

Comparative Analysis of CT Outcomes in COVID-19: Non-Vaccinated Individuals vs. Vaccine Breakthrough Cases

Dr. Aishwarya Gadwal MD, DNB, EDIR*, Dr. Vinaya Poornima, MD, Dr. Griselda P Norhona MD, DNB, FRCR, Dr. Ashvini Kumar, MD, Dr. Akshay Reshmi MD, DNB, EDIR and Vinay BS, MD

Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, India

Citation: Gadwal A, Poornima V, Norhona GP, Kumar A, Reshmi A, Vinay BS. Comparative Analysis of CT Outcomes in COVID-19: Non-Vaccinated Individuals vs. Vaccine Breakthrough Cases. *Medi Clin Case Rep J* 2024;2(2):337-341. DOI: doi.org/10.51219/MCCRJ/Aishwarya-Gadwal/91

Received: 13 June, 2024; **Accepted:** 18 June, 2024; **Published:** 21 June, 2024

***Corresponding author:** Dr. Aishwarya Gadwal MD, DNB, EDIR, Kasturba medical college, Mangalore, Manipal academy of higher education, India.

Copyright: © 2024 Gadwal A, et al., This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

A B S T R A C T

Background: In the context of the COVID-19 pandemic, this study investigates the influence of vaccination on patient demographics and clinical outcomes. Exploring disparities aids in refining public health strategies.

Purpose: To investigate and compare demographics, comorbidities, and clinical characteristics between vaccinated and unvaccinated COVID-19 patients.

Methods: This prospective observational study conducted between January 2021 and June 2022, evaluates CT outcomes in COVID-19 patients relative to vaccination status. Data collection encompasses demographics, comorbidities, and clinical details. Two radiologists independently use a CT Severity Score (CTSS) to evaluate pneumonia extent, exploring associations with age, gender, and vaccination status through statistical analyses.

Results: Out of 1020 patients, 220 were excluded. The study analysed data from 800 patients, with 450 vaccinated and 350 unvaccinated. Demographics and comorbidities showed no significant differences between groups. Dyspnoea and sore throat were more frequent in the unvaccinated group ($p < 0.05$). C-reactive protein levels were consistently elevated in both groups (>80%), indicative of COVID-19 ($p > 0.05$). These data provide a comprehensive overview of the patient population, highlighting differences in demographics, comorbidities, and clinical characteristics between vaccinated and unvaccinated individuals. There were no noticeable differences in frequency between patients who had received vaccinations and those who had not.

Conclusions: Vaccination status showed no significant correlation with comorbidity, symptom severity, or clinical outcomes. Younger individuals and females, regardless of vaccination status, showed less lung involvement. Lower CT severity scores associated with vaccination emphasize its significance in adults, guiding future COVID-19 research and strategies.

Keywords: COVID-19; Computed tomography; Demographic characteristics; Vaccination; CT severity score; Vaccine breakthrough cases

Introduction

The year 2019 marked the onset of a global crisis that transcended borders, reshaped societies, and challenged the resilience of healthcare systems worldwide the COVID-19 pandemic. Caused by the novel coronavirus SARS-CoV-2, this viral outbreak swiftly evolved from a localized health concern to a complex, multifaceted global emergency¹. In the wake of the unprecedented global health crisis sparked by the COVID-19 pandemic, the scientific community has witnessed an extraordinary convergence of efforts aimed at developing effective vaccines against the novel coronavirus, SARS-CoV-2². Vaccination campaigns, pivotal in mitigating the impact of the virus, have faced both acclaim for their role in reducing severe illness and criticism amid the emergence of breakthrough infections in vaccinated individuals^{3,4}.

Although mild to severe sickness can be brought on by breakthrough coronavirus infections, in vaccinated and unvaccinated population. However, the likelihood of a major COVID-19 infection is extremely rare, particularly in those without a chronic illness^{5,6}. Tan et al (2023)⁷ found that another coronavirus strain, omicron, more infectious than the one taken into consideration during vaccine development, caused breakthrough infection in 28% population compared to 36% of unvaccinated people. They also estimated that the risk of transmitting infection was reduced by 22%, 23%, and 40% among vaccinated breakthrough, infected prior and both vaccinated and infected priorly respectively⁷.

