Review Article

Coronavirus Disease 2019 (COVID-19): An Update on Infection, Diagnosis, Control and Prevention

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Abstract

The severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), the causative agent of COVID-19 and more than two million people have infected by the virus worldwide. Human-to-human transmission is the main reason for its rapid spread internationally. Published data from the recent studies on COVID-19 were collected from different official websites and SCI and non-SCI journals, following electronic retrieval process. The SARS-CoV-2 showed several life-threatening infections, in the community as well as health care settings. Up to date, there is no specific drug of choice to treat COVID-19. As per the WHO suggestion, in order to combat COVID-19 related global clinical issues, some mitigation strategies including self-isolation recommended. This review-based study inspects the issues on COVID-19 and its emerging global infection burden, epidemiology, detection, diagnosis, clinical symptoms, control and prevention.

Keywords: Coronavirus; SARS-CoV-2; Severe Acute Respiratory Syndrome; Coronaviral Pneumonia; Human-To-Human Transmission; COVID-19; Anti-Coronaviral Agents; Quarantine; Lockdown

Abbreviations

ACE2: Angiotensin-Converting Enzyme 2; ARDS: Acute Respiratory Distress Syndrome; CDC: Centers for Disease Control and Prevention; COVID-19: Novel Coronavirus Disease 2019; CT: Computed Tomography; CRP: C-Reactive Protein; GGO: Ground-Glass Opacity; hs-CRP: High-Sensitivity C-Reactive Protein; MERS: Middle East Respiratory Syndrome; RBD: Receptor-Binding Domain; RT-PCR: Reverse Transcription-Polymerase Chain Reaction; SARS: Severe Acute Respiratory Syndrome; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; UT's: Union Territories; WHO: World Health Organisation

Introduction

COVID-19 an emerging worldwide contagious disease, caused by a novel strain of coronavirus not previously recognized in humans and officially named as SARS-CoV-2 (novel β-coronavirus) by the International Committee on Taxonomy of Viruses [1]. Coronaviruses have a microscopic size (of about 65 - 125 nm in diameter) with a single-stranded RNA genome, belong to the family Coronaviridae in the order Nidovirales. Corona symbolises crown-like spikes (9 - 12 nm long [2]) on the external surface of the virus; thus, it was termed as a coronavirus [3]. Coronaviruses categorized into alpha (α), beta (β), gamma (γ), and delta (δ) subgroups. Maximum coronaviruses affect animals, consequently causes zoonotic transmission between animals and humans. To date, SARS-CoV-2 is latest one among seven known types of human coronaviruses [3,4] and its transmission dependent only on humans and there is no zoonotic transmission evidence up to the present date [5]. Based on the current scenario, SARS-CoV-2 is more infectious than other coronaviruses [6]. Other human coronaviruses are SARS-CoV and MERS-CoV, these have been identified as zoonotic were transmitted through civet cats (first reported in China, 2002) and dromedary camels (first informed in 2012 in Saudi Arabia) respectively, known to cause severe respiratory illnesses and even deadly [4]. An outbreak of SARS-CoV-2 (WHO recommended disease name: COVID-19 [1]) infection occurred in Wuhan, China (December 2019) showed closely related clinical symptoms like SARS-CoV and MERS-CoV including coronaviral pneumonia and ARDS [7].

During the construction of this review article, the virus is rapidly dispersing to many other regions over the globe. The number of cases has been increasing day by day, and as per WHO report on April 22, 2020, more than 24.7 lakhs confirmed cases, of these 169,006 deaths occurred globally showed a fatality rate of around 6.83% [8]. The exponential growth and transmission of SARS-CoV-2, cause effective spread to the other countries (including China, Italy, Spain, Japan, South Korea, Thailand, the USA, India etc.), appealing wide consideration all over the sphere and reflected as a pandemic by WHO on March 11, 2020 [9]. This review aimed to consider the pandemic COVID-19 characteristics in patients with new findings across the transmission, clinical symptoms and diagnosis, to know prompt treatment and preventive measures of this evolving, life-threatening infection.

