

# COVID-19: Myth and Reality

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## ARTICLE INFORMATION

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## ABSTRACT

COVID-19 is a highly contagious disease that is caused by SARS-CoV-2 that has high recombination and mutation rates. Several new viral infections have been appeared in different geographical regions in recent decades, the causative pathogens include Zika virus, Nipah virus, Ebola virus and coronaviruses. After the 1918's flu pandemic, COVID-19 has become the fifth known pandemic and it marked the third large scale coronavirus pandemic in humans. At the end of December, 2019, the emergence of SARS-CoV-2 in Wuhan city, Hubei Province of China has brought back the coronaviruses into the limelight and the outbreak has astonished us with its high transmissibility. All previous six coronaviruses species that are known to infect humans are reported to have zoonotic origin. Since the emergence of COVID-19 there has been significant discussion and debate on the origin of SARS-CoV-2. The origin of human's infecting SARS-CoV-2 is mysterious and unrevealed and is still being investigated. The pandemic puzzle revolves around three potential origins which includes the natural emergence of virus through different factors, the testing of a biological weapon or an accidental release of the deadly virus from the lab. In this article, all the three possible origins are being discussed

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## Original Research Article

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### Introduction:

The world is currently facing a pandemic of COVID-19 that has spread with alarming speed and is infecting millions of people worldwide. Hospitals in Wuhan city located in Hubei province of China reported a group of cases having pneumonia in late December, 2019. The actual cause of such sudden cluster of cases was unknown. Later the causative pathogen was identified to be a novel coronavirus through whole genome sequencing (1, 2, 3). In Wuhan, Public health authorities felt a suspected connection of the outbreak with the Seafood wholesale market as live and wild animals were illegally traded there and they sealed the market on January 21, 2020 (4). From the initially reported confirmed 41 patients, 66 percent of the patients had been exposed to that specific seafood market (5). COVID-19 was declared as an epidemic by World Health Organization and Public Health Emergency of International Concerns (PHEIC) was announced on January 30, 2020. World Health Organization named novel coronavirus pneumonia as COVID-19 on 11 February, 2020. The Study Group of the International Committee on Virus Taxonomy officially acknowledges this virus as a sister to SARS-CoV and renamed it as SARS-CoV-2 (6). The outbreak originated in Wuhan city of China and spread rapidly across the entire world (7). At the time of writing by July 31, 2020 the total reported cases worldwide

were 16,812,763. COVID-19 is a highly contagious disease that is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). It belongs to the Beta-coronavirus family that is a large class of viruses having single stranded RNA and they are prevalent in nature (8). They have high mutation and recombination rates (9). Till yet there are 7 known coronaviruses that have caused diseases in humans, these includes alpha-coronaviruses (HCoV-229E and HCoV-NL63), beta-coronaviruses that are HCoV-HKU1, HCoV-OC43, SARS-CoV and MERS-CoV (10). SARS-CoV-2 is the 7th member of the coronaviruses family (1). Several new viral infections have been appeared in different geographical regions in recent decades, the causative pathogens includes Zika virus, Nipah virus, Ebola virus and coronaviruses (11). After the 1918's flu pandemic, COVID-19 has become the fifth known pandemic (12) and it marked the third large scale coronavirus pandemic in humans (13). Since COVID-19 is reported in Hubei province of China, there has been substantial discussion and debate on the origin of SARS-CoV-2 (14). The origin of SARS-CoV-2 virus infecting humans is mysterious and unrevealed and is still being investigated. The pandemic puzzle revolves around three potential origins which includes the natural emergence of virus through different factors, the testing of a biological

weapon or an accidental release of the deadly virus from the laboratory.

### COVID-19 Originated Naturally?

The appearance and development of novel coronavirus may have been possible due to the presence and survival of multiple coronaviruses in their reservoir host, which may have accommodated the possibility of genetic recombination among coronaviruses (15). Coronaviruses undergoes high frequency mutations due to the RNA dependent RNA polymerase instability and higher recombination rates of homologous RNA, these properties leads to high genetic diversity and potential to infect the multiple host species (16). Following the previous outbreaks due to pathogen transmission from zoonotic agents, (17) has already predicted a SARS and MERS like coronavirus outbreak in China.

### Potential Origin of SARS-CoV-2

Since the pandemic has been started, tracing the natural potential origin of SARS-CoV-2 is in continuous phase. There are many possible hosts of SARS-CoV-2 that includes natural hosts, intermediate hosts and the final host (18).

### Sequence similarity of SARS-CoV-2 with MERS-CoV and SARS-CoV

genome of SARS-CoV-2, 79.5 percent resembles with SARS-CoV, which has caused epidemic back in 2003 in China and only 50 percent similarity with MERS-CoV that was originated in Saudi Arabia in 2012 (19, 20). SARS-CoV2 and SARS-CoV shares significant similarities but there are also some major variations among them. Both of the viruses bind to angiotensin – converting enzyme-2 receptor (ACE 2 receptor) to enter the cell (21,22) and induces inflammatory cytokines that results in infection and initiation of organ damage while COVID-19 is reported to be much more transmissible and infectious than SARS-CoV and MERS-CoV (23) but have low mortality rate. The receptors on the target cells are identified by coronaviruses through spike (S) proteins present on the surface of receptors. A model analysis revealed that the SARS CoV-2 binds with Angiotensin – converting enzyme 2 receptor with more than 10 times higher affinity than the SARS coronaviruses (24). Spike protein of SARS-CoV-2 having high affinity bonding with human ACE-2 is most likely the product of natural selection on human (14). The incubation period of SARS-CoV-2 is less than MERS-CoV and SARS-CoV (25).

