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Current Challenges of the 2019-COVID Pandemic: Where We Started, Where We Are, and Where do We Go?

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Abstract The current outbreak of the 2019 Novel Coronavirus Disease has disrupted the world. Many studies, clinical trials, and updates have been published with the goal of sharing information that will help prepare the world's healthcare systems for the flood of patients expected to be infected with covid-19. The goal of this literature review is to provide an extensive summary of the most recent reports and studies since the initial outbreak and provide the most up-to-date understanding of the various aspects of covid-19—its spread, diagnosis, risk factors, and currently available and effective treatment strategies—with the hope that researchers and medical practitioners can use this a branching point to other studies that our outlined here. Symptom management is currently the primary strategy that is being implemented for covid-19 treatment, especially in patients who have developed severe disease. Many promising strategies to treat covid-19 are currently being investigated while a vaccine is under development. Anti-inflammatory drugs like sarilumab and antiviral drugs like chloroquine are undergoing clinical trials, and under an emergency protocol of the US FDA, practitioners can use the antibodies from plasma in covid-19 survivors to treat those infected.

Keywords: *2019 novel coronavirus disease (covid-19, 2019-nCoV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), Acute respiratory distress syndrome (ARDS), Chloroquine*

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1. Introduction

The 2019 Coronavirus Disease (covid-19, 2019-nCoV, SARS-CoV-2) was recognized by the World Health Organization as a pandemic on March 11, 2020, due to high spread and "alarming levels of inaction." According to data from the CDC, WHO, and ECDC, as of March 25, 2020, the number of global cases has totaled 423,827 confirmed cases, with 18,925 deaths (3.9% mortality rate) and 109,172 recovered. China, where the virus was discovered to have originated from, holds the highest number of confirmed cases at 801218, with 3,281 deaths (4.4% mortality rate) and 73,650 recovered. In the United States, the number has totaled 54,916 confirmed cases, with 784 deaths (1.4% mortality rate).

In the initial period of the outbreak, the highest number of cases outside of China were discovered among cruise ships, particularly the Diamond Princess cruise, with 712 persons testing positive for covid-19 among 3,711 passengers and crew (19.2%) [1]. Unfortunately, cruise voyages had made stops in various locations, including Japan, the US, and Mexico, before active measures were implemented.

Table 1. Current treatments

Drug	Current use	Being tested?	Has shown success in covid-19 treatment?
Choloroquine [30,38]	Antimalarial	Yes	**Yes**
Kaletra (ritonavir & lopinavir) [22]	HIV	Yes	**To be further elucidated**
Interferon α-2b [21]	Hepatitis C	Yes	**To be further elucidated**
Remdesevir [30]	Experimental	Yes	**To be further elucidated**
Favipiravir [31]	Influenza	Yes	**Yes**
Actemra (tocilizumab) [24]	Rheumatoid arthritis	Approved for use in covid-19 in China, March 2020	**Yes**
Kevzara (sarilumab) [26]	Rheumatoid arthritis	Yes	**To be further elucidated**
Convalescent Plasma [42]	**Experimental**	**Yes**	**To be elucidated**

To compare these numbers, the Western Africa Ebola virus epidemic (2013 – 2016) had total cases at 28,646, and a death count at 11,323 (39.5% mortality rate) [2]. Severe acute respiratory syndrome (SARS-CoV), from November 2002 to July 2003, had a total of 8,098 cases and 774 deaths across 17 countries (9.6% mortality rate) [3]. Finally, the 2012-2015 Middle Eastern respiratory syndrome (MERS) totaled 2,506 cases and 862 deaths (34% mortality rate) [4]. While covid-19 has statistically proven itself to be a much less deadly virus in regard to its mortality rate, it is clear that it has been optimized for mild, but prolonged disease. More problematically, infected persons can be contagious when asymptomatic, with an incubation period that can surpass 14 days. Even worse, some patients have been shown to be susceptible to reinfection [5].

In a study that examined the stability of covid-19, it was found that the virus remained viable in aerosols for 3 hours, with a reduction in the infectious titer from $10^{4.3}$ to $10^{2.7}$ tissue-culture infectious dose [$TCID_{50}$] per liter of air (a similar reduction seen in SARS-CoV-1) [47]. Viable virus was detected up to 72 hours later on plastic and up to 48 hours later on stainless steel. No viable virus was detected on copper after 4 hours nor on cardboard after 24 hours. The study suggests that the differences in the epidemiological characteristics of covid-19 versus SARS-CoV-1—despite them having similar stabilities in experimental conditions—is likely due to covid-19's high viral load and shedding in the upper respiratory tract in infected persons, and the ability to be transmitted in asymptomatic persons.

