



Strategies and Guidance to Combat Novel Corona Virus (Covid-19) Disease

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Abstract

The emergence of SARS-CoV-2 outbreak which is presently reported as pneumonia of unknown etiology in a cluster of patients in Wuhan province in china has led to epicenter of pandemic of covid-19. The disease has infected >150 countries worldwide and arised as the biggest pandemic till date. The spread of this virus has raised concern as it is rapidly spreading among humans through respiratory droplets and the management of the disease has very limited options as social distancing, isolation, and quarantine. Many scientists, researches, pharmaceutical companies are working on the treatment of COVID 19 disease by either developing a vaccine or drug therapy, or by any other therapy, although some already existing drugs have already worked on for and used to manage the symptoms of the disease. In the current report the authors have compiled some strategies and guidance for combating COVID 19 diseases.

Keywords: Coronavirus; Covid-19; Quarantine; Vaccines; Management

Introduction

Coronavirus a broad spectrum viral infection which occurs in both human and animals are known to cause respiratory tract infections and gastroenteritis [1]. The novel human corona virus, a severe acute respiratory syndrome coronavirus (SARS-CoV-2) according to WHO it was first originated from Wuhan Hubei china in December 2019 [2] WHO declared it as a global pandemic on Wednesday 11th march 2020 due to the rapid transmission from human to human through respiratory droplets of infected person as reported by several studies [3] on 11th February SARS-CoV-2 was named COVID-19 after discovering its similarity to SARS-CoV and MERS-CoV, belonging to the coronavirus family which are having crown like spikes on their surface [4].

Emergence and Prevalance

In the mid-1960s, the human corona virus was discovered. Human CoV-229E (HCoV-229E) and Human CoV-

OC43 (HCoV-OC43) were first identified with symptoms of common cold in human [5]. SARS coronavirus (CoV) begins with mild respiratory symptoms and high fever which progresses to pneumonia within a short period of time [6]. MERS which emerged in the late 2012 affected several patients from 27 countries around the world and has highest number reported in Saudi Arabia as WHO reports .The main source of coronaviruses are bats although MERS-CoV have been traced to dromedary camels. SARS-CoV-2(COVID-19) cause serious respiratory flu-like problems [5-7]. SARS-CoV-2 also known as covid-19 is a beta-coronavirus and its relation to the SARS-CoV is clear [8]. As of now, the novel coronavirus has affected 213 existing countries and territories in the world, including 2 international conveyances which have shown in figure 1 & 2.

Incubation Period, Signs and Symptoms

After the data collection on the basis of exposure, onset time of illness, hospital admission and death, study showed that the mean incubation period is 5 days and 95th percentile

of incubation is 10-14 days, indicates a total quarantine period which should be less than 14 days [9].

The commonly reported signs and symptoms of COVID-19 are given in table 1. It produces symptoms like cough, shortness of breath, fever which may appear 2-14 days after exposure [10]. According to WHO; some patients

may experience nasal congestion, runny nose, pains and aches, sore throat and diarrhea [11]. The Centre for Disease Control gave list of emergency warning signs like trouble breathing, persistent pain in chest and bluish lips or face. The new symptoms reported with COVID-19 patients are loss of taste and loss of smell [10].

Geographical distribution of Covid-19 cases by Continents

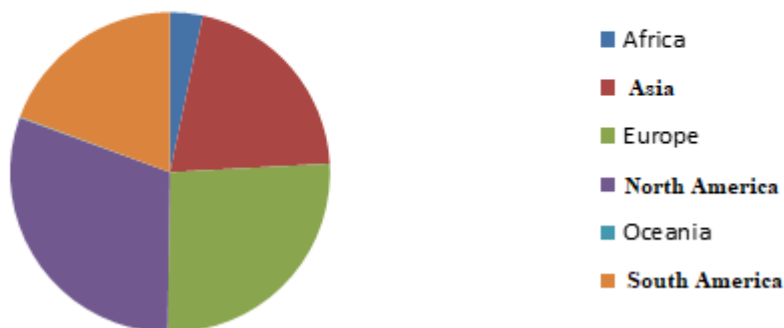


Figure 1: Geographical distribution of Total cases [13].

