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Review

Viruses, coronaviruses and COVID-19: A note for non-virology specialists

Yakubu Egigogo Raji[1*], Yahaya Muhammad Sanusi[2] and Zamberi Bin Sekawi[3]

[1]Faculty of Natural and Applied Sciences, Ibrahim Badamasi Babangida University, Niger State, Nigeria.
[2]Department of Theriogenology and Animal Production, Faculty of Veterinary Medicine, Usmanu Danfodiyo University, Sokoto, Nigeria.
[3]Department of Medical Microbiology and Parasitology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Selangor, Malaysia.

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An outbreak of a respiratory disease with severe acute respiratory syndrome (SARS) – like manifestations emerged in late December 2019 in the Wuhan city of China. The causative agent of this disease was later identified to be a novel Coronavirus. Subsequently, the disease was named coronavirus disease 2019 (COVID-19) by the World Health Organisation and later declared as a pandemic. The outbreak of COVID-19 came with many misinformation and misconceptions about viruses and the COVID-19 disease. Questions have been asked by non - virologists and the general public about what viruses are. Some wondered if viruses are living organisms or not. While some asked how big viruses are or if all viruses and the COVID-19 virus is artificially created. Yet others attributed the outbreak to the new quantum leap in the electromagnet field; the latest 5G technology. There are also concerns raised about the new virus being a bioweapon or an act of biowarfare. These numerous questions needed to be clarified concisely with available scientific knowledge. Thus, this review is providing answers to the 10 frequently asked questions aimed at informing the non - virologist in the academic field and beyond.

Key words: Virus size, virus origin, giant viruses, synthetic viruses, SARS-Cov-2, bioweapon.

INTRODUCTION

Virology and viruses are an important and fascinating area of biology. The nature of viruses, their behaviour, diversity and complexity make the area of virology a bit difficult for many specialists to understand adequately. These include health personnel, teachers and other biologists who do not major in virology. These personnel often need to explain to people a lot about viruses. However, lack of adequate understanding of the subject matter constrains their ability to offer enough and convincing explanation to satisfy the ever-growing public curiosity about viruses.

The advent of COVID-19 has been an eye opener, it exposes how little people know about viruses and their mechanisms of action. It has attracted many conspiracy

*Corresponding author. E-mail: rajiegigogoy@ibbu.edu.ng. Tel: +2348028702332.