2. Identification

A clinical update published on March 11, 2020, presented a care plan for covid-19 patients that were deemed in critical condition [6]. The principal characteristic of severe disease in this case is acute respiratory distress syndrome (ARDS), much like other previous pandemics we have seen. In line with all this, in those admitted for intensive care, the primary reason for respiratory support is respiratory failure, with two-thirds meeting the criteria for ARDS. It is clear that management of covid-19 is not very different to other viral pneumonias that cause respiratory failure. One study examined the success of identifying covid-19 in 1,070 specimen samples from various patient [7]. The authors found that bronchoalveolar lavage (BAL) fluid specimens returned the highest positive rates (14/15; 93%), followed by sputum (72/104; 72%), nasal swabs (5/8; 63%), fibrobronchoscope brush biopsy (6/13; 46%), pharyngeal swabs (126/398; 32%), feces (44/153; 29%), and blood (3/307; 1%). The 72 urine specimens did not test positive. This suggests that covid-19 could indeed be passed through feces and, additionally, could be systemic. More specimen samples from a single patient could reduce the incidence of false positives, especially important in this setting, where the number of hospital beds is the limiting factor in successfully responding to this pandemic.

2.1. Radiographic Findings

Radiographic findings were also found to be suggestive, but nonspecific: ground-glass opacities on computed tomography (CT) [8]. However, in another study that examined the correlation of chest CT to reverse transcriptase polymerase chain reaction (RT-PCR) in the diagnosis of covid-19, chest CT was found to have a high sensitivity for covid-19 [9]. The sensitivity of CT-Chest was 97% (580/601 patients) based on positive RT-PCR results. Further, in patients with negative RT-PCR results, 75% (308/413 patients) had positive chest CT findings. Additionally, 42% of cases (24/57 patients) showed improvement in follow-up chest CT before the RT-PCR results turned negative. The presence of viral shedding, even at low levels, can still result in a positive RT-PCR.

2.2. Symptoms

In a study from China that examined data from 1,099 patients, fever was found in 43.8% upon initial presentation, and developed in up to 88.7% after hospitalization [10]. In those hospitalized, severe illness developed in 15.7%. What this study showed is that the majority of patients did not initially present with fever, and most did not have abnormal radiological findings. Furthermore, as it is an indicator for disease status, worse outcomes occurred in those with a compromised respiratory status upon admission to a hospital. Another smaller study of 138 patients in Wuhan showed fever in 98.6% of the patients, fatigue in 69.6%, and a dry cough in 59.4% [11]. Other clinical indicators included lymphopenia (lymphocyte count, 0.8 x 10^9 /L [interquartile range {IQR}, 0.6-1.1) in 70.3%, prolonged prothrombin time (13.0 seconds [IQR, 12.3-13.7]) in 58%, and elevated lactate dehydrogenase (261 U/L [IQR, 182-403]) in 39.9%.

In a retrospective study that included 191 patients in China, an analysis was done to compare the 137 patients who were discharged and the 54 patients who died [12]. Using a multivariable regression, it was shown that risk factors for death included older age, a higher Sequential Organ Failure Assessment (SOFA) score, and d-dimer greater than 1 μg/mL, suggesting that medical practitioners use these variables to help identify patients with a poor prognosis early on. Relatedly, older age was also a risk factor for mortality in the setting of SARS and MERS. This was seen in a study with macaques who were infected with SARS-CoV [13]; older macaques had a stronger innate host response in increasing expression of pro-inflammatory genes and reducing those of type I interferon-β. This age-related difference could lead to deficiency in controlling viral replication and to a more prolonged inflammatory response, all contributing to poorer outcomes. The SOFA score was deemed a good indicator of sepsis and septic shock, and consequently, organ failure; in this study, more than half of the patients developed sepsis. Lastly, a d-dimer greater than 1 μg/mL was associated with a fatal outcome of covid-19, with higher levels associated with a 28-day mortality in septic patients Severe disease was also more likely to be observed in patients with lymphopenia and elevated levels

of interleukin (IL)-6, high-sensitivity cardiac troponin I, and lactate dehydrogenase, findings and conclusions that are supported in another study [14].

A correspondence was published that discussed the importance of screening for hyperinflammation in the setting of covid-19 [14]. There has been growing evidence revealing a sub-patient population of covid-19 patients that exhibit a cytokine storm syndrome. In adults, we see this often triggered by viral infections and in 3.7 – 4.3% of sepsis cases [15,16]. Pulmonary involvement of this hyperinflammation occurs in around 50% of affected patients [17]. This cytokine profile resembling secondary hemophagocytic lymphohistiocytosis (sHLH) is associated with increased covid-19 disease severity, with increased interleukin (IL)-2 and IL-7, among many other inflammatory markers [18]. In a retrospective multicenter study involving 150 confirmed covid-19 cases, predictors of fatality included elevated ferritin (mean 1297.6 ng/mL in non-survivors vs. 614 ng/mL in survivors) and IL-6 [19]. As the correspondence suggests, it seems that mortality might be due to hyperinflammation due to the virus.

