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REVIEW ARTICLE

COVID-19 outbreak: An overview and India's perspectives on the management of infection

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Abstract

Objectives: To provide an overview of COVID-19 including epidemiology, pathogenesis, transmission, clinical features, diagnosis, antiviral agents, prevention and risk management strategies in India. **Methods:** The inclusion criteria for this study were Indian population. The article discusses the COVID-19 confirmed cases, recovered and death cases from March, 2020 to till date in the Indian population. People who have been tested COVID-19 positive with aymptomatic or mild to moderate symptoms. Exclusion criteria consisted of patients with previous history of respiratory disease or other pneumonia. **Findings:** For the detection of SARS-CoV-2 infection, RT-PCR was found to be the most sensitive method. A Serological test used to detect the presence of SARS-CoV-2 antibodies present in blood serum. In India, self-quarantine and physical distancing was found to be the effective way to prevent the spread of infection**.** Few clinically approved repurposing drugs such as Favipiravir, Remdesivir, Lopinavir/ Ritonavir, Hydroxychloroquine (or chloroquine) and Dexamethasone were entered into clinical trial in human. **Improvement:** This study will also help to raise awareness of the current pandemic among primary and secondary health care providers. Simultaneously, our review also focuses on the most up-to-date COVID-19 cases and risk management strategies in India. It also highlighted about vaccines that are being developed by various countries including India against SARS-CoV-2 infection. The clinical trials are ongoing with promising outcomes against this pandemic disease.

Keywords: COVID19; epidemiology; pathogenesis; diagnosis; antiviral agents; management

1 Introduction

The world has seen the existence of new viruses in recent decades, which pose serious threats to global health. Coronaviruses (CoVs) are the largest group of viruses which may cause serious illness in humans. This virus belongs to the Nidovirales order whose member families include Roniviridae, Arteriviridae, and Coronaviridae. Torovirinae and Coronavirinae are the two subfamilies of Coronaviridae family. There are four

genera of coronaviruses, namely alpha, beta, gamma and delta based on serology and phylogenetic characterization[1,2]. They are positive-sense, single-stranded RNA viruses and their genome size ranges from approximately 27-34 kilobases, the largest among known RNA viruses. Coronaviruses are zoonotic pathogens. They can be isolated from different animal species, including birds, livestock and mammals[3]. This virus causes a wide range of clinical manifestations, including respiratory, gastrointestinal, liver and neurological infections[4].

In the history, coronavirus outbreaks include severe acute respiratory syndrome (SARS) in 2002 (Guangdong province, Southern China) and the Middle East respiratory syndrome (MERS) in 2012 (Saudi Arabia). Previously, they have been characterized as infectious agents posing a major threat to public health. The World Health Organization (WHO) has reported more than 8,000 infected cases with 774 deaths from SARS coronavirus in 2002-2003[5]. Similarly, MERS caused 858 deaths with 2,494 infected cases in 2012[6]. Recent outbreaks (2019) of the novel coronavirus posed a significant challenge to global public health. On 11 February 2020, WHO named this virus as COVID-19. The virus originated in the Huanan Seafood Market, Wuhan, China where livestock is traded. This has become the focal point of global concern due to an unexplained etiological pneumonia outbreak[7].The COVID-19 belongs to genus β-coronaviruses and primarily targets the human respiratory system[5].Based on phylogenetic and taxonomic analysis, the virus was later renamed as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV)[8].There are six known coronaviruses present in humans other than SARS-CoV-2. They are HCoV-229E, HCoV-OC43, SARS-CoV, HCoVNL63, HCoV-HKU1and MERS-CoV[9]. Since the virus is spreading worldwide, the WHO officially defined the outbreak of COVID-19 as a pandemic on 11 March 2020. WHO has now declared COVID-19 as a Public Health Emergency of International Concern. Our review focused on the epidemic, pathogenesis, diagnosis, treatment options, prevention and management strategies in India during the COVID-19 pandemic. So far, no vaccines and therapeutic drugs have not been approved for COVID-19 treatment. A better understanding of SARS-CoV-2 is therefore necessary for developing effective vaccines and therapeutic drugs.

