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Review Article

Impact of COVID-19 on assisted reproductive technologies and its multifacet influence on global bioeconomy

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ABSTRACT

Several nations of the world have issued instructions such as travel restrictions, border closure, and lockdown, plus other directives proposing that non-essential care must be withdrawn including assisted reproductive services, in an attempt to identify resources to ascertain the dissemination of SARS-CoV-2. This has led to massive shortage in medical supplies, inappropriate service delivery, hike in price, decrease in staff work load, salary cut, decrease in the utilization of qualitative maternal, and reproductive health-care services thereby creating high risk on reproductive health and global bioeconomy. The search for right candidate for the management of coronavirus disease 2019 and several reproductive health challenges begins with the screening of natural products to identify novel active constituent. Moreover, there is need to pay more attention to crucial phytochemical, bioactive fractions, phytoanalysis, and phytopharmacological investigation for effective drug discovery most especially these bioresources from beneficial microorganisms, plants, and ocean deposits that could help in mitigation of SARS-CoV-2 and reproduction health challenges through chemoinformatics, informatics, synthetic biology, nanotechnology, and metabolomics hence boosting the global economy.

Keywords: Coronavirus disease 2019, Bio-resources, Bioindustry, Bioeconomy, Assisted reproductive technologies, Health

INTRODUCTION

The incidence of coronavirus disease 2019 (COVID-19) pandemic has led to a very higher number of mortality across the globe. Furthermore, this has resulted into rapid spread of the unprecedented strain of the virus across the globe which has disrupted the global health-care system. Several nations of the world have issued instructions and directives to curb the spread by proposing that non-essential care must be withdrawn, in an attempt to identify resources to ascertain the dissemination of SARS-CoV-2. Moreover, most government have declared several restrictions strategies regarding individual freedom in the modern history linked to COVID-19 pandemic. The level of cases reported globally regarding COVID-19 has resulted into high number of admitted and isolated patients in various isolation centers most especially in developing countries where the level of health-care system has been deteriorated.[1,2]

Numerous scientific societies such as reproductive health societies, European Society for Human Reproduction and Embryology, American Society for Reproductive Medicine, Physiological societies, Embryological societies, and Biotechnological societies across the globe have implemented several restrictions by providing expert guidance based on best judgment and practices. Some of the expert advice for the practitioners and general public entails cancellation of all embryo transfers whether frozen or fresh and suspension of non-urgent diagnostic techniques plus elective surgery, postponement of novel fertility treatments which includes *in vitro* fertilization (IVF), intrauterine insemination, ovulation induction, and together with non-urgent gamete cryopreservation.[3,4] Hence, there is a need to provide an adequate care for most patients that are currently facing fertility challenges without conceding safety while there is an urgent need to suggest a remedy that could avert the long-term significances of a protracted termination of infertility management and to support regulatory authorities. The application of assisted reproductive technology (ART) treatment will go along in this situation most especially for low prognosis patients who signify approximately 30–50% of patients seeking ART.[5,6] Typical examples of such ART entails zygote intra-fallopian transfer, IVF, tubal embryo transfer, gamete intra-fallopian transfer (GIFT), pronuclear stage tubal transfer (PROST), intracytoplasmic sperm injection (ICSI), and many more. This will enhance the prevention of long-term influence of a protracted termination of infertility management and to assist regulatory authorities and embryologists recognize which patients might be ranked for the persistence of fertility care in a non-toxic environment.

Despite the fact that the ongoing COVID-19 pandemic situation has interrupted the economy of most countries across the globe, most countries still face several challenges such as increase in climatic temperature, health issues, poor quality of education, financial crisis, environmental hazards, and uncontrolled increase in human population. The world population have been stipulated to rise drastically to about 9 billion in the year 2050. More so, mankind is blessed with several natural and abundant bioresources that could be used to resolve several aforementioned challenges including reproductive health challenges. This entails the application of natural bioproducts, medicinal, and biologically active natural molecules derived from beneficial microorganism, plants, ocean deposits, and many more. Interestingly, it has been observed that the application of biogenic natural resources will go a long way toward boosting the global economy. This might be linked to several attributes which includes sustainability, availability, accessibility to pharmaceutical industries, and most especially cost effectiveness to health practitioners across the globe. Therefore, this review intends to provide a comprehensive information on the role of assisted reproduction in providing the needed economic support during COVID-19 pandemic through the utilization of bioresources for infertility treatment such as artificial insemination, IVF, gamete donation, and ICSI, reproductive health research, bioresources and bioindustry with special reference on biopharmaceutical, biotechnology, biochemical, bioproducts, and vaccine development together with issue of lockdown and second wave of COVID-19; while highlight is also placed on the influence of COVID-19 on infertility treatments, as well as current scenario and future perspectives.[7]

ASSISTED REPRODUCTION

Deep[8] defined ART as all procedures or treatment strategies involving handling of human oocytes or sperm *in vitro* to establish clinical pregnancy by circumventing different pathological barriers in human reproduction. Palermo *et al*.[9] and Schurr,[10] reported that reproductive health treatment has evolved over the years due to the development, commercialization and transnational spread of ARTs, and cross-border reproductive care and products such as IVF, surrogacy, gamete donation, physiological ICSI, and ICSI. Ferraretti *et al*.[11] revealed that Europe is the biggest market for ARTs due to affordability, legislation, reimbursement, and policies of conception and childbearing which varies across countries.

