Prevalence and severity of Computed Tomography assessed pneumonia among fully vaccinated and unvaccinated adult Filipino in-patients with COVID-19 infection: A retrospective study

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ABSTRACT

Background: The study will help give a more objective look at the effects of vaccines versus COVID-19 by comparing imaging findings of unvaccinated versus vaccinated patients. It may demonstrate the use of CT imaging in the screening for COVID-19 pneumonia in the different sub-groups of patients, as well as to help determine severity patterns of pneumonia in vaccinated and unvaccinated patients which may guide future assessment of the disease.

Methodology: A retrospective study on COVID-19 positive adult in-patients from a tertiary hospital who underwent chest CT from 2020 to 2021 was conducted. Multiple variables were collected (demographics, vaccination status, etc). Continuous data was presented using means and standard deviations, while categorical variables were presented using frequencies and percentages. For categorical variables, statistical differences between groups were determined using Pearson's chi-square test or Fisher's exact test; and for continuous variables, student's t test and analysis of variance.

Results: All 174 subjects were included in this study (68 females and 106 males) have pneumonia (77 mild, 75 moderate, and 22 severe). 113 were fully vaccinated, 4 were partially vaccinated, and 57 were unvaccinated. Based on the study, vaccinated group had mean scores of 8.637, while the other group had a mean score of 11.934. The difference was statistically significant, which implies that the vaccinated group had lower pneumonia severity scores.

Conclusion: 100% of the patients reviewed had pneumonia and patients with complete vaccination status had less severe cases of pneumonia on Chest CT.

Introduction

Since its discovery in late 2019, COVID-19 has continuously affected the entire world and has caused a variety of symptoms ranging from non-specific symptoms such as fever to more severe symptoms such as pneumonia, and in some cases even death. Imaging modalities such as the plain radiograph and Computed Tomography have been used to supplement the management of the disease, especially in symptomatic cases, and have shown to exhibit different imaging characteristics ranging from ground glass densities to presence of pulmonary nodules [1]. However, with the advent of vaccines, less people have developed severe disease. The vaccines have been shown to decrease hospitalizations and even death in fully vaccinated individuals, even those with co-morbidities [2].

COVID-19 symptoms vary and range from mild to severe and commonly include fever, cough, and shortness of breath. On CT imaging, the most common findings of COVID-19 pneumonia include multilobar as well as peripheral airspace opacities. Predominantly, ground glass opacities are the most common type seen in this type of pneumonia. These types of opacities are most demonstrated on CT scan and thus considered more sensitive than plain radiographs [3]. Aside from this, a predominance of infiltrates in the lung peripherals are observed, which has been shown to be a hallmark finding of the disease. There has also been a lack of pulmonary nodules, cavitation, and pleural effusion in COVID-19 pneumonia [1].

Non-contrast high resolution CT scan imaging has become useful in the assessment of COVID-19 in patients, particularly in individuals in early stages of the disease that receive false negative RT-PCR results. CT scan has also been used to determine the severity of COVID-19 pneumonia by using a scoring system based on visual assessment of the number of pneumonic infiltrates seen in both lungs [5]. Each lung lobe is scored individually, from 1 to 5, depending on percentage of involvement. An individual lobar score of 1 indicates an involvement of less than 5%; a score of 2 indicating 5-25% involvement; a score of 3 indicating 26-49% involvement; a score of 4 indicating an involvement of 50-75%; and finally, a score of 5 indicating a lobar involvement of greater than 75%. These scores are then summed and

may range from 0 (meaning no pneumonia) to 25 [4]. A total score of 7 or less is categorized mild, 8-17 as moderate, and 18 or more as severe. Studies have shown that these CT categorizations have significant correlations with the clinical outcome of the patients, noting increased survival rate with mild categorization and increased morbidity or mortality with the severe group [5].

As vaccines have rolled out, there has been a notable decrease in transmission and symptoms of patients afflicted with the disease. Studies have shown that vaccinated individuals have shown decreased transmission regarding the alpha, beta, and delta variants. These have been shown to decrease the viral load of COVID-19 [6]. Though vaccines may offer partial protection against the virus, breakthrough infections still occur in many individuals, especially with the advent of newer variants of the disease. In a study by Hossain, *et al.*, most vaccinated patients with breakthrough infections were shown to have mild respiratory symptoms that resolved after admission. CT findings in most of these patients initially showed the typical peripherally-located ground glass opacities and were all said to have had improvement upon follow-up CT after treatment. However, some fully vaccinated patients were noted to have required ICU admission and demonstrated CT imaging of chronic lung disease upon follow-up, denoting pulmonary sequelae [7].

