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COVID-19 Pandemic: The Existing Challenges and Available Solution; Evidence from a Systematic Review

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Abstract

Coronavirus disease (COVID-19) is presently the most important topic worldwide. However, no vaccine or specific anti-viral treatment for the disease has been shown to be effective. In this emergency, identifying risk factors, preventive measures and estimating challenges which control available drug options for COVID-19 are key to mitigating the severity of the pandemic until specific drugs or vaccines become available. Therefore, this study aims to identify possible factors which affect these drug options. This study searched PubMed database using necessary Boolean operators from December 31st to March 31st 2020 in order to identify common risk factors, preventive measures, information regarding control challenges & evidence on the available drug options against COVID-19. Risk factors were found to be human-animal interactions, males, aged people and people with co-morbidity. Furthermore, protective factors comprised of personal hygiene etiquette maintenance, rapid identification, isolation and informing (3I tools) of the COVID-19 cases and media coverage on COVID-19. Till date, anti-viral drugs like remdesivir, chloroquine, lopinavir/ritonavir and traditional Chinese medicine (TCM) are available options to fight against COVID-19 More research is needed to determine other how to control the disease until specific treatment options are available as well as risk factors, and preventive measures.

INTRODUCTION

In December 2019 lockdown of Wuhan, a central city of china has alarmed the world that it is going to face one of the biggest threats by the third pathogenic coronavirus after Severe Acute Respiratory Syndrome-Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome-Coronavirus (MERS-CoV), the disease due to this virus known as COVID-19. At first, the virus was known as "Wuhan coronavirus" named by Chinese researchers. But currently, the International Committee on Taxonomy of Viruses (ICTV) designated it as SARS-CoV-2. This virus was first initiated in the Hunan seafood market, China, and in the first month, it caused 360 fatalities and over 20 000 suspected cases (Khan et al., 2020). Researchers revealed that the genome of SARS-COV-2 is 80% identical to Severe Acute Respiratory Syndrome (SARS)-like bat CoVs

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and the cleavage site is similar to bird flu which has shown easy transmission in humans (ScienceDaily, 2020; Wu et al., 2020). It is thought that probably the virus transmitted from the bat and after genetic transformation, it achieved the ability to attack humans (Benvenuto et al., 2020). This virus can be transmitted from person to person by respiratory droplets like SARS (J. Chen, 2020). Moreover, this virus can transmit by direct contact of infected individuals. In some cases, indirect contacts like fomites and shared things of affected individuals are also shown as a cause of infection by this virus (Pung et al., 2020). The virus SARS-CoV-2 has more transmissibility than Middle East Respiratory Syndrome (MERS). The R0 (R naught) for MERS was less than 1, where the reproduction number for COVID-19 was estimated from 2.24-3.58 (Bauch & Oraby, 2013; Zhao et al., 2020). After the transmission in the human body, the virus passes an incubation period. This period was estimated around 6.4 days (95% credible interval 5.6-7.7) by a cohort study on travelers from Wuhan(Backer et al., 2020). The WHO indicated 1-14 days as the incubation period mostly the first five days for SARS-CoV-2 (WHO, 2020b).

To date, typical clinical symptoms of people affected by SARS-CoV-2 are cough, shortness of breath, fever, chest pain, headache, muscle ache, sore throat, diarrhea, rhinorrhea, nausea and vomiting (F. S. Wang & Zhang, 2020). Currently, this virus has spread over 213 countries, with 152,551 deaths recorded till April 19th, 2020 (WHO, 2020c). Case fatality rate (CFR) of COVID-19 is high among developed countries. For instance, 17.66% in France followed by the United Kingdom (13.4%), Italy (13.22%), Spain (10.44%), China (5.5%) and the United States (4.73%) (WHO, 2020c).

Vaccine or specific anti-viral treatment for COVID-19 has not yet been shown to be effective. The development of treatments may require months or years, which suggests a more immediate treatment or control mechanism should be found if possible (D. hai Zhang et al., 2020). So, a better understanding of risk factors and identifying or more promptly treating patients in high-risk groups is crucial to decrease the mortality rate (T. Chen et al., 2020a). Besides, to keep our global people healthy and secure from the infectious disease, it is essential to identify prevention strategies and treatment options to treat the disease effectively (Dexler, 2010).

Several studies have captured clinical sign symptoms, pathogenesis & mood of transmission of COVID-19 (J. Chen, 2020; N. Chen et al., 2020; W. Yang et al., 2020). Though risk factors are mostly unknown, some studies also identified the risk factors and preventive measures of the disease (Peeri et al., 2020; F. Zhou et al., 2020). Moreover, due to publishing large numbers of paper on similar topics of COVID-19 make the readers confused. Therefore, our current study aims to provide aggregated data on risk factors & preventive measures of COVID-19 from published studies around the world. Also, this systematic review tries to find the evidence on preventive measures, the challenges to control the disease and drug options available for COVID-19. We examined the study characteristics, clinical & epidemiological data, and available drug options for the treatment of COVID-19 from the study. The specific review objectives were: (1) to determine risk factors known till date; (2) to identify preventive measures and the challenges to control the disease; (3) to list out the available drug options to treat Coronavirus disease.

