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Respiratory manifestations of COVID-19

Undugodage C[1], Wanigasuriya K[1], Madegedara D[2]

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Corona virus disease 2019 (COVID-19), is the biggest health challenge faced by the world in the recent years. It rapidly spread to the rest of the world, over a short period of time, after its appearance in Wuhan, China. WHO declared it a pandemic on the 11th of March. At the time of writing, 5,556,574 people are affected worldwide with 348,223 deaths[1].

In Sri Lanka, the first local case was detected in early March 2020, and 2 months later, despite the much lower population compared to the severely affected countries such as China, US and Italy, there are over 1000 cases with 9 deaths[2].

COVID-19 is primarily a disease affecting the respiratory system. The corona virus that leads to COVID-19 is a beta coronavirus and belongs to the same subgenus as the Severe Acute Respiratory Syndrome [SARS] virus. COVID-19 virus is known as the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS COV2)[3]. The virus binds to Angiotensin Converting Enzyme 2 (ACE 2) protein to enter human cells[4]. ACE 2 proteins are expressed in the airway epithelium, lung parenchyma and vascular endothelium[5]. ACE 2 is expressed more on the apical surface of the airway epithelium as opposed to the baso-lateral surface. Thus, rendering the lung susceptible to infection by SARS COV2.

The respiratory involvement in COVID-19 can manifest in several ways –

- Upper respiratory tract infection
- Pneumonia and Acute respiratory distress syndrome [ARDS]
- Pulmonary embolism and pulmonary vascular thrombosis
- Other presentations

This article will briefly describe each of these.

Upper respiratory tract infection

Fever, cough, fatigue and dyspnoea are the commonest symptoms seen in those admitted to hospital with COVID-19, according to the data from 3 centers in Wuhan, China[6,7,8]. This is comparable to the first 100 patients from Sri Lanka[9] (Table 1). The Chinese data are from patients who required hospital admission, however in Sri Lanka, as per government policy, all patients with COVID-19 positive PCR is admitted to a hospital. Therefore, the Sri Lankan data includes patients who do not require in-ward care.

The cough is predominantly a dry cough[10]. Interestingly, occurrence of rhinorrhea is not common in the Chinese data[8]. However, in Sri Lanka, rhinorrhea is seen in 11% of patients, and nasal congestion in 21% of the patients[9]. Haemoptysis was seen in 2 out of 39 (5%) patients in one center in China[7] and in another center out of 99 patients studied, 1 patient had a pneumothorax[8].

Dyspnoea was obviously more prominent in those needing ICU care. The other symptoms didn't differ much in those needing ICU care as opposed to those in inward care. However, anorexia was noted to be more common in the former[6].

[1]*Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka,* [2]*National Hospital, Kandy, Sri Lanka.*

Correspondence: CU, e-mail: undugodage@sjp.ac.lk

http://orcid.org/0000-0001-9134-683X

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Table 1. Hospitalized patients with pneumonia from 3 centers in Wuhan, China and the first 100 patients from Sri Lanka

Symptom	*Center 1*[6] *n=138 (%)*	*Center 2*[7] *n=41 (%)*	*Center 3*[8] *n=99 (%)*	*Sri Lanka*[9] *n=100 (%)*
Fever	136 (98.6)	40 (98)	82 (83)	66
Cough	82 (59.4)*	31 (76)	81 (82)	48 (48)*
Sputum production	37 (26.8)	11 (28)	-	11 (11)
Sore throat	24 (17.4)	-	5 (5)	29 (29)
Dyspnoea	43 (31.2)	22 (55)**	31 (31)	16 (16)
Rhinorrhoea	-	-	4 (4)	11 (11)
Haemoptysis	-	2 (5)	-	-
Anorexia	55 (39.9)	-	-	-
Fatigue	96 (69.6)	18 (44)#	-	9 (9)
Myalgia	48 (34.8)		11 (11)	26 (26)
Headache	9 (6.5)	3 (8)	8 (8)	21 (21)