2 Epidemiology and COVID-19 cases in India

According to WHO, the COVID-19 ecological reservoirs are wild bats. The similarity at genome level between SARS-CoV-2 and SARS-CoV is about 70%. Some genetic variation was observed in novel SARS-CoV-2 virus compared to SARS-CoV. During the Chinese spring festival, the SARS-CoV-2 outbreak occurred. At that time, approximately three billion people were traveled countrywide. These circumstances created favorable transmission opportunities for this highly contagious disease[10,11]. Several scientific research works are under way to learn more about COVID-19 transmissibility, severity and other clinical features. The earliest cases had some kind of history of interaction with the local seafood market, China. Thereafter, the infection was found to be transmitted from human to human via close contact[9]. Transmissibility of a disease was found to be higher in COVID-19 as compared with SARS. The average incubation period of COVID-19 was estimated to be 2 to 14 days[12,13]. As of September 03 2020, WHO has confirmed a total of 26,194,004 COVID -19 cases and 8, 67,607 deaths worldwide. Countries like United States of America (USA) and Europe were severely affected by COVID-19. The first case of the COVID -19 pandemic in India was reported in Kerala on 30 January, 2020. The Ministry of Health and Family welfare in India has reported 8, 15, 538 active cases, 2, 970, 492 recoveries and 67, 376 deaths as of September 03 2020. In India, the highest number of cases has been reported in Maharashtra. The state has recorded 2, 02, 048 active cases and 25, 195 fatalities. Table 1 represents the COVID -19 cases in India by state and union territory.

Table 1. COVID-19 status in India (updated on 03rd September, 2020)

S. No.	Name of State/Union Territory	Total active cases	Recoveries	Deaths
1.	Andaman and Nicobar Islands	381	2758	47
2.	Andhra Pradesh	1, 03, 076	3, 48, 330	4125
3.	Arunachal Pradesh	1278	3075	7
4.	Assam	26, 227	88, 729	323
5.	Bihar	17, 001	1, 23, 794	646
6.	Chandigarh	2060	2670	59
7.	Chattisgarh	17, 164	18, 220	299
8.	Dadar Nagar Haveli	292	2141	2
9.	Delhi	16, 502	1, 58, 586	4481
10.	Goa	4379	14, 059	204
11.	Gujarat	15, 913	79, 929	3046
12.	Haryana	12, 622	54, 875	721

Continued on next page

Table 1 continued

13.	Himachal Pradesh	1613	4760	43
14.	Jammu and Kashmir	8053	30, 079	732
15.	Jharkhand	14, 677	29, 747	438
16.	Karnataka	94, 478	2, 60, 913	5950
17.	Kerala	21, 989	55, 778	305
18.	Ladakh	743	2007	35
19.	Madhya Pradesh	14, 337	51, 124	1453
20.	Maharashtra	2, 02, 048	5, 98, 496	25, 195
21.	Manipur	1871	4607	29
22.	Meghalaya	1186	1318	13
23.	Mizoram	359	661	0
24.	Nagaland	785	3223	9
25.	Odisha	25, 193	84, 073	514
26.	Puducherry	4936	9968	253
27.	Punjab	15, 629	39, 742	1618
28.	Rajasthan	12, 919	70, 674	1081
29.	Sikkim	431	1269	4
30.	Tamil Nadu	52, 380	3, 80, 063	7516
31.	Telangana	32, 537	1, 00, 013	856
32.	Tripura	5133	8033	126
33.	Uttarakhand	6442	14, 501	291
34.	Uttar Pradesh	56, 459	1, 81, 364	3616
35.	West Bengal	24, 445	1, 40, 913	3339
Total number of confirmed cases		8, 15, 538	2, 970, 492	67, 376

