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"Global Lessons from COVID-19: A Review of the Pandemic's Evolution"

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*Abstract:-

In early December 2019, a new outbreak of COVID-19, caused by a novel virus named SARS-CoV-2, began in Wuhan City, Hubei Province, China. By January 30, 2020, the World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern. As of February 14, 2020, there were 49,053 confirmed cases and 1,381 reported deaths worldwide. Navigating the vast and constantly expanding body of scientific research on the SARS-CoV-2 pandemic can be overwhelming. It's crucial to continuously assess and evaluate this growing body of work. Our goal was to provide a summary and critical review of systematic studies on COVID-19 in humans that were available at the start of the pandemic.

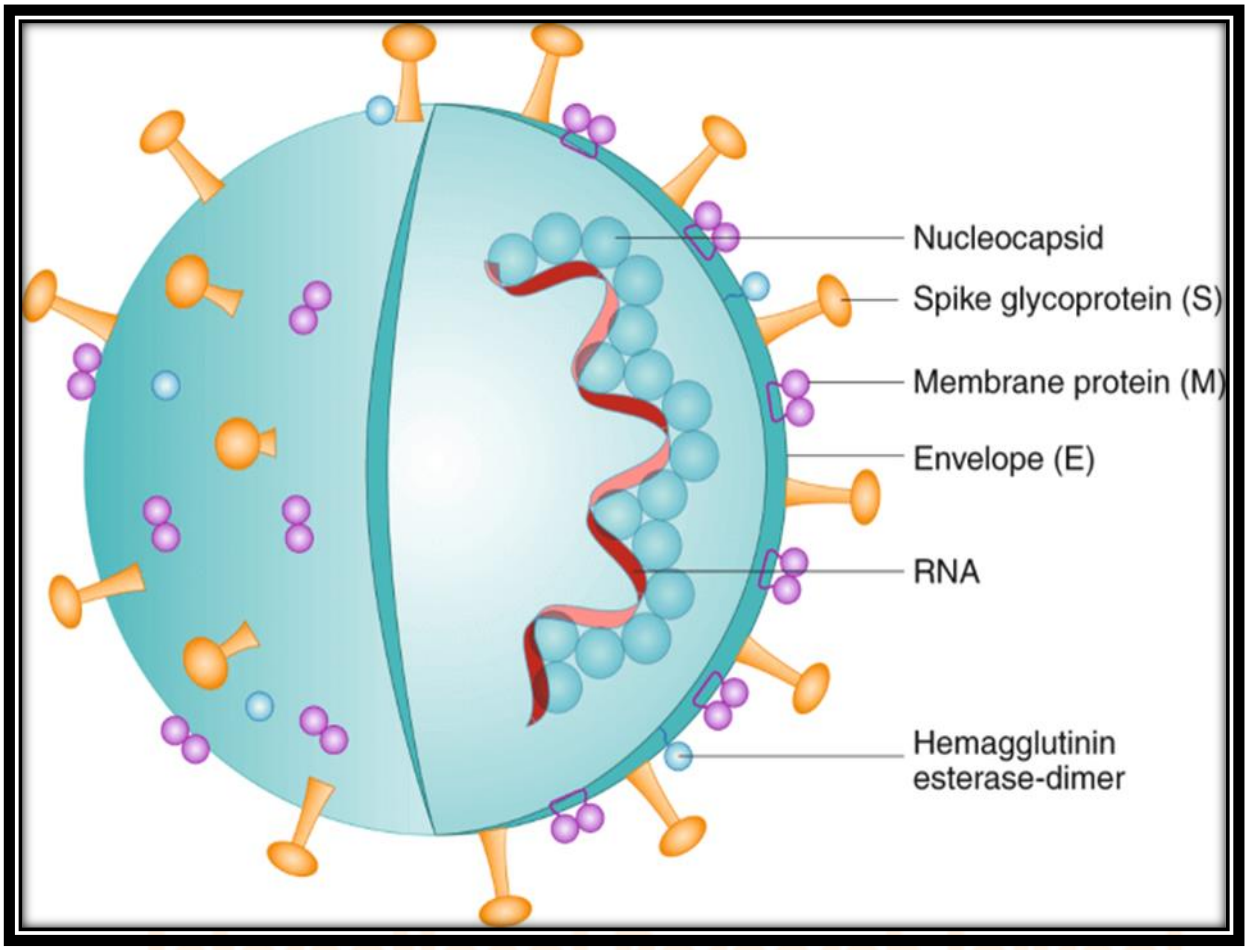
Keywords: - COVID-19, SARS-CoV-2, China, Public Health Emergency of International Concern, confirmed cases, scientific research, systematic studies, pandemic

