

From quarantine room: Physician perspective

Himmatrao Saluba Bawaskar, Pramodini Himmatrao Bawaskar

Bawaskar Hospital and Clinical Research Center, Mahad Raigad, Maharashtra, India

ABSTRACT

This write-up is a brief reflection of a rural doctor couple, Dr. Himmatrao Saluba Bawaskar (HSB) and Dr. Pramodini Himmatrao Bawaskar (PHB), working in the remote area of Maharashtra state of India during COVID-19 pandemic. During the pandemic, rural doctors are routinely exposed to symptomatic COVID-positive cases in the outpatient as well as indoor setting. The authors, both husband and wife, were in compulsory quarantine for twice at home and experienced social stigmas attached to a positive case. Here is a report the details of COVID-19 pattern and its management learned from the published scientific papers on COVID-19, and severe acute respiratory syndrome due to SARS-CoV-2 from December 2019 and their own experience in rural setting and the current literature shared in the form of personal narration. Apart from the personal experience of patients experience regarding quarantine period, COVID-19 is discussed in detail for the benefit of rural practitioners.

Keywords: COVID-19, quarantine, severe acute respiratory syndrome-SARS-CoV-2

Introduction

COVID-19 pandemic is a biggest global public health crisis of today's generation next to the influenza outbreak of 1918. The impact of COVID-19 disease is different in different countries, because of difference in culture norms. In the early August 2020, a total of cases 22857,004 and 797009 deaths in more than 200 countries were reported. COVID-19 is a zoonotic disease caused by beta-coronavirus which mimics to severe acute respiratory syndrome coronavirus (SARS-CoV-1) and Middle East respiratory syndrome coronavirus. On the basis of similar genetic proximity, SARS-CoV-2 originated from bat derived coronavirus which spread via an unknown intermediate mammal host to human. In December 2019 an atypical pneumonia cases reported from Wuhan china in those victim visited to wet market and consumed bat meat The genomic structure of human-infected SARS-CoV-2 virus is similar to the bat-carrying coronavirus which confirmed that the

primary host is bat. 80% of pages are printed for the publication on COVID-19 in the *Lancet*.^[1] First case of COVID-19 from India was reported on January 30, 2020, in the southern coastal state of Kerala in a student who had a travel history to Wuhan, China. Initially, sporadic active and fatal cases are reported from urban area; however, now, it becomes a pandemic, and by the middle of June, figure of cases is more than ten lakhs lakhs and deaths are in thousands, with the highest cases and deaths reported from Maharashtra. **Virulent SARS-CoV-2 virus flourished in a cold and high humid climate of coastal region of maharashtra including Mumbai, Thane, Raigad, Ratanagiri, Kudal and Sindhudurga were from high morbidity and mortality reported as compared to rest of Maharashtra with dry and hot climate.** High infectivity and mortality were reported from China, Germany, Spain, Italy, and the USA. Severity of COVID-19 in these developed nations with high-quality facilities is attributed to the population of these nations are very conscious about health, and they do not give chance to their body for the development of heard immunity against the virus and bacterial infection with subclinical dose. Advances of medical knowledge and gadgets, still the highest deaths as compared to India are attributed to early intubation and maximum use of invasive ventilator.

Address for correspondence: Dr. Himmatrao Saluba Bawaskar, Bawaskar Hospital and Clinical Research Center, Mahad Raigad 402 301, Maharashtra, India. E-mail: himmatbawaskar@rediffmail.com

Received: 17-05-2020

Revised: 14-06-2020

Accepted: 29-06-2020

Published: 30-10-2020

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_896_20

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Bawaskar HS, Bawaskar PH. From quarantine room: Physician perspective. *J Family Med Prim Care* 2020;9:5092-102.

Are Indian More Resistant to Infection? Age-Old Deep-Rooted Ritual

Indian villagers experience recurrent upper respiratory tract infection, fever, and loose motions. It is important to note that in rural India, there is important ritual on the 12th day of baby born called naming ceremony, for to celebrate these ritual maximum women of local area majority them are 30–60 years old are invited.

Each woman one by one takes child kiss and put in the cradle; the same is repeated by all attended women. This exercise infant get subclinical dose of different bacteria and virus and indirectly boost the infant innate immunity. This is reason why, in later life, villagers are immune for infection or carry antibodies and cross immunity against various viruses and bacteria. This ritual is no more prevalent in the urban areas; this may be one of the reasons why the urban population responds very poorly to coronavirus, in addition to overcrowding.

Pulmonary tuberculosis is taken as the fact of life in India. Every child is compulsory given Bacillus Calmette–Guerin (BCG) vaccine by a vaccinator attending almost visiting nursing homes or home deliveries. BCG is a live-attenuated strain derived from an isolate *Mycobacterium bovis* for tuberculosis even INH-resistant strain is also included in BCG. BCG vaccination acts as immunomodulators and has been reported to offer broad protection to respiratory infection. It also produces positive heterologous or nonspecific immune effects, leading to improved response against nontubercular infection. BCG vaccination enhances the secretion of the proinflammatory cytokines, specifically interleukin (IL)-1B, which plays a vital role in antiviral immunity and antagonizes the cytokine storm evoked as a respond to SARS-CoV-2 virus infection. Older people having high concentration of ACE-2 receptors. Diabetes mellitus, hypertension, cancer, obesity, and steroid consumers and on immunosuppressant and health workers are more prone to SARS-CoV-2 infection; however, because of universal BCG vaccination, these older people who are more susceptible and severely affected by COVID-19 are be protected.^[2-5] Middle- and high-income countries that have current national universal BCG policy (55 countries) had 0.78 ± 0.40 (mean \pm standard error of the mean) deaths per million people; in contrast, those countries population of middle–high- and high-income never had a universal BCG policy had a large mortality rate with 16.390 ± 7.33 deaths per million people.^[6]

What Is the Reason of Our Quarantine?

