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Review Article

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# COVID 19: A SYSTEMATIC APPROACH TO COMBAT THE DEADLY VIRUS

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**Abstract:** The COVID-19 pandemic has gripped the entire world in a medical emergency, spreading at a phenomenal rate, affecting even the most developed nations and challenging medical care infrastructure. With the precautions of social distancing and its enforcement through lockdowns, authorities have managed to buy time to flatten the curve. However, without any proven cure at hand, researchers are exploring varied approaches to treat the infected people. In this review, authors discuss the multilayered approach taken up to combat this deadly pandemic. The authors shall summarize the hospital setups, the frontline worker's struggles, the symptoms and their manifestations, preventive measures and also the current treatment approaches.

**Keywords:** Covid-19 , Favipiravir, Plasma therapy, Social distancing, Vaccine.

## INTRODUCTION

The ongoing Covid-19 pandemic with over 9.4 million cases worldwide and over 4,84,000 fatalities, has thrown the entire world in a health emergency. The deadly virus has challenged the healthcare systems of even the most developed countries, spreading at an alarming rate. A strategy to flatten the curve, by adopting lockdowns, in a bid to ensure social distancing proved effective in many countries. Health systems around the globe are currently preparing and working round the clock to manage the rise of the influx of critically ill patients. During this phase, care providers, administrators and policymakers work in coordination to understand and combat this deadly pandemic. The current knowledge about Covid-19 is limited but it is rapidly evolving with time. During this outbreak, the medical community has used evidence and experience from past outbreaks of SARS-CoV and MERS-CoV to predict Covid-19's behaviour, clinical presentation and treatment. In addition, coronaviruses (CoV) are known to cause signs and symptoms of multi organ system damage, many of which can go unnoticed even by trained medical professionals. Furthermore, frontline healthcare personnel lack a comprehensive review of the numerous clinical pulmonary and extra-pulmonary manifestations of deadly CoVs making self-education time consuming.

This engorging pandemic however could not dampen the spirits of the Covid-19 warriors. Every doctor, policeman, and health service personnel rose to the cause, risking their lives, in the face of duty. With depleting resources and increasing cases, the medical fraternity is racing against time to save lives. However, this effort comes at a huge cost that the Covid-19 warriors seem to pay on a personal level.

**The Cost of Duty**

The very definition of normal life has changed in the pandemic. With a "work from home" policy being popularized among the masses, the situation for the doctors is different. Starting from donning the PPE (Personal protective equipment) kit to spending hours in the suffocating piece of claustrophobic gear, to doffing it after dripping in every bit of sweat put in to save the patient, the doctor braves it all. These PPE kits meant to protect the wearer, severely compromises the dexterity and restricts movements from using the washroom to eating and drinking (Cheng *et al*., 2005). The sheer amount of helplessness the doctors are subjected to everyday due to lack of any standard treatment, results in a huge mental distress.

The health of the health workers is affected widely all over the country since the increasing number of cases on a daily basis overburdens the hospital setup and saturates the efficiency of a normal working capacity, the doctors are overburdened, overworked while they toil away sleepless nights in order to treat the patients. On top of that reports indicate that more than 2,000 health care workers have been infected all over India. Mental stress has become a key issue amongst doctors while balancing between their duties and quarantining themselves in isolation from family and friends so that they do not inadvertently become spreaders. The duty of a doctor also extends to procurement of masks, kits, and other safety gears to protect themselves from this deadly virus. The social stigma has become a major cause of distress amongst members of the medical community as they are being assumed as silent carriers and instances of eviction and discrimination has been reported.

In India, the Covid-19 hotspot in the state of Maharashtra has already infected over 4,000 police personnel, claiming 54 lives in the force.

**The Hospital Setup**

Due to overburdening of cases, many hospitals started setting up Fever OPD, to provide an effective measure of patient screening on the basis of Covid like symptoms. The main crux behind the establishment of fever OPD is to segregate the most suspicious ones that are most likely to incur the deadly virus inside so that the diagnosis can be quickly made in order to prevent the spread of the infection. After suitable sampling through swab testing and PCR, the diagnosed person is admitted in Covid-19 wards to undergo specific treatment, part of which is motivating the patient on a regular basis.

