Review paper

CONTRASTING THE IMPACT OF TWO CORONAVIRIDAE PANDEMICS IN PAKISTAN

Rabail Mehak[1], Syeda Hafsa Ali[1]*, Sadia Naseem[1], Syeda Ayesha Ali[2]

1. Department of Microbiology, Balochistan University Information Technology Engineering and Management Sciences, Quetta, Balochistan, Pakistan

2. Department of Biochemistry, Sardar Bahadur Khan Women University, Quetta, Pakistan

***Corresponding author:** syeda.hafsa@buitms.edu.pk*

Citation: Mehak, R.; Ali, SH.; Naseem, S and Al,i SA. CONTRASTING THE IMPACT OF TWO CORONAVIRIDAE PANDEMICS IN PAKISTAN. ***Pakistan Journal of Biochemistry and Biotechnology,*** **2022, 3 (2), x. https://doi.org/10.52700/pjbb.v3i2.82**

Received: 05-12-2021
Accepted: 11-11-2022
Published: 31-12-2022

Abstract: SARS-CoV-2 a contagious and highly transmissible virus emerged in December 2019 causing a pandemic of acute respiratory disease and therefore named 'coronavirus disease 2019' (COVID-19) as this novel strain was identified in 2019. This review aimed to provide insight to compare important features of SARS with novel COVID-19. We capitulate the current data available on the topic to provide a sound basis for the emerging issues related to these two pandemics. Both viruses belong to the same family and are accountable for two different pandemics i.e. SARS in 2003 and COVID-19 from 2019 to date. This review focuses on aspects like origin, transmission, pathogenesis, symptoms, impact, and challenges faced during the pandemic, development of immunity, possible treatments, along with possible preventive measures for personal protection. COVID-19 seems similar to SARS regarding its clinical features and high transmissibility than SARS. Although, COVID-19 belonged to the same family as SARS, yet the spread and impact of this disease bought developed and undeveloped countries to their knees. However, the current scenario shows that not only undeveloped countries but also developed countries were not prepared to cope with the challenges. Therefore, the world needs to reevaluate the health, social and economic strategies to prevent the impact at the very beginning of such outbreaks.

Keywords: Corona Virus, SARS, Pandemic, Challenges, Impact

1. Introduction

A higher ratio of the population affected by a contagious disease at a place or extended to different parts of the world at the same, the outbreak gives rise to a pandemic [1]. Such pandemics can only be intervened via preventive methods to limit the spread of the pathogen [2]. In the 21st century, Severe Acute Respiratory Syndrome (SARS) was the first outbreak reported in 2002, followed by Middle East respiratory syndrome (MERS) in 2012, Zaire EBOLA virus in 2014, while some of them turned out to be pandemics [3]. Even though development in the public health sector is up to the mark, where infectious diseases are contributing to the mortality rate. Outbreaks of diseases are not bound to happen within certain areas, it spreads from one part to another very rapidly—leaving socio-economic impacts on the community [4].

The term coronavirus was used in 1968 for its crown-like shape of spikes as observed under an electron microscope. The coronaviruses are usually enveloped, positively

stranded RNA viruses with the largest known RNA genome [4]. Viruses are emerging and reemerging due to their antigenic shift and drift. Therefore, a possible treatment for COVID-19 is a top priority for the scientific community [5]. The first case of COVID-19 was reported in November 2019 in which patients were observed with the pneumonia-like condition and the causative agent of the disease was uncertain [6,7]. Hence, declaring it novel coronavirus ncov2, COVID-19 [8]. Previously, the world experienced a similar pandemic of SARS belonging to the same Beta Coronaviridae family in November 2002 in Guangdong, China [9]. However, $220 billion in income losses were expected due to COVID-19 in developing countries [10]. Whereas Asian Development Bank projected an expected downfall from 3.3% to 2.6% in the Pakistani economy by 2020, whereas, inflation will persevere at 11.5% [11]. In both pandemics zoonotic origin was strikingly common i.e. they were transmitted from animals to human beings while the host varied in either case. SARS genome resembled the viral genome of palm civets and raccoon dogs, while the COVID-19 genome after isolation resembles with bat genome. Viral and serological investigations showed that masked palm civets and two animals that were sampled in the live market had SARS-CoV or a closely related virus. Lately, horseshoe bats in the genus Rhinolophus were discovered as a natural host of SARS-like coronaviruses. Meanwhile, the novel coronavirus was isolated from bats and was transmitted to human beings via an unidentified host in Wuhan, Hubei province, China in December 2019. COVID-19 was associated with the live market of Wuhan as infected patients had a history of visiting the market [7,12]. The incubation period in SARS was 2-10 days, while in COVID-19 it's 2-14 days [13,14].

Pakistan holds an important geographical location in the World as far as COVID-19 is concerned as it shares its border with China—the centre of origination for both novel viruses. Pakistan's health ministry confirmed the first 2 cases of COVID-19 in Karachi and Islamabad on February 26, 2020. Within 15 days of the first reported case, on 12th March, the positive number of cases reached 14 in Sindh, 5 in Gilgit Baltistan, and 1 case from a 12 year old child in Baluchistan. The infected patients had travel histories from Iran, Syria, and London. After this vigorous rise in cases, the government of Pakistan took important steps to control the spread of the disease. This research review aims to provide insight to compare the two outbreaks such as SARS with novel COVID-19. The current data available on the topic to identify similarities and differences for two pandemics i.e. SARS in 2003 and COVID-19 in 2019 till 2021. The review focuses to compare important aspects and features of SARS and COVID-19 such as: origin, transmission, pathogenesis, symptoms, impact, and challenges faced during the pandemic, development of immunity, possible treatments, along with possible preventions for personal protection. Further identifying the impact and challenges faced during SARS and COVID-19 Pandemic [15].

