

Association Between Vaccination Status and the Incidence of Breakthrough COVID-19 Infections Among University of Santo Tomas – Faculty of Medicine and Surgery Students: a Case-Control Study



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ABSTRACT

Introduction: With the introduction of COVID-19 vaccines, schools around the world have slowly started to reimplement on-site classes with guidelines to prevent outbreaks. The University of Santo Tomas has devised their own set of guidelines, including safety protocols, vaccinations and daily health declarations. These were monitored using the Thomasian Online Medical Services and Support (ThOMedSS).

Methodology: Through a case-control study design, the study aims to determine an association between the vaccination status of UST Faculty of Medicine and Surgery (UST-FMS) students and breakthrough COVID-19 infections in the first semester of the academic year 2022-2023, with population data acquired via records of students

participating in face-to-face classes from the UST Health Service Office, and categorized based on breakthrough infections and vaccination status.

Statistical Analysis: Results were analyzed using Pearson's chi-square test and Fisher's exact test ($p < 0.05$). Odds ratio was used to measure the effect of vaccination status on the incidence of breakthrough infections.

Conclusion: The study suggests that vaccination status did not have a statistically significant association ($p = 0.3451$) with breakthrough infections. The majority (99.94%) of students have received the complete primary COVID-19 vaccination series and only 6.61% of this population developed breakthrough COVID-19 infections, all occurring in those completely vaccinated. Breakthrough infections were 1.76 times more likely for those with booster shots than those without. The possible reason for this is the emergence of the Omicron variant. To improve the study, external exposures and individual behaviors must be considered as potential factors influencing infection rates.

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INTRODUCTION

Unbeknownst to Filipino students nationwide, the COVID-19 pandemic would put them out of campus beyond two weeks of class suspension. Two years later, vaccines against the virus were rolled out, and preventative protocols implemented to support and expedite the transition from online work and education settings to on-site. Aligned with this goal, the University of Santo Tomas (UST) has formulated its own COVID-19 guidelines to protect its students as they return to campus, entailing conditions such as requiring students and staff to be fully vaccinated, follow safety protocols and accomplish health declaration forms everyday.[1]

The university has made the monitoring of COVID-19 cases and vaccination status easier and more convenient through its platform, Thomasian Online Medical Services and Support (ThOMedSS). This provides a centralized database containing the health status of the Thomasian community to ensure safety during face-to-face classes. The university also seamlessly integrated its COVID-19 policies into ThOMedSS, making them more accessible to the community. Fortunately, this also provides researchers with extensive data to assess the university's guidelines for preventing COVID-19 outbreaks in its implementation of face-to-face classes.

The findings of this study will benefit not just the University of Santo Tomas but schools across the Philippines regarding the regulations and containment of COVID-19, along with the recent reintroduction of onsite face-to-face classes. With the reintroduction of onsite face-to-face classes, schools nationwide have experimented with different avenues to ensure a safe environment for their students to attend onsite classes and prevent outbreaks. Thus, schools that refer to the approach applied by results of this study will be able to make educated decisions on what kind of approach they should implement for their school. The researchers will be able to observe if the safety protocols, especially vaccination guidelines implemented by the University of Santo Tomas, have effectively contained and prevented COVID-19 within the school campus.

The general objective of this study was to determine an association between vaccination status of UST-FMS students and breakthrough COVID-19 infections in the first semester of the academic year

2022-2023. Meanwhile, the specific objectives of this research are to determine the proportion of UST-FMS medical students that have and have not received the complete primary series of COVID-19 vaccinations, which is composed of two full doses for two-dose series vaccines or one full dose for single-dose vaccines, as recommended in the national schedule for vaccines set by the Department of Health; determine the number of breakthrough COVID-19 infections among UST-FMS students for those fully vaccinated, incompletely vaccinated and unvaccinated; determine whether an association exists between the vaccination status of UST-FMS students and incidence of breakthrough COVID-19 infections; and measure the effect of vaccination status on breakthrough COVID-19 infections. The null hypothesis is that the vaccination status of UST-FMS students does not have an association with the of breakthrough COVID-19 infections.