* dry cough, # myalgia or fatigue, ** 12 (29%) patients had a respiratory rate > 24

There is a growing body of evidence for the presence of olfactory dysfunction (anosmia/hyposmia). Importance of considering anosmia as a symptom of COVID-19 was stated in a statement issued by the ENT UK and the British Rhinological Society following a number of reports on anosmia from US, France and Northern Italy[10]. A multi-center European study on olfactory dysfunction in mild to moderate COVID-19 (n= 417), showed that 85.6% had olfactory dysfunction. Interestingly the olfactory dysfunction has preceded other symptoms in 11.8% of patients. This is a very important finding as this indicates that anosmia can be an early sign to identify COVID-19 patients[11]. Similar findings were noted in several other studies across the world[12,13,14,15]. A more recent study from France looking at 54 patients with confirmed COVID-19 having anosmia found that the median duration for anosmia was 8.9 days[14]. Sri Lankan data on 58 patients show that 5% had anosmia[16].

Pneumonia and ARDS

The disease can progress to the development of pneumonia, severe pneumonia, sepsis, septic shock and ARDS[6].

Pneumonia in COVID-19 can range from mild to severe. The common radiological, including computed tomography (CT) features are multiple lung opacities and multiple types of opacities such as ground glass shadows, ground glass shadows with consolidations and bilateral consolidations. Multiple lobes are affected especially the lower lobes[17]. Crazy paving pattern and organising pneumonia are seen at a later stage in the disease[18]. Extensive con-solidation is associated with a poor prognosis[18]. Bilateral consolidations and bilateral patchy opacities were the X ray findings of 5 critically ill patients with COVID-19 in Sri Lanka[9]. However, in one patient there was a unilateral lung shadow (blunting of the costo-phrenic angle) in the chest X ray done on day 3 of the illness and patient had died on day 9. X ray chest is not sensitive to pick up subtle changes seen in early lung involvement[18].

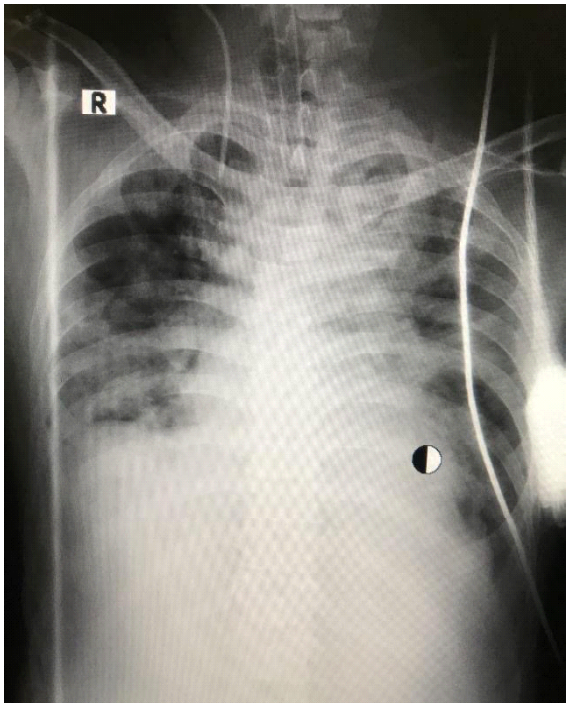
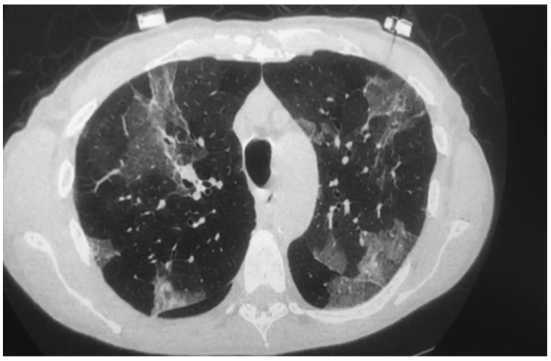


Figure 1. X ray chest image of a patient with SARS COV2 pneumonia showing bilateral lower zone shadows more prominent on the right than the left.