2. Morphology of Virus

The genome of SARS COV is 29.7 kb, a positively stranded RNA genome, based on the organization, phylogeny, and variability of the genome [16]. The spikes in COVID-19 are longer in size than the spikes of SARS [7]. The envelope comprises RNA positive-sense, single-stranded with the largest 26-32 kb genome [17]. The proteins such as spike, envelope, membrane, and nucleocapsid form the structure of a virus with the help of genome code and enable its attachment and pathogenicity and aid in the protection of the virus outside a host cell. The recombinant virus was transferred from bats to human hosts by an unknown intermediate host. The structural proteins are vital for morphology and encoded by the viral genome. The Spike proteins interact with cellular receptor angiotensin-converting enzyme 2 (ACE2), which is made up of two subunits: S1 and S2. S1 determines cellular tropism and virus-host range through the Receptor Binding Domain (RBD). S2 determines virus-cell membrane fusion. Matrix proteins are responsible for trans-mem-

brane nutrition transport and envelope formation. The host immune response is obstructed by nucleocapsid protein and envelope protein, as well as many auxiliary proteins. Aside from that, nonstructural proteins play a vital role in the replication and transcription of RNA, and numerous nonstructural proteins have unique enzymes engaged in one or more key steps in viral replication. Non-structural proteins appear to play a major role in virus-host interactions [17].

Viruses have RNA genomes with higher mutation rates than DNA viruses. Consequently, COVID-19 is reported to have mutations in at least two letters of its genome each month which is about half the rate of influenza [18]. Due to a lack of mechanism of proofreading the S gene which is responsible for a higher frequency of recombination resulted in the emergence of a novel viral strain closely associated to bat SARS-like beta coronavirus [17]. Spikes of Coronavirus range between 60 nm to 140 nm on the surface and resembles a crown under an electron microscope. The spike protein gives the virus a bulging shape and is crucial in terms of receptors present in tissues. The spike proteins of viruses attach to the receptor of the host cell and cause infection [7].

Natural selection and adaptability are important factors to provide competitive advantages to viruses for greater transmissibility or immunity evasion. Modification in COVID-19 spike protein increases the virus's ability to penetrate the cells, and evade host immunity or antibodies. Coronavirus has mutated since 2020 with new variants highly transmissible and infectious than the original strain. The alpha strain was discovered in Kent, United Kingdom, in 2020. Experts detected a mutation in the spike protein that makes infection 40 to 80 per cent more transmissible [18]. This variant was observed in other nations with a 70% high transmissibility rate and a greater fatality risk. The alpha variant mutation resulted in an abnormal spike protein with high pathogenicity [19]. The D614G mutation alters spikes phenotype which enables viruses to penetrate host cells. This mutation also increases the transmissibility of viruses potentially increasing their spread worldwide. The D614G virus outperforms and outgrows the ancestral strain by a factor of ten, and it multiplies extraordinarily well in primary nasal epithelial cells, which might be a key location for person-to-person transmission [20].

The term "double mutant" is a misnomer since it refers to a unique lineage known as B.1.617 (just like the UK variant is called B.1.1.7). Another variant (B.1.1.7) expanded rapidly in the southern UK in late 2020, accounting for about 30% of all COVID-19 infections in England. This lineage of viruses has 15 mutations, six of which affect the Spike protein and three of which are essential. The alterations occur in spike protein that interacts with the ACE2 receptor; the first boost the virus's capacity to enter cells, while the second allows for partial immune evasion. Another mutation, P681R, increases the efficiency of viral entrance into cells. The result is a virus that infects more people while simultaneously partially evading neutralising antibodies. The structural configuration showed point mutation where cytosine was added instead of thymine as a result it expresses leucine [21].

Table. 1 Variants of COVID-19

Variant	*Scientific names*	*Year*	*Country*	*Mutation in Genes*	*Phenotype/result*	*References*
Alpha	B.1.1.7	2020	Kent, UK	Mutation in spike protein	40 to 80% more transmissible	[21].
Beta	B.1.351	2020	South Africa	Mutation in asparagine to tyrosine in amino acid.	Attached easily to the host cell.	[3].

Gamma	P.1	2021	Brazil	Genetic mutation open reading frame, deletion of one codon.	Fast replicate.	[22].
Delta	B.1.617.2	2021	India	missense mutation, Fewer spike protein mutation.	Patient transmits infection into 4 individual.	[23].

The spike protein is also a target location for COVID-19 vaccines. The beta variant of the virus emerged in South Africa. The beta variant spread more easily than the original virus. In the beta variant mutation occur in asparagine to a tyrosine of the amino acid and is attached easily to the host cell. COVID-19 variant gamma emerged among people of Brazil who travel to Japan at the end of the month. The gamma variant appeared more infectious than earlier strains of the COVID-19 virus. Mutation occurs in codon caused by deletion of one codon resulting in Frame shift mutation with viral ability to fast replicate in host cell [24]. In India, the Delta variety was discovered, and it spread significantly more rapidly than other variants. Spike protein and missense mutations were rare [18]. It causes severe sickness with single infected individual capable of infecting four people. In mid-April 2021, the delta variation caused massive losses, and the identical variant was detected in more than 130 nations. The delta variation has surpassed the previous form in infectivity [25].

