






## NON-SYSTEMATIC REVIEW

## RESPIRATORY MEDICINE

## COVID-19; current situation and recommended interventions

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Email: Haitham.sd1@gmail.com**Abstract****Background:** The new coronavirus (SARS-COV-2) that emerged at the end of 2019 was stated in China and infected millions of people around the world, with the highest spread rate amongst humans compared with other coronaviruses. This paper aimed to review and analyse the published studies about COVID-19 diagnosis, prevention, and treatment.**Method:** The reviewed studies were clinical trials, in-vivo, in-vitro, guidelines, reports from the world health organization (WHO), and the centre for disease control and prevention (CDC) in addition to systemic reviews. All data extracted and analysed to stand on the latest updates and recommendations for fighting this severe attack of COVID-19.**Results:** Most important antiviral therapy of COVID-19 clinical trials is still running without clear results, but a few trials have indicated the role of numerous drugs in the treatment of COVID-19. Specific recommendations for aerosol therapy should be followed for the management of COVID-19.**Conclusion:** Nature of COVID-19 is still not very clear, however, management of the condition is similar to the previous attacks of coronaviruses.**1 | INTRODUCTION**

Coronavirus disease 2019 (COVID-19) belongs to the Coronaviridae family that is enveloped non-segmented positive-sense RNA viruses. Coronaviruses are commonly detected in most animals, but sometimes they could transform into new forms that could be able to infect humans. Since the start of the 21st century, two coronaviruses have infected humans from animal sources, causing outbreaks of the severe acute respiratory syndrome (SARS) in 2002 and the Middle East respiratory syndrome (MERS) coronavirus outbreak in 2012.<sup>1</sup> SARS started in 2002 in Asia but the first report about infected cases was in 2003. Many pieces of evidence indicated that SARS was originated in bats and then transferred to civets which infected people. SARS affected about 8098 humans, from these cases 774 patients died reflecting a death rate of about 9.6%.<sup>1</sup> The second attack, MERS, started in 2012 in Saudi Arabia. Bats transferred the virus to Camels which have infected people and results in a 2494 case from which 858 death, reflecting the highest mortality rate, about 34.4%.<sup>2</sup>

COVID-19 started in 2019 in Wuhan, China. The causing virus is SARS-CoV-2 which belongs to respiratory viruses. Bats might be the source of the virus transmission to humans, while the intermediate host that received the virus from bats has not yet been identified. Confirmed cases are millions of people from which hundreds of thousands died.

**2 | Epidemiology of COVID-19****2.1 | ROUTE OF TRANSMISSION**

The new coronavirus is transmitted from human to human via droplets and fomites during close contact with infected subjects in case of coughing and sneezing. Also, aerosol that is produced from aerosol-generating devices could lead to infection spread particularly in hospitals. Airborne spread of COVID-19 has not proven to be a major route of infection transmission based on available references, however, more preventive strategies should be considered especially in

case of indoor prevention. Human-to-human transmission of the COVID-19 virus is largely occurring in families because of close contact that provides the media for virus transmission.<sup>3</sup>

Another suspected route of infection transmission is the faecal-oral route, depending on findings from a clinical study which indicates the probability of a faecal-oral route for COVID-19 spread and that was proven by the reverse polymerase chain reaction (Real-time RT-PCR) results of stool samples for eight patients that were positive to COVID-19 even after nasopharyngeal testing was negative.<sup>4</sup> Besides another study carried by Xiao et al indicated that the genome of the virus was also detected in the oesophagus, stomach, and intestine, suggesting the gastrointestinal route of viral transmission.<sup>5</sup>

Regarding pregnant confirmed COVID-19 cases, till now, there was no evidence that the virus could affect the foetus through the intracranial route.<sup>6</sup>

## 2.2 | Incubation period

The time between infection and presentation of symptoms varies from one patient to another. The incubation period of SARS-CoV-2 is between 2 and 14 days according to recent CDC reports and about 2-10 days according to the world health organization (WHO). Recently published studies found that the incubation period could be longer than that stated by the WHO and it could be extended for about 24 days.<sup>7</sup>

## 2.3 | Conditions related to COVID-19 mortality

According to WHO, the elderly are highly affected by the infection (Age > 60) with the highest mortality rate (for those >80 years it ranged from 10% to 27%)<sup>8,9</sup> and those with underlying disorders such as hypertension, cardiovascular disease, diabetes, chronic respiratory disease and tumour.<sup>10</sup> From 72 134 cases, about 87% were between 30 and 79 years old, representing the majority of affected patients.<sup>11</sup> Disease in children less than 19 years appears to be relatively less common and mild with low percent of the total COVID-19 reported cases.<sup>12</sup> Moreover, obesity association with COVID-19 severity was investigated in several clinical trials and meta-analysis studies. Those studies reported that obese people have the potential to develop threefold higher risk of severe COVID-19 illness compared with those with normal body mass index.<sup>13,14</sup>

## 2.4 | Signs and symptoms

Most of the patients have a mild presentation to COVID-19 with the tendency to start mainly with fever followed by a dry cough that recovers without medical interventions, beside the flu-such as symptoms, headache, malaise, and muscle pain might develop early in symptomatic subjects. Mild cases were mainly related to younger patients.<sup>15</sup> But in some cases, these symptoms might develop to

### What's known

- COVID-19 is a viral disease that affects mainly the respiratory system. There are many treatment options that had been evaluated by the health care professionals.

