

# Emerging Prophylactic Strategies to Combat COVID-19: A Systematic Review

## Review Article

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## ABSTRACT

**Introduction:** In December 2019, China faced the COVID-19 outbreak. COVID-19 is a disease caused by the pathogen, SARS-CoV-2 which is a single stranded RNA virus that spreads person to person via direct contact or respiratory droplets. Since this disease has been found to be highly contagious, prevention from virus exposure seems to be a reasonable approach especially due to lack of an effective vaccination up till now. Our study is aimed at proposing the prophylactic strategies that can be implemented in Pakistan to help flatten the disease curve in order to provide more time for healthcare professionals to fight the disease better and to hopefully come up with an effective vaccination for long term disease control. **Methods:** We conducted a systematic literature review based on PRISMA guidelines. Only those articles were included which met the inclusion criteria. **Results:** The results gathered by the literature search suggested that due to the lack of any licensed vaccine or effective treatment, adopting personal and environmental protective measures, isolation and quarantine, and other community mitigation measures like temporary lockdown can help flatten the peak of the ongoing pandemic. **Conclusion:** Since there has not been any breakthrough in finding an effective vaccine, our review aims to devise an effective preventive strategy to curb this pandemic according to the present socio-economic conditions of Pakistan.

**Keywords:** COVID-19, Coronavirus, Pandemic, Prophylaxis,

## INTRODUCTION

Due to the outbreak of COVID-19 in December 2019, a significant number of pneumonia cases appeared in Hubei, China. The pathogen, SARS-CoV-2 is a single-stranded RNA virus that causes severe respiratory illness along with other complications.[1] It is highly contagious and spreads person to person via direct contact with infected people or by their respiratory droplets.[2] Human body presents host cells to which the virus binds and primarily attacks the

respiratory epithelium.[3] The common symptoms of COVID-19 infection are fever, cough, and myalgia, while less common symptoms include headache, diarrhea, dyspnea, and lymphopenia. However, these symptoms vary. They can be mild or severe. People with comorbidities like diabetes, chronic obstructive pulmonary disease and cardiovascular diseases have been found to have a higher mortality rate.[5] Due to an exponential rise in cases of COVID-19, on 31st January 2020, WHO called for a Public Health Emergency of International concern and on 11th March 2020, WHO characterized it as a pandemic.[4] As of April 9, 2020, a total of 1,539,424, confirmed cases and 90,011 deaths were reported to WHO globally.[6] In Pakistan, the situation has become quite alarming lately. As of February 29, two cases of COVID-19 were confirmed in Sindh, Pakistan. During the first two weeks after the first case in Pakistan was reported, the trajectory showed a gradual increase of less than 100 cases per day. However, after that, the incidence of new cases increased at a rate of more than 100 per day. The number of infected cases reached 4,462 by April 9, 2020; with the death toll rising to 63 and 572 patients being recovered.[7] In response to this outbreak, all the countries of the world are adopting strict measures to not only barricade the spread of this virus but also are well-equipping their health care systems for any expected or unexpected emergency while treating the COVID-19 patients, and at the same time ensuring minimum loss of



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lives. So far, no reliable treatment or vaccine has been proposed despite the untiring efforts of scientists and medical researchers all over the world.[2] Keeping in view the economic and financial status of Pakistan, the objective of our systematic review is to propose all the possible preventive strategies in order to combat the ongoing pandemic, since its prevention and control seem to be the only sane approach in this hour of public health crisis.

## METHODOLOGY Protocol

The present systematic review was performed based on PRISMA protocol for critical appraisal and quality evaluation.

### Information Sources and Search Design

Since the outbreak of SARS-CoV-2 has posed a great challenge to researchers and reviewers all over the world, there was a good deal of information on our topic. An extensive literature search was carried out in the first week of April, 2020 using pubmed and google scholar as databases. 'Prophylaxis', 'Preventive measures', 'Management' and 'Treatment' related to COVID-19 were the search terms used (Table 1). Statistical analyses were also obtained from WHO.

### Rationale for Selecting Sources

All the sources were scrutinized thoroughly and only those articles were selected which met the inclusion criteria. Two reviewers performed the data extraction and screening process. The articles which aligned with our topic were further analyzed and all the irrelevant evidence was excluded. The relevant articles were further screened for eligibility and evaluated to get the most pertinent material. All the articles published within the past five years were included. 268860 articles were the results of the search and based on the inclusion and exclusion criteria, 17 articles were included in the final review. Most of the evidence was peer reviewed and mostly of the primary source. The credentials of the sources were also taken care of (Figure 1).The findings of our literature search are shown in the PRISMA flowchart below. A total of 17 articles were finally included in the literature review.