Source: Ministry ofhealth and family welfare, India (https://www.mohfw.gov.in/)

3 Pathogenesis and routes of disease transmission

Coronavirus virions are spherical with the diameter of approximately 125 nm under cryo-electron tomography and cryo-electron microscopy[14].The COVID-19 genome encodes four main structural proteins, namely the surface spike (S) glycoprotein, the membrane (M) protein, the small envelope (E) glycoprotein and the nucleocapsid (N) protein.The spike protein, present on the surface of the virus is ~150KD glycoprotein. It contains two subunits namely S1 and S2. The S1 subunit binds to the receptor on the host cell surface, whereas S2 subunit attaches to the host cell membrane[15].The M protein is the most abundant structural protein and provides the shape of the viral envelope. It has a short N-terminal glycosylated ectodomain and a long C-terminal endodomain. It plays an important role in the assembly and budding of virus particles. The E protein (∼8–12 kDa) is found in small quantities within the virion. The E protein has N-terminal ectodomain, C-terminal endodomain and ion channel activity. The assembly and release of the virus are facilitated by the E protein. The ion channel activity of E protein is required for pathogenesis, but not required for viral replication[16,17]. The N protein is the only protein present in the nucleocapsid. It is composed of two separate domains such as N-terminal domain (NTD) and a C-terminal domain (CTD). Both domains use different mechanisms to bind RNA. N protein has multiple functions such as a nuclear localization signal, interfering cell process, virus replication and RNA package[18].Moreover, in many coronaviruses N protein is immunogenic, highly conserved and expressed abundantly during the infection. Additionally, there is a fifth structural protein known as hemagglutinin-esterase (HE) which is present in the β-coronaviruses subgroup. It enhances the S protein-mediated cell entry and spreading of virus through the mucosa[19]. Coronaviruses are zoonotic in nature and causes symptoms similar to the common cold including severe respiratory, enteric, hepatic and neurological symptoms. Angiotensin-converting enzyme 2 (ACE2), is a metalloprotease enzyme expressed on the surface of cells in various tissues including lung, intestine, liver, heart, vascular endothelium, testis and kidney. ACE2 is the host cell receptor responsible for mediating SARS-CoV-2 infection[20].Tai et al. reported that the SARS-CoV-2 enter the host cell through 'S' protein binding to ACE2 in the host cell,through the process of exocytosis, the virions are released from the infected cell. The released virions infect the lower respiratory tract, liver cells, kidney cells, intestines and T lymphocytes[21]. Previous reports stating that the SARS-CoV reduces the lymphocyte count, induce the irregular T-cell response through the stimulation of T-cell apoptosis and disrupts the immune system in human[4,22].Similarly, SARS-CoV-2 patients have a low number of leukocyte count and increased levels of plasma pro-inflammatory cytokines. In several cases, high levels of chemokines (IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα) were reported[23].

Mammals such as camels, cattle, cats and bats are the hosts for coronaviruses. Earlier SARS and MERS are reported to transmit from animals to human. Previous studies showed that the bats are the primary host for SARS-CoV and MERS-

CoV [2,24,25]. The three main transmission routes for the COVID-19 include respiratory droplet, close contact with infected patients and aerosol transmission. Respiratory droplet transmission occurs when a person is within 1 m close contact with someone who has COVID-19 symptoms (e.g. coughing or sneezing) [26]. The COVID-19 virus can be transmitted by direct contact with infected persons and by indirect contact with surfaces in the immediate environment or with items used on the infected person. Airborne transmission refers to the microorganisms present within the nucleus of the droplet, which may remain in the air for long periods of time and be transmitted to others over distances greater than 1 m.

