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Story of the Most Triggering Issue of the Globe: 2019 Novel Coronavirus (COVID-19)

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Abstract: ***Currently, the world is experiencing the most treacherous and hazardous situation with a vulnerable crisis situation by a daredevil named 2019 Novel Coronavirus. The term "coronavirus" became ubiquitous, but its origin, its reservoir of transmission from animal to human, the antiviral vaccine to fight against this corona is yet anonymous. This seems to be quite daunting task for many researchers who are working on it because of the pathetic situation which it retained on us. Across the globe, its virulence and its outspread are proliferating rapidly. It is a respiratory syndrome, which causes breathing disorders and progressively taking away many lives till date. This coronavirus and its outcomes are abruptly enduring to live in pathetic situations with a peak stage of panic levels. Is it interested to know about this daredevil? Absolutely yes! This ongoing discussion will concisely narrate about its origin, history, outbreak effects, transmission, and mechanism of prognosis, diagnosis, treatment and some of its preventive measures.***

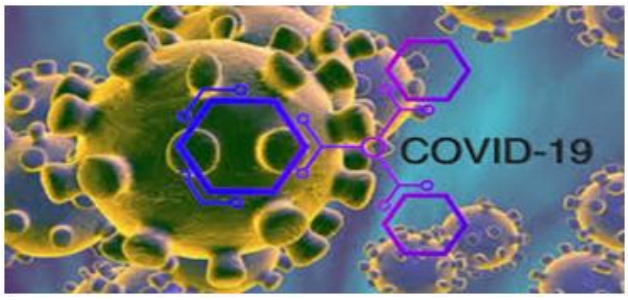
Keywords: Coronavirus, Respiratory Syndrome, Outbreak effects

1. Introduction of Novel Coronavirus

1.1 History and Origin of the disease COVID-19

***History of Coronavirus*:** Viruses continue to emerge and pose challenges to public health though decades pass. Recently, coronavirus is a threatening respiratory outbreak after SARS–CoV and MERS. In the past decades, SARS – CoV (2003) infected 8098 individuals having mortality rate of 9%, which was happened across 26 countries in the world. And now, novel coronavirus (2019) transmitted between 1,192,618 individuals with mortality rate of 3.4% which is still in a great pace of infecting virus across 205 countries and two international conveyances till the date of writing, which was estimated by WHO. Recently, in the December 2019, WHO China office informed, Wuhan, an emerging business hub of China experienced an outbreak with a sudden outbreak of pneumonia cases that killed more than 1800 and infected over 70,000 individuals within the first 50 days of the epidemic.

After further investigation, it was found that the viral particle which caused this devastating outbreak was not known previously and is completely a new one and was named as novel corona virus. A novel coronavirus (nCoV) was then isolated and identified as the causative virus by the Chinese authorities on 7 January 2020. [NOTE: As this is a new virus, what we know today, may change in future].



***Origin of Coronavirus*:** This corona virus recently at the end of 2019 shook the world with unfamiliar etiology. It is analyzed that this outbreak was initiated from the Hunan seafood market in Wuhan city of China, which sells live animals like bats, frogs, snakes, birds etc; and it rapidly infected more than 50 people immediately. On 12 January 2020, the National Health Commission of China declared that it is an unknown pneumonia outbreak.

Then, the sample from the patients is collected and the genome of the viral particle was isolated and identified as a novel coronavirus. Initially, it was indicated that the patients infected with the Wuhan coronavirus induced pneumonia in China, may have visited the Hunan seafood market where live animals were sold or patients may have consumed infected animals or birds as a source of food. Upon further investigations, it is detected that the individuals who have not visited the sea market also acquired the infection. This indicates, human to the human spreading ability of this virus, which was eventually reported in more than 100 countries in the world.

As soon as the outbreak occurred; scientists of China isolated the genomic material of the virus particle and sequenced it. This sequence showed the similarities with the SARS virus found in bats. It is identified as the mutated version or advanced version of previously observed SARS CoV and hence named as SARS CoV-2. But later on sequencing the pangolin corona virus showed the most similarity with this new virus more than that of the virus isolated from the bats. It almost showed 99% similarity, including the specific region of the S protein, which is major part to attack viruses. The amino acids present near the receptor binding regions, nearly 75 of them are found similar to the new viral genetic material when compared with the pangolin corona virus. Thus this new SARS CoV-2 is found as a chimeric of two previously existing viruses. So it is interpreted that it may be originated when both the viruses attached a similar organism and thus entered the human host cell through that reservoir.