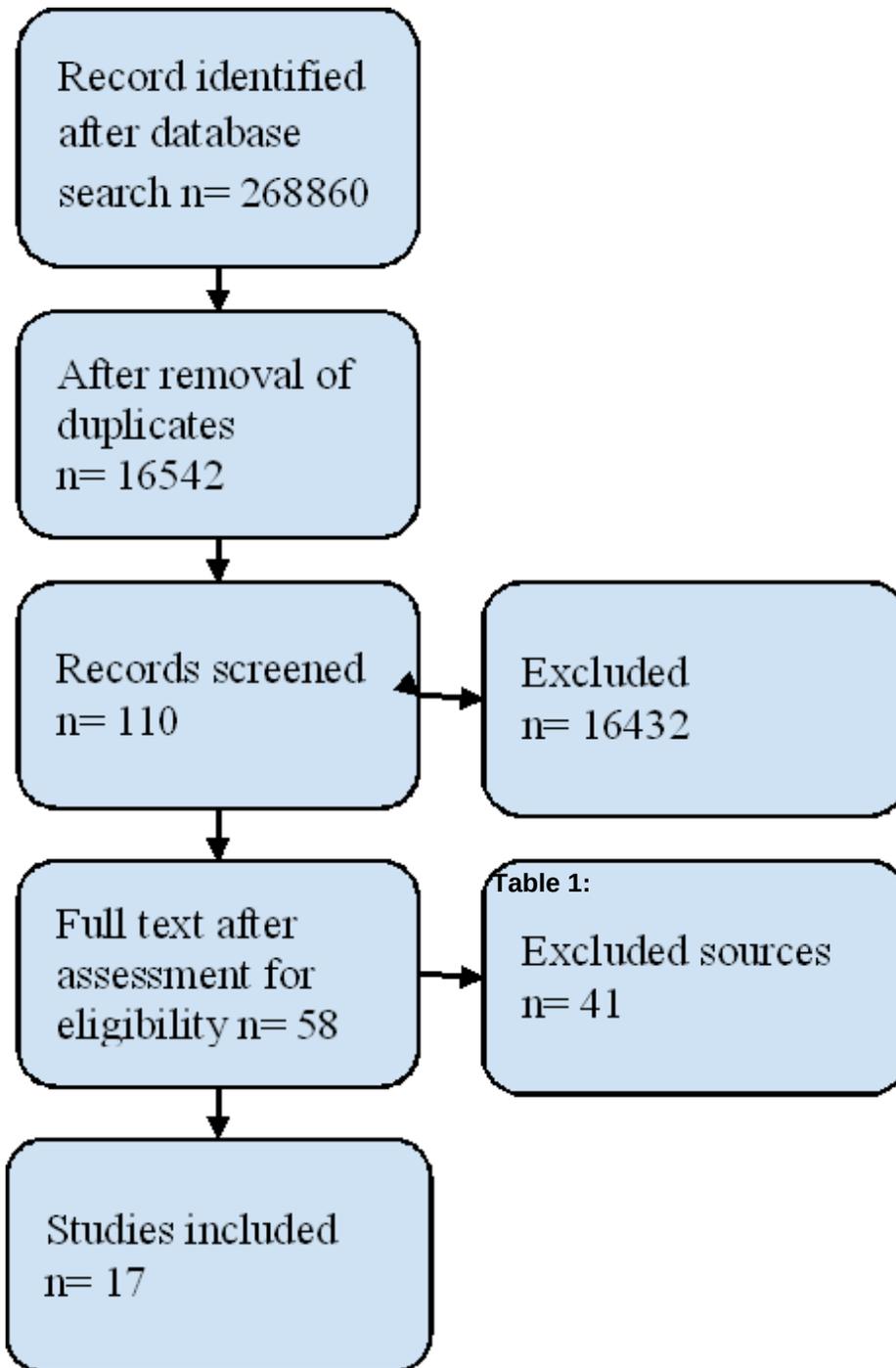
## RESULTS

In their study Chih Cheng Lai et al. described various protective measures that should be adopted by the public.[2] These include social distancing, frequent and thorough hand washing, adopting respiratory hygiene and minimizing close contact with people who show signs of acute respiratory infection. Jin yong kim et al. (Feb 2020) reported a case of a 35 year-old woman