4 Clinical manifestations and Diagnosis

The incubation period of COVID-19 virus was 14 days. The symptoms of the COVID-19 virus occur after an incubation period of 5 days. This period varies depends on the patient age and strength of the immune system [27].The most common symptoms of COVID-19 are fever, dry cough, tiredness, fatigue and diarrhea. Some patients may have a runny nose, sputum, cough, haemoptysis, diarrhea, dyspnoea and lymphopenia. In severe cases, the presence of pneumonia was identified on chest CT (Computed Tomography) scan. The irregular symptoms such as RNAaemia, Acute Respiratory Distress Syndrome (ARDS), sepsis and acute cardiac injury were also reported [28]. In certain cases, the multiple peripheral ground-glass opacities were found in subpleural regions of both lungs. The elderly and people with underlying medical problems like tumor surgery, cirrhosis, hypertension, coronary heart disease, diabetes and Parkinson's disease are at greater risk of serious illness [29].Lei et al. reported that the 80% of people with mild symptoms were recovered from COVID-19 without needing any special treatment [30].

Reverse transcription-polymerase chain reaction (RT-PCR) is the most sensitive method to detect SARS-CoV-2 infection. The respiratory samples such as oropharyngeal swabs, sputum, nasopharyngeal aspirate, deep tracheal aspirate or bronchoalveolar lavage can be used for analysis. Samples in the lower respiratory tract, in particular, may have substantially higher viral loads than the upper respiratory tract [31]. The other technique to test the samples is quantitative reverse transcription PCR (RT-qPCR) test. In this technique, the viral RNA was isolated from the sample and a portion of its genome was amplified within 4–6 hours [32,33]. In India, over one million RT-PCR tests have been conducted for the detection of COVID-19 according to an Indian Council of Medical Research (ICMR). Currently, this test is available in 292 government and 97 private facilities across the country. Serological testing is another detection method for COVID-19 infection [34].For antibody testing in 2003 SARS-CoV infection, immunofluorescence assay was performed using the S protein and a recombinant N-S fusion protein as antigens [35]. Here viral antigens or cloned viral antigens were used to detect the presence of monoclonal antibodies directed against the virus in infected patients. Recently, the Immunoassay kit containing three SARS-CoV-2 antigens, including the N protein, the S1 and S2 domains of the S protein was developed by Pharmact AG Company, Berlin. This kit was designed to detect both IgM and IgG antibodies produced during the initial and subsequent stages of an infection [32].Computed Tomography (CT) is a medical imaging technique used for COVID-19 diagnostics. In chest CT scan, most patients with COVID-19 pneumonia revealed the presence of unilateral or bilateral lung disease and most importantly, the ground glass opacities (GGO) could also be observed [29,36]. California-based molecular diagnostics company developed a diagnostic device named as point-of-care (POC) testing device. This device was approved by the Food and Drug Administration (FDA) for COVID-19 diagnosis. This newly approved test enables physicians and medical staff to make clinical decisions within minutes rather than hours [32,37]. In India, Virologist Minal Dakhave Bhosale, Research and Development Head of Mylab's, Pune developed the first COVID- 19 testing kit known as Patho Detect. This kit was developed in just six weeks and could give the diagnosis result in two and a half hours. On 18th March, the kit was submitted to the National Institute of Virology (NIV) for its analysis against SARS-CoV-2 infection. According to the ICMR, the kit showed 100% accurate results and costs around 1,200 INR or roughly US $16.