Fasouliotis and Schenker[12] showed that assisted reproduction technology practice entails patient care, research, experimentation, observation by embryologists, physicians, and other biomedical scientists. Begum[13] demonstrated that 10% of infertility cases such as bilateral tubal block, polycystic ovary, severe oligospermia, endometriosis, and plus azoospermia of any society will need the help of ART with an average pregnancy rate of 30–34% worldwide. Till today, many issues are noted as barrier to population acceptance of assisted reproduction treatment such as high cost of treatment, social stigma, superstitious believe, and poor result particularly among the developing nations. Simon and Kelly[14] showed that IVF is the cornerstone of fertility treatment with significant clinical embryological advancement. Across many centers, the success rate continues to improve with the application of cryopreservation, *in vitro* maturation, aneuploidy screening, continued research, and pre genetic implantation diagnosis. Different micromanipulation techniques have been revealed with several variants reported such as zona drilling, partial zona dissection, subzonal insemination, and ICSI. ICSI was first reported by group of Dutch scientists at Free University of Belgium working under Andre van Steirteghem who revealed the superiority of this technique over other variants in the treatment of male factor infertility. Furthermore, the development of sperm preparation techniques has led to a revival of the procedure of controlled ovarian

hyperstimulation and intra-uterine insemination in couples with cervical factor infertility.

Furthermore, the reduced implantation rates observed after IVF procedure has resulted to introducing assisted hatching either by mechanical or utilizing a YAG-erbium LASER beam. Again, the incidence of multiple pregnancies has caused increased development of novel technique of cryopreservation of embryos and gametes to maximize the chances of pregnancy from single attempt of IVF, GIFT, or ICSI. Furthermore, genetic diseases in newborn are curtailed through the utilization of preimplantation genetic diagnosis involving the use of molecular biology (fluorescent *in situ* hybridization, polymerase chain reaction [PCR], and southern blot) to analyze possible chromosomal or genetic defects or specific genes on blastomere derived from eight cell embryos. Inhorn[15] revealed that poor accessibility to effective infertility treatment is the main factor for untreated and intractable infertility in mostly rural and low-resource settings of the developing world which is equally compounded by the recent outbreak of COVID-19.

COVID-19 PANDEMIC

The current COVID-19 pandemic started in December, 2019, in the city of Wuhan, China. The word "PANDEMIC" was a rare word and seldomly found in day to day conversation however, with the outbreak of this deadly virus, the word became very popular across the media. The sample taken from the lower respiratory tract of an infected person showed the presence of a new strain of coronavirus.[16] The disease was named COVID-19 and declared pandemic by the World Health Organization on the February 11, 2020, and March 11, 2020, respectively, due to the increase in its global death rate.

There were controversies on the origin of the disease as some believed it emerged from animals and therefore it was termed as zoonosis while some persons believed it was a biological weapon from a laboratory in China. The President of the United State of America (Donald Trump) from his own perception often called the disease "Chinese virus" because it emanated from China. Some persons even linked the emergence of COVID-19 with an upcoming 5G technology from China.[17] The world Health Organization reported that the environmental samples taken from market in Wuhan, China in December 2019 tested positive for SARS-CoV-2, which suggests that the market was the source of the outbreak or played a role in the initial amplification of the outbreak.[18] Even though the origin of the disease was not clear, these were some of the issues that surround the emergence of the disease. Subsequently, COVID-19 was reported thereafter in many other countries of the world with increase fatality.[19,20] Countries such as the United State of America, Spain, Germany, Italy, Iran, and among others were severely devastated by the disease leading to shortage of hospital equipment to carter for the infected patients and increased number of death.

Studies showed that COVID-19 is an RNA virus with crown-like appearance when viewed under the electron microscope.[21] This virus may pass through the membranes of the nasal and larynx mucosa, enter into the lungs through the respiratory tract and then attack the target organs such as the lungs, heart, renal system, reproductive, and gastrointestinal tract.[22-25] The virus often commences a second phase of attack, causing the infected person's physiological condition to deteriorate around 7–14 days after onset.[26] The symptoms of COVID-19 include but not limited to fever, cough, dyspnea, headache, and sore throat. For persons with suspected infection, real-time PCR can be utilized to detect the positive nucleic acid of SARS-CoV-2 in sputum, throat swabs, and secretions of the lower respiratory tract samples.

There is no specific antiviral treatment recommended for COVID-19, and no vaccine is currently available. The treatment of symptomatic patient with oxygen therapy represents the major treatment intervention for patients with severe infection.[18] Mechanical ventilation may be necessary in cases of respiratory failure refractory to oxygen therapy, whereas hemodynamic support is essential for managing septic shock.[27] Glucocorticoids, remdesivir, chloroquine, and hydroxychloroquine, tocilizumab, lopinavir-ritonavir, bariticinib, nonsteroidal anti-inflammatory drugs, and azithromycin are among those currently tested for their efficacy against COVID-19.[28,29] At present, preventive measures such as the use of face mask, covering coughs and sneezes, washing hands regularly, avoiding contact with infected people, maintaining an appropriate social distance from people, refraining from touching eyes, nose, and mouth are the best strategies to curb the spread of the virus. Moreover, in case of infection and emergence of symptoms, seeking medical care early and following the advice given by the health-care providers is key.

