

The COVID-19 pandemic: A Comprehensive Review of the Genomic variations, Epidemiological features, Diagnosis, Treatment and Intervention schemes in South Asia

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Abstract

The ongoing respiratory disease pandemic COVID-19 caused by a newly emerging highly infectious virus Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is aggravating the world's health, economy and regular life. This unprecedented respiratory outbreak has already infected more than 43 million individuals and taken more than 1.1 million lives. The habitation of over 21% of the world's population- the SAARC region is also facing the severity of COVID-19 and comprises more than 20% of the total infected cases. Demographic analysis showed that the majority of the infected individuals of South Asia are aged between 21-30 years and males are more vulnerable than females. Similar genomic variations were observed in the countries such as variations in the ORF1ab, ORF1a, ORF3a and S genes. As no effective treatment strategy hasn't developed yet, only timely testing and tracing can mitigate the loss from the disease and hence distinct molecular and serological assays are being used for screening in different countries. Since no unanimously recognized treatment option is available, existing medicines and treatments are being taken into consideration to treat the patients. Currently, a vaccine can be the ideal solution for this rapidly evolving disease and hence two COVID-19 vaccines, BANCOVID from Bangladesh and COVAX from India are undergoing clinical trials. As the 'Second Wave of COVID-19' is approaching, it has become a matter of urgency to appraise the existing policies and strategies in order to ascertain and implement effective schemes that can mitigate the ramifications of the disease.

Keywords: COVID-19 in South Asia; Genomic variations; Epidemiological Characteristics; Diagnostic system; Treatments contrivances; Interventions.

Background

The emergence of SARS-CoV-2 has been declared as a pandemic, which is an unprecedented outbreak of pneumonia that originated in China [1, 2]. Bats were considered to be the host of this virus and 96% gene sequence homology was found between SARS-CoV-2 and a bat SARS-like-CoV whereas it only shares 79.6% similarity with SARS-CoV [3, 4]. Wild animals are regarded as the most potent natural reservoir of the coronavirus family. Two previous coronavirus epidemics- SARS and MERS were also transmitted by wild animals; from palm civets and dromedary camels, respectively [3]. On 31 December 2019, a cluster of pneumonia of unrevealed etiology was identified in Wuhan city of Hubei province in China [4]. Later, it was identified by the Chinese Center for Disease Control and Prevention (CDC) as a novel coronavirus [5]. The International Committee on Taxonomy of Viruses (ICTV) named it as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) because of its similarity with SARS-CoV and the World Health Organization (WHO) termed the disease as ‘COVID-19’ [6, 7]. The virus belongs to the family of coronaviridae and is an enveloped, single-stranded, positive-sense RNA virus [8]. It is the seventh of the already identified human coronaviruses including mild respiratory syndrome disease-causing coronaviruses HKU1, NL63, 229E, and OC43. SARS-CoV and MERS-CoV are the two other strains that have previously endangered human lives by causing two epidemics in China and the Middle East, respectively [8, 9]. Phylogenetic analysis showed that SARS-CoV-2 was intimately connected to two bat-derived SARS-like coronaviruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21, but were relatively less similar to SARS-CoV. COVID-19 is affecting 216 countries and territories around the world regardless of age, gender or race. As of 26 October 2020, around 43,837,698 confirmed cases and 1,166,142 deaths have been reported with a fatality rate of 2.66%. At the same time, 32,188,661 patients have recovered from COVID-19. Around 10,482,895 patients were taking treatment and of them, only 79,053 (less than 1%) were critical till 26 October 2020 [10]. The USA is the most affected country to date with more than 8.9 million confirmed COVID-19 cases constituting more than 20% of the total infected patients and had 231,486 deaths up to 26 October 2020. On 30 January 2020, WHO has announced the disease as a public health emergency of international concern [11]. The South Asian countries have also been devastated by this highly infectious disease with 8,856,017 infected cases and 133,969 deaths up to 26 October 2020. South Asia consists of Afghanistan, Bangladesh, Bhutan, India, Iran, Maldives, Nepal, Pakistan, and Sri Lanka. India is facing its severe ramifications being the second-most-infected country with more than 7.9 million infected

patients and 119,014 COVID-19 related deaths [12]. This review aims to outline the genome variations, epidemiological characteristics, diagnostic approaches, and treatment and prevention tactics of COVID-19 in the South Asian countries.

Main text

Genomic variations

Analysis based on accessible documented data of genetic variation of this virus suggests that like all RNA viruses, SARS-CoV-2 contains indistinguishable mutation frequency and potential mutant distributions. Among the identified variants, fewer variants can cause long-standing infections. As RNA viruses have high mutation rates, this virus is likely to develop mutations to invade the host defense mechanism. Among the South Asian countries, India has sequenced the maximum number of the SARS-CoV-2 genome (570) among South Asian countries, followed by Bangladesh (231), Pakistan (11), Sri Lanka (4) and Nepal (1) as of 15 October 2020 [13]. Afghanistan, Bhutan and Maldives have not reported any genome sequencing yet.