METHODOLOGY

With the aim of our study to investigate the association between vaccination status of UST-FMS students and incidence of breakthrough COVID-19 infections in the first semester of the academic year 2022-2023, a case-control study was deemed the most appropriate study design. In this study design as seen in Figure 1, students currently studying in UST-FMS had their data filtered using the set inclusion and exclusion criteria. From there, a categorization was made based on whether they were infected by COVID-19 as indicated by a reported positive RT-qPCR test result or not. Finally, their vaccination status, whether complete, incomplete, or unvaccinated was determined. This helped determine an association between vaccination status of these students and breakthrough infections.

The study setting is in the UST-FMS San Martin de Porres. The data obtained covered the period from the first day of face-to-face classes (9 August 2022) until the last day of face-to-face classes of the first semester of the academic year 2022-2023 (17 December 2022). Students of UST FMS participating in face-to-face classes were included. We excluded those whose data were recorded in the ThOMedSS database.

The exposure was the vaccination status of the UST-FMS students – whether they were complete,

Study Design

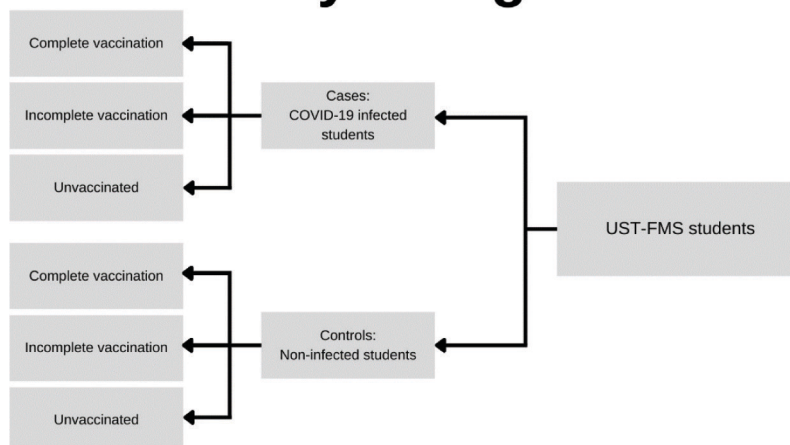


Figure 1: Study Design Diagram

incomplete, or unvaccinated. Vaccination status indicates the administration or lack thereof of the COVID-19 primary series vaccination regimen. Complete vaccination status consists of either two (2) full doses for two-dose series vaccines or one (1) full dose for single-dose vaccines, both of which may include one (1) or more doses of booster shots. Incomplete vaccination status indicates that the national schedule for vaccines set by the DOH was not followed, consisting of either one (1) full dose for two-dose series vaccines throughout the study or completion of the COVID-19 primary series vaccination regimen within the study period of 9 August 2022 to 17 December 2022. Unvaccinated status indicates no administration of any COVID-19 primary series vaccination regimen doses at all within the study period of 9 August 2022 to 17 December 2022. On the other hand, the outcomes obtained were: (1) the number of UST-FMS students completely vaccinated with the recommended primary series of COVID-19 vaccination with or without booster doses; (2) the number of UST-FMS students with incomplete vaccination of the recommended primary series of COVID-19 vaccination; (3) the number of unvaccinated UST-FMS students; (4) the total and categorized number of breakthrough COVID-19 infections among UST-FMS students. Breakthrough infection is defined as an infection with the coronavirus that causes COVID-19 despite vaccination with either primary series or a primary series with booster dose(s). Furthermore, confounding variables influenced outcomes such as the safety protocols implemented by the university,

possible external exposures of the students when they were outside the university’s premises, integrity in declaring confirmed infection among students, and lastly, local changes in the COVID-19 situation.