Vaccines, a pandemic beacon, raise questions on real-world efficacy, especially with emerging variants and waning immunity. CT outcomes in COVID-19 guide diagnosis, treatment decisions, research, public health strategies and understanding the long-term impact of the disease on the respiratory system^{8,9}. This study unravelled the impact of infections in non-vaccinated individuals and breakthrough infections among the vaccinated-on CT outcome of patients. We also compared the nuances of vaccine effectiveness on individuals from different demographic backgrounds.

Material and Methods

Study Design and Population

It was a prospective observational study conducted from Jan 2021-Jun 2022. The study enrolled 1020 patients who came for the CT scan at our hospital. Patients who agreed to be part of the study and filled patient information sheet and informed consent form were included in the study. Patients who were not interested in study and/or had a history of severe respiratory diseases were excluded from the study. Finally 800 Patients were included in the study.

Among 1020 patients, we identified 450 individuals who had received both doses of the any recommended COVID 19 vaccine between Jan 2021 and Jun 2022 and who had a documented positive SARS-CoV-2 PCR based on nasopharyngeal swab testing within 7 days of registration to our centre. These people are recognized as having breakthrough infections. We also identified 350 Individuals from the unvaccinated control group tested positive for COVID19 infection within last 14 days.

Data collection

Informed consent form and general questionnaire related to demographic data were collected from each patient. By

reviewing each case demographic, laboratory, co-morbidity and clinical data were collected. The population was divided based on age and sex (Demographic characteristics) and comorbidities (cardiovascular disease, diabetes, hypertension, and cancer) and clinical symptoms (cough, fever, sputum, myalgia, sore throat, and sensory loss).

Each patient's CT images taken during hospitalization were retrieved from the department. It was obtained within a week of symptom onset.

CT scan Interpretation

Unaware of the patient's clinical details, two radiologists (Senior and Junior) examined every image and results were compared in consensus. Person who is under training (resident) was considered as junior radiologist, whereas a radiologist with over 20 years of experience in thoracic imaging was considered as senior radiologist. Analysis was done on the amount of pneumonia on the CT scans taken within a week of onset of symptoms. Based on research predicting the severity of COVID-19 the amount of pneumonia in all five lung zones on CT scans was graded as CT Severity Score (CTSS). It ranged from 0 to 5 (score 0: no evidence of pneumonia, score 1: 1%–5% involvement, score 2: 5–25% involvement; score 3: 26–50% involvement; score 4: 51–75% involvement; score 5: > 75% involvement. Total score of all lobes ranged from 0 to 25¹⁰. A typical appearance was thought to be multifocal round ground-glass opacities (GGOs) or peripheral bilateral GGOs, with or without intralobular lines, consolidation, or a reverse halo sign. The definition of an uncertain appearance was having GGOs, either with or without consolidation, but without characteristic traits. The absence of typical or ambiguous characteristics along with distinct centrilobular nodules, lung cavitation, smooth interlobular septal thickening with pleural effusion, and/or lobar and/or segmental consolidation without GGOs were considered uncommon appearances¹¹.

Statistical analysis

Data were analyzed using statistical software (SPSS version 25.0, IBM Corp). Continuous variables were expressed as median value and interquartile range (IQR). The frequencies of demographic and clinical characteristics of populations were expressed as the number (percentage) of occurrences and were compared using the 2-tailed χ^2 test. For the CTSS assessment, the intraclass correlation coefficient (ICC) was used to compute the interobserver agreement between the two radiologists. Univariate logistic regression was performed to identify relationships between the CTSS and independent variables (age, gender, and vaccination status) and for the outcome analysis. Differences for which $p < 0.05$ were considered statistically significant.

Results

Comparative study of Demographic and clinical characteristics based on the vaccination status

A total of 1020 patients were enrolled for the present study. Among them, 220 were excluded from the study because they were either not interested in the study or had severe respiratory illness (**Figure 1**). Demographic, clinical, and laboratory data was collected for a total of 800 patients, who were included in

the study. Patients were majorly categorized into vaccinated (n=450) and unvaccinated (n=350) groups. Among the total patients, 412 were males, and 388 were females with median age 58). Gender distribution indicates that an equal proportion of vaccinated and unvaccinated individuals are male and females (Ratio 1:1). The age is reported as a median with an interquartile range (IQR), showing comparable ages between the vaccinated (60 [42, 74]) and unvaccinated (56 [44, 71]) groups. The study highlights higher prevalence of hypertension and diabetes in unvaccinated COVID-19 patients. Vaccinated individuals exhibit more frequent fever and cough, while dyspnea and sore throat are more common in the unvaccinated group. Elevated C-reactive protein levels, over 80% in both groups, are identified as a consistent COVID-19 marker. (Table 1). The data offer a comprehensive overview, revealing distinctions in demographics, comorbidities, and clinical traits between vaccinated and unvaccinated individuals, with no significant frequency differences.