### What's new

- Treatment recommendation for COVID-19 on the sight of the published clinical trials, In addition to aerosol therapy recommendations.

shortness of the breath which mainly starts within 7 days after the appearance of symptoms<sup>10</sup> and pneumonia which require the hospitalisation of the infected case, this complication mainly related to the elderly and those with comorbidities. A few percent of the severe COVID-19 cases might develop respiratory failure, multi-organ failure, or septic shock.<sup>10</sup> Other symptoms such as sore throat, runny nose, or sneezing are not common symptoms of COVID-19. Besides respiratory manifestation, a few cases had gastrointestinal symptoms such as diarrhoea and vomiting.<sup>12,16</sup> Based on a report analysis of 72 314 Chinese cases, COVID-19 mild cases were about 81%, while severe cases and critically ill patients were about 14% and 5%, respectively.<sup>11</sup> Amongst the strong predictors of COVID-19 are loss of smell and taste, particularly when presented in combination with other symptoms such as persistent cough, diarrhoea, anosmia, fever, abdominal pain, loss of appetite fatigue, and fatigue.<sup>17</sup>

New concerns have emerged about the incidence of cutaneous skin diseases related to COVID-19, especially in children who were reported to develop Kawasaki-like syndrome.<sup>18</sup> However, there is a lack of evidence whether the virus itself can cause these manifestations because of the rarity of the reported cases besides the difficulty in the recognition of unfamiliar symptoms in health care settings that are fragmented and rapidly constructed to deal with the outbreak.<sup>18-20</sup>

According to Wang et al study,<sup>21</sup> in mild cases, symptoms may last for 2 weeks, while in severe cases it takes more time (3-6 weeks).

Most studies indicated that fever is the most predominant symptom in COVID-19, while the second most common symptoms were dry cough or fatigue.<sup>15,21,22</sup>

According to symptoms, laboratory data, oxygen saturation the COVID-19 case could be considered as mild, moderate pneumonia, severe pneumonia, and acute respiratory distress syndrome (ARDS).

COVID-19 cases suffer from symptoms and manifestations after the eradication of the virus that is called post-COVID-19 syndrome. This syndrome could be defined as the persistence of symptoms for 3 weeks after the start of COVID-19 symptoms (acute) and for more than 12 weeks for chronic post-COVID-19 syndrome.<sup>23</sup> Fatigue is the most common reported manifestation as a post-COVID-19 syndrome, while more critical manifestations such as deep venous thrombosis, stroke, myocarditis, pulmonary fibrosis, and renal failure were reported by a few percent of the subjects.<sup>24</sup>

### 3 | DIAGNOSIS

Contact or exposure to confirmed COVID-19 cases in the last 2 weeks is the first step in the clinical diagnosis of the infection, but also many patients had caught COVID-19 infection without known history of exposure to confirmed cases.<sup>25</sup> The national health commission of China made the guidelines for the diagnosis of COVID-19 infections and classified the subjects into two classes, suspected and confirmed cases.<sup>26</sup> These criteria for diagnosis were based on the WHO recommendation in the first two attacks of the coronavirus family, SARS, and MERS.<sup>27,28</sup>

Suspected clustering COVID-19 cases are described when one case is confirmed and simultaneously in the same small area, there are some cases suffering from fever or symptoms of respiratory infection within 14 days. Clustering cases result from human-to-human transmission of the virus in case of exposure or close contact to the infected subject.<sup>29</sup>

#### 3.1 | Imaging examinations

Many factors could influence the finding of the imaging techniques in COVID-19 such as the severity of the disease, age of the patient, and underlying disorders of the lung.<sup>30</sup> Computed tomography (CT) imaging is the primary tool for the diagnosis of COVID-19 with high sensitivity.<sup>31</sup>

The lesion obtained from the CT scan could be single, double, or more lesions that distribute dominantly, mainly subpleural. The shape of the lesion is variable, and it could be lumpy, nodular, or patchy also other shapes could be found. The density of the lesion as described by Jin et al is showed to be ground-glass shadow and paving stones, indicating a partial filling of air spaces in the lungs by exudate or transudate, in addition to interstitial thickening, thickened walls of the bronchi, and consolidation.<sup>30,32</sup> Chest X-ray examination is less sensitive compared with the CT scan and could not detect changes in the lung at early stages.

#### 3.2 | Blood tests

The total number of leukocytes may remain normal or decrease in the early stage of the disease. In addition, lymphocytes can also show reduction, while monocytes levels may increase or remain within the normal range.<sup>30</sup>

In addition to the evaluation of the previous blood tests other laboratory data should be obtained to facilitate the clinical evaluation of the disease such as levels of ferritin, lactate dehydrogenase, liver enzymes, interleukin-6, and D-dimer which are elevated in most cases.<sup>33</sup> Besides these laboratory tests, arterial blood gases, and oxygen saturation levels are essential to evaluate the level of oxygenation.

#### 3.3 | Reverse polymerase chain reaction (Real-time RT-PCR)

RT-PCR detects the new coronavirus nucleic acid, and it has a confirmatory differentiation also it could be used for the detection of the

nucleic acid of different respiratory tract infections such as influenza A and B and chlamydia. This method is strongly recommended for the detection of SARS-CoV-2 RNA using respiratory samples.<sup>34</sup> Collection of specimens could be from the upper respiratory tract (naso- and oropharyngeal) or the lower respiratory tract (expectorated sputum, bronchoalveolar lavage, or endotracheal aspirate) according to WHO recommendations. In addition, RT-PCR should be used to follow-up the viral load of the confirmed case for the evaluation of the case response.

