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Combating Outbreak of nCoV-19: Prevention Strategies, Possible Medication and Its Predominance in Pakistan

Mubassir Shah[1], Zia Alam[1], Hajra Shahana[2], Waqar Ali[1], Latif Ullah[1], Fazal Jalil*[1]

[1]*Department of Biotechnology Abdul Wali Khan University, Mardan, KP, Pakistan*
[2]*Department of Chemistry, Women University Swabi, KP, Pakistan*

Abstract

The appearance of a novel coronavirus (nCoV-2019) is a pandemic threat which has been declared an international public health emergency. The number of infected people went out from China to other countries has increased since the discovery of the virus in late December 2019, and the epidemiological picture has changed daily. The nCoV-2019 belongs to Genera Beta coronavirus which also contains SARS and MERS i.e. (Middle East respiratory syndrome). According to the National Institute of Health (NIH), the first case reported in Pakistan was on 26 February 2020 and till 22 May 2020, the total number of confirmed cases in Pakistan are 52,013 with 16,012 recoveries and 1087 deaths. No medicine or vaccine for human coronaviruses has, sadly, yet been approved. However, it can take months to years to create new approaches. Other strategies for managing or preventing emerging nCoV-2019 infections can be envisaged including vaccines, monoclonal antibodies, oligonucleotide- treatment, peptides, interferon treatment and medication with low molecular weight molecules. In the face of the severity of the nCoV-2019 outbreak, we concentrate on the potential for recycling existing licensed or evolving antiviral agents for control of infections that are caused by different viruses especially influenza viruses i.e. SARS and MERS. Therefore, it is urgently important to identify appropriate antiviral agents to combat the outbreak of nCoV-19.

Keywords: SARS, MERS, nCov-19, Prevalence, Pakistan

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**Corresponding Author:*
Fazaljalil@awkum.edu.pk

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1. INTRODUCTION

Pathogens that arise and re-emerge are global health threats. In China (2003), a severe acute respiratory syndrome (SARS) outbreak led to the first reported significant human corona viral disease [1]. In 2012, Saudi Arabia with the Middle East Respiratory Syndrome (MERS) triggered the second epidemic of severe disease [2].

Among the many humanly pathogenic coronaviruses, the majority are related to mild clinical symptoms [3]. A novel human coronavirus in Wuhan, China was reported in late 2019 that a cluster of cases

of pneumonia having unspecified symptoms. It has spread exponentially, resulting in a Chinese epidemic and a growing number of cases worldwide in other countries. The World Health Organization named COVID-19 in February 2020 as the 2019 epidemic of coronavirus [4]. Up to date (20 May 2020) this virus infects more than 5 million individuals with more than 333,185 deaths across the globe. The COVID-19 virus is classified as an Extreme SARS-CoV-2; previously referred to as nCoV-2019. The virus is named coronavirus because of its crown like spikes on the external surface. The Orthocoronavirinae subfamily of the Coronaviridae family is classified in four types of genus CV: include alpha (α), beta (β), gamma (ć) and coronavirus delta (μ). A single strand positive-sense RNA (+ssRNA) genome of coronaviridae is present in this family of viruses (specifically in nCoV-19) with a length of 26 to 32 kilobases [3]. By comparing the current genome sequence data for identified strains of coronaviruses, we can establish that SARS-CoV-2 is a product of natural processes said Kristian Andersen, (PhD, an associate professor of immunology and microbiology at Scripps Research. The novel betacoronavirus emerging in Guangdong, South China, in November 2002, was Extreme Acute Air Syndrome (SARS-CoV) [5] and Coronavirus (MERS-CoV) in the Middle East was initially identified in Saudi Arabia in 2012 [6]. Both the disorders were responsible for the death of 1632 collectively across different countries. In December 2019, the first cases were registered [7]. Five patients with acute respiratory distress syndrome were admitted and one of these died from 18 December 2019 until 29 December 2019 [8]. This virus has been confirmed to be in the β coronavirus group[2]. The International Committee on Taxonomy of Viruses (ICTV) named the virus as SARS-CoV-2 and the disease as COVID-19 [9]. On 28 February 2020, the WHO raised the hazard to the "very big" COVID epidemic. The consequences of the current COVID outbreak are possibly yet to evolve as a result of the rapid growth of this situation.