Introduction:-

The coronavirus that emerged in 2019, initially referred to as 2019-nCoV and later named SARS-CoV-2, has spread quickly from its origin in Wuhan City, Hubei Province, China, to countries around the world. By March 5, 2020, there were approximately 96,000 confirmed cases of COVID-19 and around 3,300 deaths globally. In India, there had been 29 reported cases of the virus by that date. The corona virus disease (COVID-19) is a virus identified as the cause of the outbreak of breathing problems and respiratory illness. Right now, there are no specific antiviral drugs that are proven to effectively treat SARS-CoV-2 infection. The best approach to improving outcomes and preventing the progression of severe COVID-19 is to quickly identify patients who are at risk and provide active support for their organs. The virus is believed to spread through various means, including droplets, close contact, aerosols, and possibly faecal-oral transmission. People who are in the incubation period, even before showing symptoms, can still transmit the virus to others. Additionally, an infected person has the potential to spread active viral particles, which may change or evolve as it passes from one individual to another.

There are significant concerns about the latest strain of the coronavirus. While it appears to be transmitted from animals to humans, it is crucial to understand the specific animals and other sources involved, the transmission routes, the incubation period, the characteristics of the vulnerable population, and the survival rate. However, there is still limited clinical information available about COVID-19, and details such as the virus's age-related

impact, its animal origins, incubation time, outbreak trends, viral behaviour, transmission mechanisms, autopsy findings, and any clinical responses to antiviral treatments are still lacking in severe cases. A case was reported involving an individual from India who returned from Vienna and exposed a large group of schoolchildren at a birthday party held at a hotel in the city. Many of those who had close contact with the individual have since been placed in quarantine. The risk of disease transmission can be minimized through strategies like maintaining physical distance, cleaning surfaces regularly, and widespread use of face masks within the community. Additionally, self-isolation and self-quarantine are effective methods to prevent the spread of COVID-19.



COVID-19 Structure

The protective outer layer of the SARS-CoV-2 virus is one of the toughest among coronaviruses, making it more resilient to environmental factors and body fluids than other viruses in its family, such as MERS-CoV and SARS-CoV. Additionally, SARS-CoV-2 seems to survive longer in the environment compared to MERS-CoV and SARS-CoV, and it requires fewer viral particles to cause an infection. The exact mechanism behind COVID-19 is complex and not fully understood. However, increasing research points to the critical role of an overactive or out-of-balance immune response to the SARS-CoV-2 virus. This immune system overreaction seems to trigger a strong inflammatory response, which may be a key factor in the severity of the disease. More research into viruses and the immune system is urgently needed to better understand how COVID-19 develops. This knowledge is crucial for improving accurate diagnosis, developing better treatments, and creating effective vaccines to manage the disease. Diagnosing the SARS-CoV-2 virus is essential for controlling its spread and providing timely treatment. As a result, there has been an increasing focus on developing bio-analytical methods for detecting the virus since 2019.

Overview of SARS-CoV-2

The genomic structure of SARS-CoV-2 holds critical insights into its ability to cause disease and its various harmful traits. The full genome of the virus has been sequenced, revealing a total of 29,903 nucleotides. These nucleotides form the genetic blueprint of the virus, which is essential for understanding how it infects human cells and spreads, as well as how it interacts with the immune system. The sequence of these nucleotides also provides information about the virus's mutations, which can affect how easily it spreads or how severe the disease might be. SARS-CoV-2 is part of the Coronaviridae family and the Nidovirales order. This family has two subfamilies: Coronaviridae and Torovirinae. The Coronaviridae subfamily is divided into four genera. In simpler terms, SARS-CoV-2 belongs to a large family of viruses. Within this family, there are two main groups, and the one that SARS-CoV-2 belongs to is further broken down into four different types of viruses.