On April 14, 2020, at 10.30 AM, author Himmatrao Saluba Bawaskar (HSB) received a phone call from a doctor colleague from the intensive care unit that he admitted a 62-year-old female with recurrent loose motions since mid-night, she was acute breathless, looks toxic, extremities were cold and cyanosed, her blood pressure was 70 mmHg, oxygen saturation was 44% raised to no more than 50% with oxygen 8 L/min, she was known case of diabetes for the last 10 years, and her spot blood

sugar was 371 mg/dL. Her son gave a history that she had fever for the last 3 days before admission, with cough for which she took some injection from local doctor. Her hemoglobin was 10.1 mg/dL, leukocyte count was 3600 μ L (normal 4000–10,000), neutrophils were 82.2% (normal 50–70), and lymphocytes were 12.3% (normal 20%–40%). Neutrophil-to-lymphocytes ratio (NLR) was 6.68 (normal <3). She was in acute respiratory failure. She did not reveal any history of urinary tract infection. Her husband and son stay at Mumbai, and both returned to village on March 24, 2020 for holi celebration. Her son brought her chest X-ray to my consulting room without wearing mask. X-ray of the chest showed bilateral ground-glass opacities with bilateral pneumonias, suggestive of COVID-19 disease [Figure 1]. She was given intravenous meropenem and noninvasive ventilator and transferred to the tertiary care hospital, Mumbai. Her nasopharyngeal swab was positive for SARS-CoV-2 virus RNA. She was put on invasive ventilator and died on April 17, 2020, due to multiorgan failure. As HSB handled the X-ray, there were maximum chances of getting infection by deposited virus.

We recollected that her son who came with his mother X-ray brought his father to my clinic 8 days before with complained of severe anorexia, loss of smell sensation, with history of DM for the last 18 years, exertions dyspnea, palpitation, and giddiness with no fever. He had anal abscess. He received antibiotics from his family physician. His hemoglobin was 13 mg/dL, blood sugar was 410 mg/dL, leukocytes were 15,000/ μ L, neutrophils were 82.7%, and lymphocytes were 8.4%. The NLR was 9.84. His chest X-ray showed bilateral bronchovascular prominence with infiltration, suggestive of COVID-19, X-ray presentation of COVID-19 reported as interstitial fibrosis [Figure 2]. He was clinically improved with intravenous meropenem, moxifloxacin, and aspirin to be chewed 325 mg, hydration, plain insulin, dabigatran 110 mg twice a day, statin 80 mg, doxycycline 100 mg twice, Later, he was transferred to COVID hospital, and his nasal swab was positive. He was discharged on the 7th day. His son also was also detected positive.



Figure 1: Bilateral ground-glass appearance with pneumonia. This patient died

We ourselves became quarantine at this time for 14 days an average incubation period (5-28 Days). Now the COVID positive cases after completion of 14 days quarantine are regularly followed for next 14 days for possibility of development of symptoms. Both HSB and Pramodini Himmatrao Bawaskar (PHB) were COVID negative afterward. No servant is allowed in house. Even close friends avoid phoning us, as if virus is transmitted through the mobile phones. Somebody brought fruits, just gave a bell call, kept outside the door, and ran away [Figure 3]. However, my patient relatives daily ask for any requirements. During night, relative accompanied with serious patient; no soon they listened the words that we are in quarantine, immediately took patient and rapidly runaway as if sound and words infect them with coronavirus. However, majority of them are without mask. HSB disturbed too much and felt like a fish out of water, whenever he had to refuse the case of severe scorpion sting due to quarantine. Maximum severe scorpion sting cases are reported in June and October. However, almost all peripheral doctors and Rural Hospital Mahad doctors are trained regarding how to manage severe scorpion sting victim with pulmonary edema. We divert victim to rural hospital and guide the treating doctor at hourly interval till the patient recovered from acute pulmonary edema.

Quarantine: Few Moments of Joy

This time was the best time we have experienced and understands each others since we join the medical profession. We both woke up at 5 AM every day, read the new advance publication on COVID-19 for 1 hour, and respond to new mails. We did 1-h Zumba exercise and *Pranayama*; PHB is a trainer for Zumba. HSB clean and swab the floor with sodium hypochlorite 1:5 dilution. PHB prepared breakfast and cooked food; HSB washed the utensils, operates washing machine, and cleaned the toilet and bathroom. PHB was always busy in playing music, playing harmonium, and writing daily dairy. HSB regularly read and referred NEJM, BMJ, JAMA, LANCET regarding COVID-19 disease publication. HSB enjoyed readings and always kept in

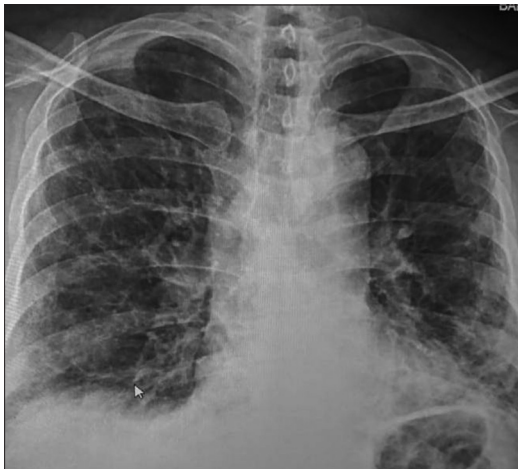


Figure 2: Diffuse bilateral infiltration

mind how application of knowledge for COVID-19 treatment as preventive or management at restricted resources at rural setting. We minimum watched the television only for news and never serials or movies. We got best chance to study in details of COVID-19 disease.

On June 4, 2020, at 16 h, a 29-year-old handicapped female due to childhood poliomyelitis complained of weakness and occasional cough for the last 2 days. Her temperature was 97°F, and she denied a history of febrile illness, no history of exposure to COVID-19 patient, or no relative returned from Mumbai or Pune. She was prescribed azithromycin 500 mg once a day. On June 5, her X-ray showed bilateral lower lobe pneumonias with ground-glass opacities [Figure 4]. Hemoglobin was 8.6 gm/dL, neutrophils were 78.8%, lymphocytes were 14.3%, NLR was 5.51, and platelets count was 125000/ μ L (normal 150,000–400,000). EC Electrocardiogram was within normal limits, and oxygen saturation was 97% on room air. There was fall of 4% while walking 6 min. She refused for to attend COVID hospital and investigations. On June 6 at 00.30 h, she was brought in acute respiratory distress; respiratory rate of 40 per minute, intractable cough, extremities cold and cyanosed, SpO₂ was 65%, pulse 124 per minute, blood pressure 90/60 mmHg. She was fully conscious. She complained of cough but not dyspnea. She was given oxygen 10 L/min by nasal prongs, and she was put on noninvasive ventilator, intravenous steroid, meropenem 1 g, dabigatran 110 mg, low molecular weight heparin 60 mg, aspirin 325 mg chewed, statin 80 mg, ivermectin 12 mg, and doxycycline 100 mg. At the end of 2 h, her oxygen saturation became 78% and her clinical status improved with a reduction in cough and cyanosis; at end of 6 h, saturation became 97% with no cyanosis and cough and dyspnea was absent with respiratory rate 20 per minute, and blood pressure raised to 100/70 mmHg. She walked herself to toilet, and oxygen saturation was maintained