5 Antiviral agents

At present, no antiviral drugs or vaccines for COVID- 19 infection has been approved for treatment. WHO has announced drug repurposing for COVID-19 treatment. Drug repurposing is defined as the alternate use of approved drugs to treat novel diseases with few side effects. Few repurposed antiviral drugs, namely favipiravir, remdesivir, lopinavir/ritonavir, hydroxychloroquine (or chloroquine) and Dexamethasone were clinically approved and entered Phase III/IV clinical trial in human. Table 2 represents the clinically approved repurposed drugs against existing disease. Chloroquine (or) hydroxychloroquine (antimalarial drugs) was the first drug approved by FDA on 3 April 2020 for the treatment of COVID-19 as an emergency. Gautret et al. reported that the hydroxychloroquine in combination with azithromycin has been effective for the eradication of virus [38].The overdose of hydroxychloroquine is associated with an increased risk of complications such as seizures, coma, and cardiac arrest. ICMR, under the Ministry of Health and Family Welfare, India, recommended the use of hydroxychloroquine for asymptomatic healthcare workers treating COVID-19 patients. The recommended dose is 400 mg twice on day 1, followed by 400 mg once a week for a total of 7 weeks. But, there is no previous evidence to support the

research findings on hydroxychloroquine treatment for COVID-19. However, the FDA approved hydroxychloroquine only for the emergency treatment of COVID-19 pneumonia. The HIV protease-inhibitor drug Kaletra, which is a combined formula of two medications, lopinavir, and ritonavir. A clinical study from South Korea showed a significant reduction of COVID-19 infection after treatment with Kaletra [39]. Furthermore, the National Medical Products Administration of China has approved the use of RNA polymerase inhibitor drug, Favilavir. This drug was shown to be effective in treating COVID-19 with minimal side effects in a clinical trial involving 70 patients [40]. Another FDA approved antiviral drug, Remdesivir have been used to target Ebola. This drug was proven to be highly effective in the control of 2019-nCoV infection *in vitro*, but it is not yet approved for human trials [41]. Generally, the cytokines were found in higher levels in the serum of COVID-19 patients. Cytokine storm is an inflammatory condition that occurs when COVID-19 patients releases tremendous amounts of pro-inflammatory cytokines such as IL-6. The increased levels of IL-6 in blood cause lung damage which leads to respiratory failure. Researchers are now considering that the use of monoclonal antibody-based drugs would limit the inflammatory response. The humanized anti-CD6 IgG1 monoclonal antibody binds to CD6 present on the T cell surface and blocks the release of IL-6 through interacting with activated leukocyte cell adhesion molecule (ALCAM), a molecule present on the antigen presenting cell. The drug named, TZLS-501 is a human anti-interleukin-6 receptor (IL-6R), helps to deplete the amount of IL-6 circulating in the body thereby reducing chronic lung inflammation. Another human monoclonal antibody drug, Gimsilumab, targets the granulocyte-macrophage colony-stimulating factor (GM-CSF) cytokine and is expected to reduce lung damage and could reduce the mortality rate in COVID-19 patients. Moreover, antibody-based drugs also have minimal side effects and proved to be effective for many human chronic inflammatory diseases [42]. An Indian biopharmaceutical company Biocon proposed the repurposed drug ALZUMAb (Itolizumab) to treat COVID-19 patients. Later, the company received the DCGI (Drug Controller General of India) approval to market the drug for emergency use in India, especially for the treatment of the cytokine storm release in moderate to severe cases. Phase II clinical trials were under process to evaluate the biological activity of the drug. In India, the convalescent plasma therapy is also showing a promising result. On May 4, 2020, ICMR approved 21 Indian institutions to initiate the randomized and open labeled phase II trials to assess the safety and efficacy of convalescent plasma therapy for COVID-19 associated complications [43].

Table 2. Clinically approved Repurposed drugs against existing disease

Sl. No	Drug	Prescribed for existing disease	Enzyme inhibition	References
1.	Hydroxychloroquine	Malaria, Rheumatoid arthritis, Chronic discoid lupus erythematosus and Systemic lupus erythematosus	Terminal glycosylation of ACE2	[44]
2.	Remdesivir	Ebola and Nipah virus	RNA-dependent RNA polymerase	[45]
3.	Lopinavir/Ritonavir	Human immunodeficiency viruses (HIV)	Protease	[46]
4.	Favipiravir	Influenza virus	RNA-dependent RNA polymerase	[47]