At the moment, it is not yet clear whether the structural proteins in COVID-19 perform similar functions. For most COVID-19 patients, the SARS-CoV-2 viral load is initially very high when symptoms first appear, and then it gradually decreases over time. In comparison, the viral load of SARS-CoV typically reaches its peak around the 10th day after symptoms start. Meanwhile, for MERS-CoV, the viral load tends to peak in the second week of illness.
Most people who get infected with the virus will have mild to moderate symptoms and will recover on their own without needing special treatment. However, some individuals can become very ill and will need medical care. Older adults and those with health conditions like heart disease, diabetes, lung problems, or cancer are more at risk of developing severe illness. While anyone can get COVID-19 and become seriously sick or even die, certain groups are more vulnerable to complications.

Clinical Features:-

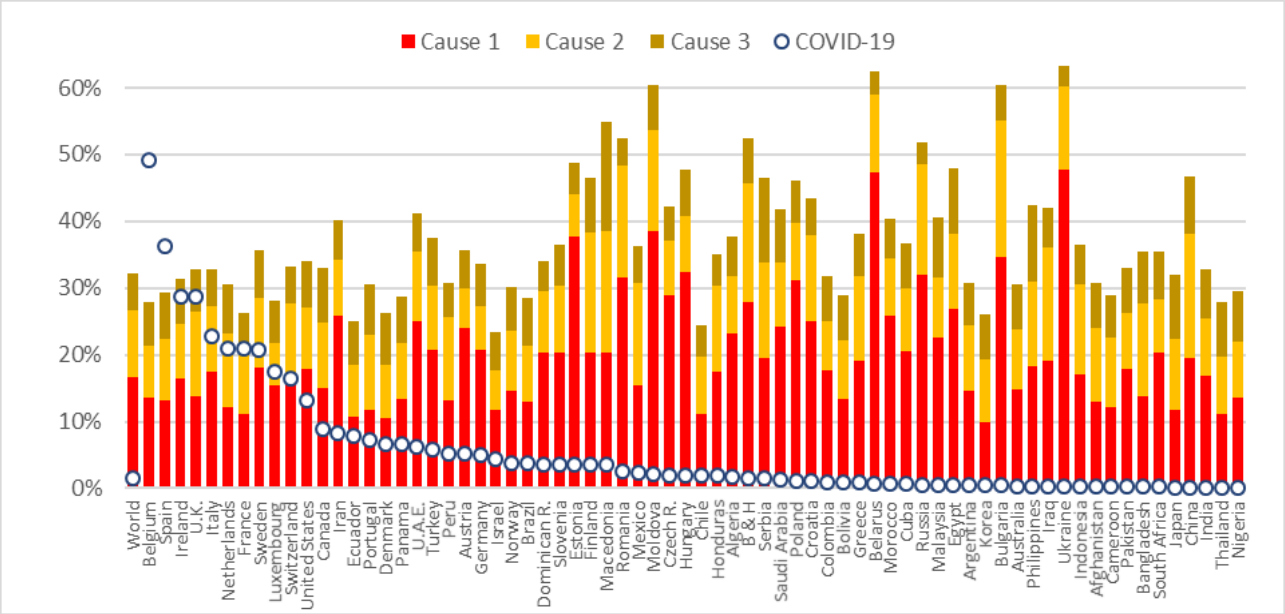
People with COVID-19 had a wide range of symptoms reported ranging from mild symptoms to severe illness. The typical symptoms of corona virus disease (CoVID-19) are fever, dry cough and fatigue and the dyspnoea in severe cases.