This disease is classified under zoonotic disease because of its transmission from animals to humans, due to spill over.

1.2 Structure of COVID-19

A Novel Coronavirus (nCoV) is a new type of virus that is not identified in humans previously. Thus this structure contains little difference, but is found almost structurally similar to SARS Corona virus which was observed in 2003.

This new SARS CoV-2 virus consists of core of genetic material and surrounded by envelope with protein spikes. This gives the appearance of crown. **In Latin,** crown is known as **"Corona"**. So this is how it acquired the name Coronavirus.

Coronavirus is the largest known RNA viruses; it is *enveloped; positive single stranded RNA* virus with the *nucleocapsid*. Helical nucleocapsid which is a lipid bilayer encloses the genetic material. The viral bilayered envelope contains few important proteins, *the spike protein(S), the membrane protein (M)* and *the envelope protein (E)* and a *hemagglutin esterase (HE)*.

Family: Coronaviridae.
Order: Nidovirales.
Subgroup: beta coronavirus.
Nick name: Wuhan Coronavirus or 2019 Novel Coronavirus (2019-n CoV)
Size: 30kb in length- and with a 5' cap structure and 3'poly A tail.
Diameter: 65-125nm.
Phylogenetically similar to: Severe Acute Respiratory Syndrome (SARS) like bat virus and Pangolin SARS virus.
Primary reservoir: bat
ICTV nomenclature: SARS-CoV-2
Disease caused: COVID-19
Others: Highly transmittable and pathogenic viral infection causing agent.