An investigation on genomes of 184 SARS-CoV-2 virus strains from Bangladesh showed that 634 mutations were located in the entire genome resulting in 274 substitutions (non-synonymous) of amino acid in 22 unrelated proteins. Amino acid substitutions were prevalent at 48 different positions of the papain-like protease (nsp3) and no mutation was detected in nsp7, nsp9, nsp10, and nsp11. Moreover, nine unique mutations were observed in comparison with the global strains in the spike proteins [14]. Another analysis of 207 genomes from different areas of the country showed that 2602 mutations were observed of which 1602 were missense mutations, 612 were synonymous, 36 were insertions and deletions, and 352 were various types. Phylogenetic analysis implicated that the virus originated from Europe and GR clade was most prevalent in this region. A significant finding in these SARS-CoV-2 genomes was 7 unique alterations of amino acid from various proteins [15].

Analysis of 566 complete or almost complete Indian SARS-CoV-2 genomes found 3384 unique mutation points of which 933, 2449 and 2 were substitutions, deletions and insertions, respectively. Besides, 64 single nucleotide polymorphisms (SNP) were found. Of them, 57 SNPs were present in six coding regions and 7 SNPs were present in 5'-UTR and 3'-UTR [16]. One comparative study found that the Indian SARS-CoV-2 strain showed a distinctive

mutation in the spike glycoprotein (A930V (24351C>T)) which was absent in further strains [17]. Additionally, another analysis showed the origin of Indian SARS-CoV-2 strains from Europe and South-East Asia followed by local transmission. All the analyzed genomes were divided into four major clades 19A, 19B, 20A and 20B along with the new Nextstrain clade nomenclature and a rare clade 19B was identified which has a low occurrence in India [18].

The SARS-CoV-2 genome strain from Nepalese isolates revealed that it was more than 99.99% identical to two previously sequenced SARS-CoV-2 genomes (MN988668 and NC_045512) from Wuhan, China with seven additional sequences. Besides, five mutations were also identified based on the reference sequence EPI_ISL_405839 [19].

Full and partial genome sequencing of eight Pakistani isolates revealed that SARS-CoV-2 strains circulating in Pakistan were GH, S, L and I clade strains which are clustered with strains from Saudi Arabia, India, USA, Australia and China. Of the eight strains, five were GH clade with mutations in S glycoprotein D614G, Ns3 gene Q57H, and RNA dependent RNA polymerase P4715L. Among others, three were L clade, two were S clade, and one strain was I clade. Additionally, Orf1ab variant L3606F was observed in one GH and one L strain which indicates further evolutionary transitions [20]. In another analysis of 4 whole genome sequences, 31 variants were identified including two causing alterations in ORF1ab gene, ORF1a and N genes with functional replication and translation. Mutations in N & ORF1a proteins showed alterations at the amino acid level [21].

Genome analysis of four SARS-CoV-2 isolates from Sri Lanka showed that the strains were clustered with strains from mostly Europe. SNP analysis revealed that the genome sequence of the first isolates showed variation in 6 nucleotide (nt) positions compared to the reference genome. The other three sequences have differed in 6 nt positions, 5 nt positions, and 4 nt positions, respectively. Amino acid variants were found in the ORF1ab protein, S protein, ORF3a gene, M gene, and N protein of four Sri Lankan whole-genome strains, while the rest of the amino acids in the genes were unaltered [22].

Epidemiological Characteristics

Among the affected South Asian countries, India continues to be the most infected country. Almost 90% of the infected individuals in the South Asian region are from India, followed by Bangladesh, Pakistan and Afghanistan. In terms of COVID-19 deaths, Pakistan was in 2nd

position after India and followed by Bangladesh. Afghanistan had the highest mortality rate (3.70%), followed by Pakistan (2.05%) and India (1.50%) as of 26 October (Table 1). Bhutan had the lowest number of infected patients; 342 individuals were infected while no one died. Around the same time, 7,923,759 (90%) patients of the South Asian nations have been cured of the disease [12].

Due to the rapid spread and infection of a large population, it is difficult to maintain the complete databases of every individual. Hence, there is a lack of information in the demographic data. Existing demographic data analysis shows that there are variations in the age distribution of COVID-19 infected cases in South Asian countries. Most of the patients, infected with SARS-CoV-2 are young adults aged between 21-30 years except for Pakistan where people aged between 31-40 years are the most vulnerable and in Sri Lanka where the majority of the patients are aged between 41-50 years (Figure 1) [23–29].