(Courtesy Dr Aruna Jayawardena, Consultant Physician (acting), Welikanda COVID-19 treatment center)

A



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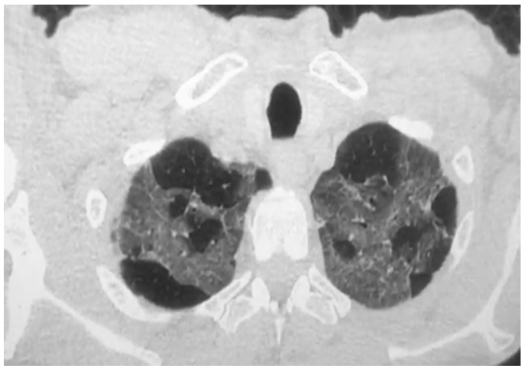
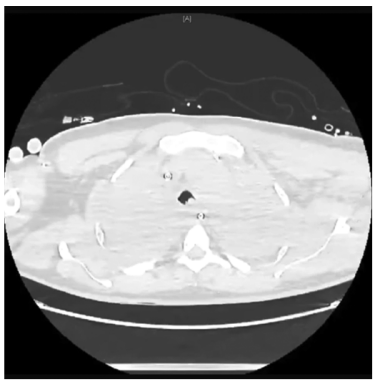


C



D

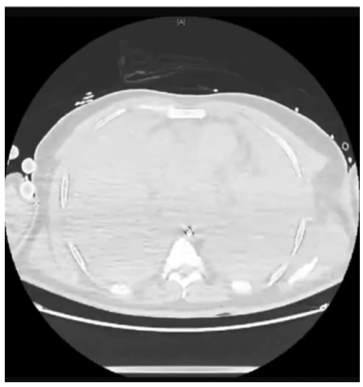


Figure 2. Chest Computed Tomographic images of a patient with severe COVID-19 pneumonia.
A & B – Bilateral ground glass shadows
C & D – Bilateral consolidation of lungs – no air visible. (The patient was moved to ECMO after failed ventilation)
(Courtesy Dr Keith Hattotuwa, Consultant Respiratory Physician, Mid Essex Hospital Services NHS Trust.)

Acute respiratory distress syndrome (ARDS): In the study by Wang et al. out of the thirty-six patients who were transferred to the intensive care unit (ICU), 22 (61.1%) had acute respiratory distress syndrome[19]. The median time from first symptom to ARDS was 8 days.

In a retrospective case series of 1591 critically ill COVID-19 patients admitted to intensive care unit (ICU) in Lombardy, Italy it was noted that, 99% (1287 of 1300 patients) required respiratory support. 88% required endotracheal intubation and 11% needed non-invasive ventilation. The mortality in the ICU was 26%[20]. However, the ICU mortality varies from center to center.

According to the Sri Lankan data of the first 100 patients, 2 were considered severely ill and 6 were critical. All critically ill patients were treated in the ICU and had required endotracheal intubation. There had been one death on admission. The rest of the critically ill patients have subsequently died following a period of stay in the ICU[9].

One of the interesting observations in COVID-19 is a category of patients with severe hypoxemia disproportionate to dyspnoea. The severe pneumonia in all patients does not behave the same way. Gattinoni et al proposed an explanation to this by observation of the presence of two different COVID-19 pneumonia phenotypes[21,22].