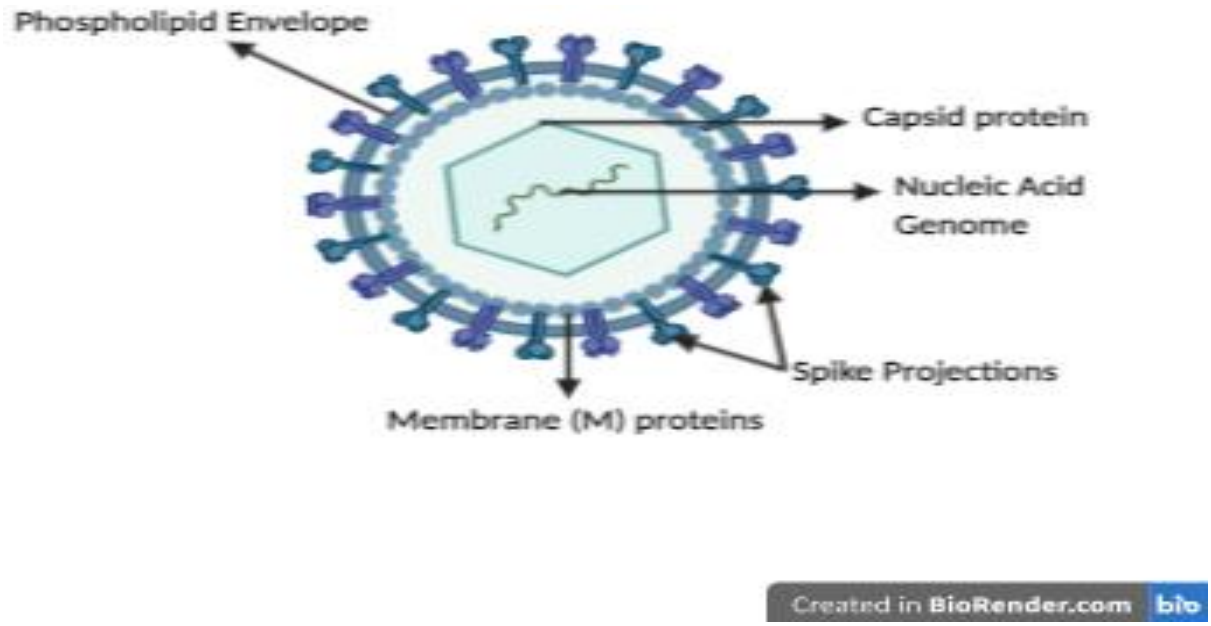

Figure 1. Schematic of a typical enveloped virus (BioRender.com: Generic Viral Life Cycle, 2020)

theories and misconceptions about viruses generally, and COVID-19 in particular. Researchers and healthcare professionals across the world have made several attempts to address some of these misconceptions (Okunlola et al., 2020; Khalid et al., 2020). However, many of these myths are yet to be fully addressed. Thus, now more than ever before is the time to empower the (unprofessional) personnel with suitable but simple enough information about viruses to adequately deal with current misinformation. This short (opinion) review aims to make information about viruses available to academics outside virology specialization and who may need the information but do not have the time for extensive study of virology now. The review answered a few questions regarding viruses and COVID-19; what has been established through scientific methods and what has not.

(1) Questions regarding what a virus is
(2) Questions regarding the origin of viruses
(3) Questions regarding whether viruses are living organisms or not
(4) Questions regarding the size of viruses
(5) Questions regarding viral replication process
(6) Questions regarding the difference between Coronavirus and COVID–19
(7) Questions regarding the available diagnostic kits for COVID -19 and whether they are produced only by China
(8) Questions regarding whether viruses in general and SARS-CoV-2 in particular are man-made
(9) Questions regarding the relationship between SARS-CoV-2 and biological warfare?
(10) Questions regarding the relationship between Electromagnetic waves (EMF) and virus epidemics.

VIRUSES WHAT ARE THEY?

A virus is an infectious agent (sub-microscopic) that can replicate only in living cells or organisms (obligate intracellular parasites). A virus can infect all forms of life (the three supper-kingdoms of life); bacteria, archaea, and eukaryotes (Sandaa and Bratbak, 2018). An infectious virus particle is called a virion; it consists of a genetic material (viral genome) which is enclosed by a protein coat (outer shell) (Chaitanya, 2019). The protein shell is known as capsid; in some viruses, a lipid membrane called an envelope surrounds the capsid (Figure 1). Therefore, viruses can be enveloped viruses (with capsid enclosed by a lipid membrane) or non-enveloped viruses. The viral genome can be DNA or RNA (nucleic acids) and varies in length (the number of DNA or RNA molecules). The viral genome can be double or single-stranded and circular or linear. The viral genetic material (DNA or RNA) encodes the protein(s) that surrounds it, thus conferring protection to the genetic material (Chaitanya, 2019).

THE ORIGIN OF VIRUSES

The origin of viruses had been, for a long time, a topic of debate, because viruses do not form fossils. The debate on viral origin is yet to be resolved completely thus the concept of viral origin is still under re-evaluation by virologists (Krupovic et al., 2019). Scientists believed that viruses have multiple evolutionary origins (Krupovic et al., 2019). The current stand is that viruses are ancient particles whose origin pre-dates the divergence of life into