Testing facilities are being increased day by day in order to increase the rate of diagnosis. The main basic test lies in swab sampling from the nasopharyngeal and oropharyngeal regions and then after PCR the results are made and analyzed, after a person turns positive the swab is taken after 5th day and 10th day. An important aspect is the viral load which plays a pivotal role in the development of symptoms and the number of days to which a person can remain positive.

**Clinical Symptoms**

The clinical manifestations range from abnormal Computer Tomography (CT) scans of the chest in asymptomatic or mild cases (Kumari and Shukla, 2020) to severe respiratory distress in acute cases according to a report by European Centre for Disease Prevention and Control. According to that report, the most common symptoms were headache (70.3%), loss of smell (70.2%), nasal obstruction (67.8%), cough (63.2%), asthenia (63.3%), myalgia (62.5%), rhinorrhea (60.1%), gustatory dysfunction (54.2%) and sore throat (52.9%); fever was reported by on 45.4% of the 1420 patients observed.

Dry cough is one of the starting symptoms for the infection present in nearly 68% of the patients. Sore throat and sputum production are relatively uncommon (5% or less).The presence of dyspnoea is very much indicative of deteriorating

severity and demands ICU admission. Ground glass opacities are common (56%), followed by consolidation in chest X-rays and interstitial abnormalities like diarrhoea are also found in some patients. There is also evidence of a higher incidence of thromboembolism in Covid-19 patients (Tang *et al*., 2020).

**Investigative Procedures**

Histopathology of the lung shows diffuse alveolar damage, denuded alveolar lining cells and interstitial fibrosis (Zhang *et al*., 2020).Ground glass opacification (GGO) pattern is the most common finding in Covid-19 infections. These are usually multifocal, bilateral and peripheral, but in the early phase of the disease, the GGO may present as a unifocal lesion, most commonly located in the inferior lobe of the right lung (Zhou S. *et al*., 2020). Initial CT-findings in Covid-19 cases include bilateral, multilobar GGO with a peripheral or posterior distribution, mainly in the lower lobes and less frequently in the middle lobe (Salehi *et al*., 2020).

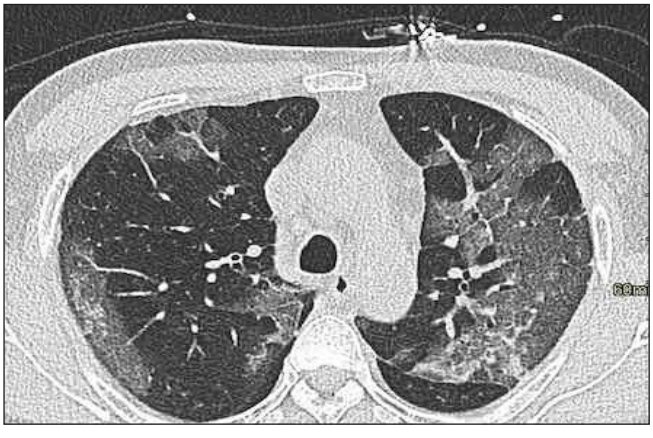

**Figure 1: CT Scan of a Covid patient's Lungs showing GGO. (Zhou S. *et al*., 2020).**

**Figure 2: Portable Chest X-Ray (left) with vague hazy densities in the right upper lobe (Black arrow) which correspond to ground glass opacities (white arrow) on coronal image from contrast enhanced CT (right) performed the same day (Jacobi *et al*., 2020).**

**Changes at Cellular Level**

At present only limited knowledge is available on the host innate immune status of SARS-CoV-2 infected patients. Effective response of innate immunity against the viral infection depends much on the interferon (IFN) type I response and its downstream cascade that results in controlling and prevention of viral replication and induction of effective adaptive immune response. The SARS-CoV and SARS-CoV-2 share the entry receptor of ACE2 while MERS-CoV uses dipeptidyl peptidase (DPP)-4 as its specific receptor (Zhou P. *et al*., 2020).

