of several ailments among residents exposed to these contaminants because some may be mutagenic, carcinogenic, or teratogenic [69–72]. Hence, it is crucial to eliminate or reduce the toxicity of such wastes using adequate treatment measures before disposal into landfills or been reused [73]. Groundwater is polluted via the percolation of toxic substances from BMW. Hence, direct disposal of such wastes into landfills without proper treatment should be strongly prohibited by the relevant authorities. Also, heavy metals in landfill leachate from BMW may cause a risk to the environment, especially in unlined landfills where dissipation of leachate into groundwater might occur [68]. Furthermore, unregulated BMW disposal may change soil quality near waste dumping sites because different contaminants may get mixed with the soil, thereby changing the constituents, reducing soil fertility, and affecting the soil ecosystem.

A study conducted in Ibadan city, Southwest Nigeria, by [74] shows that the soil samples and bottom ash of a hospital incinerator contain a higher concentration of heavy metals (such as zinc, lead, chromium, and cadmium) compared to municipal dumpsites suggesting significant soil pollution resulting from BMW generated from the hospital. This could cause a drastic deteriorating of soil quality and decrease vegetation abundance due to the dumping of BMW [75]. All the metals investigated were above the Dutch and Danish limit values for maximum permissible levels of heavy metals in good soil quality, and therefore, classified as harmful and toxic for human health. Consequently, it should be recommended that lands with an excess concentration of heavy chemicals should be closed from further use, and immediate remedial action should be implemented to minimize future pollution and potential impacts on the environment and local society [76].

It has been reported that the majority of the BMW generated are managed by burning in incinerators [77]. However, uncontrolled and improper burning of BMW may cause air pollution in the atmosphere by producing toxins and mixing different air pollutants to a level that imposes danger to human health. The primary source of these toxins is polyvinyl chloride material in the waste [78]. Arguably, greenhouse gas and particulate emissions are considered a challenging issue from municipal solid waste dumping sites [79]. The burning of BMW at these sites is a

severe threat to the environment and human health because it releases harmful chemicals (hydrochloric acid, carbon monoxide, ethane, ethylene, propane, and propylene) that cause various types of respiratory disease among the residents and workers [80]. To this end, some waste management control authorities have restricted the disposing of hazardous infectious waste in landfills without following the appropriate guidelines.

BMW and human health

Generally, the specific characteristics of BMWs implicate them as one of the most dangerous types of waste, and improper management of this waste can negatively affect health with a significant outbreak of infection and poisoning [81]. The huge health risks to humans and the environment posed by BMWs range from direct injury due to exposure and indirect injuries resulting from land, water, and air polluted with toxic chemicals from the medical waste [82] that forms significant components of these wastes [83]. Literature has shown an increasing number of epidemics and waste-related diseases resulting from inadequate waste management practices. Besides, significant health abnormalities that occurred over the years can be linked with improper handling of BMW [84–87]. Also, waste-related diseases accounted for approximately 5.2 million mortality annually, and this has been proposed to increase if adequate measures are not implemented to stop other disasters [88]. Most of the health problems linked with BMW disposal are due to the rapid and uncontrolled growth of medical care facilities and excessive use of biomedical facilities resulting in increased waste generation, improper disposal, and illegal recycling practices [89]. The potential health hazards may affect the public, especially healthcare workers, municipal employees, and rag pickers involved the recycling waste. Waste handlers and other individuals in direct contact with processing and handling of waste have a higher risk of contracting communicable diseases, majorly due to improper handling [90] and exposure via skin contact, open wound, and inhalation.

Although infectious wastes are traditionally treated by incineration, this method has been widely criticized due to the wide variety of pollutants released from the incinerator based on the component of the waste. Heavy metals, acidic and poisonous gases are significant pollutants emitted when burning BMW and may be toxic to human health. Among the possible health abnormalities associated with the burning of BMWs are increasing cancer and respiratory symptoms, eye irritation, congenital abnormalities, gastro-intestinal abnormalities, infertility, organ failure, musculoskeletal problems, and hormonal defects. At the same time, other related issues include global warming, acidification, and ozone destruction [91–93]. Therefore, newer technologies like bio-surfactants for bioremediation from beneficial microbes, hydroclaves and plasma pyrolysis, steam sterilization, microwave treatment, advanced steam sterilization, dry heat sterilization, biological treatment, plasma gasification, and alkaline hydrolysis are now proposed for the incineration of BMWs. This equipment causes reduced environmental degradation, non-significant health impacts, safe handling of treated wastes, ecofriendly, decreased running and maintenance costs, more effective reduction of microorganisms, and safer disposal [43]. Beyond a doubt, medical care is critical to life and the maintenance of health. However, the waste generated from medical activities causes additional problems for humans and the environment [94], especially during pandemics like SARS-CoV-2 (Figure 3).

Principles for effective management of BMWs

BMW should be appropriately managed (ranging from production to disposal) to protect the environment, public, and workers, especially healthcare and sanitation workers, at risk of exposure to BMW as an occupational hazard. The development and implementation of appropriate management policies can efficiently improve BMW management generated from health and related facilities in a country [96]. Practical approaches that have been identified in the management of medical waste are briefly highlighted below [97].

General principles of hygiene and sanitation

This is a vital component of a good BMW policy. This principle involves cleanliness, availability of adequate and safe water, sanitary facilities, and good ventilation to health care facilities, service providers, and other stakeholders. Implementing this principle will reduce the breeding and growth of microbes, thus, enhancing healthy living practices [98].

Waste reduction

This is another means of managing BMW, especially those generated from hospitals and laboratories. This

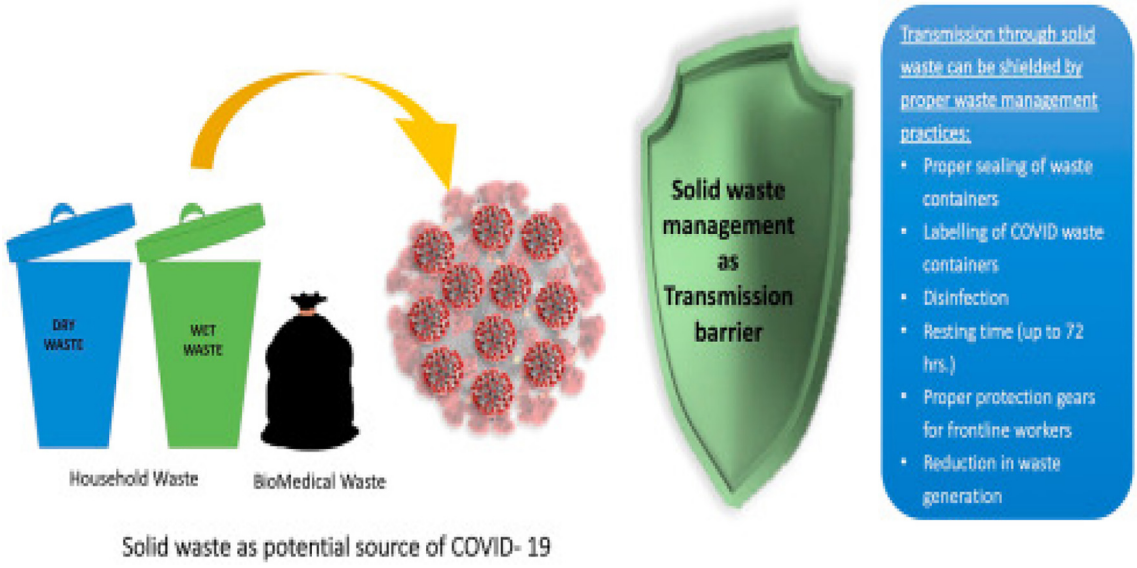


Figure 3: Solid waste management during COVID-19 pandemic [95].