6 India's role in vaccine development and ayurvedic treatment

In general, vaccination is recognized as an effective way to minimize the burden of infection. Herd immunity is a condition acquired when a sufficient proportion of the population is vaccinated [48]. In India, pharmaceutical companies have taken major efforts to develop a vaccine against COVID-19. The vaccine development is broadly based on three strategies, DNA, RNA and weakened virus known as virus-like particles (VLPs) targeting spike protein [49]. The nucleic acid based vaccines have more advantages rather than traditional methods. The vaccines targeting SARS CoV-2 spike (S) protein, which contains the receptor binding domain (RDB) could be considered to be an effective one as it will induce the neutralizing antibodies to protect a host cell from virus [50].

Many research institutes around the world have developed vaccines against SARS-CoV-2 and entered phase 1/II clinical trials. The vaccines includes Ad5-nCoV, ChAdOx1 nCoV-19, BNT162 (a1, b1, b2, c2), INO-4800, mRNA-1273, Covid-19/aAPC, LV-SMENP-DC and bacTRL-Spike [51]. The Entos Pharmaceuticals, Canada is developing DNA-Fusogenix liposome vaccine, which contains multiple protein epitopes derived from SARS-CoV-2 proteins. This could stimulate the immune response in the body to prevent COVID-19 infection. Another intranasal COVID-19 vaccine is being developed by US-based biopharmaceutical company, Altimmune. The design and synthesis of the single-dose vaccine have been completed, and animal testing is underway. Currently, the Serum Institute of India, Pune is collaborating with Codagenix Inc, a synthetic biology company, New York to develop a live-attenuated vaccine (LAV) known as CDX-005 which is a pre-clinical stage. The Serum institute has also collaborated with the University of Oxford for the mass production of ChAdOx1 nCoV-19 vaccine. The vaccine was found to be a safety in phase I trial and have entered phase II to evaluate its efficiency. Recently, India's first indigenous

COVID-19 vaccine named Covaxin has been developed by Bharat Biotech in collaboration with ICMR and NIV Pune. The vaccine has received DCGI approval for phase 1 and 2 clinical trials from July 2020 in Indian medical institutes. The Phase I study involves 375 volunteers at 12 medical institutes across the country and expected to be complete by the end of August, 2020. The phase II human trial will be expected to begin in September, 2020. Another India's based vaccine named ZyCoV-D was developed by Zydus Cadila. The drug received DCGI approval to conduct human trials in India. Phase I trial was found to be safe in healthy participants. Phase II clinical trials were under process to evaluate the safety and immunogenicity of the vaccine. The above mentioned vaccines may be the best hope to stimulate the immune response against the SARS-COV-2 infection. Alternatively, in India, AYUSH treatments including Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy have been suggested. The Ministry of AYUSH, Government of India has recommended siddha treatment named Kabasura kudineer against SARS CoV-2 infection. A team of siddha doctors in Tamil Nadu investigated on this herbal drink against fevers due to respiratory infections. The dry ingredients of Kabasura kudineer include ginger, pippali, clove, cirukancori root, mulli root, kadukkai, ajwain and many other herbs. The ingredients are powdered and combined with water, then boiling led to a one-fourth decoction of its original amount. The Government of Tamil Nadu has encouraged its use to improve immunity, although it was not approved as a medicine to treat COVID-19. Siddha medical practitioners in Tamil Nadu reported that the COVID-19 patients treated with Kabasura kudineer recovered fast compared to the standard treatment. In India, two pilot studies were conducted in the month of May and June 2020 by the National Institute of Siddha, Tambaram and SRM Medical College Hospital and Research Centre, Kattankulathur. The results revealed that the 99% COVID-19 cases were turned negative within 5 days. Many pharmacies have started to sell siddha medicines, particularly Kabasura kudineer and could be used as a complementary treatment for COVID-19.