The Th1 type immune response plays a major role in an adaptive immunity against viral infections. Antigen presenting cells culminates into a microhabitat for the cytokines that control the direction of T cell responses. Helper T cells initiate the overall adaptive response, while cytotoxic T cells are important in killing the viral infected cells. Humoral immunity, especially production of neutralizing antibodies, plays a protective role by limiting the infection at a later phase and prevents re-infection in the future. The SARS-CoV infection induces seroconversion as early as day 4 after onset of disease which was found in most patients by 2 weeks. Long lasting specific IgG and neutralizing antibodies are reported as long as 2 years after infection (Liu *et al*., 2017).

**Comorbidities**

The potential severity of the cases increased with the presence of comorbidities. The most significant of them were hypertension, diabetes and malignant tumours. The Hazard Ratio was 1.79 among patients with at least one comorbidity and 2.59 among patients with two or more comorbidities (Guan *et al*., 2020).

**Road to Treatment**

There is no standard care for the prevention or treatment of the jeopardised respiratory system in Covid-19 as of now. Medications including glucocorticoids, IL-6 antagonists, Janus kinase

inhibitors, antivirals are currently being studied as possible therapeutic options for the ongoing pandemic (Walls *et al*., 2020). A large number of trials have been done all over the world thus revoking hope in the mindset of the people. Favipiravir, Etrolizumab, Tocilizumab and Remedesivir being such agents that are being subjected to clinical trials and tested for their efficacy in managing the cytokine storm that arises amidst the infective stage of the coronavirus. Recently Favipiravir has been approved in the management protocol of Covid-19 and is been marketed in the name of FaviFlu, the basic mechanism behind the drug being inhibition of the RNA polymerase enzyme. The basic challenge in finding a suitable drug lays in the fact that the virus is mutating on a constant basis thus making it difficult for its genetic code to be tracked.

The Federal Agency of the United States, Food and Drug Administration (FDA), has determined that Chloroquine and Hydroxychloroquine are unlikely to be effective in treating Covid-19 at present for the emergency purpose. Additionally, in light of ongoing serious cardiac adverse events like PR interval (time between Atrial Depolarization and Ventricular Depolarization of the heart) prolongation, arrhythmia and other serious side effects, the known and potential benefits of Chloroquine and Hydroxychloroquine no longer outweigh the known and potential risks for the authorized use.

According to an article from Economic Times, The Indian Council of Medical Research (ICMR) has now facilitated setting up of 1,000 laboratories across the country for testing Covid-19 samples, is a major milestone towards enhanced testing in India. According to the organization, there are 730 government labs and 270 private labs for the testing. It has advised to all states, public and private institutions and hospitals to take required steps to step-up testing for Covid-19. ICMR has also asked them to deploy a combination of various tests which includes real-time RT-PCR, rapid antigen testing for detection of cases, and antibody testing for sero-surveillance. Since early diagnosis through testing and tracking and timely treatment is the only way to prevent the spread of Covid-19 infection and save lives, it is of utmost importance that testing should be made widely available to all symptomatic individuals in every part of the country and contact tracing mechanisms for containment of infection are further strengthened.

This concept of seroconversion has been used effectively in sero-surveillance trials being conducted at present by ICMR all over the country to qualitatively and quantitatively observe for the development of antibodies, if any, in doctors, nurses and frontline workers. Development of T cell immunity is also a possibility in people not having developed humoral antibody response to the infection and is currently under research.

According to an article by Times Now, India based Bharat Biotech is expected to begin human trials of its Covid-19 vaccine COVAXIN very soon. It is India's first indigenous vaccine against the novel coronavirus and has been developed by Bharat Biotech in collaboration with ICMR and NIV, Pune, will be tested on more than 1,100 people in phase 1 and 2 clinical trials.