step involves proper identification and quantification of the waste generated, achievable by keeping proper inventories, the record of wastage of consumable items, and any damages. Using this approach, the quantity of waste disposed of can also be reduced by recycling or reusing some 'wastes' such as glassware and plastics after thorough cleaning and disinfection [99].

Waste segregation and storage

This can be adjudged the most crucial step in the waste management chain as it determines the eventual amount of waste to be treated and disposed of. At this step, designated storage facilities and a central storage site should be provided within the health facilities where wastes can be temporarily stored before they are transported offsite [100]. The WHO prescribed that medical waste should be sorted and dumped into separate waste containers from the source and afterward stored in a safe place inaccessible to rodents and unauthorized people for a maximum of 48 h before treatment or disposal [101]. If this guideline is strictly followed, the quantity of medical waste eventually passed to treatment/disposal facilities will be small and manageable. However, if the wastes are all mixed, they are all treated as hazardous and become difficult to recycle without pretreatment [99]. Inadequate knowledge of the characteristics of medical waste may be responsible for the poor segregation practice [102].

Waste transportation

Transfer of BMW within the health care facility should be done by designated and adequately trained personnel using appropriate equipment like trolleys and carts, which are not used for any other purpose. Also, suitable vehicles marked with biohazard symbols should be used to transport waste to sites for disposal [101]. The personnel involved in the transportation of medical waste should be trained on the different classifications of the waste and their containers to help them handle the waste and prevent them from mixing different categories of previously segregated waste [100].

Waste treatment and disposal

The methods which have been adopted for BMW treatment and disposal include the traditional open dumping on lands or water bodies, deep burial, burning and the modern incineration, autoclaving, shredding, superheated steam sterilization, microwave disinfection, wet oxidation technology, and electron beam gun technology [103]; though the World Bank permits open burning of toxic waste as a last resort on the condition that the site of burning is in the rural area, far away from busy complexes to limit the number of people being exposed to the adverse effects of the event [104]. Modern methods that are more environmental-friendly were developed to minimize the risks posed to people and the environment by the

traditional methods. However, many modern methods are costly and not available in many developing countries [86]. Selecting suitable techniques used for waste treatment and disposal depends on the unique characteristics of the waste as well as proper separation at the point of production. The WHO also recommends that the choice of the mode of treatment and disposal should be guided by cost-effectiveness, easy implementation, and environmental friendliness [105]. However, the final disposal of these wastes is usually in a landfill. The techniques which have been documented for treatment and disposal of BMW include open dumping/burning [106], incineration [105], autoclaving [107], microwave disinfection [108], and landfilling [103]. However, in many developing countries, landfills are operated like open dumping, where all forms of waste are dumped and later burned [105]. Where the landfill is not adequately constructed, erosion may cause the waste to wash into water bodies, thus contaminating the water.

However, an international organization such as Institute for Global Environmental Strategies (IGES) has provided guidelines for adequate segregation, storage, transportation, treatment, and final disposal of BWM generated during the COVID-19 pandemic. Individual countries and authors have also suggested slight modifications to waste management during COVID-19 pandemic. These include chemical disinfection with mechanical crushing, steam disinfection/autoclave, reverse polymerization of solid wastes, while liquid waste can be subjected to chlorination, ultraviolet irradiation, ozonation, and ultrafiltration [109–111].

SARS-CoV-2 infected BMW output during pandemic

The WHO estimated that infectious diseases caused about one-quarter of all deaths worldwide [112], and approximately 50% of these deaths result from airway infections and diarrhea, which are mostly preventable with proper hygiene and adequate immunization. There is continuous emergence of new pathological infectious viral diseases that sometimes reach epidemic or even pandemic status. These ranges from HIV discovered in 1980 to various hepatitis viruses in 1990 also West Nile encephalitis virus. In the last decade, a new strain of the avian influenza virus and the SARS virus was discovered. Acute respiratory infections (ARIs) (which share some similarities with SARS-CoV-2) are the leading cause of morbidity and mortality worldwide, among other infectious diseases following self-inoculation from environmental contaminants [113]. Human activities have the aftermath of waste generation, which may carry consequences if proper handling is not instituted. The evolution of BMW as a separate category of waste dates back to the late 1970s when medical wastes were found on the USA's beaches on the east coast. This followed the enactment of the US Medical Waste Tracking Act (MWTA) in 1988. The sources of BMW are from treatment, diagnosis, immunization, research, and even to a great extent, human and animal corpses died of contagious infectious ailment [114].

Until the outbreak of human immunodeficiency virus and hepatitis B virus, BMWs were carelessly handled and improperly managed; this has woken the healthcare management to time bomb posted by a carefree predisposition to the subject [115]. Although a larger percentage of the BMW has been found not to be infectious worldwide, reevaluation of this report is critical, especially with the recent outbreak of COVID-19 in which an increase of 20% of waste becoming infectious [116]. Prüss-Üstün et al. [117] estimated the percentage of various type of BMW generated; 15% pathological and infectious waste, 80% general healthcare waste, 3% chemical/pharmaceutical waste, 1% sharps waste, less than 1% other waste, like radioactive waste or broken thermometers. It should be noted that these figures may change due to COVID 19 pandemic worldwide.

Farzadika and colleagues reported that several African countries give poor attention to the proper handling of infectious BMW as evidence by improper documentation of the amount generated, the composition, and standardized management approach [118]. Admixture of noninfectious BMW invariably makes the whole waste classified as infectious and harmful, especially in COVID-19. According to WHO, about 8–16 million new cases of hepatitis B virus yearly, 2.3–4.7 million cases of hepatitis C virus, and 80,000 to 160,000 cases of human immune deficiency virus (HIV) are due to unsafe injections and mainly due to indigent waste management systems [119]. Studies have revealed that nosocomial infections (also known as hospital-acquired infections) exert a heavy financial toll on the economy and account for significant mortality and morbidity globally, with 6–19% of patients from LMICs and approximately 8.7% of patients had infections that are secondary to infectious waste [120–123].