3. Response

Many medical researchers and practitioners followed China's initial guidelines in response to treating those hospitalized: α-interferon with Kaletra, an approved cocktail of the HIV protease inhibitors ritonavir and lopinavir [20]. Over 100 clinical trials have been put forward and accepted to deal with this increasingly dangerous disease. Chloroquine, arbidol, remdesivir, and favipiravir are some of the first-choice drugs, and have been showing promising results [21].

Table 2. Characteristics and outcomes of 21 critically ill patients with covid-19 in Washington State, taken from a research letter [48]

Baseline characteristics	No. (%) of patients	Reference range
Preadmission comorbidities		
Asthma	2 (9.1)	
Chronic obstructive pulmonary disease	7 (33.3)	
Congestive heart failure	9 (42.9)	
Diabetes	7 (33.3)	
Rheumatological disease	1 (4.8)	
Obstructive sleep apnea	6 (28.6)	
Chronic kidney disease	10 (47.6)	
End-stage kidney disease	2 (9.5)	
History of solid organ transplant	2 (9.5)	
Cirrhosis	1 (4.8)	
Immunosuppression	3 (14.3)	
Total with ≥1 comorbidity	18 (85.7)	
Admission symptoms		
Cough	11 (47.6)	
Shortness of breath	17 (76.2)	
Fever	11 (52.4)	
Temperature (range), °C	37.6 (35.3-39.2)	
Admission chest radiographic findings		
Bilateral reticular nodular opacities	11 (52.4)	
Ground-glass opacities	10 (47.6)	
Pleural effusion	6 (28.6)	
Peribronchial thickening	5 (23.8)	
Focal consolidation	4 (19.0)	
Pulmonary edema	2 (9.5)	
Venous congestion	1 (4.8)	
Atelectasis	1 (4.8)	
Clear	1 (4.8)	
Admission laboratory measures, mean (range)		
White blood cell count, /μL	9365 (2890 – 16900)	4000 – 11000
Absolute lymphocyte count, /μL	889 (200 – 2390)	1000 – 3400
Hemoglobin, g/dL	11.4 (8.0 – 13.7)	11.2 – 15.7
Platelet count, x10^3/μL	215 (52 – 395)	182 – 369
Sodium, mmol/L	137 (125 – 148)	135 – 145
Creatinine, mg/dL	1.45 (0.1 – 4.5)	0.6 – 1.2
Total bilirubin, mg/dL	0.6 (0.2 – 1.1)	0 – 1.5
Alkaline phosphatase, U/L	80 (41 – 164)	31 – 120
Aspartate aminotransferase, U/L	273 (14 – 4432)	5 – 40
Alanine aminotransferase, U/L	108 (11 – 1414)	5 - 50
Creatinine kinase, U/L	95 (45 – 1290)	21 – 215
Venous lactate, mmol/L	1.8 (0.8 – 4.9)	<1.9
Had troponin level >0.3 ng/mL, No. (%)	3 (14)	
Brain-type natriuretic peptide, pg/mL	4720 (69 – 33423)	<450
Procalcitonin, ng/mL	1.8 (0.12 – 9.56)	0.15 – 2.0
Underwent bronchoalveolar lavage, No. (%)	7 (33.0)	
After undergoing bronchoalveolar lavage		
White blood cell count, /μL	515 (174 – 1222)	0 – 5
Polymorphonuclear neutrophils, %	41.0 (13 – 77)	
Lymphocytes, %	32.0 (4 – 90)	
Monocytes, %	39.0 (12 – 72)	

In a randomized trial for hospitalized adult patients with severe covid-19, published by the NEJM on March 18, 2020, no benefit was observed with lopinavir–ritonavir treatment beyond standard care (hazard ratio [HR] = 1.24; 95% confidence interval [CI], 0.90 to 1.72) [23]. Furthermore, 28-day mortality was similar in the lopinavir–ritonavir group and the standard-care group (19.2% vs. 25.0%; difference, 5.8 percentage points; 95% CI, −17.3 to 5.7). On the other hand, severe adverse events were less common (any, 17.9% vs. 31.3%; ARDS, 12.6% vs. 27.3%). Given these results, one thing to note is that in this study, lopinavir-ritonavir treatment was started late, possibly too late for it to have its full effect. Typically, lopinavir-ritonavir should be administered early in the infection rather than when there is widespread infection, sepsis, and organ involvement. The mortality rate of the trial was 22.1%, compared to the 11 – 14.5% mortality rates of the initial descriptive studies of covid-19. This in and of itself indicates that the patients in this trial generally had more severe disease.