In another study that evaluates the clinical and imaging characteristics of COVID-19 breakthrough infections and compare them with those of unvaccinated COVID-19 patients, it was found out that fully vaccinated status was associated with a lower risk of requiring supplemental oxygen than

unvaccinated patients, as well as lower risk of intensive care unit (ICU) admission. Furthermore, patients with COVID-19 breakthrough infections had a significantly higher proportion of CT scans without pneumonia compared to unvaccinated patients. Vaccinated patients with breakthrough infections had lower likelihood of requiring supplemental oxygen or ICU admission [9].

In the study by Verma, Ashish, *et al.*, the researcher compared the high-resolution computed tomography (HRCT)–derived severity score in COVID-19 patients between those who had earlier received the vaccine against the SARS-CoV-2 and those who did not. The research retrospectively analyzed the HRCT of the chest and correlate with the vaccination status of clinically diagnosed COVID-19 patients. They looked at the variables such as evaluation of the CT severity score, whereby differential analysis of the variability on this parameter between incompletely (single dose) vaccinated, completely (both doses) vaccinated, and non-vaccinated individuals was the outcome. The results showed that the mean CT score was significantly lower in completely vaccinated patients of lower ages (≤ 60 years) compared to patients above that age. The incidence of severe disease (CT score ≥ 20) was significantly higher in the incompletely vaccinated and non-vaccinated patients compared to that in the completely vaccinated group [10].

As shown in the available literature, there is still much to discover about the imaging characteristics of the COVID-19 infection especially in the local setting where vaccination roll-outs have only just begun to finish. The study aims to show the efficacy of vaccination in regards to the presence and severity of computed tomography assessed pneumonia in the local setting.

Methodology

This is a cross-sectional retrospective study associating computed tomography findings of COVID-19 pneumonia as well as its severity with vaccination status, presence of different comorbidities, as well as demographics. Included in this study are COVID-19 confirmed patients aged over 18 years old who underwent chest CT scan at Cardinal Santos Medical Center between January 21, 2020 to December 31, 2021. Patients below the age of 18 due to lack of CT scan results in the pediatric population in the target institution and patients with incomplete records (i.e. those with no declaration of vaccination status, no co-morbid information). Sample size was calculated using OpenEpi tool for cross-sectional. Percent of unexposed with outcome (vaccinated with severe pneumonia) and percent of exposed with outcome (unvaccinated with severe pneumonia) were calculated based on the study by Modi, *et al.*, showed results of 3% and 16.8% respectively [11]. With a 95% confidence level and 5% margin of error, the computed sample size via Fleiss with CC equation shows a sample size of 174.

After ethical approval, a retrospective review of records was done from the medical records among COVID-19 positive in-patients with Chest CT scans from January 2021 to December 2021. Each medical record was then reviewed and subjected to the inclusion and exclusion criteria. Using a standard data collection form, the following variables were collected from routinely available data in the patients' medical records: demographic characteristics (age and gender), co-morbidities, vaccination status, presence or absence of pneumonia, and severity of pneumonia.

Once vaccinated and non-vaccinated individuals were determined by reviewing the in-patient records, CT scans and results of each group were then examined. Frequency of individuals (vaccinated and unvaccinated) with pneumonia were taken note of. In patients with presence of pneumonia, severity scoring was taken note of by the primary investigator by examining the official reports. Depending on the score, each individual was segregated into mild (score of 7 or less), moderate (score of 8 to 17), and severe (18 and greater).

Data analysis was mainly quantitative. Frequencies, percentages, and cross tabulations were used to describe the prevalence of pneumonia. Severity of pneumonia in the vaccinated and unvaccinated patients were also noted. Appropriate statistical treatment for variables of interest were applied to determine if with any significant difference between groups. Continuous data were presented using means and standard deviations, while categorical variables were presented using frequencies and percentages. For categorical variables (sex), statistical differences between groups were determined using Pearson's chi-square test or Fisher's exact test, and for continuous variables, student's t test and analysis of variance (ANOVA), as applicable.

Figure 1. Flowchart of Procedure

Definition of terms:

1. COVID-19 positive - Patient who are positive either RT PCR or Antigen IgM positive12

2. Breakthrough Infection - A person that is fully vaccinated- 2 doses for most available vaccine or 1 dose for Jannsen.

3. Pneumonia – infection within the lung

4. Computed Tomography (CT scan) – Radiographic imaging that uses a computer to assimilate multiple x-ray images into a 2-dimensional cross-sectional image

5. COVID 19 Severity score – Scoring system based on the visual assessment of the number of pneumonic infiltrates seen in both lungs. Each lung lobe is scored individually, from 1 to 5, depending on percentage of involvement. An individual lobar score of 1 indicates an involvement of less than 5%; a score of 2 indicating 5-25% involvement; a score of 3 indicating 26-49% involvement; a score of 4 indicating an involvement of 50-75%; and finally, a score of 5 indicating a lobar involvement of greater than 75%.