In recent times, during the Ebola outbreak in LMICs, the health worker's primary recommendation to contain the pandemic was proper disinfection and disposal of infectious waste whenever a suspected or confirmed case is being handled [124]. In the face of increased generation of infectious BMW during this pandemic, infection

prevention and control (IPC) measure is the key to averting the spread of disease to patients, health workers, and the populace.

According to WHO, proper waste management, provision of potable water, sanitization, and maintenance of an utmost level of hygiene (WASH) in health care facilities, including (public and private places) will go a long way to curb or reduce the menace posed by the COVID-19 outbreak [125]. This means that the amount of infectious waste generated from the COVID-19 outbreak invariable will increase and pose a significant health threat if not adequately managed, especially in the developing world, both in the health facilities and the community at large. There is no confirmed case of faeco–oral transmission of COVID-19, nor it close associate SARS in the past among sewage or waste management workers; despite this, such waste from a confirmed or suspected case of COVID-19 should also be treated as a biohazard and should be carefully handled [126]. In developed countries (such as Germany and Austria), there is an adequate sewerage system; unlike LMIC, the risk of the possibility of this system leak needs to be assessed to mitigate the unintentional spread of COVID-19 and careful disposal of wastes where necessary [127]. It is common knowledge that open defecation is a ban in the developing world which further poses a significant risk to infection control, especially in asymptomatic individuals. Used water for the treatment of COVID-19 should be considered infectious liquid waste, which must be adequately managed, especially in poor resource countries [128].

Survival of SARS-CoV-2 and other microorganisms in the environment

Several micro-organisms, including viruses, exist in almost every natural habitat and can be transmitted from infected hosts to the environment and vice-versa. Therefore, natural evolution and human activities that frequently change the environmental conditions can hamper or influence the survival of these organisms. Thus, the appropriate response of microorganisms to significant changes in their natural environment can enhance their adaptation and promote survival. These responses are mediated by well-adapted regulatory mechanisms that mediate genetic modifications underlying physiological responses to changes in environmental conditions. These regulatory mechanisms involve the activation of several pathways responsible for transcription and translation as well as the stability of mRNA and active proteins that elicit suitable responses observed in the microorganisms. The inhibition of these pathways involved in the survival of microorganisms can prevent the transmission of these organisms and the accompanying infections in humans.

The molecular mechanism underlying the survival of microorganism in the environment

One particular feature of microorganisms is their ability to detect changes (such as radiation, decrease nutrient, temperature, pH, and chemicals) in their natural habitat and elicit an appropriate response to such changes for growth and survival. These organisms respond to such changes by activating several transcriptions and translational processes that preserve physiological and metabolic functions under unfavorable environmental conditions [129–131]. Microorganisms utilize different measures to cope with various environmental stressors that threaten their survival. These measures include changes in their membrane morphology, formation of spores and cysts, synthesis of different molecules for relieving stress, and activation of enzymatic processes necessary repair after damage [132]. Persistent exposure to environmental stressors induces genetic modifications underlying the adaptive mechanism of these organisms against successive stresses and coping with the new condition [133]. Some organisms respond to stressors by altering their cell morphology and synthesizing toxicants against the predators to enable their continual existence in their natural environment [134]. While some microbes reduce their energy-driven and nutrient-consuming metabolic activities to survive and protect against unfavorable environmental conditions, nondividing cells secrete resuscitation-promoting factor (Rpf), a protein that promotes resuscitation and growth activity in these organisms [135–137]. Another alternative strategies used for survival by microorganisms, including viruses, is applying adequate chemotactic behavior in which these organisms move away from unfavorable environmental conditions. Also, a programmed cell death mechanism is an indirect means of survival in which some cells in the microbes naturally die under extreme environmental conditions resulting in is less competition in the microbial population. Using this strategy, some microbial populations enhance their survival by utilizing nutrients derived from the dead cells [138, 139].

Micro-organisms have a well-modified regulatory system that identifies significant deviations in

environmental conditions. These systems are very similar and well-conserved in all classes of microorganisms but are stimulated differently from an individual organism. Using different experimental approaches, it was reported that gene transcription and induction of several genes in relation to a specific change in the environmental condition provided evidence that an existing regulatory mechanism mediates adaptation to these environmental changes and the ultimate survival of these organisms [140, 141]. To ensure that these organisms survive, these regulatory genes are either upregulated or down-regulated depending on the controlling environmental conditions. This regulation occurs at both transcription and post-transcriptional levels. Regulation at the transcriptional level involves RNA synthesis (with the limiting enzyme-core RNA polymerase) and its control, altering the genetic expression. A microorganism with a well-studied survival mechanism is *E. coli*, with seven known sigma factors (σ^{70}) serving as the master regulator competing for the major component of the transcription mechanism (i.e., core RNA polymerase) [142, 143]. Other factors such as repressor, activator, sigma-binding antisigma factors, and small RNAs regulate the genetic transcription process [144–146].

Additionally, proteolysis and modulation of the transcript stability are also part of the control regulatory machinery involved in microorganism response to environmental stress [147–149]. All these biomolecules modulate genetic expression during environmental stress and create a complex regulatory network that promotes adaptation and survival despite significant deviations in environmental conditions. Thus, the survival of microorganisms in the environment is determined by their appropriate stress-response mechanism modulated by various regulatory patterns highlighted as follows; (A) control at the transcriptional stage by a specific or alternative sigma factor. This is the rate-limiting stage in the survival regulatory pattern implemented by microorganisms. These sigma factors modify the specific genes that mediate response. The action of this sigma factor is directly proportional to the environmental condition that elicits the observed response. (B) Transcriptional control by repressor binding to a DNA control element. (C) Transcriptional control by proteolysis is mediated by several auto-regulatory proteases. This mechanism can also regulate alternative sigma factors and other adaptation processes [150]. (D) Transcriptional control by small RNAs. This helps to mediate suitable responses to oxidative stress and other pathogenic stimuli [151].

Regulation at the posttranscriptional level affects all the modification processes involved in translating the genes to the active proteins. These modifications involve enhancing mRNA stability, initiating and regulating the translation processes, and the stability of the active proteins. Thus, all these control processes of transcription and translation mediate adequate physiological responses to changes in the environmental conditions and ultimate survival of these organisms [129, 130]. In addition to the above regulatory mechanism of survival, the spike protein present on the coronavirus envelope plays a vital role in SARs-CoV-2 survival. The virus uses this protein to attach to its host cell, mediate membrane fusion, and determine the solubility and infectivity of this virus. Also, the spike protein of SARS-CoV-2 has lower free energy than SARS-CoV, thereby making it more stable and able to survive at a higher temperature [152, 153].

