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# UNDERSTANDING THE CURRENT KNOWLEDGE GAPS AND THE FUTURE PERSPECTIVE OF COVID-19 INFECTIONS: A RAPID REVIEW OF LITERATURE

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## ABSTRACT

The outbreak of the novel SARS-CoV-2, the virus that causes COVID-19 has remained a serious public health challenge. The high infectivity and mortalities associated with SAS-CoV-2 infections compared to other known viruses of the same group have necessitated the introduction of various prevention guidelines which may have the potential of affecting all spheres of human life. Efforts to better understand the new virus, prevent the spread and reduce its impacts on humans, have spurred very rapid scientific research and publications among experts. The volume of these scientific publications and the rate at which new knowledge is evolving may pose some difficulties for people to stay abreast with the trend of these discoveries. This rapid article review addressed this at this critical time, and keeps the readers, researchers, and policymakers updated on the rapidly emerging research findings. Although the world is still struggling with the fourth wave and newly emerging variants, efforts have started yielding significant results in reducing community transmission and mortalities associated with COVID-19 infection.

## KEYWORDS

Coronavirus, COVID-19, SARS-CoV-2.

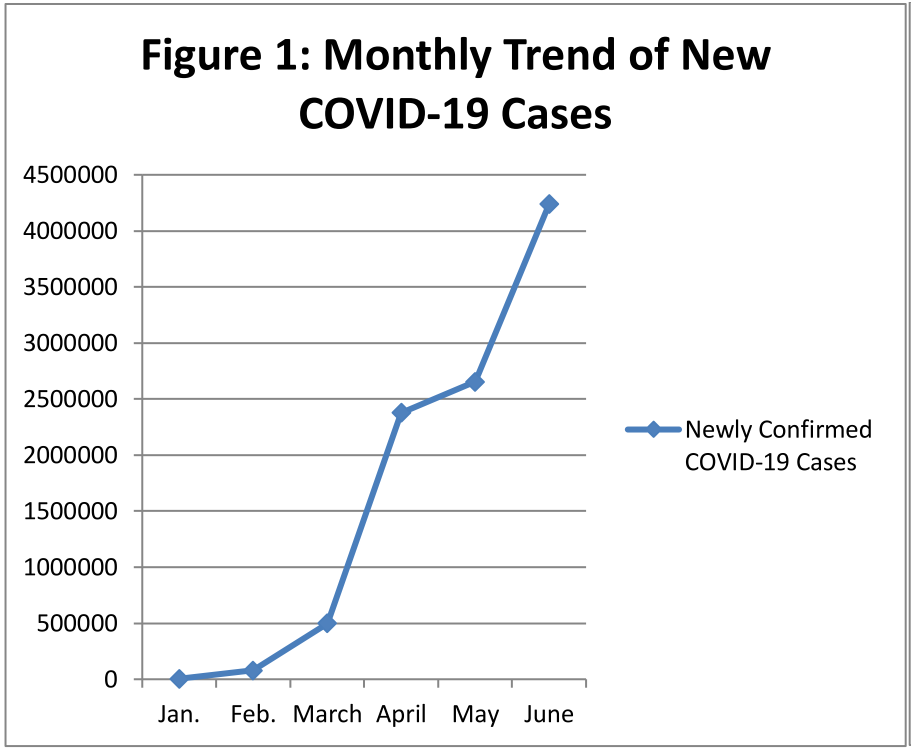
## INTRODUCTION

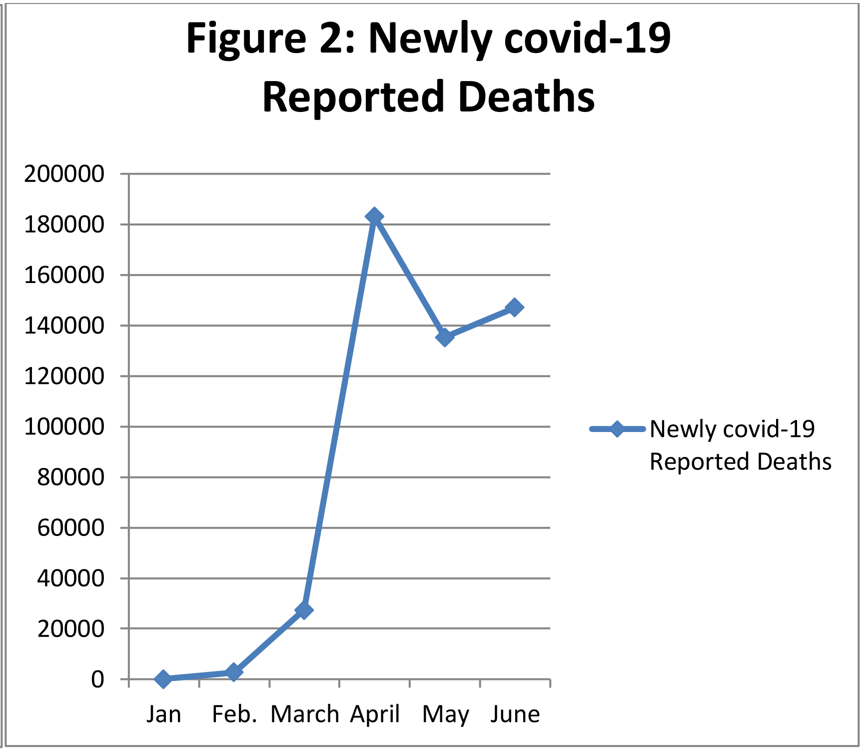
(The novel COVID-19 is a disease of the respiratory system caused by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2). It has been characterized as a threat to public health following the it's reported outbreak in Hubei Province Wuhan, China in December 2019. Both the acute respiratory syndrome coronavirus (SARS-CoV), the Middle-East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV-2 belong to β-corona virus and have all been isolated from bat. However, compared to others in the same group, SARS-CoV-2 has been noted for high infectivity and many potential hosts, including humans and animals (1).This has posed a serious challenge to the prevention and treatment strategies of COVID-19 infected individuals. A further comparative analysis of SARS-CoV-2 and the genomic sequences of MERS-CoV, SARS-CoV and bat SARS coronavirus (SARSr-CoV-RaTG13) have shown close resemblances of 50%, 79.5% and 96% respectively (**Error! Reference source not found.**). Similarly, a recent study that used macro-genomic sequencing, molecular biological detection and electron microscopic analysis, reported 99.98% similarity between SARS-CoV-2 viral strains currently infecting humans and the isolated virus strain from pangolins (1,3). These suggest that SARS-CoV-2 may have originated from bat and supports the strong suspicion on the zoonotic origin of the index case from Wuhan.