Figure 3: Fruit bag left out in front of door

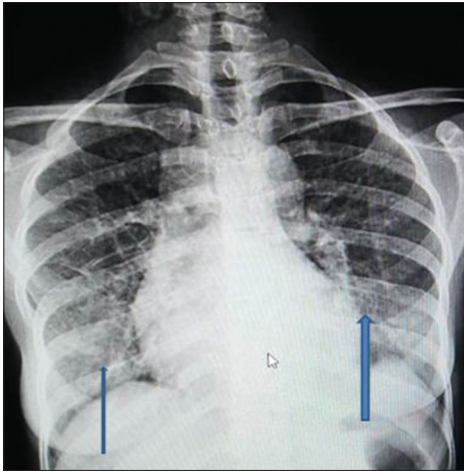


Figure 4: Bilateral pneumonia, this patient recovered at Mahad Hospital arrow shows bilateral pneumonia

94% [Figure 5] without oxygen. She walked to ambulance and transferred to COVID-dedicated hospital. She did not require further any extra treatment, and she was positive for COVID test. She was discharged on June 15. Again, we were in quarantine.

Social Stigmas

Thus, we were in quarantine twice. PHB, irrespective of regular hydroxychloroquine (HCQ) prophylaxis, became positive for COVID-19 and was home quarantine (table). HSB was negative; PHB was happy reading HSB negative report (centuries old male dominance in Indians culture and female dependency) PHB took care of HSB while wearing personal protective equipment (PPE). Thus, quarantine we became made each other and not merely a life partners. We both took ivermectin 12 mg once daily for 3 days, aspirin 75 mg, statin 80 mg, Vitamin D and C and Zinc, and doxycycline 100 mg twice a day, and floristore, metformin once a day. HSB took charge of all house requirements, everyday including food. The news in local paper declared positive PHB name in details, which is read by almost all taluk people. Many ask as if we did a social crime and injustice to society and as if infected of HIV and AIDS, stigmatized like leprosy, and felt as if outcaste; such news with name of doctor who is corona positive needs to be avoided. However, public should know if doctor became positive irrespective taking due care is certificate that he/she was actively involved in treating a serious COVID-19 case without bothering of himself and his family and not merely an observer or merely a adviser like a seniors in big hospitals. Those unfortunate health workers died of COVID-19 infection while treating COVID-19 victims should be declared as Corona-19 Martyr like soldier. This will encourage the newcomers and health workers moral while treating highly infectious life-threatening diseases. Irrespective of risk factor that HSB age 70 years, suffering from hypertension and hypothyroidism and PHB age 63 are more prone for COVID-19 infection still we treated this young women with due risk of COVID-19, otherwise she would have died. We always feel that refusing emergency is a crime. One of my friends was in quarantine for 14 days, he exclaimed



Figure 5: Himmatrao Saluba Bawaskar in PPE kit treating the severe respiratory failure patient of Figure 4 – X-ray

because of stringent law and stigmatization by society that he will henceforth never undergo for COVID-19 test. It is better to die of COVID-19 than face the social stigma which also affects the medical day-to-day practice. The person who delivers milk every morning for the last 20 years suddenly stop coming; his relative said because PHB is positive hence they decided not to visit house. A builder whose wife was serious for 2 months with acute respiratory failure we tried best and she recovered but when he noticed the COVID positive report he never call us and advice every worker not to attend the work it is though best advice but he would have at least discuss with us on phone. Even still today almost after two months we did not get maidservant and staff because of news paper news. HSB received the best certificate from PHB, when HSB ask to PHB why Irrespective of Positive report she did not disturb. She suddenly exclaimed that HSB will not allow her to die COVID-19. This is the best certificate of life time achievements.

HSB physician was called for second expert opinion and to examine case of a 54-year-old women sudden cardiac arrest preceded by chest pain at intensive care unit. HSB being in quarantine cannot go in a simple auto hence ambulance was sent for HSB; looking at ambulance by public reaching to our hospital suddenly HSB received a phone call from my surgeon friend that he was told and there is sudden news spread in Mahad that PHB became serious and ambulance is at my door.

Our relatives became more anxious and panic and asking us why you both examined and treated suspected COVID-19 cases. Younger son a DM cardiologist said, “Baba you are not going to become a martyr if you die of COVID-19 during taking care of COVID patient.” We convinced them that medical profession carries such risk, and when the patient life is at stake,

we are supposed to un-stake rather than to give shoulder to dead body. Moreover in situation like that today whole world facing threat of COVID-19 Pandemic, it is our moral duty to take active part to arrest the ongoing pandemic. Surprisingly, enough irrespective of front page news in bold red letters, no politicians inquire regarding our health, but death occurred in hospital they will repeatedly harassed us and even raised slogans and violence against doctors. A illiterate millionaire business man afraid of social stigmas attached to this disease. His wife had cough, breathlessness, fever, myalgia, lymphopenia, chest X-ray showed bilateral pneumonia, chest HCRT showed ground glass appearance, SPO₂ 89% raised serum ferritin, CRP and D-dimer, irrespective of repeated request denied for nasopharyngeal swab for viral PCR and serum antibodies levels. She recovered flavipiravir, with meropenem, low molecular weight heparin, ivermectin, doxycycline, statin 80 mg, vitamin D, C, and Zinc, nasal oxygen and prone Bi-PAP. She recently undergone angioplasty. Another woman a wife of goldsmith had signs and symptoms suggestive of COVID-19 infection CT scan chest showed ground glass infiltration. We advice for nasal swab irrespective of repeated appeal they refuse to undergo nasal swab for viral testing. She stayed in family and not in a separate room. Reason for not giving swab is that their relative will desert the family and moreover they have to close the shop. These are the culprits growing in society responsible for tertiary or community spread of these deadly virus.