Pathophysiological implications on health

The fight against COVID-19 infections caused by SARS-CoV-2 has been one of the fiercest in history that is different from SARS-CoV and MERS-CoV infections in term of biological property, transmission, and treatment strategy [154, 155]. Coronaviruses are positive-sense single-stranded RNA genomes, enveloped viruses (26–32 kb) [156]. Studies have shown that they possess about four genera of coronavirus (α, β, γ, δ). Human coronavirus is only found in α and β coronavirus genera, for α coronavirus; we have the following viruses HCoV-229E and NL63 and β coronavirus; MERS-CoV, SARS-CoV, HCoV-OC43, and HCoV-HKU1 as classified by The International Virus Classification Commission naming the novel β-CoV "SARS-CoV-2" [157, 158]. The genome of SARS-CoV-2 is closely similar to typical CoVs with more than 10 open reading frames (ORFs). Two large polyproteins are gotten from (ORF1a/b), about two-thirds of viral RNA is for nonstructural proteins [159] while the other ORFs of SARS-CoV-2 about one-third of the genomes are for main structural proteins: envelope (E), spike (S), nucleocapsid (N), and membrane (M) proteins with many accessory proteins with unknown functions [158]. The viral replicate transcriptase complex is formed from 16 nonstructural proteins (nsp1–nsp16), which are in turn processed from polyproteins (pp1a and pp1ab); the non-structural proteins rearrange the membrane produce from the rough endoplasmic reticulum by forming double-membrane vesicles, which are used for viral replication and transcription [159].

SARS-CoV-2 requires the angiotensin-converting enzyme 2 (ACE2) as a receptor to penetrate cells which is a significant step in the pathogenesis of the disease, with

the help of coronavirus S protein which helps the virus to enter into the host cell [158, 160]. Cells with ACE2, such as lungs, heart, kidneys, arteries, intestines, brain, testis, and ovary, are highly susceptible to SARS-CoV-2 attack different pathological implications based on the biological functions of the organ [161]. After binding to the receptors, there is a fusion between the virus and plasma membrane in SARS-CoV mediated by SARS-CoV S protein at position (S2') [162]. The second way it enters the cell is by clathrin-dependent and -independent endocytosis mediated SARS-CoV [163]. After successfully penetrating the cell membrane, the viral RNA genome moved into the cytoplasm, and two polyproteins and structural proteins are translated from the RNA, following which the viral genome begins to replicate [157]. New viruses are formed by combining genomic RNA and nucleocapsid protein forming the nucleocapsid, which is enclosed in envelope glycoproteins inserted into the membranes of Golgi or endoplasmic reticulum membrane and later extruded from the cell by fusing with the plasma membrane [164].

There is a paucity of information in understanding the relative effects of receptor binding and protease action predicting the infective potential of specific zoonotic coronavirus [158]. The frontier of knowledge of the pathogenesis of COVID-19 is still flawed. However, clinically they present with fever, nonproductive cough, difficulty in breathing, myalgia, fatigue, normal or decreased leukocyte counts, and X-ray evidence of pneumonia, but its pathogenesis has been likened to the mechanism of SARS-CoV and MERS-CoV [158, 165]. Antigenic peptides of the virus are presented by major histocompatibility complex (MHC; or human leukocyte antigen [HLA] in humans) by antigen presentation cells (APC), which is recognized by virus-specific cytotoxic T lymphocytes (CTLs). This is important for understanding SARS-CoV-2 pathogenesis, which is lacking [12]. Virus-specific B and T cells mediate the body's humoral and cellular immunity following stimulation by antigen presentation by producing IgM and IgG [164, 166]. Studies have shown that IgM lasts for about three months, IgG may last longer, while cellular immunity appears to wane, as evidenced by the reduction in the number of CD4+ and CD8+ T cells in the blood. This is similar to what was obtained in patients with SARS-CoV [154]. The memory cells formed in patients with SARS-CoV can last for about four years or more. The primary cause of death in these patients is ARDS, mainly resulting from cytokine storm (an excessive immunological attack on the body). The release of large amounts of proinflammatory cytokines and chemokines causes uncontrolled systemic inflammation, multiple organ failure, and eventually death [165, 167]. There is a lot to learn about the pathogenesis of SARS-CoV-2, but the knowledge about SARS-CoV and MERS-CoV helps understand the dynamic pathophysiology of the novel SARS-CoV-2.

Future perspectives and recommendations for LMIC towards BMW management

If not adequately handled by waste management agencies in LMICs, biochemical wastes could be a significant source of disease outbreaks and future pandemics that could ravage the African continent due to their inherent toxic properties. Thus, several recommendations are being made for LMIC with poor management practices. These include:

- Proper orientation of the public on the danger of improper disposal of infected BMWs.
- Significant reduction in BMW generation.
- Implementing adequate measures to monitor, evaluate, and report waste management operations.
- Developing suitable infrastructures, knowledge, and necessary skills for workers.
- Improving the existing management guidelines for effective response.
- Identifying the best equipment and provision of funds for procurement.
- Implementation and establishment of regional waste management Acts.
- Research and development in the area of BMW management by generating products like bio-surfactants from beneficial microorganisms.

Conclusions

In conclusion, the outbreak of SARS-CoV-2 that causes COVID-19 infections has become a pandemic of global challenge due to its continuous spread across the countries of the world. Studies have reported that this virus is majorly transmitted by direct contact with an infected person. Hence, strategies that create an effective barrier to minimize direct contact have been proposed to reduce the continuous outbreak of this disease. PPE plays a significant role in reducing the transmission of this virus by providing an effective physical barrier against the infected patients, thus helping manage this disease. Hence, appropriate measures must be put in place to accommodate, manage, and treat the increased rate of SARS-CoV-2 infected BMW generation. In most developing countries, BMW disposal directly into water bodies is regarded as a poor method.

However, this polluted runoff water has been linked to a significant increase in waterborne disease in LMIC because households and agricultural activities in rural communities are dependent on this water. It has been estimated that 80% of diseases worldwide are waterborne. This calls for the development of a robust, affordable, and sustainable BMW treatment plan. Also, SARS-CoV-2 infected BMWs from health care facilities accommodating COVID-19 infected patients should not be recycled without adequate treatment.