With the increase widespread in the rate of transmission of COVID-19 globally, many countries have imposed lockdown strategy which has resulted into serious economic implications. In addition to this, the World Health Organization recommends that people should take safety precautionary measures which were earlier stated. The lockdown imposed by the government of different countries was an order for the people to remain indoor or stay at home. Furthermore, the lockdown was unprecedented as no country expected or was prepared for the pandemic. Many countries ordered the closure of educational institutions, religious institutions, clubs, restaurants, industries, salon, and many more.[30] Only the workers on essential duties were exempted to be in public places with strict adherence

to COVID-19 prevention guidelines. Some countries even extended the lockdown further to flatten the curve and reduce the spread of the disease.[31] The lockdown had some beneficial and devastating effects on the people and the environments. COVID-19 lockdown caused unprecedented crisis in the socio-economic sector and due to the closure of borders and restriction of movements between countries, there was great decrease in foreign exchange and international trade.[32] This greatly affected the internally generated revenue of many nations putting them in a state of recession and depreciation in value of their currency.[33] Many organizations that offer goods and services could not cope as many were forced to lay off their staff causing job loss and unemployment. Countries whose major source of income is tourism were severely hit by the lockdown as all tourist activities were completely suspended. Many nations also shut down their markets except for those that sell essential products. Furthermore, events centers, clubs, and hotels were shut down so as not to allow social gathering that could further enhance the spread of the virus.[34] During this period, most organizations recorded sharp decrease in income generation which greatly affected their businesses. Small and medium scale enterprises (SMEs) were also badly affected as many shops were not allowed to open or operate during this period. Those SMEs (Restaurant and Salons) that could favor the fast transmission of the virus were completely shut down. Most of the countries also imposed curfew and interstate travel ban so as to limit human to human contact. They also reach out to many families in their homes through the media and advise them to adhere to COVID-19 safety protocols.

The lockdown was imposed to reduce physical contacts between people hence, even educational institutions were closed down and the students and teachers had to switch to new online or virtual learning methods.[35] This posed a big challenge as both teachers and students have to adapt and ensure that learning continues. One major challenge for the teachers is learning how to use the online platforms. Many countries that were not familiar to virtual learning methods most especially in developing nations finds it difficult to adapt to the learning software even though they are user's friendly.[36] The lockdown caused unequal learning opportunities for the students and many children of the poor people in the society do not have access to the modern learning facilities and so were deprived of learning compared to their counterparts from wealthy families.[37] In addition, there was decrease in learning time. For instance, the teachers to student's interaction time were greatly reduced and this affected the learning outcomes of the students.[38] Beyond the school environment, government of many countries mandated students to learn from home, however, this adversely affected the students as many of them were distracted and involved in social vices.[39] Even while many of these students were under their parents, they exhibit immoral behaviors such as smoking, sexual violence and rape, cybercrimes, and unwanted pregnancies.[40] The academic calendars were also disrupted most especially for those who could not cope with the E-learning methods of teaching and assessing the students.[38] Most students have always been engaged by the physical learning method; however, the lockdown imposed psychological and mental stress on them as they have to adapt, adjust, and cope with the changes experienced during this period in term of on line learning methods.[28]

The lockdown affected the psychological well-being of the people as many were faced with anxiety, depression, abnormal sleep, and eating pattern.[40] The people were frightened of not contacting the virus, so this creates fear in the minds of the people and their relatives. More so, not being engage or idleness makes some individuals to be psychologically depressed.[41] The rate of food consumption increased for those who have relatives and whose children were out of school during this period, although governments provided some palliatives to support families. Evidence have shown that stress can induce suppression in sexual behavior and fertility however, during lockdown many couple were less stressed from pressures from workplaces and so engage more in the sexual activities.[42] The quality of relationship between couples was affected and while many use that opportunity to improve their relationship and settle controversies, others breakdown theirs. Couples who do not have the opportunity to reunite during the lockdown engaged in some other alternative activities such as masturbation and pornography in other to satisfy their sexual urge.[43]

With the lockdown all over the world, many industrial activities were paralyzed and because of this, there was decrease emission of toxic gases, a blessing for nature, and the environment. During this period, there was decrease in the emission of greenhouse gases that could damage the ozone layer and expose human, animal and other living creature to the damaging effect of the ultraviolet rays from the sun.[44] Furthermore, the quality of air in the atmosphere improved because of the decrease in air pollution.[45,46] Evidence have shown that exhaust from vehicular movements greatly decreased and if these exhausts were present in the atmosphere, they could further contribute to depletion of ozone layer with resultant increase in global warming.[47] The surrounding plants were not left out as they take in carbon dioxide and not a mixture of compounds that could affect their growth and development.[48]

There was increased use of digital technology and for most private and public organizations and transaction were made online.[49] Most activities including official meetings, learning, seminars, and examinations were conducted online and

because of this, there was increased bandwidth expansion and usage.[50] In fact, some workshops and conferences took place online as well and with the ease of lockdown, many of these activities have remained online. The lockdown in a way has caused all human race to switch to digital technology which appears to be the new normal.

