National Board of Examination - Journal of Medical Sciences
Volume 2, Issue 4, Pages 371–379, April 2024
DOI 10.61770/NBEJMS.2024.v02.i04.009

ORIGINAL ARTICLE

Assessment of Lung Involvement in COVID-19 Patients on HRCT and impact of Vaccination on CT severity: Insights from the Second Wave in Kerala, India

Puthiya Maliyakkal Sinewraz[1], Praharsha Surya[2], Jeevithan Shanmugam[3] and Archana Ramachandran[2,*]

[1]*Professor, Department of Radiodiagnosis, DM Wayanad Institute of Medical Sciences, Meppadi, Wayanad, Kerala, 673577.*

[2]*Consultant Radiologist, Cloudex Radiology Solutions, Emad Tower, Fort Road, Kannur, Kerala, 670001*

[3]*Professor, Department of Community Medicine, KMCH Institute of Health Sciences and Research, Coimbatore - 641014*

Accepted: 06-February-2024 / Published Online 31-March-2024

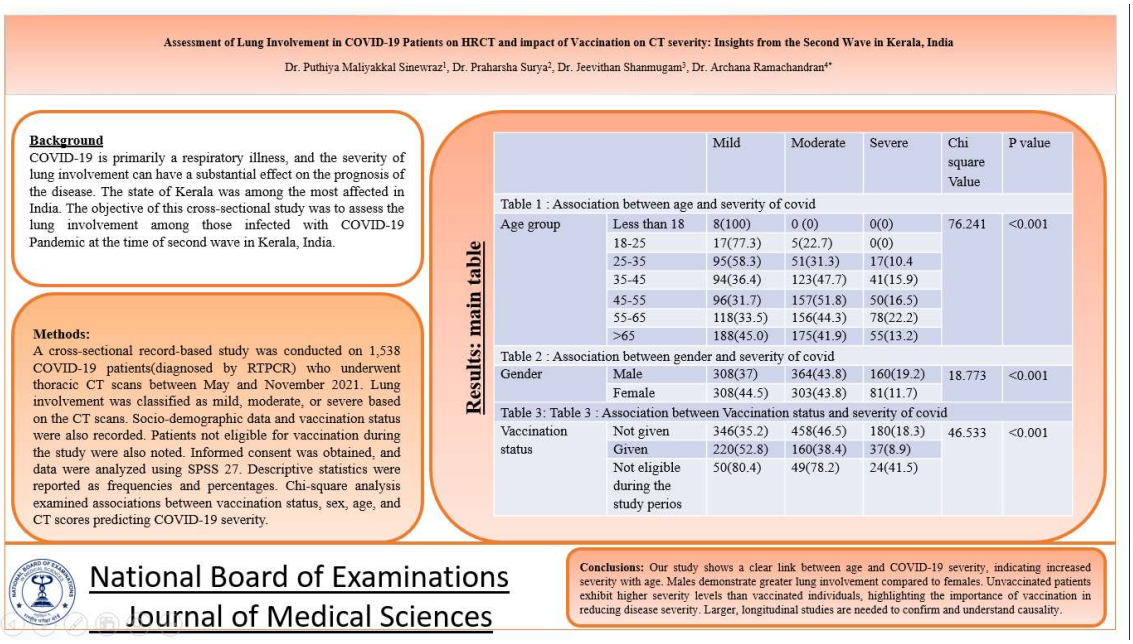
Abstract

Background: COVID-19 is primarily a respiratory illness and the severity of lung involvement can have a substantial effect on the prognosis of the disease. The state of Kerala was among the most affected in India. The objective of this cross-sectional study was to assess the lung involvement among those infected with COVID-19 Pandemic at the time of second wave in Kerala, India. **Methodology**: The study was done in 2021 and included COVID-19 patients who underwent CT scan of thorax. The socio-demographic variables and vaccine status of the patients were collected. **Results**: The results showed that the severity of lung involvement increased with age, with more than 60% of the study population being above 55 years of age. Additionally, unvaccinated patients had more severe lung involvement compared to vaccinated patients, with males being more affected than females. **Conclusion**: The study highlights the importance of vaccination and early intervention in managing severe COVID-19 cases.