Children and young people aged 18 and under can get corona virus (COVID-19), but it's usually a mild illness and most get better in a few days. The COVID-19 infection is appears in all ages of the population and median age of infection is around 50 years. In published studies, 25-30% of affected patients required admission to intensive care. Complications observed included severe lung damage, ARDS, shock, and acute kidney failure. Recovery typically began during the second or third week. For those who recovered, the average hospital stay was 10 days. Older individuals and those with existing health conditions are more likely to experience severe outcomes or death, with 50-75% of fatal cases occurring in this group.

TOP 20 COUNTRIES AFFECTED BY COVID-19

COUNTRY	TOTAL CASES	TOTAL DEATH
1.United state	111,820,082	1,219,487
2. India	45,035,393	533,570
3.France	40,138,560	167,642
4.Germany	38,828,995	183,027
5.South Korea	34,571,873	35,934
6.Brazil	38,743,918	711,380

7.Japan	33,804,284	74,707
8.Italy	26,723,249	196,487
9.Russia	24,124,215	402,756
10.United Kingdom	24,910,387	232,112
11.Turky	17,232,066	102,174
12.Spain	13,914,811	121,760
13.Vietnam	11,625,195	43,206
14.Australia	11,853,144	24,414
15.Taiwan	10,241,523	19,005
16.Iran	7,627,186	146,811
17.Greece	6,101,379	37,869
18.Canada	4,946,090	59,034
19.Israel	4,841,772	46,321



Transmission of SARs-CoV-2

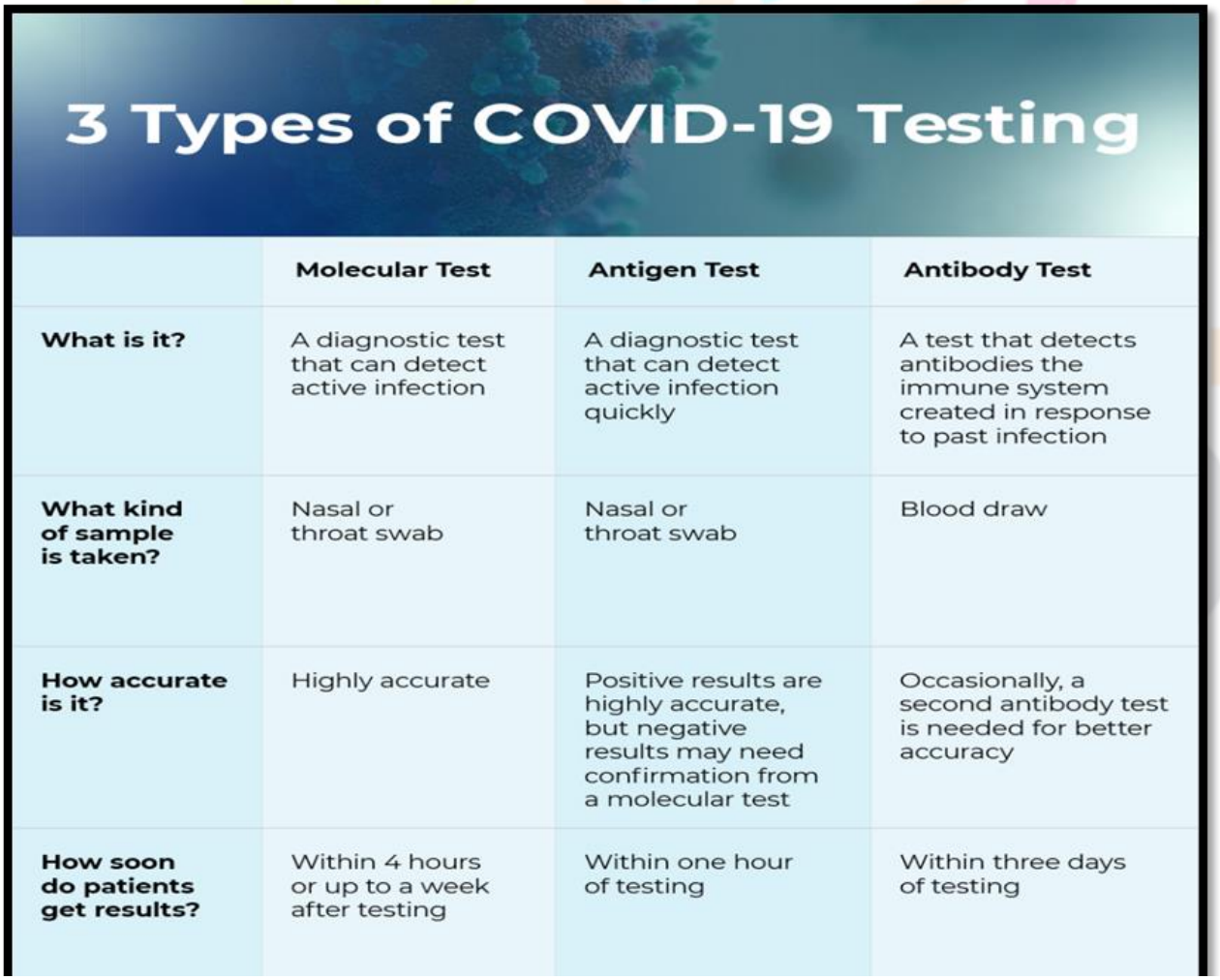
The transmission of the SARs-CoV-2 has risen in after burst of confirmed cases worldwide since December2019 is investigated. The initial one reports stated that most of the laboratory confirmed infected patient had connected to Wuhan seafood market. The SAR-CoV-2 is transmitted among humans occurs mainly, via close contact with an infected person or individual that produces respiratory droplets and aerosols while coughing or sneezing, with in a range up to 2 cm.