Though there is no scientific evidence for young people being affected at a higher rate, it is easily predictable that they are more likely to avert the interventions such as the use of face masks in public spaces, social distancing and quarantining. Regarding gender distribution, males are more susceptible to SARS-CoV-2 than females as females are genetically and immunologically more resistant to SARS-CoV-2 infection [30] (Figure 2) [23–29]. It has been found that SARS-CoV-2 utilizes angiotensin-converting enzymes 2 (ACE-2) both as receptors and the route of infection. Analysis of the expression level and pattern of human ACE-2 using a single-cell RNA-sequencing (RNA-seq) has revealed that Asian males have elevated expression of ACE 2 receptor than females and female ovaries have much lower levels of ACE-2 than male testes [31, 32]. Another reason is that the X chromosome possesses a significantly elevated amount of immune-related genes and regulatory elements. These genes and elements are directly involved in the modulation of the innate, as well as adaptive immune responses and hence, women have much immunologically stronger immunity against infectious diseases [33]. Several other social and cultural factors are deemed to be the reasons behind this. For example, smoking, tobacco use and alcohol consumption are more prevalent in men [34, 35]. Moreover, in the case of awareness and hygiene practices of the COVID-19, females act more responsibly and are reported to take necessary precautionary measures than men [36].

Diagnostics Approaches

Since the discovery of this ongoing COVID-19 pandemic, every country is trying to overcome it by following several courses of action. Among these, diagnostic measures have gotten prime concern as no reliable vaccines are available as yet.

Different methods are being used to find the presence of this fatal virus in people which are mainly categorized into molecular tests such as reverse transcriptase Real-Time Polymerase Chain Reaction (rRT-PCR) and serological tests such as rapid diagnostic test, Enzyme-Linked Immunosorbent Assay (ELISA), neutralization assay and chemiluminescent immunoassay [37]. The rRT-PCR of nasopharyngeal swabs has been regarded as the ‘gold standard’ testing method and various rRT-PCR based protocols have been uploaded to WHO technical guidance for laboratory testing of COVID-19 [38]. Though the detection of SARS-CoV-2 RNA is highly specific and less sensitive in some cases which can take a relatively long time and may produce false-negative results [39], still rRT-PCR assay is currently the most prevalent and accurate method to detect all types of coronaviruses including SARS-CoV-2 [40–42].

Among the South Asian countries, India has the highest number of testing facilities with 2134 SARS-CoV-2 detection labs including 1115 rRT PCR labs, 851 TrueNat test labs and 128 Cartridge-Based Nucleic Acid Amplification test (CBNAAT) labs [43]. In Afghanistan, there are only 14 COVID-19 designated labs, while there are 109 in Bangladesh, 6 in Bhutan, 9 in the Maldives, 76 in Nepal, 146 in Pakistan and 17 in Sri Lanka [44–51]. Table 2 lists different diagnostic methods approved and used in the South Asian countries. In terms of COVID-19 testing, most of the South Asian countries are far from reaching the target number required to test every confirmed case. Afghanistan is conducting only 2814 tests per million population, the lowest in South Asia, followed by Bangladesh (11567/1000000), Sri Lanka (13051/1000000) and Pakistan (15416/1000000) as of 26 September 2020 (Fig. 3) [68].

Treatment Strategies

In Afghanistan, a controversial drug produced by a traditional healer has become the talk of the town, which was reported to be made up of addictive substances such as morphine and codeine. Although the government and health experts have warned against this unproven drug, general people have burst with excitement to take the medication [69]. Plasma therapy has also been found to be effective in the treatment of COVID-19 patients in Afghanistan which is currently the most promising treatment for the disease [70]. The country is one of the worst

sufferers of COVID-19 as the treatment facilities are below standard and still cannot meet the requirement.

According to the "National Guidelines on Clinical Management of Coronavirus Disease-2019 Bangladesh," Chloroquine, Hydroxychloroquine and Azithromycin were prescribed to be used in the treatment of COVID-19 patients [71]. A team of doctors from Bangladesh Medical College Hospital found that a combination of antiprotozoal medicine Ivermectin in a single dose with antibiotic Doxycycline can be effective to treat COVID-19 patients though more clinical trials are needed to be done to evaluate its efficacy [72]. A Bangladeshi pharmaceutical company, Beximco had launched the world's first generic Remdesivir and currently exporting Remdesivir IV injection "Bemsivir" [73]. Favipiravir – an antiviral drug that showed efficiency against influenza A and B has also been found promising to treat SARS-CoV-2 infection in patients [74]. CP therapy has been found effective in Bangladesh, especially in critical cases when plasma therapy is the only option [75].

Among the South Asian countries, Bhutan has got special praise from the WHO for conducting timely diagnosis and treatment to combat the deadly COVID-19 pandemic. Bhutan has provided free testing facilities which resulted in timely diagnosis and treatment. As per the National Clinical Management Guideline, patients having mild symptoms with risk factors to pneumonia and other symptoms are treated with Hydroxychloroquine with or without Lopinavir/Ritonavir [76]. Additional therapies such as low molecular weight heparin, steroids and antibacterial are included for case by case usage [77].