3. Transmission of SARS and COVID-19

The transmission pathway for SARS was the dispersal of respiratory droplets from infected to healthy people. Fomites and fecal transmission were of high concern, yet not common methods of transmission [26]. About 29 countries were affected during the SARS pandemic. The reason for the SARS pandemic afflicting 29 countries was the lack of viral transmission in the asymptomatic stage. Quarantine was effective as viral peak shedding took place after 6-10 days among severely affected hospitalized individuals, consequently affected patients were isolated. All the severely ill patients who had the potential of spreading the disease were isolated from the community, hence limiting the SARS pandemic to only 29 countries. The reported case fatality rate was 15%, showing a high proportion of case fatality during a pandemic [27]. Unlike SARS, COVID-19 was rapid in spreading via respiratory droplets particularly in the asymptomatic stage [26]. Consequently, afflicting about 213 countries of the world [14]. The mortality rate of SARS was approximately 10% and 0.2% for COVID-19. This mortality rate for COVID-19 grows higher in older age groups, patients with medical conditions like cardiac patients, patients with a compromised immune system, and diabetes.

3.1 Total number of cases reported

According to the World Health Organization (WHO), about 8098 SARS cases and 774 deaths were reported during SARS pandemic [1]. Nearly 200 people remained hospitalized with the disease 25 [28]. However, in COVID-19, 48.1 million people were infected, and 1.23 million deaths were reported until 5 November 2020 [8]. ICU requirement is for 25-30% of infected patients (Singhal 2020). Moreover, about 29 countries were affected during SARS pandemic and about 213 countries were affected in the COVID-19 pandemic (see Fig.1).

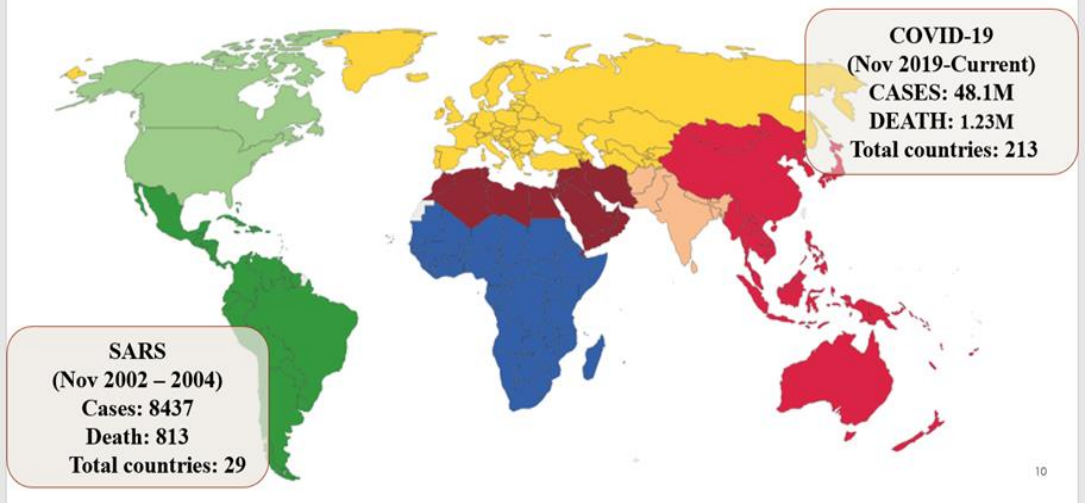

Fig.1. Shows total number of cases reported, deaths and countries affected in the world during pandemics.

3.2 Factors promoting pandemic

Wuhan with a population of more than 11 million was the epicentre of COVID-19 outbreak. During the pandemic, more than 5 million people travelled across China and around the world for the spring festival. The imposing lockdown was ineffective as people had already contracted and spread the disease to different parts of China and across the world. Hence, causing outbreaks in different parts of the World and causing miserable conditions in China. Secondly, patients were observed spreading illness in the pre-symptomatic stage. Therefore, isolating severely ill patients was of no use as they already had transmitted the virus to people around them. This phenomenon reduced the effectiveness of thermal screening. Thirdly, unknown infected asymptomatic patients caused a massive spread of the disease and proved that infected people are living normal lives [27].

3.3 Upsurge observed in the number of cases after the lockdown in Pakistan

The data during and after the lockdown recorded by the government of Pakistan was analyzed for the duration of 9th to 23rd, May 2020. The results depicted that when standard operating procedures (SOPs) were strictly followed during the lockdown phase, the cases were under control and medical care facilities were effective. However, as soon as lockdown was lifted an upsurge in the number of cases was observed which showed negligence in SOPs and a rapid increase in cases and case fatality rate (Fig.2).