COVID-19 and Rural Practitioners

Human SARS-CoV-2 viruses are enveloped nonsegmented positive sense viruses belonging to the genus *Betacoronavirus* SARS-CoV-2. It is large size with lipid enveloped positive strand RNA virus. Zoonotic transmission of the coronavirus was strongly suspected. Bats are the natural host. Primary hosts and reservoir of coronavirus are bats and pangolin (ant eater).^[7] Many studies have recently confirmed the genetic similarity between COVID-19 (SARS-COV-2) and bat SARS-related corona (SARS-COV-1); both enters cell through ACE-2 receptors.^[8] The surface spike (S) glycoprotein is critical for binding to host cell ACE-2 receptor and is to be present a key determinant of host range restriction.^[9] nCoV virus has some amino acid homology to SARS-CoV-2 and its ability to use ACE-2 as a receptor. Recently, it is shown that the processing of spike protein effected by furin-like converters in respiratory tract. This predicted pandemic potential of virus. Human-to-human transmission of COVID-19-CoV-2 occurs as evidence by infection to health workers. Analysis of two mothers milk content SARS-COV-2 virus one and other one was negative while second mother milk irrespective taking all care prevention.^[10] Patients with severe COVID-19 tend to have high viral load and long virus-shedding period. Thus, detection of circulating virus loads diagnostic criteria for the severity of COVID-19.^[11] Fecal-oral transmission has been reported. Temporal variation in frequency of types of the coronavirus was significant; the old type O was replaced by evolved virus belonging to type A2a.

The highest viral load is seen during the 1st and 2nd weeks in a mild disease, while in a severe disease, victim shed virus for a median of 21 days.^[12] In a severe diseased higher viral titers seen in third and fourth week Viral copy numbers in stool or serum were lower, detectable for 22 and 16 days, respectively, and not related to disease severity.^[13] Virus is stable from hours to days in the varies environment.^[14]

Clinical Manifestations

On set of disease, the common symptoms include recurrent fever 99°F–103°F, body-ache or myalgia, headache, chills, pain in throat, difficult in drinking water, cold but not a running nose, malaise, loose motions, hoarseness of voice, anorexia, nausea, vomiting, loss of taste and smell sensations and abdominal pain. It is important to note the weakness in COVID-19 is mild and tolerable as against in dengue there is profound weakness. Majority of patients reported on 4th or 5th days with weakness and cough always forget regarding history of febrile illness. subsequently patient experienced intractable dry and non-productive cough of tracheal type, continuous fever, difficult in respiration, breathlessness, hemoptysis, loss of taste sensation called ageusia and loss of smell sensation which can be easily detected by anosmia can smell broken onion and garlic, and there are reversible changes noted in the olfactory bulb and nucleus tractus solitarii and axon degeneration in the dorsal motor nuclei.^[15] Common presentation of COVID-19 include weakness, easy fatigue, chest pain acute myocardial infarction, stroke, intracerebral hemorrhage, toe gangrene, skin urticaria, thrombosis, hypotension, and septic shock. Signs and symptoms of acute respiratory distress syndrome; there is 30-fold increased incidence of Kawasaki disease during the pandemic of corona in Italy. Recently even Kawasaki like illness due to COVID-19 seen in adults. Oxygen saturation at rest may be 95–96 which reduces on 6-min walk to <90–92 which needs hospitalization.^[6,16-22]

Pathophysiology and Management

Infection by SARS-COV-2 virus evokes cytokine storm as a result of liberation of excessive IL -6 and autacoids result in hyperinflammation, excessive coagulation, multiple pulmonary embolism, raised antiphospholipid antibodies, alveolar changes, and alveolar capillary including hyaline membrane formation, fibrosis, exudation of fluid in alveoli-perfusion defect with preserved lung compliance. Irrespective of severe hypoxia, patient rarely complained of acute breathlessness called dead man walking hypoxia or happy hypoxia. SARS-CoV-2 virus has affinity for porphyrin molecules. It dissociates hemoglobin into hem and globin; further, hem is dissociated into porphyrin and ferritin; thus, virus distorting the hemoglobin molecule explained high requirement of oxygen flow. Thus there is no oxygen carrying hemoglobin in such situation giving liters and liters of external oxygen did not improve the hypoxia. In such situation with septic shock, methylene blue can be administered sublingually or by nebulizer so as to it directly reaches to lungs and improve the oxygenation by reconstruction of distorted haemoglobin molecule.

The randomized trial did not show any significant benefits of administering hydroxychloroquine as a postexposure prophylaxis for COVID-19.^[23] [Table] The HCQ because of its sodium channel blocking properties causes prolonged QTC interval and lethal ventricular arrhythmias, hypoglycemia, and retinal changes.^[24] There is no sound scientific evidence to justify for widespread use of HCQ for prophylaxis.^[25] Out of 30 canteen workers, 21 became COVID-positive irrespective of HCQ prophylaxis (<https://timesofindia.indiantimes.com/city/mumbai/mumbai-kem-canteen-emerges-as-its-biggest-hotspot-after-21-servants-test-covid-19-positive/artceshow/76455086.cmc>).

Ivermectin is a macrocyclic lactone with broad-spectrum antiparasitic, antibacterial, antiviral, and anticancer activities. It is a powerful antiviral. The antiviral action of ivermectin can be attributed to its role as an inhibitor of nuclear transport for the translocation of various viral species protein indispensable for their replication; this inhibition appears to affect a large number of RNA viruses including SARS-CoV-2. This action of ivermectin confirmed that it inhibits the replication of the SARS-CoV-2 virus *in vitro*.^[26] [Table] In the present cases, lymphopenia and eosinopenia altered NLR are observed in two severe cases. Macrophages release proinflammatory cytokines including IL-6, IL-10 and tumor necrosis factor-alpha. Lymphopenia, raised D-dimer, elevated serum ferritin, and C-reactive protein (CRP) along with an increase in NLR > 3 are seen in severe cases.^[27] Doxycycline cheap and easily available at rural setting an antibiotic and anticytokine agent. Other anti-inflammatory drugs like colchicine, indomethacin can be used were steroids are contraindicated antagonize the hyperinflammation due to the cytokine storm.^[5] Aspirin, dabigatran, statins, and low molecular weight heparin may prevent virus-induced endotheliitis, raised antiphospholipid antibodies, thrombosis, disseminated intravascular coagulation, and thromboembolism.^[28] Metformin suppresses the angiogenesis and inflammation;^[29] victim with high level of D-dimer and marked respiratory micro embolism in such serious stage tenecteplase a rapid thrombolysis may be life saving, the pleiotropic effects of statins include improvement in endothelial function, increase in bioavailability of nitric oxide, antioxidant, and anti-inflammatory action, and reduction in adhesion molecules and immunomodulation.^[30] Supplementation of zinc acts as an anti-infectious immunomodulator, with immune-boosting effects. It inhibits SARS-CoV-2 viral replication in the infected cells.^[31] Statin and aspirin prophylaxis prevents the development of severe sepsis and acute lung injury and also setting in of acute respiratory distress syndrome (ARDS).^[32]