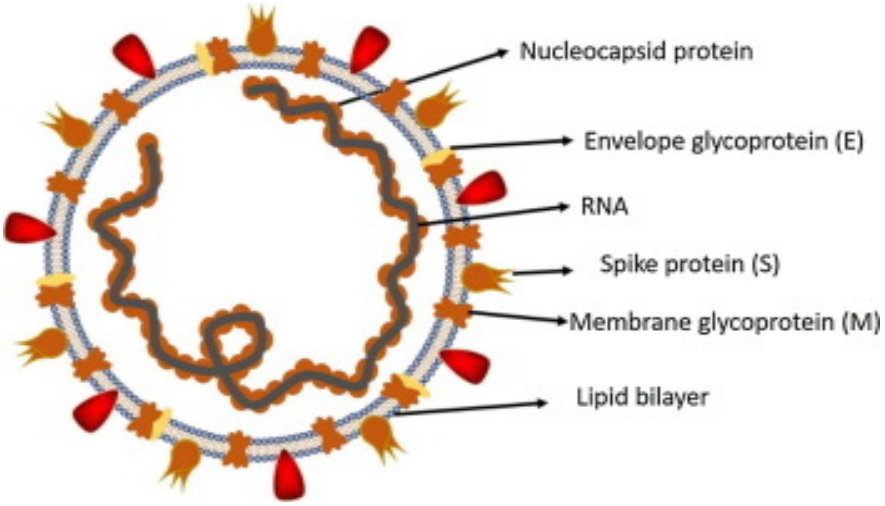

Fig. 1. Structure of nCov-19 [12]

2. COMPARISON BETWEEN nCoV-19, SARS CoV and MERS-CoV

The beta-coronavirus from the Middle East seems to be more distantly associated with the respiratory syndrome [10]. The nearest sequence of RNA is to two bat coronaviruses and bats are possibly the main source It is unclear whether COVID-19 viruses are transmitted directly by bats or through some other means (e.g. through an intermediate host) [11]. Notably, 2019-nCoV was closely linked to two bat-derived severe acute respiratory syndromes (SARS)-like coronaviruses (88 percent identity) Bat-SL-CoVZC45 and bat-SL-CoVZXC21, collected at Zhoushan in eastern China in 2018 but were more distant from SARS-CoV (about 79%) and MERS-CoV (about 50%) as shown in Fig. 2 retrieved from *Shereen et al* 2020.

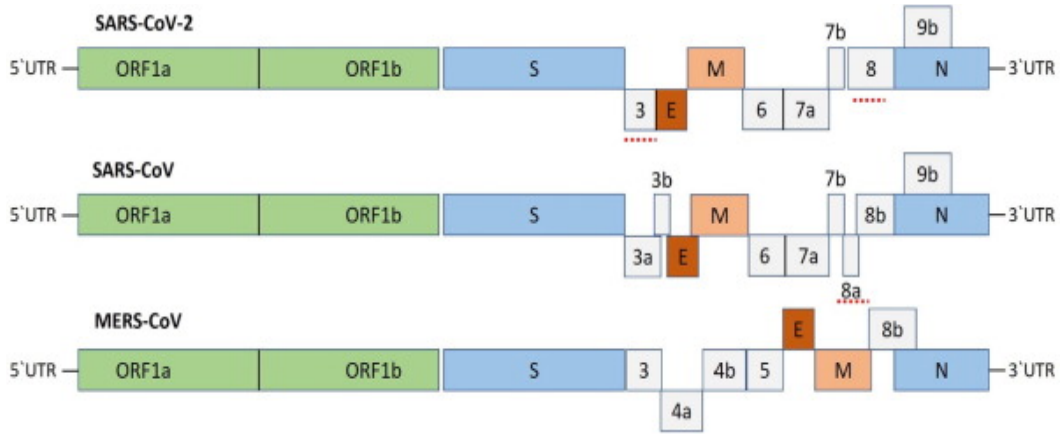

Figure 2. Betacoronaviruses Genome Organization; the 5'-untranslated region (5'-UTR) contains human betacoronavirus genome (SARS-CoV2 and MERS-CoV), Open reading frame (ORF) 1a / b (green box) non-structural protein(nsp), structural protein like spike, envelope (brass box), membrane (pink box), envelope (maroon box), Nucleocapsid (cyan box) proteins, accessory proteins (light gray boxes) such as ORF 3, 6, 7a, 7b, 8 and 9b in the SARS-CoV-2 genome, and 3'-untranslated region (3'-UTR). The red dot is the protein that shows the key variation between SARS-CoV-2 and SARS-CoV [12].