the three domains (super-kingdoms) (Thomas, 2019). However, earlier, Paleovirologists have proposed three major theories to explain the origin of viruses; (i) Virus–first hypothesis or co–evolution theory (Mughal et al., 2020). This theory proposes viruses as primitive precursors of a cellular system. This simply means viruses are the earliest phase of life's evolution, evolving from the complex molecules of nucleic acids and proteins. The principle assumes that viruses existed first before cells as self-replicating particles. (ii) Degeneracy hypothesis (Mughal et al., 2020). This hypothesis proposes that viruses originate as small parasitic cells that depend on larger cells for survival, and due to extreme parasitism over a long time, these cells lost those genes that are not required for parasitic life (degenerate). As a result, they became obligate parasites that are not capable of survival outside cells. This hypothesis is also known as the regressive or reduction hypothesis. (iii) Escape hypothesis (Mughal et al., 2020). This hypothesis suggests a cellular origin of viruses. According to this theory, viruses emerged from genes of larger organisms as break–away bits of RNA or DNA due to cell destruction (damage) of larger cellular systems. They acquired the ability to move from one gene to another, as mobile genetic elements, thereby surviving as minimal parasitic replicons (Domingo, 2020). This hypothesis is also known as cellular origin hypothesis or Vagrancy hypothesis. Each of the aforementioned hypotheses has its limitations, which makes it difficult to single out one that is correct. However, viruses might have evolved from different mechanisms. The mechanism of virus evolution might be any one of the above, a combination of two or more of them (Mughal et al., 2020) or others yet to be discovered.

VIRUSES, ARE THEY LIVING OR NOT?

Another age-long debate, among scientist, about viruses is whether they are living organisms or not. Some biologists believe that viruses are organisms at the edge of life while some consider them as non-living (Kaján et al., 2020; Shwetha, 2018). The debate is anchored on what it means to be alive. Is life about survival, growth, and reproduction? Is cell a prerequisite for life? To that end, some biologists declared that viruses are non-living because they lack cell and are not capable of independent survival, growth, and reproduction. This line of thinking became official in the year 2000 following the declaration by the International Committee on Taxonomy of Viruses (ICTV) that "viruses are not living organisms" (Zimmer, 2015). However, as years went by and with more discoveries about viruses, some scientists questioned this declaration, while some rejected it outrightly (Claverie, 2006). These group of virologists believed that classifying viruses as non–living is an old–fashioned notion. Asserting that discoveries have overtaken this old rule. They said viruses have some characteristics of life. Viruses have genetic materials (genes), reproduce (replicate) and evolve through natural selection. In addition, viruses such as giant viruses can expand their genome to acquire the ability for independent metabolism, growth, survival, and reproduction. Giant viruses also have viral factories' that act as cells (Mougari et al., 2019). As a result, some of these Microbiologists have proposed reclassification of living organisms into two groups; ribosome-encoding organisms (Eukaryotes, Archaea and Bacteria) and capsid-encoding organisms (Viruses). They, therefore, defined viruses as capsid-encoding organism that are composed of proteins and nucleic acids, capable of self-assembling in a nucleocapsid and uses a ribosome-encoding organism for the completion of its life cycle (Raoult and Forterre, 2008).

THE SIZE OF VIRUSES

One of the most remarkable features of viruses is their size. It was the uniqueness of their size that led to their discovery; viruses were able to be filtered through filters used for pathogenic bacterial filtration. Viruses are largely sub-microscopic, and their size was elucidated with the help of electron and fluorescence microscopy. There are two aspects when it comes to understanding virus size; the viral (structural) size and the genome (length of nucleic acid) size. The structural size of viruses is measured in nanometres (nm); 1×10^{-9} or 1 billionth of a metre that is, 1 billion nanometres equal 1 m. So, the size of most viruses is within the range of 5- 300 nm. However, recently discovered giant viruses are in the diameter range of 500- 1000 nm (Koonin and Yutin, 2018). Virus genome size is measured either in terms of the number of bases in the genome or their mass. The virus genome size is in the range of a few thousand bases to several hundred kilobases (O'Carroll and Rein, 2016). A few examples of viruses are listed in Table 1.