SECOND WAVE OF THE PANDEMIC

Already COVID-19 has caused devastating consequences to the world at large; having a second wave of the virus will pose a great threat to the economy and existence of human race. A second wave at a time the whole world is trying to recover and adjust to the consequences of the pandemic will pose a great danger to survival. A second wave of the virus has already been reported in European countries.[51] Therefore, a spatio-temporal assessment of the pandemic in this region will help prepare the world for a second wave.

A second wave in Europe is a signal to other continents and health-care organizations to properly prepare and take necessary measures to contain the transmission. Most of the reported cases in Europe are asymptomatic which shows the possibility of having a high rate of transmission if steps are not taken to control the spread of the virus.[52] Are countries prepared to have a possible second wave of the Pandemic? There is pressure on the government of some countries to ease the lockdown for those that are still enforcing the lockdown which has been shown to be effective in containing the disease. The ignorance pose by people most especially in the developing countries can exacerbate a second wave.[27] Some individuals believe the pandemic is over and therefore, it is no longer necessary to observe the safety protocol as recommended by the World Health Organization and this attitude may pose a big danger if re-exposed to a second wave of the virus.[53]

Researchers in health organizations may try to understand the dynamics of the past pandemics as that will provide some information on the course of the disease and how to better handle it utilizing new technologies and approaches such as chemoinformatics, nutrigenomics, informatics, synthetic biology, nanotechnology, and metabolomics. With improvement in technology, diagnosis can be made seamless for every individual. Readily available and cheap home-made diagnostic kits can be manufactured for individual use.[54] There is need to properly sensitized and informed people of the eminent danger and devastating consequences of second wave. More ventilators should be manufactured to take care of those who may likely develop complications. The World Health Organization in collaboration with research scientists is on the way to manufacture vaccines against the virus and if successful will eradicate the disease and reduce its burden on the populace.[7]

IMPACT OF COVID-19 ON FERTILITY TREATMENTS, REPRODUCTIVE HEALTH, AND RESEARCH

Choucair *et al*.[55] revealed that many laboratories across the globe due to COVID-19 pandemic and possibility of second wave have developed plans such as reducing labor needs, logistical arrangements, protective measures, and conserving supplies for managing andrology and embryology cases to safeguard the well-being of embryologists and patients. Ory *et al*.[56] showed that during COVID-19 pandemic, pregnant women are faced with unique concerns and risks such as virus induced complications in pregnancy, vertical transmission to fetus, and optimizing the use of critical health-care resources. Ajayi *et al*.[57] reported the impact of COVID-19 on assisted reproduction. They suggested that economic situation is the major reason for reduce access to IVF treatment which has equally been compounded by COVID-19 pandemic. They alluded to the fact that better understanding of the coronavirus will help to take appropriate measures in various IVF centers. The fact that coronavirus can survive in cryopreservative tanks pose a huge threat on gamete contamination, patients risk, and embryo infection. Due to the COVID-19 pandemic, several pre-implantation genetic diagnoses are discontinued.

Anifandis *et al*.[58] reported that there are several changes in reproductive plan during the COVID-19 crisis. From there study, it was revealed that in Italy the percentage of abandoners is significantly higher than in other countries such as France or Germany among younger age group. Gordon and Balsom[59] highlighted the psychological effects of reproductive treatment suspensions due to the current COVID-19 pandemic. They discovered that fertility treatment suspensions had significant negative effects on mental health or quality of life among patients. Sarah[60] also reported that COVID-19 pandemic has impacted negatively on several antenatal care services in many countries. Government directives on COVID-19 such as social distancing, lockdown, and travel restrictions have place huge burden on pregnant women who are not having ultrasound or laboratory test to keep off from attending the physical antenatal services. Younis *et al*.[61] and Olaniyan *et al*.[24,25] have implicated the male reproductive organ as a potential target for the novel coronavirus disease. The testis can be infected with the coronavirus through the angiotensin converting enzyme 2 receptor with possibility of causing orchitis, inflammation, free-radical generation, oxidative stress, sperm dysfunction, cytokine storm, and hormonal imbalance as shown in Figure 1. Ahmed[62] and Alviggi *et al*.[63] revealed that due to extended lockdown of many health-care facilities providing high-complexity fertility treatments, there has been reduction in the global rate of conception. The authors showed that 0.3% of babies are conceived through ART annually, thus the