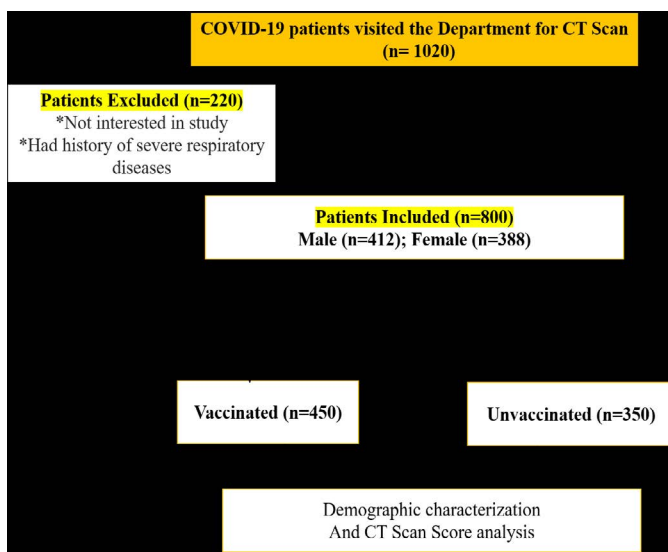


Figure 1: Flow chart of study methodology.

Table 1: Comparative analysis of demographic, clinical, and laboratory findings of vaccinated and unvaccinated population.

Variable	All patients (n = 800)	Vaccinated (n = 450)	Unvaccinated (n = 350)
Gender			
Male	412 (51.5%)	231 (51.3%)	181 (51.7%)
Female	388 (48.5%)	219 (48.7%)	169 (48.3%)
Age *	58 [40, 74]	60 [42, 74]	56 [44, 71]
Comorbidities			
No comorbidities	280 (35%)	149 (33.1%)	131 (37.4%)
Cardiovascular disease	95 (11.9%)	50 (11.1%)	45 (12.8%)
Diabetes	159 (19.5%)	70 (15.5%)	86 (24.5%)
Hypertension	180 (22.5%)	85 (18.9%)	95 (27.1%)
Cancer	10 (1.25%)	7 (1.5%)	3 (0.9%)
Others	79 (9.8%)	39 (8.7%)	40 (11.4%)
Symptoms			
Fever	612 (76.5%)	383 (85.1%)	229 (65.4%)
Cough	576 (72%)	365 (81.1%)	211 (60.3%)
Dyspnea	310 (38.8%)	151 (33.6%)	159 (45.4%)
Sore throat	710(88.75%)	3 8 0 (84.44%)	330 (94.28%)
Sensory loss	90 (11.25%)	50 (12.5%)	40 (10%)

Clinical and laboratory findings			
Leukopenia	102 (12.8%)	67 (14.9%)	35 (10%)
CRP level	696 (87%)	387 (86%)	309 (88.3%)
PaO2/FiO2 ratio	273 (34.1%)	152 (33.8%)	121 (34.6%)

*Data are expressed as median value [interquartile range (IQR)]

Table 2: Univariate analysis based on CTS score.

Variable	CTSS (Junior Radiologist)	CTSS (Senior Radiologist)
Vaccination status (all patients)		
Unvaccinated	9 [3, 21]	10 [2, 22]
Vaccinated	3 [0, 20]	3 [0, 20]
p	< 0.001	< 0.001
Vaccination status (only patients with CTSS > 0)		
Unvaccinated	13 [8, 19]	13 [9, 18]
Vaccinated	7 [4, 14]	8 [3, 14]
p	< 0.001	< 0.001
Gender		
Male	8 [0, 22]	8 [0, 23]
Female	5 [0, 22]	5 [0, 21]
p	< 0.001	< 0.001
Age		
41-58	7 [0, 19]	8 [1, 19]
59-75	10 [0, 23]	11 [0, 22]
P	< 0.001	< 0.001

Data are expressed as median value [interquartile range (IQR)].