Moreover, the increasing spread of SARS-CoV-2 infection and its associated mortalities has spurred global responses; including the development and adoption of standard operation procedures (SOP), total lockdown, social distancing, compulsory wearing of mask in public places, among others. Unfortunately, these actions against the spread of the novel COVID-19 are not without consequences. These preventive policies have been reported to affect all spheres of life, including the bio-psychosocial, cultural and economic wellbeing of nearly everyone living across the globe. Efforts to control the spread of SARS-CoV-2 infection and reduce its impacts on humans have resulted in upsurge of scientific researches. The quantity of these scientific publications and the rate at which new knowledge is evolving may pose some difficulties for people to stay abreast with the trend of these discoveries. To address this challenge and help people follow-up with the rapidly emerging research findings, we summarized current literature onCOVID-19. We also analyzed the current epidemiological trend of the disease to determine the general global impacts of various COVID-19 interventions in preventing the spread the virus.

### Prevalence of COVID-19 Infection

Globally, more than 211 countries have reported cases of COVID-19; with a total of 526.3million infections and 5.6million COVID-19-related deaths as at July 25, 2022(4).These represents a monthly average of over 2.5million infections and 81955 deaths. The infection and death rates have kept rising exponentially despite interventions (fig 1). July 25, 2022 statistics from World Health Organization shows a relatively sustained daily increase in number of COVID-19 infections, with declining daily COVID-19 related deaths. This follows the record of the highest daily COVID-19 deaths of 12,361 on April 17, 2020and the peak of COVID-19 mortalities in March 2020 (fig 2). Although measures and guidelines have long been activated to curtail the spread of the virus, the highest daily reported infections of 189,077 occurred on June 28, 2020 (4).This suggested the need for more stringent efforts to flatten the curve,




**Legend**

Figure 1 shows the monthly trend of COVID-19 new infections from the beginning of the outbreak. The curve indicate the rising new cases, suggesting that the outbreak is yet to get to its peak as community transmission continues.