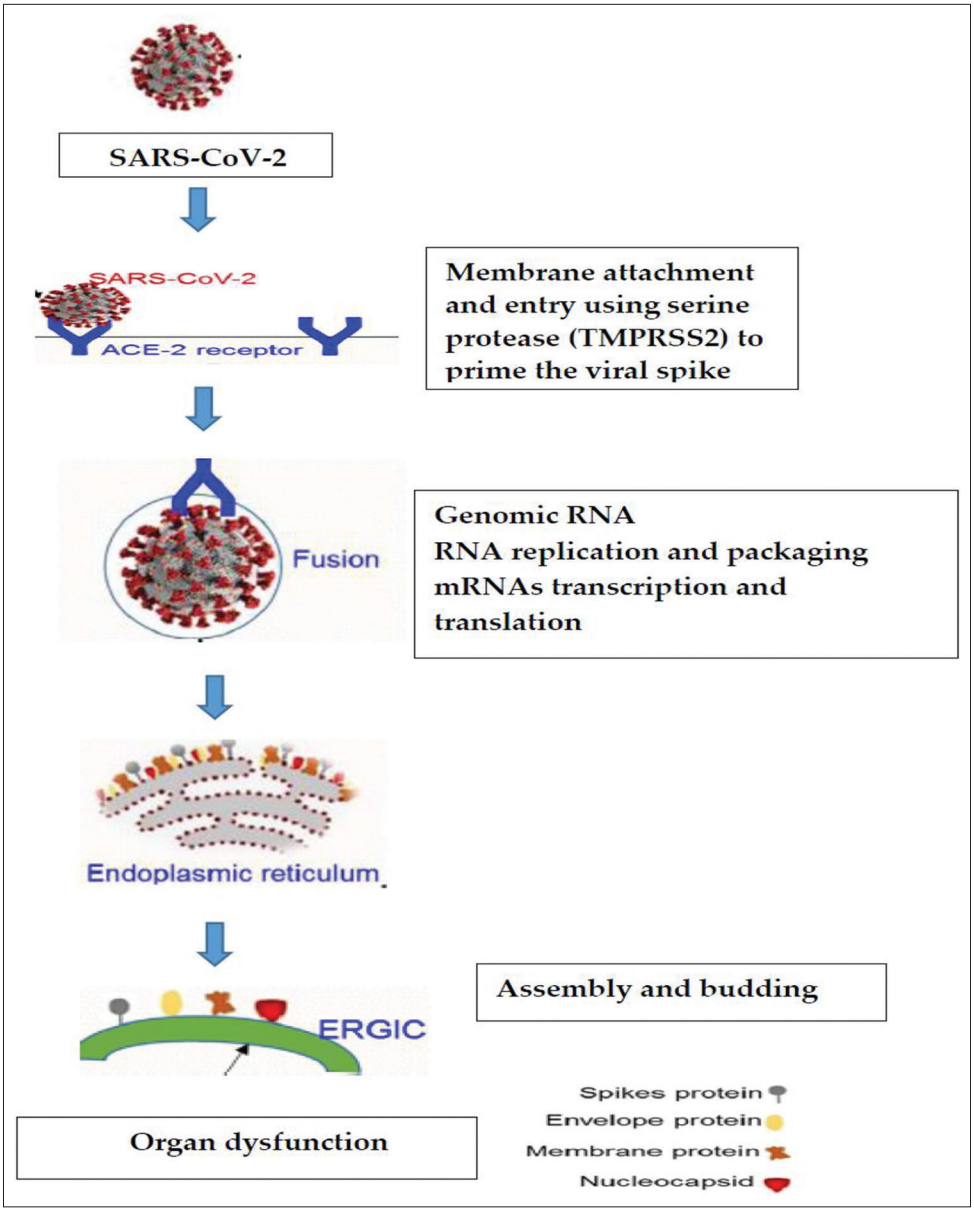

Figure 1: The pathways of SARS-CoV-2 targets in the male reproductive organ.

number of infants expected to be conceived and born will be very low.

Swartz and Graham[64] reported that all over the world, health-care facilities are over stretched due to the current COVID-19 pandemic. Thus, the authors assessed the influence of COVID-19 infection on maternal and reproductive health-care services. They discovered that shortage medical supplies, inappropriate service delivery, and increased staff work load significantly decrease the utilization and quality of maternal and reproductive health-care services particularly in the developing countries such as Ethiopia. Bateson *et al.*[65] and Monteleone *et al.*[66] showed the possible impacts of the COVID-19 outbreak on pregnant women and its potential influence on the management of assisted reproductive treatments. Human reproduction societies have recommended postponement of embryo transfers, increase utilization of telehealth and stoppage of new treatment cycles. Chen *et al.*[67] reported the role of international societies on various recommendation to postpone all ongoing cycles, embryo transfers and that morphological ultrasonography should be performed in women infected with SARS-CoV-2 at the second trimester.

Church *et al.*[68] noted that due to COVID-19 pandemic, the availability of personal protective equipment for healthcare workers is reduced, cash flow shortages as a result of reduced banking availability, loss of income in fee-paying sites

causing financial distress, travel, and movement restrictions are impacting on infertile couples and vulnerable groups, shortage, and increased pricing of pharmacy-supplied products are witnessed across the globe particularly in low resource health systems causing imbalances in health-care delivery, interruption of routine essential services, and plus redeployment of limited health personnel across health services. Furthermore, general shortages of essential medical supplies are experienced as a result of closure of medical and pharmaceutical factories, laboratory closures, restrictions on transport, reduced import and export of raw materials, bioproducts, and bioresources in countries producing medical goods such as condoms, drugs (progesterone, antibiotic, and estrogens), kits, media, reagents, antibodies, and many more. La Marca and Nelson[69] and Lavezzo *et al*.[70] reported that SARS-CoV-2 may cause increased risk of infertility, adverse pregnancy complications, fetal anomalies, as a result of lockdown and postponement of cycles, treatment suspension, scarcity, and increased pricing of pharmaceutical products during the pandemic.

