IJBPAS, February, Special Issue, 2022, 11(2): 223-233
ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)
'A Bridge Between Laboratory and Reader'

www.ijbpas.com

FACTORS ASSOCIATED WITH INTUBATION AND PROLONGED INTUBATION IN HOSPITALIZED PATIENTS WITH COVID-19

JADHAV RM[1*], NANGARE NR[2], AND KAPDI SF[3]

1: Junior Resident, Department of Surgery, Krishna Institute of Medical Sciences Deemed to be University, Karad, Maharashtra (India)

2: Professor, Department of Surgery, Krishna Institute of Medical Sciences Deemed to be University, Karad, Maharashtra (India)

3: Senior Resident, Department of Surgery, Krishna Institute of Medical Sciences Deemed to be University, Karad, Maharashtra (India)

***Corresponding Author: Dr. Rituja. M. Jadhav: E Mail: rituja.jadhav001@gmail.com**

Received 15th July 2021; Revised 18th Aug. 2021; Accepted 29th Oct. 2021; Available online 15th Feb. 2022

https://doi.org/10.31032/IJBPAS/2022/11.2.1029

ABSTRACT

Objective

To identify risk factors related to intubation and time to extubation in hospitalized patients with coronavirus disease 2019 **[1, 10]**.

Study Design

Single centre hospital based observational study.

Setting.

Krishna Hospital & Medical Research Center, Karad.

Subjects and Methods

Covid 19 Positive Patients admitted in COVID-19 ward & ICU2020were included.

We evaluated sociodemographic and clinical features related to intubation and prolonged intubation for acute respiratory failure secondary to COVID-19 infection.

- Age, sex, rate of respiration, oxygen saturation, history of diabetes and shortness of breath were factors predictive of intubation.
- Age and body mass index were the only factors independently associated with time to extubation.

Conclusion

In addition to clinical signs of respiratory distress, patients with COVID-19 who are older, male, diabetic are at higher risk of requiring intubation. And among those obese patients are at higher risk for prolonged intubation.

INTRODUCTION

- The SARS-CoV-2 virus, more commonly known as coronavirus 2019 COVID-19 is a novel respiratory virus that was first recognized in China and has now spread across the world **[4, 7]**.
- COVID-19 appears to have a lower case fatality rate but a higher rate of transmission leading to far more total deaths.
- Severe disease causes hypoxic respiratory failure requiring prolonged supportive care involving intubation and invasive mechanical ventilation **[5]**.
- The rapid transmission of the virus which can also be spread by asymptomatic individuals has led to a sharp increase in infections in a short period straining the health care system.
- Significant national concern is the limited supply of mechanical ventilators and the number needed to adequately satisfy the demand.

In this study, we aimed to identify individual risk factors related to intubation among hospitalized patients with laboratory-confirmed COVID-19 and time to extubation among these patients.