3.1. Anti-inflammatory Drugs/Corticosteroids

Despite their risks, corticosteroids have remarkable anti-inflammatory properties and are widely used, especially cancer specialties. However, they have proved to be controversial, as they have shown to be associated with exacerbation of lung injury [23], and therefore their use in the treatment of covid-19 is not recommended. However, in settings of hyperinflammation, immunosuppression has shown to be beneficial and could indeed prove to be so with covid-19 too. A multicenter, randomized controlled trial of tocilizumab (IL-6 blockade, originally licensed for cytokine release syndrome) was recently approved for use in covid-19 pneumonia and elevated IL-6 patients [24]. A very similar study examined the effects of covid-19 infection on elevated levels of cytokines [25]. Suppression of pro-inflammatory IL-1 family members and IL-6 have previously been shown to have therapeutic effects in viral infections. IL-37, on the other hand, is anti-inflammatory and immunosuppressive. It has the ability to reduce pro-inflammatory cytokines. IL-38, another anti-inflammatory cytokine, has similar immunosuppressive properties. This gives insight into potential therapeutic cytokines that can be elevated to fight covid-19. Given its association with higher fatality, the screening for hyperinflammation should strongly be considered amongst all covid-19 cases, as this could help identify patients for whom immunosuppression could be beneficial [14]. Some methods include steroids, intravenous immunoglobulins, selective cytokine blockades, and even Janus kinase (JAK) inhibition. In fact, with its approved use in China to treat patients with critical covid-19 disease, sarilumab has begun a global phase 2/3 clinical trial for the same patient population (Figure 1) [26]. Sarilumab is a fully human monoclonal antibody that inhibits the IL-6 pathway, which plays a role in the hyper-inflammatory response in the lungs. According to research, it is very possible that IL-6 may play a fundamental role in driving the inflammatory immune response that causes ARDS, and thus, the targeting of this pathway may prove beneficial for patients with severe disease.

In a similar setting, at the Jinyintan Hospital in Wuhan, China, a retrospective study was performed on a cohort of 201 hospitalized patients (aged 21 to 83 years) who were covid-19 pneumonia confirmed [27]. Of the 41.8% patients who developed ARDS, more than half died. As has been shown in other studies, ARDS seems to be a primary indicator of severe disease and worse outcomes. First, older age was associated with an increased risk of developing ARDS and death (HR = 3.26; 95% CI, 2.08-5.11; and HR = 6.17; 95% CI, 3.26-11.67, respectively), and so was neutrophilia (HR = 1.14; 95% CI, 1.09-1.19; and HR = 1.08; 95% CI, 1.01-1.17, respectively). Additionally, risk for death also appeared lower among patients with ARDS who were treated with methylprednisolone (HR = 0.38; 95% CI, 0.2-0.72). Thus, treatment with methylprednisone could be beneficial for patients who develop ARDS. It was noted that with the small sample size and lack of a double-blind randomized clinical trial, caution should be taken in following these guidelines. On another note, in a randomized controlled trial involving 277 patients with moderate-to-severe ARDS, early administration of dexamethasone was shown to reduce the duration of mechanical ventilation required [49].

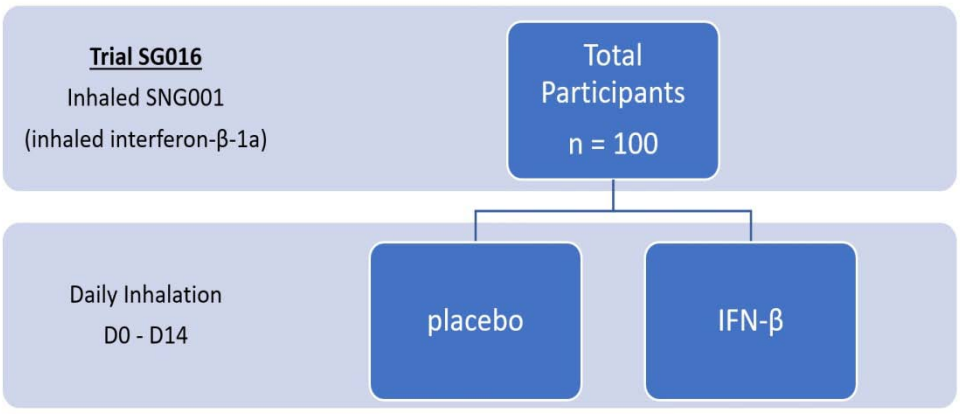

Figure 1. Phase II Trial for SNG001 [44]. IFN-β is a natural antiviral that is produced in lungs during lung infections. However, this is reduced in older patients. Successful outcomes in this trial could be a breakthrough for helping older covid-19 patients

3.2. Extracorporeal Membrane Oxygenation (ECMO)

Another seemingly successful strategy has been the implementation of oxygen therapy through high-flow nasal oxygen for those with moderately severe hypoxemia [28]. However, in the more severe cases, this might be enough, and strategies such as extracorporeal membrane oxygenation (ECMO) need to be considered. Many hospitals have expanded their ability to provide more ECMO, however, constraints still include the availability of resources, the need for training healthcare personnel, and the importance of careful patient selection, based on factors such as age and severity of disease, to prioritize those who will benefit most from therapies such as ECMO [29]. One suggestion that was made was to find a way to group critically ill patients together to optimize the delivery of ECMO.