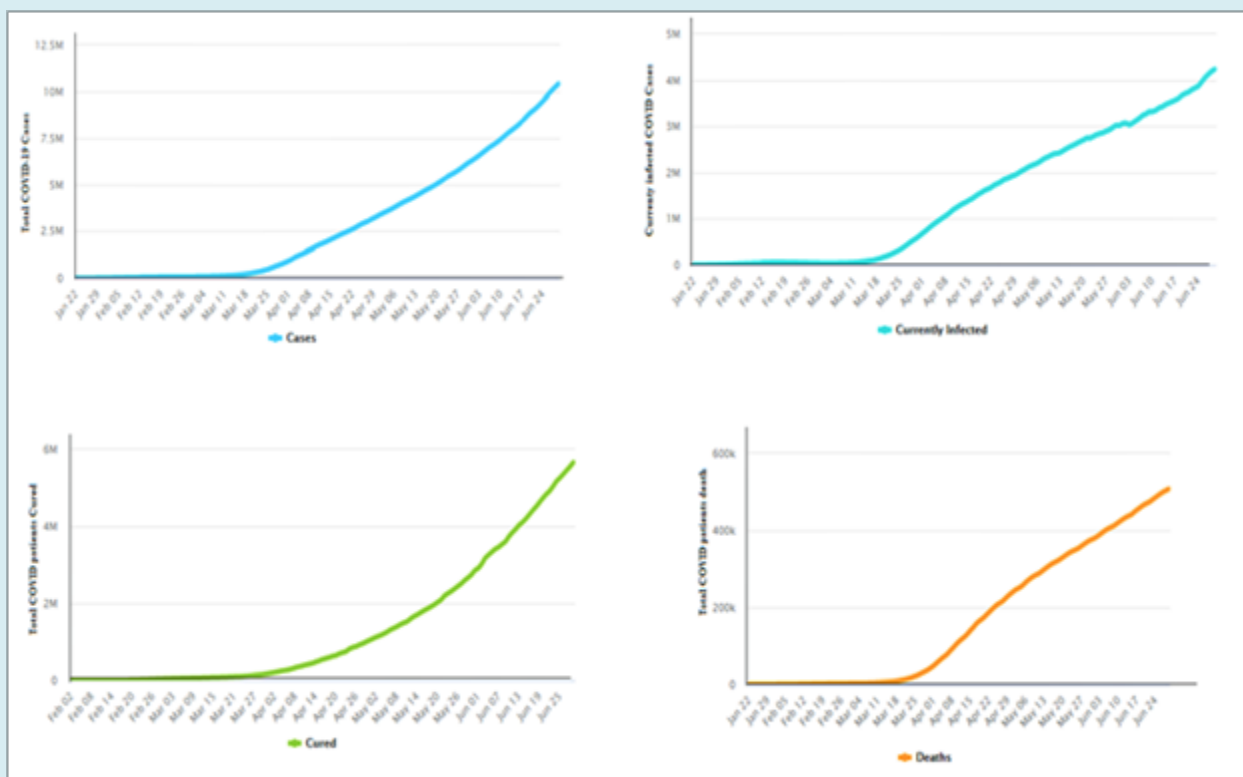


Figure 2: Current total COVID- 19 cases, active cases, cured and death prevalence growth chart [13].

| Signs and symptoms | Cold | Flu (influenza) | Covid-19 |
|-------------------------|------------------|----------------------|-------------------------|
| Fever | Mild if present | Often | Often |
| Fatigue | Occasional, mild | Common | Occasional |
| Sneezing | Common | Infrequent | Infrequent |
| Body aches | Common | Common | Occasional |
| Headaches | Very frequent | Common | Occasional |
| Sore throat | Common | Occasional | Occasional |
| Cough | Mild | Dry cough | dry cough, often severe |
| Shortness of breath | No | Rare | With mild infection |
| Difficulty in breathing | No | In severe infections | Common in severe cases |

Table 1: Signs and symptoms of common viral infections compared with COVID-19 [12].

Prevention and Control

Hygiene and Social Distancing

The best preventive measure is to avoid coming in contact to the virus, and the first step to take is personal and environmental hygiene which includes washing of hands with soap/hand wash and water, using hand sanitizer containing at least 60% of alcohol, proper use of face mask as well as properly disposing it as per WHO guidelines, covering the mouth while coughing and sneezing with the help of tissue paper and disposing it in a proper manner [14].

To avoid further spread of disease; travel restrictions have being imposed in Corona infected countries. Any person having history of travel in the past 14 days to countries having high cases of covid-19 is monitored and self-isolation and surveillance is mandatory [15].