Replication of viruses

Viral replication is the process of forming new viruses. As obligate parasites, viruses need cellular systems to replicate. To facilitate understanding, the viral replication process can be explained under the following steps; adhesion, entry, uncoating, replication, assembly, and release. The process explained here is the general rule that applies to many viruses but there are exceptions. Adsorption (adhesion); a virus attaches to a susceptible host's cell membrane at a specific position known as the receptor site using the viral attachment proteins. Entry; following attachment, the virus is engulfed into the cytoplasm of the cell through the process known as endocytosis. Uncoating; once the virus gets inside the

Table 1. Different viruses, size of their genomes and their genetic materials.

S/N	Virus name	Virus size (diameter) (nm)	Genome size	Type of genetic material
1	Poliovirus	30	7.5 Kb	RNA
2	HBV	42	3.2-3.3 Kbp	DNA
3	HCV	50	9.6- 12.3 Kb	RNA
4	HIV	120	9.2- 9.6 Kb	RNA
5	Measles virus	150	16 Kb	RNA
6	Coronaviruses	80-200	26 – 33 Kb	RNA
7	Paramyxoviruses	150 -300	13 – 19 Kb	RNA
8	Ebola virus	80 × 970	18 -19 Kb	RNA
9	Mimi virus	500	1.2 Mbp	DNA
10	Pandora virus	500 × 1000	2.8Mbp	DNA

HBV, Hepatitis B Virus; HCV, Hepatitis C Virus; HIV, Human Immunodeficiency Virus; RNA, Ribonucleic acid; DNA, Deoxyribonucleic acid; Kbp, Kilo base pairs; Kb, Kilo bases; Mbp, Mega base pairs.

cell, the viral genome is released by degradation of the capsid. Replication; this implies making a copy of the viral genome and the mechanism is dependent on genome type. For viruses with a DNA genome, the host cell's machinery is used to make a copy of the DNA, from the DNA a messenger RNA (mRNA) copy is made in a process called transcription. The mRNA is then used (translation process) for protein synthesis to make new viral capsids. While for RNA viruses, copies of viral (genomic) RNA and mRNA are synthesised. The mRNA is then translated to viral enzymes and capsid proteins. Assembly; the viral particles (viral genome and capsid proteins) are in turn packaged to form new virions. Release; this is the last step of the viral replication process and it is achieved through different means depending on the type of virus. New viruses can be released into the extracellular environment from the cell by any of these processes, apoptosis (programmed cell death), cell lysis (bursting) or budding. The newly released viruses then infect new cells and the cycle continues (Virus Replication, in Fenner's Veterinary Virology (Fifth Edition), 2017) (Figure 2).

CORONAVIRUS AND COVID – 19, WHAT IS THE DIFFERENCE?

Understanding the classification of viruses will assist in answering this question. There are two major classification systems for viruses; the ICTV and Baltimore classification systems. The ICTV classification system of viruses is similar to the classification of other cellular organisms. The ICTV system classified viruses into 15 levels starting from Realm to species. In between these levels are the Family and Genus levels. So, viruses are grouped under these levels as such viruses have 'Family', 'Genus' and 'Species' names. Names of viruses thus end with affixes 'viridae' and 'virus' for family and genus respectively. Therefore, 'Coronavirus' is a genus name of viruses under the 'Coronaviridae' family. The viruses under this family are of two distinguished genera (plural of genus) – the Coronavirus (Alpha, Beta and Gamma) that infects both humans and animals and the 'Torovirus' that infects mostly animals. The Coronavirus was discovered in 1931 and named Corona due to its spiky crown – like architecture or reminiscent of the solar corona as revealed by electron microscopy (Lalchhandama, 2020) (Figure 3). Coronaviruses are large RNA viruses with genome size ranging between 27-33 kilobases and a structural diameter of 80 – 200nm. Notable Human Coronaviruses include Human Coronavirus 229E ($HCoV\text{-}_{229}E$), $HCoV\text{-}OC_{43}$, $HCoV\text{-}HKU_1$, Severe Acute Respiratory Syndrome Coronaviruses (SARS-CoVs) and Middle Eastern Respiratory Syndrome Coronavirus (MERS-Cov). The HCoVs species usually cause common cold in humans second to Rhinoviruses with global distribution (Burrell et al., 2017; Shah et al., 2020). Common symptoms include mild fever, sore throat, rhinitis, and cough. While the SARS-CoV and MERS-CoV are known for causing severe acute respiratory diseases (Burrell et al., 2017; Shah et al., 2020). So, in late December 2019, a new SARS – like disease emerged in Wuhan City of Hubei province in China. The causative agent of this respiratory disease was later identified to be a novel Coronavirus (nCoV) after its genome was sequenced. The nCoV was not among the previously known Coronaviruses causing human infection. The virus was subsequently named Severe Acute Respiratory Syndrome Coronavirus – 2 (SARS-CoV-2) by the ICTV. On the 11th of February 2020, the World Health Organisation (WHO) named the disease caused by the SARS-CoV-2 as Coronavirus disease-2019 (COVID-19) (Vashist, 2020). Therefore, COVID-19 is the respiratory disease caused by the Coronavirus SARS-CoV-2.