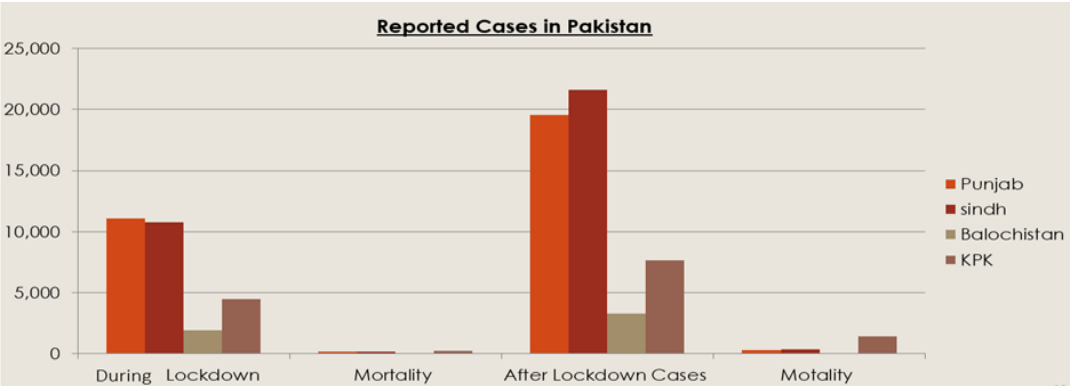

Fig.2. The total number of cases and deaths reported during and after lockdown in Pakistan.

3.4 Reasons for the second wave of COVID-19 in Pakistan

A high probability of a second COVID-19 wave is due to cold weather. Viruses' survival outside the living cell is high during the cold. The UK's Scientific Advisory Group for Emergencies (SAGE) reported that 4oC is a sweet spot for coronavirus. High UV radiations in light inactivate viruses, however, during winters there is less exposure to UV light which increases the viability of viruses. The emergence of the second wave of COVID-19 is also due to policy softening due to economic pressure and the non-serious behaviour of people. However, some countries were successful in adhering to strict policies and reducing the number of cases to a minimum such as Germany and South Korea got their testing and tracing systems functional on a large scale, allowing them to identify and trace the emergence of new cases and transmissibility of the disease. Similarly, Canberra decided to effectively impose lockdown and isolate itself from the rest of the world, while Spain banned summer visitors to relieve some of the important tourism seasons (Fig.3). Targeted regional lockdowns depended on a track and trace capacity that lets authorities control the cases [29].

Fig.3. Strategies of countries to cope with the second wave of the COVID-19 pandemic

It is an enigma how the number of cases didn't cross the threshold and the curve flattened as most of the population was not following SOPs. The second wave of COVID was officially announced by the Government of Pakistan on 28th October 2020, when 700 cases were reported in a day which led to a rise in the number of cases. Secondly, as winter emerged as a hub for viral sustenance, hence increasing the cases. The strategies opted by Pakistan to counter the growing cases included: mandatory screening tests for international travellers, wearing masks in public places and the closure of markets, restaurants, and public gatherings till 10 pm to reduce public interactions.

4. COVID-19 Is More Pathogenic Than SARS?

COVID-19 has higher transmissibility due to a high rho value than SARS. Rho value is the ability of a single infected person to further infect healthy individuals—which reflects the high transmissibility of COVID-19. Therefore, COVID-19 can transmit to further 5 individuals while SARS due to low rho value transmits to only 2 to 3 individuals [17]. While the replication of SARS is mediated by the translation of two polyproteins pp1a and pp1ab which consist of ORFs 1a and 1b encoded by the viral replicase gene. The polyproteins pp1a and pp1ab are mediated by viral proteinases which serve as a functional part

of the complex system i.e. membrane-bound replicase complex. This complex system process genomic replication and transcription of mRNAs, which helps to encode proteins that form structures such S, E, M and N. While the huge size of replicase proteins and the presence of RNA-mediated processes was not found in any other positive-stranded RNA virus which justifies the matchless complexity of the coronavirus [16].

5. Fine line to separate symptoms of SARS and COVID-19

COVID-19 has a range of symptoms that help differentiate it from seasonal flu, and cold. People normally experience cough, fever, tiredness, and myalgia in the early stage of infection. Some people, however, had uncommon symptoms such as headaches, sputum, diarrhoea, hemoptysis, and loss of smell and taste. Furthermore, people who had persistent underlying conditions such as acute heart damage, acute respiratory distress syndrome, or secondary bacterial infection had serious consequences. Patients with SARS, on the other hand, displayed symptoms such as flu, high fevers above 100.4°F, myalgia, dry non-productive dyspnea, lymphopenia, and infiltration on chest radiography during the asymptomatic period. In 38 percent of cases, pneumonia caused severe respiratory issues, necessitating the use of artificial respirators [28].

6. Relevance of Diagnostic Tests at Each Stage of Infection

6.1 Lab Based Molecular Testing

6.1.1 RT PCR

In COVID-19 and SARS, sampling can be taken from the nasal cavity, oropharynx, sputum but rarely samples from endotracheal aspirates. Bronchoalveolar lavage is sampled from the lower respiratory tract. Sampling from the lower respiratory tract is more valid than the upper respiratory tract but difficult to obtain so not frequently used. Flocked swabs of plastic and aluminium are used for sampling which is transported in the universal medium under refrigerated conditions. RNA is extracted from the sample followed by RT-PCR to detect; designed probes are used in the procedure (Table 2). Other tests are performed for confirmation of positive patients [12].

There are two mechanisms by which tests are performed by CDC and WHO:

1. CDC: they contain primer-probe sets for viral nucleocapsid genes and for human RNase P gene

2. WHO: they have a primer-probe set that target COVID-19 RNA-dependent RNA polymerase (RdRP) and envelope (E) genes.

Both methods are highly sensitive and show low cross-reactivity [30]. The threshold value of this test is 40 and undergoes 11 hours [31]. Testing in a closed system minimizes the chances of contamination, thus false-positive cases can be minimized [32]. Asymptomatic individuals hold importance as carriers shed viruses that infect surrounding people thus asymptomatic carriers can be identified using this method [33]. Meanwhile, if swabs are of calcium alginate, wood or cotton will inhibit PCR and will affect testing. Inadequate sample collection can result in false-negative tests. No matter how severely a person is affected, no serum or urine sample will work [12]. RT PCR often fails to indicate the COVID-19 severity of the disease [32].