3.3. Antiviral Drugs

According to the deputy of the China National Center for Biotechnology Development, Sun Yanrong, when the outbreak was first discovered, countless rounds of screening among thousands of existing drugs taken place to select the best contenders. Many of these drugs were previously used as treatments during the outbreaks of SARS and MERS [30].

One such antiviral drug is favipiravir, a drug developed and approved in Japan for use as an anti-influenza drug. It has shown remarkable efficacy against infections with high viral load and has mechanisms that closely resemble the anti-herpesvirus drug acyclovir, acting as a chain terminator at the site of incorporation of viral RNA, reducing viral load [31]. It has been successful in protecting against lethal infections in humans and has been used in the treatment of Ebola and Lassa viruses and rabies. Due to it and having the property of not producing favipiravir-resistant strains, it keeps its therapeutic efficacy throughout a pandemic. Thus, it is expected to play a central role in many future influenza pandemics. In a press release on March 18, 2020, Zhang Xinmin, an official at China's science and technology ministry, announced that in a 340-patient clinical trial, favipiravir had shown promise in battling covid-19. Patients tested negative for the virus after a median of 4 days, compared to 11 days without favipiravir treatment. However, doctors were concerned that favipiravir was not effective in patients with more severe disease, noting that it may not be effective if the virus has already multiplied.

Remdesivir and chloroquine were shown to effectively inhibit and control covid-19 in vitro. Another similar study echoed these conclusions about chloroquine [32], citing guidelines from South Korea and China that oral chloroquine tablets have been associated with faster time to recovery and a shorter hospital stay in regard to covid-19. Previous CDC research falls in line with these claims: chloroquine has strong potential as a prophylactic measure against coronaviruses (e.g. SARS-CoV) in vitro [33]; the paper recommended it to be used while a vaccine is under development. Chloroquine have a long track record of being used in humans for treatment of malaria and other autoimmune conditions since 1945. Chloroquine has anti-inflammatory properties, which is why it has shown efficacy in treating autoimmune conditions such as lupus or rheumatoid arthritis. Even more, in studies exploring the treatments of SARS-CoV, it was found to have broad anti-viral properties too [34]: by increasing the endosomal pH that is required for virus/cell fusion and interfering with the glycosylation of cellular receptors. This was not unique to SARS-CoV. In previous in vitro studies, chloroquine was found effective in inhibiting HCoV-229E in epithelial lung cell cultures [35,36], and averting lethal injections of HCoV-O43 in mice studies [37]. With all this, it was not surprising to see it being recommended as a treatment for the new covid-19. However, chloroquine is known for its toxicity, and there have been clear guidelines to its safe dosage level over the decades.

In the early in vitro studies of chloroquine, the Chinese Clinical Trial Registry reported that chloroquine inhibited covid-19 at very low micromolar concentrations, with a half-maximal effective concentration (EC_{50}) of 1.13 μM and half-cytotoxic (CC_{50}) concentration of >100 μM [38]. This same paper compared chloroquine and chloroquine phosphate in its treatment of covid-19 associated pneumonia throughout numerous clinical trials conducted across hospitals in China [38]. Chloroquine phosphate was found to be superior as a control and treatment strategy for inhibiting the exacerbation of pneumonia, improving lung findings, promoting a virus-negative conversion, and ultimately shortening the disease course. Since respiratory status is a predictor for worse patient outcomes, the treatment of established pneumonia is crucial in improving prognosis. Furthermore, and likely more important, there were no severe adverse reactions in patients treated with chloroquine phosphate. It was even recommended to be included in the next set of China's National Health Commission guidelines for the diagnosis, prevention, and treatment of pneumonia caused by covid-19.

On March 16, 2020, Professor Didier Raoult, at an infection hospital in Marseille, published a video online presenting the success of a trial involving hydroxychloroquine [39]. The treatment was delivered in a single arm study, dosed at 600 μg per day for 10 days with close monitoring. The conclusions from the trial showed that patients not given Plaquenil were still contagious after six days, while among those given Plaquenil, only 25% were contagious.

In addition to treating the virus, one strategy needs to be targeting the transmission rates. Antiviral drugs early after symptom onset have been shown to reduce the viral shedding in the specimens from patients. . A current trial is about to begin to investigate the prophylactic efficacy of hydroxychloroquine [45].