Diagnostic assays for COVID -19 and where they are produced

There are many available diagnostic assays for COVID-19

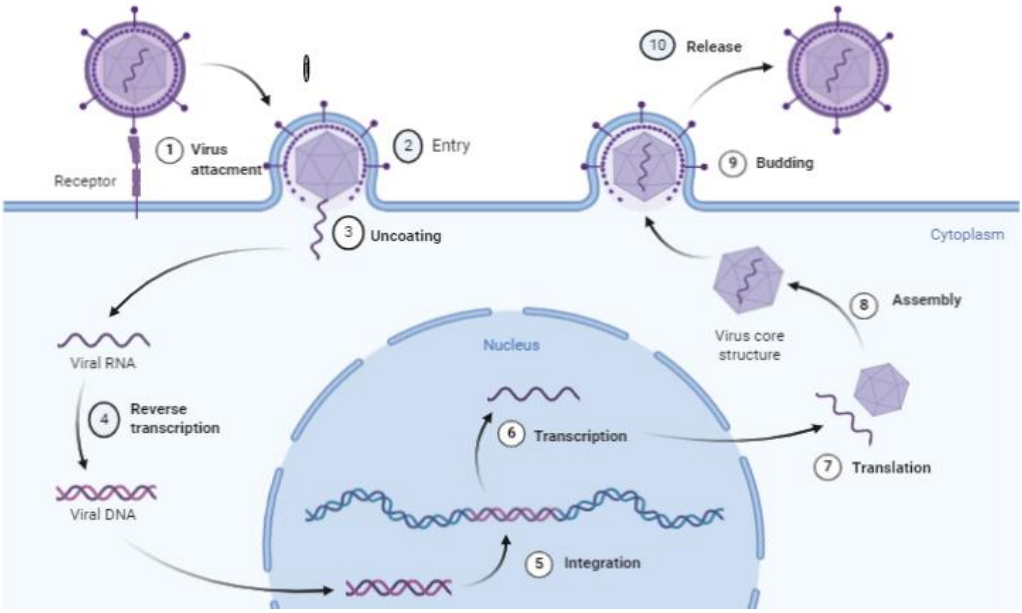

Figure 2. Diagram of viral replication process (BioRender.com: Coronavirus Replication Cycle, 2020a)

