



Research Article

THE SARS-COV-2 PANDEMIC AND EMERGING CHALLENGES AGAINST STRATEGIES

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ABSTRACT

Introduction: The SARS- CoV-2 pandemic attack; which began in Hubei province of Wuhan city of China in December 2019; is one of the serious health issues, which has challenged entire world and this is the largest outbreak since last four decades. Today there is lot of improvement in health science technology as compared to old days; still almost all countries are struggling to overcome this disease. Overall condition is same for developed as well as developing countries. For developed countries, speed of disease contamination, is not allowing settle it, while for developing countries, health infrastructure is big concern. Though the history of corona virus is quiet old, but yet there is no confirmative treatment against it. The world is familiar about corona virus since past; either in the form of severe acute respiratory syndrome corona virus (SARS-CoV); which started at Guangdong province of China in 2002 or Middle East Respiratory Syndrome corona virus infection (MERS-CoV-1) of Saudi Arabia in 2012. The virus shows continuous genetic reconstructions, with genetic mutations in human body and express as different and newer version as compared to previous corona. This is main reason, why this difficult to tackle the disease. **Objective:** To understand SARS- CoV-2 better, from past experiences, for prevention and management of this disease. **Concept Designing:** Articles collected through various search engine tools such as, Google Scholar, Ebsco host and Pub med, relevant key words inserted to search these articles such as, Corona virus, SARS, MERS and COVID tec. All articles evaluated to be as per PRISMA guidelines. **Conclusion:** The SARS- CoV-2 is altered version of previous corona virus infections, which affected entire world in respect to physical health, mental health and global economy. This pandemic disease is different from previous corona virus attacks, in respect to rapid family spreads and variations in clinical presentations. There is need of strict policies by governments which are in collaboration with private sectors and public.

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INTRODUCTION

The mankind is facing worldwide corona virus pandemic health concerns since last four decades. For current corona virus infection the responsible species is SARS- CoV-2 (Severe acute respiratory syndrome corona virus-2). Nowadays almost all countries are capable of health facilities at their levels, but still due to massive viral impact, even developed countries are struggling to control this situation. Apart from hope of corona vaccine, till date there is no definitive treatment of SARS- CoV-2. So understanding basic pathogenesis of this disease thoroughly can be a life saving measure and to generate awareness a small effort is made to write an article to shed light on this burning topic.

Aim: Obtaining maximum information about SARS- CoV-2 and associated consequences.

Objective

1. Understanding in detail about structure and behavior of corona virus.
2. To know corona virus related clinical manifestations.
3. To analyze preventive measures against this disease.

Inclusion of articles

1. Article selection from authentic source is considerable measure, during preparation of this manuscript.
2. Useful and informative articles; with substantial contents were selected.

Exclusion: Articles with inadequate information, related to study were excluded.

Acquisition of contents

Articles were searched using different search engines, such as Google scholar, Pub Med and Ebsco host. During this process of searching of articles, relevant key words i.e. Corona virus, Covid-19, Pandemic, viral infection, SARS and MERS were inserted. Currently there are limited articles on corona virus, to understand this novel pandemic disease.

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Historical Background

These kind of pandemic viral outbreaks are witnessed by human beings since past four decades. However limited sources of information technology, are responsible for delayed awareness about this viral disease among people in past. Later on due to involvement of large number of people and their health problems, this infection gained attention. This awareness generated interest among researchers about viruses to conduct multiple research works; as a result of this many informative articles were published. By virtue of these literatures since last two decades our concept about viruses, their species and virulence on human being was understood. There are many viruses which targeted human population, and had severe impact on health. Some of the species of viruses with more virulence and harmful effects are; Ebola fever, MERS, Nile infection, SARS-CoV, Nipah infection, Hendra disease, Bird flu and Swine flu etc. [1, 2]

In reality revolutionary studies with proper documentations on viruses were carried during 1960, and this was due to large scale community spreads of flu in societies. This attracted attention of the World Health Organization (WHO), who directed guidelines for preventive measures and worked for better health care measures by declaring this as health care emergency. This outbreak; on basis of involvement of virus and clinical manifestations, was termed as severe acute respiratory syndrome corona virus (SARS-CoV). Similar viral attack was evidenced in 2002, at Guangdong province of China, during this outbreak many people got affected, and that landed into deaths of more than 1000 people. [3, 4] Soon after a decade on 13th June 2012, there was another pandemic viral attack in Jeddah, Saudi Arabia. This pandemic viral attack affected to around 26 Middle East countries, and there were around similar clinical findings as previous corona virus attacks. This pandemic viral health hazard infected to around 1620 people, and killed nearly 600 people. Based on geographical involvement of Middle East countries, this viral pandemic was named as Middle East respiratory syndrome corona virus-1(MERS-CoV-1). [5]