ICU patients represent the sub-patient population that require the highest level of support. To this end, in a detailed report authored by a panel of 36 experts from 12 countries, a comprehensive guide was provided for the care of covid-19 ICU patients [40]. These included 4 best practice statements, 9 strong recommendations, and 35 weak recommendations for 53 questions relevant to the management of covid-19.

To echo the findings of interim treatment guidelines produced by UW Medicine, [41] in the case of an upper or lower respiratory tract infection without risk factors

and no immediate demand for oxygen treatment, symptomatic treatment has appeared to be enough. In the presence of a lower respiratory tract infection (LRTI) with oxygen requirement, hydroxychloroquine should be used a first-line treatment. If a LRTI requires ventilation support, hydroxychloroquine or a compassionate use of remdesivir can be considered. In the presence of a cytokine release, tocilizumab should be considered as a treatment options to manage the hyperinflammation.

3.4. Plasma from Coronavirus Survivors

On March 23, 2020, Governor Cuomo of New York announced the latest tactic: the use of plasma for coronavirus survivors to help keep patients out of the ICU [42]. The strategy, using convalescent plasma, had seen some success in the SARS and Ebola outbreaks. It was also one of the strategies utilized in China during the initial covid-19 outbreak, however, researchers have not reported on the results. Now, the hope is that it will help alleviate the immense pressure on the world's healthcare systems, by discharging patients from the hospital more rapidly. The main benefit of this strategy is that plasma from survivors is readily available in hospitals. Thanks to a tremendous joint effort from virologists, clinical-trial specialists, and statisticians, the FDA cleared researchers and medical practitioners to begin using convalescent plasma as treatment and to submit their clinical trials. If it proves successful, the future implications could be massive. A Phase I Trial for mRNA-1273, a vaccine, recently began, which marked a record speed for the start of a vaccine trial so quickly after an outbreak [43]. A Phase II Trial (SG016) for SNG001 is underway too (Figure 1) [44].

There are many ongoing trials in the treatment and prophylaxis of this virus, presented in Table 3. Many visualizations of the coronavirus cases and growth rate have also been taken from an online counter (Figure 2 – Figure 5) [46].

Table 3. A list of some of the trials that are recruiting or underway, including the arms of the trial, and the dosage information.

Trial (Trial Identifier)	N	Arms	Hydroxychloroquine Dose
Mild (NCT04307693)	150	• Lopinavir/Ritonavir • Hydroxychloroquine (HCQ) • Control	200 mg BID, 7-10 days (no loading dose)
Severe (NCT04315896)	500	• HCQ • Placebo (Pbo)	200 mg BID, 10 days (no loading dose)
Moderate to critically ill (NCT04303299)	80	• Tamiflu (Oseltamivir) +HCQ • Darunavir + Tamiflu • Lopinavir + Tamiflu • Lopinavir + Tamiflu • Favipiravir + Lopinavir • Darunavir + Tamiflu + HCQ • Darunavir + Favipiravir + HCQ	400 mg/day
Severe w/ pneumonia (NCT04321278)	440	• HCQ + Azithromycin • HCQ	400 mg BID (no loading dose)
Severe (NCT04321616)	700	• HCQ • Remdesivir • Standard of Care	• D1 = 600 mg BID • D2-9 = 200 mg TID
Hospitalized (NCT04315948)	3100	• Remdesivir • Lopinavir/R • Lopinavir + α-Interferon 2b • HCQ • Standard of Care	• D1 = 400 mg BID • D2-9 = 400 mg QD
Non-severe cases + prevention (NCT04304053)	3040	• Darunavir + HCQ 7d • Standard of Care	Infected non-severe • HCQ D1 = 800 mg • D2-7 = 400 mg (only 4 days in non-infected contacts)
Post-exposure prophylaxis (NCT04318444)	1600	• HCQ • Pbo	• D1 = 400 mg BID • D2-5 = 200 mg BID
Covid-19 Pneumonia (NCT04317092)	330	• Tocilizumab	Tocilizumab 8 mg/kg (max: 800 mg/dose), with an interval of 12 hrs
Hospitalized (NCT04315298)	400	• Sarilumab, high dose • Sarilumab, low dose • Pbo	Single intravenous dose
Vaccine Trial (NCT04283461)	45	• mRNA-1273	• 25 µg mRNA-1273 • 100 µg mRNA-1273 • 250 µg mRNA-1273