### Sequence similarity of SARS-CoV-2 with Bat SARS Coronavirus

SARS Cov-2 is much closer to bat SARS coronavirus RaTG13 than SARS-CoV. 96.2 percent of genome sequence of SARS-CoV-2 shared similarity with bat SARS coronavirus that was isolated from bats *Rhinolophus affinis* in Yunan back in 2013 according to the genome analysis (26,27). This evidence suggested that SARS-CoV-2 might have come from bats. SARS-CoV-2 has 96 percent similarity of genome sequence with two coronaviruses from bats called bat-SL CoVZX21 and bat-SL-CoVZX45 (28).

### Polybasic Cleavage Site Insertions

The polybasic cleavage site insertion genomic feature of SARS-CoV-2 at the junction of subunits of Spike(S) protein

that increases the virus infectivity is absent in bat coronaviruses (27). A comparative study revealed a cleavage site in the S protein of SARS-CoV-2 that is not present in other SARS like coronaviruses. In the S1-S2 junction of CoV, insertions, mutations and deletions can occur, it indicates that the polybasic cleavage site can emerge through a normal evolutionary cycle (29).

### Zoonotic Origin of Human Coronaviruses

From many years, mutations, variations and modifications have led the co-evolution of coronaviruses and all of their hosts (30). The standard rate of evolution for Coronaviruses is estimated roughly as  $10^{-4}$  nucleotide substitutions for each site every year (31). All previous six coronaviruses species that are known to infect humans are reported to have zoonotic origin which includes mice, bats and some domestic animals (32). The classification of animal origin of human coronaviruses is shown in Table (1). Most of the known coronaviruses came from the bats, but in those bats they are in non-pathogenic forms. They are not in pathogenic form in their natural hosts, but after interspecies transmission to a new host, they become pathogenic (30). The coronaviruses species including HCoV-229E, HCoV-NL63 and HCoV-OC43, HCoV-HKU1 usually causes diarrhea, common cold and upper tract respiratory infection, in comparison SARS-CoV and MERS-CoV are pathogenic and causes acute to chronic respiratory tract infection and the recently identified SARS-CoV-2 is also pathogenic, more transmissible and causes lower respiratory tract infection (33,34). It supports the evolutionary origin of all coronaviruses as increased transmissibility decreases the pathogenicity. The transmission zoonotic route of human coronaviruses (HCoVs) is shown in Figure (1).

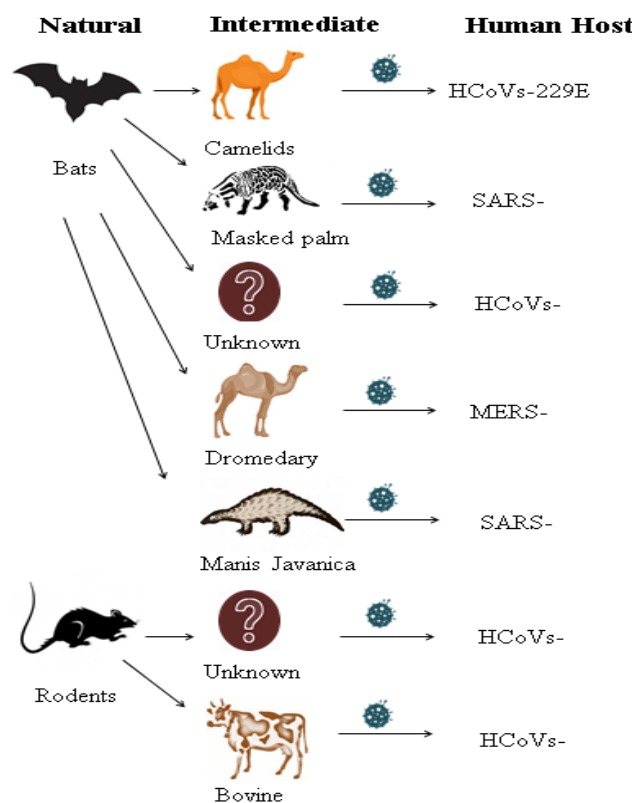


Figure 1: Transmission Route of Human Coronaviruses

A variety of animal species are reported to possess strains of coronavirus. These animals include bats, camels, rodents, rabbits, cattle, swine, horses, birds, dogs, cats, minks, snakes, marmots, pangolins, hedgehogs, and ferrets<sup>(35, 36)</sup>. A research is needed to identify their potential as reservoirs or intermediate hosts of SARS-CoV-2. China has variety of farms for several animal species that includes civets, bamboo rats, birds, mink, foxes, deer, snakes, bears and turtles. To find origin of SARS-CoV-2, these farms can be targeted<sup>(37)</sup>. The outbreak of Swine acute diarrhea syndrome coronavirus (SADS-CoV) resulted in mortality of pigs in four farms of China. SADS-CoV isolated from the pigs had a genomic similarity of 95 percent with HKU2 coronavirus found in horseshoe bat of *Rhinolophus* species indicating the bat origin of isolated virus from pigs. It also revealed that bat origin coronavirus has crossed the specie barrier and has jumped to pigs causing SADS-CoV infection. This outbreak occurred in Guangdong province of China, near the emergence location of SARS-CoV<sup>(38)</sup>.