Since, the scientific community acknowledged the transmission by airborne particles as primary route of infection, also the contaminated objects or surfaces can also cause the virus spread. The intermediate host candidate is thought to the most likely pangolins as corona virus genetic sequences from the animals and the 99% match from humans infected during the outbreak showed, which was reported by the researchers at a press conference on February 7. 2020. The aerosols are highest in concentration when people in close proximity , which leads to simply viral transmission when people are close together but airborne transmission can occur at longer distance , mainly those locations where poorly ventilated in those conditions small particles can remain occurred in the air for minute to hours.

Molecular Diagnosis:

A suspect case is characterized by symptoms such as fever, sore throat, and cough, along with a history of travel to China or regions with ongoing local transmission, or close contact with individuals who have a similar travel history or those confirmed to be infected with COVID-19. However, some cases may not show symptoms or may not have a fever. A confirmed case is a suspect case that has tested positive with a molecular diagnostic test.

Molecular diagnosis plays a crucial role in modern medicine, with its main technology being nucleic acid testing. This type of testing is valuable for identifying specific pathogens, making it ideal for precise coronavirus diagnosis. To diagnose a specific condition, molecular tests are conducted on respiratory samples such as throat swabs, nasopharyngeal swabs, sputum, endotracheal aspirates, or Broncho alveolar lavage. Laboratory tests typically don't show specific results. The white blood cell count is usually normal or low, and there may be a decrease in lymphocytes (lymphopenia). A lymphocyte count lower than 1000 is linked to more severe illness. Platelet count is often normal or slightly reduced. Inflammatory markers like CRP and ESR are usually elevated, but procalcitonin levels are typically normal. If procalcitonin is high, it could suggest a bacterial infection alongside the primary illness. Other markers, like ALT/AST, prothrombin time, creatinine, D-dimer, CPK, and LDH, may also be raised, and higher levels are linked to more severe disease.