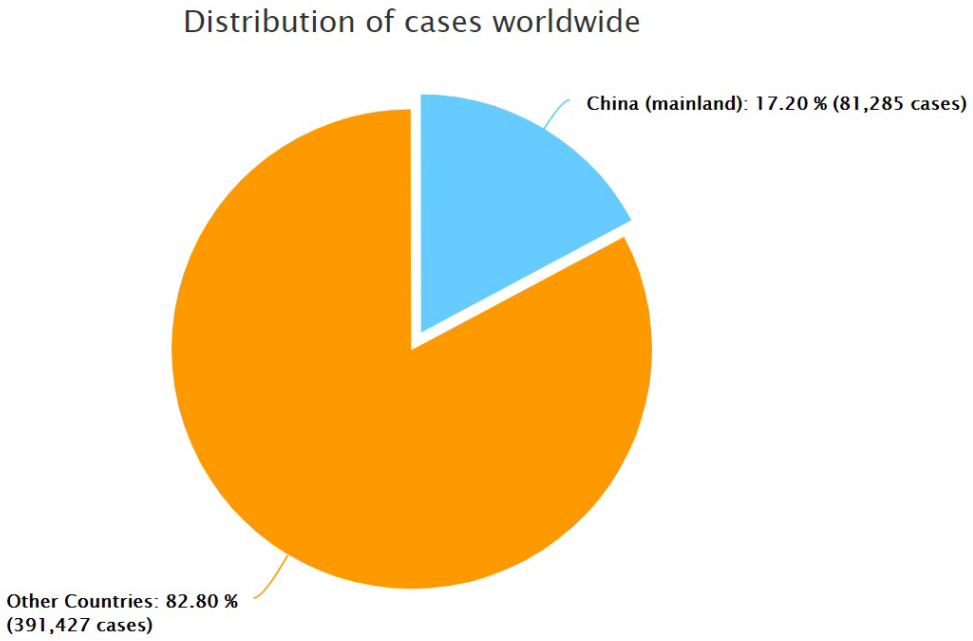

Figure 2. Distribution of cases worldwide, as of March 25, 2020 [46]

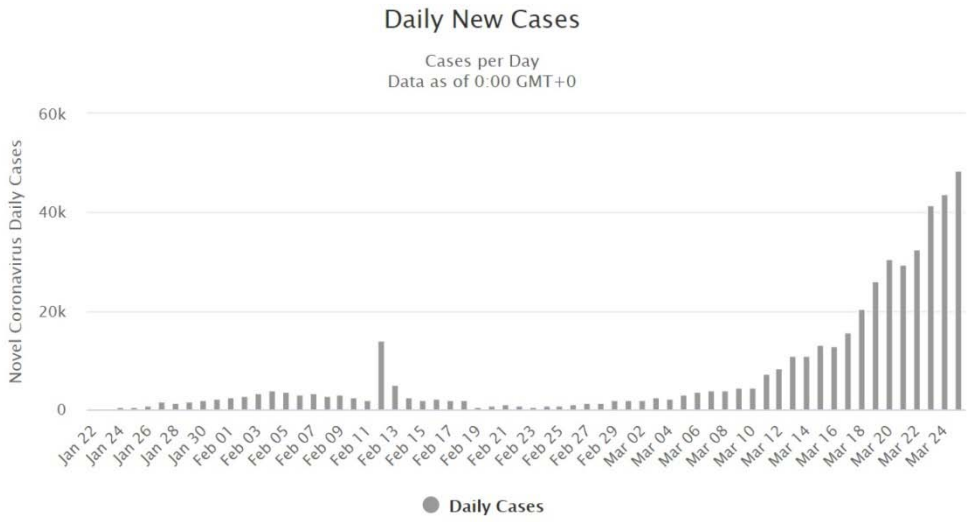

Figure 3. Daily new cases worldwide [46]

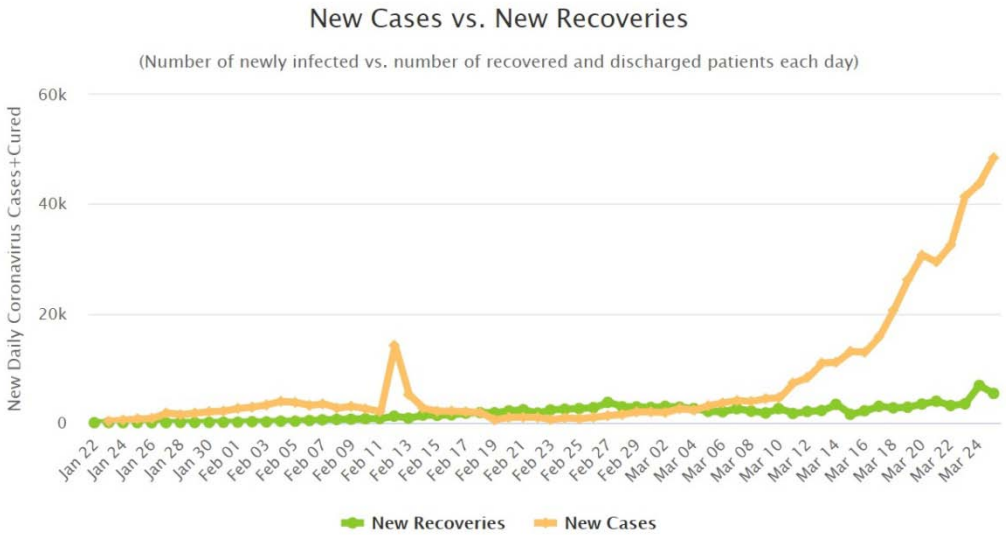

Figure 4. Daily new cases vs. recoveries [46]