**Table 1: Classification of Animal origins of Human coronaviruses (HCoV)**

HCoV	Genera	Year	Natural host	Intermediate host	Reference
HCoV-229E	$\alpha$ -CoV	1966	Bats	Camelids	(39)
HCoV-OC43	$\beta$ -CoV	1967	Mice	Bovines	(40)
SARS-CoV	$\beta$ -CoV	2003	Horseshoe bat	Palm civet	(41)
HCoV-NL63	$\alpha$ -CoV	2004	Bats	Unknown	(42)
HCoV-HKU1	$\beta$ -CoV	2005	Rodents	Unknown	(43)
MERS-CoV	$\beta$ -CoV	2012	Bats	Dromedary camels	(44)
SARS-CoV-2	$\beta$ -CoV	2019	Probably bats	Possibly Pangolins	(43)

**Bats – the natural reservoir of various Coronaviruses**

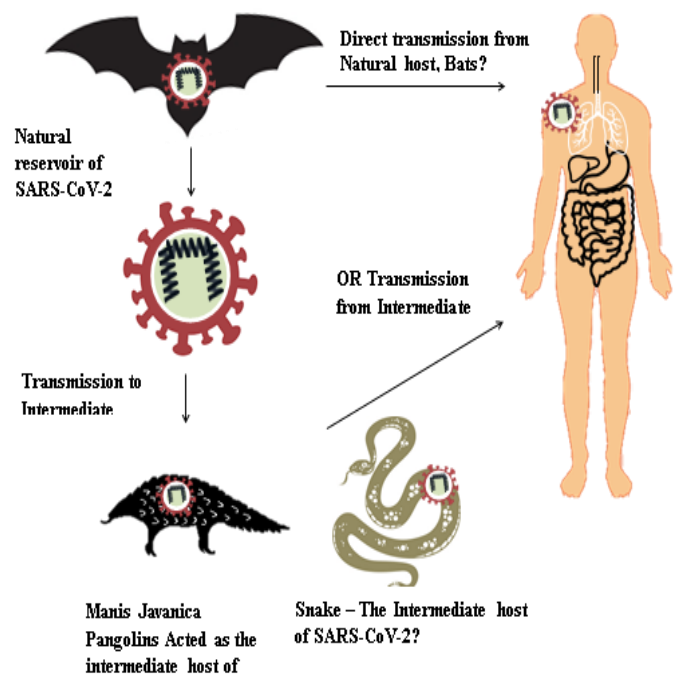
Bats have been found to be associated with more than 200 viruses and most of them are possibly RNA viruses<sup>(44)</sup>. Bats are the reservoirs of more than 30 coronaviruses<sup>(45)</sup>. It is evident that bats are the important and natural reservoirs of various coronavirus species, along with coronaviruses bats are also reservoirs of several other deadly viruses such as Ebola virus, Marburg virus and Hendra virus,<sup>(46)</sup> but it is not proper evidence that bats are reason of pandemic causing SARS-CoV-2 as the bats whose isolated coronaviruses have identical sequences with SARS-CoV-2 are not found any near to Wuhan city and the bats that are found in Hubei province are reported to be different to genomic sequence of SARS-CoV-2<sup>(47, 27)</sup>. The virus is reported to have the vast genomic diversity as till yet 200 SARS-COV-2 genomes are submitted in the records. The research studies has revealed that the bat coronaviruses are the source of alpha-coronaviruses and beta-coronaviruses genes while the genes of gamma coronaviruses and the delta coronaviruses are found in bird coronaviruses<sup>(48)</sup>. It has also been reported by several research studies that some of the bat SARSr-CoVs has ability to transfer to human

and cause infection<sup>(49,50)</sup>. Recent studies using phylogeographic Bayesian reconstruction established the most likely source of SARS-CoV-2 as SARS-like coronavirus, which circulates in the *Rhinolophus* bat family<sup>(51)</sup>.

Genomic analysis of COVID-19 reveals the indications about its origin. On the basis of the evolutionary analysis and the genome sequencing of the virus, bats are suspected to be a natural host of SARS-CoV-2<sup>(52, 53)</sup>. The genetic code of SARS-CoV-2 mutates continuously but they are only the slight mutation<sup>(54)</sup>. Coronaviruses are able to cross specie barriers. The infected bats are capable to transfer the virus to the recipient host. The recipient host behaves as an intermediated host. The virus may have been transmitted to humans from the intermediate host. There is also possibility that the virus was directly transmitted to humans from the bats<sup>(44)</sup>.

**Possible Natural Reservoir of SARS-CoV-2**

According to various research studies, the natural reservoirs of SARS-CoV-2 are considered to be bats while snakes and pangolins are stated to be as intermediate hosts<sup>(55, 56)</sup> yet a subsequent analysis found no evidence of the snakes being SARS-CoV-2 hosts<sup>(57)</sup>. The potential natural and intermediate host of SARS-CoV-2 along with their possible transmission route is illustrated in Figure (2).



