When the virus goes viral: An impetus to revisit COVID-19 scientific outrage using Web of Science platform and a recount on the lineage of pandemics

ABSTRACT

Pandemics are epidemics or disease outbreaks, which rampage across countries and continents. The ongoing corona virus disease 2019 (COVID-19) has been a full-fledged pandemic for over a year now. With the death count mounting above two million, COVID-19 has globally impacted the economy, society, public health and all spheres of human life. COVID-19 is the third type of coronavirus disease outbreak after Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome. This review paper discusses the medical perspectives of COVID-19 along with a recount on the numerous pandemics that have wreaked havoc in the past. AIDS which is ongoing, and cholera, influenza and plague have been recurring pandemics and merciless killers. Even with tremendous advancement in medical science, new pathogens continue to cause uncontrollable infections and deaths worldwide. Research in the fields of medicine, health and social sciences, psychology and so on is soaring as the world battles with COVID-19. Additionally, scientometric analysis has been performed using the Web of Science platform, a global citation database, to project the impact of COVID-19 on research in terms of scientific publications. As of 04th April 2021, 98,020 scientific works have been published of which 28 % are from the USA. Medical and health sciences have been the major focus of research globally, as the world works tirelessly to develop the *'right'* vaccine that will make COVID-19 a disease of the distant past.

Keywords: COVID-19, Coronavirus, Diseases, Pandemics, Scientometrics, Web of Science.

Review Criteria:

- Scientometric analysis of COVID-19: *Web of Science* platform (*Core Collection Citation Indexes*)
- Internationally recognised healthcare-based websites such as WHO and CDC were considered for the current updates on pandemics
- Peer-reviewed international publications were referred for gathering the other information compiled in this review paper

Message for the clinic:

- The era of COVID-19 lockdown has witnessed an *"infodemic"*. The governmental, clinicians and other societal infrastructures need to gear up with not only creating awareness among the people about public healthcare, but also to keep a check on circulation of any misleading information.
- The wide range of disciplines of immunology, psychology, ecology, public occupational health and psychiatry are the top 10 research fields to publish over 98000 papers on COVID-19.

1. Introduction

Since the start of the year 2020, the use of the word "Pandemic" has become the talk of every household. The ongoing, widely spread Coronavirus infectious disease, also known as Covid-19 has been declared as a pandemic. In this scenario, it becomes empirical to understand the fundamentals as to when a disease can be referred to as a pandemic. Fundamentally, outbreak of a disease, contained within a specific population or in a country is known as an endemic. On the other hand, an epidemic is a disease outbreak that spreads in a population of a particular region or a country. When an epidemic rampages across countries and/or continents, it is known as a pandemic. Pandemics differ from epidemics mainly because the virus or strain of a virus or any other microorganism causing the sudden outbreak of a disease is normally new and humans have very little or no immunity to it. This leads to a rapid and drastic increase in the mortality rate of the pandemic causing high socio-economic loss worldwide [1].

A glance at the history records that a regular outbreak of epidemics of cholera, smallpox, plague, yellow fever etc. has always been observed in various parts of the world time and again [1, 2]. The most recent epidemics include an outbreak of smallpox in India, meningitis and Ebola virus disease in West Africa, Cholera in Haiti and Bangladesh and influenza in the USA. These kinds of epidemics, if not controlled in time, could become a devastating pandemic [2].

The World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) are the major international organizations which work on delivering support to countries world-wide to identify, prevent and react to health care emergencies, including endemics and pandemics [3, 4]. Moreover, as a cautious approach, WHO keeps a close watch on the outbreak of about 20 diseases which include influenza, cholera, Ebola virus diseases, plague, smallpox, meningitis etc. [5].

Epidemics and pandemics such as plagues have been documented by historians over centuries. The origin, source, occurrence and mortality has varied based on the location, time period and availability of medical care. Table 1 details some pandemics which have been recorded to have the highest number of deaths till date. Cholera, influenza and plague based pandemics are witnessed as recurring pandemics in the past and are detailed in the sections

1.1, 1.2 and 1.3, respectively. The outbreak of these diseases is being vigilantly tracked by WHO to avoid any further world-wide devastation.

1.1 Cholera-based pandemics

The cholera-based pandemic is an ongoing pandemic, and this 7th cholera pandemic is the longest known, ongoing pandemic in the world having its origin in the year 1961 in Indonesia. Out of the hundreds of strains of the bacterium *Vibrio cholera*, 2 strains - *O1* and *O139* - have been identified as causing cholera outbreaks [6]. Historically, the earlier six cholera pandemics have had their origins in India with the first pandemic outbreak recorded in the year 1817. The third cholera pandemic has been referred to as the deadliest one with a death record of more than 1 million people. From medical perspective, Oral Cholera Vaccines (OCVs) are recent developments that have proven to play a major role in preventing the spread of cholera disease. One such vaccine is CVD 103-HgR (Vaxchora™) which was approved by the FDA (USA) in 2016. However, the drawbacks of this vaccine include the prescription to limited age group (18 – 64 years) of patients, requires cold chain settings for transport and have high costs [7].Table 2 depicts the details of each cholera pandemic recorded till date.

1.2 Influenza-based pandemics

The A-type strain of the influenza virus is the only known strain to cause influenza-based pandemics. Table 2 accounts the list of influenza pandemics that bear its presence since 1889. In the early part of the 20th century, the Spanish flu was the most devastating flu pandemic recording a devastating deaths of about 100 million people. It had a mortality rate higher than that of the First World War [8]. After few decades, about 1-4 million people died during the general Asian flu and the Hong Kong flu (1957 to 1970). The Swine flu pandemic of 2009 is the most recent influenza pandemic which affected both the swine and human beings alike. There are two types of vaccines licensed to be manufactured for influenza: 1) Parenterally administered non-replicating virus vaccines which are further divided based on substrate used for manufacturing, dosage route, presence of adjuvant, and type of preparation; 2) Intranasally administered live attenuated influenza vaccine (LAIV) which are live, modified influenza virus with temperature sensitivity that prevent the infection [9].

Table 1: Top 10 highest recorded mortality rate of pandemics

Name	Source	Origin	Vaccination	Time Period	No. of Deaths (millions)	Reference s
Black death	*Yersinia pestis*	Near China / Mongolia	Inactivated *Yersinia pestis*	1346-1353	75-200	[10-12]
Plague of Justinian	*Yersinia pestis*	Unknown	Inactivated *Yersinia pestis*	541-542	15-100	[11, 13, 14]
Spanish flu	Influenza A virus (H1N1)	France, China and Britain	Inactivated influenza (IIV) and live attenuated Influenza (LAIV)	1918-1919	>50	[15-17]
AIDS	HIV	Democratic Republic of Congo	Not Available	1981-Ongoing	~33	[18- 21]
Third plague	*Yersinia pestis*	China	Inactivated *Yersinia pestis*	1894-1959	12	[11, 22, 23]
Antonine plague	Unconfirmed	Mesopotamia	Not Available	165-180	2-5	[24, 25]
COVID-19	Corona virus	China	Multiple testing under observation	2019-Ongoing	2+	[26]
Asian flu	Influenza A virus (H2N2)	Asia	IIV, LAIV	1957-1958	1-2	[16, 27]
Hong Kong flu	Influenza A virus (H3N2)	Hong Kong	IIV, LAIV	1968-1970	1-2	[16, 27, 28]
Plague of Cyprian	Unconfirmed	Unconfirmed	Not Available	249-270	1+	[29]

Table 2: History of Pandemics

CHOLERA PANDEMICS

S. No.	Name	Worldwide distribution	Time Period	No. of Deaths	References
1	First cholera pandemic	India, Myanmar, Sri Lanka, Thailand, Indonesia, Philippines, China, Japan and rest of the world	1817-1824	100,000+	[30]
2	Second cholera pandemic	Central Asia, middle East, Europe, Baltic states and North America	1827-1835	100,000+	[30]
3	Third cholera pandemic	Asia, Europe, Africa and North America	1839-1856	1M+	[30]
4	Fourth cholera pandemic	Asia, Africa, France and Russia	1863-1875	600,000	[30]
5	Fifth cholera pandemic	Asia, Africa, France, Russia, Japan and Germany	1881-1896	298,600	[30]
6	Sixth cholera pandemic	Europe, Asia, north Africa, Russia, and middle East	1899-1923	800,000+	[30]
7	Seventh cholera pandemic	Indonesia, Asia and middle East	1961-present	1M+	[31]

INFLUENZA PANDEMICS

S. No.	Name	Source & Origin	Time Period	No. of deaths	References
1	Russian Flu	Influenza A virus (H1N1) – Bukhara & Russia	1889-1890	1 M	[16, 32]
2	Spanish flu	Influenza A virus (H1N1) – France, China and Britain	1918-1919	>50 M	[15, 17]
3	Asian flu	Influenza A virus (H2N2) – Asia	1957-1958	1-2 M	[28]
4	Hong Kong flu	Influenza A virus (H3N2) - Hong Kong	1968-1970	1-2 M	[28, 33]
5	Russian (Soviet) flu	Influenza A virus (H1N1) – Soviet Union	1977-1978	10,000-30,000	[16, 33]
6	Swine flu	Influenza A virus (H1N1) –USA	2009-2010	284,000	[34, 35]