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References

1. World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it; 2019. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/.
2. CDC. CDC 2019 novel coronavirus W, China; 2020. Available from: https://wwwcdcgov/coronavirus/2019-nCoV/summaryhtml [Accessed 1 Feb 2020].
3. Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A, et al. World Health Organization declares global emergency: a review of the 2019 novel coronavirus (COVID-19). Int J Surg 2020;76:71–6.
4. WHO. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV); 2020 [Internet].
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507–13.
6. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. J Am Med Assoc 2020;323:1061–9.
7. World Health Organization Novel Coronavirus (2019-nCoV) Situation Report – 12 [Internet]; 2020.
8. Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations [Internet]; 2020.
9. CDC. How COVID-19 spreads. Centers for Disease Control and Prevention (CDC); 2020.
10. Department of Health and Social Care. Official Guidance, COVID-19: guidance for infection prevention and control in healthcare settings. Version 1.0; 2020. Accessed 21.3.20 at: Department of Health and Social Care (DHSC), Public Health Wales (PHW), Public Health Agency (PHA) Northern Ireland, Health Protection Scotland (HPS) and Public Health England 2020.
11. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med 2020;382:970–1.
12. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020;382:1199–207.
13. Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: a data-driven analysis in the early phase of the outbreak. Int J Infect Dis 2020;92:214–7.
14. Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, et al. Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology 2020;295: 210–7.
15. World Health Organization Novel Coronavirus (2019-nCoV) Advice for the Public (2020) [Internet]; 2020.
16. Interim infection prevention and control recommendations for patients with suspected or confirmed Coronavirus Disease 2019 (COVID-19) in Healthcare Settings [Internet]; 2020.
17. Bae S, Kim MC, Kim JY, Cha HH, Lim JS, Jung J, et al. Effectiveness of surgical and cotton masks in blocking SARS-CoV-2: a controlled comparison in 4 patients. Ann Intern Med 2020;173: W22–3.
18. Herron J, Hay-David A, Gilliam A, Brennan P. Personal protective equipment and Covid 19 – a risk to healthcare staff? Br J Oral Maxillofac Surg 2020;58:500–2.
19. World Health Organisation. Medical devices, Personal protective equipment [Internet]; 2020. Available from: https://www.who.int/medical_devices/meddev_ppe/en/.
20. European Center for Disease Prevention and Control. Guidance for wearing and removing personal protective equipment in healthcare settings for the care of patients with suspected or confirmed COVID-19. ECDC technical report; 2020:13 p.
21. Ministry of Health New Zealand. COVID-19. Guidelines for the use of personal protective equipment for frontline health care workers. In: Health Mo, editor. Available from: https://www.health.govt.nz/system/files/documents/pages/covid-19-guidelines-use-ppe-frontline-health-care-workers-7apr20.pdf2020.
22. FDA. FDA, US. Food & Drug. Personal protective equipment for infection control. Available from: https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/02/10/2020; 2020.
23. Vozzola E, Overcash M, Griffing E. Environmental considerations in the selection of isolation gowns: a life cycle assessment of reusable and disposable alternatives. Am J Infect Control 2018; 46:881–6.
24. Alhazzani W, Hylander M, Arabi Y, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Intensive Care Med 2020;46:854–7.
25. Infection prevention and control for COVID-19 in healthcare settings [Internet]; 2020.
26. Feng S, Shen C, Xia N, Song W, Fan M, Cowling BJ. Rational use of face masks in the COVID-19 pandemic. Lancet Respr Med 2020;8: 434–6.
27. Project N95. Project N95. The national COVID-19 medical equipment clearinghouse; 2020. Available from: https://www.projectn95.org/ [Accessed 27 Mar 2020].
28. Gralton J, Tovey E, McLaws M, Rawlinson W. The role of particle size in aerosolised pathogen transmission: a review. J Infect 2011;62:1–13.

29. Public Health England. COVID-19: infection prevention and control guidance [Internet]; 2020.
30. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. World Health Organization [Internet]; 2020.
31. WHO. WHO Shortage of personal protective equipment endangering health workers worldwide; 2020. Available from: https://www.who.int/news-room/detail/03-03-2020-shortage-of-personal-protective-equipment-endangering-health-workers-worldwide.
32. WHO. Rational use of personal protective equipment (PPE) for coronavirus disease (COVID-19); 2020. Available from: https://appswhoint/iris/bitstream/handle/10665/331498/WHO-2019-nCoV-IPCPPE_use-20202-engpdf?sequence=1&isAllowed=y [Accessed 26 Mar 2020].
33. Public Health England. When to use a surgical face mask or FFP3 respirator; 2020. Available from: https://assetspublishingservicegovuk/government/uploads/system/uploads/attachment_data/file/874411/When_to_use_face_mask_or_FFP3pdf [Accessed 26 Mar 2020].
34. Gordon C, Thompson A. Use of personal protective equipment during the COVID-19 pandemic. Br J Nurs 2020;29:748–52.
35. Center for Disease Control and Prevention. Strategies for optimizing the supply of facemasks. Centers for Disease Control and Prevention; 2020. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/ppe-strategy/face-masks.html [Accessed 27 Mar 2020].
36. Colorado Department of Public Health & Environment. Interim recommendations to optimize the supply of personal protective equipment for healthcare personnel: COVID-19 response; 2020.
37. Janssen L, Zhuang Z, Shaffer R. Criteria for the collection of useful respirator performance data in the workplace. J Occup Environ Hyg 2014;11:218–26.
38. Radonovich Jr. LJ, Cheng J, Shenal BV, Hodgson M, Bender BS. Respirator tolerance in health care workers. J Am Med Assoc 2009;301:36–8.
39. WHO. Advice on the use of masks in the community, during home care and in healthcare settings in the context of the novel coronavirus (2019-nCoV) outbreak: interim guidance, 29 January 2020. World Health Organization, Geneva; 2020. Contract No.: WHO/nCov/IPC_Masks/2020.1.
40. Bauchner H, Fontanarosa PB, Livingston EH. Conserving supply of personal protective equipment-a call for ideas. J Am Med Assoc 2020;323:1911.
41. Virginia Department of Health. Optimization strategies for Personal Protective Equipment (PPE) in Long-Term Care Facilities (LTCFs). Virgina Department of Health; 2020.
42. Singh Z, Bhalwar R, Jayara J, Tilak V. An introduction to essentials of bio-medical waste management. Med J Armed Forces India 2001;57:3.
43. Manzoor J, Sharma M. Impact of biomedical waste on environment and human health. Env Claims J 2019;31:311–34.
44. Rabeie OL, Miranzadeh MB, Fallah SH, Dehqan S, Moulana Z, Amouei A, et al. Determination of hospital waste composition and management in Amol city, Iran. Health Scope 2012;1:127–31.
45. Ferronato N, Torretta V. Waste mismanagement in developing countries: a review of global issues. Int J Environ Res Public Health 2019;16:1–28.
46. Di Bella V, Alli M, Vaccari M. Constraints to healthcare waste treatment in low-income countries – a case study from Somaliland. Waste Manag Res 2012;30:44.
47. Di Maria F, Lovat E, Caniato M. Waste management in developed and developing countries: the case study of Umbria (Italy) and the West Bank (Palestine). Multidiscip J Waste Resour Residues 2018;03:171–80.
48. Tomita A, Cuadros D, Burns J, Frank Tanser F, Slotow R. Exposure to waste sites and their impact on health: a panel and geospatial analysis of nationally representative data from South Africa, 2008–2015. Lancet 2020;4:E223–34.
49. Caniato M, Tudor T, Vaccari M. International governance structures for health-care waste management: a systematic review of scientific literature. J Environ Manag 2015;153:93–107.
50. Hangulu L, Akintola O. Health care waste management in community-based care: experiences of community health workers in low resource communities in South Africa. BMC Publ Health 2017;17:448.
51. Wiedinmyer C, Yokelson RJ, Gullett BK. Global emissions of trace gases, particulate matter, and hazardous air pollutants from open burning of domestic waste. Environ Sci Technol 2014;48:9523–30.
52. Vongdala N, Tran HD, Xuan TD, Teschke R, Khanh TD. Heavy metal accumulation in water, soil, and plants of municipal solid waste landfill in Vientiane, Laos. Int J Environ Res Public Health 2018;16:22.
53. Kwikiriza S, Stewart AG, Mutahunga B, Dobson AE, Wilkinson E. A whole systems approach to hospital waste management in rural Uganda. Front Public Health 2019;7:1–9.
54. Mmereki D, Baldwin A, Hong L, Li B. The management of hazardous waste in developing countries. https://www.intechopen.com/books; 2016.
55. Zafar S. Medical waste management in developing countries. Waste Manag 2020;9:351–8.
56. Abor PA, Bouwer A. Medical waste management practices in a Southern African hospital. Int J Health Care Qual Assur 2008;21:356–64.
57. Franka E, El-Zoka AH, Hussein AH, Elbakosh MM, Arafa AK, Ghenghesh KS. Hepatitis B virus and hepatitis C virus in medical waste handlers in Tripoli, Libya. J Hosp Infect 2009;72:258–61.
58. Padmanabhan KK, Barik D. Health hazards of medical waste and its disposal. Energy from toxic organic waste for heat and power generation; 2019:99–118 pp.
59. Wilson DC, Velis CA. Waste management – still a global challenge in the 21st century: an evidence-based call for action. Waste Manag Res 2015;33:1049–51.
60. Sawadogo M, Tchini T, Sidibé S, Kpai N, Tankoano I. Cleaner production in Burkina Faso: case study of fuel briquettes made from cashew industry waste. J Clean Prod 2018;195:9.
61. Sadef Y, Nizami AS, Batool SA, Chaudary MN, Ouda OKM, Asam ZZ, et al. Waste-to-energy and recycling value for developing integrated solid waste management plan in Lahore. Energ Source Part B 2016;11:569–79.
62. Hettiarachchi H, Meegoda JN, Ryu S. Organic waste buyback as a viable method to enhance sustainable municipal solid waste management in developing countries. Int J Environ Res Public Health 2018;15:2483.
63. Arab M, Baghbani RA, Tajvar M, Pourreza A, Omrani G, Mahmoudi M. Report: the assessment of hospital waste