In second case we treated an acute presentation, with SpO₂ of 65%, with hypoxic respiratory failure and recovered with noninvasive ventilator support and oxygen. Fatality is significantly decreased in cases given non-invasive ventilator and oxygenation as compared to invasive ventilation. Prone position ventilation further improves the lungs ventilation.^[33,34] In our series, the patient had typically complained of loss of taste and smell sensation. SARS-CoV-2 virus transferred through the olfactory

nerve to olfactory bulb and the glossopharyngeal nerve to gustatory nucleus, resulting in a loss of smell and taste sensation.^[35]

It is needless to say that the victims of ARDS due to COVID-19, asphyxiate in so much so the same way as George Floyd a COVID victim suffered in his ordeal, whereby he was left gasping for air, constantly uttering “please I can’t breathe” to the police officers who continuously put pressure on his back and put a knee on his neck, virtually stealing away his breath.^[36]

Ivermectin, doxycycline, aspirin, anticoagulants, statin, metformin, and Zinc, vitamin D and C a COVID cocktail, may prevent subsequent progression of the COVID-19 diseases. At rural setting Non-invasive ventilator and oxygen is easily available to manage the COVID-19 cases with hypoxia.

Antiviral agents such as lopinvir/ritonavir are no more active against coronavirus. RLF100 a aivptadil a vasoactive intestinal polypeptide block the virus replication in lungs cells and monocytes. Recently, favipiravir and remdesivir are known to cause fast recovery in COVID-19 disease and anti-inflammatory agent, which inhibits IL-6 inhibition (tocilizumab) reduction in cytokine storm are now routinely used in tertiary care hospital with encouraging result.^[37] Vaccine and plasma therapy are under trials.

However, Intramuscular injection of autologous 2-3 ml of blood of victim suffered of COVID-19 decease, rich sources of active virulent and attenuated virus, evokes active immunity and subsequently arrest the progression of severity of disease like that used for the treatment of chronic skin disease.^[38] At the time of reading this proof lancet released a news that Vaccine successfully stimulated the immune cell and gave long term immunity. measles and rubella aminoacids are homologous of SARS-CoV-2 virus can be use in adult to evoke immunity or cross immunity against the SARS-CoV-2 RNA virus.

Summary

COVID-19 disease in India is on the way of third phase, that is, community spread, and is expected to lead to herd immunity. The COVID test in private is expensive. However, it became absolute in asymptomatic cases. It is advocated in a person 5th days of symptoms appeared. Every patient suffering of cold or upper respiratory tract infection should not be label a cases of COVID. Such symptoms should be closely observed in risky groups. Sometimes, repeated test remained positive due to dead virus. Once a positive asymptomatic person completed 10 days of quarantine period, he/she should not repeat the test. Health workers should be trained how to proper wear and unweave the PPE kit. Regular washing of hands, daily steam inhalation, gargles with betadine solution and few drops to be put in both nostril, physical distancing, proper wearing of mask, regular exercise, minimum exposure, yoga, and healthy fresh fruits, Vitamin D, C, and zinc boost the immunity. Routine use diluted betadine gargles and its nasal drops by contacts, asymptomatic carriers, high risky population at mass level about the infectivity and may arrest the community spread.

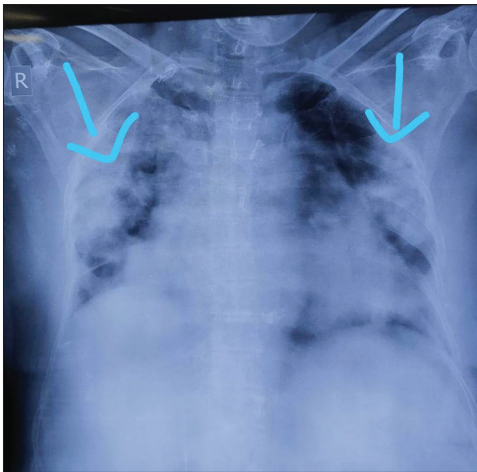


Figure 6: Bilateral peripheral diffuse ground-glass appearance patient had hemiplegia and died of respiratory failure (courtesy of Dr. Rathod from Mangaon) arrows show the peripheral ground glass appearance

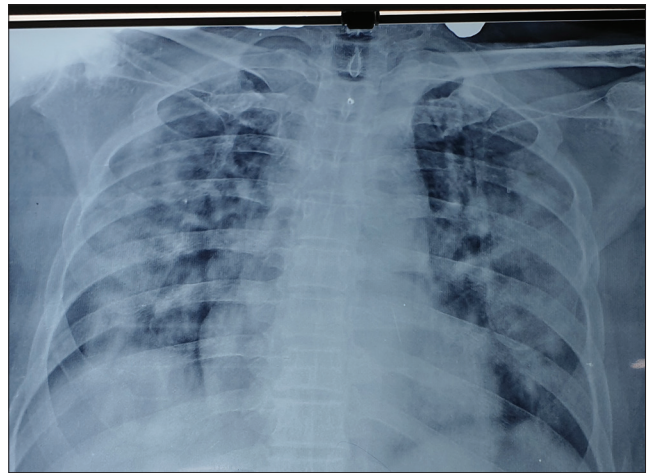


Figure 7: Diffuse bilateral peripheral lesion with ground-glass appearance typical bronchial tree infiltration

