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A REVIEW ON CORONAVIRUS-19

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ABSTRACT

Corona virus 2019(nCoV) is a large, enveloped, positive-sense, single-stranded RNA virus. Corona virus causes respiratory infection including pneumonia, cold, sneezing The corona virus disease2019 (COVID19) outbreak initiated in Wuhan, China and has spread rapidly all around the world and labeled as pandemic with almost 168,000 infected cases and 6,500 deaths globally up to March16, 2020.It is believed that children are less likely than adults to be infected with coviD-19. In this review, we summarized the up to date information regarding COVID-19's, Origin, ways of spread, patients' symptoms, treatment, and prevention.

KEYWORD:- Corona**,** covid 19, SARs, MERs, Origin, Treatment.

INTRODUCTION

The corona virus family was discovered in the 1930s Corona viruses are a diverse family of viruses. Coronaviruses are members of the family Coronaviridae, the enveloped viruses that possess extraordinarily large single-stranded RNA genomes ranging from 26 to 32 kilo bases in length[16] Corona virus have been identified in both avian hosts and various mammals, including bat, camels, dogs and masked palm civets, and are previously regarded as pathogens that only cause mild diseases in the immune competent people until the emergence of the corona virus causing acute respiratory syndrome. The severe acute respiratory syndrome corona virus (SARS-CoV), H5N1 influenza A, H1N1 2009 and Middle East respiratory syndrome corona virus (MERS-CoV) cause acute lung injury.[16] Coronaviruses are classified in four different genera. Alpha, Beta, Gamma, and Delta Corona viruses belong to the Coronavirinae subfamily that together with Torovirinae forms the Coronaviridae family in the Nidoviral order.[41]

History

Corona virus was first identified as a cause of the common cold in 1960.[33] In one study carried out in Canada in 2001, more than 500 patients presented with flu-like symptoms.[8] Virological analyses showed that 3.6% of these cases were positive for the HCoV-NL63 strain by polymerase chain reaction (PCR). Until 2002, corona virus was considered are relatively simple, nonfatal virus; however, an outbreak in2002–2003 in Guangdong province in China, which resulted in spread to many other countries, including Thailand, Vietnam, Taiwan, Hong Kong Singapore, and the United States of America, caused severe acute respiratory syndrome (SARS) and high mortality rates in over1000 patients.[8-9] After this outbreak, microbiologists and infectious disease experts focused on the understanding the pathogenesis of the disease and discovered that this infection was caused by a new form of corona virus. A total of 8096 individuals were infected with this virus, resulting in774 deaths; thus, in 2004, the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) declared a state of emergency In another report from Hong Kong, 50 patients presented with SARS, and more than 60% of these patients were positive for corona virus The evolution of this virus demonstrated that corona virus is not a stable virus and can adapt to become more virulent, even lethal, to humans. Indeed, another outbreak in Saudi Arabia in 2012 resulted in many deaths and spread first to other countries in the Middle East and then worldwide, resulting in renewed interest in studies of this new form of corona virus.[33]

Classification

The family Coronaviridae is one of three RNA virus families Nidovirales, Arteriviridae and Roniviridae. The family consists of two subfamilies Coronavirinae and Torovirinae. Members of the subfamily Coronavirinae are subdivided into four genera.

1) Alphacoronavirus
2) Betacoronavirus
3) Gammacoronavirus
4) Deltacoronavirus[30]