Data was acquired from the database of Health Declaration Checklists filled out in the COVID-19 Case Tracker tab on the ThOMedSS site by the UST-FMS students before entering the university premises for face-to-face classes. The Data Acquisition Personnel requested access to the pertinent ThOMedSS records of all students enrolled in the UST-FMS who were participating in face-to-face classes from the UST Health Service Office as approved by the Data Privacy Officer of UST. Upon receiving the records, they were turned over to the Data Storage Officer who properly handled these documents as well as concealed any type of information that may potentially reveal the true identity of participants, particularly their complete names, email addresses and student numbers. The anonymization technique employed to conceal these direct identifiers was attribute suppression using ARX 3.9.1, which was last updated on 27 November 2022. Once completely anonymized, the data became available for statistical analysis. From there, the students were categorized based on whether they were infected by COVID-19 or not. Afterwards, the students’ vaccination status, whether complete, incomplete, or unvaccinated, was determined. With the data being classified, this was tabularized accordingly with a tally of their total number for each category. Additionally, for those students with incomplete vaccination status, the vaccination date

occurring within the study period was acquired, as well as infection dates for all vaccination groups so that results could be better correlated.

Purposive sampling was applied to include data from all the UST-FMS students who attended face-to-face classes. There were 1649 students eligible for the study.

The statistical test applied were Pearson’s chi-square test and Fisher’s exact test, as both independent and dependent variables are dichotomous – complete or incomplete vaccination and unvaccinated, and COVID-19 infected and non-infected students. Using a p-value of 0.05, the statistical significance of an association found between incidences of breakthrough COVID-19 infections among completely vaccinated, incompletely vaccinated, and unvaccinated, was determined.

Since the study entails collection of sensitive data from ThOMedSS, appropriate process on protecting anonymity and data privacy was observed in the course of the study. Furthermore, the study protocol underwent review by the UST-FMS Research Ethics Board and was granted an exemption from review (REB code 2022-029-ABUNDANCIA-COVID19).

RESULTS

From 9 August 2022 to 17 December 2022, spanning the first semester of face-to-face classes of the academic year 2022-2023, 1652 UST-FMS students were vaccinated with COVID-19 vaccines, according to data recorded in the ThOMedSS database. As illustrated in Figure 2, 1540 students had no breakthrough COVID-19 infection recorded in the ThOMedSS database. Of the 112 students who had breakthrough COVID-19 infection recorded, three were excluded from the study due to missing

evidence of their COVID-19 vaccinations in the ThOMedSS database despite claiming so. Out of the 1652 students, 6.78% (112) have reported that they were infected with COVID-19. However, three of the students were excluded from this study as they had missing data in their report, such as claiming to have a COVID-19 booster with no proof of data. Hence, the final total number of participants in that category was 109, 6.60% of the total number of students (6.61% if no eligible students were removed).

Table 1 shows the demographic distribution of students and colleges of the Faculty of Medicine and Surgery and their vaccination status. There are a total of 1652 students in the year 2022 wherein 4.48% (74) are from the program “Bachelor of Science in Basic Human Studies”, 94.01% (1553) are from the program “Doctor of Medicine”, 1.33% (22) are from the program “Master in Clinical Audiology”, and 0.18% (3) are from the program “Master of Medicine in Pain Management”. Overall, the Faculty of Medicine and Surgery had 99.94% (1651) students who were fully vaccinated and 61.92% (1023) had at least one booster taken in the year 2022.

There were a total of 1649 participants from the students of the Faculty of Medicine and Surgery. There were originally 1652 participants; however, three of the students were excluded from this study as they had missing data in their report, such as claiming to have a COVID-19 booster but no proof of vaccination. As seen in Table 2, 99.94% (1648) were fully vaccinated, and 61.89% (1020) had boosters in 2022. Out of the 1649 students, 6.61% (109) reported having acquired COVID-19 as seen in Table 3. Out of the 109 students, 100% (109) were fully vaccinated, 73.40% (80) had at least one booster shot and 26.60% (29) had no booster shots.