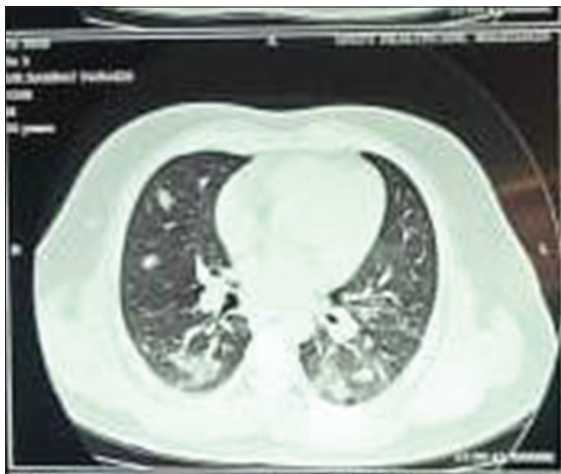


Figure 8: Ground-glass appearance in computed tomographic scan of the chest



Figure 9: Bilateral extensive ground glass shadows 54 M Covid + Breathless Meropenem, ivermectin, steroid, Remdesivir, tocilizumab, heparin, BlaPap. Oxygen 20 liters

There are a lot of controversies on HCQ (Hydroxychloroquine) as a prophylaxis against SARS-CoV-2 virus infection it but be care before using HCQ + azithromycin one should rule out prolonged QTC duration in ECG. HCQ is known to cause hypoglycemia and retinopathy. Recently, ivermectin and doxycycline covert the test rapidly in a victims tested positive for SARS-COV-2 virus. 80% of patients improved them self without any treatment Irrespective regular HCQ prophylaxis to health workers including doctors did not prevented COVID -19 viral infection [Table 1].

Many old people and young people also committed suicide by listening and viewing news of seriousness, figures of deaths, and disease on television and print media. Negative news needs to be avoided. There should be COVID-dedicated hospital and fully trained staff regarding the management of COVID-19 disease at each tehsil place senior (age 55+) and experienced doctors can advice to the young team working at COVID dedicated hospital by video conference. Death and disease of COVID-19 should

be compulsory reported to a health officer. Regular spraying of sodium hypochlorite solution will kill the virus which can stay for long time on floor.

Working oxygen cylinder with nasal prongs, pulse oximeter, nontouching thermometer for skin temperature are minimum requirements at out patient department. No patient or relative should be allowed in the consulting room without mask (N95 if possible). Doctors should wear PPE kit or N95 mask, and face shield and wash the hand with soap after examined each patient. Minimum time should be given for examination in a good ventilated room.

Symptomatic patient should be investigated for hemogram to rule out lymphopenia eosinopaenia, serum ferritin, D-dimer, chest X-ray for pneumonia and peripheral or subpleural infiltration, ground-glass appearance [Figure 6,7], computed

Table showing details doctors and nurse involved in taking care of COVID-19 victims											
no	Name	age	sex	occupation	Prophylaxis HCQ	Exposure	Risk factors	symptoms	Lymphopenia 1 st test 1 st June 20 %	Treatment	Repeat test 7 th June 20
1	DA	41	M	Nodal officer for COVID-19 Orthopedic surgeon	+	COVID -19 cases and quarantine persons	Nil	No	absent	Ivermectin 12mg three doses +doxycycline Three days Vitamin D ₃ ,and Zinc	Negative
2	SSK	41	M	Gynecologist	+	Caesarean section of COVID positive mother	Nil	No	absent	Ivermectin 12 mg three doses+doxycycline three days Vitamin D ₃ ,and Zinc	Negative
3	BYJ	52	M	Surgeon Hospital Superintendent	NO	COVID- cases of these two died	DM, HTN, Br. Asthama IHD, QTc 504ms	Weakness ,fatigue	absent	Ivermectin 6mg three doses +doxycycline five days Vitamin D ₃ ,and Zinc	Negative
4	ASD	23	F	Nurse	+	COVID-19 cases of these two died	nil	Cold and ,weakness	11	Ivermectine 12mg three doses _doxycycline five days Vitamin D ₃ ,and Zinc	Negative
5	SAP	37	M	Anesthetic	+	COVID-19 cases	nil	Fever, loss of taste sensation Breathless	13 Eosinophils 00	Ivermectin 12mg three doses +doxycycline Vitamin D ₃ ,and Zinc, Low molecular weight heparin , statin 80 mg ,asprin 75 mg See the details case in text	Negative 9 th June
6	PHB	63	F	Medical officer	+	Exposure to ARDS case due to COVID-19 cases	nil	Cold	absent	Ivermectin 12 mg three dose +Doxycycline Vitamin D ₃ ,and Zinc	Negative on 5 th day of treatment
7	GM	47	M	General practitioner	+	Outpatient department	hypertension	Cough ,fever , myalgia, breathlessness, CT cheat ground glass shadows	11 Eosinophils 00	Ivermectin 12mg three doses +doxycycline Vitamin D ₃ ,and Zinc, Low molecular weight heparin , statin 80 mg ,asprin 75 mg See the details case in text	Negative on 6 th day



Figure 10: Nebulisation of methylene blue (blue color)

tomographic scan of the chest [Figure 8], liver function test, renal profile, and troponin and ECG. If patient is in ARDS with cytokine storm, serum IL level helps for giving IL-antagonist. At time CT chest will give rapid diagnosis than waiting and confirm the entry and spread of virus in lung tissue need close monitoring. RT-PCR test may take more than 48 h. Please note once you or your doctor suspect COVID, please go ahead and meet expert and then investigate. Now lot of advance in treatment are made with almost negligible fatality provided patient report earlier. It was noted that majority of police died due to COVID-19 are reported too late when we discuss with police commissioner.

Key points

Fever, chills, cough, breathlessness, diarrhea, loss of taste and smell sensation, skin rashes, weakness, fatigue, myalgia, ARDS, $SpO_2 < 94$, leukopenia, $NLR > 3$, acute myocardial infarction, and happy hypoxia. Risk factors include old age > 55 , hypertension, DM, obesity, cancer, immunosuppression, and malnutrition. As thymus is not fully developed below 10 years children in addition there was mass campaign of MMR vaccination responsible for cross immunity against the COVID-19 infection in children, severity of disease is less. With due care and proper use of PPE kit, doctor should not be afraid of treating COVID-19 victims. No test of COVID-19 to be advocated unless victim suffered of symptoms that to on 5–10 days. False negative may be due to improper collection of swab. False positive may be due to dead virus RNA.