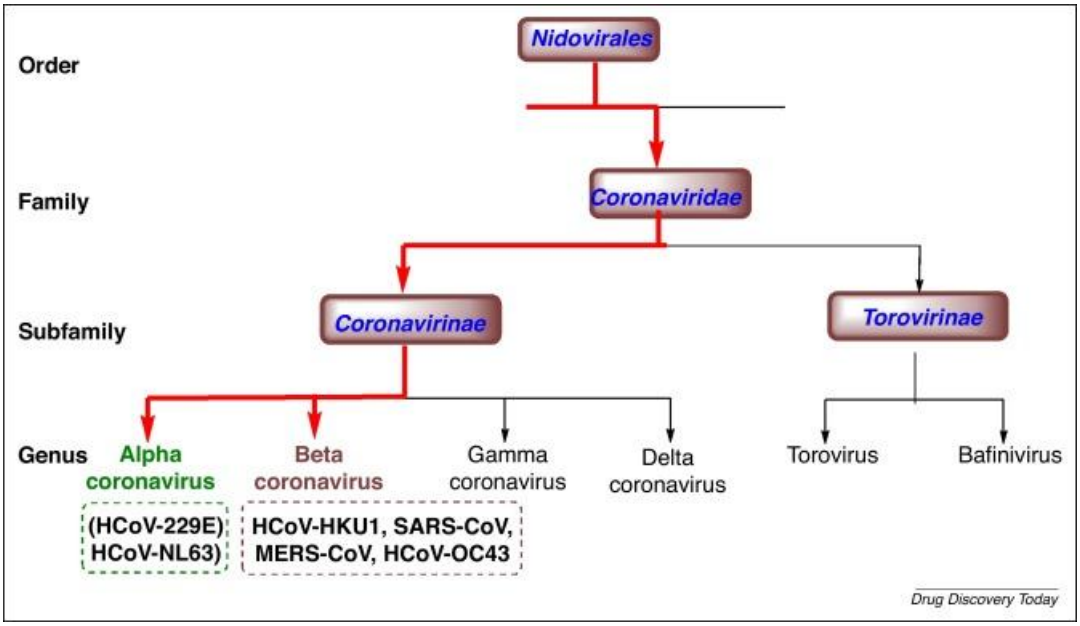

Fig. 1: Classification of corona virus.

- Alphacoronavirus- They contain human virus HCoV-229E, HCoV-NL63and animal viruses.
- Betacoronavirus-They include prototype mouse hepatitis virus (MHV), and three human viruses HCoV-OC43, SARS-HCoV, and HCoV-HKU1,
- Gammacoronavirus- contains viruses of cetaceans (whales) and birds, and the genus
- Deltacoronavirus -contains viruses isolated from pigs and birds. Corona virus include SARs and MARs[3]

SARs

The Chinese population was infected with a virus causing Severe Acute Respiratory Syndrome (SARS) in Guangdong province SARS initially emerged in Guangdong, China and then spread rapidly around the globe with more than 8000 infected persons and 776 deceases. On 29 December 4 cases were linked to Huanan Seafood wholesale market, where non-aquatic live animals, including several kinds of wild animals, were also on the sales. The local Center for Disease Control (CDC) then found additional patients linked to the same market after investigation and reported to China CDC on 30 Dec 2019.[9] The second day, World Health Organization (WHO) was informed of the cases of pneumonia of unknown etiology by China CDC The virion of SARS-CoV-2 looks like a solar corona by transmission electron microscopy imaging: the virus particle is in a spherical shape with some pleomorphism the diameter of the virus particles range from 60 to 140 nm with distinctive

spikes about 8 to 12 nm in length. The observed morphology of SARS-CoV-2 is consistent with the typical characteristics of the Coronaviridae family.

MERs

In June 13, 2012, the first reported case of MERS-CoV 1 occurred in Jeddah, Saudi Arabia. This outbreak resulted in many cases of infection, MERS-CoV were reported in almost all provinces, with Jeddah, Makka, Riyadh, and AlHassa being the most commonly affected cities June 13, 2012 until December2015, a total of 1227 cases of MERS-CoV have been reported, with 728 recovered, one still under treatment, and549 expired due to MERS-CoV related symptoms.[26] Corona virus as known to be a zoonotic virus however the MERS-CoV is a novel virus and whether zoonotic transmission occurs is not clear yet.

