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Corona Virus: Danger but Smartly Being Prevented

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Abstract: ***COVID-19 is a new illness that can affect your lungs and airways. It is caused by a virus called as coronavirus. It is a new viral infection illness that we do not know exactly how coronavirus spreads from person to person or animal to person. Similar to that corona virus, some viruses are spread in cough droplets. Corona affected or believed that person may be affected with corona need to stay in isolation or quarantine area. The name of coronavirus is given by scientists due to their 'crown' like spikes are observed on that virus surface membrane when viewed through microscope. This COVID-19 name given by WHO chief, Tedros said that 'CO'- stands for corona , 'VI'- stands for virus and 'D'- disease, while '19'- stands for that disease first entry to cause infection to 1st patient on 31st December 2019 in Wuhan, China. This review aims to study and discuss on the points such as ; structure of CORONA virus, it's molecular and microscopic study, anatomy and physiology of this virus, Tedros saying about coronavirus, diagnosis of COVID-19 and various aspects of coronavirus and its infection as well as prevention.***

Keywords: COVID-19, structural study of corona virus, affected countries patient background, treatment and vaccination

1. Introduction

The CORONA virus is a widely spreading throughout the world and causing a disease named as COVID-19. The actual mechanism of spread of this virus is not fully known, but it may spread through cough droplet, sneezing, contact with infected person, touches a surface or object that has the virus on it and then touches to mouth/nose/eyes as well as various unknown mechanisms.

But we don't need be scared off death due to the CORONA virus because the mortality rate of this virus is very slow i.e. approximately 3% to 3.8%. By using preventive measures, following the doctor's guidelines for COVID-19 and by treatment (if that disease is caused), we can fight with CORONA. [1]

Structural study of CORONA virus:-

- Synonym:-COVID-19
- Biological source:- Corona virus (present from earlier)
- Family:-caronaviridae

In the order nidovirales are genetically classified into four major general classes:-
1) Alpha-corona virus* (mammals)
2) Beta corona virus* (animals, birds)
3) Gamma corona virus
4) Delta corona virus

Transmission electron microscopic image of an isolate from the first U.S case of a COVID-19.the spherical viral particles, colorized blue, contain cross ,-section through the viral genome ,seen as block dots (as shown in figure F1). [2][3]

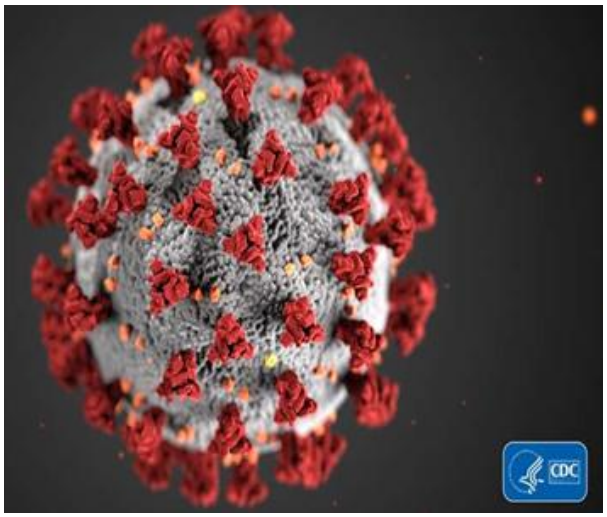

Figure F1: Microscopical structure Image shared by CDC-USA.

1.1 Brief molecular biological aspects of corona viruses

Corona viruses are enveloped, pleiomorphic with a mean diameter of approximately 120nm and have large (20nm) club -shaped surface projection-the heavily glycosylated spikes glycoprotein S. It is a large, envelope, positive-standard RNA viruses. They have the largest genome among all RNA viruses, typically ranging from 27 to 32 Kb. the genome is packed inside a helical capsid formed by the nucleocapsid protein (N) and further surrounded by an envelope. Associated with the viral envelope are at least three structural proteins. The external structure of corona virus is shown in figure F2.

a) Membrane protein (M)
b) Envelope protein (E)
c) Spike protein (S)

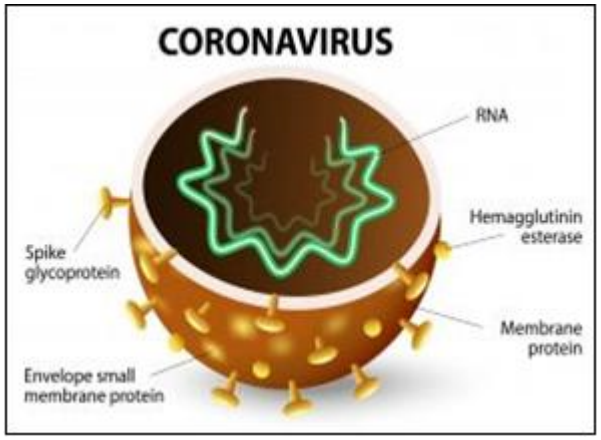

Figure F2: Corona internal structure

Some Corona viruses also encode an envelope associated haemaglutinin- esterase protein (HE). The spike protein is a dimer or trimer it has two known functions;

a) To attach the virus to receptor molecules on host cells,
b) To activate fusion of the virion membrane with host cells membranes, to release the viral genome into the cell.