India, one of the most affected countries, is facing a critical phase and looking for effective treatment methods. Hydroxychloroquine is being recommended for mild cases whereas a combination of Hydroxychloroquine and Azithromycin for severe patients in India [78]. The central government has authorized two antiviral drugs - Remdesivir and Favipiravir, but a debate has always been remaining among the medical experts about the competency in treating COVID-19 patients [79]. Itolizumab, an anti-CD6 humanized monoclonal IgG1 antibody got approval for the treatment of moderate and severe patients [80]. Another hopeful treatment that has emerged is convalescent plasma (CP), or immune plasma therapy. The Indian Council of Medical Research (ICMR) had launched clinical trials to evaluate its safety and efficacy. This treatment may serve as a short-term solution to suppress mortality rates [81].

The Maldives has published COVID-19 Quick Reference Guidelines to provide information on clinical and home management. According to this, empirical antibiotics have been

recommended based on clinical diagnosis along with Oseltamivir for mild and moderate patients [82]. As a consequence, the government has transported antiviral drugs such as lopinavir and ritonavir from India to ensure medications [83].

Most of the patients of Nepal are being treated with regular medications while Hydroxychloroquine, the controversial anti-malarial drug, was also being used in some cases. Health experts, however, emphasized that Hydroxychloroquine was not that efficient in treating COVID-19 and patients may face several side-effects including loss of vision and heart ailments [84]. The Department of Drug Administration has signed a consignment deal with Indian company Mylan to import Remdesivir, an antiviral injection used to treat COVID-19 patients with critical symptoms [85]. Nepal's health authorities have declared that their first plasma therapy treatment has become successful [86].

In Pakistan, Dexamethasone is being used to treat critical COVID-19 in patients. The WHO has addressed it as a "lifesaving breakthrough" and stated that it had reduced mortality by about one-third for patients on ventilators, and by about one-fifth for patients requiring oxygen [87]. Health experts in Pakistan prescribed Hydroxychloroquine tablets which they found efficient and secured for the patient, ignoring the warnings of the WHO [88]. The Specialized Healthcare and Medical Education Department approved Actemra – interleukin-6 inhibitor with the generic name of Tocilizumab – an immune-suppressant, for the critical SARS-CoV-2 affected patients on prescription only. However, the regional government is yet to formally approve the drug, recommended by the WHO [89]. Besides, Remdesivir is also being used for the treatment of COVID-19 patients [90]. Convalescent plasma which contains antibodies generated by the recovered patients is gaining popularity across Pakistan [91].

Sri Lankan Provisional Clinical Practice Guidelines on COVID-19 suspected and confirmed patients recommended antipyretics for mild patients [92]. Sri Lanka has been a country that promotes ayurvedic and herbal medicine to fight against COVID-19. Herbal therapy has been introduced under government supervision. An immunizing drink named "Suwadharani Immunizing Drink" and also a powder named "Sadanga Panaya" have been developed for the individuals infected with the SARS-CoV-2 virus [93, 94].

Intervention schemes

It is too tough to take essential steps for combating COVID-19 in war-torn Afghanistan. But still, the Afghan government is trying utmost to take containment measures after the first case

was identified. The measures include decreasing activity at borders entry, arranging quarantine facilities for infected people, and establishing strict restrictions on movement [95, 96]. They declared a countrywide lockdown on 28 March 2020. The authorities proposed a budget for COVID-19-related expenditure such as 6.2 billion Afghani (Af) for health packages, 23.6 billion Af for social packages including bread distribution program, and 1.7 billion Af for wheat purchase program [96]. The government received 300 million USD grants from the World Bank and another 400 million USD under the Incentive Program Development Policy Grant of the International Development Association (IDA) and Afghanistan Reconstruction Trust Fund to shore up the economy, provide aid to civil services and minimize the ramifications of COVID-19 in Afghanistan [97].

In Bangladesh, almost after two months of the Wuhan outbreak, on 8 March 2020, the first three cases were detected. To stop the spreading of pandemic throughout the country, the government declared general holidays and ordered a lockdown throughout the country on 23 March 2020 [98]. Finally, on 31 May 2020, the countrywide lockdown was withdrawn after extending several times, but the government split the country into three zones according to disease prevalence [99]. The government has made a rule for wearing a face mask and took several steps for public awareness and also opened a hotline and made sure about the quarantine of foreign returnees[100]. In addition to these, they declared 19 stimulus packages worth over 1.03 trillion USD to support various sectors for combating the COVID-19 [101]. Bangladesh is also competing in the race of vaccine development where one of the indigenous pharmaceutical companies named Globe Biotech has become successful in its two-phase animal trials in the pre-clinical stage. If they get ethical approval from the Bangladesh Medical Research Council (BMRC), then they will conduct human trials to examine whether the dose is safe and effective for humans [102].

