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COVID-19: One of the Worst Pandemic having a Mysterious Origin

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Abstract

Whole world is now struggling and suffering from CoVID-19 pandemic. The disease has already reached almost every corner of Earth and affected the entire population in a harsh way. Many Government research organizations as well as biotech companies are in a race track of vaccine development but none have gained success yet. Researchers are still trying to figure out the actual origin of the SARS-CoV-2 which may pave a helpful way in vaccine development, while most of the reports suggest its origin from Wuhan, China. While many countries are accusing China for its probable lab origin, most researchers supports it natural origin that are discussed here. This review covers the structure, evolution, current researches and the therapeutics that are now used in some countries to help patients recover from this viral infections. Some preventive measures as per the WHO and CDC guidelines are also discussed here.

Keywords: *Corona Viruses; SARS-CoV-2; 2019-nCoV; COVID-19; Viral Pneumonia of Unknown Origin*

Introduction

Corona viruses are a group of viruses belong to phylum incertae sedis, family coronaviridae, subfamily Coronavirinae and order Nidovirales [1]. These viruses have a deadly history in the USA, Italy, France, Spain, Britain, Iran, China and other European countries and also affected all countries across the world, hence at this stage there would be hardly someone ignorant about the name “Coronavirus” because of the ongoing crisis. The structure of Corona virus is illustrated as a virus cell surrounded by corona or crown like structures [2]. A certain Corona virus which is causing this pandemic is one of the 200 strains of the Corona virus family [3]. This particular strain was previously named as the “2019 Novel Corona virus” (2019-nCoV) and the disease caused by it as “COVID-19” by World Health Organization (WHO) on 11th February 2020 [4]. The international committee on Taxonomy of viruses (ICTV) has renamed the virus as SARS-CoV-2 later after analyzing its whole genome sequence data with other corona viruses [1]. The first reported case is believed to have an origin from a seafood market of Wuhan, China in December 1st 2019 and since then it has affected more than 17,73,084 people worldwide and the death toll has surged past 1,11,652 based on report provided by WHO as on April 13th [5]. Confirmed cases in some regions as reported by April 9th are: European regions (9,13,349), Regions of America (6,10,742), Western Pacific Region (1,21,426), Eastern Mediterranean Region (99,713), South East Asia region (16,883) and African region (10,259) (https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200413-sitrep-84-covid-19.pdf?sfvrsn=44f511ab_2). Although the origin of the outbreak was China, it has caused more deaths in other nations such as: Italy, Spain, USA, France and other European countries. Italy, Spain, USA and many major countries are now going through their worst and deadliest days ever in history bearing highest mortality rates and economic breakdown [Who report]. Some countries including India, USA, Italy, Spain, France have already announced the lockdown all over the country, which is leading to decrease the community spread.

Many researchers using the whole genome sequencing method that, SARS-CoV-2 is genetically more similar to the SARS corona virus, which comes under betacoronavirus family [6]. In this article we are mainly focusing on reports regarding the possible origin of the SARS-CoV-2 which is still a mystery and important for synthesis of appropriate vaccine and treatment procedures.

Structure and controversial origin of SARS-CoV-2

The origin of the virus plays a much important role in determining its classification and production of vaccines against it to prevent the outbreak. Many theories have been proposed which support its origin at the Huanan seafood market in Wuhan, China, because most of the initial cases of people infected with this had a link with the market. The first case was reported in December 2019 when a patient was diagnosed with a viral pneumonia of unknown origin which was later identified as due to corona virus [7,8]. The corona viruses are mainly of four types such as alpha/beta/gamma/delta. The alpha and beta corona viruses infects mammals including humans and the gamma and delta corona viruses infects birds. SARS-CoV-2 is a beta type, positive-sense single stranded RNA virus having a genome size of ~29,881 bp in length [8,9]. So, it's suspected that, the transmission of the virus to humans was definitely through one/two animals as a vector.

The first infection of a human with corona virus was reported by Tyrell and Bynoe in 1965 from the nasal area of a child patient having the symptoms of typical common cold. The virus was termed as B814 and it was capable of inducing common cold in others [10]. Those viruses were not considered dangerous to humans until the appearance of the fatal "Severe Acute Respiratory Syndrome" (SARS) corona virus in 2002-03 in China [11] and Middle East Respiratory Syndrome (MERS) corona virus in middle east countries just after 10 years of it [12]. SARS and MERS are now considered as the relatives of the SARS-CoV-2 having the most genetic similarity. According to the whole genome sequencing data analysis, the genome of SARS-CoV-2 shares 79% similarity with SARS-CoV and 50% similarity with MERS-CoV [6,13]. A diverse range of corona viruses resides within bats and most importantly these two corona viruses (SARS and MERS) use bats as their natural host [14]. Genetic sequence of SARS-CoV-2 shares 88% similarity with the bat corona viruses (bat-SL-CoVZC45 and bat-SL-CoVZXC21) [6,13]. As the SARS-CoV and MERS-CoV were originated from bats, so SARS-CoV-2 is likely to have an origin from bats [15,16].