**Legend**

Figure 2 shows the impact various COVID-19 treatment supports of infected individuals in lowering the mortality curve. It also shows that COVID-19-related mortality peaked in March 2022

More cases of COVID-19 infections and deaths has been reported in America and Europe compared to other regions of the world (4). This is as America and Europe respectively accounts for 50.1% and 27% of global cases; and48.8% and 39.6% COVID-19 deaths as at July 25, 2022(4).. Although the undulating curve call for caution and more research, however the unsteady rise in daily deaths suggest that the current treatment measures are helpful in the prognosis of SARS-CoV-2 infected patients. As at July 25, 2022, the top ten countries worst hit by COVID-19 infections were Russia, India, United Kingdom, Peru, Chile, USA, Spain, Italy, Iran and Mexico (4).

## COVID-19 and Age

Adults, infants and young children are at high risk forSARS-CoV-2 infection; however pediatrics infected by COVID-19 show milder symptoms compared their elderly counterparts. While the reason is still unclear, a relationship has been reported between SARS-CoV-2 viral load and COVID-19 severity (5). Infants may show low viral load as their level of expression of ACE2 is lower than adults. Earlier research has shown that ACE2 is usually expressed in abundance in epithelial cells that are well-developed and differentiated (6). Epithelial cells develop along with lungs from birth, and lower amount of ACE2 may be expressed among pediatrics. Furthermore, research has suggested that ACE2 expression may be influenced by gender(7) . The gene for ACE is on the X-chromosome, and circulating ACE2 levels are usually higher in men compared to women This perhaps, may support the difference in COVID-19 severity and mortalities among genders (male and female), both adults and children(**Error! Reference source not found.-Error! Reference source not found.**).

## Genomic Structure of SARS-CoV-2

With the recent emergence of the novel SARS-CoV-2, there are now seven known human coronaviruses. Although there are basically classified in to four; α, β, γ, and δ coronaviruses, only α and β group are known to infect humans (10). These includes those that cause mild diseases (αCoV) such as HCoV-229E and NL63229E, and the highly pathogenic group(βCoV) such as SARS-CoV, HCoVOC43, HCoV-HKU1, MERS-CoV and SARS-CoV-2 Coronaviruses (18). Like others, SARS-CoV-2 is a single-stranded RNA virus of βCoV genera, enveloped in club-shaped spikes making it appear like solar corona(10). It measures about 80-120nm in diameter, and contains four basic structural proteins: the spike (S), membrane (M), envelope (E) and the nucleocapsid (N) proteins, all of which are encoded within the 3' ends of the virus (18). These structural proteins function to; give shape to the virus (M), facilitates viral assembly and budding (E), binds to the viral RNA (N) and mediate binding of the virus to the host cell receptors surface bringing about fusion and subsequent viral entry (S).

## Transmission

No study till date has fully established the exact origin of SARS-CoV-2, however, convincing evidences show that the virus may have originated from wild animals (1,10). A study carried in Wuhan Institute of Virology revealed a very close similarity (99.8%) in the genetic sequence between SARS-CoV-2 and bat coronavirus, suggesting that bat may be a potential source of the virus (1,12). Patients infected with SARS-CoV-2 are currently considered the main source of the virus.However, the level of infectiousness of these individuals during incubation period of SARS-CoV-2 remains a controversy at the moment. Interestingly, the transmission ofSARS-CoV-2 infection has been established to mainly occur through direct contact with infected individuals and inhalation of infected respiratory droplets(18).

The entry of SARS-CoV-2 virus into the host body system triggers the viral attachment to the hosts' cell through the interaction of "S" protein and specific receptor. It takes five cyclic steps; including attachment, penetration, biosynthesis, maturation and release of mature virion into the host cells, for a full mature and infective virus to be replicated and released into the host system (10). More interestingly, SARS-CoV-2 has been found to bind in high affinity with angiotensin converting enzyme 2 (ACE2) and uses it as receptor to invade target cells (14-15).