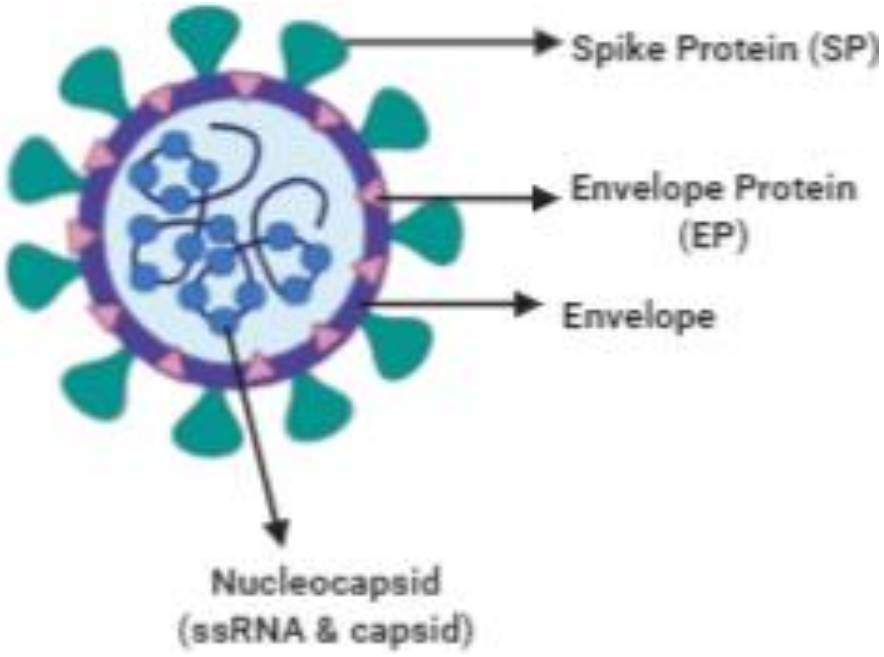

Figure 3. Diagram of a typical Coronavirus (BioRendercom: Coronavirus Replication Cycle, 2020b).

which are either molecular or serological based. Serological methods are those that detect antibodies (IgM and IgG) against SARS-CoV-2 while molecular methods tend to detect viral RNA. However, it is only the molecular method that is recommended by the world health organisation (WHO) as a confirmatory test for COVID-19 (WHO, 2020). It is also worth mentioning that molecular (PCR) methods have been used for the diagnosis of respiratory viruses including other HCoVs with remarkable outcomes (Etemadi et al., 2019). Thus,

Table 2. List of selected different manufacturers of real-time RT-PCR Kits for COVID-19 diagnosis.

S/N	Manufacturer	Viral gene target
1	China, CDC	ORF1b, N
2	India, TruPCR	E, RdRP, N
3	Thailand, NIH	N
4	Japan, NIID	SP, Pancorona & Multiple targets
5	Hong Kong SAR, HKU	ORF1b-nsp14, N
6	Germany, Charité	RdRP, E, N
7	France, IIP	RdRP (2 targets)
8	USA, CDC	N gene (3 targets), RP

CDC; centre for disease control and prevention, E; envelop protein, HKU; the university of Hong Kong, IIP; institut pasteur paris, N; nucleocapsid protein, NIH; national institute of health, NIID; national institute of infectious disease, nsp; non-structural protein, ORF; open reading frame, RdRP; RNA dependent RNA polymerase, SP; spike protein, USA; United States of America.

the confirmatory test approved for COVID-19 is based on the real–time reverse transcriptase polymerase chain reaction (real–time RT-PCR). Real–time RT-PCR for COVID-19 diagnosis is a quantitative test that amplifies targeted viral genes for RNA virus detection. Numerous real–time RT-PCR kits developed by different countries, institutions, and companies are available (FIND, 2020). A few examples of the available kits are given in Table 2.

IS SARS-COV-2 AND OTHER VIRUSES MAN-MADE?