**Figure 2: Illustration of Zoonotic origin and zoonotic transmission of SARS-CoV-2 to humans**

**Probable Intermediate Host**

SARS-CoV-2 receptor binding domain that makes it effective pathogen for humans is also present in coronaviruses that are found in *Manis javanica* pangolins and the pangolins are possible to be an intermediate host between humans and bats. They can also be the natural reservoir of SARS-CoV-2 but the sequence of covid-19 causing coronavirus matches more with the coronavirus specie present in bats than the pangolins

coronavirus (58). These receptor binding domains of SARS-CoV-2 is only 85 percent identical to that of RaTG13 (Bat coronavirus) and out of six amino acid residues, only 1 residue is similar (27). Similarly out of six receptor binding domain amino acids, five residues are different between SARS-CoV-2 and SARS-CoV (14). But all six key receptor binding domain residues of SARS-CoV-2 are similar to some pangolin coronaviruses and similarity is as at E (100%), M (98.2%), N (96.7%), and S genes (90.4%) (58, 59). It indicates that the spike protein of SARS-CoV-2 engineered to bind to human like Angiotensin-converting enzyme 2 resulted through natural selection (59). These *Manis javanica* pangolins are reported to be illegally imported in Guangdong and Guangxi provinces in south China. Pangolins are considered to be a delicacy in China. An additional insertion of the amino acid PAA at the S cleavage site is also recognized in another bat coronavirus RmYNO2 that was isolated in 2019 from *Rhinolophus* which indicates that it is a natural evolution of coronavirus but RmYNO2 coronavirus has only 72 percent similarity in Spike protein with Covid-19 causing coronavirus (27).

Research conducted by (60) and (61) revealed the 90-99 percent resemblance of the nucleotide sequence of SARS-CoV-2 infecting the humans with SARS-CoV-2 isolated from the pangolins. SARS-CoV-2 has specific RRAR motif in the S protein that is not present in pangolin-isolated coronaviruses, indicating that SARS-CoV-2 does not derive directly from pangolins. This research also adds up to the fact that pangolins are intermediate hosts of the covid-19 causing virus. Although till yet, the actual origin of SARS-COV-2 virus infecting humans is mysterious and is still being investigated. The genomic sequence identity comparison of SARS-CoV-2 with other coronavirus species is shown in Table (2).

**Table 2: Genomic sequence identity comparison of SARS-CoV-2 with SARS-CoV, Bat SARS-CoV RaTG13, Bat SARSr CoV ZC45 and pangolins**

CoVs	Full length	S protein	E protein	M protein	N protein	Referen
SARS-CoV	79.6%	73.4/76.9%	94.7/96.0%	85.6/90.0%	88.8/91 %	(62)
Bat-CoV RaTG13	96.2%	93.1/97.7%	99.6/100%	95.5/99.6%	96.9/99%	(4)
Bat SARSr CoVZC45	88.1%	77.8/82.3%	98.7/100%	93.4/98.6%	91.1/94%	(3)
Pangolins	90%	90.4%	100%	98.2%	96.7%	(58)

#### **Link of SARS-CoV-2 and SARS-CoV with live animal market**

The outbreak of SARS-CoV was linked to the wildlife meat industry (63). According to the epidemiological analysis data, SARS coronavirus had links with live animals as they had history of contact with specifically palm civets. Serological examination revealed that the anti-SARS-CoV antibody IgG was indicated higher in animal traders than the general population (Control & Prevention, 2003). During the pandemic of SARS-CoV, in live animal markets, a raccoon dog and Paguma larvatapalm civets were recognized to contain SARS-CoV like virus that was nearly similar with SARS-CoV that causes SARS disease. After terminating all the civets from the live animal markets by killing them, no more SARS had been identified neither reported anywhere. Though, palm civets from the farms or wilds without access to live animal markets have been reported to be mostly

negative for SARS-CoV, indicating that palm civets were only serving as the intermediate host, but they aren't the natural hosts carrying SARS coronavirus (64, 65). Various other mammal species from the live markets were reported to have anti-SARS-CoV antibodies that supported the possibility of multiple species being intermediate hosts. *Rhinolophus* bats coronavirus was revealed to be closely related to SARS-CoV and they were also detected positive for anti-SARS-CoV antibody and their coronavirus's genome sequence is 88-92 percent similar to SARS-CoV, it provides an evidence of those bats being natural reservoirs of SARS-CoV (66,67). WIV1 virus is said to be the one ancestor of SARS-CoV in bats as it shares 95 percent genome sequence with the epidemic causing SARS-CoV virus (68).

As the animals from the live animal market have previously been listed as the intermediate hosts of the SARS outbreak in a province of China (64), it is proposed that the outbreak of SARS-CoV-2 emerged from the seafood market of Wuhan with its earliest transmission from live wild animals to humans accompanied by human-to-human transmission is most probable and convincing (69). Although a recent study has stated that the first patient who was reported to be diagnosed with COVID-19 on 1st December, 2019 had no any link of contact with the market (70, 69). Several ongoing research studies have disclosed that the potential source of SARS-CoV-2 could be bat. Although there is no confirmed evidence till yet that SARS-CoV-2 emerged from the seafood market (13). Yet, the cause and the origin of the disease remains an unresolved mystery. Chinese people's eating habits include consumption of wild animal foods as they believe that wild animals have medicinal value. In China, bats and pangolins are sold at live animal markets for food purposes and they are also an important part of Traditional Chinese Medicine. The scales of pangolins are used for medical purposes (56, 71).