Assessment of CT severity score (CTSS) according to Vaccination Status

There was good agreement between junior and senior radiologists in the interobserver variability analysis (ICC of 0.89) for the CTSS assessment. The median time interval between symptom onset and CT scan was 6 days^{4,7} for vaccinated and unvaccinated patients (p=0.312). (Tables 2) represent the specified findings as reported by both junior and senior radiologists. According to the senior radiologist, the CTSS results of all patients showed a significant difference between vaccinated and unvaccinated patients (p < 0.001), with a median value of 3 [0, 20] for vaccinated patients and 10 [2, 22] for unvaccinated patients. A similar statistical difference between the two groups was confirmed (p < 0.001) when patients without lung involvement (CTSS = 0) were excluded. The median CTSS was 8 and 13 for vaccinated and unvaccinated individuals (Table 2). Males showed a higher median value (8) compared with females (5). When parenchymal involvement was compared based on age, senior citizens were noted with significantly (p < 0.001) higher median CTS scores compared to adults (Table 2).

According to both radiologists, GGO was the most common pattern in both vaccinated and unvaccinated individuals, followed by crazy-paving and consolidation; among vaccinated patients, GGO and crazy-paving patterns were more common (p < 0.001). Regarding the existence of pleural effusion and swollen lymph nodes, there were no differences between individuals who had received vaccinations and those who had not.

Assessment of the Proportions of Chest CT Scores

Overall, of the 800 patients included in the study, 480 patients (60%) underwent chest CT during hospitalization; of these, 37% of unvaccinated patients and 45% of fully vaccinated patients had negative CT scans (CTS Score 0). The proportion of negative CT scans was higher in the fully vaccinated group than in the unvaccinated group (p < 0.005) (Figure 2). Approximately 25% of unvaccinated and vaccinated patients had a CT score of 1. Additionally, 13% of unvaccinated patients and 10% of vaccinated patients had a CT score of 2. The number of cases

was not significantly different for CT scores 3, 4, and 5 (Figure 2).

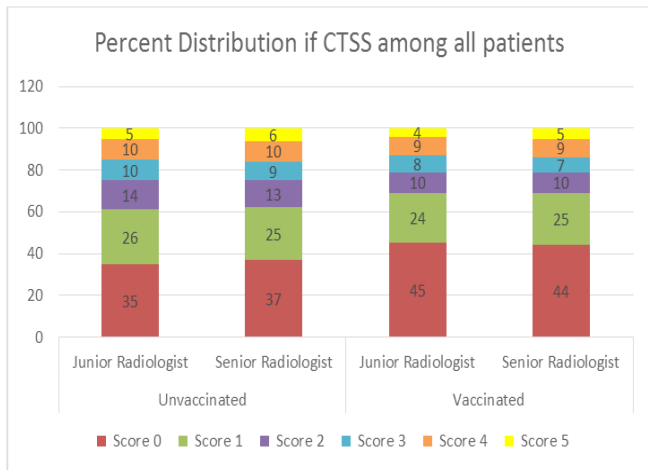


Figure 2: CT scan scores of all unvaccinated and vaccinated patients involved in the study.

Results of vaccinated and unvaccinated patients having CTSS more than zero were also in agreement between both radiologists. The severity of the disease was low in the case of vaccinated people. Significantly a greater number of cases were distributed for scores 1 and 2 for vaccinated patients. There was a significant difference in frequencies of patients with higher CTSS 3, 4, and 5. It was 15, 16, and 11 for unvaccinated and 12, 9, and 6 for vaccinated patients respectively (Figure 3).

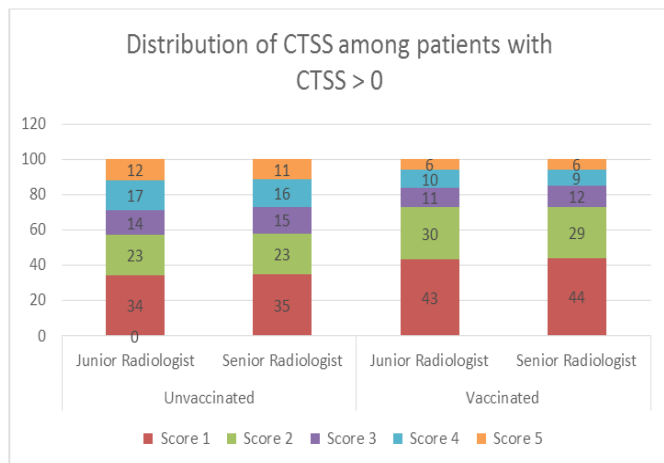


Figure 3: Distribution of unvaccinated and vaccinated patients having CT scan scores more than 1.