Recently it is reported that patient with blood group O is less susceptible for severe manifestations of COVID-19 disease while group A will develop severe manifestations due to COVID-19. Rest of blood groups is less susceptible. Since march 2020 we treated 160 moderate patients of COVID-19 with raised

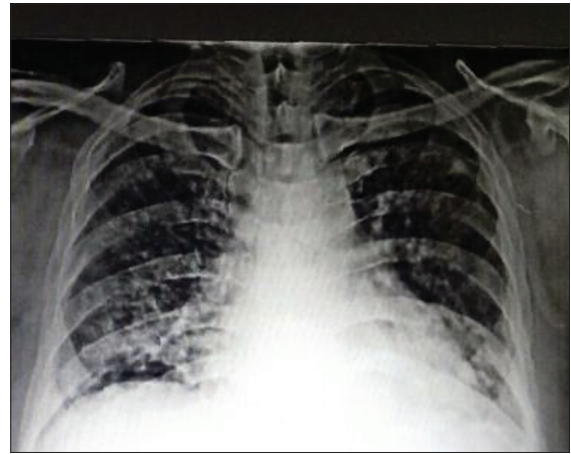


Figure 11: Remarkable improvement in lungs shadows SpO_2 maintained 96% without Oxygen after daily for three days doses of methyl blue nebulisation 1:4 dilution

inflammatory bio-markers with HCRT showed 25-75% lesion in both lung, of these three required BiPaP ventilator reported 10 days after initial infection. In our series 48%, 10%, 22%, 7%, were from blood group A, AB, O and B respectively.

These cases recovered with oral flaviparavir, doxycycline, ivermectin, aspirin, dabigatran 110 mg or low molecular weight heparin once a day, statin 40–80 mg, metformin 500 mg vitamin C, Zinc, and D. all are given warning how to use betadine gargles and nasal drops to patients and all his contacts exposures and family members. Nasal mucosal cells ACE-2 receptors concentration is 200–700 times higher than rest of tissue. It confirms virus first accumulate in the nostril mucosa. Iodine is viricidal. we both authors daily add iodine nasal drops three times a daily with gargling in addition to N19 mask, face shield. this prevented us getting infection, Irrespective of daily exposure to 8-10 COVID-19 symptomatic cases.

Recent advances

Post manuscript note

Irrespective of almost three months lockdown in India, the COVID-19 disease reached to third phase of infection. Thus “DEAD LOCKDOWN” for two weeks and nobody should leave the house. Essentials will be provided on request by state reserved police (SRP) or military personnel who are repeatedly tested for COVID-19 test confirmed they are non infectious. Then and then possible to brake the vicious chain of virus. This SARS-CoV-2 virus donot give long term immunity. Postinfection immunity or IgG antibodies only detected up to 8-12 months, confirmed community infection will give a transient herd immunity. Vaccine is deemedly needed to arrest the community spread.

In cases of severe terminal phase with ARDS and respiratory failure with shock one should be very aggressive in the management rather than stick to routine protocol. In such situation intravenous methylene blue to reconstruct damage

hemoglobin to oxygen carrying hemoglobin, improve the oxygen carrying capacity. Intravenous thrombolytic agent such as tenecteplase to improve the pulmonary circulation by dissolving the microthrombi. Injecting remdesivir by puncturing the crico-thyroid membrane to lungs to attack the virus attached to ACE-2 receptors and reduce the viral load and in case of normal procalcitonin IL antagonist and dexamethasone can be injected if this is not possible one can give these drugs through nebulizer.

Furin content of lung potentiates the infectivity of SARS-CoV-2 virus, subsequently result in chronic lung fibrosis lead to chronic obstructive pulmonary disease a life time crippler, a report from KEM hospital Mumbai, cured patients from COVID-19 of these 22 returned to KEM hospital with pulmonary fibrosis (<http://mumirror.indiatimes.com://coronavirus/news/cured-of-covid-22-returned-to-kem-with-pulmonary-fibrosis/articleshow/77340422>), similar report of interstitial pneumonia and fibrosis.^[39] Early administration of Metformin to arrest the neovascularization in lungs and Furin antagonist Pirfenidone at the time of hyper-inflammation stage. In our two patients with ARDS with SPO₂ <80 improved oxygenation by 10-12% by giving methylene blue inhalation by nebulizer, one ML methylene diluted in four ML of normal saline, methylene blue reconstructs the distorted hemoglobin by converting liberated ferric ion into ferrous sulphate [Figures 9-11]. Routine MMR (measles, mumps and Rubella) vaccination gives cross immunity against SARS-CoV-2 virus in children that is the reason the morbidity and mortality in children are negligible. Adults born before 1957 or in those measles antibodies not detected specifically in old people and having risk factors can receive MMR vaccine to protect. Both authors took MMR and BCG vaccine and their serum measles antibodies are more than 300.^[40] Recently it is observed that nitric oxide plays an important role in the pathogenesis of ARDS. Bradykinin stimulates the nitric oxide synthase enzyme. Methylene blue inhibits the nitric oxide synthase enzyme and improves the alveolar capillary perfusion.^[41]