A structural model analysis revealed that the binding affinity of SARS-CoV-2 with ACE2 is 10-folds higher compared to SARS-CoV, and at a threshold far higher than that which is required for viral infections (1). ACE2 are available in kidney, bladder, intestines and in the epithelial cells of the Lungs. These, particularly the lungs are the commonest access point for binding of SARS-CoV-2 and ACE2. In addition to ACE2, SARS-CoV can also bind with dendrite-cells specific intercellular adhesion molecule-3-grabbing non-integrin (DC-SIGN) and DC-SIGN-related protein (DC-SIGNR, L-SIGN) [(10],16).

In addition, researchers have identified SARS-CoV-2 in stool, intestines, tears, conjunctival secretions, saliva and urine, suggesting these may be potential routes of SARS-CoV-2 infection(1). Findings from studies conducted on pregnant women with COVID-19 have ruled out the possibility of intrauterine vertical transmission from mother to child. This further supports the experts reports that the major route of COVID-19 transmission is by direct contact and inhalation of infected respiratory droplets. Furthermore, it has been found that the incubation period of SARS-CoV-2 ranges from 3-6 days with 14days median time from onset of symptoms to death (1). This compared to MERS-CoV with a latency period of 7days; SARS-CoV-2 has a maximum latency of 24days, which increases the risk for its transmission. Elderly (75years and above) are 2-folds more susceptible to SARS-CoV-2 infection and fatality compared to younger individuals; and may require more attention than any other group. Also, individuals with other chronic diseases such as diabetes, heart diseases, hypertension among others, are more vulnerable to SARS-CoV-2 infection, and at greater risks of poor prognosis (13).

## Clinical Characteristics of SARS-CoV-2 Infection

Patients infected with SARS-CoV-2 present with various symptoms ranging from mild to severe respiratory and multi-organ failures. However, a proportion of the population with SARS-CoV-2 infection may never show symptoms throughout the period the disease. A study (17), show that 17.9% of people infected with SARS-CoV-2 are asymptomatic carriers who will never show clinical symptom. However, majority of cases of COVID-19 may present with fever (often approximately 39$^{o}$C), cough, sore throat, dyspnoea, rhinitis fatigue, vomiting and diarrhea [(18]-19).In severe cases, there may be varying degrees of complications, including respiratory distress syndrome, respiratory failure, cardiac injuries and lung tissues damage. Some studies have also reported neurological symptoms, cardiac arrhythmia, renal failure and abnormal liver function (1,20).

## Laboratory and Radiological Features of COVID-19 Patients

Diagnosis of SARS-CoV-2 Infection requires laboratory detection of SARS-CoV-2 ribonucleic acid (RNA) using polymerase chain reaction. Moreover, the conventional practice of combining the laboratory tests, clinical symptoms and radiological images, particularly CT Scan support accurate diagnosis of COVID-19 and gives clearer picture of the severity and level of damage to organs involved.

Like pneumonia, computed tomography (CT scan) of the chest is a vital tool in diagnosis of SARS-CoV-2 infection. Radiological examinations of COVID-19 patients have consistently shown important typical imaging features of frequent ground glass opacification, lung tissues consolidations, air bronchogram, thickening of inter-lobular septa and adjacent pleura, and lower lobe involvement (1, 21).Research has also found that the sensitivity of chest CT scan in accurately suggesting COVID-19 case was 97%(22). These further suggest the importance of CT scan imaging features in the diagnosis of COVID-19.

Laboratory tests have continued to show various biochemical and physiological features of patients with COVID-19. Wang et al (2020) reported that 82.1% of COVID-19 patients have lymphopenia while 36.2% showed features of thrombocytopenia. Although most patients show normal leucocytes counts, a significant proportion (33.7%) may show leucopenia, elevated creatinine, kinase, lactate dehydrogenase, and transaminase. Compared to ordinary bacterial pneumonia, COVID-19 patients show lower oxygenation index, with the disease progression often aggravated by cytokinine release syndrome (Wang et al. 2020). Patents with COVID-19 are also reported to show laboratory increase in plasma concentration of pro-inflammatory cytokines, including interleukins (IL)-6, IL-10, granulocyte-colony stimulating factor (G-CSF), monocyte chemo-attractant protein 1 (MCP1), macrophage inflammatory protein (MIP)1α, tumor necrosis factor (TNF)-α and lowered CD4 +T (10, 20,23-24). In addition, a rapid (1hour) SARS-CoV-2 detection test kit has been reportedly developed using SHERLOCK technology (25). Furthermore, some researcher in Peking University also recently published a new method for quick transcriptome sequence SHERRY library construction, which is reportedly helpful in rapid SARS-CoV-2 sequencing(26)  These when proven valid, may help to speed up SARS-CoV-2 screening and diagnosis.