#### **SARS-CoV-2 a recombinant virus**

Lu et al., (20) in his research study also considered the factor of SARS-CoV-2 as a recombinant virus. He stated that the coronaviruses and the saberviruses experiences recombination naturally as from the SARS-COV-2 analysis there are evidences of recombination at multiple locations. So a recombination can be among SARS-COV, pangolin coronaviruses and RaTG13 or RmYN02 (56). Among coronaviruses, the genome changes due to the gene exchange, recombination, insertion and deletion of genes are constant and persistent (72). There has been proof of natural recombination in HCoV-OC43 and HCoV-HKU1, also there is evidence in batCoV-HKU9 and bat SL-CoV. A third specie having contact with pangolins and bats might have been responsible for the recombination of SARS-CoV-2 (73, 30). The possible recombination of SARS-Cov has been identified with alpha-coronavirus and gamma- coronavirus lineages. Specific recombination regions were found in nsp9 and nsp10 and also in RNA dependent polymerase (74). SARS-CoV-2 RNA genome sequence analysis has reported that it is a recombinant virus and identified the recombination to be in between bat coronavirus and another coronavirus that is unknown. The recombination has been occurred within the spike glycoprotein that is responsible cell surface receptor

recognition (55). There are still some pieces missing in the puzzle regarding the zoonotic roots of SARS-CoV-2.

#### **COVID-19 – Testing of a biological weapon**

Biological weapon is referred as the intentional and calculated use of microbial agents and their toxins as weapon against population for mass destruction as bioterrorism or as biodefense strategy. It causes high mortality and morbidity. The biological agents selected as biological weapon mostly has aerosol route of transmission and they are manipulated by genetic engineering (75). The use of microbial pathogens as biological weapons has history from ancient times. One of such examples is of 14th century, when Hittites sent infected rams to cause Tularemia (76). The first ever use of biological warfare is considered to be by Mongols who were suffering from a plague and to beleaguer the Caffa City, they threw the dead bodies of their suffering companions over the wall of the Caffa. The plaque causing bacteria was quickly spread into living beings from the corpses by some fleas and caused massive destruction there (77). The mass production of microorganisms to be used as biological weapons was started by Japan and it is claimed by (77) that Japan attacked almost 11 cities of China with those biological agents by directly spraying them from the aircraft at that time. United States initiated the Biological weapon program as a defense strategy against the possible attack by Germany. They filled almost 5000 bombs with germs.

#### **SARS-CoV-2 is a biological weapon?**

Biological weapons have pandemic potential and similarly COVID-19 has rapidly caused a pandemic situation. The first case of SARS-COV 2 was revealed in Wuhan city of Hubei Province, then it spreads to other cities of China and now the pandemic virus has almost covered the whole world (4). The origin of SARS-CoV-2 is not provable till yet and being unsustainable is a renowned characteristic of biological weapons (78).

#### **Classification of potential biological terrorizations**

Potential biological terrorizations are classified into three categories by U.S. Center of disease Control and Prevention (CDC). According to their categories, COVID-19 totally falls in Category A and Category C, which is undeniable proof of it to be a biological weapon (79).

##### **A Category:**

- Having high mortality rates
- Transmission from individual to individual
- Cause Social disruption
- Reason of public panic

##### **C Category:**

- These pathogens lead to low immunity in population
- High Mortality and Morbidity rates
- Are engineered for Mass propagation

#### **Genetic Modifications**

A research study has stated that genes of COVID-19 contain pShuttle-SN sequences. These pShuttle-SN sequences are remainders of sequence of genetic engineering that is used for insertion of genes into viruses and microbes. Some expert researchers have revealed that there is a greater possibility that COVID-19 must have been genetically engineered with HIV's key structural proteins. These key structural proteins are HIV-1, Gag and gp120. This revealing provides

undeniable proof that SARS-COV 2 is not naturally originated but has been genetically engineered in the laboratory (80). Scientists in Thailand have reported that RNA segments of COVID-19 resemble more with HIV than SARS and MERS (81). According to Coutard et al., (29) genome of COVID-19 has expressed that it is recombinant of HIV and SARS origins. HIV and SARS are two different species of viruses and they belong to different and distinct ancestors and pedigrees. The recombinant of these two species can never be emerged in a natural environment and process because of their different existence duration and space. Thus, from this fact it cannot be a product of natural process but instead it is definitely a genetic engineering product (29). The sequence of spike protein has revealed that an additional proline is inserted in the sequence; hence the sequence inserted is PRRA. It has been stated by Andersen et al., (14) that addition of polybasic cleavage site through recombination or insertion converts the low pathogenic form of virus into high pathogenicity (14). Furthermore, it is reported in Jewish Press that Covid-19 patients are responding to the treatment used for HIV. These medications include Lopinavir, Ritonavir (81).

#### **Failed Vaccine Development of SARS?**

However, there is difference of opinion between these experts that whether it is testing of a biological weapon or either it's a failed vaccine development experiment against SARS virus. A researcher has concluded that the comparison of this sequence with other proteins has revealed that SARS protein is also present in COVID-19 sequence which can be result of an objective to produce reactogenic vaccine (6).