management: a case study in Tehran. Waste Manag Res 2008; 26:304–8.
64. Mohee R. Medical wastes characterisation in healthcare institutions in Mauritius. Waste Manag 2005;25:575–81.
65. Taghipour H, Mosaferi M. The challenge of medical waste management: a case study in northwest Iran-Tabriz. Waste Manag Res 2009;27:328–35.
66. Patwary MA, O'Hare WT, Sarker MH. An illicit economy: scavenging and recycling of medical waste. J Environ Manag 2011; 92:2900–6.
67. South Africa National Standard. SANS 10248-3 Management of health care waste. SABS Standards Division, Pretoria, South Africa; 2011.
68. Al Raisi S, Sulaiman H, Suliman F, Abdallah O. Assessment of heavy metals in leachate of an unlined landfill in the Sultanate of Oman. Int J Environ Sci Dev 2014;5:60–3.
69. Green AES, Wagner JC. Toxic products of medical waste incineration. In: Green AES, editor. Medical waste incineration and pollution prevention. Boston: Springer; 1992:1–36 pp.
70. Singh S, Prakash V. Toxic environmental releases from medical waste incineration: a review. Environ Monit Assess 2007;132: 67–81.
71. Sharma R, Sharma M, Sharma R, Sharma V. The impact of incinerators on human health and environment. Rev Environ Health 2013;28:67–72.
72. Gautam V, Thapar R, Sharma M. Biomedical waste management: incineration vs. environmental safety. Indian J Med Microbiol 2010;28:191–2.
73. Heera S, Rajor A. Bacterial treatment and metal characterization of biomedical waste ash. J Waste Manag 2014;2014:1–6.
74. Auta T, Morenikeji O. Heavy metal concentrations around a hospital incinerator and a municipal dumpsite in Ibadan City, South-West Nigeria. J Appl Sci Environ Manag 2013;17: 419–24.
75. Ali SM, Pervaiz A, Afzal B, Hamid N, Yasmin A. Open dumping of municipal solid waste and its hazardous impacts on soil and vegetation diversity at waste dumping sites of Islamabad city. J King Saud Univ Sci 2014;26:59–65.
76. Demie G, Degefa H. Heavy metal pollution of soil around solid waste dumping sites and its impact on adjacent community: the case of Shashemane Open Landfill, Ethiopia. J Environ Earth Sci 2015;5:9.
77. Javied S, Tufail M, Khalid S. Heavy metal pollution from medical waste incineration at Islamabad and Rawalpindi, Pakistan. Microchem J 2008;90:77–81.
78. Zhao L, Zhang FS, Wang K, Zhu J. Chemical properties of heavy metals in typical hospital waste incinerator ashes in China. Waste Manag 2009;29:1114–21.
79. Karthikeyan S, Balasubramanian R, Iouri K. Particulate air pollution from bushfires: human exposure and possible health effects. J Toxicol Environ Health 2006;69:1895–908.
80. Vimercati L, Baldassarre A, Gatti MF, De Maria L, Caputi A, Dirodi AA, et al. Respiratory health in waste collection and disposal workers. Int J Environ Res Publ Health 2016;13:631.
81. Marceta M, Nadj I. Effect of medical waste on health of population and environment in the Republic of Serbia. Res Rev Dep Geogr Tour Hotel Manag 2018;47:18.
82. Kuchibanda K, Mayo AW. Public health risks from mismanagement of healthcare wastes in Shinyanga Municipality Health Facilities, Tanzania. Sci World J 2015;2015:981756.
83. Patil GV, Pokhrel K. Biomedical solid waste management in an Indian hospital: a case study. Waste Manag 2005;25:592–9.
84. Bokhoree C, Beeharry Y, Makoondlall-Chadee T, Doobah T, Soomary N. Assessment of environmental and health risks associated with the management of medical waste in Mauritius. APCBEE Procedia 2014;9:36–41.
85. Lekwot V, Nunyi B, Ifeanyi E, Okafor CI, Adamu B. Public health implication of improper hospital waste disposal in Zonkwa district of Zangon-kataf local government area, Kaduna state. J Res Environ Sci Toxicol 2012;1:6.
86. Maseko Q. Critical evaluation of medical waste management policies, processes and practices in selected rural hospitals in the Eastern Cape; 2014.
87. Harhay MO, Halpern SD, Harhay JS, Olliaro PL. Health care waste management: a neglected and growing public health problem worldwide. Trop Med Int Health 2009;14:1414–7.
88. WHO. World health statistics: monitoring health for sustainable development goals; 2018.
89. Sharma HB, Vanapalli KR, Cheela VS, Ranjan VP, Jaglan AK, Dubey B, et al. Challenges, opportunities, and innovations for effective solid waste management during and post COVID-19 pandemic. Resour Conserv Recycl 2020;162:105052.
90. Santappa M, Kumar V. RE: Hospital Waste Management Committee and salient features of biomedical wastes. In: Proceedings of southern regional conference on biomedical waste management organized by Tamil Nadu Pollution Control Board, Chennai, India; 2002.
91. Giusti L. A review of waste management practices and their impact on human health. Waste Manag 2009;29:2227–39.
92. Ephraim PI, Ita A, Eusebius IO. Investigation of soils affected by burnt hospital wastes in Nigeria using PIXE. Springerplus 2013; 2:208.
93. Rushton L. Health hazards and waste management. Br Med Bull 2003;68:183–97.
94. Mathur P, Patan S, Shobhawat S. Need of biomedical waste management system in hospitals – an emerging issue – a review. Curr World Environ 2012;7:7.
95. Tripathi A, Tyagi VK, Vivekanand V, Bose P, Suthar S. Challenges, opportunities and progress in solid waste management during COVID-19 pandemic. Case Stud Chem Environ Eng 2020;2:100060.
96. Ezirim I, Agbo F. Role of national policy in improving health care waste management in Nigeria. J Health Pollut 2018;8:180913.
97. Deva L, Shah C, Yagnik B, Solanki H, George L. Principles and practices of biomedical waste management: a case study of selected hospitals of Ahmedabad city. Univ Rev 2019;8:451–9.
98. Mara D, Lane J, Scott B, Trouba D. Sanitation and health. PLoS Med 2010;7:e1000363.
99. Ali M, Wang W, Chaudhry N, Geng Y. Hospital waste management in developing countries: a mini review. Waste Manag Res 2017;35:581–92.
100. Vumase B. An evaluation of operational and administrative procedures for health care waste management in Public District Hospitals of South Africa; 2009:40 p.
101. WHO. World Health Organization Management of solid healthcare waste at primary healthcare centres (a decision-making guide). Geneva, Switzerland; 2005:36–7 pp.
102. Gabela S. Health care waste management in Public Clinics in the Ilembe District: a situational analysis and intervention strategy; 2007.