Strcture

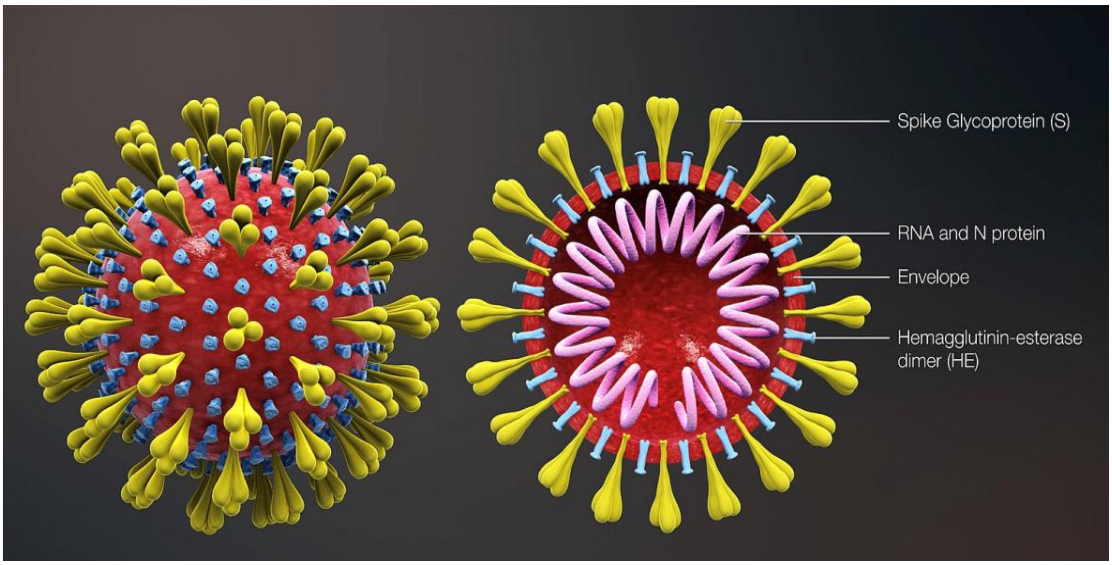

Fig. 2: Structure of corona virus.

Coronaviruses are medium-sized RNA viruses with a very characteristic appearance in electron micrographs of negatively stained preparations The nucleic acid is about 30 kb long, positive in sense, single stranded and poly acetylated. The RNA is the largest known viral RNA and codes for a large poly protein. This polyprotein is cleaved by viral encoded proteases to form RNA-dependent RNA polymerase and an ATPase helicase a surface hemagglutinin esterase protein present on OC43 and several other group II corona viruses; the large surface glycoprotein (S protein) that forms the petal-shaped surface projections; a small envelope protein (E protein); a membrane glycoprotein (M protein); and a nucleocapsid protein (N protein) that forms a complex with the RNA. The coding functions of several other

ORFs are not clear.[22] The corona virus replicase is encoded by two large over lapping ORFs (ORF1a and ORF1b) occupying about two-thirds of the genome and is directly translated from the genomic RNA.[23]

Origin

First case of corona virus was notified as cold in 1960. According to the Canadian study approximately 500 patients were identified as Flu-like system. 17-18 cases of them were confirmed as infected with corona virus Corona In 2003, various reports published with the proofs of spreading the corona to many countries such as United States America, Hong Kong, Singapore, Thailand, and Vietnam and in Taiwan. In 2012, Saudi Arabian reports were presented several infected patient and deaths. COVID-19 was first identified and isolated from pneumonia patient belongs to Wuhan, china.[9]