METHODS

Search Strategy

We systematically utilized the PubMed database to identify articles related to COVID-19. "Coronavirus", "Novel Coronavirus", "2019-nCov", "2019 novel coronavirus", "n Coronavirus", "Covid-19","SARS-CoV-2","severe acute respiratory syndrome coronavirus 2", “Wuhan coronavirus" were used as search term. The “OR” Boolean operator was used to combine the category (Virus and disease). Further, we filtered the search to literature related to humans, having full text, in English and were published from December 1st, 2019 to March 31st, 2020. In addition, Center for Disease Control and Prevention (CDC), WHO report on COVID-19, were accessed to get updated information and to get real-time statistics on COVID-19.

Inclusion Criteria

We included the original published studies based on the following inclusion criteria: (1) studies had information on risk factors or preventive measures or challenges to control COVID-19 or current drug options for coronavirus disease; (2) Studies published from December 31st, 2019 to March 31st, 2020; (3) Studies having epidemiological or clinical data related to humans and virus, excluded studies related to virus structure and diagnosis of disease.

Exclusion of Studies

A total of 550 studies were screened out. We found 547 studies in PubMed till 31st march, 2020 and 3 studies were collected from reference screening. Among them, 427 studies were excluded which did not meet our inclusion criteria. A total of 123 studies were screened out, where 88 studies were excluded due to letter, comments, correspondence, and reviews. Finally, 35 studies were selected for qualitative synthesis. However, two studies were excluded during analysis because of full texts of the-

se articles could not be found.

Data Extraction

Most of the included studies were published from China as the pandemic started from Wuhan, China and published in March 2020. We tried to obtain the information regarding risk & protective factors, prevention, challenges to control and current anti-viral treatment to resist this pandemic. Mainly the title and abstract were the screening point to select desired studies. However, in some cases, result and method part also screened to get a deep understanding of the studies. We extracted the following information from included 33 full texts available full text articles: (1) author, publication date; (2) Title; (3) Study design; (4) Risk factors; (5) preventive measures; (6) Challenge to control the disease; (7) Drug options for the treatment COVID-19.

Analysis Plan

We collected & listed out the studies in a table (Table 1). The information from the studies was added with the respective title of the study. The table was divided into four parts, including risk factors, preventive measures, the challenge to control and drug options to treat COVID-19. The tabulated information arranged the result section. Where some studies provided information related to risk factors, few discussed the preventive measures and challenges to control the disease and some listed the available drug options for COVID-19. From which we synthesized and analyzed the findings. We tried to find out the relationship within and between studies and overall assessment of the robustness of the evidence. The PRISMA flow diagram described by Liberati et. al.is shown in Figure 1 (Liberati et al., 2009).