103. Yawson P. Assessment of solid waste management in healthcare facilities in the Offinso Municipality; 2014.
104. World Bank. World Bank. Guide to HCW management 2002 [Online]; 2002. Available from: http://www.essentialaction.org [Accessed 02 Oct 2017].
105. Hossain MS, Santhanam A, Nik Norulaini NA, Omar AK. Clinical solid waste management practices and its impact on human health and environment – a review. Waste Manag 2011;31: 754–66.
106. Nemathaga F, Maringa S, Chimuka L. Hospital solid waste management practices in Limpopo Province, South Africa: a case study of two hospitals. Waste Manag 2008;28:1236–45.
107. Jang Y, Lee C, Yoon O, Kim H. Medical waste management in Korea. J Environ Manag 2006;80:9.
108. Windfeld ES, Brooks MS. Medical waste management – a review. J Environ Manag 2015;163:98–108.
109. Wang J, Shen J, Ye D, Yan X, Zhang Y, Yang W, et al. Disinfection technology of hospital wastes and wastewater: suggestions for disinfection strategy during coronavirus disease 2019 (COVID-19) pandemic in China. Environ Pollut 2020;262:114665.
110. Belhadi A, Kamble SS, Khan SAR, Touriki FE, Kumar MD. Infectious waste management strategy during COVID-19 pandemic in Africa: an integrated decision-making framework for selecting sustainable technologies. Environ Manag 2020;66: 1085–104.
111. Singh N, Tang Y, Zhang Z, Zheng C. COVID-19 waste management: effective and successful measures in Wuhan, China. Resour Conserv Recycl 2020;163:105071.
112. Kindhauser MK. Communicable diseases 2002: global defence against the infectious disease threat. Geneva: World Health Organization; 2003.
113. WHO. Infection prevention and control of epidemic and pandemic-prone acute respiratory infection in health care; 2014.
114. Hegde V, Kulkarni R, Ajantha G. Biomedical waste management. J Oral Maxillofac Surg 2007;11:5–9.
115. Pasupathi P, Sindhu S, Ponnusha B, Ambika A. Biomedical waste management for health care industry: a review. Int J Biol Med Res 2011;2:14.
116. Rajor A, Xaxa M, Mehta R. An overview on characterization, utilization and leachate analysis of biomedical waste incinerator ash. J Environ Manag 2012;108:36–41.
117. Prüss-Üstün A, Giroult E, Rushbrook P, World Health Organization. In: Prüss A, Giroult E, Rushbrook P, editors. Safe management of wastes from health-care activities. Geneva: World Health Organization; 1999.
118. Farzadkia M, Moradi A, Mohammadi M. Hospital waste management status in Iran: a case study in the teaching hospitals of Iran University of Medical Sciences. Waste Manag Res 2009;27:5.
119. WHO. Unsafe injection practices and transmission of blood borne pathogens. Bull World Health Org 1999;77:787–819.
120. Umscheid CA, Mitchell MD, Doshi JA, Agarwal R, Williams K, Brennan PJ. Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality and costs. Infect Control Hosp Epidemiol 2011;32:101–14.
121. Rosenthal VD, Maki DG, Mehta Y, Leblebicioglu H, Memish ZA, Al-Mousa HH, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 43 countries for 2007–2012. Device-associated module. Am J Infect Control 2014;42:942–56.
122. Yallew WW, Kumie A, Yehuala FM. Point prevalence of hospital-acquired infections in two teaching hospitals of Amhara region in Ethiopia. Drug Healthc Patient Saf 2016;8:71–6.
123. Pandey S, Dwivedi A. Nosocomial infections through hospital waste. Int J Waste Resour 2016;6:1–3.
124. Ebola Waste Management. Ebola waste management guide; 2014. Available from: https://www.in.gov/isdh/files.
125. WHO. Water, sanitation, hygiene, and waste management for the COVID-19 virus: interim guidance coronavirus disease (COVID-19) advice for the public. World Health Organization, Geneva; 2020. Available from: https://www.who.int/emergencies/diseases/novelcoronavirus-2019/advice-for-public [Accessed 3 Mar 2020].
126. WHO. Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected: interim guidance, 25 January 2020. World Health Organization, Geneva; 2020. Available from: https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-whennovel-coronavirus-(ncov)-infection-is-suspected-20200125 [Accessed 3 Mar 2020].
127. WHO. Sanitation safety planning: manual for safe use and disposal of wastewater, greywater and excreta. World Health Organization, Geneva; 2015. Available from: https://apps.who.int/iris/handle/10665/171753 [Accessed 3 Mar 2020].
128. Kalpana V, Sathya D, Prabhu D, Vinodhini S, Devirajeswari V. Biomedical waste and its management. J Chem Pharm Res 2016; 8:670–6.
129. Ron EZ. Bacterial stress response. In: Rosenberg E, DeLong EF, Lory S, Stackebrandt E, Thompson F, editors. The prokaryotes: prokaryotic physiology and biochemistry. Berlin, Heidelberg: Springer Berlin Heidelberg; 2013:589–603 pp.
130. Yamaguchi N, Park J, Kodama M, Ichijo T, Baba T, Nasu M. Changes in the airborne bacterial community in outdoor environments following Asian dust events. Microbes Environ 2014;29:82–8.
131. Ikeda S, Sasaki K, Okubo T, Yamashita A, Terasawa K, Bao Z, et al. Low nitrogen fertilization adapts rice root microbiome to low nutrient environment by changing biogeochemical functions. Microbes Environ 2014;29:50–9.
132. Storz G, Hengge R. Bacterial stress responses, 2nd ed. Washington, DC: ASM Press; 2011.
133. Kulkarni G, Wu CH, Newman DK. The general stress response factor EcfG regulates expression of the C-2 hopanoid methylase HpnP in *Rhodopseudomonas palustris* TIE-1. J Bacteriol 2013; 195:2490–8.
134. Müller S, Strack SN, Ryan SE, Kearns DB, Kirby JR. Predation by *Myxococcus xanthus* induces *Bacillus subtilis* to form spore-filled megastructures. Appl Environ Microbiol 2015;81:203–10.
135. Hoehler TM, Jørgensen BB. Microbial life under extreme energy limitation. Nat Rev Microbiol 2013;11:83–94.
136. Dewi Puspita I, Uehara M, Katayama T, Kikuchi Y, Kitagawa W, Kamagata Y, et al. Resuscitation promoting factor (Rpf) from *Tomitella biformata* AHU 1821(T) promotes growth and resuscitates non-dividing cells. Microbes Environ 2013;28: 58–64.
137. Puspita ID, Kitagawa W, Kamagata Y, Tanaka M, Nakatsu CH. Increase in bacterial colony formation from a permafrost ice wedge dosed with a *Tomitella biformata* recombinant resuscitation-promoting factor protein. Microbes Environ 2015; 30:151–6.