In December 2019, adults in Wuhan, capital city of Hubei province and a major transportation hub of China started presenting to local hospitals with severe pneumonia of unknown cause. On December 31st 2019, China notified the outbreak to the World Health Organization. On 7th January the virus was identified as a corona virus that had >95% homology with the bat corona virus and >70%similaritywiththeSARSCoV Huanan sea food market so tested positive, signicant the virus originated from. there By 23rd January, the 11 million population of Wuhan was placed under lock down with restrictions of entry and exit from the region. Soon this lock down was extended to other cities India, which had reported only 3 cases till 2/3/2020, has also seen a sudden spurt in cases. By 5/3/2020, 29cases had been reported; mostly in Delhi, Jaipur and Agra in Italian tourists and their contacts. One case was reported in an Indian who traveled back from Vienna and exposed a large number of school children in a birthday party at a city hotel .Many of the contacts of these cases have been quarantined.[5]

Epideiology

As with many respiratory infections, spread is by direct contact between infected individuals or via formites. two viruses together account for 5 to 30% of all common colds.[3] The first reported patients happened in December 2019 At the beginning, morbidity was very low. in January 2020 it hit a turning point. A significant rise in infected patients occurred in cities WHO reported over 10,000 cases of COVID-19 infections across China in late January 2020 On 13 February 2020, 13332 new cases were registered from Hubei for the first time n April 17, 2020, a total of 2,200,358 infected cases were reported all over the world with 1,494,415

active cases and 705,907 closed cases. The total active cases, 1,437,938 (96%) were found to have mild symptoms, and 56,477 (4%) were tagged as serious or critical cases. Among closed cases, 558,168 (79%) are recovered to their normal conditions and discharged, while 147,787 (21%) deaths occurred.[18]

Clinical features

The clinical features of COVID-19 are varied, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction There is no cross-immunity between human coronavirus-229E and human coronavirus-OC43, and it is likely that new strains are continually arising by mutation selection The common clinical features include fever (not in all), cough, sore throat, headache, fatigue, headache, myalgia and breathlessness Thus, they are indistinguishable from other respiratory infections. Asymptomatic infections are frequent as measured by the detection of virus in the upper respiratory tract. HCoV 229E, OC43, NL63 and HKU1 have all been identified in bronchoalveolar avages in immuno compromised patients with lower respiratory tract disease suggesting that they contribute to severe respiratory illness in these patients.[20]

Genome strucure of coronairus

Coronaviruses encode five structural proteins in their genomes. These are the Spike (S), Membrane (M), Envelope (E) glycoproteins Hemagglutinin Esterase (HE) and Nucleocapsid (N) protein All envelope proteins and N protein is present in all virions but HE is only present in some beta coronaviruses.[39]

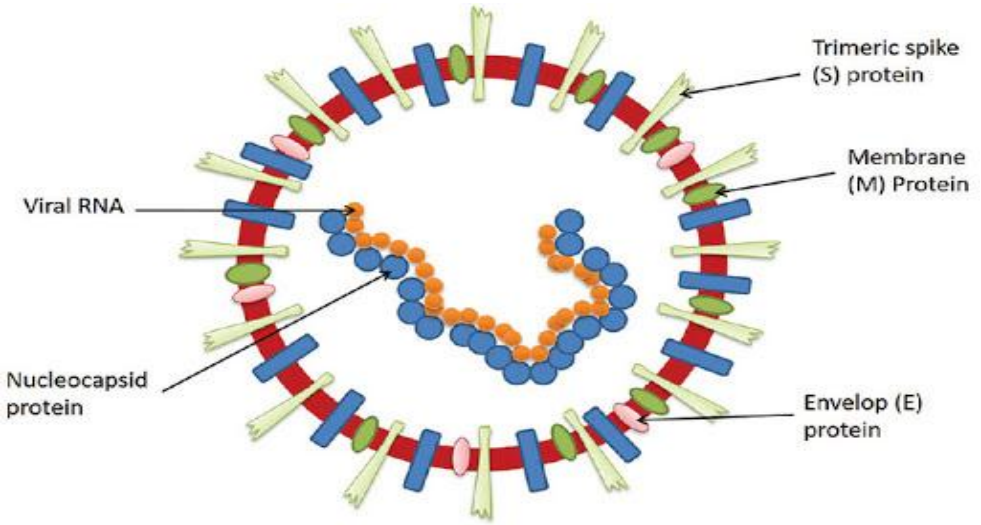

Fig. 3: Genomic structure of corona virus.