The sensitivity of RT-PCR reported by different studies is about 78% compared with 75 for Ct scan.<sup>35</sup>

#### 3.4 | Rapid tests (serological tests)

However, the diagnostics of COVID-19 subjects by RT-PCR is both efficient and specific, but also crucially in need of rapid tests (serological tools) for investigating antibody responses for rapid and easy diagnosis besides assessing potential herd immunity.<sup>36</sup> Most studies indicated that sensitivity of rapid tests is higher (69.9%: 98.9%) at least 3 weeks from the onset of COVID-19 symptoms, while at the start of the disease the sensitivity of serological tests is low (13.4%: 50.3%).<sup>37</sup> According to a recent review that analysed findings from 40 studies, the sensitivity and specificity of these tests are low especially at the start of the disease and the current evidence does not support the continued use of existing point-of-care serological tests.<sup>37</sup>

### 4 | PREVENTION

Preventive measures should be performed by both the patient and the people in contact with them.<sup>20,38</sup>

Preventive measures should be performed by suspected or confirmed COVID-19 cases to minimise the spread of the infection to the surrounding community. Subjects that should follow the preventive measurements are those with suspected, under investigation, or confirmed COVID-19 with a mild case that does not need hospitalisation or those that are medically stable after hospitalisation and have been discharged.

Subjects with confirmed or suspected COVID-19 should avoid direct contact with others to prevent the disease spread, also it is recommended to wear a mask in case of contact with other people. For suspected cases, they should call the medical emergency number specified by each country.

The previous attack of SARS provided the medical researchers and healthcare professionals with important findings of aerosol producing procedures and devices, also their role in viral diseases spread.<sup>39</sup> Previous studies showed a higher rate of viral infections amongst the medical staffs that performed noninvasive ventilation (NIV), endotracheal intubation, and other aerosol-generating procedures.<sup>39</sup>

Aerosol therapy using nebulisers during mechanical ventilation also can be a source for spreading COVID-19 infection amongst healthcare providers, hence, it is recommended not to use aerosol producing tools such as pressurised metered dose inhaler (pMDI) or nebulisers if possible or using nebulisers with the extra protective

measures.<sup>40-42</sup> The ability of nebuliser to carry the viral infection to the medical team or other close contacts to the subject is based on the emitted aerosol particles from the nebuliser that produce particle size ranging from 1 to 5 µm, these respirable fine particles can carry the virus and come back from the lung through the exhaled air.<sup>43</sup>

#### 4.1 | Safety of intensive care providers (personal protective equipment)

All healthcare providers in close contact with COVID-19 subjects are at increased risk of contracting the viral infection.<sup>44,45</sup> Therefore, all healthcare workers in the intensive care unit (ICU) should follow preventive measures through using a medical protective mask (preferable to be an N95 mask), gloves, disposable surgical cap, gown, and full-face respirator protective device.<sup>46</sup> The findings of two randomised clinical trials designed to compare the protective effect of the N95 mask with that of the surgical mask against the spread of influenza to the healthcare providers indicated that there is a non-significant difference between them, but also it is still considered that the use of the surgical mask for ICU medical staff dealing with COVID-19 subjects is not recommended.<sup>47,48</sup> In addition, using sanitisers that contain alcohol can be beneficial, however, it is not superior to washing hands with soap and running water.<sup>49</sup> Healthcare providers should wear double gloves in case of handling subjects' related biological samples.<sup>50</sup>

There are several types of gowns such as surgical, non-surgical, and overall gown. In case of healthcare provider who deals with COVID-19 subjects, it is recommended to wear the coverall gown for the optimum benefits.<sup>50</sup>

## 5 | TREATMENT

### 5.1 | Drug therapy

#### 5.1.1 | Antiviral

There is a weak recommendation for using lopinavir/ritonavir alone or in combination based on its use during the previous two attacks of SARS and MERS.<sup>51-53</sup>

The essential key to gain benefits from using antiviral therapy is the early start of treatment because delayed treatment has no significant effect in reducing mortality.<sup>30</sup>

A clinical trial carried on 199 patients with confirmed COVID-19 indicated a lack of difference in results between the two study groups, one group received lopinavir 400mg/ritonavir 100mg for 14 days and the second group received the standard therapy. This finding suggests that no significant benefits have been gained from using lopinavir/ritonavir.<sup>54</sup>

Remdesivir plus chloroquine in-vitro study indicated an inhibitory effect on COVID-19.<sup>55</sup> However, a recent study indicated a

beneficial role of Remdesivir reflected by the clinical improvement of about 68% of hospitalised COVID-19 subjects that received the drug, but also a large randomised clinical trials are needed to prove the beneficial effect.<sup>56</sup>

Favipiravir is a prodrug approved in Japan for the treatment of influenza which has broad-spectrum antiviral activity, is now used in Japan for the treatment of COVID-19. An open-label controlled study compared Favipiravir plus inhaled interferon with the control group indicated a significant impact of Favipiravir on virus clearance and disease progression.<sup>57</sup> The dose of Favipiravir on the first day of treatment was 1600 mg twice daily followed by a maintenance dose of 600 mg twice daily for 14 days.<sup>57</sup> While comparing Favipiravir with arbidol resulted in a non-significant difference regarding the clinical recovery rate in day 7 as showed by a randomised clinical trial.<sup>58</sup> The adverse effects of Favipiravir were mild and easily managed.<sup>58</sup> The National Medical Products Administration of China approved Favilavir for the treatment of COVID-19 but still under investigation and there are no confirmed findings.<sup>59</sup>

#### 5.1.2 | Antibiotics

In the case of secondary bacterial infection, the patient should receive the appropriate antibiotic regimen. Critically ill COVID-19 patients with suspected or confirmed diagnosis should receive empiric antimicrobial therapy.<sup>34</sup> The antibiotic should cover the community or hospital-acquired pneumonia, such as azithromycin, amoxicillin, fluoroquinolones,<sup>30</sup> and recently doxycycline.<sup>60,61</sup>

Vancomycin could be considered in case of a risk factor to MRSA.