To answer this question, we need to understand the magnitude of virus diversity. Viruses are the most numerous life forms on planet earth. Viruses are found in virtually every single ecosystem on earth. Viruses are present in oceans, lakes, rivers, under the Antarctic ice and in other life forms (Zimmer, 2015). To estimate the numbers of viruses in existence, “try multiplying a billion by a billion then, multiply the product by ten trillion”. The result: 10 to the 31st power “is the mind boggling–number estimate of how many individual viral particles are estimated to populate the planet” (Bruce, 2020). Viruses are also diverse in their composition; they are either RNA or DNA, single stranded or double stranded, linear or circular, and enveloped or naked (non-enveloped). Viruses are of different sizes and structures, different hosts range, mode of transmission and mechanism of replication. Scientists can indeed manipulate microbes and studies have shown how viruses can be chemically synthesised without an existing template. So, improvement in biotechnology and synthetic virology has made it possible to modify and artificially create viruses (Thiel, 2018). Certainly, the process involved in chemical synthesis of viruses is not perfect but successful infectious viruses have been produced using the technique (Thiel, 2018). However, the same advancement in biotechnology has means of verifying modified or artificially created viruses. Comparative genome analysis is a means by which gene sequences are examined and compared between organisms. With comparative genomics, unique and conserved genes among species are identified. This technique can be used to scientifically determine the origin of different organisms. So, to establish whether SARS-CoV-2 was artificially created, Kristian Andersen and colleagues conducted a comparative analysis of available Coronavirus genomic data. Their analysis revealed that SARS-CoV-2 was neither artificially constructed nor was it purposefully modified (Andersen et al., 2020). At this stage, considering the innumerability, diversity and architectural complexity of viruses, it is only rational to say that though it is true that viruses can be man–made, but all the viruses cannot be man-made. For SARS-CoV-2, to date there is no proven evidence that the virus is man-made but it has been proven that the virus is not man–made.

SARS-COV-2 AND BIOLOGICAL WARFARE

To answer this question effectively, there is a need for basic knowledge of biological weapons, the history of biological warfare and biotechnology. Biological warfare (BW), is the use of pathogenic agents or microbes to kill humans, animals or plants (Rao, 2011; Oliveira et al., 2020). The agents that can be used in BW include bacteria, fungi, viruses, insects or biological toxins (Berger et al., 2016; Pal et al., 2017). The BW agents are known as bio–agents or bio–weapons and can be used during war or for bioterrorism. Bio-weapons can be naturally occurring highly infectious agents or artificially created (Berger et al., 2016; Pal et al., 2017). History has shown evidence of BW right from antiquity to the modern ages. Arrowheads, swords, and wells have been poisoned with biological toxins during wars in ancient times. Also, ancient means of BW include sending plague

victims or their dead bodies into the enemy's territories to cause plague epidemics or the use of beasts to attack the opponent (Rao, 2011; Oliveira et al., 2020). In modern history, there have been reports of attempted or alleged use of smallpox by the British army on Native Americans and the Aboriginal population in the USA and Australia respectively (Carus, 2017). During world war II, nations such as the USA, Russia, UK, Canada, Japan, and France established BW centres and successfully weaponised different highly infectious agents for war purposes (Rao, 2011; Carus, 2017). Although some countries never had to use these weapons, some did with some level of success. Japan conducted human experiments of these weapons on prisoners and launched it against Chinese soldiers and civilians (Rao, 2011). Biosecurity concerns were heightened even more with the advent of novel advancements in biotechnology. Advancement in biotechnology has enabled Scientists to manipulate the genetic materials of microbes for different purposes. Improved understanding of genomics and genetic engineering has led to the development of novel vaccines, drugs, modified foods, and beverages. Newer technologies for genome editing such as the Clustered, Regularly Interspaced, Short Palindromic Repeat (CRISPR) system, has made manipulation of micro-organisms even faster and easier (Adli, 2018). Therefore, there is the potential of using the knowledge of these technologies to enhance pathogens for BW. Although natural pathogens can indeed be used for BW, it is equally possible to enhance the efficiency of these pathogens using genetic engineering (Berger et al., 2016; Pal et al., 2017). Also, as stated above, viruses can be chemically synthesised (Thiel, 2018). However, for any pathogen to qualify as an ideal bioweapon it must be highly infectious, lethal, efficiently transmissible, environmentally robust, and massively produced with sustained pathogenicity (Clark and Pazdernik, 2016). Additionally, treatment or vaccine for the agent must have been established by the developers of the bio-agent for their protection. These features thus, make a bioweapon or BW a highly dangerous concept with unimaginable consequences. In view of the dare consequences of Bio-agents and BW, a proposal for banning of bioweapons was presented to the United Nations (UN) by selected countries. Accordingly, in 1969, the then US president Richard Nixon made a statement that bioagents are "repugnant to the conscience of mankind" and it has the potential to "cause massive, unpredictable and potential uncontrollable consequences" (Rao, 2011). This proclamation by Nixon, led to the termination of the US BW programme and the destruction of all its existing bioweapons. Accordingly, the proposal presented to the UN led to the Biological Weapon Convention (BWC); a treaty that came into force in 1975 and so far, over 180 nations have either ratified or acceded to it (Geneva, 2020). The BWC bans the development, creation and stockpiling of all forms of bioweapons and provided for the destruction of the existing ones (Rao, 2011). Finally, bioweapons and BW are possibilities, but SARS-CoV-2 couldn't have been a bio-agent or an act of BW due to three reasons. Firstly, BW contravenes international laws as stipulated by the BWC and ratified by over 180 nations. Secondly, the devastating outcome of a BW on a global scale is unimaginable and is too much of a risk for any country to contemplate. Thirdly, SARS-CoV-2 does not meet the requirement of an ideal bioweapon. Although it is highly infectious, the disease mortality is less than 4% and no country seems to have any available cure or vaccine for the disease.