6.1.2 Serology

The clinical specimens were obtained from blood and saliva. The specificity of the test is higher than 99% with a sensitivity of 96% [34]. Coronaviruses have four structural proteins: spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins [35]. Two proteins are antigenic sites to detect COVID-19, one of them is the S protein encoded by the S gene containing two subunits S1 and S2, both viruses are capable to bind to human angiotensin-converting enzyme 2, which is part of respiratory cells, gastrointestinal cells and renal cells of the human being [36]. N protein forms the structure of helical nucleocapsid and acts as an antigenic site in early diagnosis of COVID-19, against which antibodies are produced that are detected in patients [37]. Moreover, N proteins play a vital role in epidemiology and to determine previous exposure among asymptomatic patients (Table 2). Negative results are drawbacks if recent exposure to the virus has occurred [38]. Production of antibodies requires weeks to be detected and cross-reactivity to antibodies is also a potential problem [39,40].

6.1.3 Antigen detection test

This test identifies previous exposure to virus SARS-CoV-2 by identifying neutralized antibodies in the given specimen. Antibodies are produced as a result of the immune response against the antigen. The sample is obtained from nasal cavity, after which monoclonal antibodies are generated for nucleocapsid protein against SARS-CoV-2, which will serve as a foundation for antigen rapid detection test [33]. The detected antibodies are IgM and IgG. The advantages of conducting this test are easy to run, fast, and capable to detect low level of viral load (Table 1). While demerits of the test are poor sensitivity and possible missing of cases due to sampling variability [41].

6.1.4 Rapid antigen testing

It is the modification of antigen testing where a COVID-19 kit is used to detect antigens specifically in nasopharyngeal secretions. The mechanism follows with colloidal gold nanoparticles which use monoclonal antibodies to identify conserved nucleoprotein antigen of SARS-CoV and SARS-CoV-2, while another set of monoclonal antibodies is conjugated with gold colloidal and immobilized on nitrocellulose membrane. The test is performed by utilizing nasopharyngeal secretions and LY-S dilution buffer in a tube and analyzing the result in strips. As nasal secretions encounter the strip, the solubilized conjugate passively diffuses to drift with the sample and react with antibodies that are immobilized on the membrane. The test is interpreted by the presence of the control line and a positive line. A single control line depicts a negative test while line formation on control and positive sites indicates a positive test (Table 1). The specificity of the test to separate the true negatives is 100%, while the sensitivity of this test to identify true positives is 30.2% [42].

6.2 Imaging

6.2.1 Chest X-ray examination

Sampling is not required to perform the test. The radiological images helps in diagnosis, management of a patient, follow-up, it resemble the X-ray of pneumonia. The images can show no lung changes. Chest X-ray may show alveolar opacities which are multifocal bilateral in progressing stage of disease, which intend to cover complete opacity of lung (Table 1). Meanwhile, linked Pleural effusion could be observed. Chest X-ray has low sensitivity in diagnosing the initial stages of infection [30].

6.2.2 Chest computed tomography

This test is used as a confirmatory test after PCR, may not require any sample and help detect early infected individuals. The affected lungs of COVID-19 patients having pneumonia can easily be detected by CT scan due to multiple regions having prominent opaque glass-like areas called "ground or ground glass" (GG) in posterior regions and lower lobes of the lung with prominent intralobular septal thickening. The CT-scan progress over time, during the initial infection of 0 to 4 days GG is prominent, with lower lobes involved and the partial reticular pattern called crazy paving. As the infection progresses from day 5 to 8, the expansion of GG can be observed with abundant crazy paving arrangements. During the peak stage when the sign and symptoms are prominent during 10 to 13 days of infection, a consolidation pattern is hallmark of the infection (Table 2) [30].

6.2.3 Lung ultrasound

The lung ultrasound has higher sensitivity to detect abnormality and identify the infection. It can be performed if the main interstitial pattern of "white lung" with sub-pleural fusions are observed. During the disease, the first phase is identified by looking for focal areas of fixed B lines emerging at the pleural line of the lungs. The initial stage of COVID-19 has multiple B lines with thickening of the subpleural, as the infection proceeds posterior consolidations are noticeable. This test is conducted within 24 hours among suspected individuals, while the severity of affected individuals can be monitored by conducting his test every 48 hours. Thereby, severely ill patients can be shifted on a mechanical ventilator. The distinguishable features commonly observed among COVID-19 patients include irregular, discontinuous and thickening of pleural lines. Sub-pleural lesions are consolidations or nodules lines are often coalescent, static cascade that White lung Thickening of bilateral and posterior regions of lungs are prominent in COVID-19 patients (Table.2) [30].