In spite of the presence of indigenous platforms till date, SARS-CoV-2 vaccine development proves to be a challenging one. The virus spike protein is a promising immunogen for protection, optimizing antigen design is very much crucial to ensure optimal immune response. Vaccine development is a lengthy, expensive process which is tiresome and gruelling. It usually takes multiple candidates and many years to manufacture a licensed vaccine.It is because of the cost and high failure rates, developers usually follow a linear sequence of protocols, with a series of many bottlenecks for data analysis or manufacturing-process checks (Gouglas *et al*., 2018).

Plasma therapy is an upcoming and promising mode of treatment in the recent Covid infection according to an article in The Print. According to WHO, management of Covid-19 has mainly detailed on prevention, early case detection and monitoring and supportive care along with symptomatic and conservative treatment of the positive cases. However, there is no specific anti-SARS-CoV-2 treatment that is recommended because of the lack of proper evidence. Most importantly, the current guidelines dictate that systematic corticosteroids should not be given on

a routine basis for the treatment of Covid-19. Evidence at present shows that convalescent plasma from patients those have recovered from viral infections can be used as a treatment without the occurrence of severe adverse events in them. Therefore, it might be worthwhile and fruitful to test the safety and efficacy of convalescent plasma transfusions in SARS-CoV-2-infected patients (Cheng *et al.*, 2005).

**PREVENTION**

In order to reduce the general risk of transmission of Covid-19, WHO has recommended some precautionary measures such as avoiding close contact with people suffering from acute respiratory illness, regular hand washing with soap and water for 20 seconds or hand sanitizer particularly after direct contact with sick people or their environment, maintaining cough etiquette, and avoiding unprotected contact with farm or wild animals etc. (Verma and Prakash, 2020).

According to Centres for Disease Control and Prevention, the most important ways to prevention include cleaning hands after touching surfaces that might have been contaminated by fomites of infected persons and covering our faces with a mask so as to prevent inhalation of airborne droplets from an infected person. Social distancing and isolation or quarantine is the best way to prevent the infection.

Social distancing practices are changes in human behaviour that can possess the ability to prevent disease transmission by decreasing the contact rates between susceptible individuals and infected persons who may transmit the disease to other people. Social distancing norms can decrease the aggression of a pandemic, but its benefits depend on the extent to which it is used by individuals (Reluga, 2010).

This concept of social distancing has been adopted by India and worldwide and it has worked miraculously to limit the spread of the infection. In India it has been supplemented with lockdown of states on an individual basis in which restrictions have been imposed on the daily working habits of the inhabitants so as to prevent further spread of covid infection. Implementation of this on a larger scale is definitely a big challenge in itself since it requires equal coordination of all the states with the central agencies and communication between them needs to be immaculate.

The lockdown of states has crippled the economic and financial status of the country and many others worldwide (Verma and Prakash, 2020), which has created joblessness and instilled a sense of panic in the minds of the people due to scarcity of food and produce. It has hampered the mental peace of the people and has pushed them into a state of panic and mental frenzy. After reinstating the working of daily lives in a phased manner, normalcy has once again taken its course and slowly the economy is stabilizing along with the mental mind-set of the people. In spite of the challenges faced in the implementation of social distancing and lockdown, it has aided a lot in reducing the spread of infection and thus decreasing the number of cases.

**DISCUSSION**

Retrospectively speaking the ongoing pandemic could have been prevented or delayed all over the world by early preparedness and active participation in initiating the social distancing and early case diagnosis and treatment could have paved the way for a better future. The main challenge lies in the future that speaks of a suppressed fear that lingers on in the minds of the people regarding the persistence of the infection in the community and in the environment. Fears of a second wave of infection are also at large as is seen in a recent uptick in cases in China. It might happen that the infection can regress to an endemic and persist in the community. As much as it is hard to accept the new terms of leading the normal life, wearing masks being an important aspect of which, nevertheless the entire world needs to come together in combating the deadly virus and preventing further spread in the community. The contribution of the medical personnel, and those who delivered essential services, risking their lives as the entire world stayed locked up, shall never be forgotten. Better facilities and attention should be taken by governments across the world for the care of the frontline warriors. Every step in the ladder of

science is being used, as the entire world looks forward to researchers as they toil to find a cure. Their hopes high, their heads tired, but firm in their resolve.

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