In addition to mediating virus entry, the spikes is a major determinant of viral host range and tissue tropism and major inducer of a host immune responses. The Corona virus spike protein contain three segments:-

a) Large ectodomain
b) Single -pass transmembrane anchor
c) Short intracellular tail.

IBV and other, thought not all, corona viruses, have protein in a cleaved from as two subunits.

Ectodomain consist of:-

1) Receptor- binding subunit (S1)
2) Membrane- fusion subunit (S2)

For IBV these comprise a little over 500 and 600 amino acids ,respectively.bulbous head of the S protein is believed to be formed largely by the S1 subunit .the S prokein is anchored in the membrane by the carboxy terminal portion of S2.the cleavage site is usually associated with one or more pairs of basic amino acids. For example, Arg-Arg-Ser-Arg-Arg is a common S1-S1 connecting peptide of IBV.apart from the S protein ,all Corona viruses have a large copy number of a smaller ,integral membrane glycoprotein(M; approximately 230 amino acids)and low amounts of very small ,membrane associated E(approximately 100 amino acids)both of these proteins are required for virus particle formation.the S protein interacts with the transmembrane region of M closely associated with the RNA genome (to form a ribonucleoprotein ,RNP) is the nucleocapsid protein (N; approximately 420 amino acids). The Corona virus is a single stranded ,positive -sense RNA of 27000 to 32000 nucleotides.[4]

1.2 Spike protein of coronavirus-How it works at molecular level:-

During virus entry ,S1 binds to a receptor on the host cell surface for viral attachment, and S2 fuses the host and viral membranes ,allowing viral genomes to enter host cells.(S)spike glycoprotein binds to the cell membrane protein -angiotensin-converting enzyme 2(ACE2) to enter into human cells.receptor binding and membrane fusion are the initial and critical steps in the corona virus infection cycle ,they also serve as primary targets for human inventions.

Two major domains in coronavirus S1:-

1) C-terminal domain(S1-CTD) contains two subdomains
   a) Core structure
   b) Receptor -binding motif (RBM)
2) N-terminal domain (S1-NTD)

The core structure is a five standard anti --parallel beta-sheet.

The RBM presents a gently concave outer surface to bind ACE2.the base of this concave surface is a short, two -standard parallel beta sheet, and two ridges are formed by loops. The beta sheet is a common motif of regular secondary structure in proteins. Beta seets consist of beta -stand interconnected hydrogen bonds, forming a generally twisted sheet. A beta strand is a stach of polypeptide chain typically 3 to 10 amino acids long with backbone in an extended confirmation.[5]

What are the symptoms of covid- 19?

Patients with covid -19 have had mild to severe respiratory illness with symptoms of

- Fever
- Cough
- Shortness of breath.

The sign-symptoms are as shown in figure F3.[6]

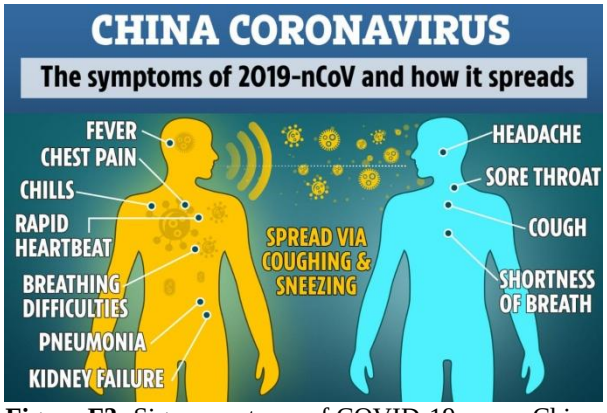

Figure F3: Sign-symptoms of COVID-19 as per China reports

Is there a vaccine?

There is currently no vaccine to protect against COVID- 19 the best way to prevent infection is to avoid being exposed to the virus that causes COVID-19.

Clinical information:-

Corona viruses mainly cause respiratory tract infection.
The authors of the Chinese CDC report divided the clinical manifestations of the disease by three severities:-

1) Mild disease (81%)

a) Non-pneumonia
b) Mild pneumonia

2) Sever disease (14%)
   a) Dysnea
   b) Respiratory frequency>30/min
   c) Blood Oxygen Saturation (SPo2)<93%
   d) Lang infiltrates>50% within 24 to 48 hours.
3) Critical disease (5% Cases)
   a) Respiratory failure
   b) Septic shock
   c) Multiple organ dysfunction (MOD) or failure (MOF)

2. Treatment

No specific antiviral treatment /no vaccine is currently available.