7 Prevention and risk management in India

The Centers for Disease Control and Prevention (CDC) recommends basic measures to prevent the transmission and risk of SARS-CoV-2. On 22 January 2020, the National guidelines published National Health Commission to prevent COVID-19 for medical institutes. In India, The Ministry of Health and Family Welfare have raised awareness about the COVID-19 outbreak and have taken necessary action to control the infection. Isolation remains the best and the most effective measure to prevent the rapid spread of infection. The public has also been told to do frequent hand washing for at least 20 seconds by using soap and water. Alternatively, hand sanitizers with at least 70% of alcohol can be used [52].Touching mucosal surfaces such as the mouth and the nose with unwashed hands should be avoided. To prevent aerosol transmission, patients and the general public are recommended to cover the mouth while coughing and sneezing. Immunocompromised individuals and elders are mostly advised to avoid public gatherings. Healthcare professionals at hospitals and medical centers should strictly follow personal protection, including gloves, gowns, N95 masks, FFP3 masks, eye protection and hand hygiene [53,54].

In India, the Government has strongly instructed the "self-quarantine" of people returned from foreign countries at home for 14 days. On 24 March 2020, the Government of India has announced the nationwide lockdown for a period of 40 days around the entire 1.3 billion population of India till 3 May 2020. But at the end of the lockdown period, the Government has extended the lockdown period till 17 May 2020. The possibility of spreading infection was reduced during this lockdown period. Physical distancing is one of the best ways to slow down the spread of infection. The strategies adopted in India includes testing the symptomatic people with international travel history, previous contacts with positive cases, quarantine and restrict the people movement from one place to another [55]. The Indian Government locked down the public transport services, closed public and private offices, academic institutes and industries. Due to the COVID-19 outbreak, Indian economy has severely disrupted [56,57]. Apart from this, the three main factors were considered for the low mortality rate in India. Firstly, the largest youth population could be one of the reasons for the infection resistant. Secondly, nearly 94% of worldwide infections occur at the maximum temperature of below 17°C. Currently, in India the temperature is around 40 °C and hence the temperature might weaken the virus. Thirdly, the Bacillus Calmette-Guerin (BCG) vaccine has been used as an effective weapon to prevent tuberculosis in children. This vaccination is a part of India's universal immunization program and administered to millions of children soon after birth since 1948. In Spain, the vaccination program was discontinued in 1981. In Italy, it was terminated after 2001 and in the USA the vaccine has never been given to children. Currently, it was believed that people with COVID-19 and tuberculosis showed similar symptoms such as cough, fever and difficulty in breathing. Both diseases attack primarily the lungs, but, however, still more investigation is needed to evaluate the efficiency of the BCG vaccine against this highly contagious disease.

8 Conclusion and Future directions

In this study, the novel coronavirus epidemiology, pathogenesis, transmission, clinical manifestations, diagnosis, prevention, treatment options and the risk management in India have been discussed. Since December 2019, the novel coronavirus (COVID-2019) has caused the pneumonia outbreak in Wuhan and spread rapidly throughout the world. Compared with SARS or MERS, a tremendous increase in the SARS-CoV-2 infection rate has been observed. WHO guidelines have been released to serve the medical professionals, healthcare practitioners, public health individuals and researchers to tackle the infection. In India, self-quarantine was found to be the effective way to prevent the spread of infection. However, still there are no specific clinically approved antiviral treatments or vaccines available. Hence, there is an urgent need for studies in the disease preventive domain to minimize the impact of the outbreak. Only few studies have been focused on clinical practice because the guidelines to develop clinical practice were difficult. The main reason for this gap was due to rapid development of COVID-19 outbreak and understanding of the novel virus spread is not clear. Hence, it is taking more time to conduct clinical studies. Our review would help researchers to fill these research gaps including the research on existing drugs or vaccines to handle the COVID-19 outbreak.

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Compliance with Ethical Standards

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Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical approval

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Not required

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