Keywords: COVID-19, Lung involvement, HRCT

*Corresponding author: Archana Ramachandran
Email: archu.ram@gmail.com

Graphical Abstract



Introduction

The COVID-19 pandemic, due to SARS-CoV-2 virus, has emerged as one of the most severe public health catastrophes in recent years, causing extensive morbidity and mortality worldwide. As of February 2022, the pandemic has affected over 40 crore humans, with over 60 Lakh deaths reported globally. India has been severely impacted by the pandemic, with a high number of COVID-19 cases and also deaths [1]. Kerala was one of the worst impacted areas during the second wave of the pandemic in India [2]. COVID-19 is primarily a respiratory illness that affects the lungs, and the severity of lung involvement can have a significant impact on the prognosis of the disease. A computed tomography (CT) scan of the thorax has been proven to be an efficient method for detecting lung involvement in COVID-19 patients [3].

Several studies have been conducted to evaluate the extent of lung involvement in COVID-19 patients using CT scan imaging. These studies have shown that COVID-19 primarily affects the lungs, with characteristic features such as ground-glass opacities, consolidations, and crazy-paving patterns observed in CT scans of the thorax. These features are indicative of varying degrees of lung involvement and can be used to assess the severity of the disease [4,5].

Ai et al. in China discovered that CT scan imaging was more sensitive than reverse transcription-polymerase chain reaction (RT-PCR) testing in diagnosing COVID-19 infection in patients presenting with clinical symptoms. The authors also reported that the extent of lung involvement observed on CT scans was associated with the severity of the disease and the need for hospitalization [6,7]. A similar study conducted by Long et al. in the United States reported that CT scans were more sensitive in the detection of COVID-19 infection than RT-PCR testing and also

showed a significant association between the extent of lung involvement observed on CT scans and disease severity [8].

In this research, we designed to evaluate the severity of lung involvement in COVID-19 infection during the second Pandemic wave in Kerala, India, using CT scan imaging. We also assessed the impact of socio-demographic variables and vaccine status on the severity of lung involvement.

Materials and Methods

A cross sectional record based study was done on a sample of 1,538 patients of COVID-19 who underwent CT scan of thorax between May and November 2021. Complete enumeration of all the patients who were diagnosed as COVID-19 infection positive by RTPCR and referred for CT thorax were included. Based on the CT scan of thorax the lung involvement in COVID-19 patients, were classified into mild, moderate, or severe. In addition socio-demographic data and vaccine status of the patients were recorded. When the study was designed, the vaccination against the infection was given in a phased manner starting with the elderly, front line and health care workers with gradual shift towards younger population in decreasing order of age. So those who were not in the age group for vaccination during the study period were considered as Not eligible for vaccination. Prior written Informed consent was obtained. Microsoft excel was used for data entry and SPSS 27 was used for analysis. Descriptive results were presented as frequency and percentages. Chi square analysis was performed to measure the association between Vaccination status, sex and age with CT scores predicting the COVID 19 disease severity.

Results

A total of 1,538 COVID-19 patients who underwent CT scan of thorax were included in the study. The study population consisted a slight majority of males (55%). The majority of the patients (70.4%) were above 45 years of age, with more than 60% of the study population being above 55 years of age (Table 1).

Majority of about 91.9% were eligible for vaccination during the study period. About 27.4% among the total had received at least one dose of any of the approved COVID-19 vaccine, with 11% having received both the recommended doses then. In total about 72% had not received the vaccine.

The CT scores showed that 40.4% of the patients had mild lung involvement, 43.8% had moderate lung involvement, and 15.8% had severe lung involvement. Higher proportion of people in the age group of more than 45 years had severe disease than who were 45 and below ($p<0.01$) (Table 2). Significantly a higher proportion of males had severe lung disease than the females (Table 2). The severity of lung involvement was also significantly higher among unvaccinated patients (18.3% in not received and 19.5% in the not eligible category) compared to vaccinated patients (8.9%). Majority of them in the not eligible category (40.6%) and those having received vaccine (52.8%) had CT scores suggestive of mild disease. Whereas among those who were eligible but had not taken the vaccine majority (46.5%) were in the moderate category (Table 3). The severity of lung involvement increased with age, with the highest percentage of patients with severe lung involvement being above 55 years of age.