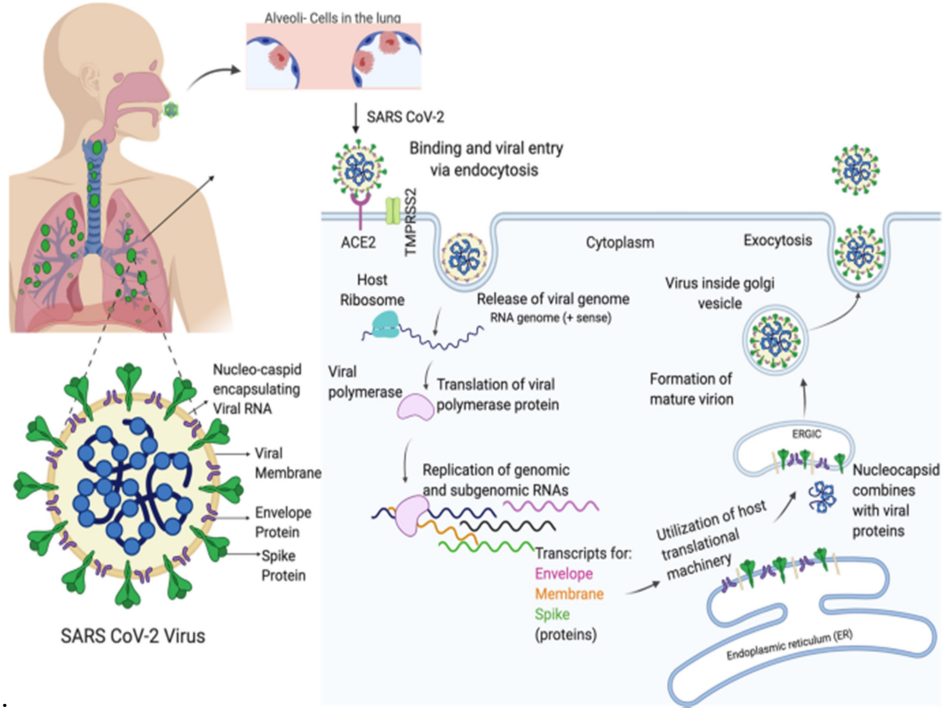
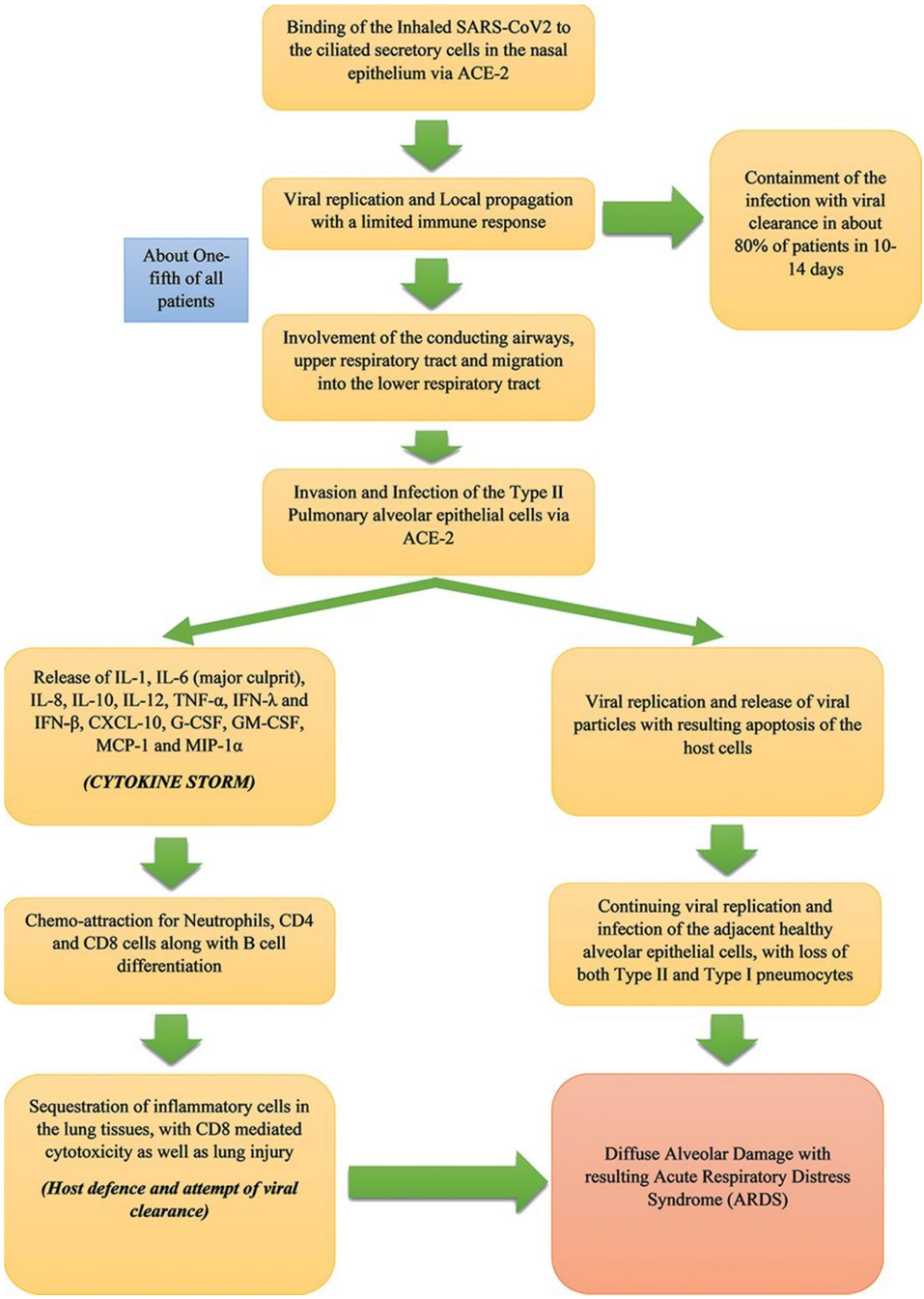