POSSIBILITY OF VERTICAL TRANSMISSION OF SARS-COV-2 FROM MOTHER TO FETUS

Álvaro *et al*.[71] reported that vertical transmission of SARS-CoV-2 from mother to the fetus has not been recorded so far from different studies conducted but the possibility of transmission during delivery cannot be ruled out plus physiological deterioration of pregnant women infected with SARS-CoV-2. They revealed the possibility of the mother to develop different cardiopulmonary disorders coupled with acid-base imbalance and postpartum hemorrhage. Karimi-Zarchi *et al*.[72] reported from their findings that no evidence of vertical transmission was detected in the amniotic fluid, cord blood, placental, pharyngeal secretion, neonate blood, or neonate in all the cases investigated but revealed that some of the mothers developed cardiorespiratory complications. However, in contrary, Fornari[73] reported the possibility of vertical transmission of COVID-19 from infected mother to fetus suggesting that vertical transmission could not be ruled out.

Moreno *et al*.[74] investigated the possibility of vertical transmission of SARS-CoV-2 particularly during the during the third trimester. They reported that in all the COVID-19 infected mother during the third trimester, the neonates tested negative thus suggested that symptomatic COVID-19 mothers during the third trimester of pregnancy was not linked with vertical transmission to the neonates. Wang *et al*.[75] investigated the possibility of intrauterine viral infection during pregnancy. Thus, tested different samples such as placental, cord-blood neonatal pharyngeal swab plus amniotic-fluid collected immediately after delivery in nine pregnant women infected with COVID-19 particularly during the third trimester. From their findings, it was revealed that all the samples tested negative, thereby ruling out the possibility of vertical transmission.

SIGNIFICANCE OF BIORESOURCES FOR EFFECTIVE MANAGEMENT OF COVID-19 AND REPRODUCTIVE CHALLENGES

Bioresources entails several natural products and their derivatives that have been recognized as a source of structural diversity and therapeutic agents which could be applied for effective management of several illness and health challenges including numerous reproductive disorders, hormonal imbalance, and dysfunction. The natural bioresources are multidimensional chemical structures which could be modified to enhance the functionality of the main active constituents. Therefore, the search for right candidate for the management of COVID-19 and several reproductive health challenges begins with the screening of natural products to identify novel active constituents. Moreover, the procedure involves in the detection of natural products that could serves as the best drug candidate requires several experience and expertise. Furthermore, there is need to establish the chemical structure and their biodiversity identify some novel technologies which could led to rapid identification of natural products and discovery of novel drugs most especially for the management of COVID-19 and several reproductive health challenges.[76]

These techniques provide a unique opportunity to affirm the potential of natural products as a significant source for drug discovery. The procedure involves in the drug discovery entails isolations, identification, characterization, and application of biologically active constituents obtained from natural products as a potential drug candidate. Some of these techniques entail chemoinformatics, informatics, synthetic biology, nanotechnology, metabolomics, and many other.[77-82] Moreover, there is need to pay more attention to crucial phytochemical, bioactive fractions, phytoanalysis, and phytopharmacological investigation for effective drug discovery most especially the bioresources that could help in mitigation of COVID-19 and reproduction health challenges.[24,83]

Studies have shown that polluted air with virus and toxic compounds can adversely affect the health and air quality. Thus, many approaches can be utilized to improve the quality of air. Some of these methods are generally expensive and require sophisticated equipment. It has been revealed that plant can serve as source of bioresources for the development of bioproducts through plant based technology to clean polluted environment (air phytoremediation biotechnology). Some of these plants, ocean deposits and microorganisms are also utilized as source of bioresources for the development

of bio based chemicals and other bioproducts to fight against SARS-CoV-2 and other environmental pathogens.[84]

Forest based materials and resources are of great benefits for the development of industrial based biomaterials and bio based raw materials for the manufacturing of various pharmaceutical and medical products such as media, buffers, drugs, enzymes, consumables, kits, and instruments which are constantly being utilized in different assisted reproductive techniques.[85] The critical role of bioresources in the sustainable development of human and environment can never be overemphasized. Serious attention has been given to the beneficial roles of bioresources in the development and application in various industrial based biomaterials. Studies have revealed that many bioresources do not eventually enter the global market to derive or generate income, but they significantly contribute to the economic, nutrition, and livelihood of the people. Specifically, wild foods, leaves, fruits, nuts, berries, bush meats, insects, fungi, and grass seeds contribute significantly about 20% to the nutrition status of deprived populace of some India, Sudan, Tanzania, Uganda Communities.

Many of these bioresources and raw materials such as raffia, rattan, and reeds are converted to drugs, and pharmaceutical products and medical devices such as honey, waxes, fuel, clothing, animal feeds, biofertilizers, and other industrial raw materials. In general, it has been reported that many of these bioresources are utilized for the production of raw materials useful for protection against detrimental effects of climate change, production of agro chemicals, medicinal constituents or genetic resources and vaccines.[86] Ngbolua *et al*.[87] reported that many plants constituents such as Solanum genus and Ocimum species are utilized as source of flavors, food, additives, and drugs such as antiviral agents particularly for the fight against COVID-19. The phenolic constituents and essential oil derived from these plants such as glycoalkaloids have been shown to interact with SARS-CoV-2 protease and respiratory tract infections. They recommended the consumption as source of nutraceuticals to curb the negative impact of SARS-CoV-2.[88]