The treatment is symptomatic and oxygen therapy represents the major treatment intervention for patient with severe infection.

Mechanical ventilation may be necessary in cases of respiratory failure refractory to oxygen therapy, where as hemodynamic support is essential for managing septic shock. [7]

2.1 Potential future treatment option include:-

1) Remdesivir (GS-5734), an investigational nucleoside analogue:-
   - Remdesivir has been administered to several hundred patients with confirmed ,severe SARS-cov-2 infection in the United States ,Europe and Japan thought expanded Access compassionate use programs (g).Compassionate use requests must be submitted to the drug manufacturer by the treating physician.
   - A clinical trial evaluating the efficacy of remdesivir in patients infected with SARS-COV-2 is currently being conducted in China. data from this trial are expected by April 2020.
   - In preclinical trials, remdesivir has demonstrated significant activity against corona virus and a high genetic barrier to residence.
   - Data suggest remdesivir (GS-5735) inhibits activity of 2002 SARS-COV, MERS-COV, and bat COV strains that have the ability to replicate in human epithelial cells and mediate entry via human COV receptors.
   - Remdesivir has shown prophylactic and therapeutic efficacy against 2002 SARS-COV mouse model. Resistance mutations have not been identified.
2) Sofosbuvir in combination with rebavirin:-
   Data from molecular docking experiment using the SARS-COV-2 RNA dependent RNA polymerase (RdRp) model identified tight binding of sofobuvir and ribavirin to the Corona virus RdRp, there by suggesting possible efficacy of sofobuvir and ribavirin in treating the covid-19 infection.[8]

2.2 To protect yourself from Corona virus:-

1) Wash your hands often.
2) Use mask properly and when necessary.
3) Have your temperature checked for fever.
4) Avoid large crowds and stay home if you're sick.
5) Never touch your face with unclean hands.
6) Thoroughly cook meat and eggs.
7) Avoid close contact with those who show signs of flu.
8) Cover nose and mouth when coughing and sneezing with tissue or flexed elbow.
9) Avoid unprotected contact with live wild of farm animals.

Primary patient's history:-
Three adult patients presented with severe pneumonia and were admitted to a hospital in Wuhan on December 27, 2019. Patient first was a 49- years -old woman, patient two was a 61 -year -old man and patient 3 was a 32 -year -old man. Clinical profile was available for patients 1 and 2. Patient 1 reported having no underlining chronic medical conditions but reported fever (temperature 37°c to 38°c) and cough with chest discomfort on December 23, 2019. Four days after the onset of illness, her cough and chest discomfort worsened, but the fever was reduced; a diagnosis of pneumonia was based on computed tomography (CT) scan. Her occupation was retailer in the seafood wholesale market.

Patient 2 initially reported fever and cough on December 20 ,2019. Respiratory distress developed 7 days after the onset of illness and worsened over the next 2, days at which time mechanical ventilation was started he had been a frequent visitor the sea food wholesale market. Patients 1 and recovered and were discharged from the hospital on January 16, 2020. Patient 2 died on January 9, 2020 no biopsy specimens were obtained.[9]

2.3 Corona virus study report:

1) December 10, 2019: Wei Guixian, 57 years old, a seafood merchant in this city's Huanan market started to suffer and eight days later situation worsened. Hear global health and financial paralysis started from (China) CHINA.
2) December 31, 2019: In Wuhan, the metropolitan area in the China Hubei province, and epidemic of cases with unexplained the respiratory infection detected, and first reported to the WHO country office in the China. Media houses raised question "why China's administration delayed this reporting?"
3) Early January 2020: Initially, the new virus was called 2019-nCov. Subsequently, the task of experts of the international committee on taxonomy of viruses (ICTV) termed in the SARS-cov-2 virus (as it is very similar to the one that caused the SARS-cover break and possess 90% of its DNA with SARS-COV.
4) January 30, 2020:- The international health regulations, the outbreak was declared by the WHO a public health emergency of international concern (PHEIC)as it had spread to 18 countries with four countries reporting human -to -human transmission(according to WHO Corona viruses are zoonotic, meaning these can transmitted between animal and people).
5) February 11, 2020:- WHO named the disease covid -19 -short corona virus disease. On the same day that the disease was named The "novel corona virus" was given a

name ,by the international committee on taxonomy of viruses(ICTV).novel corona viruses is the name being used by Goal of present for public advisory advertisements.