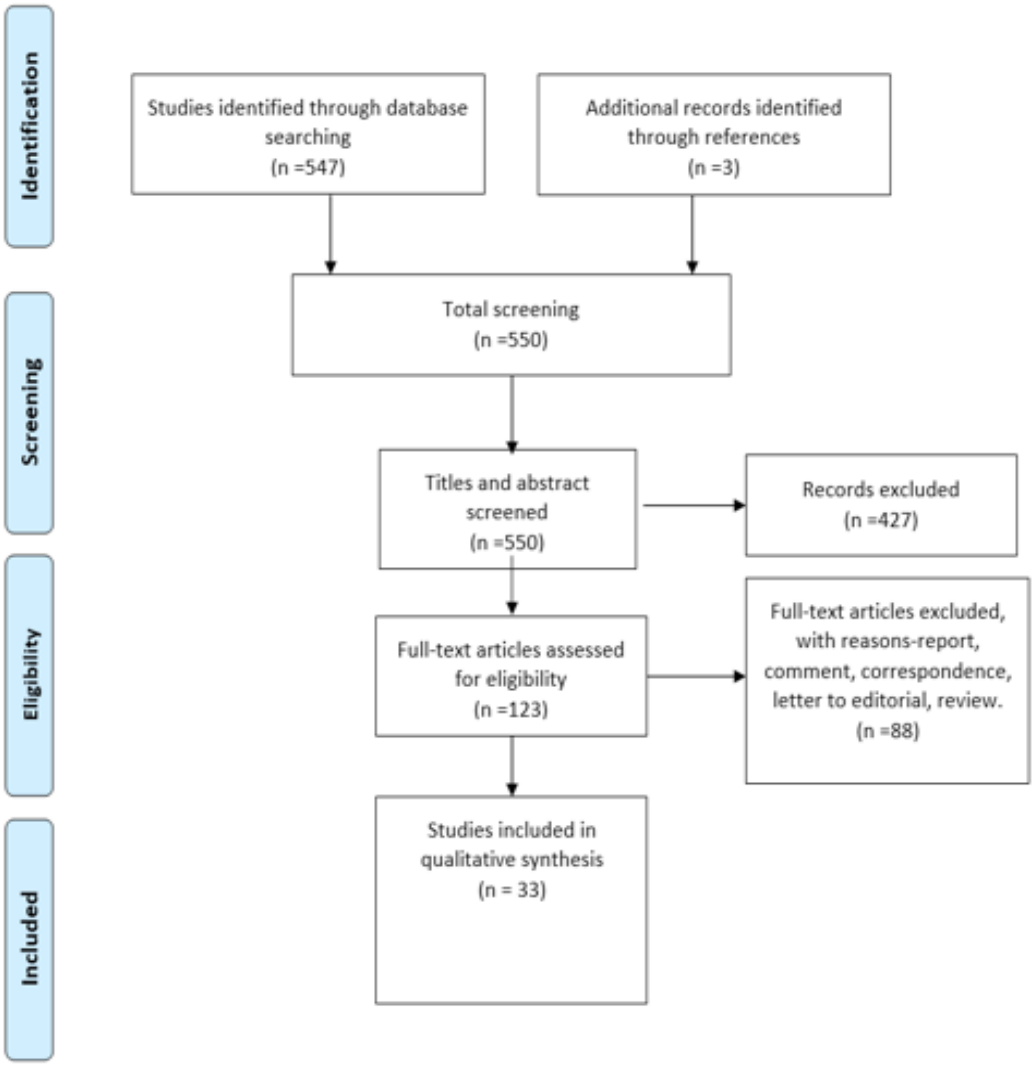

Figure 1. Flow Diagram Showing Inclusion of the Studies for Analysis.

RESULTS AND DISCUSSION

Risk Factors

TThe COVID-19 pandemic is ongoing. Within a short period of time, it is difficult to predict risk factors of the disease. Though different studies considered some factors as the risk of COVID-19. These risk factors are extracted from the studies published recently. Interactions between humans and animals and the poor level of environmental biosecurity increases the risk of the emergence of new zoonotic diseases (H.-Y. Li et al., 2020). Human-animal interaction just incepts the zoonotic disease like COVID-19. In January2020, in Illinois, the USA, the first case of COVID-19 was identified to a woman who had traveled to China. Her husband was further diagnosed with the virus due to prolonged, unprotected exposure with her wife (Ghinai et al., 2020).

Being male and age below 40 or above 60 years old with Covid-19 are at higher risk of severe cases and need to ventilate or be admitted in intensive care units (ICU) or ultimate death (G. Zhang et al., 2020). A cohort study in Wuhan reported being older is one of the major risk factors for this disease. It also indicated that a higher sequential organ failure assessment (SOFA) score or organ dysfunction score during admission related to the death of patients (F. Zhou et al., 2020). In addition, having hypertension make the patients more vulnerable (N. Chen et al., 2020; Shi et al., 2020). Patients who had a previous history of cardiovascular cerebrovascular disease and other complex diseases were associated with critical illness than patients without such diseases (N. Chen et al., 2020; T. Chen et al., 2020b).

Table 1. Data synthesis from included studies

Title	Author; Year; and Study Location	Study Design	Risk Factors	Preventive Measures	Drugs Options for COVID-19	Challenges to Control
A qualitative study of zoonotic risk factors among rural communities in southern China	Li HY et al.; March 2020; China.	Qualitative study	Human-animal interaction can increase the possibility of zoonotic disease emergence. Lack of environmental biosecurity concern as free-range allowed interactions between domestic and wild animals.	Not reported	Not reported	Not reported
First Known Person-To-Person Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in the USA	Isaac Ghinai et al.;	Case reports	This article suggests that prolonged and unprotected exposure with symptomatic COVID-19 patients might result in a person to person transmission.	Not reported	Not reported	Not reported

Title	Author; Year; and Study Location	Study Design	Risk Factors	Preventive Measures	Drugs Options for COVID-19	Challenges to Control
Clinical Course and Risk Factors for Mortality of Adult Inpatients with COVID-19 in Wuhan, China: A Retrospective Cohort Study	Fei Zhou et al.;	Retrospective Cohort Study	In virus shedding period it might cause recurrent infection without isolation and anti-viral therapy. The potential risk factors of older age, high Sequential Organ Failure Assessment score (SOFA).	Not reported.	Not reported	Prolong (37 Days) viral shedding was observed
Analysis of Clinical Characteristics and Laboratory Findings of 95 Cases of 2019 Novel Coronavirus Pneumonia in Wuhan, China: A Retrospective Analysis	Zhang G et al.;	Retrospective Analysis	Age below 40 or above 60 years old, male, lower platelet and higher Creatinine level count also seemed related to severe 2019 novel coronavirus pneumonia and composite endpoint.	Not reported	Not reported	Not reported
Host Susceptibility to Severe COVID-19 and Establishment of a Host Risk Score: Findings of 487 Cases Outside Wuhan.	Yo Shi et al.;	Retrospective cohort	Male elderly age patients with hypertension have a risk of developing COVID-19.	Not reported	Not reported	Not reported