The first COVID-19 case was identified on 6 March 2020 in Bhutan and the government immediately closed its border and educational institutes for 2 weeks and extended this closure several times [103]. They made it compulsory for foreign returnees to be quarantined [103]. The government built two mobile apps named “Stay Home App” and “Druk Trace App” for helping and providing accurate information about COVID-19 and for tracing people who come in direct contact with COVID-19 affected people [104, 105].

India declared ‘Janata Curfew’ on 22 March 2020, after confirming the first case and countrywide restriction on movement on 25 March 2020 [106]. India has launched a mobile

app called 'Aarogya Setu' for raising awareness of the COVID-19 and a WhatsApp chatbot called 'My Gov Corona Helpdesk' for ensuring accurate information and to stop rumors [107]. The government took an initiative to set up 2 million retail shops called 'Suraksha Stores' to ensure everyday essentials to citizens by maintaining safety measures throughout India [108]. To prevent the massive SARS-CoV-2 infection, the Indian government suspended all visas and closed all educational institutes. The government has declared an incentive package of USD 280 Billion to decrease economic loss and keep a balance between health practices and the economy [109]. India-based companies named Zydus Cadila and Bharat Biotech, in partnership with ICMR, are leading the spurt of COVID-19 vaccine development in the country. Bharat Biotech's Covaxin has got approval to conduct the Phase III trials whereas, Zydus Cadila's COVID vaccine is undergoing the phase II trials after obtaining promising and positive results [110].

The Maldives detected its first case on 7 March 2020, and the government imposed a lockdown on 16 April 2020 [111, 112]. In addition to this, they have turned an island into a quarantine facility called the world's first coronavirus resort [113]. The country has been divided into six zones so that each zone can be graded individually for engagement, preparedness and response. Moreover, the government developed a training plan for increasing professional skills among the health workers and introduced risk allowance for the civil servants who are working in the frontline in COVID-19 response [114].

Nepal first confirmed its SARS-CoV-2 positive case on 23 January 2020 [115]. The Nepal government has taken several strategies to prevent transmission of the virus such as they suspended all international flights and formed a multi-agency coordination committee to stop the spread of COVID-19 [116]. They increased the number and facilities of self and institutional isolation and quarantine wards in hospitals of all the provinces [117]. Nepal also closed all educational institutions and declared a countrywide lockdown on 24 March 2020. All of their existing public health and community-based networks and other line ministries and development partner networks are coordinately working for ensuring public awareness and providing accurate information [118]. Nepal is also volunteering in the third-phase clinical trials of three COVID-19 vaccines conducted by three companies from China, Russia, and the UK. If they got approval from the Nepal Health Research Council, they will begin the trials soon [119].

The government of Pakistan has taken many effective steps after confirming the positive case. They formed a National Coordination Committee to monitor COVID-19 situation regularly and took necessary steps such as closing all educational institutions along with the border and banning all public gatherings till 5 April 2020 [120]. Pakistan accepted 'Smart lockdown strategies' instead of blanket lockdown by recognizing 500 hotspots and imposed a lockdown on those areas [121]. The government has announced a stimulus package of 7.79 billion USD to assist businesses, emergency response, and to cover relief to residents [122]. Pakistan will also get the benefit of the vaccine trial from China. The phase 3 trial of the Chinese vaccine for COVID-19 will be held in Karachi's Indus Hospital [123].

A Chinese tourist was first detected as COVID-19 positive on 27 January 2020 in Sri Lanka and as a result, the government banned all international transports across the country. They banned all foreign travels and shut down all educational institutes [124]. To restrain and control the pandemic situation the government took some effective measures such as developing an active response mechanism team who are communicating directly with the root level people for growing awareness and for stopping the rumors [125].

Discussion

Genome analysis of SARS-CoV-2 suggests that this virus is rapidly evolving and numbers of distinct variants exist in most of the strains [126]. Simultaneously it is noticeable that most of the strains are still causing mutation and framing new emerging variations of those viral strains though there are common frequencies of mutation distributed in neighboring countries. Analysis of the sequenced genomes from the South Asian countries found that most of the strains adopted several mutations, mostly as insertions and/or deletions. Variations in the ORF1ab, ORF1a, ORF3a and S gene are most prevalent. Additionally, SNPs are significantly usual. Alterations in the levels of the amino acid markedly vary in the genome of SARS-CoV-2 isolates of these countries.

Though most of the infected patients of COVID-19 are younger adults, mortality rate is higher among the geriatric population [127]. Similarly, it has been observed that males are more vulnerable to SARS-CoV-2 than females. So, males and young people who have to expose more to the outside due to work and other duties, need to be more aware of the hygiene practices. The use of face masks during traveling, maintaining social distance and continuous

use of disinfectants to stay safe from the virus are some common health practices for COVID-19.

