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Review Article

Viral Infection- A Looming Catastrophe

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ABSTRACT

The common cold, influenza, chickenpox, human immunodeficiency virus (HIV), SARS-CoV-2, and other disease-causing (pathogenic) viruses crop up when most people hear the word "virus." Infectious diseases are predicted to account for over one-third (i.e., 20 million) of annual deaths worldwide, as per the World Health Organization (WHO). The rising globalized health sector has made major contributions to the improvement of human health. However, long-standing, developing, and re-emerging infectious disease risks continue to haunt the globe. With a pandemic on the scale of COVID-19, Antibiotic resistance is a veiled concern looming behind the COVID-19 pandemic, which has already claimed thousands of lives before the global breakout. With the worrisome rise in antibiotic resistance incidences only few new antimicrobial drugs on the horizon, it's essential to keep monitor of pathogen epidemiology in ways that will improve treatment decisions. This review article aimed to outline recent findings of the origin, transmission, diagnosis, precautionary measures, antimicrobial resistance, reinfection and repurposing of drugs for the treatment and prevention of COVID-19 depending on the previous literature.

Keywords: COVID-19, Reinfection, Transmission, Repurposing, Antimicrobial Resistance

INTRODUCTION

Colonization, enslavement, and combat all contributed to the rising propagation of deadly diseases in archaic times, with disastrous effects Concurrently, animal illnesses like rinderpest spread along trade routes and with travelling regiments, ravaging on livestock and dependent human populations.[1] Major epidemics, some of which marked as pandemics, have occurred in the twenty-first century, exacerbated by old diseases such as typhoid, flu, as well as arising ailments such as severe acute respiratory syndrome (SARS), Ebola, Zika, Middle East respiratory syndrome (MERS), HIV (although technically endemic), influenza A (H1N1), and lately, COVID-19.[2] It is believed that 25% of the approximately 400 reported emerging diseases are human pathogens.[3] According to some of the other estimates, over 175 species have been linked to developing diseases, with approximately 75 percent of them being of zoonotic origin.[4] Increased human-animal contact has resulted in the spread of the majority of these zoonotic

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pathogens..[5,6] These zoonoses account for roughly 44%, 30%, 11%, 9%, and 6% of viruses, bacteria, protozoa, fungus, and helminths, correspondingly.[7] In the post-1980 period, some zoonotic pathogens were responsible for outbreaks, such as E. coli O157 in the 1980s, the avian flu strain in Hong Kong in 1997 West Nile virus in 1999 the increase in the prevalence of chikungunya in Italy in 2007, the outbreak of Query fever in the Netherlands, the pandemic of severe acute respiratory syndrome (SARS) in 2002 exacerbated by very virulent strains of new coronaviruses, Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012, and avian influenza, such as A/H1N1 in 1997 in Hong-Kong, A/H7N7 in 2004 in the US, A/H7N2 in 2007 in the UK, and A/H7N9 in China. During 2013 and 2016, major Ebola virus disease (EVD) epidemics endangered communities in West African regions, with 28,603 patients and 11,310 deaths, and between 2018-2020 in the Democratic Republic of the Congo (DRC), with 3444 patients and 2264 deaths. The whole world is currently witnessing an unusual epidemic induced by a new coronavirus strain identified as coronavirus infection 2019. (COVID-19). In this paper, we looked at notable superbugs that have impacted humanity throughout history, how they were managed in the earlier, and how they are managed currently. Viral infections continue to pose a hazard to human health as microbes can spread quickly via global trade and travel. Global monitoring strategies are therefore needed to locate and recognize pathogens that spread from animals to humans, and also to combat water-borne pathogens and vector-borne ailments Moreover, adequate non-pharmaceutical and pharmaceutical interventions for disease prevention and control are needed to restrict their transmission in the human population.