#### 5.1.3 | Chloroquine and hydroxychloroquine

An in-vitro study carried on chloroquine as antiviral for treating COVID-19 indicated a beneficial antiviral effect of the drug before or after cell infection by the virus.<sup>55</sup> Not only the in-vitro results were positive, but also, several in vivo studies. A study carried out by Gao et al showed that chloroquine significantly had a role in reducing hospital stay and improving the evolution of COVID-19 pneumonia.<sup>62</sup> This could lead to a recommendation of a 500 mg dose of chloroquine twice daily for all cases of COVID-19.<sup>63</sup>

A study carried out by Gautret et al indicated the beneficial role of hydroxyquinoline 600 mg daily in decreasing the virus load in COVID-19 patients.<sup>64</sup> These results are promising especially hydroxychloroquine has a better long-term safety profile and fewer interactions compared with chloroquine.<sup>65,66</sup>

#### 5.1.4 | Immunosuppressant and corticosteroids

Laboratory testing and HScore<sup>67</sup> for screening and subgrouping of hyper-inflammation should be performed with all COVID-19

**TABLE 1** Target level of oxygen saturation for different COVID-19 patients<sup>30</sup>

Condition	Target level
Adult and non-pregnant patient	SpO <sub>2</sub> ≥ 90%
Pregnant patient	SpO <sub>2</sub> ≥ 92%-95%
Children	SpO <sub>2</sub> ≥ 90%
Children or adults with dyspnea, severe respiratory distress, apnoea, coma, shock, and central cyanosis	SpO <sub>2</sub> ≥ 94%

severe cases. For patients whom immunosuppressants could be of benefit, they could receive tocilizumab, corticosteroids, or immunoglobulin. A study carried by Xu et al including 20 cases with severe COVID-19 indicated the efficacy of tocilizumab on the management of hyper-inflammation of severe cases and resulted in the improvement of symptoms in addition to decreasing case deterioration.<sup>68</sup>

Using corticosteroids during coronavirus infection is controversial depending on results from previous studies carried on the two previous attacks (SARS and MERS). Studies on SARS indicated some survival benefits of using corticosteroid and potential harms such as delayed clearance of the viral infection, vascular necrosis, and psychosis.<sup>69</sup> Regarding corticosteroid administration during the MERS attack, a study carried by Arabi et al indicated no benefit from using it in decreasing mortality, in addition to reducing the rate of viral clearance from the lung.<sup>70</sup> Based on these findings the routine use of corticosteroid is not preferred and it should be reserved for selected patients (COPD and asthma exacerbation, and septic shock).<sup>71</sup> Methylprednisolone (40-80 mg) could be used in case of severe illness rapid progressive disease to improve the symptoms of the patient and reduce the rate of progression, but it does not affect the length of hospital stay.<sup>30,72,73</sup>

Recent randomised clinical trial (RECOVERY trial) tested the effect of corticosteroid administration on the mortality rate of COVID-19 subjects, administration of 6 mg/day for 10 days of dexamethasone resulted in decreased death by about one-third compared with control group.<sup>74</sup>

### 5.1.5 | Anticoagulant

COVID-19 subjects are at increased risk of thrombotic events such as venous thromboembolism, hence, the use of anticoagulant therapy is essential to reduce this risk and decrease mortality.<sup>75,76</sup> Case reports provided evidence of these thrombotic events such as pulmonary embolism and deep venous thrombosis.<sup>77</sup> Beside case reports, a study carried by Cui et al, indicated that about 25% of severe COVID-19 subjects have a thrombotic event and elevated levels of D-dimer who were not receiving anticoagulant therapy.<sup>78</sup> According to these findings, the International Society on Thrombosis and Haemostasis (ISTH) recommended that all COVID-19 subjects who require hospital admission should receive a prophylactic dose of low molecular weight heparin (LMWH), unless they have contraindications to anticoagulant therapy such as active bleeding and platelet count <25 × 10<sup>9</sup>/L.<sup>79</sup> In case the anticoagulants are contraindicated,

mechanical thromboprophylaxis could be used such as pneumatic compression devices. Receiving anticoagulant therapy appeared to be effective for reducing mortality amongst COVID-19 subjects.<sup>75,80</sup>

### 5.1.6 | Lactoferrin

Lactoferrin is an iron-binding glycoprotein that belongs to the transferrin family. Lactoferrin expressed antiviral activity against several viral infections such as rotavirus, poliovirus, hepatitis B, hepatitis C, and influenza A virus.<sup>81,82</sup> Serrano et al, conducted a study to demonstrate the preventive and curative effect of lactoferrin on COVID-19 subjects and members in contact with them.<sup>83</sup> The findings of the study showed that the administration of liposomal lactoferrin (32 mg/10 mL) dosed every 4-6 hours for 20 days has a curative effect for all included subjects in the study. Also, other members in direct contact with the patient received half of the dose and it reflected a preventive effect. Addition of lactoferrin to the treatment regimen is preferred because of its proven beneficial effect.

## 5.2 | Oxygen therapy

For subjects with hypoxia, respiratory distress, severe respiratory infection there is a strong recommendation for oxygen therapy.<sup>30</sup> No need for oxygen for patients with pneumonia without signs of severe manifestations.<sup>71</sup> The patient should receive oxygen with titratable rate until the target oxygen saturation (SpO<sub>2</sub>) is achieved. The target SpO<sub>2</sub> differs according to the clinical conditions as shown in Table 1.

If oxygen therapy through a nasal cannula or facial mask is not effective or the subject has hypoxic respiratory failure, mechanical ventilation should be considered.<sup>30</sup> Invasive mechanical ventilation (IMV) is recommended for moderate to severe cases of ARDS, while mild cases could be supported by non-invasive ventilation (NIV).<sup>84,85</sup> Low tidal volume ventilation is related to low mortality in ARDS.<sup>86</sup> In addition to NIV continuous positive airway pressure (CPAP) could be beneficial for the management of COVID-19 associated respiratory failure.