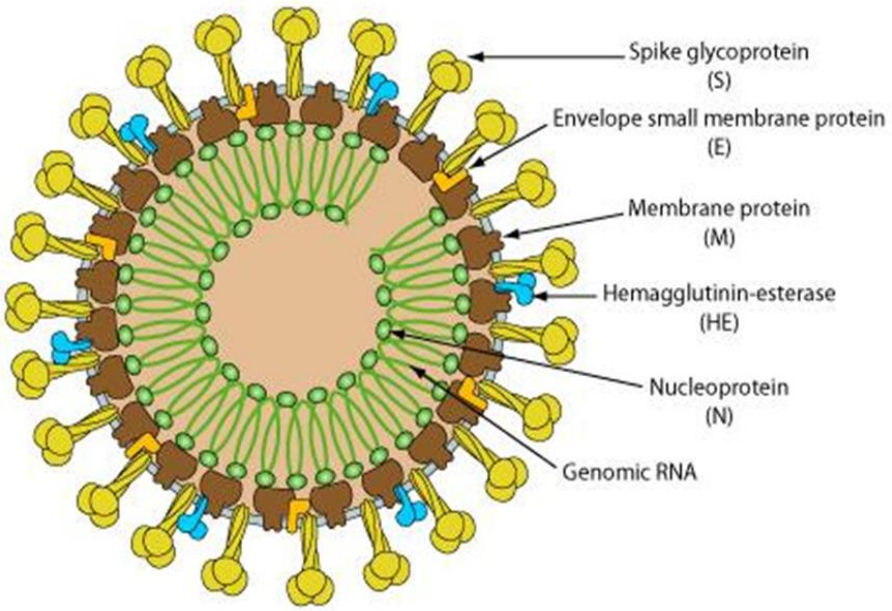


Figure: Structure of COVID-19

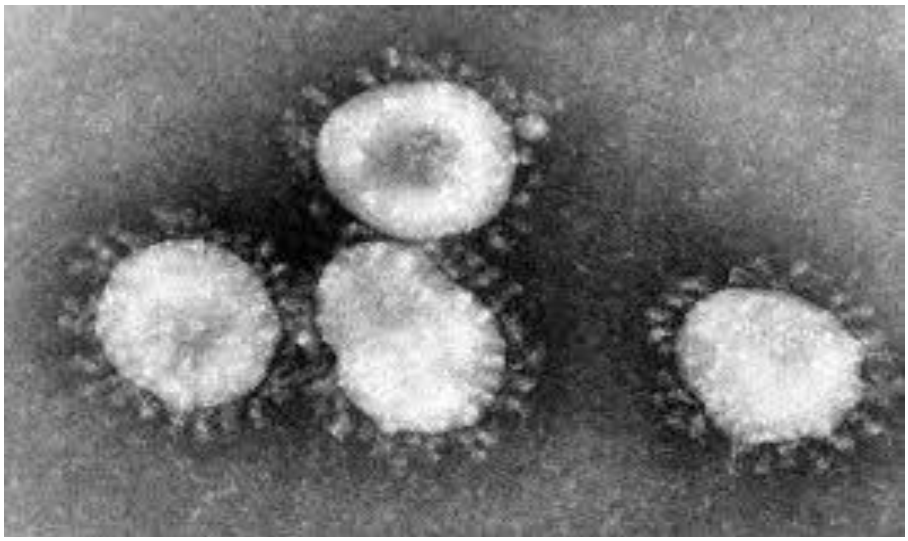
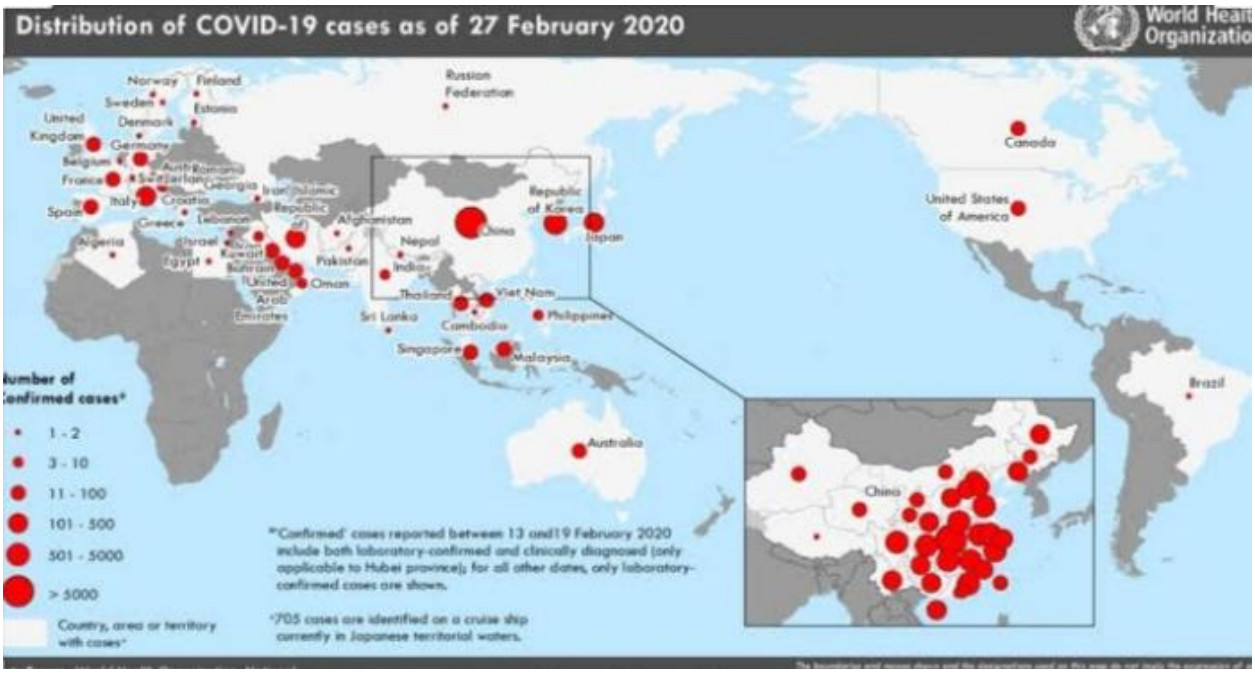


Figure: Microscopic view of Corona Virus

1.3 Epidemic of COVID-19



Initially on 31 December 2019, the outbreak of this disease was observed. Later on it was informed to WHO by the Chinese government. As of 23 February 2020, the countries affected are:

China, Canada, USA, Australia, Malaysia, Singapore, Cambodia, Philippines, Sri Lanka, Thailand, Vietnam, India, Nepal, Republic of Korea, Japan, Russia, Iran, United Arab Emirates, Egypt, Israel, Lebanon, Italy, Germany, Spain, France, Belgium, UK, Sweden, Finland.

This widespread outbreak is still in an emerging progress and infecting lakhs of people across the globe.

As of April 8th 2020, the virus still continued to attack and nearly 83143 individuals died globally (according to Johns Hopkins University).