Every nation of South Asia is trying to expand its screening facilities by equipping more hospitals with rRT-PCR and other amenities. This early identification of SARS-CoV-2 infection may bring the COVID-19 pandemic under control by inhibiting the community transference. Although many months have passed, still there is no benchmark testing method like rRT-PCR in diagnosing COVID-19 infected patients. However, other COVID-19 confirmation methods like the Feluda test, TrueNat, CBNAAT, rapid antigen and antibody tests are also gaining popularity to soar up the number and availability of diagnostic tests. Apart from these, to reduce the cost of tests, Pakistan has invented their own kits for RT-PCR named N-CovKit. Over time, the massive spread and spontaneous mutation of SARS-CoV-2 have led the way of the development of new diagnosis methods having greater efficacy with quick result time such as Rapid Dot Blot in Bangladesh and Feluda paper strip test in India. Only proper testing, tracing and treatment can minimize the loss due to this virus but still, there is a lack of testing kits and diagnostic facilities in many South Asian Countries. Already vaccines of SARS-CoV-2 are under investigation in 198 countries of the world, and of them, 42 have been going under clinical trials [21]. Bangladesh (BANCOVID vaccine) and India (COVAX vaccine) are two South Asian countries competing and their vaccines are still undergoing clinical trials where they are working with various national and international collaborators to develop a promising vaccine soon. At this moment, an effective vaccine can be the best hope for all the countries.

Though no effective treatment has been discovered yet, all the South Asian countries are experimenting with the existing medicines and treatment strategies to strive against the pandemic. Specifically designed randomized clinical trials are urgently needed to determine the most appropriate evidence-based treatment. To stop the spread of COVID-19 and prevent the burden of any future outbreak, an effective modality of treatment is essential.

Almost every country has taken necessary actions to safeguard its people, but particularly Pakistan applied an innovative approach called ‘Smart Lockdown’ which helped stabilize their economy. India and Bhutan have developed several Apps for public awareness, while Bangladesh and Maldives have taken varied lockdown strategies according to disease prevalence to handle the pandemic situation properly. As all of the countries have been infected

by either transborder movement or returnees from overseas, they need to be more careful about their borders and quarantine facilities and implement effective social containment strategies with a balance between economy and health practices.

Conclusion

The COVID-19 pandemic is a matter of global concern that has hampered every sector, from health to economy to society. No gender, nation and ethnic groups could evade the massive and rapid spreading of this highly infectious virus. Due to rapid and unpredictable transmission, classical health contrivances and surveillance measures are the only means to combat this pandemic. International and regional co-operations among the South Asian countries are mandatory to strive against the pandemic. Policymakers, government officials and experts of various fields from these countries should come forward to work hand in hand to establish response operations. Local and regional co-operative organizations have to work with the authorities of the countries to promote knowledge and awareness of the COVID-19 among their populations.

Lists of Abbreviations

COVID-19: Coronavirus Disease 2019; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus; MERS-CoV: Middle East Respiratory Syndrome Coronavirus; WHO: World Health Organization; SNP: Single Nucleotide Polymorphism; ACE2: Angiotensin-Converting Enzyme 2; rRT-PCR: reverse transcriptase Real-Time Polymerase Chain Reaction; CBNAAT: Cartridge-Based Nucleic Acid Amplification Test; CT: Computed tomography; CDC: Centers for Disease Control and Prevention; DGDA: Directorate General of Drug Administration;

CRediT authorship contribution statement

AAN, JEE, RIM, MSI, FS, MShI- Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Visualization, Writing - original draft, Writing - review & editing.

SS, NM, MMK, AAM and TJ- Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing - original draft, Writing - review & editing.

Availability of data and material

All data and material are available upon request.

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Table1: Case distribution of COVID-19 in South Asian countries

Country	Total confirmed case	Total deaths	Mortality rate (%)	Total recovered
Afghanistan	40,833	1,514	3.70	34,129
Bangladesh	398,815	5,803	1.45	315,023
Bhutan	342	0	0	307
India	7,909,959	119,014	1.50	7,137,228
Maldives	11,505	37	0.32	10,524
Nepal	158,089	847	0.53	111,670
Pakistan	328,602	6,739	2.05	311,075
Sri Lanka	7,872	15	0.19	3,803

Table-2: COVID-19 diagnostic methods in South Asian countries.