#### **Tested biological weapon potential?**

It is claimed in different studies that strain of coronavirus was retrieved from a Saudi old man who was diagnosed with SARS virus in 2012. His Egyptian physician who is a virologist, Dr. Ali Mohamed Zaki sent the biopsy of lung tissues of patient for genetic sequencing of the virus strain to Dr. Ron in Holland. Later, In May 2013, Canada National Microbiology Laboratory's Scientific Director Dr. Frank Plummer acquired this biopsy sample. Appropriate cell lines were used to cultivate the viral sample in Dutch Laboratory. They also performed animal inoculation of this deadly virus to know their susceptibility. It is claimed that deadly viruses were smuggled to China in 2019 which is mysterious (82). At Canada National Microbiology Laboratory which is located in Winnipeg, researchers alerted that smuggled viruses were deadly and have strong potential to be a reason of pandemic (82). Later the inquiry on smuggled viruses has traced that Chinese scientists including Dr. Xiangguo, Dr. Keding Cheng and other research team members were accused to smuggle these deadly viruses from Canada National Microbiology Laboratory. These scientists were formerly working in this Laboratory. They smuggled these viruses to different China's Research Institute of Virology which are located in Beijing, Hubei and Changchun. These particular Chinese institutes are well known for biological weapon program (83, 84).

#### **Wuhan Institute of Virology?**

The initial cover up of the Covid 19 spread and the removal of the Wuhan's senior health official has also raised questions on the origin of Covid-19. It is also a fact that Wuhan Virology Lab located in Wuhan Institute of Virology (WIV)

has potential and capacity for originating and developing biological weapons (85). Washington Times in January has claimed in its two articles that coronavirus is a part of biological weapon program of China (86) later the claim was rejected by them but again in February, Tom Cotton who is senator of US has proposed that it can be Chinese biological weapon (87). Wuhan institute of Virology was upgraded in 2015 to National Biosafety Laboratory (Level 4). This laboratory was involved in coronaviruses research and they were investigating on the causative agents of SARS-CoV which was emerged in 2003. Shi Zheng Li, the Wuhan institute's lead virologist, all of his research studies on bat-related Coronaviruses were based in Yunnan's southern subtropical regions. It revealed that virologists of Wuhan Institute of Virology were researching on bat related coronaviruses (88).

There are in fact earlier known studies in which modifications have been made to the coronavirus. The collaborative research project on coronavirus was carried out between Wuhan Institute of Virology and University of North Carolina. Menachery et al. in an article in 2015 (49), has explained about their laboratory project on gain of function studies on coronaviruses. The author has pointed out to the earlier research papers of Chinese and American researchers explaining and addressing how modern chimera viruses have been engineered using SARS-coronavirus. He has referred to some research studies (49). World renowned Chinese scientist Dr. Zheng-Li Shi and his colleagues has led a research project at Wuhan Institute of Virology in 2008 that has demonstrated the technological potentials to exchange RBDs between human coronaviruses and bat coronaviruses.

#### **United States Originates COVID-19 as a Strategy against China?**

China has 2nd largest economic power in the world after United States but their growth rate is higher than US. It has been forecasted according to Iranian's student news agency in 2020, the global economic growth of china's share will be 27 percent. Covid-19 pandemic has disastrous and destructive effects on China's economy, so here a though arise that which country will get benefit from downturn of Chinese economy (90) (Iranian Students' News Agency, 2020). It is claimed by Law (91) that it's an undeniable fact that USA has originated the COVID-19 as a biological weapon for consolidating and preserving their international economic and political dominance, authority and power.

He stated that SARS like Coronavirus named "SL-COVs" were isolated from horseshoe bats in 2008. The N terminus of the spike protein of these "SL-COVs" was combined with a pseudovirus system that was HIV based system and it was further combined with cell lines that express ACE2 molecules of civet, human and horseshoe bat (91). It was also reported by Ren et al., (92) that different sequence of SARS Coronavirus were inserted into backbone of "SL-COVs" to construct series of "S Chimeras". Some animal models have ACE2 receptor that is very similar to human ACE2 receptors. The cells of these animal models were infected. The chimeric Spike proteins gained their ability of entering into cells through these human angiotensin converting enzymes receptor sites and the small segment of RP3-S was replaced with BJ01-S. These changes made it possible for "SL-COVs"

to convert from non-ACE2 binding to ACE2 binding (92). It is stated by Sahin et al.,(9) that both SARS and Covid-19 has occurred during the most well-known and popular festival of China that is called as "The Spring Festival". Almost 3 billion people travel during this festival. These circumstances are the ideal conditions for the transmission of this extremely infectious disease (9).