### Therapeutic Management of COVID-19

Till date, there is yet a conventionally approved drug for the treatment of SARS-CoV-2 infection. Although, world health organization in June 2020 approved the use of dexamethasone, a corticosteroid, in the treatment of critically ill COVID-19 patients requiring Oxygen and ventilators supports, however, the same drug was reported to have no benefit on other categories of COVID-19 patients (27). Nevertheless, the often management option is treatment with broad-spectrun anti-viral drugs such as nucleoside analogues and HIV-protease inhibitors in order to attenuate viral replication awaiting specific anti-viral discovery.

More so, several anti-viral drugs have been documented to have some levels of potential efficacy in the inhibition of SARS-CoV-2 replication. Remedesivir, an anti-rviral drug used in the treatment of Ebola disease, has been reported efficacious in the treatment of a wide range of RNA viruses. Meta-analysis of randomized control trials that evaluated the efficacy of remedesivir on patient with SARS-CoV-2 infection shows that remedesivir may exhibitsignificant control of the virus in-vitro, but with consequent adverse effects (28-29). Although the United States and European union recently approved the use of Remedesivir in the treatment of SARS-CoV-2 infections in the regions, the drug has not been proven a sure cure to covid-19. Similarly, a clinical controlled trials has reported the immuno-modulatory activities of chloroquine in the inhibition of SARS-CoV-2 in-vitro, suggesting that it may be effective in COVID-19 treatment (30-30). Also, studies have shown that Arbidol, an indole derivative,not only could block viral fusions in hepatitis and influenza A and B viruses, but efficient in SARS-CoV-2 treatment, particularly in reducing the incidence of severe cases. In addition, nucleoside analogues, peptide EK1, neuraminidase inhibitors, ritonavir among others, could also be helpful in the treatment of SARS-CoV-2 infection(1). However, their levels of efficacy and safety have remained the concerns of experts and health decisions-making bodies. While researches to arrive at the appropriate treatment drugs and vaccines are ongoing, use of broad-spectrum antiretroviral drugs and symptomatic management of people infected with SARS-CoV-2 has generally remained the common practice.

In addition, some researchers have suggested other palliative therapies that could enhance the treatment outcome and reduce associated complications of COVID-19(1).These measures are based on potential biochemical and patho-physiological changes in COVID-19 patients, and includes; convalescence therapy, auxiliary blood purification therapy, immuno-enhancement therapy and the Chinese decoction therapy.

### Prevention of COVID-19 Infection

Till date, there is yet a conventionally and scientifically proven drug or vaccine for COVID-19. Although ongoing researches, including clinical trials are promising, current efforts aims to bridge the sources and routes of transmission of SARS-CoV-2, while using already existing drugs and means to proactively control the spread and progress of the disease(1). This is achieved through protection of outside body, reduction of heat, wind and dampness with the viral agent, and promotion of self-resistance through recommended approaches, including-good personal and environmental hygiene, healthy lifestyle, adequate nutrition and rests, wearing of appropriate masks, good ventilation, and strict social distancing.

## Recommendation

While hopes are high for the discovery of drugs and vaccines that could control SARS-CoV-2 infection, current clinical treatment of the viral disease has been limited to palliative care. This underscores the urgent need for scientists to work harder in order to develop drugs that can efficiently prevent and cure COVID-19. SARS- CoV-2 is a ribonucleic acid (RNA) virus, therefore, earlier developed vaccines for RNA viruses such as polio, measles, influenza, among others, may be potential alternatives. Clinical trials should be conducted using these available vaccines for RNA viruses to determine their efficacy in preventing Person to person transmission of SARS-CoV-2 to vulnerable population, including elderly, children, health workers and non-infected general population. Continuous personal and environmental hygiene, including decontamination of public facilities are necessary. Public sensitization on other potential routes of transmission such as urine, saliva and faecal matter would be of immediate and future help. Epidemiological data would also provide a framework for more specific public health measures that can help prevent the SARS-CoV-2 infections.

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