TABLE 2. Relevance of diagnostic tests in SARS and COVID-19

Tests	*Sample*	*Procedure*	*Performed for*	*Advantages*	*Disadvantages*	*References*
RT PCR	Sputum, Endotracheal Aspirates, Bronchoalveolar Lavage	RNA extraction, Sens: 70 %	SARS, COVID-19 A/Symptomatic stage	Low-complexity, rapid, low false-positive	Chance of false-negative test, cannot indicate severity	[12,30,31,32,33].
Antigen detection test	Mucus from nose or throat	Ag-Ab conjugation (use of IgG, IgM) Sens: 73% Spec: 94%	SARS, COVID-19 A/Symptomatic stage	Rapid identification, low-cost	Poor sensitivity in early infections due to variability of viral load	[33,41].
Rapid antigen testing	Mucus from nose or throat	Ag-Ab conjugation, (use of Monoclonal Ab) Sens: 30.2%, Spec: 100%	SARS, COVID-19 A/Symptomatic stage	Easy collection of samples, inexpensive	Require weeks to be detected, chance of Cross reactivity	[42].
Serology	clinical specimens (such as	Ag-Ab conjugation Spec: 99% Sens: 96%	SARS, COVID-19 A/Symptomatic stage	Rapid identification of asymptomatic patients	Early diagnosis is impossible, Time consuming for precise	[34,36,38,39].

	blood or saliva)				identification, cross-reactivity of antibody	
				IMAGING		
Chest X-ray examination	No sample is required	Radiological images	SARS, COVID-19 Symptomatic Stage	Sampling not required, prompt identification	Early stage detection is not possible	[31].
Chest computed tomography	No sample required	Radiological images	COVID-19, Symptomatic Stage	Can detect infection in initial stages.	Several non-specific patterns similar to other infections can be observed	[31].
Lung ultrasound	No sample required	Radiological images	SARS, COVID-19 Symptomatic Stage	No sample required Immediate results obtained	None	[31].

7. Challenges To Control

7.1 The challenges faced in two pandemics

During SARS the insufficient stocks of safety kits for the public, along with ineffective delivery regarding viral infection by the Chinese government led to terror. Medical care authorities were ill-prepared. Deficiency of support such as hospitals, and medical supplies added complications to viral control. Similarly, in the COVID-19 pandemic, countries couldn't cope as they were not adapted to handle upsurges in cases. The shortage of basic medical supplies and laboratory facilities for diagnosis of the disease matched with SARS. Patients showing no symptoms were capable of transmitting infection, making the situation difficult to conclude the duration of the epidemic and estimate the total number of cases. During the COVID-19 pandemic, when travel was suspended millions of Chinese citizens had already travelled and were affected, spreading the disease in the region—unaware of the risks [26].

7.2 Impact

Pandemics come with a price to pay either economically or psychologically. The pandemic cost the global economy an estimated amount of $30–$100 billion. In 2003 SARS-CoV outbreak emerged in Singapore. Among various impacts of the SARS epidemic, 27% of paramedic staff reported depression and psychiatric symptoms [26]. The mental effects of SARS shared with travel caused a huge financial loss for the airline industry and the world economy [27]. COVID-19 devastating impact on the airline industry around the

world. Medical workers in the world dealt with high-risk infectious diseases with inadequate protection. Overwork, frustration, discrimination, isolation, pessimistic, and exhaustion was commonly observed among individuals living far away from home or facing financial strains due to lockdown. The mental health issues were widely observed among all individuals, especially healthcare workers which influenced their decision-making capacity to fight against COVID-19 [7].

7.3 Challenges faced by Pakistan

Pakistan—being a developing country faced an early phase of the outbreak and had limited resources. The diagnostic kits used to detect affected patients were not available and samples initially were sent to foreign countries for identification. Due to a large amount of demand in China for face masks, the export of masks readily increased causing a scarcity of masks in the market, hence resulting in high prices of face masks. The establishment of quarantine centers with a limited number of beds was not sufficient to cope with the large population of Pakistan. Moreover, some mosquito nets that were used at dengue fever outbreaks were used in quarantine centers imposing another health hazard. The thermal screening was not very effective in detecting patients of COVID-19 and many patients were missed in the scenario [15].

Pakistan encountered multiple problems during covid-19 due to instable economy, high inflation people living below poverty line, food insecurity, and natural disasters. According to a report of the Multidimensional Poverty Index 24% of the population is living below the poverty line and 38.8% are living in poor states. Diagnostic kits were sent by China and the primers were provided by Japan—making the detection of patients possible [15]. Iran was a tremendously affected country with a great number of patients, it also shares its border with Baluchistan, so a quarantine center was set up at the border to effectively isolate the affected patients and after proper testing sends back the unaffected individuals to their homes and hospitalizing the affected ones. Moreover, NIH played a vital role in making protocols to prevent transmission and prevent people from disease. Awareness campaigns were organized to spread awareness to people which explained the proper usage and disposal of PPE, face mask, gloves, proper hand washing, and body hygiene. Pakistan surveillance unit was established by collaborating with provinces. The media played a pivotal role in explaining protection strategies. Moreover, the lockdown was imposed by the Government of Pakistan to ensure safety for all. Later, due to the financial status of people smart lockdown was imposed by which provinces decided to close markets on particular days. No schools, colleges, or universities were allowed to open [15].

8. Treatment

SARS-CoV proteins serve as a target site for drugs or vaccines [28]. (Stadler et al., 2003). During viral replication, the enzymes used are appealing candidates for the production of antiviral molecules. The glycoproteins can be exploited in vaccines such as (S), (M) glycoprotein on the inner side of the viral envelope and N protein forms helical nucleocapsid [1,2,3]. By that time, β-interferon, as it is recorded to inhibit replication of SARS in the laboratory, was considered to treat patients. Although the rapid mutation in the viral genome has reduced treatment options for COVID-19 due to the phenomenon of antigenic drift such that COVID-19 is vigorously achieving new mutations that possibly facilitate the virus to mask from antiviral drugs that were supposed to be effective in treating it [28].