PLAGUE PANDEMICS

S. No.	Name	Origin	Time Period	No. of Deaths	References
1	Antonine plague	Mesopotamia	165-180	2-5 M	[24, 25]
2	Plague of Cyprian	Unconfirmed	249-270	1M+	[29]
3	Plague of Justinian	China and North East India	541-542	15-100M	[13, 14]
4	Black death	Near China or Mongolia	1346-1353	75-200M	[10-12]
5	Plague in kingdom of Naples	Naples	1656-1658	1.25M+	[36]
6	Third plague	China	1894-1959	12M	[22, 23]

†where M denotes millions of deaths

1.3 Plague-based pandemics

Plague has been mainly caused by a deadly bacteria called *Yersinia pestis*. In the start of the first millennium, more than a 100 million people lost their lives with the occurrence of plague in 3 different time periods (see Table 2). The Black Death alone which occurred in the 14th century caused the death of around 200 million people. There is an ambiguity in the naming and time periods of plague-based pandemic occurrences among historians and researchers because the first and second plague-based pandemics consisted of numerous outbreaks with sporadic distribution globally. However, the latest plague-based pandemic of previous century is collectively called as third plague-based pandemic as it was rampantly spread [18]. Although vaccines for treatment of plague is an active research area, yet none are currently recommended by WHO for the general public. However, plague can be readily cured by modern day antibiotics and medical care if diagnosed during the early stages. 'Killed whole-cell *Y. pestis*' vaccine, initially produced in Australia and the USA was found to be ineffective in the long term and was discontinued. In 1920s, the 'Live attenuated *Y. pestis'* vaccines, EV series was made. This has been administered to people in Indonesia, Madagascar, Vietnam, and the Soviet Union in millions [37]. However, the EV series of vaccines has not been accepted worldwide because the previous large scale immunization did not provide with any safety data and there is no uniformity seen in the genetics of the strain of vaccines after multiple passages [38]. Molecular vaccines such as rF1-V (USA), RypVax (UK) and SV1 (China) have been patented but not yet licensed [39]. According to the WHO, the regions of Asia, Africa, Western USA, and North America have been recognized as a natural plague foci; the most recent outbreaks being in Madagascar, Uganda, China, and Democratic Republic of Congo [40].

1.4 AIDS (Acquired Immunodeficiency Syndrome)

AIDS is an ongoing pandemic which was initially reported in the USA in 1981. By the end of 1985, it had spread around the globe to be declared as a pandemic. AIDS is caused by HIV (Human Immunodeficiency Virus) which infects CD4 cells, weakening a patient's immune system. It is believed to have originated from Central Africa and started to infect humans in the 1930s. This disease has since then caused a huge impact on life expectancy, economic growth and orphaned millions of children worldwide [41].

Data suggests that AIDS has claimed the death of about 33 million people till date with around 690,000 deaths worldwide in 2019 alone. This virus can be transmitted through infected blood, semen or vaginal fluids and from a mother to the fetus. No successful vaccines are available for HIV infection yet, however, the virus can be controlled by antiretroviral drugs (ARVs) preventing its transmission to other people [42].

2. Corona-based pandemics

The term corona virus was derived from the Latin word "*corōna*" which means crown or garland. The virus was given this name because of its halo like structure when observed under an electron microscope. Coronavirus is known to be of the *Orthocoronaviridae* subfamily (order: *Nidovirales*, subordination: *Cornidovirineae*, family: *Coronaviridae*) [43, 44]. The coronavirus sub-family is subdivided into four genera: alpha, beta, gamma, and delta coronaviruses. HCoVs are coronaviruses infecting humans and these belong to alpha and beta coronaviruses. Middle East respiratory syndrome coronavirus (MERSCoV), the severe acute respiratory syndrome coronavirus (SARS-CoV), and SARS-CoV-2 belong to beta coronaviruses genera [44].

The genome of all corona viruses have a single-stranded ribonucleic acid (RNA) with a 5′→3′ orientation of RNA base sequence corresponding to the later messenger RNA (mRNA). The virus is the largest known RNA genome having a length of 26.4–31.7 kilobases [45]. The error prone RdRp of the virus which is responsible for duplication of genetic information causes it to have a high mutation rate [46]. The diverse nature of corona viruses enables them to infect numerous species. It was in the year 1937 that the Infectious Bronchitis Virus (IBV), the first coronavirus discovered was isolated from chicken embryos [47]. Since then, many types of corona viruses have been observed in farm animals, wild animals and pets. However, many of these viruses do not show any symptoms in the animals infected. These pathogens are considered to be of zoonotic origin since they are present in a variety of animal species and are further transmitted to humans [48, 49]. Over the past years, 3 diseases caused by coronaviruses have been of primary importance for researchers: ***Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and Corona virus disease 2019 (COVID-19).*** A comparison of the above mentioned diseases is detailed in Table 3.

2.1 Severe Acute Respiratory Syndrome (SARS)

In 2003, SARS outbreak in Guangdong Province of China was caused by SARS-CoV. As per WHO, a total of 774 people out of the 8,098 people infected died in the 2003 outbreak [50]. The origin of SARS-CoV is considered to be a bat since it shares similarity with two novel bat SARS-related CoVs and utilized the same receptor (ACE2) [51]. Since SARS-CoV transmits only through close contact with an infected person, the outbreak was easily contained. According to CDC, close contact in the case of SARS included caring for or living with a SARS patient or directly being exposed to body fluids or respiratory secretions of a SARS patient [50]. This pandemic witnessed high mortality, especially in the regions of Southeast Asia and Canada. The consequence of this pandemic was also the subsequent economic loss worldwide that accounted to nearly 40 billion dollars [52].

2.2 Middle East Respiratory Syndrome (MERS)

The SARS-CoV outbreak was followed by the MERS-CoV outbreak in Saudi Arabia in the year 2012. MERS-CoV related respiratory tract infections were mainly seen in Middle East countries. The main animal reservoir host of MERS-CoV is said to be dromedary camels though the exact role of the camels in virus transmission is unknown. Like the spread of SARS-CoV, MERS-CoV transmits through close contact with an infected person [53]. Since the year 2012, MERS cases have been reported in 27 countries, of which 80% of the cases reported are from Saudi Arabia [53]. Treatments and vaccines for MERS is still under development. Until 31st March 2020, WHO has received reports of 2553 MERS-CoV cases globally which includes 876 associated deaths [54].

2.3 Corona virus disease 2019 (COVID-19)

In the end of December 2019, there was a sudden outbreak of pneumonia of unknown cause in Wuhan City, Hubei Province of China. A total of 44 cases of pneumonia with 11 cases being in critical condition was reported to WHO as of January 3, 2020 [55, 56]. Investigation showed that majority of the patients had visited Huanan Seafood market, a local market of fish and wild animal. Initial observation of isolated virus from lung fluid and throat swabs of patients showed striking similarity to coronavirus and the epidemiology of the outbreak was also very similar to the outbreak of SARS in 2003 giving it the name SARS-CoV-2 [56, 57]. On 30th January 2020, the outbreak of COVID-19 was declared to be a Public Health Emergency of International Concern by WHO. WHO officially named the new coronavirus disease on 11th February 2020 as COVID-19 [58].

Though each of the three corona viruses has caused respiratory disease outbreaks, they have their own unique features. COVID-19 is more infectious and spreads easily among people, increasing the number of cases. The fatality rates of SARS and MERS are significantly higher than that of COVID-19. In spite of the lower case fatality rate, when compared to SARS and MERS, COVID-19 has higher overall number of deaths. MERS is an ongoing public health concern, while the number of cases recorded of SARS is nil for over a decade [59].

2.4. Economic impact due to corona-based pandemics

Ceylan and Ozkan have studied the impact of SARS, MERS and COVID-19 on the economic conditions, labour market and income level. The extent of spread of the disease is a major factor controlling the economy. SARS was more fatal and had a depreciating effect on all economies when compared to MERS which was restricted to a few countries. It has been shown that both supply and demand effects are very evident for COVID-19, giving a bi-directional economic impact [60]. With the risk of being exposed to the virus when outside the house, the demand for online shopping has been tremendous. Unemployment has been on the rise; the reduced income and productivity has further discouraged leisure spending [61]. This has impacted almost every economic sector that entail human workforce. Lockdown and quarantine rules all over the world have been a huge set-back for the aviation and tourism sector. The construction industries have been faced with unavailability of labors and a fluctuation in the prices of construction materials [62]. With the impact that the ongoing pandemic has had on the day to day life, the recovery of the economic conditions to normality might take several years.