Treatment and Management

The rapid spread of covid-19 has created a matter of concern to develop a treatment approach relates to drug development or vaccine development as shown in table 2.

| Drug & Dosage form | Class | Action in COVID | Reference |
|------------------------------------|----------------------|--|-----------|
| Chloroquine (Oral) | Anti-malarial | Chloroquine was found to block SARS-CoV-2 infection at low micromolar concentration. Chloroquine with azithromycin needs careful monitoring, and can be used only in hospital and clinical settings only. | [20] |
| Interferon - α (Inhalation) | Anti-viral | a broad-spectrum antiviral that is usually used to treat hepatitis, though it is reported to inhibit SARS-CoV reproduction in vitro. | [23] |
| Lopinavir / Ritonavir (Oral) | Antiretroviral | It has anti-SARS-CoV activity in vitro and in clinical studies, but no clinical trials available to support use in Covid-19 | [24] |
| Ribavirin (IV infusion) | Antiviral | It can prevent the replication of RNA and DNA viruses by suppressing the activity of inosine monophosphate dehydrogenase, which is required for the synthesis of guanosine triphosphate (GTP) | [27] |
| Arbidol (Oral) | Antiviral | Arbidol can effectively inhibit SARS-CoV-2 infection at a concentration of 10-30 μ M in vitro. | [25,26] |
| Favipiravir (Oral) | Anti -viral | Favipiravir is capable of blocking the replication of flavi-, alpha-, filo-, bunya-, arena-, noro-, and other RNA viruses. | [28] |
| Remdesivir (IV -infusion) | Antiretroviral | The <i>in vitro</i> study showed that remdesivir potently blocked SARS-CoV-2 infection at low-micromolar concentrations and showed a high selectivity index.Reduced the duration of hospital stay in Covid-19 patients | [25,29] |
| Ivermectin | anti-parasitic agent | A FDA-approved anti-parasitic previously shown to have broad-spectrum anti-viral activity <i>in vitro</i> , is an inhibitor of the causative virus (SARS-CoV-2), with a single addition to Vero-hSLAM cells 2 h post infection with SARS-CoV-2 able to effect ~5000-fold reduction in viral RNA at 48 h. | [30] |

Table 2: Current Status of Drugs In Management Of Covid-19 Disease.

Till date, no drug or vaccine has been approved as anti covid-19 drug, but some drugs can be used as an emergency treatment for management of the disease together with some traditional methods [16] and benefits to the body to develop natural immune response which plays a significant role in fighting of viral infection either by the adaptive immune response or T-cell response [17].

The initial strategy to treat the symptoms of COVID- 19 are with either use of interferons- α nebulization, broad-spectrum antibiotics, and anti-viral drugs which can reduce the viral load. [18-20].

However the use of a broad spectrum nucleotide analog antiviral drug remdesivir has revealed promising effect against the virus. The use of remdesivir alone or in combination with chloroquine or interferon beta significantly blocked the SARS-CoV-2 replication and patients were stated as clinically recovered [20-22].

Lopinavir -Ritonavir are drugs that have showed preliminary effect against Covid-19, the results suggested that this combination showing little to no benefit treatment beyond standard care which may be due to the late treatment time in patients [23,24].

While the results from the adaptive Covid-19 treatment trials revealed that patients administered with remdesivir showed 31% faster recovery rate than those given the

placebo [25,26].

Vaccines

There are several approaches in the development of vaccine, the recombinant subunit vaccine is said to have more advantages than other vaccines as it has less side effects. Clover biopharmaceuticals together with GSK have made an announcement of improving the body's response to immunity by bringing together their S-Trimer and GSK's adjuvant. Inovio and Applied DNA sciences are on the preclinical stage of developing a vaccine focused on S protein [31,32].

The use of mRNA is a new technological approach in combating the infectious diseases and can be a potential vaccine candidate, the mRNA based vaccine (mRNA-1273) by Moderna and Vaccine Research Centre NIH has successfully completed phase 1 clinical trial after having shown success in animal models. The other companies working in clinical trials of vaccines are China's casino vaccine which has progressed to second stage of trials, Vaccine by AstraZeneca plc. And Oxford University started trials in the month of April [32] as shown in table 3. The vaccine by Indian Council of Medical Research (ICMR) and Bharat Biotech International Limited (BBIL) came to the phase 1 and 2 clinical trials in July 2020 as per the permission granted by Drug controller general of India. The other institutes as Wuhan institute of biological products, Sinovac, Pfizer-BNTECH vaccine working persistently for the vaccine development.

| Company/Sponsor | Vaccine Candidate | Status |
|--|-----------------------------|-----------------------------------|
| Moderna | mRna-1273 | phase 2 clinical trials |
| Oxford and AstraZeneca | AZD1222 | advanced stage of trial phase 2/3 |
| Pfizer and BNTEch | BNT162 | phase 1 and 2 trials |
| Inovio pharmaceuticals | INO-4800 | phase 1 trials |
| CoronaVac | SinoVac | phase 1and 2 trials |
| University of Melbourne and Murdoch children's research institute, Radboud university medical center; Foustman lab at Massachusetts General Hospital | BCG live attenuated vaccine | phase 2and 3 trials |

Table 3: Latest research on covid-19 vaccines [32].