1.4 Brief of the COVID-19 Disease

1) ***Source of Transmission*:** Usually this infection occurs when a SARSCoV-2 virus enters the body, increases in number, and then affects the tissues in the body. In general, respiratory viruses are usually transmitted through droplets created, when an infected cough or sneezes or through something that has been contaminated with virus.
2) ***Mode of Transmission*:** Microorganism or the virus is transmitted through the any of the ways.
   a) **Direct Mode**
      - Direct Contact – Touching an infected individual may transmit the viral particle to others; which are present on the infected individual due to infected droplets which reside on them.
      - Contact with viral contaminated surfaces, contact with infected individual nasal secretions, vegetation or any abiotic factor which contain viral particle can also make a way for spread of disease to healthy individual.
      - Droplet Spread – It refers to spray of infected droplets with relative large or shorter-range aerosols produced by sneezing or coughing.

   b) **Indirect Mode**
      - Indirect Contact – It refers to the transfer of an infectious agent from a reservoir to a host.
      - Airborne transmission- The droplets which contain viral particle present in the air can also cause the infection (within the short range of distance), which is classified as air borne transmission.
3) **Portal of entry and incubation period**
   a) **Portal of entry:** After the virus coming into contact with the human body it takes the portal entry through nose and enters the respiratory tract.
   b) **Incubation period:** It is the period between exposure to an infection and the appearance of the first symptom. A current estimate about the incubation period of COVID-19 range is 1-14 days (median 5-6 days). The viral particle takes 8 days to progress and stabilize itself in the human body to show symptoms, and then it causes illness and shows symptoms.

4) **Signs or Symptom**

After the incubation period, people may be sick with the virus for the next 7 days of viral cycle. The most common symptoms of corona virus disease (COVID – 19) are dry cough, cough with sputum, sneezing, running nose, loss of smell, head ache, fever, sore throat, difficulty in breathing, shortness of breath, multiple organ failure, diarrhea, pneumonia, bronchitis, and in severe cases can lead to death.

5) **Mechanism of COVID-19:**

MECHANISM: A mechanism is a systematic procedure of any microbe interacting with the parts of the body and

metabolic pathways that produce one or more effects. The structure of SARS CoV -2 is well built to enter into the host cells and attack the tissues or cells of throat, trachea, and pulmonary tract on its onset with pneumonia like adverse affects and eventually leading to the damage of the other tissues and cells of the body causing multiple dysfunctions of organs and severing the condition of the host leading to death. The mutation caused in the SARS corona virus structure promised a great challenging structure to the world.

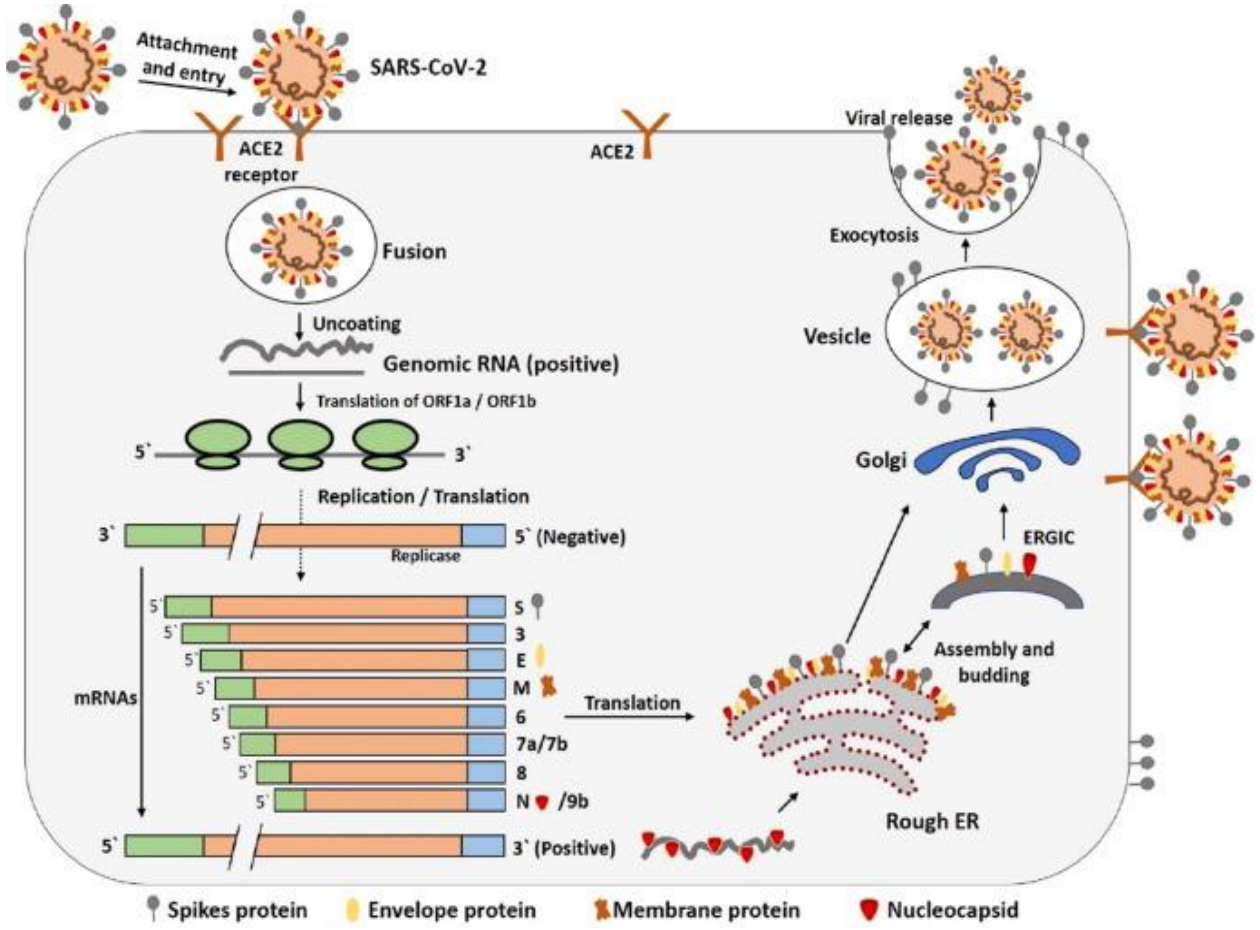
6) Mode of entry of the pathogen into the human cell