If a direct comparison is made for the SARS-CoV, MERS-CoV and SARS-CoV-2, the per capita GDP was not affected much during the first corona-based pandemic. Hong Kong felt the most of tremors during 2002-2003 with a decline of 2.79% and a brief economic volatility in China and South Korea followed by a slow growth rate across the world for few years. However, the impact caused by MERS-CoV was far more visible. A decline in the real per capita GDP was witnessed in the gulf countries, especially a decline of 12% in the UAE, 16% is Saudi Arabia, 25% in Qatar and 32% in Kuwait [60]. Nevertheless, the economic impact of the ongoing COVID-19 pandemic is far more overwhelming as it is neither concentrated to the far East or West Asian bloc of countries, but on a worldwide scale. A study conducted by McKibbin and Fernando [63] rightly indicated a strong decline in the global income by 6.7% as per the predictions made after considering the 2019 figures with a reflection on the first half of 2020. Certain projections made by international organizations like International Labor Organization and International Monetary Fund were quite devastating. The former estimated a loss of 309 million full-time jobs in the second quarter of 2020 and the latter forecasted a global growth rate shrinkage of -6.3% [60].

2.5. Impact on medical psychology due to corona-based pandemics

With a prior experience of the devastation caused by epidemics and pandemics, the importance and seriousness of keeping a check on possible outbreaks of diseases has increased. With a larger population of people being affected across the globe at an alarming rate, it becomes necessary to take drastic measures to contain the spread of the disease. Quarantine and social distancing are the initial rule that the government imposes on the general public whenever disease transmission is by close contact. These lockdown and quarantine rules greatly impact the psychological state of an individual, causing distress, depression, anxiety and PTSD (post-traumatic stress disorder).

Joel Vos has performed a meta-analysis on the psychological impact of SARS, MERS and COVID-19 on the human population [64]. This study showed that during the pandemics of SARS and MERS, 15% of the general population, 31% of the patients and 33% of health care workers experienced various psychological symptoms. The study showed that during the ongoing pandemic 25% of the general population and 32% of the patients suffer from various psychological symptoms. 59% of health care workers experience post-traumatic stress and 37% experienced depression, insomnia and anxiety [64]. The COVID-19 pandemic seems to have a larger and more severe impact on the psychological state of individuals. In the present scenario, with the increase in COVID-19 cases, access to medical care for other treatments has drastically reduced. Patients requiring routine checkups, medications and treatments get more anxious which further affects their mental and physical health [65, 66]. Moreover, health care workers are overburdened with increased working hours coupled with the higher risk of infection at the workplace [66, 67].

Lastly, a study by Gonzalez et al., in Spain focused on the effect of the pandemic on higher education [68]. This study showed that the shift of classes to an online system has enabled the students to develop the habit of studying on a more continuous basis. An improvement in the efficiency of the student is expected in the future [68]. However, educational sector that requires real-time training such as research, medicine, engineering to mention a few have faced major setbacks [69, 70].

Table 3. Evaluation of the epidemiology, pathogenesis and clinical characteristics between three corona-based pandemics

Corona based pandemics	SARS-CoV	MERS-CoV	SARS-CoV-2	References
		Epidemiology		
Year of outbreak	2003	2012	2019	[44]
Place of origin	Guangdong, China	Saudi Arabia	Wuhan, China	[44]
Animal reservoir	Bats	Bats	Bats	[44]
Intermediary host	Palm civet	Dromedary camel	Pangolin	[71]
Incubation period (Days)	2-7	5-6	4-14	[72-74]
Time to infect first 1000 people (Days)	130	903	48	[44]
Case fatality rate	9.5%	34.4%	2.2%	[72, 75, 76]
No. of cases confirmed	8096	2468	130,422,190	[72, 75, 76]
No. of Countries affected	29	27	>223	[72, 75, 76]
Reproductive Number† (R_o)	1.7-1.9	0.7	2-2.5	[77]
Route transmission	Respiratory droplets transmission or direct person-to person transmission through local contact	A blend of long-range airborne and nearby contact routes	Airway, contact transmission and aerosol transmission	[71]
		Pathogenesis and clinical characteristics		
Cell receptor in humans	Angiotensin-converting enzyme 2 (ACE2)	Dipeptidyl peptidase 4 (DPP4)	Angiotensin-converting enzyme 2 (ACE2)	[44]
Respiratory tract symptoms	Upper respiratory, gastrointestinal symptoms	Upper respiratory, gastrointestinal symptoms	Pneumonia, lower respiratory symptoms	[71]
Key symptoms	Breathing difficulties, cough, diarrhoea, fever, headache, lethargy, muscle pain, shivering and sore throat	Abdominal pain, cough, fever, muscle pain, shortness of breath and vomiting	Cough, difficulty to breathe, fever, shortness of breath and pneumonia	[77, 44]

†Reproductive number (RO) is defined as the transmission potential of a disease.

3. Roadmap on medical perspective of COVID-19

Ever since COVID-19 was declared as a pandemic, there has been an insurgence amongst researchers to divert their attention on this topic. However, with the social media being hyperactive regarding COVID-19 and the general public going haywire, an abundance of misleading information is under circulation. As a disastrous consequence, an *'infodemic'* is witnessed whereby, a situation is created leading to inaccessibility of legit information on the medical perspective of COVID-19. For simplification, this section highlights the key developments for the diagnosis and treatment of COVID-19 along with a note on the role of nanotechnology to tackle the ongoing pandemic.

3.1. Covid-19: Diagnosis & treatment

An interesting study by Menni et al., summarizes their extensive work on real-time prediction of potential COVID-19 cases based on self-reported symptoms. Along with common flu-like symptoms that include fatigue, persistent cough and loss of appetite, loss of smell and taste is recognized as a major potential predictor of individuals infected with coronavirus 2 [78].

The prior experience of detecting SARS-CoV (coronavirus) paved the way for identifying the current COVID-19 virus in a much relatable manner. Earlier, SARS-CoV was identified using transmission electron microscopy in the span of 5 months whereas SARS-CoV-2 was identified by genome sequences technique in just 18-20 days [79, 80]. The rapid detection and sequencing facilitated the immediate improvement of nucleic acid tests for SARS-CoV-2. The quick realization of the existence of a deadly virus played a vital role in the efforts to curb the outbreak and bolstered the researchers to have an in-depth utilization of the diagnostic tools to detect and limit the spread of coronavirus 2 [80-82]. These include real-time reverse-transcription PCR (rRT-PCR) [80, 83], loop mediated isothermal amplification (LAMP) [80], computed tomography (CT) scan [84, 85], ELISA [81, 83] and conventional antigen-antibody interactions [78].

As there is no specific vaccine that has been commercialized for treating patients with COVID-19, an alternative method that has been widely recommended is 'drug repurposing'. Various attempts in the form of clinical trials and investigation on drug repurposing have been carried out. These infer that viable analysis of medical condition of humans is the faster and cost-effective way of identifying drugs for treating various clinical characteristics [86-88]. Durojaiye et al., accounted *in silico* studies hypothesizing that cefuroxime can be the drug repurposed for tackling COVID-19 as it may inhibit three key proteins of coronavirus 2, namely, main protease (Mpro), RNA dependent RNA polymerase and angiotensin converting enzyme 2(ACE-2) spike protein binding complex. However, the realization of the multi-target inhibitor to combat COVID-19 pandemic depended on the clinical efficacy and safety profile of cefuroxime [89]. Furthermore, in the second half of 2020, chloroquine phosphate and hydroxychloroquine (HQC) were tested for treatment and it displayed a noteworthy result for many of the COVD-19 infected patients with better lung image and overall improvement [90-93]. However, the search for the 'right vaccine' is still an ongoing journey.

3.2. Covid-19: Vaccine and medicine

Pandemics are associated with the disease spreading worldwide at a catastrophic rate. Providing with an effective vaccination has been the primary approach to control such disease outbreaks. As mentioned in section 1, vaccines have been developed in the past for diseases such as influenza, plague, cholera etc. The entire process starting from the initiation to production of vaccines take many years, with the involvement of a large work force turning it into a very expensive and time consuming process [94]. Since the outbreak of COVID-19, medical and vaccine research for a solution has been fast tracked worldwide with varied outcomes.

A wide variety of vaccines are being designed, produced and tested worldwide for COVID-19 by various approaches such as immunotherapy, mRNA, to name a few [86, 95-99]. However, the continual mutations in the genome sequence coding has shed uncertainty to these methods. Antibody therapy which was successful in the Ebola outbreak caused immune dysregulation when tested against coronavirus 2 infection [100]. Since the beginning of this pandemic, researchers have also explored pre-existing medicines such as chloroquine and remdesivir for the treatment of COVID-19. HCQ, FaviPavir and remdesivir were found to block coronavirus 2 while paronavir & INF2 inhibited the infection [92, 93, 101].