Table 1. Association between age and severity of covid

Age group	Mild		Moderate		Severe		Chi square Value	P value
	Number	%	Number	%	Number	%		
Less than 18	8	100	0	0	0	0	76.241	<0.001
18-25	17	77.3	5	22.7	0	0		
25-35	95	58.3	51	31.3	17	10.4		
35-45	94	36.4	123	47.7	41	15.9		
45-55	96	31.7	157	51.8	50	16.5		
55-65	118	33.5	156	44.3	78	22.2		
>65	188	45.0	175	41.9	55	13.2		

Table 2. Association between gender and severity of covid

Gender	Mild		Moderate		Severe		Chi square Value	P value
	Number	%	Number	%	Number	%		
Male	308	37	364	43.8	160	19.2	18.773	<0.001
Female	308	44.5	303	43.8	81	11.7		

Table 3. Association between Vaccination status and severity of covid

Vaccination status	Mild		Moderate		Severe		Chi square Value	P value
	Number	%	Number	%	Number	%		
Not given	346	35.2	458	46.5	180	18.3	46.533	<0.001
Given	220	52.8	160	38.4	37	8.9		
Not eligible during the study perios	50	80.4	49	78.2	24	41.5		

Discussion

This cross-sectional study aimed to assess the correlation between vaccination status and the extent of lung involvement among COVID-19 patients in Kerala, India, amidst the second wave of the pandemic.

Age and COVID 19 disease

The findings indicated a positive correlation between patient age and the severity of lung involvement, aligning with existing research demonstrating a higher incidence of COVID-19 among older individuals. Aging is often associated with a compromised immune system, rendering individuals more susceptible to viral infections. Moreover, elderly populations frequently contend with underlying health issues, further heightening their risk of experiencing severe manifestations of COVID-19. In this discourse, we will examine pertinent literature elucidating the connection between age and COVID-19 incidence, alongside exploring potential mechanisms underpinning this association.

A research endeavor carried out by scientists in Italy revealed a notable rise in COVID-19 incidence corresponding to age, with the most pronounced rates observed among individuals aged 80 years or older [9]. Another study conducted in China similarly highlighted a greater incidence of COVID-19 among older adults, emphasizing that individuals aged over 60 faced an elevated risk of infection [10]. A comprehensive systematic review and meta-analysis encompassing 22 studies from diverse countries revealed a substantial escalation in the risk of severe COVID-19 illness and mortality in tandem with advancing age [11].

Several factors may underlie the heightened incidence of COVID-19 among older adults. One potential mechanism is immunosenescence, which denotes age-related alterations in the immune system leading to a diminished capacity to mount a robust immune response against viral infections [12]. Additionally, the prevalence of underlying health conditions, including cardiovascular disease, diabetes, and chronic respiratory ailments, tends to be higher among older individuals, thereby amplifying the susceptibility to severe manifestations of COVID-19 [13].

Moreover, older adults may face an elevated risk of virus exposure owing to factors like residing in long-term care facilities, which have been sites of COVID-19 outbreaks. Social dynamics also play a role, with age-related declines in social support and heightened social isolation potentially contributing to the heightened vulnerability of older adults to COVID-19 [6,14].

Yang et al. [15] have demonstrated that advanced age stands as a significant risk factor for severe COVID-19 disease and its associated complications. Numerous studies further corroborate age as a pivotal risk factor for both the incidence and severity of COVID-19. The mechanisms underscoring this correlation encompass immunosenescence, underlying health conditions, and heightened susceptibility to virus exposure. These insights underscore the critical importance of prioritizing older adults for vaccination and implementing preventive measures to mitigate the risk of COVID-19-related morbidity and mortality.

Gender and COVID

Multiple studies have consistently observed a higher severity of lung involvement in male COVID-19 patients compared to females. This gender disparity has been documented across various

regions worldwide, including the United States, China, and Italy. For instance, a study conducted in New York City, USA, underscored that male individuals diagnosed with COVID-19 faced a greater risk of severe lung disease and a heightened mortality rate compared to their female counterparts [16]. Similarly, a study conducted in Wuhan, China, highlighted that male COVID-19 patients exhibited a higher incidence of severe pneumonia and a heightened mortality rate compared to females [17]. Likewise, findings from Italy underscored that male individuals diagnosed with COVID-19 had a higher incidence of severe respiratory failure in comparison to female patients [18].

The underlying reasons behind the gender disparity in COVID-19 lung involvement remain somewhat elusive. Some studies propose that biological factors could contribute to this phenomenon. For instance, research indicates that females often exhibit more robust immune responses compared to males, potentially shielding them from severe manifestations of COVID-19 [19]. Additionally, the female hormone estrogen has been posited as a protective factor against severe COVID-19. Estrogen is known for its anti-inflammatory properties and may aid in mitigating the cytokine storm, a potentially harmful immune response associated with severe COVID-19 cases [20].

Indeed, behavioral and environmental factors could also contribute to the observed gender differences in COVID-19 lung involvement. For instance, males often exhibit higher rates of smoking compared to females, which is known to compromise lung health and elevate the risk of severe COVID-19 outcomes. Additionally, males are more likely to engage in occupations that entail exposure to air pollution, a factor that can also impair lung function and heighten susceptibility to severe COVID-19 complications. These behavioral and environmental disparities may contribute to the increased vulnerability of males to severe lung involvement in COVID-19 [21].