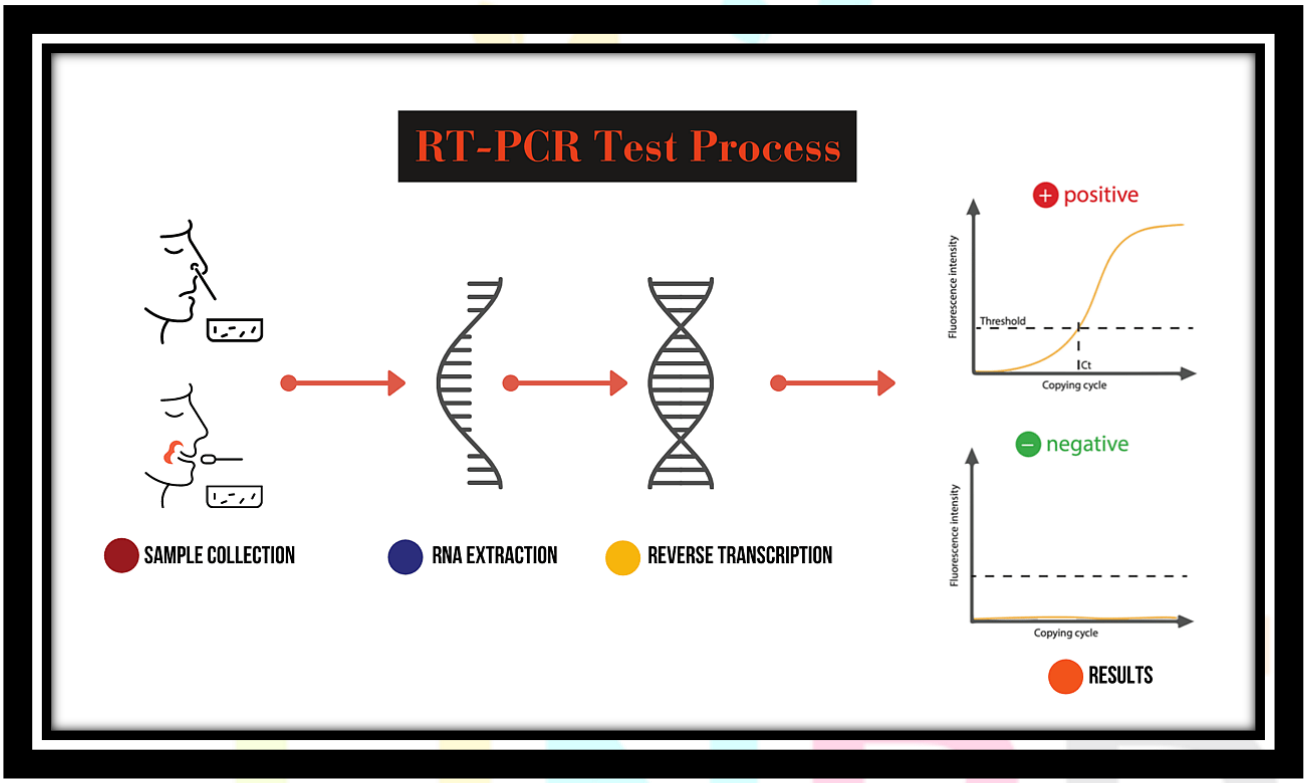


Detection of SARS-CoV-19:

1. Detection of RNA by RT-PCR:

RTPCR, or Reverse Transcription Polymerase Chain Reaction, is a type of molecular test that detects the virus's genetic material. It is also referred to as Real-Time Polymerase Chain Reaction, and it works by converting RNA into DNA and then amplifying specific segments of the virus's genetic code to identify its presence

The gold standard for COVID-19 virus detection is considered to be the reverse-transcription polymerase chain reaction (RT-PCR) test. PCR is widely used to detect viral nucleic acid by amplifying DNA samples, allowing for precise identification of the virus. This technique was developed by Kary B. Mullis, who was awarded the Nobel Prize in Chemistry in 1993 for his invention. Mullis passed away in 2019 due to complications from pneumonia.