9. Prevention

SARS is a contagious disease and can be prevented by avoiding person-to-person contact such as isolating patients and by quarantining them in hospitals. By maintaining appropriate human distance, and community control measures [27]. Similar preventive measures were followed in the case of COVID-19 such as segregation of confirmed or suspected cases. Restrain from public places and delay unnecessary travel to places. Cough hygiene should be maintained by coughing in the sleeve/ tissue rather than the hands. Wearing masks, and gloves in crowded areas and washing hands for 20 seconds after coming back each time [7].

5. Conclusions

COVID-19 seems similar to SARS, but it varies in the receptor-binding domain. As people followed SOPs the number of cases was under control but an exponential rise in cases was observed after lockdown due to violations in SOPs. For diagnosis, RT PCR is a widely used test because it is capable of detecting asymptomatic and symptomatic patients. Upon comparison with SARS, the impact showed both pandemics imposed psychological and economic impacts on the world's economy. Challenges that were faced by the world considering both pandemics were not different, showing the world is not ready to cope with pandemics. Pakistan is an under-developing country that coped with the COVID-19 pandemic with limited possible resources and tried to control possible reasons for the pandemic, yet we are not prepared and fully equipped to deal with future pandemics.

Acknowledgments: The authors are grateful to senior professors for their valuable feedback.

Conflicts of Interest: All authors declare no conflict of interest regarding this article.

López-García, P.; & Moreira, D. (2012). Viruses in biology. Evolution: Education and Outreach, 5(3), 389-398

References

1. WHO (2007). https://www.who.int/csr/resources/publications/who_cds_epr_2007_6c.pdf.
2. CDC (2019). https://www.cdc.gov/coronavirus/2019-ncov/index.html
3. WHO (2016). https://www.who.int/csr/disease/coronavirus_infections/october-2016/en/
4. Weiss, S. R.; & Navas-Martin, S. Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. MMBR 2005, 69(4), 635-664.
5. Nguyen, T. M.; Zhang, Y.; & Pandolfi, P. A potential treatment for 2019-nCov (SARS-CoV-2) and other RNA viruses. VIR 2020.
6. Wu, J.; Liu, X.; Zhou, D.; Qiu, G.; Dai, M., Yang.; Q., & Wu, P. Identification of RT-PCR-negative asymptomatic COVID-19 patients via serological testing. Public health Fornt 2020, (8), 267.
7. Singhal. T. a review of coronavirus disease-2019 (covid-19). Indian J. Pediatr 2020, (13), 1-6.
8. Shah, S. K.; Miller, F. G.; Darton, T. C.; Duenas, D.; Emerson, C.; Lynch, H. F.; ... & Rid, A. Ethics of controlled human infection to address COVID-19. Science 2020, 368(6493), 832-834.
9. Zu, Z. Y.; Jiang, D.; Xu, P. P.; Chen, W.; Ni, Q. Q.; Lu, G. M.; & Zhang, L. J. Coronavirus disease 2019 (COVID-19) China. Radio 2020, 296(2), E15-E25.
10. UNDP (2020). https://www.undp.org/content/undp/en/home/coronavirus.html
11. Augustine, R.; Hasan, A.; Das, S.; Ahmed, R.; Mori, Y.; Notomi, T.; & Thakor, A. S. Loop-mediated isothermal amplification (LAMP): a rapid, sensitive, specific, and cost-effective point-of-care test for coronaviruses in the context of COVID-19 pandemic. Biol. Rev. 2020, 9(8), 182.
12. Wang, W.; Xu, Y.; Gao, R.; Lu, R.; Han, K.; Wu, G.; & Tan, W. Detection of SARS-CoV-2 in different types of clinical specimens. JAMA 2020, 323(18), 1843-1844.