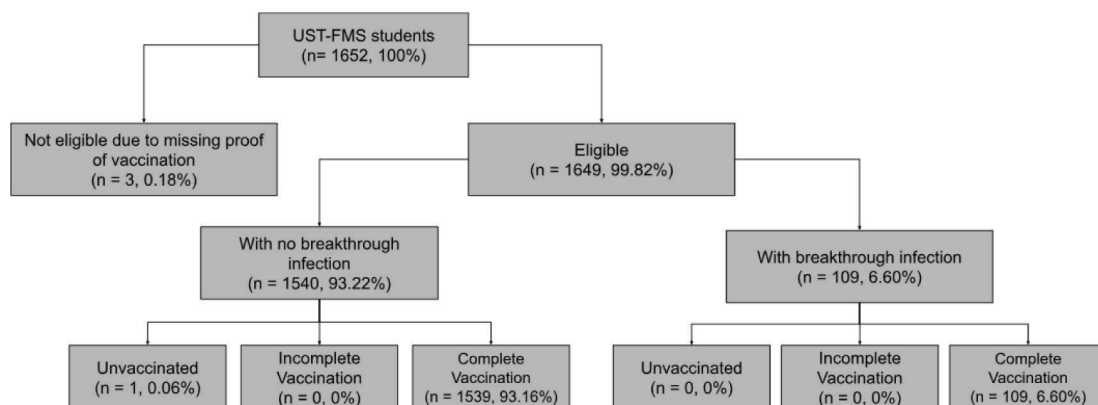


Figure 2: Selection of study sample

Table 1: Students and Colleges of Faculty of Medicine and Surgery and Vaccination status.

Year Level	No. of Students	Fully Vaccinated	Booster
Bachelor of Science in Basic Human Studies			
1	74	74 (100%)	39 (52.7%)
Total for Program	74 (4.48%)	74 (100%)	39 (52.7%)
Doctor of Medicine			
1	423	423 (100%)	261 (61.7%)
2	455	455 (100%)	277 (60.88%)
3	378	378 (100%)	249 (65.87%)
4	297	297 (100%)	177 (59.6%)
Total for Program	1553 (94.01%)	1553 (100%)	964 (62.07%)
Master in Clinical Audiology			
1	17	16 (94.12%)	15 (88.24%)
2	2	2 (100%)	2 (100%)
3	1	1 (100%)	0 (0%)
4	2	2 (100%)	1 (50%)
Total for Program	22 (1.33%)	21 (95.45%)	18 (81.82%)
Master of Medicine in Pain Management			
1	3	3 (100%)	2 (66.57%)
Total for Program	3 (0.18%)	3 (100%)	2 (66.57%)
Total for College	1652	1651 (99.94%)	1023 (61.92%)

Table 2: Vaccination status and booster status of UST-FMS students

	Number of Students	Percentage of Students
Complete Vaccination	1648	99.94
Incomplete Vaccination	1	0.06
Total	1649	100
	Number of Students	Percentage of Students
With Booster	1020	61.89
Without Booster	628	38.11
Total	1648	100

Table 3: Presence of breakthrough infections among UST-FMS students

	Number of Students	Percentage of Students
With Breakthrough Infections	109	6.61
Without Breakthrough Infections	1540	93.39
Total	1649	100

While data acquired from the ThOMedSS reflects records of the students' vaccination status as well as the number of students with COVID-19 exposure despite being vaccinated, potential confounders such as possible external exposures of students, when they are outside the university's premises and integrity in declaring confirmed infection among

students, could affect the association between vaccination status and incidence of breakthrough COVID-19 infections among the UST-FMS students.