2. Molecular Approaches for Detection of SARS-CoV-2 Infection:

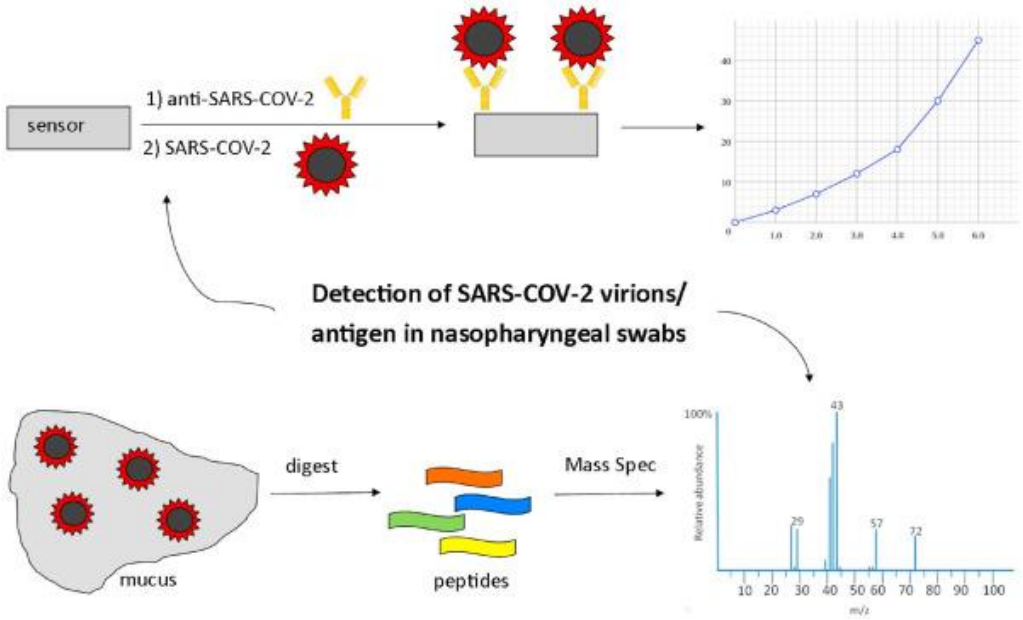
Many companies and research organizations have created diagnostic tools for this single-stranded, positive-sense RNA virus. The full genetic sequence of the virus was uploaded to the Global Initiative on Sharing All Influenza Data (GISAID) platform, which has provided the necessary information for molecular identification of the genome.

Molecular diagnostics represent a critical frontier in modern medicine, with nucleic acid testing serving as its foundational technology. This method is particularly effective in identifying specific pathogens, making it ideal for precise coronavirus diagnosis. Current nucleic acid detection techniques include gene sequencing, CRISPR, and nucleic acid amplification tests such as PCR or isothermal nucleic acid amplification. PCR relies on thermal

cycling, offering high sensitivity and specificity in virus detection. On the other hand, isothermal nucleic acid amplification provides a rapid testing option that operates at a constant temperature, eliminating the need for thermal cycler adjustments. The genome and proteome structures of the virus were identified by March 24, 2020, although the host's reaction to SARS-CoV-2 was not yet fully comprehended at that point.

3. Detection of antigens:

To control the spread of the virus, practical and scalable surveillance methods that involve frequent, large-scale, and rapid testing would be more effective than relying on nucleic acid amplification-based testing limited to suspected cases (Larimore et al., 2021). Consequently, developing a reliable onsite detection method is urgently needed. SARS-CoV-2 can be diagnosed either by detecting viral antigens directly or by identifying antibodies produced by the body's immune system in response to SARS-CoV-2 infection.



4. Detection of Antibody:

An antibody test can't diagnose if you currently have COVID-19 because it doesn't detect the virus (SARS-CoV-2) itself. Only COVID-19 diagnostic tests can tell if you're currently infected. A positive antibody test result can help identify people who may have had a past infection with SARS-CoV-2 or COVID-19. This test doesn't show if you have an active infection, as antibodies are part of the body's immune response, and the test only looks for those antibodies, not the virus. Plus, it can take days or even weeks after the infection for your body to produce enough antibodies to be detected.