When it is difficult to maintain SpO<sub>2</sub> more than 92% and/or not improved dyspnea through standard oxygen therapy, application of high flow nasal oxygen (HFNO) is recommended. HFNO could be initiated at 30-40 L/min and FiO<sub>2</sub> 50%-60% and it should be adjusted according to the clinical response of the subject.<sup>33</sup> After 1 hour with flow more than 50 L/min and FiO<sub>2</sub> more than 70%, if the patient symptoms are not improved switch to NIV.<sup>33</sup>

**TABLE 2** Factors affecting aerosol delivery during mechanical ventilation and recommended settings<sup>42,88,89</sup>

Factor	Recommendations
Nebulizer type	It is preferred to use VMN instead of traditional jet nebulizer (JN) as the VMN drug chamber is completely separated from the exhaled air pathway. If available use VMN for aerosol delivery during mechanical ventilation.
Nebulizer position	Placing the VMN prior to the humidifier could improve the efficiency of the aerosol therapy and further reduce retrograde contamination from the infected subject. JN (if used) should be placed close to the ventilator.
Position of pMDI attached to spacer	pMDI + spacer should be placed at least 15 cm away from the endotracheal tube.
Nebulizer fill volume	Add at least 2 ml of the vehicle to the drug for JN. Adding saline to the nebulized drug solution would increase the delivered fraction of the inhalable drug. Increasing the fill volume of VMN is not important.
Residual dead volume	The dead volume that remains in the nebulizer chamber affects the amounts of aerosol that could be delivered to the patient. Also, this amount of drug could be contaminated with microorganisms in case of jet nebulizers. In case of using JN, it should be disinfected and discarded carefully after end of nebulization. VMNs are recommended if available.
Filters	It is recommended to Attach a HEPA filter to the expiratory limb of the ventilator to reduce the exposure to the fugitive aerosol and avoid the transmission of contaminated droplets through the ventilator circuit.

### 5.3 | Aerosol therapy during mechanical ventilation

Aerosol therapy for respiratory disorders is important for providing targeted drug delivery with less systemic absorption. Bronchodilators, corticosteroids, and antibiotics are the most common agents to be delivered through aerosol. Aerosol producing devices that could be used during mechanical ventilation are nebulisers and pressurised metered-dose inhaler (pMDI) but should be used with caution to avoid the infection of the surrounding personals by fugitive aerosol.<sup>87</sup>

Several factors that could control the aerosol delivery during mechanical ventilation are summarised in Table 2 with recommended settings.<sup>42,88,89</sup>

### 5.4 | Symptomatic treatment

#### 5.4.1 | Fever

Temperature up to 38°C is acceptable without using antipyretics, starting from 38.5°C antipyretic drug that could be used.<sup>30</sup> Antipyretic drugs such as paracetamol or non-steroidal anti-inflammatory drugs could be used.

Regarding anti-inflammatory such as ibuprofen, there is a warning against its use because it is thought to aggravate and worsen COVID-19, whoever there is no strong evidence for ensuring this warning and a big clinical trial should be carried to confirm the findings.<sup>90</sup>

### 5.5 | Nutrition

Malnutrition of the patient is a predictor of the prognostic direction for those with respiratory failure and mechanically ventilated

subjects. Malnutrition could be caused by different deficiencies, one of them is a low level of albumin, which is related to case prognosis.<sup>91</sup>

Synthesis of proteins and division of immune cells need a high amount of amino acids. Hence, protein-energy malnutrition (PEM) is believed to be the main cause of immunodeficiency worldwide.<sup>92-94</sup> Recent studies recommended the measuring and balancing of the nutritional status of COVID-19 subjects at the time of admission for enhancing the immune system and supporting the therapeutic agents.<sup>30,95</sup> Patients that are malnourished at admission should receive nutritional supplementation as early as possible, particularly increasing the oral intake of amino acids.<sup>30</sup> A sufficient protein intake of about 1.5 g/d should be maintained for all subjects with confirmed COVID-19 even they are presented with signs of malnutrition.<sup>30</sup> Anti-inflammatory and antioxidant properties of some vitamins and elements could be the explanation of their involvement in the nutritional plan in case of COVID-19.<sup>95</sup> In addition to proteins several vitamins and trace elements could enhance the immune response of the infected patient to fight against the viral infection. Vitamins that had a beneficial effect during viral infections are vitamin A, C, D, and E, also zinc and selenium have a good impact on enhancing the immunity of the subject.<sup>96-102</sup>

## 6 | CONCLUSION

Supportive care including oxygen therapy and mechanical ventilation is the backbone for the management of COVID-19. Chloroquine and hydroxychloroquine have a controversial effect on treating this viral infection. there is no antiviral therapy that has been proved to effectively cure SARS-CoV-2 infection. Tocilizumab results are promising. Finally, the essential key to fight this attack is the prevention

strategies against virus spread. Vitamins and trace elements could enhance the immune response of the infected subject to fight against the infection. vibrating mesh nebuliser is the recommended type for aerosol delivery during mechanical ventilation. Lactoferrin is a promising effective agent for the treatment and prevention of COVID-19.

## AUTHORS CONTRIBUTIONS

Conception and design: Haitham Saeed; Administrative support: All authors; Provision of study materials or patients: All authors; Collection and assembly of data: All authors; Data analysis and interpretation: All authors; Manuscript writing: All authors; Final approval of manuscript: All authors.

## DISCLOSURE

The authors have declared no conflicts of interest for this article.

## DATA AVAILABILITY STATEMENT

The datasets analysed during the current study are available from the corresponding author on reasonable request.