Jin et al. [22] in their study also revealed that the severity of lung involvement was higher among males than females, reported that males have an increased risk of severe COVID-19 infection and mortality. The evidence that are currently available suggests that COVID-19 lung involvement is higher in males compared to females, although the reasons for this gender difference are not entirely clear. Biological factors such as immune response and hormone levels may play a role, as well as behavioral and environmental factors. Further research is imperative to comprehensively unravel the mechanisms underlying the gender disparity in COVID-19 lung involvement.

Vaccination and Covid Severity

The study underscores a crucial finding: unvaccinated patients exhibit a higher severity of lung involvement in contrast to vaccinated individuals, highlighting the protective efficacy of COVID-19 vaccination against severe disease and its associated complications. Numerous studies corroborate this observation, consistently demonstrating elevated COVID-19 lung involvement among unvaccinated individuals compared to their vaccinated counterparts. The principal rationale behind this trend lies in the demonstrated effectiveness of vaccines in preventing severe COVID-19 illness and mitigating the risk of hospitalization and mortality [23,24].

A substantial retrospective cohort study conducted in the United States unveiled that unvaccinated individuals faced a heightened risk of hospitalization and mortality in comparison to vaccinated counterparts [24]. Similarly, a study carried out in the United Kingdom highlighted that individuals who were either unvaccinated or partially vaccinated exhibited a greater propensity for hospitalization and mortality when contrasted with fully vaccinated individuals [23].

The mechanism behind the higher COVID-19 lung involvement among unvaccinated individuals is related to the immune response. Vaccines stimulate the production of neutralizing antibodies that can bind to the virus and prevent it from entering cells. They also activate T cells that can identify and kill infected cells. Thus, vaccinated individuals are more likely to have a robust immune response that can prevent severe lung involvement in case of COVID-19 infection [25].

Moreover, unvaccinated individuals are at a higher likelihood of COVID-19 exposure and subsequent severe disease development. Vaccines play a crucial role not only in safeguarding individuals but also in curbing virus transmission within communities. Consequently, the overall risk of exposure diminishes as the spread of the virus is mitigated through vaccination efforts [26]. The COVID-19 lung involvement is higher among unvaccinated individuals compared to vaccinated individuals. This is due to the fact that vaccines stimulate a robust immune response that can prevent severe lung involvement in case of COVID-19 infection. Additionally, vaccines reduce the risk of exposure to the virus in the community. Therefore, it is important to promote vaccine uptake to reduce the severity of COVID-19 disease and prevent its spread.

Conclusion

The results of our study indicate a direct correlation between age and the severity of lung involvement in COVID-19 patients, with increasing age corresponding to heightened severity. Additionally, our findings reveal that males exhibit greater severity of lung involvement compared to females. These observations underscore the critical role of COVID-19 vaccination in mitigating the risk of severe disease, as evidenced by higher lung involvement among unvaccinated patients relative to vaccinated counterparts. To further validate these findings and ascertain causality, future studies with larger sample sizes and longitudinal designs are warranted.

Limitations: The data was gathered from a single center, and the sample size was modest. The cross-sectional study design makes it more difficult to prove causation. The effect of comorbidities on lung involvement in COVID-19 participants was not assessed in this study.

Conflicts of interest

The authors declares that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

References

1. Ministry of Health and Family Welfare. (2021). COVID-19 Statewise Status. Retrieved from https://www.mohfw.gov.in/
2. India Today. (2021). Kerala records highest single-day Covid-19 spike, 29,682 new cases reported. Retrieved

from https://www.indiatoday.in/coronavirus-outbreak/story/kerala-records-highest-single-day-covid-19-spike-29-682-new-cases-reported-1848514-2021-08-22