#### **Gain of Function Technology?**

It also raised question on the origin of SARS by quoting Ren et al., (92) statement that SARS coronavirus protein failed to use RpACE2 of bats as a receptor. The use of different combinations of virus recombination, gain of function (GOF) that is a DNA engineering technology and host switching has already been studied in past and successful experiments has already been achieved. Law (91) has called COVID-19 as one of the biological weapon at its best. He has also illustrated the inserts of HIV envelope protein on the binding site of COVID-19's glycoprotein. He further reported that it has potential and ability to attack and kill any organism that has similar human ACE2 receptors (91). An article published in Nature Medicine by Menachery et al in 2015 (49) has alerted a pandemic as a post threat to human emergence. The authors of that article were from USA and two of them were Chinese scientists and it was for American "Gain of Function" technology (49). Revealing and assembling all these facts, Law(91) has claimed that it was GOF technology that has enable and made it possible for SARS Cov and HIV recombinant to become a one of the most powerful biological weapon named "COVID -19" or "SARS COV2". According to Courtard et al., (29) COV-19 Spike protein has 12 additional nucleotides Law,(91) called them the genetic engineering "insertions" According to Prof. Francis Boyle, GOF has no medical use and it is a DNA engineering technology for "turbo-charging" threatening, high risk pathogens and biological substances (91).

#### **COVID-19 accidental release from Laboratory**

One of the extraordinary secrets of the Covid-19 pandemic is the manner by which, precisely, the SARS-CoV-2 infection made the jump from wildlife life into people. Researchers who've examined the infection's genome are confident that it is possibly originated from a bat in China. But Chinese epidemiologists have not revealed much about how or where the first patients get infected. The outbreak became exposed before the end of 2019 when early cases were connected to a food market in Wuhan. A virology institute in Wuhan studied on SARS-related corona virus. The lab was warned regarding safety issues, in 2018. In any case, in spite of widespread online hypothesis, there is no proof of any sort that the SARS-CoV-2 infection (which causes COVID-19) was discharged inadvertently from a lab.

#### **A Killer Corona Virus Probably Originated From A Lab In Wuhan:**

Early research found that SARS-CoV-2 focuses on the ACE2 receptor, which is found in East Asians at around five-times the pace of other worldwide population, showing that the Wuhan SARS-CoV-2 strain was possibly developed as a part of an addition-of-function protective undertaking possibly connected to immunotherapy or immunizations, never intended to escape the laboratory, but meant to provide as a Red Team to combat against, not as a threatening weapon

since the infection is probably wired to be substantially more destructive among Asian populations (95).

A research article published in *The Lancet* revealed that 41 individuals in Wuhan were reported to have the acute respiratory disorder and 27 of them had link with Hunan Seafood Market. SARS-CoV-2 was reported in 33 of 585 samples collected on the market following the outbreak of virus. The market was considered being the origin of this pandemic, and was sealed as per the standard of quarantine the origin source during a pandemic (5). The bats conveying CoV ZC45 were initially found in Zhejiang province or Yunan, the two of which were in excess of nine-hundred kilometers from the fish sea food market. Bats were regularly found to live in caverns and trees. Be that as it may, the seafood market is in a heavy populated area of Wuhan, a metropolitan of ~15 million individuals. The possibility was exceptionally less for the bats to travel to the market. As indicated by metropolitan reports and the declarations of 31 residents and 28 travelers, the bat was never a food source in the Wuhan city, and no bat was exchanged in the market. There was conceivable characteristic recombination or middle of the road host of the crown infection, yet minimal confirmation has been reported (95). The area around seafood market is screened and recognized two labs directing examination on bat corona-virus

Inside ~280 meters away from the market, The Wuhan Disease Control and Prevention Center (WHCDC) was located

WHCDC facilitated animals in labs for research reason, one of which had practical experience in pathogens assortment and recognizable proof. In one of their investigations, 155 bats were caught, including *Rhinolophus affinis*, in Hubei region, and in the Zhejiang region, 450 other bats were caught. In the Author Contributions (JHT) the professionals in collection was noted. Besides, he was communicated for gathering infections on across the nation papers and sites in 2017 and 2019. He reported that he was once assaulted by bats and a bat blood shot on his skin. He knew the outrageous threat of the contamination so he isolated himself for 14 days (96). In another mishap, he isolated himself again in light of the fact that bats peed on him. He was once excited for catching a bat conveying a live tick (97). The enclosed livestock were medically examined and DNA, RNA extraction and sequencing was carried out by tissue testing. The tissue tests and contaminated junks were source of pathogens. They were just ~280 meters away from the fish showcase. The WHCDC was additionally adjoining the Union Hospital where the primary gathering of specialists was infected during this epidemic. It is conceivable that the infection spilled around and some of them tainted the underlying patients in this epidemic, however strong verifications are required in future investigation (98).

The subsequent research center was ~12 kilometers from the fish market and had a place with Wuhan Institute of Virology (WIV)

This research center detailed that the Chinese horseshoe bats were normal repositories for the extreme intense respiratory condition SARS-CoV which caused the 2002-2003 pandemic. The principle analyst took an interest in an undertaking which created a chimeric infection utilizing the

SARS-CoV turn around hereditary qualities framework, and announced the potential for human development. An immediate hypothesis was that SARS-CoV or its subordinate may spill from the lab (99). A research facility in Wuhan is licensed to work with the most dangerous pathogens in the world. The move is a piece of an arrangement to work somewhere in the range of 5 and 7 biosafety level-4 (BSL-4) labs over the China. A few researchers outside China panic about pathogens escaping from the labs, and the expansion of an organic measurement to international pressures among China and different countries (85).

Officials of the State Department expressed concern at Wuhan's security in 2018. This does not, however, prove that its scientists were inadequate.