138. Oku S, Komatsu A, Nakashimada Y, Tajima T, Kato J. Identification of *Pseudomonas fluorescens* chemotaxis sensory proteins for malate, succinate, and fumarate, and their involvement in root colonization. Microbes Environ 2014;29: 413–9.
139. Ramisetty BC, Natarajan B, Santhosh RS. mazEF-mediated programmed cell death in bacteria: "what is this?" Crit Rev Microbiol 2015;41:89–100.
140. Hatfield GW, Hung SP, Baldi P. Differential analysis of DNA microarray gene expression data. Mol Microbiol 2003;47:871–7.
141. Neidhardt F, Phillips T, VanBogelen R, Smith M, Georgalis Y, Subramanian A. Identity of the B56.5 protein, the A-protein, and the groE gene product of *Escherichia coli*. J Bacteriol 1981;145:8.
142. Ishihama A. Functional modulation of *Escherichia coli* RNA polymerase. Annu Rev Microbiol 2000;54:499–518.
143. Burgess RR, Anthony L. How sigma docks to RNA polymerase and what sigma does. Curr Opin Microbiol 2001;4:126–31.
144. Narberhaus F, Obrist M, Führer F, Langklotz S. Degradation of cytoplasmic substrates by FtsH, a membrane-anchored protease with many talents. Res Microbiol 2009;160:652–9.
145. Vogel J, Luisi B. Hfq and its constellation of RNA. Nat Rev Microbiol 2011;9:11.
146. Storz G, Vogel J, Wassarman KM. Regulation by small RNAs in bacteria: expanding frontiers. Mol Cell 2011;43:880–91.
147. Caron M, Lafontaine D, Masse E. Small RNA-mediated regulation at the level of transcript stability. RNA Biol 2010;7:5.
148. Hengge R. Proteolysis of sigmaS (RpoS) and the general stress response in *Escherichia coli*. Res Microbiol 2009;160:667–76.
149. Shenhar Y, Rasouly A, Biran D, Ron EZ. Adaptation of *Escherichia coli* to elevated temperatures involves a change in stability of heat shock gene transcripts. Environ Microbiol 2009;11:2989–97.
150. Jenal U, Hengge-Aronis R. Regulation by proteolysis in bacterial cells. Curr Opin Microbiol 2003;6:163–72.
151. Podkaminski D, Vogel J. Small RNAs promote mRNA stability to activate the synthesis of virulence factors. Mol Microbiol 2010; 78:1327–31.
152. Gui M, Song W, Zhou H, Xu J, Chen S, Xiang Y, et al. Cryo-electron microscopy structures of the SARS-CoV spike glycoprotein reveal a prerequisite conformational state for receptor binding. Cell Res 2017;27:119–29.
153. Riddell S, Goldie S, Hill A, Eagles D, Drew TW. The effect of temperature on persistence of SARS-CoV-2 on common surfaces. Virol J 2020;17:145.
154. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8:420–2.
155. Wu YC, Chen CS, Chan YJ. Overview of the 2019 novel coronavirus (2019-nCoV): the pathogen of severe specific contagious pneumonia (SSCP). J Chin Med Assoc 2020;83:217–20.
156. Su S, Wong G, Shi W, Liu J, Lai ACK, Zhou J, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trends Microbiol 2016;24:490–502.
157. Perlman S, Netland J. Coronaviruses post-SARS: update on replication and pathogenesis. Nat Rev Microbiol 2009;7: 439–50.
158. Li X, Geng M, Peng Y, Meng L, Lu S. Molecular immune pathogenesis and diagnosis of COVID-19. J Pharm Anal 2020;10: 102–8.
159. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol 2015;1282:1–23.
160. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020;579:270–3.
161. Olaniyan OT, Dare A, Okotie GE, Adetunji CO, Ibitoye BO, Bamidele OJ, et al. Testis and blood-testis barrier in Covid-19 infestation: role of angiotensin-converting enzyme 2 in male infertility. J Basic Clin Physiol Pharmacol 2020;31:1–13.
162. Belouzard S, Chu VC, Whittaker GR. Activation of the SARS coronavirus spike protein via sequential proteolytic cleavage at two distinct sites. Proc Natl Acad Sci USA 2009;106:5871–6.
163. Kuba K, Imai Y, Ohto-Nakanishi T, Penninger JM. Trilogy of ACE2: a peptidase in the renin-angiotensin system, a SARS receptor, and a partner for amino acid transporters. Pharmacol Ther 2010; 128:119–28.
164. de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol 2016;14:523–34.
165. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
166. Li W, Moore MJ, Vasilieva N, Sui J, Wong SK, Berne MA, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature 2003;426:450–4.
167. Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. Semin Immunopathol 2017;39:529–39.