The recent corona outbreak is noticed on 16th December 2019, the epicenter of this disease noticed in Hubei province of Wuhan city of China. Considering the year of incidence of this viral spread, initially this was termed as novel corona virus-2019 (n-CoV-19) or CoVid -19 (corona virus disease-19). This is still unclear that, why the term novel is used in this context but may be associated with genetic framework and clinical entity. Later on by considering its clinical manifestations; this term was reconsidered as SARS-CoV-2 (severe acute respiratory syndrome corona virus- 2). [6-11]

Understanding the corona virus

Terminology of corona virus was derived from the Latin word "Coronam" which means crown. The reason behind this terminology is that, morphology of corona virus shows multiple spikes on its outer surface and resembles like crown and this is correlated with Latin word "Coronam." [12]

These spikes on surface are made up of glycoprotein, and they are termed as protein S, further subdivided as S1 & S2. These spikes play important role during adhesion of virus on surface of host or target. This virus is made up of RNA, which has only one strand, but there are around 29891 nucleotides and 9860 chains of amino acids. This is one of the biggest virus

with average size of 60 nm to 140 nm, and length of 30 kb, 5' cap and 3' end part. [13-14]

The present studies suggest that, there are number of corona species out of these, infectious species to human population are associated with eighth subfamily; that ranks fifteenth. This is forty-ninth species in twenty-seven subgenera and five genera. Further Coronaviridae family is classified as many subfamilies; including Cornidovirineae, Nidovirales, and Riboviria etc. [15, 16]

Out of all corona species only some species have capacity to infect human beings and these are 229E, OC43, NL63, HKU1, MERS-CoV, SARS-CoV AND SARS-CoV-2. [17]

According to variations of serotypes corona viruses are further classified and subdivided in different types such as; α (alpha), β (beta), γ (gamma) and δ (delta), out of all these variants β (beta) corona virus is comparatively more infectious to humans. [18, 19]

Learning from past

This was unexpected health impact on entire world with remarkable pandemic outbreak of SARS-CoV-2. Some countries are recovering, while some are still struggling for substantial health measures. Gradual increase in graph of SARS-CoV-2 positive cases is mainly due to two reasons, first lack of cooperation among people to follow physical/ social distancing strictly, and limited sources of medical facilities and infrastructure, mainly in developing countries. [20]

The pandemic attack of MERS-CoV of 2012 affected 1600 people with 600 deaths, which was as good as 30%. The reason behind this was, paralysis of health care system due to spread of infections among health care workers, including doctors, nurses and paramedical staff. The situation was out of control to restrict deaths, so world health organization (WHO) announced an emergency. These previous experiences can be helpful to handle current scenario of corona outbreak. The coordination issues between the countries during early phase of disease, was deciding factor in the spread of disease. There would have been less number in these pandemic cases, if information was shared at right time. [21, 22]

Source of infection

The corona viral attack in past was around two decades earlier, this reflects that, frequency of virus attack is irregular, but as per old literatures large group of population was affected by SARS-CoV and MERS-CoV. Though previous attacks show some associations with recent attack of SARS-CoV-2, but recent virus shows advanced genomic alterations as compared to previous species. These genetic alterations are responsible for complicated changes in structure of this virus, making more challenging for researchers, and rightly state this virus species as novel. [23] This particular group of viruses transmits via airborne zoonotic droplets. Once the surface is available; the replication of virus begins; mainly in ciliated epithelium, leading to further cellular damage, further accompanied with inflammatory reactions at the site of viral aggregations. [24, 25] There are many sources for spread of corona viruses, i.e. bats, whales, pigs, birds, cats, dogs, mice and camels. According to different studies, there is zoonotic spread to human beings which leads to rapid spread of infections in to the localities; through droplets or direct surface contact, either from animal to human or vice versa. [26-30]