ROLE OF BIOINDUSTRY IN THE MANAGEMENT OF COVID-19 AND REPRODUCTIVE CHALLENGES

Heidaran *et al*.[89] examined the influence of COVID-19 on the engineering of genes and cells by way of biotech and therapeutics, through medical trials of scenery. The authors reported that the new COVID-19 is a pathogen from the coronavirus (SARS-CoV-2) which has affected medical trials scenery globally in very quick months. This pathogen belongs to the family Coronaviridae, which can affect animals and human, thus results in pathogenic and communicable symptoms such as colds, catarrhs sneezing, and loss of breath. The authors revealed that serious concerns on issues relating to adulteration of biologics and medical supply needed for human utilization to curb the spread of the virus is beginning to emerge due to the lockdown and travel restrictions witnessed in many bioindustrial sectors. However, a good engineering consideration and practice for responding to the novel COVID-19 contagion in workers in the biological and drug products of the pharmaceutical industries should establish safety guidance or follow extant industrial guidelines established by the FDA 2020 for the management and control of the novel coronavirus guidelines. Although the hazard of the novel coronavirus on medical products such as biopharmaceuticals is minimal as regard the pathways. Besides, the route of the chain of supply needs to be checked to control and strike a balance on risk, control, and management. They concluded by suggesting that the coronavirus safety approach should be the primordial measure in the enhancements and adjustments of biotechnological materials.

Hofman *et al*.[90] evaluated the influence of COVID-19 on biospecimens sourced from biobanks linked to cancer research and other biomedical industry. The authors recounted that the COVID-19 pandemic has pinpointed the hazards linked to the assemblage and dispensation of biospecimens from humans who have potential COVID-19 status whether for research, therapeutics, and diagnostic. Biological samples from cancer banks sourced from patients during this pandemic have been fingered to have possible COVID-19 strains. Biospecimens such as organs, swabs, biofluids, and tissues are being infected by COVID-19 exempting the human urine. The authors reported that COVID-19 is likely to be active in a temperature of 133°F (56°C), paraffin, and formalin. However, it can thrive in various superficial regions making it a highly infective virus. Hence, it is important to ship, handle, store, and prepare biospecimen samples from humans to ensure that they are not exposed to the virus during the routes of the transfer. This can be achieved through standard safety protocols set by regulatory bodies for bioindustries.

Simeon-Dubach and Henderson[91] evaluated the risks and opportunities of the COVID-19 pandemic on biobank research centers. They revealed that COVID-19 pandemic has caused serious effects on public health and research. For over 100 years, the COVID-19 pandemic has been one of the most devastating diseases globally affecting scientific, political, social, public, and private lives worldwide. In the clinical sector, the virus has greatly impacted the productions and utilization of bioproducts because they may have been contaminated by the virus and the human capacity has been reduced, due to high morbidity and mortality cases. The storage, processing, and collection of biosamples into

biobanks have been very slow and restricted because of the global impact of the virus to survive well in cryopreservative tanks. Nonetheless, the COVID-19 pandemic also creates opportunities for research industries to develop a data biobank and also provides the medium for the development of protective vaccines, treatment options, drugs from natural biomolecules to manage, and combat the virus. The authors concluded by suggesting that the biobank sector has a key role to play in the area of research and drug development which could be explored in the nearest future. Besides, the sector can also use the medium to signal and forecast future occurrences of the pandemic through the information and biodata store in the biobanks.

Rewari *et al*.[92] examined the impact of the novel coronavirus (COVID-19) on the worldwide supply ladder of HIV drugs (antiretroviral) and vaccines. The recent pandemic caused by coronavirus has ravaged the supply ladder of the distribution of antiretroviral medications specifically in the middle- and low-income countries. Some of the greatest challenges encountered in the distribution of this antiretroviral medication are the inability to access the active materials and other bioresources for drug development, increase in cost of production of bioproducts, and shipping delays as a result of lockdown and travel restrictions. Furthermore, the dependence on the markets from the developed nation to source biomaterials for the synthesis of the antiretroviral drugs and vaccines was one of the toothing problems. The findings from their pilot study showed that there is a need to foster long-term ordering of the antiretroviral drugs to eke the buffer and dispensing monthly stocks. The management of the inventory and information gotten from the real-time computerization of the antiretroviral products should be put into cognizance to ensue evenly distribution. More so, the bioindustry and manufacturing associations should have constant and official interaction with major stakeholders in addressing cut in the supply chains particularly during this pandemic. They concluded by suggesting safety and strategic management measures to enhance the flexibility of antiretroviral drugs and vaccines supply ladder and distribution of stocks during and after the pandemic.

Barshikar[93] assessed the novel impact of COVID-19 on biopharmaceutical, biomedical, biochemical, and biological industrial sectors globally. Based on the recent developments and impacts of the novel corona virus, different industrial sectors across the globe have been negatively affected due to the spreading and transmission of the coronavirus, thereby reducing productivity and economic growth. The impact of the virus has affected the operational and manufacturing sectors, thus the health of the personnel and products is influenced also. There is need to protect this sector by imbibing the protocols set by regulatory bodies to forestall continuity of the manufacturing of different bioproducts to safeguard the health of the personnel and the consumables. More so, the biopharmaceutical sectors have to ensure that the virus does not spread rapidly during the handling, exit and entry, plus distribution of the bioproducts to the end consumer. Key protocols such as the use of 70% alcohol hand sanitizers, nose mask, face gears, frequent washing of the hand with water and soap, and social isolation should be adhered to. Staff not engaged with research activities should stay or work from home to ensure workplace safety.