#	Search Strategy	No. of results
1	Prevention	1729477
2	Precautionary measures	1190
3	#1 OR #2	1730302
4	Management [MeSH terms]	1508020
5	Treatment	2456799
6	Prophylaxis	1466048
7	#4 OR #5 OR #6	6556423
8	Covid-19	3633
9	Sars-CoV-2	1504
10	nCoV-2019	415
11	#8 OR #9 OR #10	3633
12	#3 OR #7 AND #11	268860

**Table 1:** Data retrieved from PubMed search

who had come from Wuhan, China to Korea and developed the symptoms of COVID-19 including fever, cough, fatigue. On the fifth day, she developed pneumonia.[9] Since early symptoms of COVID-19 are common to any other acute respiratory infection so they emphasized the importance of taking the travel history of a patient for early diagnosis. They especially highlighted the importance of HRCT (high resolution computed tomography) for early detection of pneumonia, even before the symptoms of pneumonia develop. They concluded that screening of all the symptomatic individuals is a safe approach, as many individuals might not develop pneumonia, or develop it later so a diagnosis can be suspected by travel history and other symptoms like fever and dry cough. In the Clinical Guidance for COVID-19 outbreak in the US, Anita Patel et al. (Feb 2020) stressed upon the early diagnosis of COVID-19 patients.[10] It was advised to isolate the patient immediately after the diagnosis is confirmed. Since no vaccine or treatment is available, they suggested medical care of the patients to be the only solution for the time being. People showing signs and symptoms of COVID-19 and having a travel history should be evaluated and their specimens of upper and lower respiratory tract should be tested. Other samples of urine and stool should also be stored. However they advised that patients with seasonal flu and other acute



**Figure 1:** Prisma Flowchart

respiratory infections must also be evaluated at the earliest. They suggested that PUIs (patients under inspection) must be isolated and health care personnel entering the room should use standard precautions, contact precautions, airborne precautions, and eye protection (e.g. goggles or a face shield). They emphasized that preventive measures are implemented only to slow the spread of illness, to flatten the curve and to provide time for the health care systems to be ready and to better combat the illness by diagnostics, therapeutics and vaccines.

Disinfection of surfaces is important since a lot of studies have suggested that viruses may persist on inanimate surfaces and it might be a route of their

transmission into the human body. G. Kampf et al. (March 2020) studied the persistence of coronaviruses on different inanimate surfaces and they assumed the same for SARS-CoV-2.[26] It was observed that viruses stay active for about 2 to 9 hours on inanimate surfaces therefore it is necessary to disinfect the surfaces which are frequently touched by biocidal agents having a mixture of ethanol and propanol to minimize the spread by this route of transmission. In their study, P Conti et al. (March 2020) suggested that among various ways to minimize the spread of COVID-19, quarantine can prove to be significantly fruitful.[11] They also speculated that people with good immunity and those who have been previously vaccinated for

bacterial or viral infection are less likely to develop complications. Due to lack of vaccines and therapeutics, they suggested that non therapeutic interventions (NPIs) should be initiated to curb the transmission of the disease. A wide range of NPIs including school closures, banning of mass gatherings and isolation of ill persons will prove valuable in decreasing transmission of COVID-19 as they brought fruitful results in case of influenza pandemic (H1N1 virus), but these measures will affect the low income families so they should be provided with free meals and funds. In a perspective review, Benjamin J. Cowling et al (March 2020) also suggested that personal protection by adopting hand hygiene and using face masks along with isolation and quarantine of the ill has proved successful in the past for SARS and MERS and so they might work out in curbing the COVID-19 pandemic too.[12] This has been consistent with yet another study by A Wilder Smith et al. (Feb 2020) in which they jotted down the classical methods of preventing the spread of viral infections like these.[13] They mentioned that isolation of infected patients, social distancing, quarantine and lockdown can be significantly beneficial in order to prevent the spread of disease. In a review, Aparna Visnath et al. stated that personal protection of health care workers is extremely important as they are responsible for patient's safety. [14] Regarding the protection of health care workers and paramedic staff, they highlighted the importance of surgical masks and N95 respirators to prevent aerosol spread. The inanimate surfaces as door knobs, furniture, tables and chairs must be frequently decontaminated. Regarding the protection and safety of HCWs, they provided following suggestions:

1. PPEs should be properly disposed of.
2. Hospitals should have isolated units.
3. Time of exposure to ICUs should be divided among the health care workers.
4. Staff with comorbidities must minimize their exposure.
5. The number of personnel entering the operating rooms should be minimized.
6. Telemedicine departments should be formed.