6. Vaccinated individual – Based on WHO guidelines, individuals at least 2 weeks from receiving 2 doses of a COVID-19 vaccine, (1 dose for those given Johnson & Johnson vaccine).

7. Unvaccinated individual – Individuals without or with incomplete vaccination.

Results and Discussion

There was a total of 174 COVID-19 positive in-patients from January 21, 2020 until December 31, 2021 who underwent chest CT scan were included in this study.

Table 1 summarizes the demographic profiles of the patients in the final sample. Among the 174 patients, 68 (39.08%) are females and 106 (60.92%) are males. The mean age of the patients is 63.87, with a standard deviation of 18.36 and median of 66.50.

Table 2 summarizes the clinical profiles of the patients. Among the 174 patients, 113 (64.94%) are fully vaccinated, 4 (2.30%) are partially vaccinated, and 57 (32.76%) are unvaccinated. The most common symptoms are cough (47.13%), fever (44.25%), and difficulty of breathing (27.01%). 11 (6.32%) patients are asymptomatic. As for co-morbidities, the most common are hypertension (35.06%), diabetes mellitus (32.76%), and dyslipidemia (21.84%). 58 (33.33%) patients do not have any co-morbidities.

Table 3 presents the sex and age distribution of the COVID-positive patients. Among the 113 fully vaccinated patients, 43 (38.05%) are female

Table 1. Demographic profiles of the patients

Profiles[1]	Frequency (n = 174)	Percentage
Age		
18 to 25 years old	3	1.72%
26 to 33 years old	9	5.17%
34 to 41 years old	18	10.34%
42 to 49 years old	10	5.75%
50 years old and above	134	77.01%
Mean (± Standard Deviation)		63.87 (± 18.36) years old
Median		66.50 years old
Interquartile Range		52.25 – 77.50 years old
Sex		
Female	68	39.08%
Male	106	60.92%

[1]Frequencies and percentages are presented for categorical variables, while the mean, standard deviation, median, and interquartile range are presented for continuous variables.

Table 2. Clinical profiles of the patients

Profiles[1]	Frequency (n = 174)	Percentage
Vaccination Status		
Fully vaccinated	113	64.94%
Partially vaccinated	4	2.30%
Unvaccinated	57	32.76%
Symptoms		
Anosmia	4	2.30%
Body Malaise	9	5.17%
Chest Pain	1	0.57%
Colds	14	8.05%
Cough	82	47.13%
Desaturation	23	13.22%
Diarrhea	10	5.75%
Difficulty of breathing	47	27.01%
Dyspnea	3	1.72%
Fever	77	44.25%
Headache	5	2.87%
Loss of appetite	1	0.57%
Palpitations	1	0.57%
Sore throat	4	2.30%
Vomiting	3	1.72%
Asymptomatic	11	6.32%
Co-morbidities		
Coronary artery disease	9	5.17%
Chronic kidney disease	6	3.45%
Cardiovascular disease	4	2.30%
Diabetes mellitus	57	32.76%
Dyslipidemia	38	21.84%
End-stage renal disease	4	2.30%
Heart failure	1	0.57%
Hypertension	61	35.06%
Ischemic heart disease	2	1.15%
Liver cirrhosis	1	0.57%
None	58	33.33%
Presence of Pneumonia		
Yes	174	100.00%
Severity Score		
Severe	22	12.64%
Moderate	75	43.10%
Mild	77	44.25%
Mean (± Standard Deviation)		9.79 (± 6.38)
Median		9.00
Interquartile Range		4.00 – 14.00

[1]Frequencies and percentages are presented for categorical variables, while the mean, standard deviation, median, and interquartile range are presented for continuous variables.

Table 3. Sex and age distribution of COVID positive patients

Profiles	Fully Vaccinated (n = 113)		Partially Vaccinated and Unvaccinated (n = 61)		p-values[1,2]
	n	%	n	%	
Sex					
Females	43	38.05%	25	40.98%	0.705
Males	70	61.95%	36	59.02%	
Age					
18-25	3	2.65%	–	–	0.682
26-33	6	5.31%	3	4.92%	
34-41	13	11.50%	5	8.20%	
42-49	6	5.31%	4	6.56%	
50 and above	85	75.22%	49	80.33%	

[1]The Pearson chi-squared test of independence is used to determine whether there is an association between the indicated profiles and vaccination status of the patients.
[2]A p-value threshold of 0.05 is used to determine whether to accept or reject the null hypothesis. If the generated p-value is less than 0.05, the null hypothesis is rejected. P-values that are less than the threshold are presented in bold.