Either through any of the mode, the virus enters the human body and makes its way to survive. This novel corona virus-19 has the structure similar to the SARS CoV and is hence named as SARS CoV-2.

1) This SARS CoV-2 virus enters the body through the respiratory tract and mainly targets the goblet cells and ciliated cells on the first line in order to survive and colonize.
2) Goblet cells help in covering the respiratory tract with mucous so that mucous entraps the pathogens or foreign particles. On the other hand, ciliated cells provide the mechanical movement in the respiratory tract and thus sweep away the foreign particles and pathogens away from the body through coughing and sneezing. Thus these cells provide first line physical defense to the respiratory infections.
3) Thus it enters into the human body and now infects the epithelial cells of the body, mainly respiratory tract cells. The virus comes into contact with the help of receptor binding regions (RBD) present on the viral particle and the receptors present on the host cells.
4) The angiotensin-converting enzyme-2 (ACE-2) receptor, found on the host cells provide affinity for the viral particle to bind with the host cell. The virus particle uses its specialized glycoproteinacious spikes present on its outer coat- contain 394 glutamine residues to recognize 31 lysine residues on the ACE-2 receptor. Thus the receptor-viral interaction is observed. The detailed mechanism is yet unknown, but some experts believe it to be like lock and key mechanism.
5) The receptor-viral complex shows the conformational changes on the cell membrane and facilitates the entry of the viral genetic material into the cells and the phenomenon called endocytosis occurs.
6) Thus the viral particle makes a way to enter into the cell host and transports its genetic material for replication, transcription and translation.

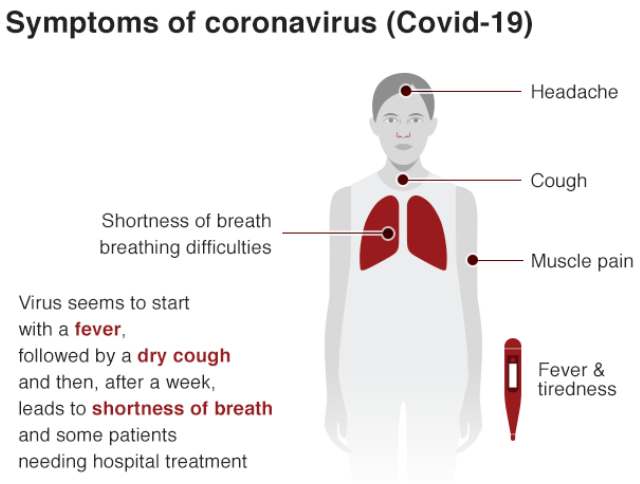
7) Life cycle of SARSCoV-2 in the human cell