The Chinese government's helpless transparency Record; the way that the WIV, a research place with offices in a similar city where the infection initially showed up, was considering risky pathogens, including bat corona virus; and US authorities' interests about the lab's safety guidelines in 2018, per the Washington Post (100). The Washington Post paper announced data got from strategic links on 14 April. They show that, in 2018, US science ambassadors were sent on repeated visits to a Chinese exploration office. Authorities sent two warnings to Washington about the lab. The segment says the authorities were stressed over safety and the executive's shortcomings at the WIV and called for more assistance (100) likewise declare negotiators were concerned the lab's examination on bat corona infections could hazard another SARS-like pandemic. The paper says the links fuelled later conversations in the US government about whether the WIV or another lab in Wuhan could have been the source of the infection behind the current pandemic. The outbreak became exposed before the end of last year when early cases were connected to a food market in Wuhan. In any case, in spite of wild online hypothesis, there is no proof of any sort that the SARS-CoV-2 infection (which causes Covid-19) was discharged accidentally from a lab (101).

#### **What kind of security measures do labs use?**

Research centers studying the virus and bacteria are adopting a BSL standard, in which the BSL standard demonstrates the degree of biosafety. Four levels are tested based on the kind of organic operator and the insurance controls are required to distinguish them.

- Biosafety Level 1 (BSL-1) is the least used and does not present a danger to people at laboratories occupied by natural operators.
- The safety measures regulations increase across levels until they hit Biosafety Level 4 (BSL 4), the highest, saved for laboratories that handle the most dangerous disease pathogens, for which no antibodies or medicines are available at all: Ebola, Marburg infection accounts for two foundations in the United States and in Russia, it is the small pox.

The Biosafety Labs measures are applied universally, however with some restorative varieties.

Dr. Filippa Lentzos, a biosecurity master at King's College London said that the Russians have the highest control laboratories as 1 and the least guideline labs as 4, and the standard is particularly backward, but the certified practices and requirements for establishments are relative.. In any case,

while the World Health Organization (WHO) has distributed a manual on the various levels, the principles are not upheld by any arrangements. "They have been made to be in the prosperity for working safely, for laboratory workers who might lean toward not to corrupt themselves or their area, and for the earth to keep up a key good ways from accidental releases," says Dr. Lentzos (101).

#### **What kinds of security/safety failures were the cables describing?**

There is no any accurate answer. For the most part talking, there are various ways that security measures can be penetrated at labs managing organic specialists. As per Dr. Lentzos, these include: "Who approaches the lab, the preparation and boost preparing of researchers and professionals, strategies for record-keeping, signage, stock arrangements of pathogens, mishap notice rehearses, crisis systems."

#### **Be that as it may, how unordinary were the concerns communicated in the diplomatic cables?**

In 2014, mishap occurs in a research area next to Washington; over-the-counter vials of smallpox were found in a cardboard box. In 2015, the US military mistakenly sent Bacillus' live test to nine laboratories and a military base in South Korea rather than dead spores. SARS infection was accidentally released in laboratories, Singapore, Taiwan and Beijing, between 2003 and 2004. The vast number of laboratories at the lower end of the BSL scale has various security procedures and several smaller breaches are not into the news (101).

#### **Conclusion:**

Since the pandemic started, tracing the potential origin of newly emerged coronavirus SARS-CoV-2 is in continuous phase. Genomic similarity with bat-SARS-CoV RaTG13 has suggested that the natural reservoir of SARS-COV-2 is considered to be bats while Manis Javanicapangolins are stated to be as intermediate hosts. But there are still some pieces missing in the puzzle regarding the zoonotic roots of SARS-CoV-2 as how bats and pangolins came into contact resulted in recombination of coronavirus and if the origin of SARS-CoV-2 has zoonotic roots then why there are a lot of differences in the genomic sequence of SARS-CoV-2 with other coronaviruses. The revealing of presence of genetically engineered sequences in genome of SARS-CoV-2, the potential of SARS-CoV-2 being exceptionally well adjusted to infect human population, ongoing research on bat related coronaviruses and SARS-coronavirus in laboratories of China and USA before the emergence of pandemic and the experiments on the gain of function technology leads to the suspected link of SARS-CoV-2 as testing of a biological weapon but the bioweapons are meant to affect only the enemy not one's own people and country, so in case of COVID-19, it is impossible to only affect enemy or as a purpose of testing because its transmissibility potential is so high that a country can't save its own people from it. Scientific evidence reinforces the conclusion that corona virus may come out of nature either from Wuhan market or elsewhere. An excessive number of surprising incidents would have needed to occur for it to have escaped or leaked from a lab. In any case, the Chinese government has yet not been willing to give data that would explain waiting inquiries concerning any

conceivable pretended by either Wuhan lab. That is the reason insight organizations are as yet investigating that chance, regardless of how remote it might be. So, there is no solid evidence or proof, that the corona virus was accidentally released from Wuhan Lab. COVID-19 probably has the natural origin as the evidences of bats being the natural host and pangolins being the intermediate host of SARS-COV-2 has more potential than being it to be a biological weapon or an accidental release from lab. But the possibility of other origins of SARS-CoV-2 should not be ruled out; it needs further higher level research on its suspected testing as a biological weapon or an accidental release from labs.

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