3. Kanne JP, Little BP, Chung JH, Elicker BM. (2020). Essentials for radiologists on COVID-19: an update-radiology scientific expert panel. Radiology. 2020; 296(2): E113-E114. https://doi.org/10.1148/radiol.2020200527
4. Salehi S, Abed A, Balakrishnan S, Gholamrezanezhad A. (2020). Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients. AJR. American journal of roentgenology.2020; 215(1): 87-93. https://doi.org/10.2214/AJR.20.23034
5. Simpson S, Kay FU., Abbara S, Bhalla S, Chung JH, Chung M, Henry TS, Kanne JP, Kligerman SJ, Ko JP, Litt H, Maldjian P, Reilly C, Tomography C. (2020). Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. Radiology: Cardiothoracic Imaging.2020; 2(2): e200152. https://doi.org/10.1148/ryct.2020200152
6. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, Tao Q, Sun Z, Xia L. 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. doi: 10.1148/radiol.2020200642.
7. Li K, Wu J, Wu F. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. *Invest. Radiol.* 2020;55(6):327–331. doi: 10.1097/RLIK.0000000000000672
8. Long C, Xu H, Shen Q, Zhang X, Fan B, Wang C, Zeng B, Li Z, Li X, Li H. Diagnosis of the Coronavirus disease (COVID-19): rRT-PCR or CT? *Eur. J. Radiol.* 2020;126:108961. doi: 10.1016/j.ejrad.2020.108961
9. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA. 2020;323(18):1775–1776.
10. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239–1242.
11. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia - A systematic review, meta-analysis, and meta-regression. Diabetes Metab Syndr. 2020;14(4):395–403.
12. Nikolich-Žugich J. The twilight of immunity: emerging concepts in aging of the immune system. Nat Immunol. 2018;19(1):10–19.
13. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential Effects of Coronaviruses on the Cardiovascular System: A Review. JAMA Cardiol. 2020;5(7):831–840.
14. Burton JK, Bayne G, Evans C, et al. Evolution and effects of COVID-19 outbreaks in care homes: a population analysis in 189 care homes in one geographic region. Lancet 2020.;1(1):E21-E31.
15. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475-481.
16. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-20. doi:10.1056/NEJMoa2002032

17. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020;368:m1091. doi: 10.1136/bmj.m1091
18. 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
19. Klein SL, Dhakal S, Ursin RL, et al. Biological sex impacts COVID-19 outcomes. PLoS Pathog. 2020;16(6):e1008570. doi:10.1371/journal.ppat.1008570
20. Bukowska J, Frazier-Jessen M, Ries W. COVID-19 susceptibility and outcomes: A sex-specific and hormonal perspective. J Clin Med. 2020;9(5):1645. doi:10.3390/jcm9051645
21. Bhopal SS, Bhopal R. Sex differential in COVID-19 mortality varies markedly by age. Lancet. 2020 Aug 22;396(10250):532-533. doi: 10.1016/S0140-6736(20)31748-7.
22. Jin JM, Bai P, He W, et al. Gender differences in patients with COVID-19: Focus on severity and mortality. Front Public Health. 2021;9:152.
23. Keehner J, Horton LE, Pfeffer, MA, Longhurst CA, Schooley RT, Currier JS, Shah NH. Real-world evidence for lower morbidity and mortality of mRNA COVID-19 vaccination. Med.2020: 2(7); 779-790.e4. https://doi.org/10.1016/j.medj.2021.05.005.
24. Tenforde MW, Self WH, Zhu Y, Naioti EA, Gaglani M, Ginde AA, Jensen K, Talbot HK, Casey JD, Mohr NM, Zepeski A, McNeal T, Ghamande S, Gibbs KW, Files DC, Hager DN, Shehu A, Prekker ME, Erickson HL, Gong MN, Mohamed A, Johnson NJ, Srinivasan V, Steingrub JS, Peltan ID, Brown SM, Martin ET, Monto AS, Khan A, Hough CL, Busse LW, Lohuis CT, Duggal A, Wilson JG, Qadir N, Chang SY, Mallow C, Rivas C, Babcock HM, Kwon JH, Exline MC, Botros MM, Lauring AS, Shapiro NI, Halasa N, Chappell JD, Grijalva CG, Rice TW, Jones ID, Stubblefield WB, Baughman A, Womack KN, Rhoads JP, Lindsell CJ, Hart KW, Turbyfill C, Olson S, Murray N, Adams K, Patel MM; Influenza and Other Viruses in the Acutely Ill (IVY) Network. Protection of Messenger RNA Vaccines Against Hospitalized Coronavirus Disease 2019 in Adults Over the First Year Following Authorization in the United States. Clin Infect Dis. 2023: 8;76(3):e460-e468. doi: 10.1093/cid/ciac381.
25. Bar-On YM, Goldberg Y, Mandel M, Bodenheimer O, Freedman L, Kalkstein N, Mizrahi B, Alroy-Preis S, Ash N, Milo R, Huppert A. Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel. New England Journal of Medicine.2021; 385(15): 1393–1400. https://doi.org/10.1056/nejmoa2114255
26. Krammer F. SARS-CoV-2 vaccines in development. Nature.2021: 586(7830), 516–527. https://doi.org/10.1038/s41586-020-2798-3.