A case study of the relation between the mortality rate by COVID-19 and the MMR (measles, mumps and rubella) vaccine was performed in Cambridge [102]. Sequence homology was observed between coronavirus 2 and measles, mumps and rubella viruses. This study showed that the MMR vaccine could play a vital role in minimalizing the transmission of the COVID-19 disease [97, 102]. A phase 1 trial of an adenovirus type-5 vectored COVID-19 vaccine carried out in Wuhan evaluated the T-cell responses after intramuscular vaccination. No serious adverse effects were reported even after 4 weeks of vaccination while specific T-cell response peaked after the initial 2 weeks. This vaccine was demonstrated as acceptable and immunogenic after 4 weeks of vaccine administration [86]. As per the official website of Centers for Disease Control and Prevention (CDC), Pfizer-BioNTech COVID-19 vaccine and Moderna's COVID-19 vaccine are the currently recommended vaccines to prevent the spread of this pandemic [26]. Furthermore, as per CDC's reports updated on 15th January 2021, in the USA, phase 3 clinical trials of AstraZeneca's, Janssen's and Novavax's COVID-19 vaccines are in progress [26]. Continuous updates of medical advancements in the treatment of COVID-19 are periodically provided by the World Health Organization (WHO) [103].

Nanotechnology, a modern approach, is being explored effectively to alleviate the pandemic situation. The use of nanotechnology to produce effective carriers (nanocarriers) of medicine to the target has been widely studied in the past years. The major drawback of a nanocarrier can be its compatibility with the host cell. The effective and safe use of nanotechnology for COVID-19 treatment is currently being explored thoroughly as described in the following section [104, 105].

3.3. Covid-19: Solution from nanotechnology?

Various nuances of nanotechnology are being exploited as effective means for early diagnosis of Covid-19 due to the availability of highly specific & sensitive nanodevices [106-109]. These nanodevices are employed to study the biological mechanism of virus and subsequently, to develop a suitable vaccine for annihilation of the virus [110-112]. Currently, advances in nanotechnology has resulted in manufacture of gloves, goggles, masks, PPE kits and filters to inhibit the spread of virus [113]. From a medical perspective, nanomaterials are a hot topic studied fervently for the detection, treatment and prevention of viruses. These materials have been previously used as promising antiviral agents. A classic example is that of silver nanoparticles displaying promising results to tackle Hepatitis B, herpes, monkeypox to mention a few [109, 112]. On the other hand, studies have strongly suggested that graphene can be used for screening and designing nano-biosensors for the detection of viruses and for drug efficiency testing [108]. Moreover, a new class of nanomaterial that uses external magnetic field for biosensing tactics are super-paramagnetic nanoparticles that have caught the attention of researchers to detect COVID-19 [114].

Nanomaterials are reported to have antimicrobial activities that inhibit viruses. One such example is TiO_2 nanoparticles that annihilate nipah virus [106, 107, 115]. Various other nanoparticles such as gold or lipid nanoparticles are used to block S protein, the initiator of virus life cycle [116]. Thus, for the effective vaccination against coronaviruses, S protein, the immunodominant antigen in coronavirus 2 is targeted. Potential alternatives currently under study include chiral gold nanohybrids with quantum dots and nanostructured boronic acid-functionalized quantum dots that easily enter the genome and prevent the replication of coronavirus [117, 118]. As per the ongoing scientific trends and ever increasing publications in the field of nanomedicine, a finite and promising role of nanotechnology in combating the current pandemic is expected in the near future.

4. Web of Science™

Web of Science™ (WoS), which was known previously as web of knowledge, is a global, citation database which is publisher independent and owned by Clarivative™ analytics [119]. The work of Dr. Eugene Garfield, who created the world's first citation index, led to the formation of WoS. It is a multidisciplinary platform which connects research data and publications from all over the world, across various research categories. Clarivative™ claims that the core collection of WoS is highly selective and the indexing is accurate, complete and consistent over at least 50 years [119]. The Core Collection of WoS Citation Indexes consists of 6 online database: Science Citation Index Expanded, Social Sciences Citation Index, Arts & Humanities Citation Index, Emerging Sources Citation Index, Conference Proceedings Citation Index- Social Science & Humanities and Conference Proceedings Citation Index - Science. Some of these databases cover research from the year 1900 [120]. WoS also has a Core Collection of Chemical Indexes which include Current Chemical Reactions and Index Chemicus.

In this review the Web of Science Core Collection Citation Indexes was used. The data discussed in this article was collected on the 04th of April 2021. Since the number of publications on the ongoing pandemic is increasing rapidly on a daily basis, collection of all the data on the same day normalizes the results. The term "COVID-19" was used as the keyword and the search was carried out by *Topic*. Based on the filters available such as countries of publication, categories of research, funding agencies, language etc., an understanding of the impact of COVID-19 on research publications was studied.

4.1. Results

The search by topic option of the Web of Science™ platform was used to obtain the results. This search would give back results of every kind of scientific publication related to the input keyword. A search of "COVID-19" as the keyword returned 98,020 scientific works of which 54,304 were research articles and 10,223 were review articles. The first scientific publication as per WoS was in 2019 with 76,940 works published in 2020. Figure 1 details the various types of scientific documents available on COVID-19.

Fig. 1 WoS - Types of documents available on COVID-19 [120]

4.1.1. Publications by language and region

COVID-19 related literature has been published by researchers from over 220 countries. USA, China and England are ranked in the top three with 27334, 10732 and 9574 number of works, respectively. Figure 2 illustrates the distribution of literature across the continents. Europe has published the highest number of works with a total of 51,637 publications (52.7% of the total). 95.3% of the total publications (93,404), the majority, was in the English language followed by Spanish and German as the next highest.

Fig. 2 Literature available on COIVD-19 across continents [120]

4.1.2. Categories of research

Research on the ongoing pandemic has spread rapidly across numerous fields in the scientific world since December 2019. Figure 3 depicts the top 25 categories on WoS with the highest number of publications on COVID-19. Publications in health sciences is booming with 13,738 works on General Internal Medicine, 8,340 on Public Environmental Occupational Health and

4,668 on Infectious Diseases. This number is only expected to tremendously increase in the near future.

Fig. 3 WoS Search: “COVID-19” filtered by Research Areas [120]

4.1.3. Journals, authors and citations

Table 4 depicts the quantity and quality of the COVID-19 based research publications wherein BMJ-British Medical Journal published by British Medical Association (UK) has more than 1000 papers in their repository. It is impressive to see that a journal of high repute with impact factor more than 30 ranks first in terms of quantity of the pandemic based publications. This also hints at the workload witnessed during the peer-review process. Moreover, the top 5 journals that have published works on COVID-19 constitute over 5 % of the total published papers on this pandemic. A single virus has led to substantial variety of research that is being published in innumerous scientific disciplines. Furthermore, in terms of quality of the journals indicated by their impact factor, the top 5 journals with highest impact factor in 2020 have reported around 1 % of the total publications based on COVID-19. Among these 5 journals, Lancet journal ranks highest to publish 494 articles having impact factor of over 60. These results are in accordance with the general trend of research wherein a small fraction of very high quality of research gets published in the best journals in scientific community.

The statistics of the top 10 papers with highest citations is detailed in Table 5. One of the pioneering work by Guan W. *et al.,* on the ‘Clinical Characteristics of Coronavirus Disease 2019 in China’ has received over 7,500 citations. This paper published in 2020 by New England Journal of Medicine has an impressive impact factor of around 75. The second in this list is the work published by Zhou F. *et al.,* in Lancet journal which also has a remarkable impact factor of over 60. The work titled ‘Clinical Course and Risk Factors for Mortality of Adult Inpatients with COVID-19 in Wuhan, China: A Retrospective Cohort Study’ has received 6,764 citations. These two papers indicate that around 15 % of the total papers published so far have cited these two works. A closer look at the list of top 10 papers suggests the dominance of Chinese origin researchers in this field of research. Furthermore, the trend follows the general perception that biological sciences receive more citations, as COVID-19 based research has received most citations for the works conducted in clinical pathology, immunology, virology, neurology to mention a few. The current trend also emphasizes that conducting pioneering research in a hot topic attracts more scientific views and subsequent citations.