Acknowledgement

We are grateful to Pranav Ajmera professor of radiology DY Patil medical college Pune for editing the manuscript. Dr R.S. Mohite for Figures 9-11.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Editorial. COVID-19: Learning from exercise. *Lancet* 2020;395:1011.
- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054-62.
- Curtis N, Sparrow A, Ghebreyesus TA, Netea MG. Considering BCG vaccination to reduce the impact of COVID-19. *Lancet* 2020;395:1545-6.
- Miller A, Reandelar MJ, Fasciglione K, Roumenova V, Li Y, Gonzalo H Otazu *Medrxiv* Correlation between universal BCG vaccination policy and reduced morbidity and mortality for COVID-19: An epidemiology study. doi: <https://doi.org/10.1101/2020.03.24.20042937>
- Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, *et al*. COVID-19: Consider cytokine storm syndromes and immunosuppression. *Lancet* 2020;395:1033-4.
- Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol* 2020;17:259-60.
- de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: Recent insights into emerging coronaviruses. *Nat Rev Microbiol* 2016;14:523-34.
- Paraskevis D, Kostaki EG, Magiorkinis G, Panayiotakopoulos G, Sourvinos G, Tsiodras S. Full-genome evolutionary analysis of the novel coronavirus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. *Infect Genet Evol* 2020;79:104212.
- de Wilde AH, Snijder EJ, Kikkert M, van Hemert MJ. Host factors in coronavirus replication. *Curr Top Microbiol Immunol* 2018;419:1-42.
- Groß R, Conzelmann C, Müller JA, Stenger S, Steinhart K, Kirchhoff F, *et al*. Detection of SARS-CoV-2 in human breastmilk. *Lancet* 2020;395:1757-8.
- Liu Y, Yan LM, Wan L, Xiang TX, Le A, Liu JM, *et al*. Viral dynamics in mild and severe cases of COVID-19. *Lancet Infect Dis* 2020;20:656-7.
- Biswas NK, Majumder PP. Analysis of RNA sequences of 3636 SARS-CoV-2 collected from 55 countries reveals selective sweep of one virus type. *Indian J Med Res* 2020 [doi: 10.4103/ijmr.IJMR_1125_20].
- Msoraca A, Margiotti K, Vila A, Cima A, S. paracino D, Giorlandino C. Evaluation of SARS-CoV-2 viral RNA in fecal samples. *Virology Journal* 2020;17:86 <https://doi.org/10.1186/s12985-020-01359-1>.
- van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, *et al*. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. *N Engl J Med* 2020;382:1564-7.
- von Weyhern CH, Kaufmann I, Neff F, Kremer M. Early evidence of pronounced brain involvement in fatal COVID-19 outcomes. *Lancet* 2020;395:e109.
- Li T, Lu H, Zhang W. Clinical observation and management of COVID-19 patients. *Emerg Microbes Infect* 2020;9:687-90.
- Chow EJ, Schwartz NG, Tobolowsky FA, Zacks RLT, Huntington-Frazier M, Reddy SC, *et al*. Symptom screening at illness onset of health care personnel with SARS-CoV-2 infection in King County, Washington. *JAMA* 2020;323:2087-9.
- Diaz-Guimaraens B, Dominguez-Santas M, Suarez-Valle A, Pindado-Ortega C, Selda-Enriquez G, Bea-Ardebol S, *et al*. Petechial skin rash associated with severe acute respiratory syndrome coronavirus 2 infection. *JAMA Dermatol* 2020;doi.org/10.1001/jamadermatol.2020.1741
- Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, *et al*. Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med* 2020;382:2268-70.

20. Bhatia R, Srivastava MV. COVID-19 and stroke: Incidental, triggered or causative. *Ann Indian Acad Neurol* 2020;23:318-24.
21. Chen D, Li X, Song Q, Hu C, Su F, Dai J, *et al.* Assessment of hypokalemia and clinical characteristics in patients with coronavirus disease 2019 in Wenzhou, China. *JAMA Netw Open* 2020;3:e2011122.
22. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, *et al.* An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: An observational cohort study. *Lancet* 2020;395:1771-8.
23. Boulware DR, Pullen MF, Bangdiwala AS, Pastick KA, Lofgren SM, Okafor EC, *et al.* A randomized trial of hydroxychloroquine as postexposure prophylaxis for COVID-19. *N Engl J Med* 2020. doi: 10.1056/NEJMoa2016638.
24. Funck-Brentano C, Salem JE. Chloroquine or hydroxychloroquine for COVID-19: Why might they be hazardous? *Lancet* 2020. doi: 10.1016/S0140-6736(20)31174-0.
25. Rathi S, Ish P, Kalantri A, Kalantri S. Hydroxychloroquine prophylaxis for COVID-19 contacts in India. *Lancet Infect Dis* 2020;doi: 10.1016/S1473-3099(20)30313-3.
26. Rizzo E. Ivermectin, antiviral properties and COVID-19: A possible new mechanism of action. *Naunyn Schmiedebergs Arch Pharmacol* 2020;393:1153-6.
27. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, *et al.* Clinical and immunological features of severe and moderate coronavirus disease 2019. *J Clin Invest* 2020;130:2620-29.
28. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, *et al.* Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in COVID-19. *N Engl J Med* 2020;383:120-8.
29. Han J, Li Y, Liu X, Zhou T, Sun H, Edwards P, *et al.* Metformin suppresses retinal angiogenesis and inflammation *in vitro* and *in vivo*. *PLoS One* 2018;13:e0193031.
30. Davignon J. Beneficial cardiovascular pleiotropic effects of statins. *Circulation* 2004;109:III39-43.
31. Rahman MT, Idid SZ. Can Zn be a critical element in COVID-19 treatment? *Biol Trace Elem Res* 2020. Doi: <https://doi.org/10.1007/s12011-020-02194-9>.
32. O'Neal HR Jr., Koyama T, Koehler EA, Siew E, Curtis BR, Fremont RD, *et al.* Prehospital statin and aspirin use and the prevalence of severe sepsis and acute lung injury/acute respiratory distress syndrome. *Crit Care Med* 2011;39:1343-50.
33. Ferreyro BL, Angriman F, Munshi L, Del Sorbo L, Ferguson ND, Rochweg B, *et al.* Association of noninvasive oxygenation strategies with all-cause mortality in adults with acute hypoxemic respiratory failure: A systematic review and meta-analysis. *JAMA* 2020. Doi: 10.1001/jama.2020.9524 PMID: 32496521.
34. Wilcox SR. Management of respiratory failure due to COVID-19. *BMJ* 2020;369:m1786.
35. Spinato G, Fabbris C, Polesel J, Cazzador D, Borsetto D, Hopkins C, *et al.* Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. *JAMA* 2020;323:2089-90.
36. Hardeman RR, Medina EM, Boyd RW. Stolen breaths. *N Engl J Med* 2020;383:197-9.
37. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): A review. *JAMA* 2020;323:1824-36.
38. Oomen-Welke K, Huber R. Intramuscular autologous blood therapy-A systematic review of controlled trials. *BMC Complement Altern Med* 2019;19:248.
39. Raghu G and Wilson KC. COVID-19 interstitial pneumonia: Monitoring the clinical course in survivors. *Lancet Respir Med* 2020. Available from: [https://doi.org/10.1016/S2213-2600\(20\)303349-0](https://doi.org/10.1016/S2213-2600(20)303349-0). [Published online 2020 Aug 03].
40. Fidel PL and Noverr MC. could an unrelated live attenuated vaccine serve as a preventive measure to dampen septic inflammation dissociated with COVID-19 infection? *mBio* 2020;11:e00907-20.
41. Ghahestania MS, Shahabb E, Karimic S, Madanid MH. Methylene blue may have a role in the treatment of COVID-19 *Medical Hypothesis* 2020;144:110163.