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## REFERENCES

- Wong G, Liu W, Liu Y, et al. MERS, SARS, and Ebola: the role of super-spreaders in infectious disease. *Cell Host & Microbe*. 2015;18:398-401.
- Willman M, Kobasa D, Kindrachuk JJV. A comparative analysis of factors influencing two outbreaks of Middle Eastern respiratory syndrome (MERS) in Saudi Arabia and South Korea. *Viruses*. 2019;11:1119.
- Mez J, Daneshvar DH, Kiernan PT, et al. Clinicopathological evaluation of chronic traumatic encephalopathy in players of American football. *JAMA*. 2017;318:360-370.
- Xu Y, Li X, Zhu B, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med*. 2020;26(4):502-504.
- Xiao F, Tang M, Zheng X, et al. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterology*. 2020;158(6):1831-1833.
- Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: A retrospective review of medical records. *Lancet*. 2020;395:809-815.
- Zhou D, Zhang P, Bao C, Zhang Y, Zhu N. Emerging understanding of etiology and epidemiology of the novel coronavirus (COVID-19) infection in Wuhan, China. 2020.
- COVID C. Severe outcomes among patients with coronavirus disease 2019 (COVID-19)—United States, February 12–March 16, 2020.
- El-Gendy AO, Saeed H, Ali AM, et al. Bacillus Calmette-Guérin vaccine, antimalarial, age and gender relation to COVID-19 spread and mortality. *Vaccine*. 2020;38:5564-5568.
- Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054-1062.
- Wu Z, McGoogan JMJJ. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323(13):1239-1242.
- Zimmermann P, Curtis NJTPIDJ. Coronavirus infections in children including COVID-19. *Pediatr Infect Dis J*. 2020;39(5):355-368.
- Cai Q, Chen F, Wang T, et al. Obesity and COVID-19 severity in a designated hospital in Shenzhen, China. *Diabetes Care*. 2020;43:1392-1398.
- Gao F, Zheng KI, Wang X-B, et al. Obesity is a risk factor for greater COVID-19 severity. *Diabetes Care*. 2020.
- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395:497-506.
- Xia W, Shao J, Guo Y, Peng X, Li Z, Hu DJ. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. *Pediatr Pulmonol*. 2020;55(5):1169-1174.
- Menni C, Valdes A, Freydin MB, et al. Loss of smell and taste in combination with other symptoms is a strong predictor of COVID-19 infection. *MedRxiv*. 2020;26(7):1037-1040.
- Wollina U, Karadağ AS, Rowland-Payne C, Chiriac A, Lotti T. Cutaneous signs in COVID-19 patients: a review. *Dermatol Therapy*. 2020.
- Viner RM, Whittaker EJTL. Kawasaki-like disease: emerging complication during the COVID-19 pandemic. *Lancet*. 2020;395:1741-1743.
- Elgendy MO, El-Gendy AO, Abdelrahim ME. Public awareness in Egypt about COVID-19 spread in the early phase of the pandemic. *Patient Educ Counsel*. 2020;103(12):2598-2601.
- Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061-1069.
- Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513.
- Greenhalgh T, Knight M, Buxton M, Husain L. Management of post-acute covid-19 in primary care. *BMJ*. 2020;370:m3026.
- Kamal M, Abo Omirah M, Hussein A, Saeed H. Assessment and characterisation of post-COVID-19 manifestations. *International Journal of Clinical Practice*. 2020;http://dx.doi.org/10.1111/ijcp.13746
- Zu ZY, Jiang MD, Xu PP, et al. Coronavirus Disease 2019 (COVID-19): A Perspective from China. *Radiology*. 2020;296(2):E15-E25. <http://dx.doi.org/10.1148/radiol.2020200490>
- Committee GOoNH. Office of state administration of traditional Chinese medicine. Notice on the issuance of a programme for the diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (trial fifth edition)(2020-02-26)[EB/OL].
- World Health Organization. WHO guidelines for the global surveillance of severe acute respiratory syndrome (SARS): updated recommendations. October 2004.
- Azhar El, El-Kafrawy SA, Farraj SA, et al. Evidence for camel-to-human transmission of MERS coronavirus. *New Engl J Med*. 2014;370:2499-2505.
- Chan JF-W, Yuan S, Kok K-H, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating

- person-to-person transmission: a study of a family cluster. *Lancet*. 2020;395:514-523.
30. Jin Y-H, Cai L, Cheng Z-S, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res*. 2020;7:4.
  31. Ai T, Yang Z, Hou H, et al. Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. *Radiology*. 2020;296(2):E32-E40. <http://dx.doi.org/10.1148/radiol.2020200642>
  32. Zhou S, Wang Y, Zhu T, Xia LJ. CT features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. *Am J Roentgenol*. 2020;214:1287-1294.
  33. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. *Features, Evaluation and Treatment Coronavirus (COVID-19)*. Statpearls [internet]: StatPearls Publishing; 2020.
  34. Alhazzani W, Møller MH, Arabi YM, et al. Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Intensive Care Med*. 2020;46(5):854-887.
  35. Waller JV, Allen IE, Lin KK, Diaz MJ, Henry TS, Hope MD. The limited sensitivity of chest computed tomography relative to reverse transcription polymerase chain reaction for Severe Acute Respiratory Syndrome Coronavirus-2 infection: a systematic review on COVID-19 diagnostics. *Invest Radiol*. 2020;55(12):754-761.
  36. Hoffman T, Nissen K, Krambrich J, et al. Evaluation of a COVID-19 IgM and IgG rapid test; an efficient tool for assessment of past exposure to SARS-CoV-2. *Ecol Epidemiol*. 2020;10:1754538.
  37. Bastos ML, Tavaziva G, Abidi SK, et al. Diagnostic accuracy of serological tests for covid-19: systematic review and meta-analysis. *BMJ*. 2020;370:m2516.
  38. Elgendy MO, Abd Elmawla MN, Abdel Hamied AM, El Gendy SO, Abdelrahim MEA. COVID-19 patients and contacted person awareness about home quarantine instructions. *International Journal of Clinical Practice*. 2020;<http://dx.doi.org/10.1111/ijcp.13810>
  39. Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PLoS One*. 2012;7.
  40. Hui DS, Chow BK, Chu LC, et al. Exhaled air and aerosolized droplet dispersion during application of a jet nebulizer. *Chest*. 2009;135:648-654.
  41. Wang Y, Zhu L-Q. Pharmaceutical care recommendations for antiviral treatments in children with coronavirus disease 2019. *World Journal of Pediatrics*. 2020;16(3):271-274. <http://dx.doi.org/10.1007/s12519-020-00353-5>
  42. Ari A. Practical strategies for a safe and effective delivery of aerosolized medications to patients with COVID-19. *Respiratory Medicine*. 2020;167:105987. <http://dx.doi.org/10.1016/j.rmed.2020.105987>
  43. Amirav I, Newhouse MT. Transmission of coronavirus by nebulizer: a serious, underappreciated risk. *CMAJ*. 2020;192:E346.
  44. Cheung JC-H, Ho LT, Cheng JV, Cham EYK, Lam KN. Staff safety during emergency airway management for COVID-19 in Hong Kong. *Lancet Respir Med*. 2020;8(4):e19.
  45. Chang D, Xu H, Rebaza A, Sharma L, Cruz CS. Protecting health-care workers from subclinical coronavirus infection. *Lancet Respir Med*. 2020;8:e13.
  46. Arabi YM, Fowler R, Hayden FG. Critical care management of adults with community-acquired severe respiratory viral infection. *Intensive Care Med*. 2020;46:315-328.
  47. Radonovich LJ, Simberkoff MS, Bessesen MT, et al. N95 respirators vs medical masks for preventing influenza among health care personnel: a randomized clinical trial. *JAMA*. 2019;322:824-833.
  48. Loeb M, Dafoe N, Mahony J, et al. Surgical mask vs N95 respirator for preventing influenza among health care workers: a randomized trial. *JAMA*. 2009;302:1865-1871.
  49. Hirose R, Nakaya T, Naito Y, et al. Situations leading to reduced effectiveness of current hand hygiene against infectious mucos from influenza virus-infected patients. *MSphere*. 2019;4:e00474-00419.
  50. Chen X, Shang Y, Yao S, Liu R, Liu H. Perioperative care provider's considerations in managing patients with the COVID-19 infections. *Transl Perioper Pain Med*. 2020;7:216-223.
  51. Lai ST. Treatment of severe acute respiratory syndrome. *Eur J Clin Microbiol Infect Dis*. 2005;24:583-591.
  52. Chu C, Cheng V, Hung I, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax*. 2004;59:252-256.
  53. Que T, Wong V, Yuen KJ. Treatment of severe acute respiratory syndrome with lopinavir/ritonavir: a multicentre retrospective matched cohort study. *Hong Kong Med J*. 2003;9:399-406.
  54. Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *New Engl J Med*. 2020;382(19):1787-1799.
  55. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res*. 2020;30:269-271.
  56. Grein J, Ohmagari N, Shin D, et al. Compassionate use of remdesivir for patients with severe Covid-19. *New Engl J Med*. 2020;382:2327-2336.
  57. Cai Q, Yang M, Liu D, et al. Experimental treatment with favipiravir for COVID-19: an open-label control study. *Engineering*. 2020;6(10):1192-1198.
  58. Chen C, Huang J, Cheng Z, et al. Favipiravir versus arbidol for COVID-19: a randomized clinical trial. *MedRxiv*. 2020. <https://doi.org/10.1101/2020.03.17.20037432>
  59. Elfiky A A. Anti-HCV, nucleotide inhibitors, repurposing against COVID-19. *Life Sciences*. 2020;248:117477. <http://dx.doi.org/10.1016/j.lfs.2020.117477>
  60. Conforti C, Giuffrida R, Zalaudek I, Di Meo N. Doxycycline, a widely used antibiotic in dermatology with a possible anti-inflammatory action against IL-6 in COVID-19 outbreak. *Dermatol Ther*. 2020.
  61. Sayed AM, Khalaf AM, Abdelrahim MEA, Elgendy MO. Repurposing of some anti-infective drugs for COVID-19 treatment: a surveillance study supported by an in silico investigation. *Int J Clin Pract*; 75(4):e13877.
  62. Gao J, Tian Z, Yang XJ. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends*. 2020.
  63. Colson P, Rolain J-M, Lagier J-C, Brouqui P, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *International Journal of Antimicrobial Agents*. 2020;55(4):105932. <http://dx.doi.org/10.1016/j.ijantimicag.2020.105932>
  64. Gautret P, Lagier J-C, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *International Journal of Antimicrobial Agents*. 2020;56(1):105949. <http://dx.doi.org/10.1016/j.ijantimicag.2020.105949>
  65. Yao X, Ye F, Zhang M, et al. In vitro antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Clin Infect Dis*. 2020.
  66. Marmor M, Carr R, Easterbrook M, Farjo A, Mieler WJ. American Academy of Ophthalmology. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy: a report by the American Academy of Ophthalmology. *Ophthalmology*. 2002;109:1377-1382.
  67. Fardet L, Galicier L, Lambotte O, et al. Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. *Arthritis Rheumatol*. 2014;66:2613-2620.