Title	Author; Year; and Study Location	Study Design	Risk Factors	Preventive Measures	Drugs Options for COVID-19	Challenges to Control
Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study	Nanshan Chen et al.; January 2020; China.	A retrospective study	2019-nCoV is more likely to infect older adult males with chronic co-morbidities than female.	Not reported	Not reported	Not reported
Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study	Chen T et al.; March 2020; China.	Retrospective study	Both pulmonary and systemic inflammation, acute respiratory distress syndrome and type I respiratory failure, acute cardiac injury and heart failure may also contribute to the critical illness state associated with high mortality.	Not reported	Not reported	Not reported
Immediate Psychological Responses and Associated Factors During the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic Among the General Population in China	Chuiyan Wang et al.; March 2020; China	Cross-sectional	Not reported	Lower psychological impact (stress, anxiety, and depression) is associated with accurate up-to-date specific health information and with specific protective measures (e.g., wearing a mask, hand hygiene).	Not reported	Not reported

Title	Author; Year; and Study Location	Study Design	Risk Factors	Preventive Measures	Drugs Options for COVID-19	Challenges to Control
Effects of Media Reporting on Mitigating Spread of COVID-19 in the Early Phase of the Outbreak	Zhou WK et al.; March 2020; China	Cross-correlation analysis	Not reported	While in the initial stage of the outbreak, to curb the spread of COVID-19, media coverage can be considered as an effective way, with insufficient resources and data.	Not reported	Not reported
Corona Virus (COVID-19) "Infodemic" and Emerging Issues through a Data Lens: The Case of China	Jinling Hua et al.; March 2020; Japan	Data analysis.	Not reported	Humanitarian issues need to prevail over other priorities and giving correct and timely information with good governance and citizen participation, factors to key to success over combating COVID-19.	Not reported	Not reported
Investigation of Three Clusters of COVID-19 in Singapore: Implications for Surveillance and Response Measures	Rachael et al.; March 2020; Singapore	Descriptive study	Not reported	To minimize widespread transmission enhanced surveillance and contact tracing is important	Not reported	Not reported
2019-nCoV: The Identify-Isolate-Inform (3I) Tool Applied to a Novel Emerging Coronavirus	Kristi L et al.; January, 2020; Singapore	Descriptive study	Not reported	Identify, Isolate, and Inform (3I) tool for preventing the spread of COVID lesson learned from Ebola	Not reported.	Not reported

Title	Author; Year; and Study Location	Study Design	Risk Factors	Preventive Measures	Drugs Options for COVID-19	Challenges to Control
Characteristics of COVID-19 Infection in Beijing	Sijia Tian et al.; February 2020; China	Descriptive study	Not reported	To prevent COVID-19 infection early isolation of patients should be focused, and quarantine for close contacts and communities are also needed. The median incubation period was 6.7 days.	Not reported	Not reported
Evaluation of the Effectiveness of Surveillance and Containment Measures for the First 100 Patients with COVID-19 in Singapore - January 2nd –29 February, 2020	Yixiang et al.;	Descriptive study	Not reported	Rapid identification and isolation of cases, quarantine of close contacts, and active monitoring of other contacts have been effective in suppressing expansion of the outbreak	Not reported	Not reported
Effect of delay in diagnosis on transmission of COVID-19	Rong XM et al.;	Dynamic modelling	Not reported	Improving the richness of diagnostic resources and diagnosis efficiency can shorten the peak time, new infection, and new confirmed cases.	Not reported	Not reported

Title	Author; Year; and Study Location	Study Design	Risk Factors	Preventive Measures	Drugs Options for COVID-19	Challenges to Control
Passengers' Destinations from China: Low Risk of Novel Coronavirus (2019-nCoV) Transmission into Africa and South America	Najmul Haider et al.; February, 2020; UK	Cross-sectional	Not reported	To migrate future spread of diseases, increase public health response is needed with early case recognition, isolation of identified case, contract tracing, targeted airport screening, and vigilance of health workers.	Not reported	Not reported
Active Monitoring of Persons Exposed to Patients with Confirmed COVID-19 — United States, January–February 2020	Rachel et al.; March 2020; USA	Case Reports	Not reported	To migrate the community spread of SARS-CoV-2, patients with their household members and health care providers should strictly follow prevention and infection control measures combination with contact tracing activities	Not reported	Not reported
A Mathematical Model for the Novel Coronavirus Epidemic in Wuhan, China	Yang CY et al.;	Mathematical modelling	Not reported	These analytical and numerical results indicate that the coronavirus infection would remain endemic, which necessitates long-term disease prevention and intervention programs.	Not reported	Not reported

Title	Author; Year; and study location	Study design	Risk factors	Preventive measures	Drugs options for COVID-19	Challenges to control
Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia.	Li Q et al.;	A descriptive study	Not reported	Not reported	Not reported	The mean incubation period was 5.2 days, the epidemic doubled in size every 7.4 days, the basic reproductive number was estimated to be 2.2
Spatial -temporal distribution of COVID-19 in China and its prediction: A data -driven modeling analysis	Rui Huang et al.;	Data driven modeling analysis	Not reported	Not reported	Not reported	Calculated reproduction number R for the range of 2.23-2.51
Data-based analysis, modelling and forecasting of the COVID-19 outbreak	Rosso L et al.; March 2020; Italy	Model based data analysis study	Not reported	Not reported	Not reported	The estimated average value of R0 was found to be ~2.6 based on confirmed cases
Feasibility of Controlling COVID-19 Outbreaks by Isolation of Cases and Contacts	Joel Helwell et al.; February 2020;	Mathematical analysis	Not reported	Not reported	Not reported	When the basic reproduction number (R0) was 2.5 to 3.5 and more transmission before symptom onset, then the probability of controlling outbreaks decreases with the number of initial cases.