1) After the endocytosis the viral particle oozes its genetic material into the cell. This genetic material is single stranded RNA (+ssRNA). This genetic material uses the host cells machinery by plundering.
2) This +ssRNA advanced its structure that it need not enter into the nuclear region to replicate its genomic material. Thus +ssRNA uses the ribosome's as its basic machinery to replicate the +ssRNA strand and forms – ssRNA.
3) This is usually through translation of the Open Reading Frames (ORF) 1a and 1b, which results in the formation of the two important polypeptides 1a and 1ab. These polypeptides are cleaved to proteins using viral proteinases and combine with –ssRNA. (+ ssRNA is the sense stranded RNA and- ssRNA is the anti sense stranded RNA.)
4) Two main mechanisms are observed- replication and translation at this phase. Thus the new daughter viral particles are formed.
   a) Replication of the – ssRNA results in the formation of + ssRNA, this acts as the genetic material for the daughter viral particles.
   b) Discontinuous translation, on the other hand, results in the formation of the sub-genomic mRNA. The translation of these sub-genomic mRNA results in formation of protein components of the viral particles, mainly S spike protein, M protein, E protein and other important components.
5) All these individually formed nucleoprotein from ribosomes and glycoproteins, other proteinaceous parts and other components from endoplasmic reticulum are packed into fine viral structures in the golgi complex and are transported into the vesicles.
6) These vesicles bud off (exocytosis) from the host cell and burst out to release new viral daughter cells.
7) As the cell undergoes much pressure during the viral replication, transcription and translation, the cell is subjected to apoptosis, mean cell death.
8) Thus the new viral particles are formed and they in turn attack the new neighboring cells and thus damage the tissues and organs of the host body and worsen the clinical condition of the host body.



8) Pathophysiology

1) The SARS CoV-2 virus particle mainly targets the pneumocytes. There are two types of pneumocytes-type 1 and type 2 cells. *Type 2 pneumocytes are primarily affected.*
   - Type 1 pneumocytes help in gaseous exchange and
   - Type 2 pneumocytes help in production of surfactant, which decreases the surface tension in the lungs and reduces the collapsing of the alveoli
2) As the virus particles progress in the human body, hosts immune system identifies the pathogens, and trigger neutrophils, macrophages and other complement proteins to eradicate the viral particle invasion.
3) In type 2 pneumocytes, the interaction of the immune cells and protein complexes with the pathogen causes inflammation; and thus causes the dilation of the epithelial cells of capillary tubes beneath the alveoli and also increases the capillary permeability. Thus it results in leaking of the interstitial fluid into the alveoli. This is clinically called as *alveolar edema*. This accumulation of fluid in the alveoli objects the exchange of gases and creates much pressure in the lungs to meet the required oxygen level. Thus causes the *difficulty in breathing and shortness of breath*. Thus *increased heart rate* and *breathing rate* is observed. Thus this CoVID-19 is evidencing the symptoms of pneumonia. If this clinical condition progresses it may eventually lead to *death*.
4) Due to decrease in partial pressure of oxygen, *hypoxemia* is observed.
5) The debris, due to interaction of pathogen and body's immune proteins, cells and the interstitial fluid, due to alveolar edema, is expelled out in the form of cough. Thus *coughing up with sputum* is observed as a symptom.
6) Due to the damage of goblet cells, no production of mucous is observed and infection in throat leads to *dry cough*. Hence due to continuous cough *sore throat* is seen.
7) Macrophage releases Interleukin 1(IL-1), Interleukin 6 (IL-6) and Tumor Necrosis Factor-alpha (TNF-alpha). These released factor IL-1. IL-6, TNF-alpha acts on the hypothalamus of the brain to release prostaglandins which further releases the pyrogens, factors that cause fever. Thus *fever* is evidenced in CoVID-19.
8) Due to the dilation of capillaries, *blood pressure decreases* and thus blood volume. This results in *lowering the perfusion*. This causes the *multi system organ dysfunction* due to lack of oxygen and supplements to the organs.
9) Not only the respiratory tract but also the gastro intestinal tract is affected, because of the presence of ACE-2 receptors. Thus due to disturbed gastro-intestinal tract, *diarrhoea* is observed.



***Fatal Consequences*:** When untreated and in rare conditions, this virus leads to fatal conditions.
Three important stages of infection are mild disease, severe disease, and critical disease

- Mild disease is characterized by non-pneumonic or less pneumonic condition and is found in most of the cases.
- Severe disease is characterized by respiratory diseases, dyspnea, low level of oxygen and its supply in the body, this occurred in few cases.
- Critical disease is the last stage of the disease and septic shock, multiple organ failure and respiratory failure are associated. This is seen in very low cases.