13. Zhang, T.; Wu, Q.; & Zhang, Z. Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. Curr. Bio 2020, 30(7), 1346-1351.
14. Ceccarelli, M.; Berretta, M.; Rullo, E. V.; Nunnari, G.; & Cacopardo, B. Editorial–Differences and similarities between Severe Acute Respiratory Syndrome (SARS)-CoronaVirus (CoV) and SARS-CoV-2. Would a rose by another name smell as sweet. Eur Rev Med Pharmacol Sci 2020, 24(5), 2781
15. Saqlain, M.; Munir, M.; Rehman, S. U.; Gulzar, A.; Naz, S.; Ahmed, Z.; & Mashhood, M. Knowledge, attitude, practice and perceived barriers among healthcare workers regarding COVID-19: a cross-sectional survey from Pakistan. JHI 2020, 105(3), 419-423.
16. Thiel, S. L.; Weber, M. C.; Risch, L.; Wohlwend, N.; Lung, T.; Hillmann, D.; ... & Paprotny, M. Flattening the curve in 52 days: characterisation of the COVID-19 pandemic in the Principality of Liechtenstein–an observational study. Swiss Med. Wkly 2020, (4142), 150
17. Baxi P.; & Saxena S.K. emergence and reemergence of severe acute respiratory syndrome (sars) coronaviruses [in coronavirus disease 2019 (covid-19)]. Springer. Sci. Rev 2020, (55), 151-163.
18. Callaway E. Fast-spreading COVID variant can elude immune responses. Nature 2021, 589(7843), 500-501
19. Mass E. Covid-19: UK approves Oxford vaccine as cases of new variant surge. BMJ 2020, 371:m (4968), 1-2
20. Arora, P.; Pöhlmann, S., & Hoffmann, M., (2021). Mutation D614G increases SARS-CoV-2 transmission. Signal Transduction and Targeted Therapy 2021, 6(1), 1-2.
21. Emameh, R. Z.; Eftekhari, M.; Nosrati, H.; Heshmatnia, J.; & Falak, R. Identification and characterization of a silent mutation in RNA binding domain of N protein coding gene from SARS-CoV-2. BMC Res. Notes 2021, 14(1), 1-6..
22. Touzard-Romo, F.; Chantal Tapé, B. A.; & Lonks, J. R. Co-infection with SARS-CoV-2 and human metapneumovirus. R. I. Med. J. 2020, 103 (3), 48-49.
23. Costa, E.; Rodríguez-Domínguez, M.; Clari, M. Á.; Giménez, E.; Galán, J. C.; & Navarro, D. Comparison of the performance of 2 commercial multiplex PCR platforms for detection of respiratory viruses in upper and lower tract respiratory specimens. Diagn. Microbiol. Infec. Dis 2015, 82(1), 40-43.
24. Vaidyanathan G. Vaccine makers in Asia rush to test jabs against fast-spreading COVID variant. Nature 2021, (63), 99-11
25. Mahase E. Covid-19: What have we learnt about the new variant in the UK? BMJ. 2020, 371(44), 1-2
26. Peeri, N. C.; Shrestha, N.; Rahman, M. S.; Zaki, R.; Tan, Z.; Bibi, S.; ... & Haque, U. The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned? Int. J. Epidemiol 2020, 49(3), 717-726.
27. Wilder-Smith, A.; Chiew, C. J.; & Lee, V. J. Can we contain the COVID-19 outbreak with the same measures as for SARS? Lancet Infect. Dis 2020, 20(5), e102-e107.
28. Stadler, K.; Masignani, V.; Eickmann, M.; Becker, S.; Abrignani, S.; Klenk, H. D.; & Rappuoli, R. SARS—beginning to understand a new virus. Nat. Rev. Microboil 2003, 1(3), 209-218.
29. BBC (2020). https://www.bbc.com/news/health-53515077
30. Corman, V. M.; Landt, O.; Kaiser, M.; Molenkamp, R.; Meijer, A.; Chu, D. K.; & Drosten, C. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro surveill 2020, 25(3), 2000045.
31. Torales, J.; O'Higgins, M.; Castaldelli-Maia, J. M.; & Ventriglio, A. The outbreak of COVID-19 coronavirus and its impact on global mental health. Int. J. Psychiatry 2020, 66(4), 317-320.
32. Wu, J.; Liu, X.; Zhou, D.; Qiu, G.; Dai, M.; Yang, Q.; & Wu, P. Identification of RT-PCR-negative asymptomatic COVID-19 patients via serological testing. Public Health Fornt. 2020, (8), 267.
33. Pan, Y.;Zhang, D.; Yang, P.; Poon, L. L.; & Wang, Q. Viral load of SARS-CoV-2 in clinical samples. The Lancet Infet. Dis. 2020, 20(4), 411-412.
34. Scohy, A.; Anantharajah, A.; Bodéus, M.; Kabamba-Mukadi, B.; Verroken, A.; & Rodriguez-Villalobos, H. Low performance of rapid antigen detection test as frontline testing for COVID-19 diagnosis. J. Clin. Virol 2020, (129), 104455..
35. Cascella, M.; Rajnik, M.; Aleem, A.; Dulebohn, S.; & Di Napoli, R. Features, evaluation, and treatment of coronavirus (COVID-19). StatPearls 2021, (565), 84.
36. Chan, C. M.; Tse, H.; Wong, S. S. Y.; Woo, P. C. Y.; Lau, S. K. P.; Chen, L.; ... & Yuen, K. Y.Examination of seroprevalence of coronavirus HKU1 infection with S protein-based ELISA and neutralization assay against viral spike pseudotyped virus J. Clin. Virol 2009, 45(1), 5
37. Cui, J.; Li, F.; & Shi, Z. L. Origin and evolution of pathogenic coronaviruses. Nat. Rev. Microbiol 2019, 17(3): 181-192.
38. Liu, Y.; Eggo, R. M.; & Kucharski, A. J. Secondary attack rate and superspreading events for SARS-CoV-2. Lancet 2020, 395(10227), e47
39. Wölfel, R.; Corman, V. M.; Guggemos, W.; Seilmaier, M.; Zange, S.; Müller, M. A.; ... & Wendtner, C. Virological assessment of hospitalized patients with COVID-2019. Nature 2020, 581(7809), 465-469.
40. Guo, L.; Ren, L.; Yang, S.; Xiao, M.; Chang, D.; Yang, F.; ... & Wang, J. Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). Clin. Infect. Dis 2020, 71(15), 778-785.
41. Prendergast, C.; & Papenburg, J. Rapid antigen-based testing for respiratory syncytial virus: moving diagnostics from bench to bedside?. Future Microbiol 2013, 8(4), 435-444.
42. Sizun, J.; Arbour, N.; & Talbot, P. J. Comparson of immunofluorescence with monoclonal antibodies and RT-PCR for the detection of human coronaviruses 229E and OC43 in cell culture. J. Virol. Methods 1998, 72(2), 145-152.