Figure 1: Pathophysiology of COVID-19 Disease


Binding of the Inhaled SARS-CoV2 to the ciliated secretory cells in the nasal epithelium via ACE-2
Viral replication and Local propagation with a limited immune response
Containment of the infection with viral clearance in about 80% of patients in 10-14 days
About One-fifth of all patients
Involvement of the conducting airways, upper respiratory tract and migration into the lower respiratory tract
Invasion and Infection of the Type II Pulmonary alveolar epithelial cells via ACE-2
Release of IL-1, IL-6 (major culprit), IL-8, IL-10, IL-12, TNF-α, IFN-λ and IFN-β, CXCL-10, G-CSF, GM-CSF, MCP-1 and MIP-1α
(CYTOKINE STORM)
Viral replication and release of viral particles with resulting apoptosis of the host cells
Chemo-attraction for Neutrophils, CD4 and CD8 cells along with B cell differentiation
Continuing viral replication and infection of the adjacent healthy alveolar epithelial cells, with loss of both Type II and Type I pneumocytes
Sequestration of inflammatory cells in the lung tissues, with CD8 mediated cytotoxicity as well as lung injury
(Host defence and attempt of viral clearance)
Diffuse Alveolar Damage with resulting Acute Respiratory Distress Syndrome (ARDS)

METHODS

Data source

- Data is collected after permission from concerned authority & informed consent from samples on basis of inclusion criteria.
- Data on hospitalized patients with laboratory-confirmed COVID-19 infection during or prior to admission was identified **[12]**.
- A confirmed case was defined as a positive result on a reverse transcriptase polymerase chain reaction assay of a specimen collected by a nasopharyngeal swab.

Inclusion criteria

- COVID-19 positive patients admitted with co-morbidities in KH & MRC, Karad.

Exclusion criteria

- COVID-19 negative patients with respiratory distress.
- All COVID-19 negative patient with comorbidities.
- Hospitalized patient with documented Do Not Resuscitate / Do Not Intubate (DNR/DNI).
- Those who left hospital against medical advice (DAMA i.e Discharge against Medial Advice).
- Patients who had missing data on investigated predictor variables and did not reach a clinical endpoint of intubation.

Measures

- Sociodemographic information was collected including age, sex, race, ethnicity and history of tobacco use **[11]**. Symptom and clinical history obtained on the day of admission, including recent travel and get in touch with individuals infected with COVID-19 was manually extracted from the medical history. Vital signs included systolic and diastolic blood pressure, pulse rate, respiratory rate, maximum temperature, lowest documented oxygen saturation, and body mass index (BMI) measured in the emergency room.
- Medical history included all comorbidities documented on admission.
- Comorbid disease was classified into diabetes, hypertension, cardiovascular disease, organ transplantation, immune-suppression, cancer, obstructive sleep apnea, pulmonary disease and chronic kidney disease. Cardiovascular disease included myocardial infarction, stroke, congestive coronary failure, valvular heart condition and

arrhythmias. Pulmonary disease included asthma, chronic obstructive pulmonary disease, acute interstitial pneumonitis, sarcoidosis, hypersensitivity pneumonitis, interstitial pneumonia.

- Chest radiographic imaging results were reviewed on the day of admission and classified as having positive findings if the radiologist documented any evidence of ground-glass opacity, consolidation or infiltrates.
- The primary outcome of this study was intubation with an oral endotracheal tube and attachment to a mechanical ventilator during the hospitalization. The secondary outcome was time required for extubation.

	Intubated	Not intubated	Total
Age -			
<60	**15**	**25**	**40**
>60	**35**	**25**	**60**
Sex -			
Male	**35**	**25**	**60**
Female	**18**	**22**	**40**
BMI -			
<30	**19**	**15**	**34**
30-39	**30**	**16**	**46**
>40	**12**	**8**	**20**
Diabetes	**41**	**22**	**63**
Symptoms -			
Cough	**70**	**16**	**86**
Shortness of breath	**40**	**27**	**67**
Past history of Covid-19	**28**	**15**	**43**
Vitals on admission -			
Pulse>100	**47**	**25**	**72**
RR>24	**41**	**27**	**68**
SpO2<90	**36**	**22**	**58**
SBP<90	**24**	**16**	**40**
Temperature>100.4°F	**32**	**20**	**52**

Investigations -			
CXR(opacities/infilteration)	**50**	**36**	**86**
HRCT Score on admission-			
≤7(Mild)	**22**	**13**	**35**
8-17(Moderate)	**28**	**17**	**45**
≥18(Severe)	**17**	**3**	**20**
O2 supplementation	**64**	**24**	**88**

BMI – Basal Metabolic Rate; RR – Resoiratory Rate; SpO2 – Saturation of oxygen; SBP – Systolic Blood Pressure; CXR – Chest Xray; HRCT – High Resolution Computed Tomography; O2 – Oxygen

RESULTS

Clinical Presentation

- A minority of hospitalized patients endorsed recent traveller contact with a confirmed individual with COVID-19 infection **[9]**.
- The most commonly reported symptoms were cough, fever, shortness of breath and fatigue.
- As compared with nonintubated patients, intubated patients were more likely to present with shortness of breath respiratory rate>24/min, temperature >100.4^{0}F and oxygen saturation <90%. Intubated patients were also more likely to have evidence of opacities, infiltrates or consolidation on chest radiographs.