Dan Zhou et al (March 2020) proposed that hydroxychloroquine can be preferably used over chloroquine for the treatment of COVID-19 since it has been found to have fewer adverse effects.[15] They stated that HCQ is an antirheumatic drug with a chemical structure similar to CQ and by elevating the intracellular pH it inhibits lysosomal activity in antigen-presenting cells which reduces T cell activation and the

cytokine storm. CQ exerts an antiviral effect by interfering with the glycosylation of angiotensin-converting enzyme 2 (ACE2) which blocks the fusion of viruses with host cells. Thus, the binding of the virus to the receptors on the cells is impeded and infection is prevented. However, a recent study done in the US has shown no benefits and increased side effects of HCQ. [34] In addition, Thachil J. (April 2020) studied the significance of heparin in prophylaxis and treatment of COVID-19 patients.[16] Coagulopathy in corona virus infection is associated with lung inflammation, impaired gas exchange, Acute Respiratory Distress Syndrome (ARDS), and endothelial dysfunction. It has been suggested that the use of Lower Molecular Weight Heparin with a proper dosage according to BMI of COVID-19 patients can help resolve these harmful effects. They observed that the anti-viral role of heparin as seen by its interaction with SARS-CoV2 spike protein receptor binding domain opened new fields of discovery and treatment. Moreover, Mrudula Phadke and Sujata Saunik (March 2020) studied the repurposing of drugs to treat COVID-19 patients until an effective vaccine is developed.[17] These include Angiotensin Receptor 2 blockers, to prevent the virus entry into the host cells. Clinical trials using statins which have anti-inflammatory and immune-modulatory prophylaxis to prevent acute lung injury by COVID-19 infection should be performed.

Michael Day (March 2020) studied that in people showing COVID-19 symptoms, use of paracetamol should be preferred over ibuprofen and other NSAIDs. [18] This has been supported by many scientists and senior physicians all over the world due to possible deleterious effects of anti-inflammatory actions of NSAIDs on COVID-19 patients. Antiviral therapy has also been tried. Bin Cao et al (March 2020) from China conducted a study on 199 adult COVID patients out of which 99 were in the Lopinavir-Ritonavir group and 100 were given standard care and it was concluded that Lopinavir-Ritonavir provided no significant clinical benefit if not backed by standard care.[19]

Critical steps during operations of Covid-19 patients need to be followed. Liah Kah Ti et al. (March 2020) from National University of Health System Singapore, shared the Operation room (OR) protocol for treating COVID-19 patients.[20] This included a setup of 5 interconnected rooms, with negative pressure in ante rooms and Anesthesia rooms. OR proper, preparing rooms and scrub rooms had positive pressure. Anesthesia machines were specific for COVID-19 treatment only. Heat and Moisture Exchange (HME), and soda lime

were renewed each day. Drug trolleys, disposable equipment, video laryngoscopy, bispectral index motors, transports ventilators were also used. PPEs were provided with a powered air purifying respirator (PAPR) for ICU personnel. These were comprehensive measures to protect healthcare workers while treating COVID-19 patients. Stress has been given on the safety measures during deliveries of pregnant females suffering from COVID-19. Kang X. et al (May 2020) studied the anesthesia management in Pregnant females, as COVID-19 affects the cardiopulmonary function of pregnant mothers.[21] For ordinary COVID-19 patients, spinal anesthesia is preferred in the cesarean section; whereas in critically ill patients, general anesthesia via endotracheal intubation is adopted. Level III standard protection should also be adopted by the anesthetists. It was suggested that special attention should be given to pregnant females to reduce their anxiety before operation. Xuwen et al. (Feb 2020) reported that severe and critical patients with COVID-19 pneumonia were more likely to develop ARDS. According to their report noninvasive and invasive positive pressure ventilation support was required for treatment.[22] Although medication is the direct weapon against this disease, even way before it all starts, the prevention is being emphasized in the countries with the epicenter of this outbreak. Stefano Spina et al. (February 2020) studied Milan's Emergency Medical System (EMS) to confront the COVID-19 outbreak.[23] After the declaration of COVID-19 as a pandemic by the WHO, the Italian Govt. implemented various protective measures including interruptions in flights, organizing repatriation flights and isolation of suspects of COVID-19. A helpline in Lombardy caters all the emergency cases, with a team consisting of healthcare workers and technicians. Moreover, the COVID-19 response team collaborates with Regional Medical Authorities to design and punctually update a procedural algorithm for detection of suspected cases of COVID-19. The Emergency Medical System response team along with local Medical authorities are working tirelessly to fight the Pandemic. Antonio Pesenti et al. (March 2020) studied the critical care measures adopted by Lombardy to treat the Corona crisis.[24] This included increasing ICU capacity and forecasting the demand over-time. It also included containment measures by the local Health Authorities of quarantining different towns and cities in a systematic manner [Supplementary Material 1].