VIRUS EPIDEMICS AND ELECTROMAGNETIC FIELD (EMF), IS THERE A RELATIONSHIP?

EMF is simply defined as waves propagated or radiating through space carrying radiant energy (Funk et al., 2016). The EMF is thus, a spectrum of waves (fields) that includes gamma rays, X-rays, ultraviolet radiations, visible light, infrared, microwaves, radio waves and extremely low frequencies (ELF) in decreasing order of frequency and increasing wavelength (Funk et al., 2016). The energy emitted by each field is directly proportional to its frequency. This implies that high frequency waves have greater energy while low frequency fields have less energy (Funk et al., 2016). EMFs with high frequencies thus can directly cause cellular damage. Remember that biological molecules present in cells include DNA and RNA. The high energy EMFs achieve cellular damage by breaking water molecules to produce reactive oxygen species (ROS) known as free radicals. As a result, they are called ionizing radiations. These waves can damage DNA molecules causing mutations that can lead to cancers. On the other hand, the low frequency waves are non–ionizing because they do not lead to the production of free radicals. However, since all EMFs are packets of energy, they can generate heat at sufficient levels (intensity). A perfect example of this is the heat generated by the microwave oven. Therefore, low frequency waves can generate heat leading to cell damage. Now, the critical issue to be resolved is to establish whether non–ionizing radiation at low intensities can cause cell damage or lead to health hazards. Over the years, scientists have conducted association studies to link low frequency EMFs to various health risks including cancers (Carpenter, 2013; Miller et al., 2019). Also, there are correlation studies linking quantum leap in EMF usage in history to virus epidemics (Lauer, 2015). These correlation studies and the escape theory of virus origin explained earlier are the reason given for linking non–ionizing radiation to virus disease outbreaks. However, it is important to note that correlation or association does not mean causality. Proving causality effect needs empirical evidence and a strong mechanism of causation. On this note, it is safe to say that there is no

identified mechanism by which low energy EMFs at sub-thermal intensities induce cellular damage resulting to cancer or ill health. Nevertheless, there is the need for more research to decipher this lingering theory.

CONCLUSION

As the world battles against SARS-CoV-2, the need to clear arising misconceptions cannot be underestimated. Understanding the fascinating world of viruses will certainly help in the fight against the COVID-19 pandemic. However, it is worth stating that within the last four decades, the world has witnessed outbreaks of viral infectious diseases. From HIV-AIDS, SARS, MERS, Zika, H1N1 influenza to Ebola and now the COVID-19 pandemic. This goes to show that viruses and particularly zoonotic RNA viruses are major sources of emerging and re–emerging infectious diseases. Therefore, it is of utmost importance for the world to unite with a common goal of fighting the scourge of these emerging infectious diseases and prepare for subsequent pandemics.

Data availability statement

Data sharing not applicable to this article as no data were used to support this study.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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