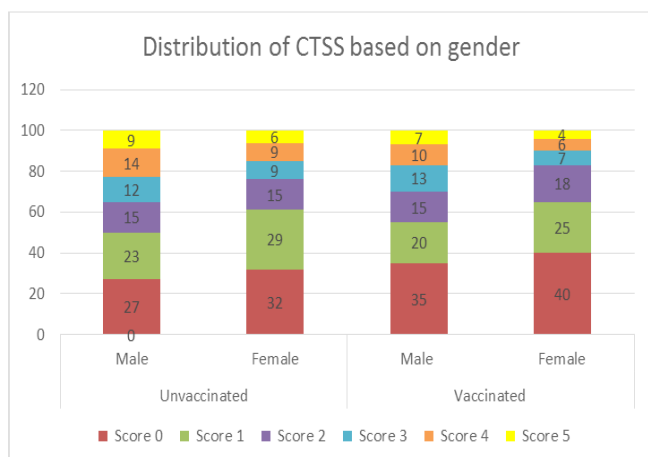


Figure 4: Distribution of CT scan scores of all unvaccinated and vaccinated patients based on gender.

We noted that vaccination was effective in controlling lung damage for both males and females. However, a greater number of females were unaffected (CTS score 0) than males in vaccinated and unvaccinated groups. The severity of COVID-19 (scores 4 and 5) in females was less in vaccinated group (6,4) compared to the unvaccinated group (9, 6 respectively). A similar trend was observed in males as well (Figure 4).

Comparing the age groups and vaccination statuses, it appears that there are variations in the distribution frequency of both group for CTS scores. However, in both age ranges, a higher number of vaccinated individuals have lower CTS scores compared to the unvaccinated group. This trend is also observable in the 59-75 age group. On comparing scores on each group, comparatively higher number of patients were distributed towards scores 1 and 2 for 41-58 years and 3,4 and 5 for 59-75 years (Figure 5).

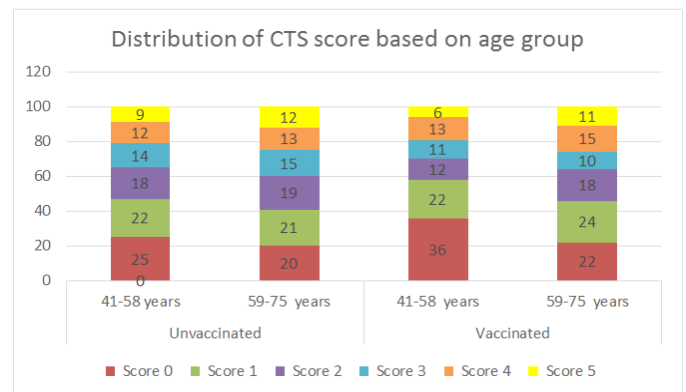


Figure 5: Distribution of CT scan scores of all unvaccinated and vaccinated patients based on age groups.

Discussion

The investigation focused on the comparison of CT scan scores among vaccinated and unvaccinated patients based on multiple factors such as age, sex, co-morbidity, and symptoms. The CT scan was scored from 0-5 based on the severity of lung involvement¹⁰. The findings of this study indicate that vaccination status had no significant correlation with the presence of co-morbidity, the severity of symptoms, and clinical outcomes in COVID-19 patients.

Interestingly, lower lung involvement was noted in younger people and females, irrespective of their vaccination status. This analysis supported the recent findings, demonstrating Chest CT features of COVID-19 patients¹¹, however¹² did not found any co relation among COVID-19 symptoms with age, sex. This could be due to the inherent immune responses across different age groups and genders¹². According to¹³ men are more susceptible than women because they produce more testosterone (TLT). Women’s immune systems are stronger and can fend off severe SARS-CoV-2 viral disease because they express more of the TLR7 gene, which is located on the X chromosome and encodes Toll-like proteins. This means that women’s dendritic cells can produce more interferons and antiviral proteins¹³. However, a deeper exploration into the underlying causes of this observation is needed to develop a comprehensive understanding of the disease progression in different demographic groups.

The study observed a potential link between vaccination and lower CT scores, indicating potentially milder lung involvement in COVID-19-infected vaccinated individuals, aligning with prior imaging studies^{10,11,14,15}.

It underscores the importance of vaccination in adults for potentially reducing the severity of the disease. Although further studies are required to establish a definitive correlation, these findings provide preliminary evidence supporting the role of vaccination in disease management.