Disease aetiology

According to Lu., *et al.* (2020) [10], SARS-CoV-2 was closely associated (approximately 88%) to two SARS-like coronaviruses related to bat (bat-SL-CoVZXC21 and bat-SL-CoVZC45) from Zhoushan, eastern China (2018) and were distantly allied to MERS-CoV and SARS-CoV of about 50% and 79%, respectively. Corona-

viral genome coded the spike (*S*) envelope protein among four key structural proteins that can bind with human ACE2 receptor which consequently supports to the fusion between the envelope and host cell membranes to help viral access into the host cell [11]. Research indicates α-CoV C-domains may alter to gain ACE2-binding capacity through divergent evolution, whereas divergent evolution and convergent evolution both occur subsequently for α-coronavirus NL63-CoV and β-coronavirus SARS-CoV C-domains to acquire ACE2-binding roles [12]. Previous literature proved that the versatile presence of ACE2 protein in many human organs like brain, lung (in alveolar epithelial cells), stomach, small intestine (in enterocyte cells), colon, spleen, liver, kidney, lymph nodes, thymus, bone marrow, nasopharynx including skin, arterial as well as venous endothelial cells, oral and nasal mucosa etc. These all mentioned organ and organ associated ACE2 surface protein might provide potential routes of entry for the SARS-CoV resembling viruses [13]. The SARS-CoV-2 poses high affinity to create S-protein - ACE2 binding may contribute to the spread from human to human. Several reports suggest that human-to-human transmission of coronaviruses also exaggerated by various factors, viz. viral replication competence, or virus modification/mutation rate and the host's immune response [14].
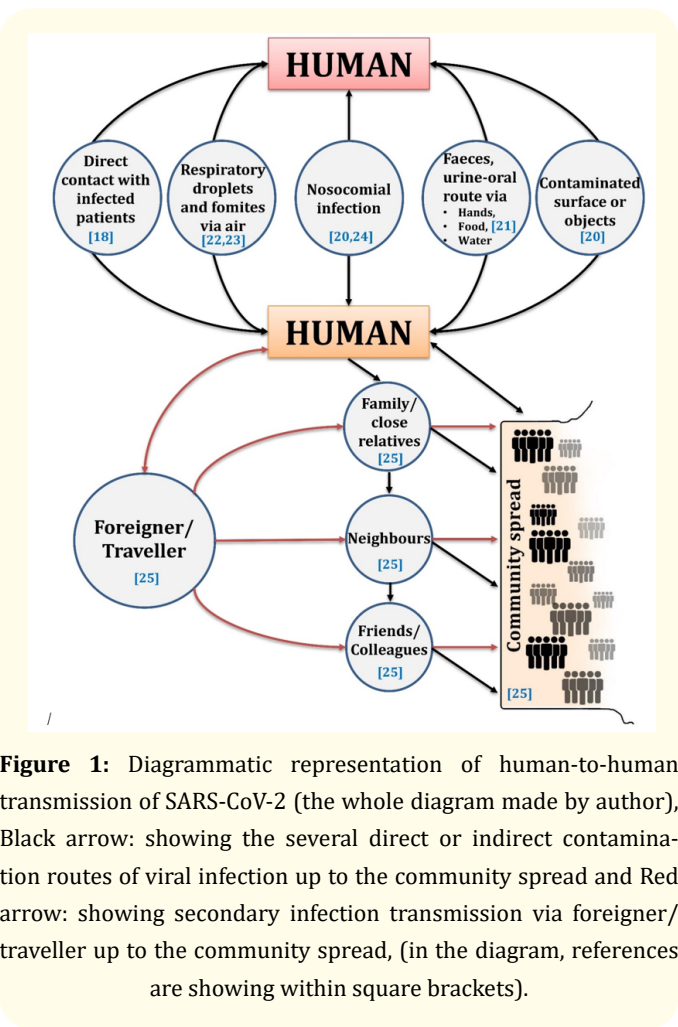
Transmission