Country name	Screening Method	Synopsis	References
Afghanistan	rRT-PCR	Sample: Oropharyngeal and nasopharyngeal swab.	[52]
Bangladesh	rRT-PCR	Sample: Nasopharyngeal swab, oropharyngeal swab, nasal swab, throat swab, sputum. Result: within 24 -48 hours.	[53]
	GeneXpert Covid-19 Test	Sample: Saliva. Result: within 45 mins.	[54]
	Rapid Dot Blot	Sample: Blood Result: within 15 mins. Reliability: 90% accuracy.	[55]
Bhutan	rRT-PCR	Sample: Upper respiratory sample (nasal and throat swab)	[56]
	Rapid Diagnostic Test	Sample: Blood Result: 30 mins Reliability: 90% sensitivity.	[57]
India	rRT- PCR	Sample: Nasal, oral and throat swab, sputum. Result: within 3-8 hours	[58]
	Feluda-CRISPR Test	Sample: Nasal or throat swab. Result: within 45 mins. Reliability: 96% sensitivity, 98% specificity	[59]
	Rapid Antibody Test	Sample: Blood. Result: within 20-30mins.	[58]
	Rapid Antigen Test	Sample: Nasal swab.	[58]

		Result: within 30 mins.	
	TrueNat	Sample: Nasal swab, oral swab. Result: within 60 mins.	[58]
	CBNAAT	Result: within 60 mins	[60]
	ELISA based antibody test	Sample: Blood serum or plasma. Reliability: 92.37% sensitivity, 97.9% specificity.	[61]
Maldives	rRT-PCR	Sample: Combined oropharyngeal and nasopharyngeal swab, sputum.	[52]
	GeneXpert Test	Sample: Swab sample. Result: Within 45 mins.	[62]
	Rapid Antigen Test (BinaxNOW COVID-19 Ag Card)	Reliability: 97% sensitivity, 98.5% specificity.	[63]
	Antibody Test	Reliability: 100% sensitivity, 99% specificity.	[64]
Nepal	rRT-PCR	Sample: Nasal swab or throat swab.	[52]
	Rapid Diagnostic test	Sample: Blood. Reliability: 50% sensitivity, 99.5% specificity.	[65]
Pakistan	rRT-PCR (N-CovKit)	Sample: Nasopharyngeal swab, oropharyngeal swab. Reliability: 90% accuracy.	[52]
	Rapid Digital Test	Sample: Blood Result: within minutes. Reliability: 95% accuracy.	[66]

Sri Lanka	rRT-PCR	Sample: Nasopharyngeal swab, oropharyngeal swab, sputum.	[67]
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Figures Title:

Figure-1: Age distribution of COVID-19 infected patients in South Asian countries¹.

Figure-2: Sex distribution of COVID-19 infected patients in South Asian countries².

Figure-3: COVID-19 testing per million populations in South Asian countries.

¹ [Demographics data was not available for Bhutan and unspecified cases are not indicated in Afghanistan (5%), Maldives (14.5%) and Pakistan-(6%)]

² [Demographics data was not available for Bhutan]