Title	Author; Year; and study location	Study design	Risk factors	Preventive measures	Drugs options for COVID-19	Challenges to control
Isolation, Quarantine, Social Distancing and Community Containment: Pivotal Role for Old-Style Public Health Measures in the Novel Coronavirus (2019-nCoV) outbreak.	Wilder-Smith A et al.; March 2020; UK	Perspective issue	Not reported	Not reported	Not reported	Isolation, quarantine, social distancing, and community containment will not be sufficient if the patients are asymptomatic as it reports as old-style public health measures
Estimating the Asymptomatic Proportion of Coronavirus Disease 2019 (COVID-19) Cases on Board the Diamond Princess Cruise Ship, Yokohama, Japan, 2020	Kenji et al.; March 2020; Japan	A descriptive study	Not reported	Not reported	Not reported	It was observed that in Diamond Princess cruise ships, Japan 17.9% cases with 95% credible intervals 15.5-20.2% were asymptomatic
Effectiveness of Airport Screening at Detecting Travelers Infected with Novel Coronavirus (2019-nCoV)	Quilty BJ et al.; 2020 February; UK	Descriptive study	Not reported.	Not reported	Not reported	Airport screening by thermal scanner could prove as an ineffective strategy to prevent infected person's mobility in different regions. Which ultimately increases wide transmission risk.

Title	Author; Year; and study location	Study design	Risk factors	Preventive measures	Drugs options for COVID-19	Challenges to control
Learning from the Past: Possible Urgent Prevention and Treatment Options for Severe Acute Respiratory Infections Caused by 2019-nCoV.	Jared S Morse et al.; February, 2020; USA	Computational analysis	Not reported	Not reported	An ACE2-based peptide, remdesivir, 3CLpro-1 and a novel vinylsulfone protease inhibitor can be the useful treatment approach for the COVID-19 patients.	Not reported
Tilorone: A Broad-Spectrum Antiviral Invented in the USA and Commercialized in Russia and beyond	Ekins s et al.;	Data analysis	Not reported	Not reported	Deserves further reassessment in light of corona virus pandemic	Not reported
Anti-HCV, nucleotide inhibitors, repurposing against COVID-19	Abdo A et al.; February, 2020; Saudi Arabia	Computational analysis	Not reported	Not reported	Sofosbuvir, Ribavirin, and Remdisivir can be used against the new strain of coronavirus that emerged with promising results	Not reported
Traditional Chinese medicine: an effective treatment for 2019 novel coronavirus pneumonia (NCP).	DU HZ et al.; March, 2020; China	Data analysis of TCM	Not reported	Not reported	Traditional Chinese medicine has exhibited decent effect in the fight against Novel Corona Pneumonia.	Not reported

Title	Author; Year; and study location	Study design	Risk factors	Preventive measures	Drugs options for COVID-19	Challenges to control
Clinical characteristics and therapeutic procedure for four cases with 2019 novel coronavirus pneumonia receiving combined Chinese and Western medicine treatment	Wang. Z et al.; February 2020; China	Clinical study	Not reported	Not reported	Lopinavir/ ritonavir, arbidol and SFJDC report significant improvement in pneumonia on the base of supportive care	Not reported
Case of the Index Patient Who Caused Tertiary Transmission of Coronavirus Disease 2019 in Korea: The Application of Lopinavir/ Ritonavir for the Treatment of COVID-19 Pneumonia Monitored by Quantitative RT-PCR	LimJ. et al.; February 2020; Korea	Clinical study	After isolation patient-reported psychiatric symptoms such as insomnia, suicidal thoughts, depression, and also experienced stress from media reports about COVID-19	Not reported	Reduced viral loads and improved clinical symptoms were observed after treatment with lopinavir/ritonavir	Not reported
Diagnosis and clinical management of severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) infection: an operational recommendation of Peking Union Medical College Hospital (V2.0)	Thisheng Li et al.; March 2020; China	Model based study	Not reported	Not reported	For general treatment, supply of energy and fluid can be effective but hypoxemia and symptoms with ARDS patients should be treated with oxygen therapy and protective ventilation strategy.	Not reported

Title	Author; Year; and study location	Study design	Risk factors	Preventive measures	Drugs options for COVID-19	Challenges to control
					Lopinavir/ ritonavir can be used as an anti-viral treatment. Still, for severe patients at an early-stage glucocorticoid, for critically ill patient human immunoglobulin and oral antibiotics for community-acquired pneumonia are suggested in this article.	