So far, among these animal sources, bats share more than 95% genomic contents which are noticed in SARSCoV-2. However some workers do not agree for this, because genetic sequence RaTG13 does not use angiotensin converting enzyme (ACE-2) receptor as binding domain. Similarly Pangolins also share 90% genetic sequences, with 94% amino acids and is routine source of diet in South China, but due to some variations, this is also doubtful to be a primary source. The route of viral spread is mainly through droplets, but studies also suggest that, fecal contamination is also responsible for SARSCoV-2 infection. [31, 32] There are different groups and sub groups of corona viruses such as, alpha-CoV, beta-CoV, gamma-CoV and delta-CoV. Out of these; only some groups are infectious to humans and this is determined by genetic structures of viruses. Out of these, alpha-CoV and beta-CoV show genomic resemblance with bats and rodents, however delta-CoV and gamma-CoV are associated with avian species [33] Beta-corona virus is responsible for human infections, and this is further classified in different sub families i.e. lineage A-to -D. In this B- lineage is responsible for SARS-CoV and SARS-CoV-2 while; C lineage is responsible for MERS-CoV infections. [34-37]

Mechanism of transmission

The virus cannot enter directly into the human body, rather there is need of receptor and binding surface, called receptor binding domain (RBD), and there is variation in mechanism of entry for different species of viruses. The corona viruses have spikes on their surfaces i.e. glycoprotein spikes (S) which are subdivided as S1& S2. Surface preparation and attachment on receptor domain is by S1, while S2 is useful in penetrating the membranes. (Figure1). [14]

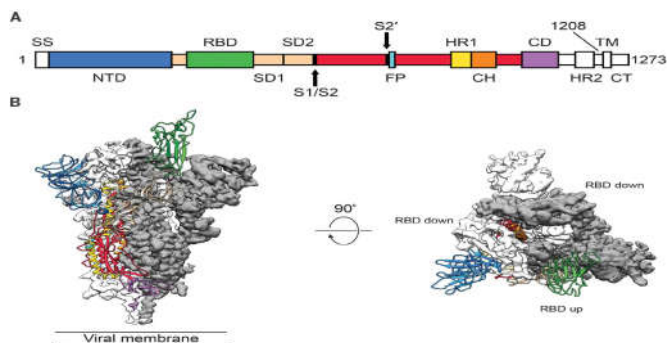


Figure 1 Shows process of attachment and entry of SARS-CoV-2 in the body.

1. Structure of virus showing different domains. Signal Sequence(SS), Location of cleavage (S2'), Fusion Peptide (FP), Heptad Repeat one (HR1), Central Helix (CH), Connector Domain (CD), Heptad Repeat two(HR2), Transmembrane Domain (TM), Cytoplasmic Tail (CT) and arrow shows site of cleavage.
2. Upper and lateral aspect of SARS-CoV-2, Protein S having one RBD, with up position, while 2 down RBDs in gray or white color. [38]

The SARS-CoV needs angiotensin converting enzyme -2 i.e. (ACE-2), while MERS-CoV; binds with the help of enzyme dipeptidyl-peptidase 4 (DPP-4). But C lineage group of viruses like HKU4 need extracellular trypsin and DPP-4 to bind on surface. [39,40] Thus entry of virus within the body is really difficult task, it needs many processes, such as; cellular adhesion, contact with receptor, utilization of enzyme and entry in to the cell surface. [41]

Clinical presentations

Entry of virus in body is in two stages, first binding on the surface and second after entry, it starts aggregating in that site. During early binding step protein spikes play important role during attachment on receptor binding domain (RBD) and gradually there is local colonization of viruses. [42,43] While reaching towards distant locations, protein S1 shows typical movement to reach at domain sites, at the same time there are continuous up and down movements, which help to approach the targeted binding surface and once proper adhesion is achieved, gradually there is stability. [44-46]

Spread of all types of corona viruses is through nasal or oral droplets, but carrier animals for different viral species are different, and also have variable incubation periods for different species of viruses. Such as, infection of MERS-CoV shows zoonotic spread through droplets and the carrier animal of this virus is camels, which has around 2- 4 days incubation period. [47] Similarly SARS-CoV also transmits through zoonotic source i.e. bats or pangolins, and they show incubation period of 2-10 days. Viruses enter human body either from oral cavity or nose, and gradually transported to distant areas by multiplication and manage to infect distant organs such as lungs, heart and kidneys. [48]

Once virus is entered in organs, it starts multiplication, enhances virulence and gradually damages to the respective organs. The symptoms of disease depend on involvement of organs, degree of destruction of tissues and immunity of body against this infection. The symptoms range from mild infections such as; respiratory illness, fever, cough and loose motions, whereas severe infections leading to failure of organs. [49]

This corona virus shows varying clinical manifestations, ranging from mild signs like cough, cold and sore throat to severe systemic disturbances such as; pulmonary complications, heart damage and shock. Later on these mild/moderate clinical findings can be landed in to complications; once they are accompanied with, smoking, immunocompromised status, secondary infections, hematopoietic abnormalities and old age. [50]