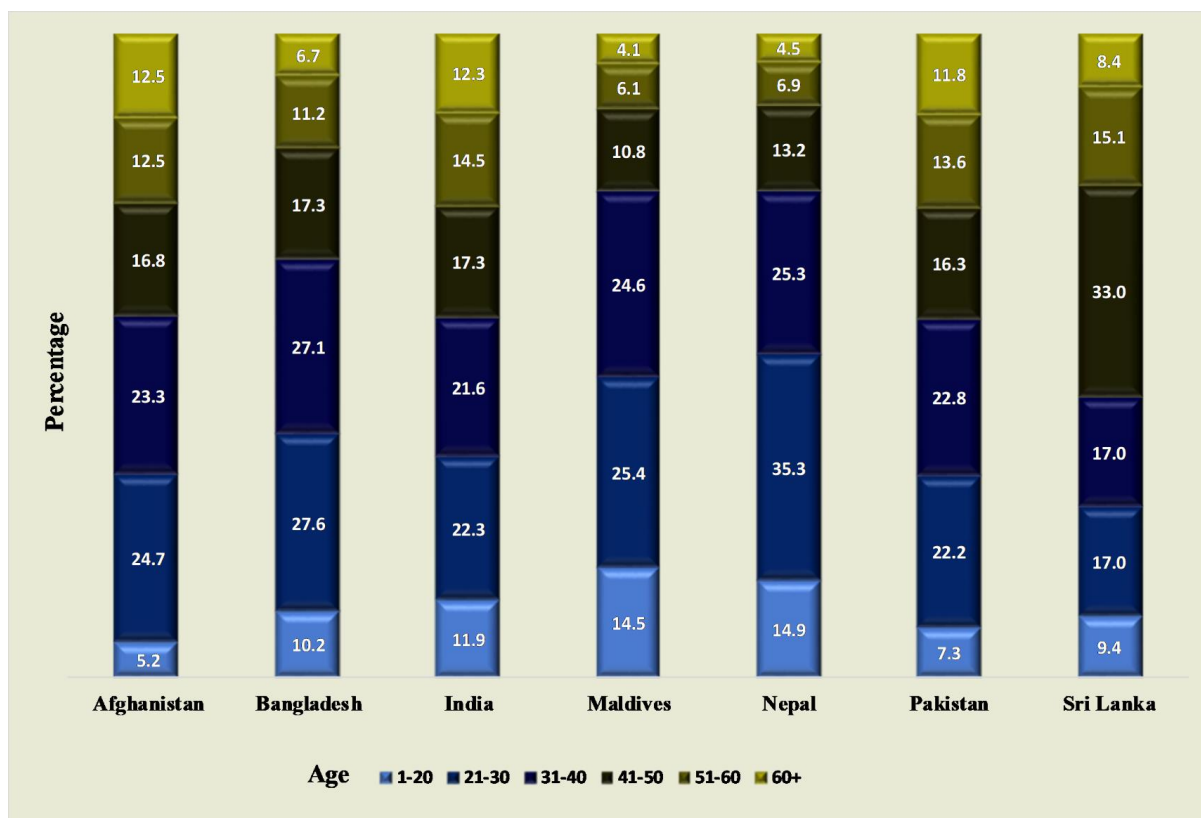


Figure 1

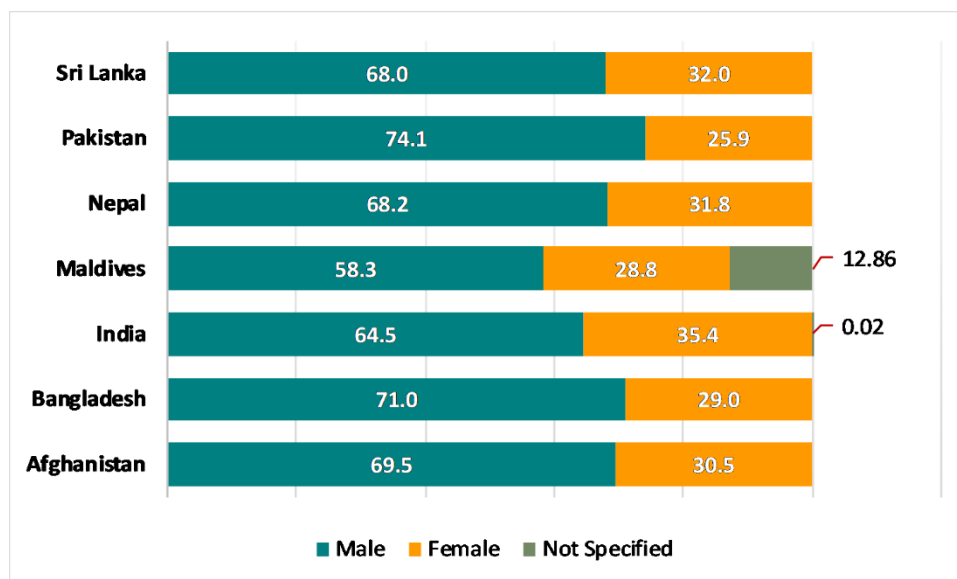


Figure 2

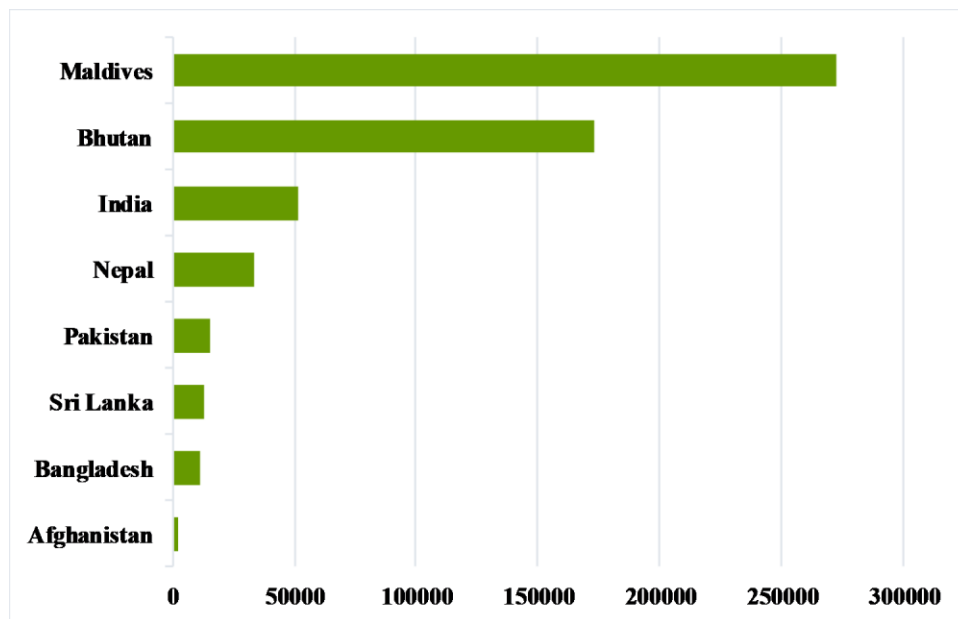


Figure 3