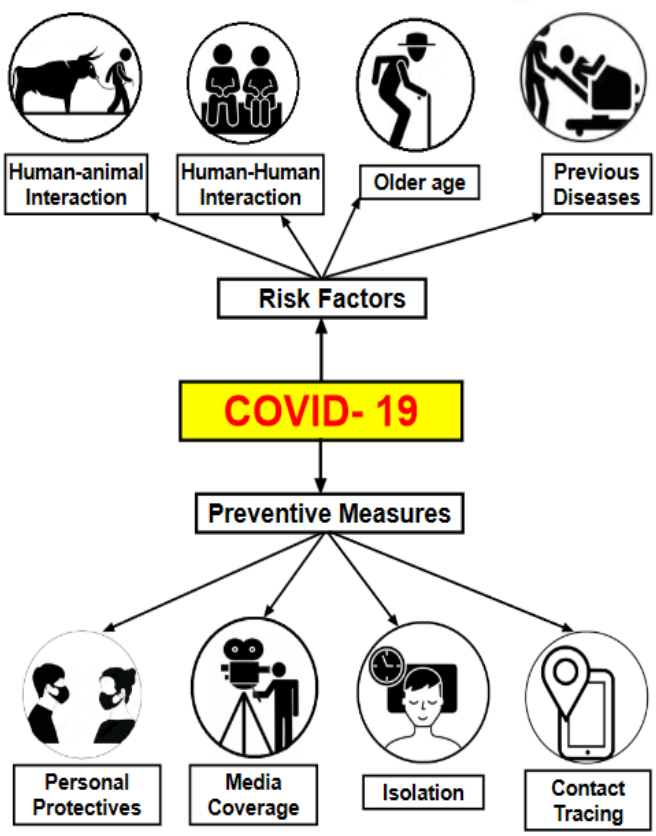

Figure 2. Graphical visualization of risk factor and preventive measure against SARS-CoV-2 to prevent further transmission.

Preventive Measures and Challenges to Control

Some preventive measures have been mentioned by studies on coronavirus side by side of risk factors of COVID-19. Personal hygiene etiquette could be effective against noble coronavirus. For instance, washing hands with alcohol-based detergent or soap, avoiding mouth-nose contact, sneezing, and coughing on tissue or elbow, wearing surgical masks, and maintaining distance from symptomatic respiratory persons. These types of personal precautionary measures and update and dissemination of authentic information on disease spread and treatment were also effective against depression, anxiety and stress during pandemic situations (C. Wang et al., 2020). Media coverage on COVID-19 to aware the public at rudimentary stages of outbreak carries an impact on reducing transmission of disease (W. Zhou et al., 2020). Moreover, active community participation and effective governance are essential to prevent the spread of disease (Hua & Shaw, 2020). Due to the high transmissibility of this virus in the community setting, contact tracing and surveillance strategy should be considered strictly to mitigate community transmission (Pung et al., 2020).In addition, effective management of COVID-19 by modified (3I) tools (originally used for Ebola management) Identify, Isolate and Inform could be vital resources for healthcare providers (Koenig et al., 2020). Fast isolation and quarantine of closely contacted person in family and community is essential for reducing wide transmission (Tian et al., 2020; Ng et al., 2020). Furthermore, rapid diagnosis, reducing of diagnosis waiting time and isolation onset time could be effective in reducing reproduction number, transmission risk and eventually prevent Covid-19 endemic (Rong et al., 2020). Airport screening, public awareness and public health workers prompt response could help to reduce the severity of the pandemic (Haider et al., 2020). Combined efforts on prevention and infection control by healthcare providers, patients and their family members are necessary to combat with the disease (Burke et al., 2020). A study emphasized long term intervention and preventive measures to fight against the disease (C. Yang & Wang, 2020).

Still there are challenges to control this pandemic by COVID-19 virus. Some studies estimated reproduction number (R0) is 2.2-2.6 (Anastassopoulou et al., 2020; Huang et al., 2020; Q. Li et al., 2020). A study warned when the reproducibility is between 2.5 and 3.5, contact tracing and isolation become ineffective (Hellewell et al., 2020). Again, isolation of suspected and confirmed Covid-19 cases is essential for resisting transmission. However, this public health measure becomes ineffective when patients are asymptomatic (Wilder-Smith & Freedman, 2020). It was observed that in Diamond Princess cruise ships, Japan 17.9% cases with 95% credible intervals, 15.5-20.2% were asymptomatic (Mizumoto et al., 2020). Due to asymptomatic cases and a specific incubation period of 2019-nCov, airport screening by thermal scanner could prove as an ineffective strategy to prevent an infected person's mobility in different regions. Which ultimately increases wide transmission risk (Quilty et al., 2020). Another challenge could be the viral shedding. A retrospective cohort study in Wuhan shows this virus can shed for 37 days long in a deceased person and about 20 days among survivors (F. Zhou et al., 2020).