Based on Table 4, using Fisher's exact test for count data $p = 1$ ($p > 0.05$), which is found to be not significant, therefore, there is no statistically significant association between COVID-19

Table 4: Odds ratio and Fisher’s exact test of vaccination status and the presence of breakthrough infections among UST-FMS students

Observed	With Breakthrough Infections	Without Breakthrough Infections	
Complete Vaccination	109	1539	1648
Incomplete/No Vaccination	0	1	1
Total	109	1540	1649

Table 5: Odds ratio and Pearson’s chi-squared test of booster status among fully vaccinated UST-FMS students and the presence of breakthrough infections

Observed	With Breakthrough Infections	Without Breakthrough Infections	
With Booster	80	940	1020
Without Booster	29	599	628
Total	109	1539	1648

vaccination status and breakthrough infections. The odds ratio is infinite (Z statistic = 0.944; p = 0.3451).

Based on Table 5, using Pearson’s chi-squared test using Yates’ continuity correction (R software), the chi-square statistic is 6.5463 (p = 0.010511). The chi-square statistic with Yates correction is 6.0345 (p = 0.014029). This means that there is an association between the COVID-19 booster vaccination and breakthrough infections. The odds ratio is 1.7579 (95% CI = 1.1355 to 2.7214; Z statistic = 2.530; p = 0.0114), therefore, UST-FMS students with COVID-19 booster vaccines are 1.76 times more likely to have breakthrough infections compared to those without booster vaccine. The incidence rate of breakthrough infections (109) among the 1649 UST-FMS students who fit the inclusion criteria is 6.61% (0.05387409, 0.07869249).

DISCUSSION

From the results, out of 1652 students enrolled in the UST-FMS, only 1649 were eligible and 109 (6.61%) students had breakthrough COVID-19 infection in the first semester of the academic year 2022-2023. Totally, 1648 (99.94%) students have received the complete primary series of COVID-19 vaccination as recommended in the national vaccine schedule set by the DOH. One hundred and nine of 1648 fully vaccinated students had a breakthrough COVID-19 infection while 0 of the 1 unvaccinated student had a breakthrough COVID-19 infection. Using Fisher’s exact test for count data, a p-value of 1 was obtained inferring that there is no statistically

significant association between COVID-19 vaccination status and breakthrough infections. The vaccination status of the UST-FMS students had no effect on breakthrough COVID-19 infections.

This study has limitations based on the method of how data was collected through ThOMedSS as it was user-dependent. It would rely on students’ due diligence in reporting for the day, reporting data honestly, such as in symptoms and exposure, and even vaccinations to some extent. Data would only be included based on the inclusion and exclusion criteria, but no clarification of data that was input would be done. Additionally, the research did not take into account specific vaccine brands per participant, other than taking into account how many doses constitute a complete primary series vaccination, as well as the severity of breakthrough COVID-19 infections.

COVID-19 vaccines are highly effective in preventing serious illness, hospitalization and death. [2] Thus, with the reopening of schools for hybrid face-to-face classes for 2022, the UST Office of the Secretary-General, in compliance with IATF Resolution No. 155, released a memorandum requiring all of its staff and students that will be allowed onsite, whether for work or study, be fully vaccinated, following a “No Vax Card, No Entry” policy.[3] However, there are few conditions that would exclude an individual from being vaccinated,[4] such as (1) if they have a history of anaphylaxis or severe allergic reaction to any of the components used in the formulation of COVID-19 vaccines, or (2) they had a fever over 38.5°C on the day of their vaccine appointment to which they are

asked to have their vaccination day rescheduled. The COVID-19 vaccines are considered safe for pregnant women,[5] infants 6 months of age and older, children, adolescents,[6] and geriatrics aged 65 and older.[7] However, even with its students' compliance to vaccination requirements, it does not guarantee complete protection against breakthrough infections. Infection breakthroughs were observed with the study's finding of correlating an association between the COVID-19 booster vaccination and breakthrough infections. It was found that the UST-FMS students with COVID-19 booster vaccines are 1.76 times more likely to have breakthrough infections compared to those without booster vaccines (seen in Table 5). One reason could be attributed to the presence of comorbidities. Soegiarto, et al., (2022) found that the risk of breakthrough infection was greater among vaccinated patients with comorbidities, such as diabetes, hypertension and obesity, when compared to vaccinated patients without these conditions. Lower lymphocyte count and chronic systemic inflammation seen in these comorbidities impair the immune response to vaccines.[8]