Hospital Course

- During their admission, a majority of patients infected with COVID-19 received oxygen supplementation, antibiotics, and hydroxychloroquine.
- The number of daily intubations for patients infected with COVID-19 gradually increased reaching a peak in last week of March 2020 and then declined in the days afterward.
- A significantly higher percentage of intubated patients received oxygen supplementation, antibiotics, hydroxychloroquine, an IL-6 receptor inhibitor or remdesivir as compared with non-intubated patients.

DISCUSSION

- COVID-19 induces acute respiratory distress by hypoxia, tachypnea, dyspnea.
- Intubation & mechanical ventilation are strategic treatment for covid-19 distress or hypoxia.
- Severe respiratory distress, hypoxia, unconsciousness are important reasons for intubation.
- Increase level of D-dimer, ferritin, lipase in common with hyproxia are related to ICU admission and intubation.
- Daily intubations for patients infected with COVID-19 gradually increased in March until peaking in last week of March 2020.
- About a third of intubated patients were intubated upon presentation in the emergency room, a sign of the rapid clinical deterioration experienced by a subset of patients infected with COVID-19.
- Increasing time between admission & intubation is associated with increase in mortality.
- Experts recommend early intubation.

- Early intubation is defined as intubation at admission or within 2 days of having documented FiO2 greater than or equal to O.5.
- For severe and critical COVID-19 patients, early intubation with invasive respiratory support is recommended to reduce mortality.
- Identifying and treating at-risk patients early in the infection may provide benefit in preventing progress of disease.
- Medical staff should have high level protection during intubation **[2]**.
- Certain clinical findings were associated with the need for mechanical ventilation during hospitalization.
- Shortness of breath was reported by 80% of intubated patients.
- Oxygen saturation <90% and increased respiratory rate were also predictors for intubation.
- In our study advanced stage was strongly associated with intubation and time to extubation.
- Age was reported as a predictor of mortality.
- Increasing age was also associated with mortality among ICU patients.
- The pathophysiology underlying the increased risk of a more severe clinical presentation in older patients is an area of active research **[3]**.
- COVID-19 induced reduction of ACE2 (angiotensin converting enzyme 2) which regulates inflammation and is already present in lower levels in the elderly has been proposed as a possible mechanism leading to higher disease severity.
- ACE2 is also a component of Leydig cells within the male testes leading to a potential site of infection and viral safe harbor which may contribute to the higher percentage of male patients with COVID-19 as compared with females.
- BMI was also a significant risk factor predictive of time to extubation among intubated patients with COVID-19.
- Obese patients may have a higher likelihood of being admitted and placed on mechanical ventilation.
- All of us are aware regarding the impact of obesity on severity of disease obesity is already associated with decreased pulmonary function and with the addition of COVID-19 injuring lung tissue, adequate ventilation would inevitably become more difficult.

- Obesity is also associated with higher levels of inflammatory cytokines which may be exacerbated by the release of TNF-α and IL-6 from infected pneumocytes and pulmonary cells.
- The most common comorbidities among patients in this study were hypertension, diabetes, cardiovascular disease and chronic obstructive pulmonary disease (COPD).
- These risk factors are associated with admission to the ICU, placement on invasive mechanical ventilation or death.
- Metabolic disorders have been associated with the impairment of macrophages and lymphocytes.
- As a result, diabetic patients may be at higher risk of an inadequate immune response to a COVID-19 infection.
- Open tracheostomy has a high risk of transmission of COVID-19 to health workers as it is an aerosol-generating procedure.
- There are several limitations to this study that should be considered -

  1) Several patients in this study were still hospitalized at the time of last follow-up; as a result, some clinical outcomes were not known such as mortality.

  2) Deciding when to intubate a patient is a complex clinical decision based on many factors and different health care providers may have different criteria for deciding when to intubate patients with COVID-19. While this study included patients treated at several hospitals, the results might not be generalizable to other institutions.