The SARS-CoV-2 might be from initially introduced by bats (sold at the Huanan seafood market) and might have been spread to humans via pangolin [15] or other wild faunas [10,16] and later via human-to-human transmission occurred [17]. A recent investigation revealed that returning from epidemic areas significantly correlated with early and late period infection [18]. The most interesting report on the disease COVID-19 causing viral transmission is the virus may spread via a known asymptomatic carrier [19]. According to Doremalen., *et al.* (2020), SARS-CoV-2 can transmit via aerosol and fomite also, remain infectious dependent on the presence of viral content capacity (may remain active on surfaces up to days and in aerosols for hours) [20]. The previous study confirms the presence of COVID-19 causing live virus in the stool of patient that indicates the virus can also be spread through the faecal-oral path and consequently may cause infection by entering the respiratory mucosa, conjunctiva, oral cavity etc. [21]. Evidence of various probable routes of human-to-human transmission of SARS-CoV-2 summarized in figure 1.

Epidemiology summary

As per the current situation report (No. 93) circulated by the WHO on 22 April 2020 [8], calculated 2,471,136 confirmed COVID-19 cases informed globally (details in figure 2), of these, 84,287 cases from China; 2,04,178 cases from Spain; 7,76,907 cases from the United States of America and other countries in Europe, Eastern Mediterranean Region, South-East Asia, African Region also affected.

Several investigations showed, COVID-19 has an average incubation period of 3 days (range: 0 - 24 days), with the latent asymptomatic transmission [22]. Fan., *et al.* (2020) demonstrated the epidemiology of the outbreak of COVID-19 outside of Wuhan (China). Their research data establish statistically significant differences


Figure 1: Diagrammatic representation of human-to-human transmission of SARS-CoV-2 (the whole diagram made by author), Black arrow: showing the several direct or indirect contamination routes of viral infection up to the community spread and Red arrow: showing secondary infection transmission via foreigner/traveller up to the community spread, (in the diagram, references are showing within square brackets).

between patients who required care in the early and late stages of distinguished age and profession related divisions, but there was no significant score observed for patient sex (between male and female) or living location (between urban and rural areas) [18].

In India, a total of 19,984 COVID-19 cases [8] reported from 32 States/UTs [26]. Prime Minister of India called for 'Janata curfew' (lockdown) on 22 March and later extended up to 30 April 2020, instructed people to stay at home except those in essential services, implementing public led social distancing participations [8, 26]. Due to COVID-19 pandemic situation, mental health care is an immediate need for medical workers and public, who have been facing psychological problems (anxiety, depression, and stress) [27].