6) February 24, 2020:- Clinical and epidermal logical data from the Chinese CDC and regarding 72,314 case records (confirmed, suspected, diagnosed and asymptomatic cases) were shared in the journal of the American medical association (JAMA).
7) March 03, 2020: Data provided by the WHO health emergency Dashboard; 87,137 conferred cases worldwide since the beginning of the epidemic.2977 (3.42%) reported to the fatal.
8) March 14, 2020: Many Indian states government declared holidays to schools, officers. In India, till now Maharashtra and Kerala reported many cases of suspects and confirmed patients. Private sector especially these dealing with "health sciences" role are unclear yet.

The report of development of corona virus disease in world is shown in figure (F4) and the fatality rate report of mainland China is shown in figure (F5).[10]

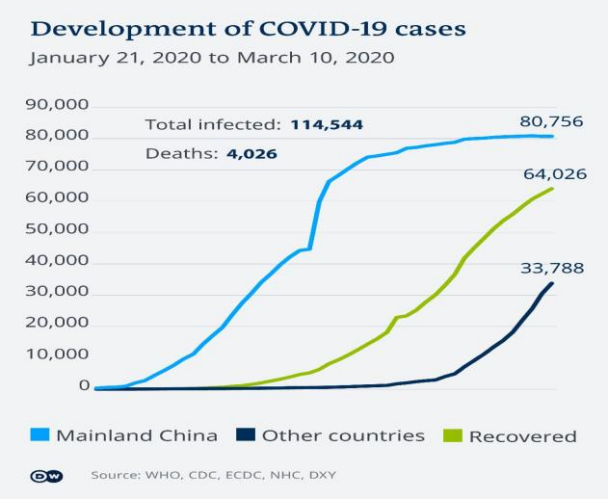

Figure F4: The report of development of corona virus disease in world

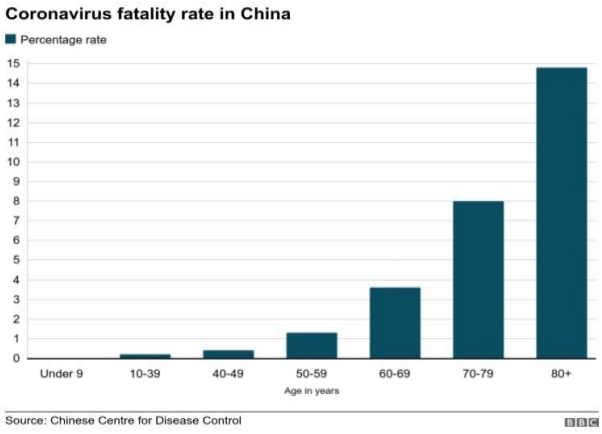

Figure F5: The report of corona fatality rate in China [10]

2.4 Corona virus life cycle

The best studied model for corona virus replication and pathogenesis has been the group 2 murine corona virus, mouse hepatitis virus, and much of what is known of the stages of the corona virus life cycle has been determined in animals and in culture using this virus. Thus this discussion will focus on SCoV and other corona virus. This is appropriate because bioinformation analyses suggest that SCoV, while a distinct virus, has significant similarities in organization, putative protein function and replication to the group II Corona virus, particularly are sites for replicase gene translation and replicase polyprotein processing, and also for viral RNA synthesis. Replicase gene proteins likely mediate positive-strand, negative-strand, sub genomic, and genomic RNA synthesis, as well as processes of capping, polydenylation, RNA unwinding, templet switching during viral RNA synthesis and discontinuous transcription and transcription attenuation. The corona virus replicase polyprotein and mature replicase proteins represent the largest and most diverse repertoire of known and predicated distinct enzymatic recombinant and of host range determinants in the S protein ,the development of targeted recombination has allowed more defined and detailed studies of the accessory and structural genes of MHV ,transmissible gastroenteritis virus [TGEV], and feline infectious peritonitis virus [FIPV] [Haijema et al.,2003;kuo et al.,2000; masters et al., 1994]. studied with natural variant and targeted recombination genetic studied have demonstrated that the S protein is the major determinant of host range, tropism, and pathogenesis; other genetic elements, possibly in the replicase, may influence these characteristics of different corona viruses encoding of accessory function that are flexible and tolerant of changes, or conversely group or host - specific roles that are subject to pressure for more rapid change.[11]