Current Scenario of Viral Diseases and Their Global Impact

Throughout history, infectious ailments with pandemic potential have arisen and propagated on a frequent basis. Many infectious diseases that trigger superbugs are caused by zoonoses that have disseminated to humans as a consequence of growing contact with animals through breeding, hunting, and global finance activities. Furthermore, landscape utilisation and climate emergency are thought to contribute infection transmission from wildlife to humans.[8] As a corollary, monitoring techniques must be established as soon as feasible to detect the onset of illnesses with the propensity for virus propagation at the animal-human interface. Coronaviruses have provoked three prominent outbreaks in the recent couple of decades, beginning in 2002 with SARS-CoV, followed by MERS-CoV in 2012, and now SARS-CoV-2 (COVID-19).[9] Coronaviruses (CoVs) are eminent causes of significant ailments in humans and in number of animal hosts, notably pulmonary, enteric, and systemic diseases CoV infections have been detected in livestock, small animals like pigs, rats, cats, dogs, bats, palm civets, ferrets, horses, rabbits, snakes, and a variety of other wild mammals and birds.[10] This SARS-CoV epidemic resulted in around 8000 reported clinical infection and 774 deaths (a 9.5 percent mortality rate) as a consequence of its going global.[11] Initially, the outbreak occurred in captive Himalayan palm civets, which have been deemed to be the virus's natural host Following the Crisis in 2003, a comparable CoV designated HKU3-1 to HKU3-3 was confirmed in non-caged horseshoe bats from Hong Kong in 2005.[12] Following, bats have been identified as the primary host and probable repository species accountable for any eventual CoV epidemics and/or pandemics. Several instances of pneumonia were reported in Wuhan, Hubei Province, China, during the first week of December 2019.

The patients had previously visited the surrounding Huanan seafood market, which sold several live animals, and zoonotic (animal-to-human) transmission was regarded as the primary root of disease origin. As per the Ministry of Health and Family Welfare (MoHFW), a total of 266 598 confirmed COVID-19 cases had been reported from 32 states/union territories since around June 9, 2020. The majority of the cases were detected from Maharashtra, Tamil Nadu, Delhi, and Gujarat. So far, the MoHFW has reported 7471 deaths due to COVID-19, amounting in a case-fatality rate of 2.8 percent. As per a MoHFW assessment provided on April 6, 2020, 76 % of the estimated number of cases reported were male. People under the age of 40 accounted for 47 percent of instances, while those over the age of 60 accounted for 19 percent. Contrastingly, people aged 60 and up accounted for 63 percent of all deaths. Case fatality rates were 0.40 %, 2.36 %, and 8.89 %, accordingly, in age categories: 40 years, 40 to 60 years, and more than 60 years. Additionally, 86 percent of the deaths occurred amongst individuals who had underlying ailments, most notably diabetes mellitus, hypertension, renal illness, and/or coronary heart disease. Although overall mortality rates vary by country, ranging from 0.7 percent in Germany to 10.8 percent in Italy. The finding that death owing to COVID-19 rises and the presence of comorbidities is comparable across all nations. According to another report from the Indian Council of Medical Research (ICMR), 80 percent of cases in India are either undiagnosed or moderate**.** This is congruent with whatever is observed from the largest Chinese dataset**.**[13]

Transmission

The major route of transmission of 2019-nCoV is from person to person. As yet, there seems to be no indication of animal-to-human transmission. Although not everyone who is infected suffers the disease, asymptomatic carriers of the virus are at high risk of becoming superinfectors. This is a worry that countries across the world have noted, with the Indian government voicing concern about how to detect and control asymptomatic carriers, who might account for up to 80% of those affected. Human-to-human transmission is predominantly by droplets, which are released during coughing, conversing, or sneezing and inhaled by a healthy individual. They can also be transmitted to people indirectly when they rest on surfaces that are touched by a healthy person, who may subsequently touch their nose, mouth, or eyes, allowing the virus to enter the human body. In such disorders, fungi are also a frequent issue. Despite the findings of SARS-CoV-2 RNA in blood and fecal samples[14] and the culture of viable SARS-CoV-2 from faeces in some COVID-19 patients[15] A joint WHO-China investigation concluded that the fecal-oral conveyance route did not show up to be a big aspect in the dissemination of virus. It should be highlighted that a study of COVID-19 patients' sperm and testicular material revealed that SARS-CoV-2 could not be transferred during sexual contact[16] While women who are pregnant are at a greater threat of acquiring COVID-19, it is critical to investigate the possibility of transmission of COVID-19. An infant born to a sick mother tested negative for seven duplicate specimens of neonatal blood, faeces, and nasopharyngeal. Recent findings, however, revealed immunoglobulin M antibodies to SARS-CoV-2 in newborn infant blood, implying that transmission of SARS-CoV-2 from mother to foetus cannot be winnow out.