The two phenotypes described are L type and the H type. The L type is characterized by low elastance; therefore, the lungs are compliant, and are easy to oxygenate. The amount of non-aerated lung tissue is very low. The low ventilation perfusion (V/Q) ratio leading to hypoxemia is believed to be a consequence of vasoplegia, or the loss of hypoxic vasoconstriction of the pulmonary vasculature. Hypoxemia increases the minute ventilation by stimulation of the peripheral chemoreceptors. Partial pressure of CO_2 ($PaCO_2$) in the blood is the main determinant of the respiratory rate. In the presence of near normal lung compliance, a slight increase in minute volume will decrease the PCO_2 and therefore an increase in respiratory rate is not seen. This explains the severe hypoxemia without dyspnoea noted in certain patients[21]. The High-resolution computed tomography (HRCT) images of the lungs in L type show bilateral ground glass opacities, mainly in the subpleural areas and along the fissures. The H type on the other hand has a low lung compliance. The lungs are heavy, sometimes the lung weight is > 1.5kg with areas of non-aerated lung tissue[7]. There is a high right to left shunt because of the pulmonary perfusion to non-aerated tissue. This is associated with a high lung recruitabilty. This is the basis for prone ventilation in such patients. The HRCTs show bilateral consolidations.

L type can either remain as it is or progress to H type. The differentiation between the 2 types is important as the ventilator strategies employed are different.

Pulmonary embolism and pulmonary vascular thrombosis

Pulmonary embolism (PE) is common in COIVD-19 pneumonia[23]. In a series of 107 patients admitted to ICU with pneumonia, it was noted to have high number of PE (20.6%). This was compared with a similar number of ICU admissions with pneumonia during the same time interval the previous year. The frequency of PE in the COVID-19 series was twice as high as the frequency in the control period. A similar study done in a center in Paris, found 24% of COVID-19 patients with pneumonia had PE[24].

PE should be suspected in those with sudden worsening of hypoxia, hypotension, tachycardia and new onset arrhythmia. It is more common in patients in critical care units and in those requiring mechanical ventilation[25]. An advice paper from the European Society of Radiology and the European Society of Thoracic Imaging suggested that PE should be suspected if supplementary oxygen is needed in a patient with limited disease extension and an additional contrast-enhanced CT acquisition may be indicated[18].

There is increased evidence of thrombosis of the pulmonary vessels[3]. Post mortem histology of pulmonary vessels in patients with COVID-19 has widespread thrombosis with microangiopathy. Alveolar capillary microthrombi were 9 times as prevalent in patients with COVID-19 than in patients with influenza[26].

Other presentations

Patients with coexisting lung diseases like asthma, chronic obstructive pulmonary disease, bronchiectasis, interstitial lung diseases and other chronic lung diseases, may present with features of an exacerbation of their lung condition secondary to an infection with COVID-19.

Even though many extra pulmonary manifestations have been described in COVID-19, severe disease, need for ICU care and mortality are almost always related to the respiratory involvement. More research is clearly needed into the pulmonary pathophysiology, and a better understanding of this will go a long way in saving lives.