## DISCUSSION

The results built on the existing literature suggest that prevention and precaution against the ongoing pandemic is of paramount importance since no effective treatment has yet been proposed. Various studies have stressed upon the following protective measures that should be strictly adopted by the public:

1. A distance of 3 feet should be maintained between individuals as it protects them from inhaling respiratory droplets of an infected person when he/she coughs or sneezes. Face masks are recommended at workplaces and in health care departments.[10,12,31]
2. People should boycott mass gatherings in order to avoid interactions.
3. Hand washing with alcohol based sanitizers for at least 20 seconds has been proven effective as it kills pathogens. However, sanitizers are inflammable, so they shouldn't be used prior to cooking.[25]
4. A pea sized drop of hand sanitizer has been recommended. Usage of water should also be wisely managed.
5. Coughing/sneezing etiquettes should be followed. If a tissue paper or handkerchief is used, it should be properly disposed of however it is better to cough into the elbow.
6. If mild symptoms appear and the patient has no comorbidity, it is advisable to isolate him/her at home in order to provide room in the hospitals for those who are at a high risk of developing complications.[25]

The stability of viruses on plastic, steel and other inanimate surfaces has also been suggested and therefore it is necessary to disinfect the surfaces which are frequently touched by water and detergents.[26,27]

This is especially important at workplaces where a number of employees are at a risk of contracting the infection by touching contaminated surfaces.[28]

Isolation, social distancing and lockdowns have been proven fruitful previously in controlling the spread of epidemics, especially the respiratory epidemics.[13] A study in Italy and Spain has shown that lockdown has helped flattening the curve of pandemic. These actions should be enforced by the government.[32]

Safety of healthcare workers (HCWs), physicians and paramedic staff is of prime importance because they are at a high risk of contracting the infection.[29] Regarding their rights and responsibilities WHO states that they should be given proper training on prevention and control and should be provided with personal protective equipment (PPE). They should critically

follow all the protective measures as well. Due to shortage of PPE, a study has suggested that though PPE is not designed to be reprocessed, it can still be disinfected if the supplies are limited.[33] Telephone outpatient clinics should be conducted to reduce the load of patients in hospitals with non-emergent clinical conditions or diseases.[14,30]

Since there is no effective treatment up till now and prevention from the spread of the virus is the need of the hour, it is important for the public to spread awareness among masses via posters or meetings and stay updated about the present conditions in Pakistan.

## CONCLUSION

There is a dire need to conduct randomized clinical trials to get better knowledge of the possible treatment of COVID-19. Efforts to use the serum of recovered patients to produce a vaccine and pharmaceutical interventions for COVID-19 must be the prime goal of health professionals. Hand hygiene practices, getting proper rest, eating immunity boosting meals must be preached along with the proper usage of safety measures like N-95/ surgical masks, gloves and sanitizers. The awareness to seek medical attention if symptoms of COVID-19 are observed is of paragon importance. Screening tests should be stressed upon. Psychiatrists need to play their role as well to prevent people from going into mental health issues due to the depressing statistics of new cases and deaths on a daily basis. The world is in a state of crisis due to the outbreak of COVID-19. It is needed that we learn from the experiences of countries like China, the USA, Italy, etc. and adopt effective measures which suit our socio-economic status to curb this situation at the maximum. Vaccines are currently under evaluation, so it is suggested that the best way to cope with the current situation is to responsibly implement all the preventive measures, both individually and collectively and enforce community-wide containment procedures. Spreading awareness in backward areas is of prime importance in the prevention of disease. Minimizing the spread of disease by practicing social distancing and isolating infected patients can also prove significantly helpful in control of COVID-19. Higher authorities should also keep noticing the situation so we can respond better to it.

## LIMITATIONS

As the outbreak is still recent and only a few months have passed by hence the evidence is limited and more time is needed to research and find effective protective and management skills and vaccines to minimize the rapidly rising death toll. Moreover, the

economic challenges that every country is facing is hindering the progress of confronting this pandemic. Much of the recommendations on treatments are based on short case series or anecdotal data without strong evidence of benefit. Caution should be measured when adopting a treatment for COVID-19 infection given lack of strong evidence and treatment should be individualized as per risk benefit balance.

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