In a recent study, researchers analyzed the genome of SARS-CoV-2 with the genome of corona viruses that infects diverse animals such as; hedgehogs, marmots, birds, bats, and snakes to find the patterns in the genetic code that may reveal the host of the virus [17]. Based on their study, they suspected that the SARS-CoV-2 may have been originated from snakes. It seems obvious because snakes were also sold at the Huanan seafood market. As the beta corona viruses can only infect mammals and birds and they cannot infect snakes, this leads to another controversies about its origin.

Another study was conducted by comparing patterns of the amino acid variation of the S1 proteins (i.e. membrane protein) from Pangolin-CoV, SARS-CoV-2, RaTG13 and other representative of SARS CoV [18]. They found that the SARS-CoV-2 uses the same receptor angiotensin converting enzyme 2 (ACE2) like the SARS-CoV [18,19]. So, they suspected that the virus was transmitted from bats to humans but there might be an intermediate host. This again supports the theory of its transmission from bats.

In another research it was reported that, whole genome sequence of SARS-CoV-2 shares 91.02% similarity to Pangolin-CoV [20]. It was also identified that the S1 protein of this Pangolin-CoV is more identical to S1 protein of SARS-CoV-2 than that of the RaTG13 (Bat-CoV). Thus, the Pangolin-CoV stands as the second most close relative to SARS-CoV-2 after RaTG13. Here the point is to be considered that in Huanan seafood market Pangolins were sold illegally as it is banned in china and other countries. As some cases have already confirmed the illegal trading of this endangered species in china, it is probable that the virus may came from the pangolins sold at that market.

Wei Ji., *et al*. (2020) supports the natural origin of the virus by investigating the possible virus reservoir like snakes, bats and other farm animals which were mostly sold at Huanan seafood market [21]. They performed an evolutionary analysis using the relative synonymous codon usage (RSCU) to study the codon usage biases between viruses and their hosts which could reveal the possible host reservoir of SARS-CoV-2 [21]. The results suggested that it might be a recombinant between a bat corona virus and an unknown origin corona virus. The recombination might have occurred within the viral spike glycoprotein indicating a sign towards cross species transmission that was caused by homologous recombination. Another report regarding the mutations in receptor binding domain of SARS-COV-2 supports its natural origin [22]. According to the report, the high-affinity binding of the SARS-CoV-2 spike protein to human ACE2 receptor protein is most likely to be a result of natural selection [22].

Although most of the scientific researches regarding the origin of the deadly virus supports the natural origin theory but there are many controversies about its lab origin as recombinants can be natural as well as a lab construct. However, based on research reports published in most of the reputed journals, it seems SARS-CoV-2 virus have a natural origin rather than biologically engineered origin and the controversies are nothing but seems like a conspiracy theory.

Evolution of SARS-COV-2

While the epidemic has progressed to a global pandemic, more viral genomes of SARS-COV-2 isolated from patients across different countries are being sequenced. We know that nucleotide substitution is one of the most important mechanisms of natural viral evolution [23]. The earlier samples isolated from patients of Wuhan were showing little genetic diversity among them due to mutations [24]. The genetic variations might help for determining the evolution of SARS-COV-2 but it'll also create problem in determining the exact phylogeny of the original virus, as the mutations might have taken place rapidly within the viral genome during this recent period of outbreak. Also based on the virus transmissibility, it's not yet understood that if the mutations can radically change phenotypes [25]. Another study also reported a total of ninety three mutations over the entire SARS-CoV-2 genome [26]. They found eight missense mutations in the spike surface glycoproteins [26] which are essential for binding to receptors on host cells [27]. These mutations can result in conformational changes which in turn might lead to change in its antigenicity [26]. Recently, researchers from University of Cambridge tracked down the evolutionary path adopted by the virus to enhance its resistance through mutations. They labelled 3 variants of the virus as type A (in USA and Australian patients), Type B (Main Wuhan virus) and Type C (found in patients of European countries) [28]. These findings can truly help in preventing further outbreaks in other nations. So further studies are required to investigate the evolutionary pattern of the virus to determine whether its evolution is driven by genetic mutations or not.