68. Xu X, Han M, Li T, et al. Effective treatment of severe COVID-19 patients with Tocilizumab. *ChinaXiv*: 20200300026, 2020.
69. Stockman LJ, Bellamy R, Garner P. SARS: systematic review of treatment effects. *PLoS Med*. 2006;3(9):e343.
70. Arabi YM, Mandourah Y, Al-Hameed F, et al. Corticosteroid therapy for critically ill patients with Middle East respiratory syndrome. *Am J Respir Crit Care Med*. 2018;197:757-767.
71. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance, 13 March 2020; 2020.
72. Zhao Z, Zhang F, Xu M. Clinical analysis of 190 cases of outbreak with atypical pneumonia in Guangzhou in spring, 2003. *Zhonghua yi xue za zhi*. 2003;24:73-76.
73. Meng Q, Dong P, Guo Y, et al. Use of glucocorticoid in treatment of severe acute respiratory syndrome cases. *Zhonghua yu fang yi xue za zhi*. 2003;37:233-235.
74. Ledford H. Coronavirus breakthrough: dexamethasone is first drug shown to save lives. *Nature*. 2020;582:469.
75. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost*. 2020;18:844-847.
76. Tang N, Bai H, Chen X, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost*. 2020;18:1094-1099.
77. Danzi GB, Loffi M, Galeazzi G, Gherbesi E. Acute pulmonary embolism and COVID-19 pneumonia. A random association? *Eur Heart J*. 2020;41:1858.
78. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. *J Thromb Haemost*. 2020.
79. Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *J Thromb Haemost*. 2020;18:1023-1026.
80. Iba T, Di Nisio M, Levy JH, Kitamura N, Thachil J. New criteria for sepsis-induced coagulopathy (SIC) following the revised sepsis definition: a retrospective analysis of a nationwide survey. *J Thromb Haemost*. 2017;7(9):e017046.
81. Berlutti F, Pantanella F, Natalizi T, et al. Antiviral properties of lactoferrin—a natural immunity molecule. *Molecules*. 2011;16:6992-7018.
82. Van der Strate B, Beljaars L, Molema G, Harmsen M, Meijer DJ. Antiviral activities of lactoferrin. *Antiviral Res*. 2001;52:225-239.
83. Serrano G, Kochergina I, Albors A, et al. Liposomal lactoferrin as potential preventative and cure for COVID-19. *Int J Res Health Sci*. 2020;8:8-15.
84. Bellani G, Laffey JG, Pham T, et al. Noninvasive ventilation of patients with acute respiratory distress syndrome. Insights from the LUNG SAFE study. *Am J Respir Crit Care Med*. 2017;195:67-77.
85. Frat J-P, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *New Engl J Med*. 2015;372:2185-2196.
86. Needham DM, Yang T, Dinglas VD, et al. Timing of low tidal volume ventilation and intensive care unit mortality in acute respiratory distress syndrome. A prospective cohort study. *Am J Respir Crit Care Med*. 2015;191:177-185.
87. Saeed H, Mohsen M, Eldin AS, et al. Effects of fill volume and humidification on aerosol delivery during single-limb noninvasive ventilation. *Respir Care*. 2018;63:1370-1378.
88. Saeed H, Mohsen M, Fink JB, et al. Fill volume, humidification and heat effects on aerosol delivery and fugitive emissions during non-invasive ventilation. *J Drug Deliv Sci Technol*. 2017;39:372-378.
89. Saeed H, Mohsen M, Eldin AS, et al. Effects of fill volume and humidification on aerosol delivery during single-limb noninvasive ventilation. *Respir care*. 2018;63:1370-1378.
90. Day M. Covid-19: ibuprofen should not be used for managing symptoms, say doctors and scientists.
91. Caccialanza R, Laviano A, Lobascio F, et al. Early nutritional supplementation in non-critically ill patients hospitalized for the 2019 novel coronavirus disease (COVID-19): rationale and feasibility of a shared pragmatic protocol. *Nutrition*. 2020;74:110835.
92. Delafuente JC. Nutrients and immune responses. *Rheum Dis Clin North America*. 1991;17:203-212.
93. Ritz BW, Gardner EM. Malnutrition and energy restriction differentially affect viral immunity. *J Nutr*. 2006;136:1141-1144.
94. Maggini S, Wintergerst ES, Beveridge S, Hornig DH. Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune responses. *Br J Nutr*. 2007;98:S29-S35.
95. Zhang L, Liu Y. Potential interventions for novel coronavirus in China: a systematic review. *J Med Virol*. 2020;92:479-490.
96. Zhang J, Taylor EW, Bennett K, Saad R, Rayman MP. Association between regional selenium status and reported outcome of COVID-19 cases in China. *Am J Clin Nutr*. 2020;111:1297-1299.
97. Read SA, Obeid S, Ahlenstiel C, Ahlenstiel GJ. The role of zinc in antiviral immunity. *Adv Nutr*. 2019;10:696-710.
98. Grant WB, Lahore H, McDonnell SL, et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients*. 2020;12:988.
99. Truwit JD, Hite RD, Morris PE, et al. Effect of vitamin C infusion on organ failure and biomarkers of inflammation and vascular injury in patients with sepsis and severe acute respiratory failure: the CITRIS-ALI randomized clinical trial. *JAMA*. 2019;322:1261-1270.
100. Patel N, Penkert RR, Jones BG, et al. Baseline serum vitamin A and D levels determine benefit of oral vitamin A&D supplements to humoral immune responses following pediatric influenza vaccination. *Viruses*. 2019;11:907.
101. Huang Z, Liu Y, Qi G, Brand D, Zheng SG. Role of vitamin A in the immune system. *J Clin Med*. 2018;7:258.
102. Hemilä H, Kaprio JJ. Vitamin E supplementation and pneumonia risk in males who initiated smoking at an early age: effect modification by body weight and dietary vitamin C. *Nutr J*. 2008;7:33.

**How to cite this article:** Saeed H, Osama H, Madney YM, et al. COVID-19; current situation and recommended interventions. *Int J Clin Pract*. 2021;75:e13886. <https://doi.org/10.1111/ijcp.13886>