2.5 Expression of structural and accessory Genes-

Only the 5' most replicase gene is translated from the input positive- strand genome RNA. THE Genome contains multiple other genes for the known structural proteins S, E, M, and N. as well as other genes for expression of proteins that have been labeled as "nonstructural" or "accessory" because they have been presumed to not though to tested MHV replicase protein have been shown to localize to replication complexes at the earliest Time of detection, likely both by membrane integration and by protein-protein and protein-RNA interaction [bost et al ., 2000;Dension, et al ., 1999; prentice and Dension,in press; shi et al., 1999; sims et al., 2000;van der meer et al.,1999]. Further, replicase protein likely mediates the process of double- membrane vesicle formation, likely by induction of cellular autophagy pathway [E. Prentice, unpublished results]. Corona virus replication complexes are sites for replicase gene translation and replicase genome is encapsulated by multiple copies of the nucleo-capsid protein [N], and has the conformation of a helical RNA/ Nucleocapsid structure. The S protein has been a focus of pathogenesis studied in mice because it appears to be the critical determinant of cell tropism, species specificity, host selection , cell tropism, and diseases [Navas and Weiss,2003; Navas et al., 2001; Rao and Gallagher,1998]. Virus replication is initited by binding of the s Protein to specific receptors on the host cell surface. for MHV, the primary receptor has been shown to be the carcino- embryonic antigen- cell adhesion molecule [CEACAM] been shown that subpopulation of replicase proteins and the structural nucleocapsid [N] translocate from replication complexes to sites of assembly and may

mediate the process in association with cellular membrane/ protein trafficking pathways [bost et al .,2000]. virus assembly in the ERGIC involves interaction of genome RNA(n) , the membrane protein [M], and the small membrane protein [E], resulting in budding of virus in to the lumen of ER/Golgi virosomes [opstetten et al .,1995]. Further maturation of virus particles occurs during movement through the Golgi, resulting in virosome filled with mature particles. Trafficking of the virosomes to the cell surface has not been well characterized but is presumed to occur via normal vesicle maturation and exocytic processes. The outcome is the nonlytic release of the vast majority of mature virions into the extracellular space. For MHV and several other corona viruses that can directly fuse with cells, there is a characteristic and rapidly detectable cytopathic effect of cell-cell fusion into multinucleated syncytia. Production of infectious virus continues even after the majority of cells are fused. Syncytia were recently reported as readout of SCoV receptor expression and cell infection (lee et al., 2003).

2.6 Virus replication complex formation and fuction:-

Following entry and uncoating, the 5' most replicase gene of the input positive strand RNA genome is translated into two co-amino terminal replicase polyproteins that are co- and post- translationally processed by viral proteinase to yield 15 to 16 mature replicase proteins, as well as intermediate precursors. The nascent replicase polyproteins and intermediate precusrors likely mediate the formation of viral replication complexes in the host cell cytoplasm. Interestingly, corona virus replication requires continuous replicase gene translation and processing throughout the life cycle to maintain productive infection (Kim et al 1995; Perlman et al., 1987; Sawicki and sawicki, 1986). Replication complexes of MHV replicase proteins have been shown to co-localize to replication complexes at the earliest time of detection, likely both by membrane integration and by protein – protein and protein – RNA interactions (Bost et al., 2000; Dension et a., 1999; Prentice and Dension in press; Shi et al., 1999; Sims et al., van der Meer et al., 1999). Further replicase proteins likely mediate the process of double- membrane vesicle formation, likely by induction of cellular autophagy pathways (E. Prentice, unpublished results).

Corona virus replication complexes are sites for replicase gene translation and replicase polyprotein processing, and also for viral RNA synthesis. Replicase gene proteins likely mediate positive-strand, negative-strand, ad genomic RNA synthesis as well as processes of capping, polyadenylation, RNA unwinding, template switching during viral RNA synthesis, and discontinuous transcription and transcription attenuation. The corona virus replicase polyproteins and mature replicase proteins represent the largest and most diverse repertoire of known and predicted distinct enzymatic functions of any positive-strand RNA virus family. Until recently, of the 15 or more mature replicase proteins, only the proteinase, RNA helicase and RNA-dependent RNA polymerase activities had been predicted or experimentally confirmed (Brockway et al., 2003; Heusip et al., 1997; Lee et al.,1991; Ziebuhr et al., 2000). With the advent of SARS, more extensive bioinformatics analyses have resulted in predictions of several additional functions involved in RNA processing, including methyltransferase and exonuclease activities (Snijder et al., 2003; Thiel et al., 2003). Even with inclusion of distant predicted relationships, up to eight of the replicase proteins remain without predicted or confirmed functions. In summary, it is likely that corona viruses have exploited their genetic capacity to encode proteins in the replicase gene with distinct functions in RNA synthesis and processing, as well as proteins with specific roles in induction or modification in host cellular membrane biogenesis and trafficking, delivery of replication products to sites of assembly, and possibly virus assembly. Thus, replication translation, replicase polyprotein processing, and mature replicase proteins constitute important targets for interference with corona virus replication, virus – cell interactions, or viral pathology.