S Glycoproteins:- S Glycoproteins are located outside the virion and give the virion the typical shape S proteins bind to the virion membrane via the C-terminal transmembrane regions and they interact with M proteins.[39]

M Glycoproteins:- The most abundant structural protein in the virion is the membrane (M) protein. It is a small (25-30 k Da) protein with 3 transmembrane domains and thought to give the virion its shape.[39] The M protein plays a key role in regenerating virions in the cell. N protein forms a complex by binding to genomic RNA and M protein triggers the formation of interacting virions in this endoplasmic reticulum-Golgi apparatus intermediate compartment (ERGIC) with this complex.[33]

E Glycoproteins:- E Glycoproteins are small proteins that are composed of approximately 76 to 109 amino acid.[39] About 30 amino acids in the N-terminus of the E proteins allow attachment to the membrane of viruses Corona virus E proteins play a critical role in the assembly and morphogenesis of virions within the cell E protein has a N-terminal ectodomain and a C-terminal endodomain and has ion channel activity. The ion channel activity in SARS-CoV E protein is not required for viral replication but is required for pathogenesis**.**[33]

N Glycoproteins:- The N protein constitutes the only protein present in the nucleocapsid. It is composed of two separate domains, an N-terminal domain (NTD) and a C-terminal domain , both capable of binding RNA in vitro, but each domain uses different mechanism to bind RNA**.**[39] It has been suggested that optimal RNA binding requires contributions from both domains N protein is also heavily phosphorylated and phosphorylation has been suggested to trigger a structural change enhancing the affinity for viral versus non-viral RNA. N protein localizes in both the replication/ transcriptional region of the coronaviruses.[33]

Sign and Symptoms

Sign include

- Fever
- Cough
- Runny nose
- Fatigue
- Fever a pharyngitis in rare cases
- Shortness of breath

- Exacerbated asthma attack[18]

Symptoms:- COVID-19 triggers flu-like symptoms, such as fever and cough. These symptoms can develop into pneumonia, chest strain, chest pain, and difficulty to breath. It begins with a fever and leads to dry coughing. One week after infection the conditions become harsh and lead to breath shortening with approximately 20% of patients requiring hospital treatment and medication A few patients may develop pain or hemoptysis and many may also be completely asymptomatic. Older people with serious alveolar injury.[18]

The human angiotensin-converting enzyme 2 (ACE2) is the receptor for 2019-nCoV. In addition, other studies reported the high expression of ACE2 in the kidney, testicular tissue, and kidney damage in patients with 2019-nCoV-infected.[1]

Transmission:- The Corona virus spreads from one person to other person through the respiratory droplets which form when the patient coughs or sneezes. These droplets fall inside the noses or mouths of nearby people or maybe inhaled to their lungs. The transmission may also occur by direct contact with contaminated objects or surfaces, followed by touching the face. Furthermore,[23] The lung epithelial cells are the essential objective of the infection. The infection could likewise spread when an individual contacts a surface or item polluted with irresistible beads at that point contacted his/her mouth, nose or eyes (SARS, 2017). The normal brooding time frame or SARS inside human is 4 to 6 days, albeit once in a while it tends to be as short as 1 day or up to 14 days (SARS, 2003). SARS patients mystery the infection discharge in respiratory.[30]

Prevention:- To date, there are no specific antiviral treatments or vaccines for COVID-19 Prevention of infectious diseases by traditional Chinese Medicine has been recorded for a long time in Chinese history, The six most commonly used Chinese herbal medicines are astragalus, liquorice, fangfeng, baizhu and honeysuckle. maintaining a strategic distance from movement to high hazard zones Studies have shown that vitamin C may prevent the susceptibility of lower respiratory tract vitamin C supplementation may be a way to prevent COVID-19 proper supplementation of vitamin D and vitamin E may enhance resistance to SARS-CoV-2.infection under certain conditions.[28]