Table 4: WoS studies on the various journals publishing COVID-19 based articles [120]

TOP 5 JOURNALS WITH HIGHEST NUMBER OF PAPERS PUBLISHED				
S. NO.	NAME OF JOURNAL	PUBLISHER	IMPACT FACTOR	NO. OF PUBLICATIONS
1	BMJ-British Medical Journal	British Medical Association, UK	30.22	1440
2	International Journal of Environmental Research and Public Health	Multidisciplinary Digital Publishing Institute (MDPI), Switzerland	2.85	1120
3	PLOS ONE	Public Library of Science, USA	2.74	889
4	Journal of Medical Virology	Wiley Publishers, USA	2.02	768
5	Cureus	Cureus, Inc., USA	NA	700
TOP 5 HIGHEST IMPACT FACTOR JOURNALS AND THE PAPERS PUBLISHED				
S. NO.	NAME OF JOURNAL	PUBLISHER	IMPACT FACTOR	NO. OF PUBLICATIONS
1	CA-A Cancer Journal for Clinicians	Wiley Publishers, USA	292.28	4
2	New England Journal of Medicine	Massachusetts Medical Society, USA	74.70	340
3	Nature Reviews Materials	Nature Publishing Group, UK	71.19	5
4	Nature Reviews Drug Discovery	Nature Research, UK	64.80	23
5	LANCET	Elsevier, Netherlands	60.40	494

Table 5: List of top 10 research publications with most citations related to COVID-19 [120]

S. No.	Title of Publication	Authors	Journal of Publication	Journal Impact Factor	Citation Count
1	Clinical Characteristics of Coronavirus Disease 2019 in China	Guan, W. *et al.*, 2020	New England Journal of Medicine	74.699	7677
2	Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study	Zhou, F. *et al.*, 2020	LANCET	60.392	6764
3	Pathological findings of COVID-19 associated with acute respiratory distress syndrome	Xu, Z. *et al.*, 2020	Lancet respiratory medicine	25.094	2520
4	Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area	Richardson, S. *et al.*, 2020	JAMA-Journal of the American Medical Association	45.540	1923
5	Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial	Gautret, P. *et al.*, 2020	International Journal of Antimicrobial Agents	4.621	1913
6	Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China	Wu, C. *et al.*, 2020	JAMA Internal Medicine	18.652	1843
7	A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19	Cao, B. *et al.*, 2020	New England Journal of Medicine	74.699	1680
8	Neurologic Manifestations of Hospitalized Patients with Coronavirus Disease 2019 in Wuhan, China	Mao, L. *et al.*, 2020	JAMA Neurology	13.608	1590
9	The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2	Gorbalenya, A. E. *et al.*, 2020	Nature Microbiology	15.540	1564
10	Immediate Psychological Responses and Associated Factors during the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic among the General Population in China	Wang, C. *et al., 2020*	International Journal of Environmental Research and Public Health	2.849	1480

Conclusions

Man-made and natural disasters have been witnessed by humankind for time immemorial. The pages of history have always been stirred whenever the casualties are deaths of humans. Healthcare organizations across the world have put in innumerable efforts to either prevent or counter such devastating instances, including endemics, epidemics and pandemics. As this century witnesses one of the most impactful achievements in terms of telecommunication and digitalization, the byproduct is intensification of any incidence, positively or negatively. In this scenario, the era of COVID-19 lockdown has to bear the imprints of *"infodemic"*. The governmental and other societal infrastructures need to gear up with not only creating awareness among the people about public healthcare, but also to keep a check on circulation of any misleading information. Although the preceding pandemics have seen much more deaths than COVID-19, the current pandemic has shaken the roots of so many infrastructural entities. Universal change of order in daily routine has become a necessity. The world being locked inside houses and the global experiment of 'work from home' has led to numerous alarming possibilities of devastating nature that includes bioterrorism. This paper has attempted to simplify the lineage of pandemics and distinguish the other related endemics or epidemics. Moreover, a detailed account of the coronavirus based health scare and its biological differentiation has been presented for varied scientific discipled readers.

Since the effects of COVID-19 are far stretched, the scientific community too has faced its beats. In the present age of social media going haywire, any instance turning viral is a new norm. This review also captures the ongoing scientific research trends impacted by COVID-19. Remarkably, in over 15 months of this bioterror, more than 98,000 publications have been added to the scientific literature, out of which 56 % are experimental-based journal papers. Interestingly, scientometric analysis reveals the plethora of scientific backgrounds that are interested to conduct research engulfing COVID-19. The wide range of disciplines of immunology, psychology, ecology, public occupational health and psychiatry are in the top 10 research fields to publish papers on COVID-19. Moreover, the journal to publish the largest number of papers on COVID-19 is BMJ-British Medical Journal, which is having an impact factor of over 30. This testifies that groundbreaking research is being carried out to address the present need. Furthermore, a jump in the scientific rating of a researcher working on COVID-19 is expected with the rise in *h-index* and *i10-index* due to the increased citations. To sum up, every problem accompanies an opportunity that holds true to the scientific community as well.

References

[1] Madhav, N., Oppenheim, B., Gallivan, M., Mulembakani, P., Rubin, E., and Wolfe, N. (2017). Pandemics: risks, impacts, and mitigation, 3rd ed., pp.315-345, DOI: 10.1596/978-1-4648-0527-1_ch17.

[2] WHO: "Disease outbreaks by year" https://www.who.int/csr/don/archive/year/en/, Visited 11 February 2021.

[3] WHO: "Emergencies preparedness, response," The Weekly Epidemiological Record, 13 May 2016, https://www.who.int/csr/disease/epidemic-focus/global-epidemic-response/en/, Visited 11 February 2021.

[4] CDC: Emergency preparedness and response https://emergency.cdc.gov/index.asp, Visited 11 February 2021.

[5] WHO: "Emergencies: Disease outbreaks," United Nations Economic and Social Council, https://www.who.int/emergencies/diseases/en/, Visited 11 February 2021.

[6] Preston, T. (2020) Pandemic: A Brief History of Influenza, The Plague, Cholera, and other Infectious Diseases That Have Changed the World; How They Started, How They Ended, and the Lessons Learned by Humanity. Independently published. ISBN: 9798640289725.

[7] Saluja, T., Mogasale, V. V., Excler, J. L., Kim, J. H., and Mogasale, V. (2020) An overview of Vaxchora™, a live attenuated oral cholera vaccine. Hum. Vaccines Immunother, 16(1), 42-50. DOI: 10.1080/21645515.2019.1644882.

[8] Khan, U., Mehta, R., Arif, M. A., and Lakhani, O. J. (2020) Pandemics of the past: a narrative review. Public Health, J. Pak Med Assoc. 70(5), 34-37.

[9] Neuzil, K. M., and Ortiz, J. R. (2016) Influenza vaccines and vaccination strategies. In The Vaccine Book, 2nd ed., pp.423-444, Academic Press.

[10] Benedictow, O. J. and Benedictow, O. L. (2004) The black death. *The Complete History: Boydell and Brewer*, pp.1346-1353.

[11] CDC: "Plague Vaccine," https://www.cdc.gov/mmwr/preview/mmwrhtml/00041848.htm, Visited 11 February 2021.

[12] DeLeo, F. R., & Hinnebusch, B. J. (2005). A plague upon the phagocytes. Nat. Med., 11(9), 927-928. DOI: 927-928. 10.1038/nm0905-927.

[13] Mordechai, L., Eisenberg, M., Newfield, T. P., Izdebski, A., Kay, J. E., and Poinar, H. (2019) The Justinianic Plague: an inconsequential pandemic?. *Proc. Nat. Acad.of Sci.s*, *116*(51), 25546-25554. DOI: 10.1073/pnas.1903797116.

[14] Sarris, P. (2002) The Justinianic plague: origins and effects. *Continuity and change*, *17*(2), 169-182. DOI: 10.1017/S0268416002004137.

[15] Patterson, K. D., and Pyle, G. F. (1991) The geography and mortality of the 1918 influenza pandemic. *Bull.Hist. Med.*, *65*(1), 4-21.

[16] WHO: "Types of seasonal influenza vaccine," https://www.euro.who.int/en/health-topics/communicable-diseases/influenza/vaccination/types-of-seasonal-influenza-vaccine, Visited 11 February 2021.

[17] CDC: 1918 Pandemic (H1N1 virus) https://www.cdc.gov/flu/pandemic-resources/1918-pandemic-h1n1.html, Visited 11 February 2021.

[18] Sharp, P. M., and Hahn, B. H. (2011) Origins of HIV and the AIDS pandemic. *Cold Spring Harbor Perspect. Med.*, *1*(1), DOI: 10.1101/cshperspect.a006841.

[19] WHO: "HIV Vaccines- WHO," https://www.who.int/hiv/topics/vaccines/Vaccines/en/, Visited 11 February 2021.

[20] Fauci Anthony, S., and Fauci, M. D. (2017) An HIV Vaccine is Essential for Ending the HIV/AIDS Pandemic.*, J. Am. Med. Assoc., 318(16), 1535.* DOI:10.1001/jama.2017.13505.

[21] WHO: The Global Health Observatory (GHO) data https://www.who.int/gho/hiv/en/, Visited 11 October 2020.

[22] Lynteris, C. (2019) Pestis Minor: The History of a Contested Plague Pathology. *Bull. Hist. Med.*, *93*(1), 55-81. DOI: 10.1353/bhm.2019.0002.

[23] Bramanti, B., Dean, K. R., Walløe, L., and Chr. Stenseth, N. (2019) The third plague pandemic in Europe. *Proc. R. Soc. B*, *286*(1901), 20182429. DOI: 10.1098/rspb.2018.2429.

[24] C. Haas, (2006) The Antonine plague, Bull. Acad. Natl. Med., 190(4), 1093-1098. DOI: 10.1016/s0001-4079(19)33258-3.