2.7 CORONA virus replicase protein expression and processing:-

The proteinase activities for all coronaviruses include both papain- like proteinase (PLP) and picornavirus 3c-like proteinase activities that are encoded within the replicase polyproteines and mediate both cis and trans cleavage events (ziebuhr et al., 2001). Specifically, there are both conserved and divergent regions of the replicase polyproteins by amino acid identity and similarity, with the sequences and predicted mature proteins beginning, with the sequences and predicted mature proteins beginning with the 3C- like proteinases through the carboxy terminus of the replicase polyprotein retaining higher identity and similarity across the predicted proteins. In contrast, the amino terminal third of the replicase demonstrates the most variation in proteins, cleavage site locations, and the number of proteinases that mediate the maturation processing. SCoV appears to have the general organization of, and similar protein sizes to, the group 2 corona viruses such as MHV in this part of the genome (Snijder et al., 2003). However, SCoV likely uses only one PLP to mediate the cleavages, similar to the group 3 corona virus infectious bronchitis virus (IBV). Thus this region of the replicase may experience the most variability, suggesting into virions either the encoding of accessory functions that ares flexible and tolerant of changes, or conversely group or host-specific roles that are subject to pressur for more rapid change.

2.8 Expression of structural and accessory genes:-

Only the 5' most replicase gene is translated from the input positive-strand genome RNA. The gnome contains multiple other genes for the known structural proteins S, E, M, and N, as wellas other genes for expression of proteins that have been labeled as "non structural" or "accessory" because they have been presumed to not be required for replication, and are not thought to be incorporated into virions . MHV encodes six of these genes, while SCoV encodes possibly up to structural and accessory genes, which are expressed from sub genomic mRNA (Snijder et al., 2003). Sub genomic RNA transcription occurs during minus- strand RNA synthesis by acquisition of the anti leader RNA sequences from the 5' end of the genome via homology to a transcriptional regulatory sequence (TRS, also known as an

intergenic sequence (TRS, also known as intergenic sequence), and requiring a discontinuous activity of the nascent minus- strand template and polymerase complex to acquire the leader (Sawicki and Sawicki, 1998). The outcome of transcription is the generation of a "nested set" of sub genomic negative- strand RNAs that all contain the ant leader sequences that serves as template for similar size sub genomic mRNAs. This transcriptional strategy exposes different genes as the 5' ORF in different mRNAs, all of which also contain the gene, including the 3' non-translated region of the genome. For MHV genes 3, 5b, 6, and 7 encodes S, E, M, and N, respectively. Genes 2, 4, and 5a are not required for replication in culture , and have been mutated to block expression, deleted, or substituted with non-corona virus genes such as GFP (de Haan et al., 2002; Ortego et al., 2003; Sarma et al., 2002). because all corona viruses retains these genes in various combinations in the face of presumed pressure for genetic economy and apparent lack of functions in RNA synthesis, it is presumed that the genes serve role in modification of host cells, pathogenesis or interaction with the immune system. SCoV encodes larger and more complex array of these genes than MHV or other corona viruses, which may reflect its evolution in its original animal host (Ksiazek et al., 2003; Marra et al., 2003; Snijder et al., 2003; Thiel et al., 2003). In addition, the report of a deletion within one of the accessory genes in human isolates of SCoV suggests that this may be a gene involved in host range or adaptation for replication and transmission in humans (Guan et al., 2003). [11]

2.9 Corona virus genetics

Until recently, the genetics of corona virus replication and pathogenesis have largely been studied using natural variants, host range mutants, passaged virus, and mutagenized viruses selected for temperature sensitivity and specific phenotypes. Classical complementation of functions made it possible to define at least eight genetic groups for MHV ,with most of the complementation groups localized to the replicase gene (stalcup et al., 1998).Taking advantage of naturally high rates of homologous RNA-RNA recombination and of host range determinants in the S protein , the development of targeted recombination has allowed more defined and detailed studies of the accessory and structural genes of MHV, transmissible gastroenteritis virus (TGEV), and feline infectious peritonitis virus(FIPV) (Haijema et al., 2003; Kuo et al., 2000; Masters et l., 1994) studies with natural variants and targeted recombination genetic studies have demonstrated that the S protein is the major determinant of host range, tropism, and pathogenesis; other genetic elements, possibly in the replicase, may influence these characteristics of different corona viruses (Navas and Weiss).[12] [13]

3. Treatment

How chloroquine will act as a prophylactic drug and is acting as a therapeutic agent against COVID-19 infection and Why Trump is saying chloroquine is a game changer in fight against the COVID-19.

Chloroquine acts on host target respiratory cells by:

Chloroquine increases the endosomal pH required for the virus- host target cell fusion. Increase in the pH disrupts the normal viral function.

In SARS-corona virus, which is a sister to COVID-19, chloroquine was found to interfere with the glycosylation of cellular receptors of the virus. This interference eventually resulted in no association between the host target cell and the virus.

Chloroquine acts as an ionophoric agent for Zinc ions and thus increases the influx of zinc ions into the cytoplasm of host target cells regardless whether the host target cells are infected or not.