3. PREVALENCE OF nCoV-19 IN PAKISTAN

The outbreak of this new type of coronavirus named SARS – COV2 is now microscopically described and epidemiologically evolving. The borders between Pakistan and China and Iran are one, with the epicenter, and the other, over the past few months, an unprecedented rise in the number of incidents. The increasing influx of air, ground, and sea travellers puts Pakistan in increased danger of spreading the virus further from Iran and China. There is a very high risk of the virus being imported into Pakistan that calls for strict precautions and rigorous action in order to identify possible cases and to avoid further spread of the virus. Yet internationally, Pakistan is as fragile as any other developing country. According to the National Institute of Health (NIH), In Pakistan the first case of COVID-19 was reported on 26 February 2020 and till 22 May 2020, the total number of confirmed cases in Pakistan are 52,013 with 16,012 recoveries and 1087 deaths. The following graph shows the prevalence rate of nCoV-19 in Pakistan as shown in Fig. 3.

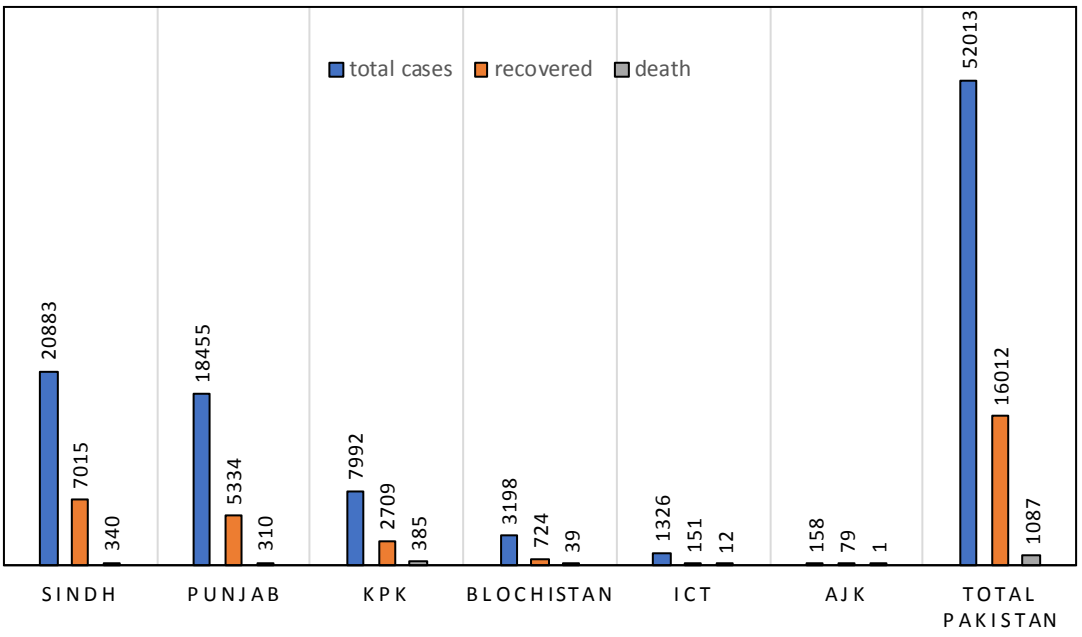

Fig. 3. Prevalence rate of nCov-19 in different regions of Pakistan.

4. SIGN AND SYMPTOMS

Following an incubation time of around 5.2 days, COVID-19 signs appear[13]. During 6 to 41 days, the average time of the onset of COVID-19 symptoms was 14 days [14]. This time depends on the patient's age and immune system status. Fevers, cough (30%), and fatigue are the most common symptoms at COVID-19 onset. Other indications include sputum, vomiting, haemoptysis, diarrhoea, dyspnea, and lymphopenia [8,15]. In certain cases, multiple peripheral opacifications of the ground glass were found in subpleural areas of both lungs [16].

5. POSSIBLE TREATMENT AND MEDICATION

Several therapies and vaccines to cope with the coronavirus pandemic have been suggested. Different treatment methods have been suggested and certain older pharmaceutical products tend to be correlated with positive results. Modern vaccines must be developed and tested rigorously and checked safely in clinical trials before widespread human use. Therefore, it is urgently important to identify responsible antiviral agents for combating the disease. Here is some therapeutic option which could counter the Cov-19 before the vaccine. Some medicines were used in SARS or MERS patients, i.e. ribavirin, interferon, lopinavir-ritonavir or corticosteroids but some medicines remain controversial in their effectiveness [17].

5.1 Remdesivir

Remdesivir is not developed specifically for the destruction of SARS-CoV-2. However, it removes a specific piece of machinery in the virus, known as "RNA polymerase," which were used by viruses to replicate. Remdesivir is an exploratory agent with a wide variety of antiviral activities, were used against SARS-CoV and RNA Respiratory Syndrome. The efficacy is still under consideration and more thorough research is required before it is a general SARS-CoV-2 therapy. Remdesivir has only recently been recognized in the cultured cells, mouse and non-human primates (NHP) models as a promising antiviral against a large range of RNA viruses (including SARS / MERS-CoV5) [18]. Remdesivir is an adenosine analog that integrates in nascent viral RNA chains and leads to a premature ending.