Probable Drug Options for COVID-19

SARS-CoV2 receptor-binding domain, angiotensin-converting enzyme as well as membrane fusion, are an ideal target for vaccines and anti-viral treatment against SARS-CoV2 infection (Morse et al., 2020). Moreover, both the drugs statins and angiotensin receptor blocker counter endothelial dysfunction (Fedson et al., 2020). RdRp inhibitors are nucleoside analog, which inactivate exonuclease activity and effectively inhibit viral RNA replication (Morse et al., 2020). For instance, both remdesivir and chloroquine are broad-spectrum anti-viral drugs. At low-micromolar concentration, both drugs blocked virus infection. They also showed a high selectivity index (M. Wang et al., 2020). On the other hand, Tilorone activates innate Immunity pathways such as the RIG-I-Like receptor pathway (Ekins et al., 2020). In addition, a molecular docking model based upon WUHAN COVID-19 showed DX-184 and Sofosbuvir, remdesivir are potent drugs against Covid-19 (Elfiky, 2020). Moreover, 3CLpro-1, has an IC50 value against SARS-CoV of 200 nm and such potency is strong enough to combat towards the 2019-nCoV (Morse et al., 2020).

A retrospective study from China revealed that two out of three patients had significant improvement after treating with lopinavir/ritonavir (Kaletra®), arbidol, a traditional Chinese medicine(TCM), SFJDC (ShufengJiedu Capsule) (Z. Wang et al., 2020). Traditional Chinese Medicine (TCM) were widely recommended in china as the response rate was over 90% among of 214 cases in the clinic There and 88% patients were receiving TCM (DU et al., 2020).In addition, Lopinavir/ritonavir has been shown as a viral load reducer(Lim et al., 2020). According to the severity of diseases, patients should receive general treatment, empirical antimicrobial therapy, Intravenous immune globulin, Glucocorticoid therapy, anti-viral treatment, oxygen therapy (T. Li, 2020).

Discussion

By carefully considering published reports and systematically considering characteristics, our study evaluates risk factors, preventing measures & challenges to control of this, and also drug options for Covid-19. The source of SARS-CoV-2 is still unknown. Though it is primarily analyzed that the virus spread from the Hunan seafood market in China where different kinds of animals were sold. Scientists estimated more than 60% of known infectious disease and around 75% of the emergence of new infectious disease in humans is due to direct or indirect contact with animals (CDC, 2020c). Although, the virus rarely gets the ability to adapt and spread within new host without prior exposure. However, frequent exposure or due to acquisition of variations leads to find a new host and which ultimately results in devastating outbreaks (Parrish et al., 2008).

Due to the high transmissibility of this virus, it can attack those with unprotected and prolong exposure with the infected one. The World Health Organization (WHO) emphasizes avoiding close contact, maintain physical distance and unprotected contact (WHO, 2020a). According to our findings, being male with older age and having co-morbidity increases the score of attack by the newest emerged virus. Older male patients are at higher risk to coronaviruses like SARS, MERS and now SARS-CoV-2. However, the presence of 'X' chromosome and sex hormones in women provides strong natural immunity and make them less susceptible to this virus (Channappanavar et al., 2017; Jaillon et al., 2019; Rahman & Sarkar, 2019). Our findings from different studies are similar to an early-stage study on the SARS virus and MERS virus. Which reported male sex, people with older age and having co-morbidity like hypertension, diabetes, cardiovascular diseases and other chronic diseases are at more risk than others (Assiri et al., 2013; Fehr et al., 2017). These factors are considered as risk factors in the regular updating of the Center for disease control and prevention (CDC) (CDC, 2020b).

SARS-CoV-2 is a virus that can easily transmit through person to person more precisely when a healthy person is exposed to an infected person. Our findings from different studies recommend personal hygiene etiquette (PHE) is essential to prevent this disease or reduce the transmission. It is observed that hand hygiene is one of the effective strategies to reduce infectious diseases and transmission of disease (Han, 2018; Dexler, 2010). Personal protection is essential and can play effective roles in reducing transmission. SARS-CoV-2 can also enter through different parts of the human body like previous human coronavirus (Leung et al., 2020; Raboud et al., 2010).Additionally, Our finding suggests that using this kind of personal protection helps to decrease anxiety and psychological impact during the epidemic (C. Wang et al., 2020).

Our findings also enumerate accurate information helps to maintain psychological stability. In this case media can play vital roles to provide authentic information about the pandemic. It can delay the epidemic peak and reduce the severity of the outbreak. Not only we can delay the epidemics but also regular and prompt updates of the pandemic by administrative authority helps the health authority to take action immediately along with updating researchers of the world about an unknown fact (Gralinski & Menachery, 2020; Xiao et al., 2015). However, media is not only the catalyst for inhibiting or preventing this disease. If we want to win this fight against this unseen enemy, combine effort of the community, government along with public health workers is essential. The community should plan for vulnerable peoples who demand humanitarian assistance during pandemic like Covid-19. Active participation and engagement of community people will help to mitigate the pandemic attack (Blendon et al., 2008).