Personal Precautionary Measures: -

If severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is present in the community, occupants are generally urged to exercise social distancing by seeking to avoid crowds and keeping a distance of two meters from those around when out in public. [17] Individuals should avoid up - close interaction with sick people for instance. While stepping out in open, it is also recommended that people wear masks. Also Because of greatest possible risk of transmission has now been outlined between these residential contacts of COVID-19 sick people [18] retaining the household safe necessitates physical separation, and use of some other public health interventions compiled here, and notably, appropriate and effective usage face masks (outside the household and in some instances within the household) to thwart SARS-CoV-2 emergence and propagation. Comprehensive diagnosis is a key approach for limiting the passive spreading of SARS-CoV-2 among asymptomatic and presymptomatic individuals. Yet, as the responsiveness of existing tests and the duration of exposure fluctuate wildly, a test result might provide some undue affirmation; hence, all preventative methods, including the use of face masks and upholding social distance, should be implemented. A flow of data from six large nations revealed that high levels of investigation, along with good contact tracing, can significantly limit SARS-CoV-2 transmission[19]

Reinfection –

In CoVID-19 individuals, elevated liver enzymes and inadequate lymphocyte levels (lymphocytopenia) are common, as are elevated C-reactive protein (CRP) values. Acute respiratory distress syndrome (ARDS) and mortality could arise as a result. In a limited subset of individuals, recent studies show indications of virus recurrence after an undetectable CoVID-19 infection. According to recent findings, SARS-CoV-2 could exhibit identical symptoms and reawaken in individuals with previously confirmed CoVID-19 infection, causing sickness and dissemination from person to person. CoVID-19 reinfection is more pervasive in older patients with comorbidities. According to investigations, there are 3 key pathways for CoVID-19 reinfection: a short-lived, inefficient, and strain-specific immune response. Subsequent medical conditions such as super infection, deep vein thrombosis, or chronic RNA virus that can be detected in respiratory samples in medically recovered CoVID-19 individuals must be distinguished from CoVID-19 recurrence following recovery. Various investigations have found that reinfection is unlikely and that post infection protection is only temporary. According to South Korea,116 CoVID-19 recovered cases were determined to be positive once more. Reinfection risk of novel covid 19.[20] Individuals infected with distinct genetic variants of SARS-CoV-2 verified via PCR were considered to have reinfected with COVID-19. Also, findings with available viral genome sequencing for both infectious events were included in this review to differentiate between true reinfection and continuous viral shedding, as research has also shown that only a certain number of cases may carry the virus even after treatment and prior negative PCR tests.[21] Those who healed from COVID-19 were assumed to have a considerable immune response that cleared the virus. It needs to be seen, however, if the initial infection gives a protective immunity against later infections. Recent research shows that a positive COVID-19 antibody from the initial infection may confer safeguard against reinfection in the majority of patients in the study, but reinfection still seems to be probable in some people**.** Despite the presence of antibodies, reinfection with critical human coronaviruses is common.[22] Highlighting the prospect of underreporting and the preceding report's inclusion of only studies with genomic data, there seem to be many more cases of reinfection than have been recognized. Yet, estimating the true rate of COVID-19 reinfection may be problematic due to the lack of comprehensive genomic data in most COVID-19 infections and the fact that many patients with minor symptoms were not screened during the initial stages of this outbreak. Furthermore, as patients with asymptomatic reinfections became less likely to be identified, determining the true prevalence of COVID-19 reinfection is challenging without community analyses, which could be a future research hotspot. Several studies contained in our review found major nucleotide variations between the sequenced viruses, although new variants have recently been detected in parts of the UK where cases are emerging[23].

Repurposing-

Acute respiratory distress syndrome (SARDS) is a condition that occurs when the virus that causes coronavirus disease is coronavirus type 2 (SARS-CoV-2) (COVID-19). SARS-COV-2 is an enclosed positive Coronaviridae virus. Single-stranded RNA viruses are viruses that have only one strand of RNA.[24] Repurposing is the process of discovering new uses for obsolete medications Indications for currently available medications and considered as an effective and efficient, low-cost strategy. The expense of the new drug discovery process is also referred as repositioning, re-profiling, re-tasking, and drug rescue. Amounts to more than a billion it will last for a long time with an accuracy rate of only 2.01% over a period of ten to fifteen years. Examining current antiviral and other medications for SARS-CoV2 is cost-effective as compared to the time and money necessary to develop new therapeutics. Existing medications have recently been reused for treating a wide range of diseases. WHO has identified one of the most effective medicines, including a mixture of the two HIV drugs (lopinavir and ritonavir), anti-malarial drugs (chloroquine and hydroxychloroquine), and investigational antiviral molecule called remdesivir.[4] The drug repurposing technique accelerates the drug development process and has engaged researchers from a wide array of scientific domains. Drug discovery phases are simplified due to the availability of in-vitro and in-vivo testing data, overall chemical optimisation, safety studies, bulk manufacturing, formulation design, and pharmacokinetics profiles of FDA-approved medications.[5] Medications that have recently been repurposed to function on virus-related targets like the RNA genome:

Remdesivir:

Remdesivir, which was used to treat SARS-CoV2 infection, is being examined as a prospective candidate medication for treatment against COVID-19. Remdesivir is a nucleotide analogue (adenosine) that is linked to the virus's replicate DNA and creates a triphosphate state that competes with adenosine triphosphate (ATP) for the role of RDRP substrate. Upon finishing the developing RNA strand, Remdesivir inserts 3 main nucleotides. The 3 extra nucleotides might safeguard the action of the 3′- 5′ viral exonuclease clearance inhibitor[7] Remdesivir is also one of the main contentious medication candidates in COVID-19 clinical trials. Against RNA viruses in especially, the medication has demonstrated sufficient reliability and all-encompassing effects[25] Remdesivir (Veklury) has now been licenced by the FDA to cure COVID-19 in adults and children aged 12- and up. Individuals who have been hospitalised with COVID-19 may be administered Remdesivir. It's injected into the skin with a needle (intravenously).[7]

A further clinical trial with remdesivir in serious COVID-19 patients without mechanical ventilation showed no difference between the 5-day and 10-day courses of remdesivir treatment on day 14, but by day 14, 64 percent of participants in the 5-day group and 54 percent of participants in the 10-day group had improved by two points or more on the ordinal level out of a 7-point ordinal level.[4]

Favipiravir:

Favipiravir (promoted as AVIGAN) is a nucleoside precursor that suppresses a wide spectrum of influenza virus strains. It was created by a Japanese company, Toyama Chemical Co., Ltd., and it has been approved in Japan against Influenza since 2014. The medication effectively blocks the RDRP enzyme.[4] Toyama Chemical (a branch of Fujifilm, Japan) produced the medication favipiravir, which is marketed as Avigan. By matching the molecular makeup of endogenous guanine, favipiravir uses competitive inhibition to change the action of RNA-dependent RNA-polymerase.[26] Repurposing favipiravir against COVID-19 is more difficult due to the drug's lack of preclinical trials relative to remdesivir, despite the fact that their effects are similar. The number of favipiravir clinical trials (NCT04445467, NCT04434248, NCT04411433, and others) is growing, as are the stakes.[25] Favipiravir has a dose-dependent antiviral effect. It has a near-100 percent pharmacokinetic properties and a short half-life of 2–5.5 hours. Favipiravir binds to plasma proteins 54% of the time in humans. Favipiravir is metabolised by aldehyde oxidase (AO) and xanthine oxidase (XO) in the hepatocytes, and the inactive oxidative metabolite (T-705 M1) is excreted by the kidneys.[25,27]

Ribavirin:

Ribavirin is just a guanosine analogue that has been licenced for treatment of hepatitis C virus in combination and respiratory syncytial virus monotherapy.[28]The efficiency of a mixture of IFN-1b, lopinavir/ritonavir, and ribavirin in the management of SARS-CoV-2 infected people was investigated in a phase two randomised, open-label research.[3,7] The monophosphate form of ribavirin blocks the enzyme inosine monophosphate dehydrogenase (IMPDH), which regulates intracellular guanosine triphosphate (GTP) pools. The exhaustion of the intra-cellular GTP pool inhibits the viral RDRP enzyme indirectly. It also disrupts the capping of mRNA. Ribavirin (500 mg 2–3 times/day) given intravenously in conjunction with the other medications such lopinavir/ritonavir or interferon (IFN) for no more than ten days make SARS-CoV2 infected people more resistant to respiratory distress syndrome and mortality.[4]

Antimicrobial resistance-

Nonetheless, since the onset of the COVID-19 crisis, there has been raising concerns about an increase in antimicrobial resistance as a consequence of elevated antibiotic therapy for COVID-19 patients.[29] Three factors influence the spread of AMR in a population: emergence, transmission, and infection burden at the population health. Selective pressures on microbial populations within people, animals, and the atmosphere can all contribute to the onset of AMR. Such selection pressures enable resistance acquiring mechanisms like gene mutations or horizontal transfer of genes encoding resistance to one or more antibiotics when they are subjected to the 'drug and bug' of concern.[30] The transfer of these newly emerging antimicrobial-resistant organisms (AROs) among humans, animals, and environments may be influenced or prevented as a consequence of natural circumstances and behaviors. The frequency and variety of infections, as well as the availability, effectiveness, and safety of alternate therapies, will determine the severity of ARO-related illnesses.[31]

CONCLUSION

The pandemic situation and overall outbreak affect the globally. The SARS-CoV-2 Omicron VOC is highly transmissible among fully vaccinated young and middle-aged people, according to preliminary findings from our outbreak investigation. With the pharma industry's ever-increasing roadblocks, drug repurposing is the best strategy for lowering the risks associated with new drug development. Vaccines are often believed to be the only way to provide long-term immunity and avoid viral infections.

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