[25] Rigau-Pérez J. G. (2006) The Power of Plagues. *Emerging Infect. Dis.*, 12(10):1625-1626. DOI:10.3201/eid1210.060803.

[26] CDC: Different COVID-19 Vaccines https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines.html, Visited February 2021.

[27] CDC: 1957-1958 Pandemic (H2N2 virus) https://www.cdc.gov/flu/pandemic-resources/1957-1958-pandemic.html, Visited 11 February 2021.

[28] CDC: (1968) Pandemic (H3N2 virus) https://www.cdc.gov/flu/pandemic-resources/1968-pandemic.html, Visited 11 February 2021.

[29] Harper, K. (2015) Pandemics and passages to late antiquity: Rethinking the plague of c. 249–270 described by Cyprian. *J. Roman Archaeol.*, *28*, 223-260. DOI: 10.1017/S1047759415002470.

[30] J. N. Hays, "Epidemics and pandemics: their impacts on human history," 2005. [Online]. Available: https://archive.org/details/epidemicspandemi0000hays. [Accessed 4 September 2020].

[31] Azizi, M. H., and Azizi, F. (2010) History of Cholera Outbreaks in Iran during the 19th and 20th Centuries. Middle East J. Dig. Dis. *2*(1), 51.

[32] Ewing, E.T., Kimmerly, V. and Ewing-Nelson, S. (2016) Look out for 'la grippe': Using digital humanities tools to interpret information dissemination during the Russian flu, 1889–90. *Medical history*, *60*(1), 129-131. DOI: 10.1017/mdh.2015.84.

[33] Kilbourne, E. D. (2006). Influenza pandemics of the 20th century. *Emerging infect. Dis.*, *12*(1), 9.

[34] Rozo, M., and Gronvall, G. K. (2015) The reemergent 1977 H1N1 strain and the gain-of-function debate. *MBio*, *6*(4), 1-6. DOI: 10.1128/mBio.01013-15.

[35] Girard, M. P., Tam, J. S., Assossou, O. M., and Kieny, M. P. (2010) The 2009 A (H1N1) influenza virus pandemic: A review. *Vaccine*, *28*(31), 4895-4902. DOI: 10.1016/j.vaccine.2010.05.031.

[36] Scasciamacchia, S., Serrecchia, L., Giangrossi, L., Garofolo, G., Balestrucci, A., Sammartino, G., and Fasanella, A. (2012) Plague epidemic in the Kingdom of Naples, *Emerging infect. Dis.*, *18*(1), 1656–1658. DOI: 10.3201/eid1801.110597.

[37] Sun, W. and Singh, A., K. (2019) Plague vaccine: recent progress and prospects. npj Vaccines, 4(11), DOI: 10.1038/s41541-019-0105-9.

[38] Meyer, K. F., Smith, G., Foster, L., Brookman, M., and Sung, M. (1974) Live, attenuated Yersinia pestis vaccine: virulent in nonhuman primates, harmless to guinea pigs. *J. Infect. Dis.*, *129*, 85-120. DOI: 10.1093/infdis/129.Supplement_1.S85.

[39] Demeure, C. E., Dussurget, O., Fiol, G. M., Le Guern, A. S., Savin, C., and Pizarro-Cerdá, J. (2019). Yersinia pestis and plague: an updated view on evolution, virulence determinants,

immune subversion, vaccination, and diagnostics. *Genes & Immunity*, *20*(5), 357-370. DOI: 10.1038/s41435-019-0065-0.

[40] Bertherat, E.(2019) Plague around the world in 2019. *Weekly Epidemiological Record*, *94*(25)*, 289-292*.

[41] Peters, P. J., Marston, B. J., and De Cock, K. M. (2014) HIV: Epidemiology in the Tropics. In Manson's Tropical Infectious Diseases (pp. 68-78). WB Saunders. DOI: 10.1016/B978-0-7020-5101-2.00010-8.

[42] WHO: HIV/AIDS https://www.who.int/health-topics/hiv-aids/#tab=tab_1, Visited 12 February 2021.

[43] Fan, Y., Zhao, K., Shi, Z-L. and Zhou, P. (2019) Bat coronaviruses in China. *Viruses*, *11*(3), 210. DOI: 10.3390/v11030210.

[44] Rabaan, A. A., Al-Ahmed, S. H., Haque, S., Sah, R., Tiwari, R., Malik, Y. S., Dhama, K., Yatoo, M. I., Bonilla-Aldana, D. K. and Rodriguez-Morales, A. J. (2020) SARS-CoV-2, SARS-CoV, and MERS-CoV: a comparative overview. *Infez. Med. 28*(2), 174-184.

[45] Ludwig, S., and Zarbock, A. (2020) Coronaviruses and SARS-CoV-2: A brief overview. *Anesth. Analg. 131*(1), 93–96. DOI: 10.1213/ANE.0000000000004845.

[46] Lai, M. M. (1992) RNA recombination in animal and plant viruses. *Microbiol. Mol. Biol. Rev. 56*(1), 61-79.

[47] Bijlenga, G., Cook, J. K. A., Gelb, Jr, J. and de Wit, J. J. (2004) Development and use of the H strain of avian infectious bronchitis virus from the Netherlands as a vaccine: a review. *Avian Pathol. 33*(6), 550-557. DOI: 10.1080/03079450400013154.

[48] Wong, G., Bi, Y-H., Wang, Q-H., Chen, X-W., Zhang, Z-G. and Yao, Y-G. (2020) Zoonotic origins of human coronavirus 2019 (HCoV-19/SARS-CoV-2): why is this work important?. *Zool. Res. 41*(3), 213-219. DOI: 10.24272/j.issn.2095-8137.2020.031.

[49] Ye, Z-W., Yuan, S., Yuen, K-S., Fung, S-Y., Chan, C-P. and Jin, D-Y. (2020) Zoonotic origins of human coronaviruses. *Int. J. Biol. Sci.*, *16*(10), 1686–1697. DOI: 10.7150/ijbs.45472.

[50] CDC: Basic Factsheet for SARS https://www.cdc.gov/sars/about/fs-sars.html, Visited 12 February 2021.

[51] Ge, X-Y., Li, J. L., Yang, X. L., Chmura, A. A., Zhu, G., Epstein, J. H., Mazet, J. K., Hu, B., Zhang, W., Peng, C., Zhang, Y-J., Luo, C-M., Tan, B., Wang, N., Zhu, Y., Crameri, G., Zhang, S-Y., Wang, L-F., Daszak, P. and Shi, Z. -L. (2013) Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature*, *503*(7477), 535-538. DOI: 10.1038/nature12711.

[52] Fehr A.R. and Perlman S. (2015) Coronaviruses: An Overview of Their Replication and Pathogenesis. In Coronaviruses. Methods in Molecular Biology, (Maier H., Bickerton E., Britton P., eds). Vol 1282, pp. 1-23. Humana Press, New York, NY. https://doi.org/10.1007/978-1-4939-2438-7_1

[53] WHO: Factsheet for MERS-CoV https://www.who.int/news-room/fact-sheets/detail/middle-east-respiratory-syndrome-coronavirus-(mers-cov), Visited 12 February 2021.

[54] WHO: MERS-CoV – Disease Outbreak News https://www.who.int/csr/don/05-may-2020-mers-saudi-arabia/en/, Visited 12 February 2021.

[55] WHO: Pneumonia of unknown cause – China https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/, Visited 12 February 2021.

[56] Lu, H., Stratton, C. W. and Tang, Y-W. (2020) Outbreak of pneumonia of unknown etiology in Wuhan, China: the mystery and the miracle. *Journal of medical virology*, *92*(4), 401-402. DOI: 10.1002/jmv.25678.

[57] Sohrabi, C., Alsafi, Z., O'Neill, N., Khan, M., Kerwan, A., Al-Jabir, A., Iosifidis, C. and Agha, R. (2020) World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *Int. J. Surg. 76*, 71-76. DOI: 10.1016/j.ijsu.2020.02.034.

[58] WHO: WHO Director-General's Remarks at the Media Briefing on 2019-nCoV on 11 February 2020 https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020, Visited 12 February 2021.

[59] Luo, M., Guo, L., Yu, M., Jiang, W. and Wang, H. (2020) The psychological and mental impact of coronavirus disease 2019 (COVID-19) on medical staff and general public–A systematic review and meta-analysis. *Psychiatry Res. 291,* 113190. DOI: 10.1016/j.psychres.2020.113190.

[60] Ceylan, R. F. and Ozkan, B. (2020) The economic effects of epidemics: from SARS and MERS to COVID-19. *Res. J. Adv. Humanit. 1*(2), 21-29.

[61] Baker, S. R., Farrokhnia, R. A., Meyer, S., Pagel, M. and Yannelis, C. (2020) How does household spending respond to an epidemic? Consumption during the 2020 COVID-19 pandemic. *Rev. Asset Pricing Stud.* 10(4), 834-862. DOI: 10.1093/rapstu/raaa009.