The lack of association between vaccination status and the presence of co-morbidity, severity of symptoms, and clinical outcomes might seem intriguing. It could be inferred that vaccination may not directly influence these factors, but have a role in controlling the extent of lung damage, as indicated by lower CT scan scores. However, many studies noted a significant correlation of Co-morbidities and clinical outcomes with CT severity score^{16,17}.

Conclusions

Vaccination status had no association with the presence of co-morbidity, the severity of symptoms, and clinical outcomes of COVID-19 patients. Lesser lung involvement was noted for younger people and females irrespective of vaccination status. A potential association between vaccination and lower CT scan scores was noted, which highlights the importance of vaccination in adults. These findings could be instrumental in shaping future research and strategies for COVID-19 treatment and prevention.

Acknowledgements: none

Conflicts of Interest: nil

Funding: None

References

- Ciotti M, Ciccozzi M, Terrinoni A, Jiang WC, Wang CB, Bernardini S. The COVID-19 pandemic. *Crit Rev Clin Lab Sci* 2020;57(6):365-388.
- Ciotti M, Ciccozzi M, Pieri M, Bernardini S. The COVID-19 pandemic: viral variants and vaccine efficacy. *Crit Rev Clin Lab Sci* 2022;59(1):66-75.
- Le TT, Cramer JP, Chen R, Mayhew S. Evolution of the COVID-19 vaccine development landscape. *Nat Rev Drug Discov* 2020;19(10):667-668.
- Bok K, Sitar S, Graham BS, Mascola JR. Accelerated COVID-19 vaccine development: milestones, lessons, and prospects. *Immunity* 2021;54(8):1636-1651.
- Lang R, Humes E, Coburn SB, et al. Analysis of severe illness after postvaccination COVID-19 breakthrough among adults with and without HIV in the US. *JAMA Netw Open* 2022;5(10):2236397.
- Butt AA, Yan P, Shaikh OS, Mayr FB, Omer SB. Rate and risk factors for severe/critical disease among fully vaccinated persons with breakthrough severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in a high-risk national population. *Clin Infect Dis* 2022;75(1):849-56.
- Tan RY, Wong B, Lim R, Lee CL, Tan J, Tan KB, Wee LE. Factors associated with delayed diagnosis of symptomatic adult COVID-19 cases presenting to primary care: A population-wide study during transition from Delta to Omicron BA. 1 in Singapore. *Lancet Reg Health-West Pac* 2023;41.
- Cromb  A, Bensid L, Seux M, et al. Impact of Vaccination and the Omicron Variant on COVID-19-related Chest CT Findings: A Multicenter Study. *Radiology* 2023;307(3):222730.
- Lee JE, Hwang M, Kim YH, et al. Imaging and clinical features of COVID-19 breakthrough infections: A multicenter study. *Radiology*. 2022;303(3):682-692.
- Lee JE, Hwang M, Kim Y-H, et al. Imaging and clinical features of COVID-19 breakthrough infections: A multicenter study. *Radiology* 2022;303:682-692.
- Masci GM, Izzo A, Bonito G, et al. Chest CT features of COVID-19 in vaccinated versus unvaccinated patients: use of CT severity score and outcome analysis. *La radiologia medica* 2023;128(8):934-943.
- Statsenko Y, Al Zahmi F, Habuza T, et al . Impact of age and sex on COVID-19 severity assessed from radiologic and clinical findings. *Front Cell Infect Microbiol* 2022;11:1395.
- Zovi A, Ferrara F, Langella R, Cavallaro F, Vitiello A. Sex affects immune response capacity against COVID-19 infection. *Rev Med Virol* 2023;33(4):2450.
- Verma A, Kumar I, Singh PK, A et al. Initial comparative analysis of pulmonary involvement on HRCT between vaccinated and non-vaccinated subjects of COVID-19. *Eur Radiol* 2022;32(6):4275-4283.
- Vishwanath T, Rajalakshmi BR, Sadananda KS, Manjunath CN. Association of Chest CT Severity Scores and Vaccination Status in COVID-19 Disease: A Cross-sectional Study. *J Clin Diagn Res* 2022;16(2).
- Carbonaro L, Braga F, Gemma P, et al. Chest computed tomography of suspected COVID-19 pneumonia in the Emergency Department: comparative analysis between patients with different vaccination status. *Pol J Radiol* 2023;88(1):80-88.
- Sharma R, Thakker V, Sharma RB, Arora M, Sarda P, Ahuja M, Randhawa LS, Azad RK. Effect of vaccination on the HRCT profile of COVID-19 patients-A single-center experience. *J Fam Med Prim Care* 2022;11(6):2938.