Clinical symptom spectrum

The clinical symptoms of COVID-19 are indicated nonspecific and were measured minimum 3 - 6 days required to generate detectable symptoms from the day of exposure [28]. Primarily nausea and diarrhoea may occur for a few days before common symptoms including fever (≤ 37.3 - >39°C [29]) and consequently cough, myalgia and fatigue may arise [23]. Research study advocated that the fever is dominant but not the final determining symptom of the infection. Several studies on COVID-19 patients indicates lower white blood cell counts, lymphopenia and thrombocytopenia, or thromboplastin activation and amplified C-reactive protein level [17,22,30]. Most of the patient showed upper respiratory tract infection with pneumonia [31]. Lung parenchymal and airway abnormalities were common in symptomatic patients, while asymp-
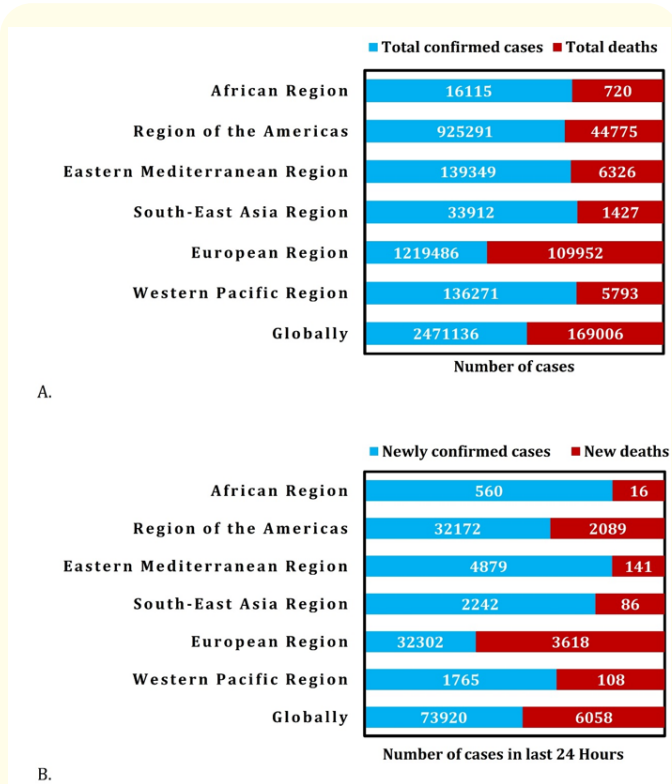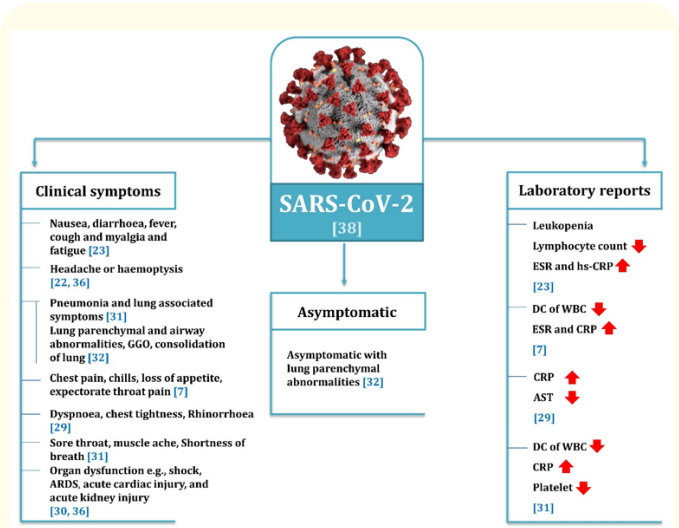
Figure 2: Areas with reported laboratory-confirmed COVID-19 cases and deaths (Data source: WHO report, 22 April 2020) [8]. A: represents total case report up to date, B: newly added cases in last 24 hours.

Figure 3: Diagrammatic view (made by author) of several clinical symptoms and laboratory report associated with COVID-19, Red upward arrow: showing the increased amount, Red downward arrow: showing a decreased amount. ARDS: Acute Respiratory Distress Syndrome; GGO: Ground-Glass Opacity; AST: Aspartate Aminotransferase; hs-CRP: High-Sensitivity C-Reactive Protein; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; WBC: White Blood Cell; DC: Differential Count (in the diagram, references are showing within square brackets).

tomatic cases showed lung parenchymal alterations on CT in up to 54% with a significant prevalence of GGO. On the other hand, consolidation of the lung was frequent in symptomatic patients [32]. Outcomes of CT imaging share numerous resemblances with previously discovered coronaviruses (SARS-CoV and MERS-CoV) [33]. Some more interesting investigation indicates infected aged men may show comorbidities with respiratory failure due to severe alveolar damage [31], but children appear to be at lower risk for COVID-19 than adults although some children and infants have been sick with COVID-19 [34]. Another report on pregnant women showed COVID-19 may increase the risk of preterm delivery, intrauterine growth restriction and spontaneous miscarriage [35]. SARS-CoV-2 may cause organ impairment and even death depending upon severity [30,36]. Limited data available from different locations over the globe demonstrated that anosmia or hyposmia and dysgeusia are symptoms may be related to the COVID-19 pandemic [37]. All the clinical symptoms and laboratory reports associated with COVID-19 portrayed in figure 3.