Treatment and preventions

Still we have not been able to develop a clinically approved vaccination which can totally work against the virus SARS-COV-2. Considering the genetic similarities between SARS-COV-2 and SARS CoV, some health experts are using the same antiviral drugs that were prescribed to the SARS affected patients [29,30]. China's Academy of Military Medical Sciences in collaboration with the Hong Kong-listed biotech firm CanSino Biologics has designed some specific vaccines and will carry out the human trial soon [31]. An mRNA based vaccine prepared by the US National Institute of Allergy and Infectious Diseases against SARS-CoV-2 is under its phase 1 trial but the major problem is that, animal models are not vulnerable to this virus, so it would be useless to use them for vaccine development [32]. Some countries like USA has banned use of human fetal tissue which is preventing some researchers of NIH from designing some valuable vaccines [33].

Some potential drug treatments, now being used just to suppress the viral replication upto a limit of 85% in infected patients are oseltamivir (75 mg every 12h orally), ganciclovir (0.25g every 12h intravenously) and lopinavir/ritonavir tablets (400/100 mg, that are given twice daily orally [29,30,34]. Along with these medications some types of antifungal agents, empirical antibiotics, intravenous alpha/gamma immunoglobulins and systemic steroids are also used in some treatment procedures [29,30,34]. Some traditional Chinese medicines like ShuFeng JieDu or Lianhua Qingwen capsules are also being used to treat the infections in China [35]. A recent study by Wang., *et al*. revealed that, remdesivir and chloroquine/ hydroxyl chloroquine are working effectively in the control of 2019-nCoV *in vitro* studies, so now are widely used across the world [36]. Although the SARS-CoV-2 pneumonia shows a promising clinical response to remdesivir, further clinical studies of remdesivir therapy are still required to verify its therapeutic efficacy. Since the SARS-CoV-2 is similar in many aspects (except its S1 domain) with the other Human corona viruses, some studies also suggests repurposing of drugs which were approved by FDA (Food and Drug Administration) to treat CoV related diseases before such as: lopinavir and ritonavir (SARS and MERS-CoV) [37-40], Arbidol (Influenza, Flavivirus) [41], Resveratrol, antimalarial drugs like Amodiaquine and Mefloquine (MERS-CoV), Chlorpromazine (SARS and MERS CoV) [42], Chloroquine (Nipah, Ebola and HIV) [43], Oseltamivir (Influenza inhibitor, currently under phase-IV trials for SARS-CoV-2) [NCT04255017] [44] and Galidesivir (SARS, MERS, Ebola and Several RNA virus related diseases) [45] etc.

However, the Center for Disease Control and Prevention (CDC), World Health Organization (WHO) and China CDC (China Center for Disease Control and Prevention) including other health ministries of different countries have taken major steps to stop the outbreaks. Awareness programs are being held across all countries through media/social networking/newspapers to give proper knowledge about the CoVID-19 outbreak, its symptoms and preventions. Some important steps need to be considered, includes maintaining a distance of at least 1.5 feet from an affected person or a symptomatic person, washing hands frequently for at least 20 sec most importantly after traveling outside, avoiding contact with farm animals, covering face with masks or handkerchiefs/use tissue paper while coughing and sneezing and enhanced protocols should be used by all people to avoid the mass spreading.

Conclusion

There is a saying that “Precautions are better than cure” which now exactly applies to break the transmission of virus during this CoVID-19 outbreak. To break the chain of transmission, many countries are announcing complete lockdown but they must be prepared economically before the announcement. It has not been confirmed yet if the virus can enter the body only through facial or oral routes or any other routes [46]. It also have not been confirmed that whether the SARS-COV-2 is present in the environment or not. Previous studies have shown that the SARS-CoV and other corona viruses could survive on environmental surfaces, so there is a chance that the SARS-CoV-2 is present in the environment [47]. However, the CoVID-19 is going to be the fifth pandemic of history and still the knowledge about its origin remains unknown. This stands as a huge challenge for the researchers to develop either drugs or vaccines. Scientists around the globe are undoubtedly giving their highest efforts for the development of drugs and vaccines as soon as possible to combat the outbreak. As the virus seems to have an origin from the seafood market in Wuhan (China), the governments around the world must take strict actions to close the wet markets in different cities where live animals are being slaughtered and sold. Many animal welfare organizations like PETA (People for the Ethical Treatment of Animals) are protesting such activities worldwide. The public must step forward to support this and must follow the instructions to adopt the preventive methods suggested by the Government Health Ministries until the development of a drug. Therefore, the public, the government and the health workers, by working together can have a major impact on stopping the CoVID-19 outbreak worldwide.

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