5.2 Favipiravir

Favipiravir is an antiviral that is intended to combat RNA viruses which also contain coronaviruses and influenza viruses. It is also known as Avigan. The drug is intended to interfere with a mechanism for replicating viruses within the cells. The mechanisms of its action are considered related to viral-RNA-dependent RNA polymerase selective inhibition [19]. Favipiravir leads to lethal mutations in the transverse RNA, which create a viral phenotype that is not viable [20]. Preliminary results of Faviravirs moderate antiviral effect on Covid-19 have emerged from study in china, although the parent company of the drug (Fujifilm Pharmaceuticals, japan) has not confirmed the drug's efficacy[29].

5.3 Chloroqine and Hydroxychloroquine

Chloroqine has recently been identified as a possible broad-based antiviral medication, a commonly used medicine for antimalarial and autoimmune disease [21]. Chloroquine is believed to prevent viral infection by growing the virus ' endosomal pH /cell fusion and by interfering with cellular glycosylation of SARS-CoV receptors [22]. Chloroquine is a low cost and effective drug used for 70 years, which makes it easier to treat 2019 nCoV clinically. Hydroxychloroquine is an analog of chloroquine that has fewer concerns about drug-drug interactions. In the previous SARS outbreak, hydroxychloroquine was reported to have anti-SARS-CoV activity in vitro [28]. For COVID-19 patients for three to six days, we show hydroxychloroquine is successful in clearing the SARS-CoV-2 virus in most patients. A substantial difference was found between the patients treated with hydroxychloroquine and the controls even after day 3 [23]. According to FDA Hydroxychloroquine and Chloroquine has no longer safe and effective for treating or preventing COVID-19. During clinical trials doctors notice that hydroxychloroquine and Chloroquine can cause abnormal heart rhythms such as QT interval prolongation and a dangerously rapid heart rate called ventricular tachycardia. Therefore, this is threatening to Heart dysfunction patients as well as other patients to limit the use of hydroxychloroquine and Chloroquine.

5.4 Lopinavir–Ritonavir

MERS patient case reports of treatment programs like lopinavir-ritonavir were related to beneficial outcomes of diseases, like defervescence, serum and sputum viral clearance and survival [24]. The enzyme 3-chymotrypsin-like protease ($3CL^{pro}$) plays a crucial role in processing in viral RNA. Lopinavir-ritonavir are the protease inhibiters (PI) and can inhibit ($3CL^{pro}$) proteases. Owing to in-vitro and in-vivo activity against MERS-CoV, lopinavir-ritonavir and IFN-β1b therapies have been developed for clinical trials in hospitalized Saudi-Arabia MERS patients [25]. The MERS CoV marmoset (Primate) model has contributed to mild improvements in MERS disease effects in oral care, Lopinavir-ritonavir showing lower penetration of the chest x-ray pulmonary, less interstitial pneumonia and lower weight loss [26].

5.5 Nitazoxanide

Nitazoxanide is a generic antiprotozoal agent with a wide range of antiviral ability. These drugs target host-regulated processes involved in viral replication, it inhibits replication of DNA and RNA viruses. Inhibited nCoV-2019 at a low micromolar concentration, including animal coronaviruses (EC_{50} = 2.12 µM; CC_{50} > 35.53 µM; SI > 16.76) [27]. It is recommended that this drug is further tested in vivo against nCoV-2019 infection which could be the possible way to combat the deadly nCoV-19.

6. PREVENTION

This epidemic is unprecedented, and it is completely necessary to alter habits to avoid the spread. The WHO provides many preventive methods to shield yourself from infection. The virus spread from individual to individual and has been transmitted worldwide. Wash your hands at least for 20 seconds. Cough and sneeze into your elbow. Don't touch your face, mouth, and ear as the virus enters the body through these parts of the body. Similarly, if you have visited a place where COVID-19 spreads, isolate yourself for 14 days.

7. CONCLUSIONS

Many other medications are being tested are considered for prophylaxis or COVID-19 clinical trials in the United States and other countries. The different finding suggests that different antiviral drugs especially that were used against the SARS-Cov and MERS would be highly effective in the combat of nCoV-19 outbreak in vitro. These different combinations of drugs must, therefore, be used in nCoV-19 patients with a safety record and demonstrated to be effective against different illnesses. Therefore, we suggest, human patients with a novel coronavirus disease should test them. The combination of different antiviral drugs (cocktail) should possibly block the nCoV-19 life cycle, at different stages either changing the pH of the cellular membrane, release of RNA to host cell, replication of RNA etc.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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