All the above-mentioned mechanism is on the host cells and COVID-19 cannot mutate and cause resistance to these 3 mechanisms. First 2 mechanisms inhibit the virus-target host cell union. Chloroquine results in disablement of ACE-2 (Angiotensin converting enzyme 2) terminal glycosylation which leads to the morphological change; ACE-2 is a surface receptor found on target host cell. This results in the disruption in the association between the COVID-19 and target host cell as COVID-19 requires ACE-2 receptor to attach to a cell.

Because the action is on the target host cell, Chloroquine won't develop resistance therapeutically. If a person uses Chloroquine as a prophylactic agent (500mg once in a week for adults and 8.3 mg per kg once in a week for children) against COVID-19 then, it will act pre-infection and post-infection. If a person does not get exposed to the COVID-19 infection after taking Chloroquine (say for 3 weeks) and then some viruses enters and try to infect target host cells, Chloroquine mechanism "a" and mechanism "b" will prevent the union of virus-target host cell. If some of the viruses enters the target host cell, there Zinc ions are waiting to adhere to the RNA dependent RNA polymerase enzyme of the virus and stops COVID-19 polymerization intracellularly. If COVID-19 mutates inside the cell several times, even then the Zinc ions will actively inhibit the viral multiplication inside the host respiratory cells, irrespective of the viral strain. Even if COVID-19 virus manages to escape from Zinc ions trap and releases from the host target cell cytoplasm into the interstitial matrix, intercellular space, and tried to re-infect some of the healthy target host cells, Chloroquine will prevent the re-union of viral genome with target host cells via mechanism 'a' and mechanism 'b' and the infection will halt in the preliminary stages itself and complications like COVID-19 pneumonia will not develop. Chloroquine molecules will not lose its effectivity in an individual pre and post infection.

Zinc is present in ample amount in the human body. In normal conditions, the Zinc is not present in free state in the cell. The increased level of Zinc ions is not toxic to the cells and cells excrete the extra Zinc ions into the extracellular space. Zinc is commonly present in red meat, legumes, nuts, milk, cheese, eggs, whole grains etc. Garlic increases the absorption and bioavailability of Zinc inside the body. So, some persons who aren't taking Zinc rich foods in ample amount should eat zinc supplements or garlic daily.

Safety of Chloroquine is well tested as it is given for Malaria prophylaxis, autoimmune diseases like rheumatoid arthritis Lupus erythematosus. Now a days it is indicated into the SARS infection as it is a broad antiviral agent. Through it ionophoric action for its zinc intracellular influx, chloroquine is also used as anti-cancerous drug.

The long-term use of chloroquine (4 years together) may cause its accumulation in the eye. There are some concerns of its use in glucose-6-phosphate dehydrogenase enzyme deficient children but the recommended prophylactic and therapeutic doses, Chloroquine is safe to be used in these children. Some persons may complain of acidity and nausea, but it can be resolved if Chloroquine is taken post meal.

Prophylactic dose in malaria is 500 mg once a week in adults and 8.3 mg per kg once a week in children.

In these doses it will be effective against COVID-19 prophylaxis. The therapeutic doses against COVID-19 as used in China, America and India are Chloroquine 500mg BD for 5 days with other anti-viral drugs like Oseltamivir, Lopinavir, Ritonavir etc. and in complicated COVID-19 pneumonia cases, Chloroquine may be used for 10 or more days in the same amount.

Now comes the actual catch of its technicality to be used prophylactically against COVID-19 action. In India as it is a very cheap, safe and easily available drug and can be prescribed against the Malaria as a prophylactic drug as the summer season approaches. It will surely work prophylactically against the COVID-19 outbreak and we can use this opportunity to prescribe it in larger amount as Malaria is endemic in India. It will act on Malaria and COVID-19 infection prophylactically without it being included in the guidelines.

Trump's excitement for chloroquine in his announcement can be related with the fact that American researchers are currently working on the Chloroquine drug. Many companies have donated chloroquine to the US for research purpose. Hydroxychloroquine is less toxic but original Chinese work is based on chloroquine phosphate. Hydroxychloroquine can be used with equal efficacy. If one starts prophylactically with Chloroquine, then one must stick with chloroquine and must not switch to hydroxychloroquine and vice-versa. This switch may result in increase QT interval.[14]

The figure F6 shows the data of recovered patients from corona.