Detection and diagnosis

The prime need is to find recent travel or residence history or close association with people from outbreak location or COVID-19 positive individual in the past 14 days. After checking the exposure history, physical examination of severe clinical symptoms (2 - 3 in number) is the most considerable measure to detect suspected patient [39]. To detect COVID-19 pneumonia, NGS (next-generation sequencing), RT-PCR (real-time reverse-transcription-polymerase-chain-reaction) and chest CT scans are the foremost choices for clinicians [29]. The RT-PCR used as the reference standard for CO-

VID-19 infection with high accuracy [28]. The CT findings confirm the lesions in the peripheral zone of the lung, patchy GGO, GGO with consolidation and vascular thickening. According to imaging features in COVID-19 are nonspecific and can show initial chest imaging abnormality, subpleural and peripheral areas with GGO and consolidation [40]. Diverse molecular assays in the various country to detect the SARS-CoV-2 have been and are presently under progress using different gene targets viz. ORF1ab and N (China), RdRP, E, N (Germany), ORF1b-nsp14, N (Hong Kong), Pancorona and multiple targets and spike protein (Japan), N (Thailand), three targets in N gene (US) and two targets in RdRP (France) [41].

Prevention and control

Based on the current situation, prevention and control of COVID-19 must include prompt detection, diagnosis, treatment, and quarantine to avoid human-to-human spread as well as to reduce secondary contaminations up to the level of community transmission [42]. For COVID-19 patients specially controlled chambers are needed including single occupancy, negative pressure room with minimum six air alterations per hour, access to the room should be reduced and well-disciplined healthcare worker should enter the room [43].

Presently there are no specific drugs, vaccines, monoclonal/polyclonal antibodies available for SARS-CoV-2 but a previous study revealed chloroquine has the efficacy to glycosylate ACE2 receptor which helps to prevent SARS-CoV-ACE2 receptor binding and entry of infections [44]. We know that SARS-CoV-2 also shares the ACE2 pathway to initiate infection and may be inhibited by the way above mentioned [45]. Gao., *et al.* (2020) showed chloroquine phosphate could suppress the infection of COVID-19 pneumonia at low-micro-

molar concentration and decrease the length of treatment [46]. According to Wang., *et al.* (2020), SARS-CoV-2 is extremely sensitive to the high temperature that would prevent the virus from spreading but more specific studies are wanted to find accurate temperature dependency of its [36]. Artificial intelligence-based learning algorithms can be useful to find COVID-19 suspects, through a mobile phone dependent survey upon the quarantined population and it's a crucial preventive measure to stop new transmission from home quarantined COVID-19 positive persons to others [47]. Some investigators trying to find newer treatment regimen to inhibit coronaviruses including SARS-CoV-2, are briefly represented in table 1.

Before going to the worst situation, we should maintain some community mitigation strategies as follows:

I. Use of social distancing procedures to decrease contagious spread between people in the community and the prohibition of mass gathering may reduce the risk of transmission [59].

II. Restrictions in transport, including reduced national and international public transport without compromising essential need [60,61].

III. Voluntary or mandated quarantine of domestic associates is useful to hinder the disease spread [60]. Though there is no