Table 4. Distribution of severity of pneumonia among vaccinated and unvaccinated patients

Severity of Pneumonia	Fully Vaccinated (n = 113)		Partially Vaccinated and Unvaccinated (n = 61)		p-values[1,2]
	n	%	n	%	
Mild	57	50.44%	20	32.79%	**0.032**
Moderate	46	40.71%	29	47.54%	
Severe	10	8.85%	12	19.67%	

[1]The Pearson chi-squared test of independence is used to determine whether there is an association between the severity of pneumonia and vaccination status of the patients.
[2]A p-value threshold of 0.05 is used to determine whether to accept or reject the null hypothesis. If the generated p-value is less than 0.05, the null hypothesis is rejected. P-values that are less than the threshold are presented in bold.

Table 5. Differences in pneumonia severity scores of vaccinated and unvaccinated patients

Groups	Mean Scores (± SD)	Standard Error	Difference (95% CI)	p-values[1,2]
Vaccinated	8.637 (± 5.951)	0.849	3.297	**0.001**
Partially Vaccinated and Unvaccinated	11.934 (± 6.633)	0.560	[1.354, 5.241]	

[1]The Student's t test is used to determine whether the differences in the means are statistically significant.
[2]A p-value threshold of 0.05 is used to determine whether to accept or reject the null hypothesis. If the generated p-value is less than 0.05, the null hypothesis is rejected. P-values that are less than the threshold are presented in bold.

and 70 (61.95%) are male. 85 (75.22%) of the fully vaccinated patients are 50 years old and above. For the 61 partially vaccinated and unvaccinated patients, 25 (40.98%) are female and 36 (59.02%) are male. 49 (80.33%) of the partially vaccinated and unvaccinated patients are 50 years old and above.

All patients in the final sample have pneumonia, with 77 (44.25%) categorized as mild, 75 (43.10%) as moderate, and 22 (12.64%) as severe. Table 4 presents the distribution of severity of pneumonia among vaccinated and unvaccinated patients. Among the fully vaccinated patients, 57 (50.44%) have mild pneumonia, 46 (40.71%) have moderate pneumonia, and 10 (8.85%) have severe pneumonia. On the other hand, 20 (32.79%) of the partially vaccinated and unvaccinated patients have mild pneumonia, 29 (47.54%) have moderate pneumonia, and 12 (19.67%) have severe pneumonia.

The result of the Pearson chi-squared test of independence shows that the differences in the distribution of severity of pneumonia are statistically significant.

Previous studies have also shown that vaccinated individuals have been shows to have lesser incidence of pneumonia on CT scan, however, the study fails to duplicate this showing all participants to have CT imaged pneumonia.9 Studies have also shown that individuals who have had complete vaccination had decreased incidence of severe disease compared to individuals with incomplete or no vaccination [10]. A study by Lakhia and Trivedi focused on the CT severity scores of completely vaccinated, partially vaccinated, and unvaccinated individuals with COVID-19 infections. Their study showed that there was a significant difference between the three groups, demonstrating lower severity scores in those with complete vaccinations compared to those that were partially vaccinated and unvaccinated [8]. These findings are consistent with the results of the study.

Table 5 presents the results of the student's t test, which allows us to verify which group had lower severity scores. Based on the table, we find that the vaccinated group had mean scores of 8.637, while the partially vaccinated and unvaccinated group had mean scores of 11.934. The difference of 3.297 is statistically significant (p = 0.001), which implies that the vaccinated group had lower pneumonia severity scores.

Based on the studies, vaccinated patients have been shown to have lower severity scores as compared to those unvaccinated individuals, which is consistent with the results [10].

In a study by Modi, *et al.*, it was shown that there is a significant difference, in regards to the presence and severity of pneumonia, in vaccinated patients versus unvaccinated patients. It was shown by the study that patients with vaccinations had lower CT severity scores compared to those who are unvaccinated. Better overall outcome was seen in vaccinated patients compared to unvaccinated patients [11].

Limitations

A major limitation of this study was that all data used was based on in-patients only, which may have caused a bias on the absence or presence of pneumonia on the sample population. Another limitation of the study includes the lack of differentiation between vaccine types, which may have had an effect on the severity of the pneumonia.

The assessment of the severity of pneumonia of each patient may also be a limitation since the CT-scan studies were reviewed by differing radiologists which may have their own subjective biases.

Conclusions

Among the 174 COVID-19 positive in patients reviewed, 100% were seen to have pneumonia.

Based on this study, patients with complete vaccination status compared to those who were unvaccinated or partially vaccinated had overall less severe cases of pneumonia on Chest CT scans.

Recommendation

For future studies, a larger population is recommended, which may include outpatients which may diversify the results. The variable of vaccine type can also be explored since these may also affect the presence or absence of pneumonia as well as its severity. A total review of the imaging studies by one or two licensed radiologists can also be done in future studies to limit the subjective biases as well as make the severity grading more consistent.

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