  3) Laboratory results were not collected and could contribute as additional predictive factors for intubation and prolonged intubation.

  4) Although data were derived directly from medical records they were originally collected for clinical care and thus suffer from rapidly evolving practice guidelines, which may lead to bias. We utilized several statistical methods to reduce bias and confounding effects.

CONCLUSION

- Acute respiratory distress in COVID-19 requires endotracheal intubation, mechanical ventilation.
- Age, male sex and a history of diabetes were independent risk factors associated with intubation in hospitalized patients with COVID-19 **[8]**.

- Early intubation was not associated with worse clinical outcome compared to delayed or no intubation.
- Early intubation may reduce virus aerosolization.
- Time to extubation is also influenced by age and obesity.
- Obesity and elderly age are associated with difficult or delayed extubation.

Acknowledgement

I am thankful to Mrs. Rupali Salunkhe for secretariat help, Department of Surgery, Krishna Institute of Medical Sciences Deemed to be University, Karad, Maharashtra (India).

REFERENCES

[1] Hur K, Price CP, Gray EL, Gulati RK, Maksimoski M, Racette SD, *et al*., <? covid19?> Factors Associated With Intubation and Prolonged Intubation in Hospitalized Patients With COVID-19, Otolaryngology–Head and Neck Surgery, 163(1), 2020, 170-8.

[2] Ranney ML, Griffeth V, Jha AK, Critical supply shortages—the need for ventilators and personal protective equipment during the Covid-19 pandemic, New England Journal of Medicine, 382(18), 2020, e41.

[3] COVID C, Team R, COVID C, Team R, COVID C, Team R, *et al*., Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019—United States, February 12–March 28, 2020, Morbidity and Mortality Weekly Report, 69(13), 2020, 382.

[4] Jernigan DB, COVID C, 19 Response Team (2020) Update public health response to the coronavirus disease 2019 outbreak US Feb 24, 2020, Morbidity and Mortality Weekly Report, 69, 216-9.

[5] Jordan RE, Adab P, Cheng K, Covid-19: risk factors for severe disease and death.

[6] Starren JB, Winter AQ, Lloyd-Jones DM, Enabling a learning health system through a unified enterprise data warehouse: the experience of the North western University Clinical and Translational Sciences (NUCATS) Institute, Clinical and translational science, 8(4), 2015, 269.

[7] Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, *et al*., Characteristics and outcomes of 21 critically ill patients

with COVID-19 in Washington State, Jama, 323(16), 2020, 1612-4.

[8] Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, *et al*., Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana, New England Journal of Medicine, 367(5), 2012, 423-34.

[9] Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, *et al*., The Northwell COVID-19 Research Consortium Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area, Jama, 323(20), 2020, 2052-9.

[10] Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, *et al*., the Northwell COVID-19 Research Consortium Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area, Jama, 323(20), 2020, 2052-9.

[11] Myers LC, The Permanente Medical Group KPNC, Oakland, Parodi SM, The Permanente Medical Group KPNC, Oakland, Escobar GJ, The Permanente Medical Group KPNC, Oakland, Liu VX, The Permanente Medical Group KPNC, Oakland: Characteristics of Hospitalized Adults With COVID-19 in an Integrated Health Care System in California, JAMA, 323(21), 2020, 2195-8.

[12] Du RH, Liang LR, Yang CQ, Wang W, Cao TZ, Li M, *et al*., Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study, European Respiratory Journal, 55(5), 2020.

[13] Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, *et al*., Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy, Jama, 323(16), 2020, 1574-81.

[14] Mercuro NJ, Yen CF, Shim DJ, Maher TR, McCoy CM, Zimetbaum PJ, *et al*., Risk of QT interval prolongation associated with use of hydroxychloroquine with or without concomitant azithromycin among hospitalized patients testing positive for

coronavirus disease 2019 (COVID-19), JAMA cardiology, 5(9), 2020, 1036-41.

[15] Douglas GC, O'Bryan MK, Hedger MP, Lee DK, Yarski MA, Smith AI, *et al*. The novel angiotensin-converting enzyme (ACE) homolog, ACE2, is selectively expressed by adult Leydig cells of the testis, Endocrinology, 145(10), 2004, 4703-11.

[16] Chooi YC, Ding C, Magkos F, The epidemiology of obesity. Metabolism, 92, 2019, 6-10.

[17] Ogden CL, Fakhouri TH, Carroll MD, Hales CM, Fryar CD, Li X, *et al*., Prevalence of obesity among adults, by household income and education—United States, 2011–2014, MMWR, Morbidity and mortality weekly report, 66(50), 2017, 1369.