Type	Name of agents	Administered against	Experimental outcomes	References
Synthetic/ Semisynthetic drugs	Combination of lopinavir/ ritonavir and interferon-β1b	MERS-CoV	MIRACLE trial in hospitalized patients with laboratory-confirmed MERS displayed standard supportive care	[48]
	Chloroquine	SARS-CoV-2	i. Alter virion assembly and budding, ii. Preventing the ACE2 - SARS-CoV-2 binding to target cells and iii. Replication cycle inhibited.	[49]
	Remdesivir and chloroquine	SARS-CoV-2	*In vitro* study using Vero E6 cells, showed effective % inhibition of virus and low cytotoxicity.	[50]
	Hydroxychloroquine and Azithromycin (an open label non-randomized clinical trial)	SARS-CoV-2	For virus elimination, Azithromycin-hydroxy-chloroquine combination therapy was significantly more efficient than hydroxychloroquine alone.	[51]
	Lopinavir-ritonavir combination (a randomized, controlled, open-label trial)	SARS-CoV-2	Treatment did not significantly accelerate clinical improvement but decrease mortality, or reduce throat viral RNA inoculum in patients.	[52]
	Teicoplanin	Laboratory prepared virus or pseudovirus, containing spike (S) gene of SARS-CoV-2	Required very low amount of 1.66 μM to inhibit 50% of viruses (IC_{50}).	[53]
Chinese medicines using herbs	*Radix astragali, Radix glycyrrhizae, Radix saposhnikoviae, Atractylodis macrocephalae Rhizoma, Lonicerae japonicae flos and Fructus forsythia*	SARS causing pathogens	Combination of traditional Chinese medicinal herbs can prevent SARS associated clinical symptoms.	[54]
Others	CTL-epitope based vaccine	SARS-CoV-2 structural proteins	IEDB epitope cluster analysis tool was used. CTL-epitope based vaccine showed high immunogenicity against SARS-CoV-2 structural proteins in terms of high HLA binding affinity, high TAP transport efficiency and high C-terminal proteasomal cleavage.	[55]
	Convalescent serum of human	SARS-CoV-2	Works in a prophylactic manner or passive antibody therapy involve preventing the virus.	[56]
	Microneedle array (MNA) delivered recombinant coronavirus vaccines	MERS-CoV and SARS-CoV-2	Coronavirus spike (S) protein-based MNA delivered recombinant vaccines can generate higher levels of a potent neutralizing antibody (after 2 weeks of immunization in mice).	[57]
	Saquinavir and Beclabuvir used with two receptor structure of AutoDock PDBQT format (Vina and SMINA)	SARS-CoV-2	Virtual Screening based prediction: Form complex and inactivates Mpro (Main protease) of SARS-CoV-2 displayed through the molecular docking method.	[58]

Table 1: Several experimental anti-coronaviral agents and their efficacy

TAP: Transporter Associated with Antigen Processing, HLA: Human Leukocyte Antigen, MIRACLE: MERS-CoV Infection treated with A Combination of Lopinavir/ritonavir and interferon-β1b, IEDB: Immune Epitope Database, CTL: Cytotoxic T Cell.

evidence of zoonotic transmission of SARS-CoV-2, to suppress the risk factor distance should be maintained from domestic as well as wild animals.

IV. To slow down the spread of SARS-CoV-2, country lockdown (for three to several weeks depending on the situation) displayed a significant effect in China where positive differences documented before and after the start of the lockdown period [61]. So, the other COVID-19 epicenters should follow the country lockdown strategy.

V. Use of preventive measures like frequently cleaning of hands with hand sanitizers (alcohol-based), hand wash or soap for self-use and disinfectants to manage the households recommended. Public awareness is essential and correlated to reduce the attack rate in terms of mitigating and delaying the COVID-19 pandemic [62].

VI. Wearing a mask is necessary if coughing or sneezing persists or in the period of association with suspected COVID-19 patients [63].

VII. Use of personal protective measures or PPE (personal protective equipment) viz. disposable or reusable goggles, face shields and isolation gowns are mandatory for healthcare workers [43].

VIII. Some fruit (citrus, pear, strawberry, carrot and yellow watermelon) juice should be consumed by COVID-19 patients to check their body temperature. However, selective vitamins (vitamin C, E and D) and antioxidant drugs also may enhance the immune system of COVID-19 patients [64].

IX. We have to go without unnecessary panic and communication with health experts is necessary to confirm real information beyond fake news and rumours [60].

X. Remarkable awareness is needed to eliminate falsified medical goods that claim to detect, prevent or cure COVID-19 [65].

Conclusion

Up to the time, there is no specific medicine to treat SARS-CoV-2, although few are in progress and particular drug or agents may be available soon. To control this situation community mitigation strategies along with clinical decision based medical care would be the preferable target for the early prevention and control of COVID-19.

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Conflict of Interest

Not applicable.

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