Self-Protection:- Hand washing for at least 20 seconds after visiting public place Soap or hand sanitizer with at least 60% of ethanol is recommended Avoid touching the denoted

facial T-zone. Avoiding contact with people who are already presenting with symptoms, as well as avoiding gathering or crowded places hand cleanliness measures are additionally suggested, including successive hand washing and the utilization of PPE, for example, face covers.[15]

Object surface disinfection

Article surface is cleaned with 1,000 mg/L chlorine-containing disinfectant, cleaned twice with 75% ethanol for non consumption obstruction, when at regular intervals.

Equipment disinfection:- The gear in the sullied territory is cleaned with 2,000 mg/L chlorine containing disinfectant. The DR and CT gantry in the tainted territory are cleaned with 75% ethanol. The hardware in the cushion region is cleaned with 500 to 1,000 mg/L chlorine containing disinfectant or liquorr containing dispensable disinfectant wipes two times every day.

Diagnosis

Nucleic Acid Detection Technology

Real-time quantitative polymerase chain reaction (RT-qPCR**):** It is the golden test for the diagnosis of SARS and COVID-19.

A. **High-throughput sequencing:** The authoritative identification method for SARS-CoV-2
B. **Computed tomography (CT)**
C. **Chest X-rays**

Drugs under cinical trials forcovid-19treatment

To date, there are no proven effective antiviral therapies for the infection caused by SARS-CoV-2. Treatment in several hospitals includes the use of prophylactic antibiotics to prevent secondary infection. Initial reports have shown that some antiviral with antibiotics combination can be given orally with benefits.

Chloroquine:- Chloroquine, a commonly used antimalarial and autoimmune medication, has recently been identified as a possible broad spectrum antiviral drug chloroquine is reported to be a variable bioactive agent Chloroquine is known to prevent infection of the cells by the virus through increasing the endosomal pH needed for virus for cell fusion, and interfering with the glycosylation of SARSCoV cell This treatment was especially successful in the in vitro experiments with SARS-CoV-2 infection of a human cell line.

Remdesivir:- Remdesivir (GS-5734) is a nucleoside inhibitor that is the strongest candidate from COVID-19 treatment. it was recognized as a potential antiviral medication against a broad variety of RNA viruses The EC90 value of remdesivir in Vero E6 cells against SARS-CoV-2 was 1.76 μM, indicating that its working concentration is likely to be attained in NHP models.

Lopinavir and Ritonavir:- The lopinavir and ritonavir combination has also been shown to be effective against SARS in vitro The current Chinese guidelines for COVID-19 treatment include a PO 50 mg-200 mg dose BID for a duration of 10 days.

Favipiravir:- Favipiravir is an inhibitor of a new type of RNA-dependent polymerase RNA The value of Favipiravir EC50 in Vero E6 cells was as high as 67μM. Preliminary results from a total of 80 patients (including the experimental group and the control group) have shown that favipiravir has a more potent antiviral effect than lopinavir/ritonavir.

CONCLUSION

The episode of the COVID-19 has become a clinical risk of everybody and medicinal services laborers around the world. This new virus outbreak has challenged the economic, medical and public health infrastructure of China and to some extent, of other countries especially, its neighbours. Corona virus was spreading human to human to transmission by close contact via airborne droplets generating by coughing, sneezing. As per WHO and ECDC guideline avoid the contact with sick person and also avoid the market or public place as per possible. For corona there is no clinical treatment or prevention strategies have been developed against human coronaviruses. However, the researchers are working to develop efficient therapeutic strategies to cope with the novel coronaviruses. Various broad-spectrum antivirals previously used against influenza, SARS and MERS coronaviruses. Remdesivir, Lopinavir, Ritonavir, and Oseltamivir significantly blocked the COVID-19 infection in infected patients.

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