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References

1. COVID-19 Worldometer. https://www.worldometers.info/coronavirus/
2. Health Promotion Bureau, Sri Lankahttps://www.hpb.health.gov.lk/en
3. Gorbalenya AE, Baker SC, Baric RS, et al. Severe acute respiratory syndrome-related coronavirus: The species and its viruses – a statement of the Coronavirus Study Group. *bioRxiv* 2020. https://www.biorxiv.org/content/10.1101/2020.02.07.937862v1
4. Jia H, Look DC, Shi L et al. ACE2 receptor expression and severe acute respiratory syndrome coronavirus infection depend on differentiation of human airway epithelia. *Journal of Virology.* 20025; **79**(23): 14614-21. doi:10.1128/JVI.79.23.14614-14621.2005
5. Leisman DE, Deutschman CS, Legrand M. Facing COVID-19 in the ICU: vascular dysfunction, thrombosis, and dysregulated inflammation [published online ahead of print, 2020 Apr 28]. *Intensive Care Medicine* 2020; 1-4. doi:10.1007/s00134-020-06059-6
6. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China [published online ahead of print, 2020 Feb 7]. *JAMA* 2020; **323**(11): 1061-9. doi:10.1001/jama.2020.1585
7. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **39** (10223): 497-506.
8. 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): 507-13. doi:10.1016/S0140-6736(20)30211-7
9. Clinical and Epidemiological Characteristics of the Confirmed COVID-19 Patients in Sri Lanka. Status Report Based on the Interim Analysis of the First 100 COVID-19 Patients Following Hospital Discharge or Death. Ministry of Health and Indigenous Medical Services, Colombo, Sri Lanka, 10 May 2020.
10. ENT UK and BRS joint statement: Non-recognition of lost sense of smell or taste as symptoms of COVID-19 infection – 13th of May 2020. entuk.org
11. Lechien JR, Chiesa-Estomba CM, De Siati DR, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study [published online ahead of print, 2020 Apr 6]. *European Archives of Oto-rhino-laryngology* 2020; 1-11. doi:10.1007/s00405-020-05965-1
12. Yan CH, Faraji F, Prajapati DP, Boone CE, DeConde AS. Association of chemosensory dysfunction and Covid-19 in patients presenting with influenza-like symptoms. *International Forum Allergy & Rhinology* 2020. Accepted Author Manuscript. doi:10.1002/alr.22579
13. Seyed H, Alimohamed et el Coincidence of COVID 19 epidemic and olfactory dysfunction outbreak. medRxiv (preprint) http://doi.org/10.1101/2020.03.23.20041889
14. Klopfenstein T, Kadiane-Oussou NJ, Toco L, et al. Features of anosmia in COVID-19. MÃ©decine et Maladies Infectieuses 2020. https://doi.org/10.1016/j.medmal.2020.04.006
15. Mao L, Wang M, Chen S, et al. Neurological Manifestations of Hospitalized Patients with COVID-19 in Wuhan, China: a retrospective case series study. *MedRXiv.* 2020. https://doi.org/10.1101/2020.02.22.20026500
16. Weekly COVID update – issue 3. Published on the 20th of April 2020 by Ceylon College of Physicians https://www.ccp.lk/covidweekly
17. Fu F, Lou J, Xi D et al. Chest computed tomography findings of coronavirus disease 2019 (COVID-19) pneumonia. *European Radiology* 2020. https://doi.org/10.1007/s00330-020-06920-8
18. Revel M, Parkar AP, Prosch H, et al. COVID-19 patients and the radiology department – advice from the European Society of Radiology (ESR) and the European Society of Thoracic Imaging (ESTI). *European Radiology* 2020. https://doi.org/10.1007/s00330-020-06865-y
19. The ARDS Definition Task Force. Acute Respiratory Distress Syndrome: The Berlin Definition. *JAMA.* 2012; **307**(23): 2526-2533. doi:10.1001/jama.2012.5669
20. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020; **323**(16): 1574-1581. doi:10.1001/jama.2020.5394
21. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? *Critical Care* 2020; 24, 154. https://doi.org/10.1186/s13054-020-02880-z

22. Gattinoni L, Chiumello D, Caironi P, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? *Intensive Care Medicine* 2020. https://doi.org/10.1007/s00134-020-06033-2

23. COVID-19 group. Pulmonary Embolism in COVID-19 Patients: Awareness of an Increased Prevalence. *Circulation* 2020. doi: 10.1161/CIRCULATIONAHA.120.047430.[Epub ahead of print]. PMID: 32330083.

24. Bompard F, Monnier H, Saab I, et al. Pulmonary embolism in patients with Covid-19 pneumonia. *European Respiratory Journal* 2020; (in press) https://doi.org/10.1183/13993003.01365-2020

25. Grillet F, Behr J, Calame P, et al, Acute pulmonary embolism associated with COVID-19 pneumonia detected by Pulmonary CT angiography, Radiology online, April 23 2020.https://doi.org/10.1148/radiol.202020 1544

26. Hariri L, Hardin CC. Covid-19, Angiogenesis, and ARDS Endotypes. *New England Journal of Medicine* 2020. DOI: 10.1056/nejme2018629