2. Identification of the Pathogen and its Detection

Detection of the SARSCoV-2 is the most crucial part of the Corona virus outbreak. Diagnosis involves in collection of specimen or sample, preserving and transporting the sample to the laboratory, and then finally processing it.

2.1 Collection of Specimen or Sample

Specimen is usually collected from the lower or upper respiratory tract; blood, and sometimes urine and feces can also be used as specimen. Before collecting the sample, the individuals are allowed to rest for some time to bring the body to homeostatic condition. Then the areas from where the sample is collected are cleaned and then sample is collected. This has to be done by the specialist and has to be done very carefully under specific conditions (use of gloves, protective goggles, respiratory mask, and gown). Specimen has to be collected in the plastic swabbing kit only, in order to avoid the damages caused to both the individual and the viral particle.

- *Upper respiratory tract specimen collection*: Usually nasopharyngeal and oropharyngeal swab specimen is collected. For the nasopharyngeal sample, the swab is inserted into the nose to the post nasopharynx and swabbed for the viral particle. In oropharyngeal swabbing, the swab is inserted through the mouth and swabbing is done at the back wall of throat region. The specimen has to be collected carefully without touching the other parts of the nose or mouth.
- *Lower respiratory tract specimen collection*: Usually sputum, endotracheal aspirate, alveolar lavage can be collected. Sputum is collected into the sterile container.
- *Blood* is collected using needle. Usually pricking is done.

After collecting the sample it has to be labeled with patients' name, CoVID number, date of the sample collected and other details.

2.2 Transportation of specimen

- Samples are carefully stored and transported. Specimen or sample is generally stored at 2-8oC.
- If the specimen will reach the laboratory in less than 72 hours, store and ship at 4oC.
- If the specimen will reach the laboratory in more than 72 hours, store at -80OC and ship on dry ice and liquid nitrogen.

2.3 Processing of specimen

The sample or specimen is processed for detecting the presence of the viral particle. For molecular analysis assays the genetic particle is extracted and for serological studies directly the sample can be used. In molecular analysis assays the genome is selected and amplified and for the serological assays, detection of antibodies which are produced against the virulence of virus particles as a part of defense mechanism are tested.

a) Detection of virus using PCR test or molecular analysis :

***Materials and Methods*:** real time Reverse Transcriptase-PCR is used for the molecular analysis of virus.

Patients appearing with suspected symptoms are to be screened further for the detection of the virus using amplification tests (NAAT), like real time Reverse Transcriptase –Polymerase Chain Reaction (rRT-PCR). The SARSCoV-2 virus consists of single stranded RNA. N, E, S and RDRP genes which are present on the viral genome, are targeted and sequenced first using primers and probes. Then the sample is tested for the presence of the selected sequence using other primer and probe. The targeted patients sequence is amplified to produce complementary DNA (cDNA) at first and followed by ds cDNA and then it is qualitatively and quantitatively analyzed using fluorescent dyes.

Observation and Interpretation

1) Control shows no targeted sequence is detected in the patient sample.
2) Negative condition: no similar amount of targeted RNA sequence is amplified in the patient sample.
3) Positive condition: very high amount of targeted RNA sequence is amplified in the patient sample.

This test, since it is highly specific for the nucleotide sequence, is only used for the complementary sequencing of viral RNA genes. It is costly and when negative results are found for symptomatic individuals the test has to be repeated, because that may occur due to fault at any stage of the protocol followed.

b) Detection of virus using Non – PCR test or Serological analysis

Materials and Methods: Rapid COVID-19 Kit is used for the serological analysis in the Non – PCR test. (different kinds of kit are in usage in different countries).

This test is now highly accepted by FDA and is now in rapid use. Since it takes less time usually 15 min, results can be obtained as early as possible. This is also known as kit method. Different types of kits are now used globally and are manufactured by their own country. This kit contains different blocks like control Ig G, Ig M, sample and buffer slots. The sample and buffer are introduced into the kit and allowed to run for 15 minutes.

Observation and Interpretation

1) Indicating a mark in the control region is must for both the antibodies, since it indicates the kit quality. Absence of control indicates the damage of the kit.
2) Negative condition: Indicating only the control regions and no antibodies indicate that sample contains no viral particle.
3) Positive condition:
   - Indicating the presence of only Ig M antibodies in the sample shows the recent infection of viral particle in the body.
   - Indicating the presence of only Ig G antibodies indicate the advancement of the infection and patient need advance care.
   - Indicating the presence of both the antibodies shows that infection is caused in the body while ago and the individuals' body is trying to resist the body.