Indian Senario for Covid -19 Investigations

As the COVID-19 pandemic inception started in India,

Indian Council of Medical research (ICMR) is working for the evaluation of molecules, regimens by AYUSH ministry, products/technologies/ diagnostic kits, etc. (Table 4)

| Investigational technologies/ products /diagnostic devices | Indian Research Institutions/Labs | | | |
|--|--|--|--|-------------------------|
| | DST | DBT | CSIR | ICMR |
| Synthetic molecules/ drugs-repurposed drugs | IACS, Kolkata JNCASR, Bengaluru | ICGEB, New Delhi RCB, Faridabad ILS, Bhubaneswar THSTI, Faridabad RGCB, Kerala | IICT, Hyderabad NCL, Pune CDRI, Lucknow NIIST, Thiruvananthapuram IIIM, Jammu NEIST, Jorhat | NIV, Pune NARI, Pune |
| Synthetic molecules/ drugs- New molecules | IACS, Kolkata JNCASR, Bengaluru | ICGEB, New Delhi RCB, Faridabad ILS, Bhubaneswar THSTI, Faridabad RGCB, Kerala | IICT, Hyderabad | NIV, Pune NARI, Pune |
| Nano particles | IACS, Kolkata JNCASR, Bengaluru | ICGEB, New Delhi ILS, Bhubaneswar THSTI, Faridabad RGCB, Kerala | NCL, Pune NIIST, Thiruvananthapuram | ----- |
| Plant extracts (Crude extracts/oils/ purified products) | ARI, Pune JNCASR, Bengaluru | RCB, Faridabad ILS, Bhubaneswar IBSD, Manipur THSTI, Faridabad RGCB, Kerala ICGEB, New Delhi | IICB, Kolkata NBRI, Lucknow IIIM, Jammu | ----- |
| Herbal formulations | National Innovation Foundation, Gandhinagar JNCASR, Bengaluru | RCB, Faridabad ILS, Bhubaneswar IBSD, Manipur THSTI, Faridabad RGCB, Kerala ICGEB, New Delhi | IIIM, Jammu NBRI, Lucknow NIIST, Thiruvananthapuram | ----- |
| Ayurveda based formulations | JNCASR, Bengaluru | RCB, Faridabad ILS, Bhubaneswar THSTI, Faridabad RGCB, Kerala ICGEB, New Delhi | IIIM, Jammu | ----- |
| Siddha based formulations | JNCASR, Bengaluru | RCB, Faridabad RGCB, Kerala ICGEB, New Delhi | TKDL, New Delhi | ----- |
| Homeopathy based formulation | JNCASR, Bengaluru | RGCB, Kerala ICGEB, New Delhi | TKDL, New Delhi | ----- |
| Surface Disinfectants | SCTIMST, Thiruvananthapuram IACS, Kolkata, JNCASR, Bengaluru | ----- | ----- | ----- |
| Hand sanitizers | ARCI, Hyderabad IACS, Kolkata ARI, Pune JNCASR, Bengaluru | IBSD, Manipur | ----- | ----- |
| Diagnostic/ventilators/ supportive devices etc | SCTIMST, Thiruvananthapuram ARI, Pune | THSTI, Faridabad (only in vitro diagnostics) RGCB, Kerala | NAL, Bengaluru CMERI, Durgapur CSIO, Chandigarh | ----- |
| UV based equipment's/ small portable unity ozone based units/ Ion generator | SCTIMST, Thiruvananthapuram ARCI, Hyderabad IACS, Kolkata | ----- | CMERI, Durgapur CSIO, Chandigarh | ----- |

| | | | | |
|----------------------------|---|-------|---|-------|
| PPE-Fabrics, Masks, Gloves | ARCI, Hyderabad IACS, Kolkata JNCASR, Bengaluru | ----- | NAL, Bengaluru NCL, Pune CMERI, Durgapur | ----- |
| AI-Health tools | JNCASR, Bengaluru | ----- | IGIB, New Delhi CEERI, Pilani | ----- |
| Mobile applications (Apps) | IACS, Kolkata JNCASR, Bengaluru | ----- | IGIB, New Delhi CEERI, Pilani | ----- |

Table 4: List of Indian Research Institutions and Labs working for products/technologies/ diagnostic kits [33].

Conclusion

Due to the spreading of COVID-19 pandemic, scientists around the world are actively exploring various treatments, therapies, diagnosis that would be potentially effective in combating COVID-19. Generally, till date there are no finally verified antivirals specific to COVID-19 treatment at present. Hence, the safety and efficacy of drug candidate used in the treatment of COVID-19 need to be confirmed in further preclinical and clinical trials.

Conflict of Interest

No conflict of interest has been declared by the author.

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