Guerin *et al*.[94] investigated the influence of COVID-19 on the worldwide stock of biomedical products. The globe currently is facing the hit of the novel coronavirus which has caused serious economical and health damages. In line with the call for a safe environment, policymakers and stakeholders in the environmental, economic, and health sectors have to respond swiftly to minimize this outbreak and possible health and economic impacts. The biopharmaceutical sector has been largely hit by this pandemic where a lot of medical bioproducts have been lost due to contamination, reduction in work force, and reduction production line. This has also reduced the health-care distribution systems where vaccines, bioproducts, tools, and equipment for diagnostics, and drugs are economically impeded with the worth of over 1.3 billion dollars globally. The control and mitigation of this pandemic around the globe are paramount at this time of community transmission especially in the low-income countries. In the nearest future, the biopharmaceutical, biotechnology, and biochemical industries will determine the rate at which the pandemic will be controlled or completely eradicated. However, incomparable actions should be carried out to maintain and support the functioning and the production of plant-based medical drugs for the control of the virus because of its high potencies, accessibility, affordability, availability, sustainability, and other chattels found therein.

Ayati *et al*.[95] evaluated the long- and short-term influence of COVID-19 on the biomedicinal sector. The new COVID-19 has been characterized by the World Health Organization early March 2020 as a worldwide pandemic. This virus has affected the health sector especially the biomedicinal sector thus decreasing the economics of the sector. The outcome of their study showed that the pandemic contributed to short-term changes in the R and D (research and development), the demand and supply ladder of the biopharmaceutical sector. Besides, the growth rate of the sector declined, the production, demand, and supply ladder crashed, and the sector moved to self-sufficiency which has a serious ethical impasse. In the long-term, there is possible anticipation of the influence of the virus on the sector at the local and global levels. In conclusion, the authors suggested a primary assessment and identification of gray effects on this sector to enable policymakers and stakeholders to inform decision in the mitigation and management of the COVID-19 pandemic.

CURRENT SCENARIO AND FUTURE PERSPECTIVES

Today, the practice of assisted reproduction has evolved to the point where a prospective parent can go to the web, drop a vial of sperm from a donor with specific selected characteristics into a "shopping cart" and have that sperm delivered in 24 h. Furthermore, selection of eggs from women with desired characteristics can be done online with delivery. Over the past few years, advancement in the development of sophisticated reproductive technology has created a global market and economic growth such as pharmaceutical industry, embryo laboratories, suppliers, infertile consumer, gamete middlemen plus brokers, representative organizations, and resulting into annual revenue of 7 billion dollars in the United States alone. This figure continues to grow with the establishment of international sperm supply industry, entrepreneurial facilities, and sperm/stem cell banks with a net worth of about 100 million dollars.

Despite this recognition, the market of ARTs is currently being threatened by the COVID-19 pandemic demonstrating a pervasive impact across multiple sectors including pharmaceutical, medical, research, agricultural, and the global bioeconomic insecurity. The suspension of new treatment cycles, canceling planned embryo transfers, minimizing in-person interaction, and stoppage of elective surgeries aimed at achieving pregnancy by the American Society of Reproductive Medicine and European Society of Human Reproduction and Embryology declared on the March 17, 2020, coupled with global lockdown, travel restriction, social distancing, closure of factories, and pharmaceutical industries has created higher risk on reproductive health and global bioeconomy.[96-98] Robertson *et al*.[99] reported that the impact of COVID-19 on global economy is staggering with a negative growth rate of –4.9% in 2020 with recovery rate projected to be gradual. Many sectors with large private component such as infertility care and ARTs have been revealed to witness widespread economic uncertainty, with many centers struggling to cope. Again, during this pandemic many household economies may face income reduction resulting into delayed conception with resultant future spike in fertility service demand and post-COVID-19 patients seeking for ART due to adverse effects of coronavirus on reproductive organs.

Morganti and Morganti[100] revealed that COVID-19 pandemic has increased the rate of consumption of non-biodegradable natural raw materials resulting into waste generation. ART procedures also consume large of these polypropylene non-biodegradable materials such as gloves, cannulas, face and nose mask, vials, dishes, syringes, and nylons. Today, bio-industries utilizes natural biomolecules from beneficial microorganisms, plants, and ocean deposit such as lignin and chitin which are biodegradable to produce many bioproducts, surgical, and medical goods plus drugs which are utilized in assisted reproductive procedures thereby generating revenue for bioeconomic growth. Thus serious attention should be given to the identification and development of novel bioresources and bioproducts for the management of COVID-19 and other reproductive health issues such as premature ovarian insufficiency, hormonal imbalance, endometriosis, polycystic ovarian syndrome, and many more. Natural bioresources can be utilized in the development of novel *in vitro* activators and biostimulants, drugs, vaccines, bioproducts, polymers, reagents, media, contraceptives, enzymes, biosurfactants, and many more.

CONCLUSION

This review provides a perspective to assist competent authorities and health-care providers such as embryologists, physicians, and pharmaceutical industries to urgently identify priorities or remedies for many infertile patients impacted by the COVID-19 pandemic lockdown and travel restrictions. At the moment when preventing reproductive complications and regulating burdens on health-care systems, the accurate prognostic classifications and identification of patients in a time-sensitive manner are crucial for guiding the steady resumption of ART services so as to boost global bioeconomy.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

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