Like SARS and MERS-CoV, SARS-CoV-2 is a respiratory infection, and this disease also spreads through respiratory droplets. Identifying the spreader, isolate the close contacts and inform the local health authorities are the utmost emergency to stop transmission of disease. If the spreader is not detected quickly, then he will spread to other close contacts. Contact tracing, quick identification as well as quarantine or isolation of close contacts are essential to stop the chain of transmission (CDC, 2020a). We have to face challenges to defend the COVID-19. The basic reproduction number indicates the transmissibility of a virus. A review on reproduction number(R0) of coronavirus shows it is ranging from 1.4-6.49 which is higher than SARS and MERS virus (Liu et al., 2020). Our findings also warned higher transmissibility of this virus. However, the estimated R0 can be miscalculated or misinterpreted due to biological, environmental and social effects on this value (Delamater et al., 2019).

Another challenge could be the asymptomatic characters of this disease. An asymptomatic patient can become a super spreader in the community. Who can infect their close contact, it is observed in a case report mother and son were asymptomatic cases while the father was an active case of COVID-19. Strict vigilance is key here to mitigate transmission (Pan et al., 2020; Yu & Yang, 2020). Along with asymptomatic cases, coronavirus challenged us by its shedding. It is common coronavirus can shed in the blood or plasma of human, which increases the risk of transmission through blood product. In addition,

without monitoring and optimum anti-viral therapy to the patient after discharge from the hospital can increase the transmission chain (Chang et al., 2020; F. Zhou et al., 2020).

Until now there are no certain drugs available for COVID-19 yet. Researchers are trying to establish a drug in this outbreak based on the clinical symptoms of the patients affected by this virus. As this virus resembles the genome sequence of SARS-CoV and MERS-CoV, previous medicinal studies, along with existing databases, are conducive to establishing a new drug for COVID-19. Moreover, based on genome structures of the disease as well as redevelopment of the existing drugs are common target features for researchers to establish a drug to combat COVID-19. Broad-spectrum anti-viral drugs are used as a standard treatment for this virus. For instance, remdesivir is one of the common drugs that have been used for COVID-19 due to its high anti-viral activity. China is negotiating with Gilead for the possible use of this drug to treat the virus. Combinational therapy, for instance, remdesivir and 3CLpro-1, lopinavir/ritonavir have been used to treat the viruses (N. Chen et al., 2020; Lim et al., 2020; H. Lu, 2020; Thompson, 2020). Though, one study from China showed that the lopinavir and ritonavir combination did not have a significant outcome compared to single therapy (Agrawal et al, 2020). Another randomized trial also reported recently in severe cases, and these drugs have no benefit for the primary endpoint (Stower, 2020). Besides, TCM is highly recommended by the Govt. of China to treat individual patients as TCM exhibits a decent effect against this virus. It would be an option to treat the viruses apart from China to the rest of the world. It is observed that TCM can reduce severe symptoms of the disease and would be an option of interest for the world as China (Rasmussen et al., 2020). However, numbers of anti-virals are under clinical trials like chloroquine, arbidol, remdesivir, and favipiravir. However, the efficacy and safety of these drugs are in the queue for rigid confirmations to treat solely in COVID-19 through various clinical trials. For a sustainable solution, vaccines are essential (Dong et al., 2020; S. Lu, 2020).

Several global coronavirus epidemics served as a reminder of how novel pathogens can rapidly emerge and spread through the human population and cause a public health crisis. Without proper treatment, these options are not enough to hold the current and upcoming outbreaks. The combined role of the internet of things and related technology can play a vital role in preventing zoonotic infection by smart disease surveillance systems (Peeri et al., 2020). In 2003, SARS-CoV was successfully controlled by taking appropriate steps like increased awareness, education, and vigilance to infection control procedures (Fowler et al., 2004). So, strict vigilance, heightened prevention, control policies, intervention strategy should follow strictly to prevent further transmission and spread of SARS-CoV-2. Besides, probably it is not the last pandemic, and these outbreaks help us to learn about the responses to the outbreak in the different political systems and suggest that the world needs total political commitment to pandemic preparedness (Kickbusch & Leung, 2020). As the pandemic is still ongoing, further research should be done to gather more data on unknown's challenges and its solution.

We have enlisted the risk factors, preventive measures, challenge to control the disease and available drug options to treat the disease till date. From the best of our knowledge, it is the first systematic review on the existing challenges and solutions related to COVID-19. However, we limited our search from the PubMed database. However, we tried to provide available resources and strategies published throughout the world within a short period of time.

CONCLUSION

This review tries to find out existing information about risk factors, preventive measures, the challenges to control the disease and available drug options. When a pandemic is existing in this modern era, combine effort from health professionals, researchers, media, and community are essential to mitigate and ultimately stop the pandemic. More studies and data are urgently needed from around the world on preventive measures and available resources to tackle this pernicious virus. Human-animal interaction, male, aged people with co-morbidity are at more risk of this disease. Personal hygiene etiquette (PHE), media coverage, 3I tools identify, isolate, and inform are preventive measures though asymptomatic cases, high reproducibility of virus and viral shedding could challenge us more in future. Antiviral drugs like remdesivir, chloroquine, lopinavir/ritonavir, and traditional Chinese medicine (TCM) could be an option against COVID-19 until vaccine development.

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