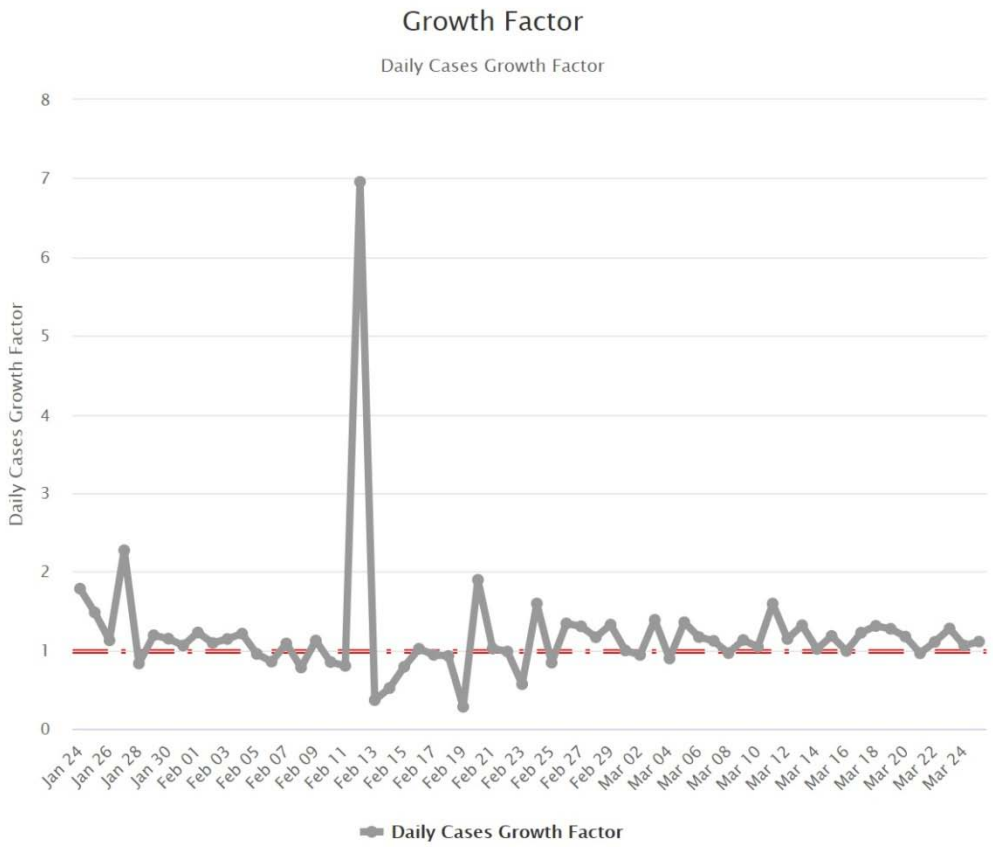

Figure 5. Growth factor of the daily cases worldwide [46]

4. Conclusion

Over this short period of time since the outbreak, countless clinical trials have been approved with the goal of discovering the optimal strategy for treating covid-19. The goal of this review is to provide a quick summary of various aspects of this current pandemic, as well as to act as a reference to the some of the ongoing studies.

The primary risk factors for worse outcomes and difficulty in treatment include being over 60 years old, having existing pulmonary disease, chronic kidney disease, transplant, diabetes mellitus, hypertension, cardiovascular diseases, cardiomyopathy, biologic immune modulators, detectable HIV or a CD4 count of <200 cells/mm^3, and other immunosuppressive medications including chronic corticosteroid treatment at the equivalent of >20 mg of oral prednisone daily.

The current strategy for covid-19 cases is supportive treatment and symptom management. Targeted treatment trials are underway to secure lower mortality rates and improve prognosis. The strongest evidence seems to lead us to antiviral treatments. Chloroquine has established itself as a very promising player in improving patient outcomes and hospital courses and lowering levels of contagiousness for those infected.

The utilization of plasma from covid-19 survivors seems to be a promising strategy too. Under the emergency protocols of the FDA, doctors can treat patients with coronavirus antibodies, despite it not being officially approved. The hope is that this will help clear out the already flooded hospitals. This could prove to be an effective treatment strategy while a vaccine is still under development.

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