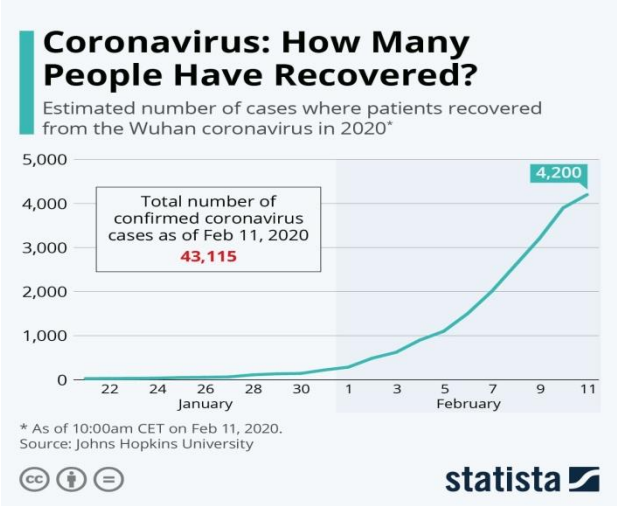

Figure F6: Data of recovered patients from COVID-19

4. Discussion

During the initial phase of the covid-19 outbreak, the diagnosis of the disease was complicated by the diversity in symptom and imagine findings and in the severity of disease at the time of a presentation. Fever was identified in43.8% of the patients on presentation but developed in 88.7% percent after hospitalization, after illness occurred in15.7% of the patients after admission to a hospital. No radiologic abnormalities were noted on initial presentation in2.9% of the patients with severe disease and in of 17.9% of those with non severe disease.

Despite the number of deaths associated with covid-19, SARS-COV-2 appears to have a lower causing fatality rate than either SARS-COV-2 or MERS-COV.

Approximately 2% of the patients had a history of direct contact with wildlife, whereas more than three quarters were either residents of Wuhan, had visited the city or had contact with City residents.

These findings Echo the latest reports, including the outbreak of a family cluster, transmission from an asymptomatic patient, and the three -phase outbreak patterns. Our study cannot preclude the presence of patients who have been termed" super-spreaders". Conventional routes of transmission of SARS-COV-2, MERS-COV, and highly pathogenic influenza consist of respiratory droplets and direct contact, mechanism that probably occur with SARS-COV as well.

The term covid-19 has been applied to patients who have laboratory-confirmed symptomatic cases without apparent radiologic manifestations.

A better understanding of the spectrum of the disease is needed, since in 8.9% of the patients, SARS-COV-2 infection was detected before the development of viral pneumonia or viral pneumonia did not develop.

In, concert with recent studies, we found that the clinical characteristics of covid-19 mimic those of SARS-COV.

Fever and cough were the dominant symptoms and gastrointestinal symptoms were uncommon, which suggest a difference in viral tropism as compared with SARS-COV, MERS-COV and seasonal influenza.

Our findings were more similar to the national official statistics, which showed a rate of a death of 3.2% among 51,857 cases of covid-19 as of February 2020, since patients who were Mildly ill and who did not seek medical attention were not included in our study, the case fatality rate in real world scenario might be even lower. Early isolation, early diagnosis ,and early management might have collectively contributed to the reduction in mortality in Guangdong.

Our study had some notable limitation:-

Some cases had incomplete documentation of the exposure history and laboratory testing, given the variation in the structure of electronic data bases among different participating sites and the urgent timeline for data extraction.

Some cases were diagnosed in outpatient setting where medical information was briefly documented and incomplete laboratory testing was performed ,along with a shortage of infrastructure and training of medical staff in non speciality hospitals.

We could estimate the incubation period in only 291 of the study patient who had documented information the uncertainty of the exact dates might have inevitably affected our analysis.

We no doubt Missed patients who were asymptomatic or had mild cases and who were treated at home, so our study conchort May represents the more severe end of COVID-19.

Many patients did not undergo sputum bacteriologic or fungal assessment on admission because, in some hospitals, medical resources were overwhelmed.

Data generation was clinically driven and not systematic. COVID-19 had spread rapidly since it was first identified in Wuhan and has been shown to have a wide spectrum of severity. Some patients with covid-19 do not have fever or a radiologic abnormality is on initial presentation, which has complicated the diagnosis.[15]

5. Conclusion

During the first 2 months of the current outbreak, covid-19 spread rapidly throughout China and caused varying degrees of illness.

Patient often presented without fever and many did not have abnormal radiologic findings(funded by the national health commission of China and others).

Author contribution statement

1) Shweta S. Kulkarni and Jayashri S. Kolsure presented idea, developed theory and performed the computations. Deepak A. Joshi (asst. professor) verified the literature survey and encouraged Shweta S. Kulkarni and Jayashri S. Kolsure to investigate (a specific aspect) and supervised the survey report of this work. All authors discussed the results and contributed to final manuscript.
2) Shweta S. Kulkarni and Jayashri S. Kolsure collected information and wrote the manuscript with support from Deepak A. Joshi (asst. professor) and fabricated, helped to supervise the project. Shweta S. Kulkarni and Jayashri S. Kolsure conceived the original idea and Deepak A. Joshi (asst. professor) supervised the project.
3) All authors contributed to final version of the manuscript and supervised the project of review article, designed and directed the project.

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