[62] Gamil, Y. and Alhagar, A. (2020) The Impact of Pandemic Crisis on the Survival of Construction Industry: A Case of COVID-19. *Mediterr. J. Soc.Sci. 11*(4), 122-128. DOI: 10.36941/mjss-2020-0047.

[63] McKibbin, W. and Fernando, R. (2020) The Economic Impact of COVID-19. In *Economics in the Time of Covid-19*, (Baldwin, R. and di Mauro, B. W., eds), Centre for Economic Policy Research pp. 45-51.

[64] Vos, J., (2020) Prevalence and predictors of the early psychological impact of the COVID-19 pandemic compared with SARS and MERS: A systematic literature review and meta-analysis. Psyarxiv Preprint as stated in DOI: 10.31234/osf.io/mupk2

[65] Singh, A., Goyal, N., Chouksey, D., Telang, K., Jain, R. and Sodani, A. K. (2020) COVID-19 pandemic: impact of lockdown and hospital classification on neurological patients. *Int. J. Community Med. Public Health*, *7*(8), 1. DOI: 0.18203/2394-6040.ijcmph20203097.

[66] Ying, Y., Ruan, L., Kong, F., Zhu, B., Ji, Y. and Lou, Z. (2020) Mental health status among family members of health care workers in Ningbo, China, during the coronavirus disease 2019 (COVID-19) outbreak: a cross-sectional study. *BMC psychiatry*, *20*(1), 1-10. DOI: 10.1186/s12888-020-02784-w

[67] Dewangan, R. L. (2020) Mental Health and related issues during COVID-19. *Indian J. Soc. Psychiatry* (Accepted Manuscript) Available at https://www.researchgate.net/publication/343039664.

[68] Gonzalez, T., de la Rubia, M. A., Hincz, K. P., Comas-Lopez, M., Subirats, L., Fort, S. and Sacha, G. M. (2020) Influence of COVID-19 confinement on students' performance in higher education. *PloS one*, *15*(10), e0239490. DOI: 10.1371/journal.pone.0239490.

[69] Rose, S. (2020) Medical Student Education in the Time of COVID-19. *J. Am. Med. Assoc.* 323(21), 2131-2132. DOI: 10.1001/jama.2020.5227.

[70] Ahmed, H., Allaf, M. and Elghazaly, H. (2020) COVID-19 and medical education. *Lancet Infect. Dis. 20*(7), 777-778. DOI: 10.1016/S1473-3099(20)30226-7.

[71] Zhang, X-Y., Huang, H-J., Zhuang, D-L., Nasser, M. I., Yang, M. H., Zhu, P. and Zhao, M-Y. (2020) Biological, clinical and epidemiological features of COVID-19, SARS and MERS and AutoDock simulation of ACE2. *Infect. Dis.Poverty*, *9*(1), 1-11. DOI: 10.1186/s40249-020-00691-6.

[72] CDC: SARS (10 Years After) https://www.cdc.gov/dotw/sars/index.html, Visited 12 February 2021.

[73] CDC: MERS Clinical Features https://www.cdc.gov/coronavirus/mers/clinical-features.html, Visited 12 February 2021.

[74] CDC: Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19) https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html, Visited 12 February 2021.

[75] WHO: Middle East respiratory syndrome coronavirus (MERS-CoV) https://www.who.int/emergencies/mers-cov/en/, Visited 12 February 2021.

[76] WHO: Coronavirus disease (COVID-19) pandemic https://www.who.int/emergencies/diseases/novel-coronavirus-2019, Visited 4 April 2021.

[77] Petrosillo, N., Viceconte, G., Ergonul, O., Ippolito, G. and Petersen, E. (2020). COVID-19, SARS and MERS: are they closely related?. *Clin. Microbiol. Infect.* 26(6), 729-734. DOI: 10.1016/j.cmi.2020.03.026.

[78] Menni, C., Valdes, A. M., Freidin, M. B., Sudre, C. H., Nguyen, L. H., Drew, D. A., Ganesh, S., Varsavsky, T., Cardoso, M. J., Moustafa, J. S. E-S., Visconti, A., Hysi, P., Bowyer, R. C. E., Mangino, M., Falchi, M., Wolf, J., Ourselin, S., Chan, A. T., Steves, C. J. and Spector, T. D. (2020) Real-time tracking of self-reported symptoms to predict potential COVID-19. *Nat. Med. 26*(7), 1037-1040. DOI: 10.1038/s41591-020-0916-2.

[79] Udugama, B., Kadhiresan, P., Kozlowski, H. N., Malekjahani, A., Osborne, M., Li, V. Y., Chen, H., Mubareka, S., Gubbay, J. B., and Chan, W. C. (2020) Diagnosing COVID-19: the disease and tools for detection. *ACS Nano*. 14(4), 3822-3835. DOI: 10.1021/acsnano.0c02624.

[80] Nguyen, T., Duong Bang, D., and Wolff, A. (2020) 2019 novel coronavirus disease (COVID-19): paving the road for rapid detection and point-of-care diagnostics. *Micromachines*. 11(3), 306. DOI: 10.3390/mi11030306.

[81] Sethuraman, N., Jeremiah, S.S. and Ryo, A. (2020) Interpreting diagnostic tests for SARS-CoV-2. *JAMA*, 323(22), 2249-2251. DOI: 10.1001/jama.2020.8259.

[82] Perera, N. (2020) Diagnosis of COVID-19: the present and the future. *J. Ceylon Coll. Physicians.* 51(1), 48-52. DOI: 10.4038/jccp.v51i1.7887.

[83] Xu, X., Sun, J., Nie, S., Li, H., Kong, Y., Liang, M., Hou, J., Huang, X., Li, D., Ma, T., Peng, J., Gao, S., Shao, Y., Zhu, H., Lau, J. Y-N., Wang, G., Xie, C., Jiang, L., Huang, A., Yang, Z., Zhang, K. and Hou, F. F. (2020) Seroprevalence of immunoglobulin M and G antibodies against SARS-CoV-2 in China. *Nat. Med. 26*(8), 1193-1195. DOI: 10.1038/s41591-020-0949-6.

[84] de Luna, G., Habibi, A., Deux, J-F., Colard, M., d'Orengiani, P. H. D. A-L., Schlemmer, F., Joher, N., Kassasseya, C., Pawlotsky, J. M., Ourghanlian, C., Michel, M., Mekontso-Dessap, A. and Michel, M. (2020) Rapid and severe Covid-19 pneumonia with severe acute chest syndrome in a sickle cell patient successfully treated with tocilizumab. *Am. J. Hematol.* 1-3. DOI: 10.1002/ajh.25833.

[85] Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X. and Cheng, Z., Yu, T., Xia, J., Wei, Y., Wu, W., Xie, X., Yin, W., Li, H., Liu, M., Xiao, Y., Gao, H., Guo, L., Xie, J., Wang, G., Jiang, R., Gao, Z., Jin, Q., Wang, J. and Cao, B. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*, *395*(10223), 497-506. DOI: 10.1016/S0140-6736(20)30183-5.

[86] Zhu, F. C., Li, Y. H., Guan, X. H., Hou, L-H., Wang, W-J., Li, J-X., Wu, S-P., Wang, B-S., Wang, Z., Wang, L., Jia, S-Y., Jiangm H-D., Wang, L., Jiang, T., Hu, Y., Gou. J-B., Xu, S-B., Xu, J-J., Wang, X-W., Wang, W. and Chen, W. (2020) Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial. *The Lancet*. *395*(10240), 1845-1854. DOI: 10.1016/S0140-6736(20)31208-3.

[87] Smetana, K., Rosel, D., and BrÁbek, J. (2020) Raloxifene and Bazedoxifene could be promising candidates for preventing the COVID-19 related cytokine storm, ARDS and mortality. *in vivo*. *34*(5), 3027-3028. DOI: 10.21873/invivo.12135.

[88] Karim H. M. R. and Ahmed, G. (2020) Hydroxychloroquine prophylaxis for SARS-CoV-2 infection among healthcare workers, *Indian J. Med. Res.* 152(1), 119-120. DOI: 10.4103/ijmr.IJMR_2372_20.

[89] Durojaiye, A. B., Clarke, J-R. D., Stamatiades, G. A. and Wang, C. (2020) Repurposing cefuroxime for treatment of COVID-19: a scoping review of in silico studies. *J. Biomol. Struct. Dyn.* 1-8. DOI: 10.1080/07391102.2020.1777904.

[90] Khaliha, H., Bendalla, I. B., Saed, A. and Daw, S. Hydroxychloroquine And Dexamethasone are both possible for treatment of Covid-19. *Int. J. PharmTech Res.* 13(3), 305-308. DOI: 10.20902/IJPTR.2019.130323.

[91] Mustafa, N. (2020) Therapeutic preferences for Coronavirus 2 (SARS-CoV-2) patients. *Int. J. Qual. Res. 15*(1), 1-35. DOI: 10.21203/rs.3.rs-19507/v1.