This can be concluded as because, as soon as the viral particle enters the body the first antibodies triggered are Ig M for the primary infection and then the Ig G antibodies come into the role to eliminate the viral particle during later stages.

Thus the presence of viral particle is detected.

3. Treatment

This SARS-CoV-2 virus can be eradicated by some effective measures. In the case of infection of virus into the human body, both the mechanical and chemical methods are used to treat the patient.

a) Mechanical treatment include intubation, ventilation to support the breath through artificial mechanisms
b) Chemical treatments include the use of drugs to inhibit the viral progression in the body using either inhibitors or anti-metabolites.

- Hydrochloroquine, is the most potent drug, being used for diagnosis with different combinations, chloroquine, azythromycin. This helps in reduction of fever and blocks the receptor binding site (ACE-2), in order to prevent interaction of virus particle.
- Antiviral agents like Lopinavir/ Ritonavir and Remdesivir (GS5734), Ribavirin, Avigan can inhibit the viral particles. Remdesivir, can also inhibit RNA polymerase.
- Kaletra, Actemra and Kevzara acts as inflammation reducing agents and inhibits interleukins mainly IL-6, thus prevents the alveolar edema, fever etc.
- Avigan is also used for treatment because of its action to reduce influenza.
- Recently drug called teicoplanin is being used which can inhibit the release of RNA into the host cell.
- Antibodies are also being used, mainly antibody AbCR3022 acts to reduce viral infection by binding to the receptor binding domain. Research on hyperimmune globulin called TAK-888 is going on to treat COVID-19.
- Recent investigations showed an oral drug called EIDD-2801can induce mutations in the genetic material of virus and thus inhibit the viral replication.
- Glucocorticoids like Tocilisumab (TCZ), are effective in treating this disease by blocking JAK inhibitors, thus reduces inflammation. Corticosteroids reduces lung inflammation hence acts against this virus.
- Various interferons, immune boosters, anti pyragenics are used in treating this disease. Patients have to be hydrated with some fluids also if necessary.

4. Result

By the usage of some of these chemical drugs, the viral infection can be diminished and ceased in various ways either by inhibiting the IL (interleukin) functions, by inhibiting RNA polymerase function or by acting against the viral replication or by inducing mutations. Whereas, in other cases, by using the antibodies of the recovered COVID-19 patients, infected individuals can be treated by receiving blood from the donor to fight against the virus and to boost up their immune system . Many ongoing trails are happening around the world to further identify the mechanism and virulence of the virus in detail and over a month or within short time, after successful clinical trials, many chemical drugs and therapies are going to manifest their functions and effectiveness in solving this perplexed problem.

5. Prevention

a) Basic Physical Methods

Some of the physical methods which are need to be followed by the patients and also by the individuals surrounding them, in order to prevent the further spread of virus in a group includes:

Maintaining the hygienic conditions by washing hands frequently, considerably after having direct contact with the

symptomatic and diseased ones is important. Not being in close contact with the respiratory infected people. Maintaining social distance with symptomatic people is preferable. People identified with acute symptoms like fever, cough, difficulty in breathing, they are suggested to wear a medical mask and are advisable to seek medical help. In case of health care setting, proper use of Personal Protective Equipment (PPE) is mandatory. While consuming animal source as food, ensure that it is washed thoroughly and cooked completely. It is obligatory to isolate and stay individually, in case of unwell, by avoiding mass gatherings.

b) Vaccines

Treatment using vaccines are in developmental stages. No clinically approved antiviral vaccine is available till date to be used against COVID-19.

6. Conclusions

To conclude up, the analysis of WHO report of this daredevil COVID-19 is 14, 50,249 corona registered cases having 83,476 deaths and 3, 09,358 recovered cases till the day of writing. So, the only finest and healthier remedy to prevent from COVID-2019 is being isolated from others, avoiding mass gathering, and by following the guidelines of WHO. Everyone should be in a motto of "**NO TO LIVE IN SOCIETY BUT TO LIFE FOR THE SOCIETY",** which in turn protects not only them, but also their family, surroundings, community, and finally it helps to eradicate the disease. A small change in our conscious mind to isolate ourselves can bring immense pleasure results to fight against the daredevil. Stay safe and stay healthier because "*HEALTH IS WEALTH*".

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