The outbreak of SARS-CoV -2 showed rapid spread within communities, at same time it showed different clinical findings in same family. Reason behind this could be immunity of person, which restricted power of virulence during attachment on host surface and after entry in the body. [51] The species of beta CoV; particularly lineage A, (HCoV-OC43, and HCoV-HKU1); show mild symptoms. However lineages B and C have tremendous capacity of widespread attack, leading to target larger group of populations, and they are presented with different types of clinical manifestations. Due to more aggressiveness and larger involvements of people, these later lineages show remarkable death rates of around 10% to 35% [52]

A new version of corona family

The SARSCov-2 is definitely a stronger version as compared with previous corona species. These species have different genomi reconstruction, with stronger attachment capacity on the host surface and long term survival. This virus is unaffected with climate, temperature or location; that's why we are facing its pandemic effects throughout the world. However; this particular virus shows tremendous capacity of

multiplication and adapt to produce more virulence in consecutive sequences of human contacts. That is the reason; why SARSCov-2 shows no complete genetic match with the previous corona viruses. ^[53]

Lab tests for corona virus

This is very important part; that determines possible outcomes of controlling the corona virus. During this many stages are involved, starting from sampling to running the samples on analyzer, and all stages are equally important for correct diagnosis. For sampling it needs well trained medical and paramedical teams, along with different types of kits; including protective kits, while for applying test, it needs highly automated equipment and skilled technical staff to monitor the test. In short; process of swab collection of corona population and its investigation by RT-PCR is tedious and costly matter, and sometimes there are chances of false negative cases if there is even a minor mistake during entire procedure. ^[54-55]

The performance of RT-PCR depends on, up-regulation of protein E, open reading frame-1a (ORF-1a) and open reading frame-1b (ORF-1b). The PCR is considered positive; when it locates two specific genome locators or one positive sequence and one more positive PCR at another location. In short when RT-PCR for E-protein (up) is positive, should be assessed with RT-PCR; ORF- 1a, its positive result decides confirmation. In other case if RT-PCR with up-E; is positive, it should be confirmed with any of genomic ligand i.e. N assay and Rd-Rp, if still shows positive result the test is finally confirmed. ^[56-64]

Management

Till date there is no proper drug or vaccine to treat this highly pandemic disease; infected by SARS-Cov-2, as a result its treatment is symptoms based. Nowadays hydroxychloroquine is used as prophylactic adjunct against SARS-Cov-2. The basic working of this drug is to raise cellular Ph and restrict binding efficiency of receptor cells (APC). This will limit capacity of major histocompatibility complex-II (MHC-II) to donate antigens to T cells, leading to deficiency of supportive proteins i.e. CD4 and CD154. The HCQ delays the binding process, by altering the toll like receptors, which provide base for viral adhesion. Apart from this chloroquin also act as antiviral agent by stabilizing intra cellular Ph. ^[65] Sometimes virus stays in incubation zone, and these people are asymptomatic and recovered but test results may be positive. ^[66] This group of people, who are asymptomatic and positive, may become threat to society. After completion of lockdown and control over corona infection, these positive carriers; contribute to contaminate other people. Because mass screening and sampling is economic burden on developing and underdeveloped countries, so even 2% asymptomatic carries can be responsible for severe pulmonary disturbances and later on they may be source of infection. ^[67] These viruses can be deactivated by chloroform, chlorine mixtures, ethyl alcohol and peroxy- acetic acid. ^[68] Corona outbreak affected almost all sectors of life including, physical health, mental status, unemployment, and growth of economy, and to tackle this is going to be tough for governments and stake holders of world. This is need of an hour that all countries should come together, to set up the strategy against these crucial; but basic challenges, so as to repair massive worldwide damage. ^[69]

CONCLUSION

The SARS-CoV-2 is a unique corona virus pandemic attack, which is different from previous corona virus infections. The community spread of this virus is rapid with higher rates of contamination and adaptation in human body. On the other hand, this shows variations in clinical presentations which are one of the reasons to have difficulty during interventions; even in same families it shows different clinical findings. Today entire world is facing challenges in the form of physical health, mental issues, unemployment and massive economic loss. In this worldwide pandemic attack; health infrastructure of almost all countries is tested and found inadequate. However lock down policies, critical awareness by media and social networks, found effective to restrict SARS-CoV-2 associated complications and mortalities. Even after this phase is over, there is need to frame policies by governments and private stake holders to strengthen people in their physical, mental and economical crises.

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