[92] Gao, J., Tian, Z. and Yang, X. (2020) Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *BioSci. Trends.* 14(1), 72-73. DOI: 10.5582/bst.2020.01047.

[93] Yao, X., Ye, F., Zhang, M., Cui, C., Huang, B., Niu, P., Liu, X., Zhao, L., Dong, E., Song, C., Zhan, S., Lu, R., Li, H., Tan, W. and Liu, D. (2020) In vitro antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Clin. Infect. Dis. 71*(15), 732-739. DOI: 10.1093/cid/ciaa237.

[94] Gouglas, D., Le, T. T., Henderson, K., Kaloudis, A., Danielsen, T., Hammersland, N. C., Robinson, J. M., Heaton, P. M. and Røttingen, J-A. (2018) Estimating the cost of vaccine development against epidemic infectious diseases: a cost minimisation study. *The Lancet Global Health*. *6*(12), e1386-e1396. DOI: 10.1016/S2214-109X(18)30346-2.

[95] Jackson, L.A., Anderson, E.J., Rouphael, N.G., Roberts, P.C., Makhene, M., Coler, R.N., McCullough, M.P., Chappell, J.D., Denison, M.R., Stevens, L.J. and Pruijssers, A.J., (2020) An

mRNA vaccine against SARS-CoV-2—preliminary report. *N. Engl. J. Med. 383,* 1920-1931. DOI: 10.1056/NEJMoa2022483.

[96] Baker, D., Roberts, C. A., Pryce, G., Kang, A. S., Marta, M., Reyes, S., Schmierer, K., Giovannoni, G. and Amor, S. (2020) COVID−19 vaccine−readiness for anti−CD20−depleting therapy in autoimmune diseases. *Clin. Exp. Immunol. 202*(2), 149-161. DOI: 10.1111/cei.13495.

[97] Gold, J.E., Tilley, L. and Baumgartl, W., 2020. MMR vaccine appears to confer strong protection from COVID-19: few deaths from SARS-CoV-2 in highly vaccinated populations https://www.researchgate.net/publication/341354165_MMR_Vaccine_Appears_to_Confer_Strong_Protection_from_COVID-19_Few_Deaths_from_SARS-CoV-2_in_Highly_Vaccinated_Populations. Visited 12 February 2021.

[98] Le, T. T., Andreadakis, Z., Kumar, A., Roman, R. G., Tollefsen, S., Saville, M. and Mayhew, S. (2020) The COVID-19 vaccine development landscape. *Nat Rev Drug Discov*. *19*(5), 305-306. DOI: 10.1038/d41573-020-00073-5.

[99] Lurie, N., Saville, M., Hatchett, R. and Halton, J. (2020) Developing Covid-19 vaccines at pandemic speed. *N. Engl. J. Med. 382*(21), 1969-1973. DOI: 10.1056/NEJMp2005630.

[100] Sewell, H. F., Agius, R. M., Kendrick, D. and Stewart, M. (2020) Vaccines, convalescent plasma, and monoclonal antibodies for covid-19. *BMJ. 370*, m2722. DOI: 10.1136/bmj.m2722.

[101] Dong, L., Hu, S. and Gao, J. (2020) Discovering drugs to treat coronavirus disease 2019 (COVID-19). *Drug Discoveries Ther. 14*(1), 58-60. DOI: 10.5582/ddt.2020.01012.

[102] Young, A., Neumann, B., Fernandez, R., Joannides, A., Reyahi, A., Modis, Y. and Franklin, R. (2020) Homologous protein domains in SARS-CoV-2 and measles, mumps and rubella viruses: preliminary evidence that MMR vaccine might provide protection against COVID-19. *medRxiv*. DOI: 10.1101/2020.04.10.20053207.

[103] WHO: COVID-19 Vaccines https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines?gclid=Cj0KCQjwoJX8BRCZARIsAEWBFMJMDlIsQL0Fj068BmlAw8EfMXlgy2gVSN9oKHwDC88mkjNoco_Kg9YaAq3CEALw_wcB, Visited 12 February 2021.

[104] Theobald, N. (2020) Emerging vaccine delivery systems for COVID-19: Functionalised silica nanoparticles offer a potentially safe and effective alternative delivery system for DNA/RNA vaccines and may be useful in the hunt for a COVID-19 vaccine. *Drug Discovery Today, 25(9),* 1556-1558. DOI: 10.1016/j.drudis.2020.06.020.

[105] Chauhan, G., Madou, J. M., Kalra, S., Chopra, V., Ghosh, D. and Martinez-Chapa, S. O. (2020). Nanotechnology for COVID-19: therapeutics and vaccine research. *ACS nano*, *14*(7), 7760-7782. DOI: 10.1021/acsnano.0c04006.

[106] Palestino, G., García-Silva, I., González-Ortega, O. and Rosales-Mendoza, S. (2020) Can nanotechnology help in the fight against COVID-19?. *Expert Rev. Anti-Infect. Ther. 18*(9), 849-864. DOI: 10.1080/14787210.2020.1776115.

[107] Weiss, C., Carriere, M., Fusco, L., Capua, I., Regla-Nava, J. A., Pasquali, M., Scott, J. A., Vitale, F., Unal, M. A., Mattevi, C., Bedognetti, D., Merkoçi, A., Tasciotti, E., Yilmazer, A., Gogotsi, Y., Stellacci, F. and Delogu, L. G. (2020) Toward nanotechnology-enabled approaches against the COVID-19 pandemic. *ACS nano*, *14*(6), 6383-6406. DOI: 10.1021/acsnano.0c03697.

[108] Palmieri, V. and Papi, M. (2020) Can graphene take part in the fight against COVID-19?. *Nano Today*, 33, 100883. DOI: 10.1016/j.nantod.2020.100883.

[109] Aydemir, D. and Ulusu, N. N. (2020) Correspondence: Angiotensin-converting enzyme 2 coated nanoparticles containing respiratory masks, chewing gums and nasal filters may be used for protection against COVID-19 infection. *Travel Med. Infect. Dis.* 101697. DOI: 10.1016/j.tmaid.2020.101697.

[110] Chan, W. C. W. (2020) Nano research for COVID-19. *ACS nano. 14*(4), 3719–3720. DOI: 10.1021/acsnano.0c02540.

[111] Kostarelos, K. (2020) Nanoscale nights of COVID-19. *Nat. Nanotechnol.* 15, 343–344. DOI: 10.1038/s41565-020-0687-4.

[112] Galdiero, S., Falanga, A., Vitiello, M., Cantisani, M., Marra, V. and Galdiero, M. (2011) Silver nanoparticles as potential antiviral agents, *Molecules. 16*(10), 8894-8918. DOI: 10.3390/molecules16108894.

[113] Sportelli, M. C., Izzi, M., Kukushkina, E. A., Hossain, S. I., Picca, R. A., Ditaranto, N. and Cioffi, N. (2020) Can nanotechnology and materials science help the fight against SARS-CoV-2?. *Nanomaterials*, *10*(4), 802. DOI: 10.3390/nano10040802.

[114] Szunerits, S., Saada, T. N., Meziane, D. and Boukherroub, R. (2020) Magneto-optical nanostructures for viral sensing. *Nanomaterials*, *10*(7), 1271. DOI: 10.3390/nano10071271.

[115] Kerry, R. G., Malik, S., Redda, Y. T., Sahoo, S., Patra, J. K. and Majhi, S. (2019) Nano-based approach to combat emerging viral (NIPAH virus) infection. *Nanomed. Nanotechnol. Biol. Med. 18*, 196-220. DOI: 10.1016/j.nano.2019.03.004.

[116] Abd Ellah, N. H., Gad, S. F., Muhammad, K., Batiha, E. G. and Hetta, F. H. (2020) Nanomedicine as a promising approach for diagnosis, treatment and prophylaxis against COVID-19. *Nanomedicine*, *15*(21), 2085-2102.DOI: 10.2217/nnm-2020-0247.

[117] Ahmed, S. R., Nagy, É. and Neethirajan, S. (2017) Self-assembled star-shaped chiroplasmonic gold nanoparticles for an ultrasensitive chiro-immunosensor for viruses. *RSC adv. 7*(65), 40849-40857. DOI: 10.1039/C7RA07175B.

[118] Łoczechin, A., Séron, K., Barras, A., Giovanelli, E., Belouzard, S., Chen, Y. T., Metzler-Nolte, N., Boukherroub, R., Dubuisson, J. and Szunerits, S. (2019) Functional carbon quantum dots as medical countermeasures to human Coronavirus. *ACS Appl. Mater. Interfaces*, *11*(46), 42964-42974. DOI: 10.1021/acsami.9b15032.

[119] Web of Science https://clarivate.com/webofsciencegroup/solutions/web-of-science/, Visited 12 February 2021.

[120] Web of Science Platform www.webofknowledge.com, Visited 04 April 2021.