Recently, diagnostic tests for detecting anti-SARS-CoV-2 antibodies in blood and tissue samples have been developed. These tests include enzyme-linked immunosorbent assay (ELISA) and immunochromatography assays. Zhang's team used ELISA to identify immunoglobulins M and G (IgM and IgG) from serum samples. The detection rates of the two ELISAs (one targeting the spike protein and the other targeting the nucleocapsid protein) were 82.2% for IgM and 80.4% for IgG. Additionally, the spike protein-based ELISA demonstrated

higher sensitivity in detecting anti-viral IgM compared to the nucleocapsid protein-based ELISA. Both IgG and IgM detection rates increased as the number of days after infection grew. A noticeable increase in detection rates for both IgG and IgM was observed after 10 days from disease onset, but IgM detection declined after 35 days. Furthermore, both the spike protein- and nucleocapsid protein-based IgM and IgG ELISAs showed detection rates below 60% during the first 10 days post-infection. These findings suggest that ELISAs could serve as valuable supplementary tests to nucleic acid-based methods for detecting anti-viral antibodies, particularly in serum samples from patients after 10 days from disease onset.

Signs and Symptoms:

The following are not all potential symptoms. Symptoms may evolve with new COVID-19 variants and may differ based on vaccination status. Some possible symptoms are:

- Fever or chills
- Coughing
- Difficulty breathing or shortness of breath
- Sore throat
- Nasal congestion or runny nose
- Sudden loss of taste or smell
- Tiredness
- Muscle or body pains
- Headaches
- Nausea or vomiting
- Diarrhoea

Treatment:

The management and treatment of COVID-19 involve both supportive care, such as symptom relief, fluid management, and oxygen support when necessary, along with an expending
range of approved medications. The widespread use of highly effective vaccines has significantly lowered the mortality rate linked to SARS-CoV-2. However, for individuals still awaiting vaccination and for the millions of immunocompromised individuals who may not respond effectively to the vaccine, ongoing treatment continues to be essential.

Most COVID-19 cases are mild. For these, supportive care typically involves medications like Paracetamol or NSAIDs to alleviate symptoms such as fever, body aches, and cough, along with staying hydrated, getting plenty

of rest, and breathing through the nose. Practicing good hygiene and maintaining a balanced diet are also suggested. The National Institutes of Health (NIH) highlights two primary processes that contribute to the development of COVID-19. In the initial phase of the illness, the virus replicates within the body. As the disease progresses, a disordered immune and inflammatory response to the SARS-CoV-2 virus occurs, causing widespread tissue damage throughout the body. Essentially, COVID-19 begins with the virus multiplying in the early stages, and later, an overactive immune response leads to severe damage to various organs and tissues. Remdesivir is the sole antiviral medication approved by the U.S. Food and Drug Administration (FDA) for the treatment of COVID-19. Ritonavir-boosted nirmatrelvir, molnupiravir, and high-titer COVID-19 convalescent plasma are authorized under Emergency Use Authorizations (EUAs) for treating COVID-19. Additionally, the combination of tixagevimab (300 mg) and cilgavimab (300 mg) monoclonal antibodies has received EUAs, permitting their use as preexposure prophylaxis (PrEP) against SARS-CoV-2 in specific patients.

Oxygen may be delivered through a tube in the nose. In some cases, a tube may need to be inserted into the airway to assist with air flow into the lungs. This process is called mechanical ventilation. In extremely critical situations, a device known as extracorporeal membrane oxygenation (ECMO) can be used to replicate the heart and lung functions.

Treatment	**Who (Among people who are at high risk of getting sick)**	**When**	**How**
Nirmatrelvir with Ritonavir (Paxlovid)	Adults; children ages 12 years and older	Start as soon as possible; must begin within 5 days of when symptoms start	**Taken at home by mouth (orally)**
Veklury (remdesivir)	Adults and children	Start as soon as possible; must begin within 7 days of when symptoms start	**Intravenous (IV) infusions at a healthcare facility for 3 consecutive days**
Molnupiravir (Lagevrio)	**Adults**	**Start as soon as possible; must begin within 5 days of when symptoms start**	**Taken at home by mouth (orally)**

Conclusions:-

The ongoing COVID-19 pandemic is undoubtedly a global public health challenge. Significant progress has been made in understanding the virus, its mechanisms of infection, and its impact on health. Given the fast spread of the virus, it is crucial for countries worldwide to enhance their disease surveillance systems and

strengthen their preparedness and response efforts. This includes the creation of rapid response teams and the improvement of national laboratory system capacities.

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