Furthermore, although it has been a year since the COVID-19 vaccine became available in the Philippines in March 2021, it was said that the newly emerged Omicron variant of COVID-19 had posed a new challenge in terms of its precedent speed of transmission.[9] While vaccination against COVID-19 does not provide 100% protection from getting infected, post-vaccine immune protection varies among individuals and wanes over time, contributing to the individual's susceptibility to acquiring the Omicron variant.[10]

The Omicron variant was reported to be 100-fold greater than the Delta variant in terms of transmissibility and infection rates, replacing Delta as the dominant variant.[11] By March 2022, it was established that almost 90% of the global population had developed antibodies against the COVID-19 virus either through infection or vaccination.[12] It was found that vaccination alters the kinetic property of viral shedding, which reduces the transmission of COVID-19, as well as the viral load and symptoms of individuals.[11] This would account for the reduced impact of Omicron on those who are vaccinated. [12] When the UST opened its doors for face-to-face classes in August 2022, the Omicron variant was still the dominant variant, specifically the BA.5

lineage, which was reported to be more infectious and had a higher reinfection rate.[11] This would account for the incidence of breakthroughs amongst students of UST-FMS.

A similar study was conducted in Wales by Bedston, et al., (2023) wherein they conducted a prospective, national-scale, observational cohort study of healthcare workers (HCWs) comparing the infection breakthrough amongst healthcare workers who were vaccinated with COVID-19 booster and those with primary, and second dose vaccines only during the period of September 2021 up until February 2022.[4] It was found that the overall crude rate of infection was higher for HCWs who received a booster dose compared to those who received only the second dose. Here, it was taken into account that during the uptake of booster vaccines, the predominant variant transitioned from Delta to the more transmissible Omicron variant. It was further reported that out of the 63,580 HCWs who had received a second dose were susceptible after 14 days of administration wherein 9.1% (5,820) became infected at a rate of 160 per 1,000 person-years. As compared to the 55,500 HCWs who received a booster dose and were similarly susceptible, they had a higher percentage of 15.3% (8,500) HCWs who became infected and at a higher rate of 510 per 1,000 person-years. These findings were similar to our study in terms of evidently showing that individuals who had booster vaccines were more likely to have breakthrough infections compared to those without booster vaccines. However, the difference between their study and ours would be the participants' exposure since the HCWs are more prone to be exposed to patients with COVID-19 than students. However, this does not rule out possible external exposures of students when they are outside of the university's premises, which is a confounding factor that may account for their breakthroughs. Piehlmaier, et al., (2023) found that overconfidence in one's knowledge of COVID-19 also led to a laxer attitude and lower levels of concern towards the virus, ultimately leading to less engagement in protective behaviors, such as social distancing and wearing of masks.[13]

Despite the breakthrough infections, in a study consisting of vaccinated healthcare and non-healthcare workers, the majority were either asymptomatic or only mildly symptomatic, emphasizing the benefit-to-risk ratio of getting

vaccinated.[14] However, this study did not evaluate the severity of symptoms of breakthrough infections reported by students.

The samples were representative of the UST-FMS students from the academic year 2022-2023 and clearly identified between completely vaccinated, incompletely vaccinated and unvaccinated individuals. There was also the inclusion of booster dose status. The exposure and outcomes were measured and acquired through the ThOMedSS website and database managed by the UST Health Service Office. The exposure period of the first semester of A.Y. 2022-2023 was also the first widespread implementation of face-to-face classes; hence, a good time period to measure the association between vaccination status and breakthrough infections. The appropriate statistical analysis was also used as it accommodated the presence of 0 to 1 as the input value via Fisher's exact test. Pearson's chi-squared test was also used to determine the association between booster status and breakthrough infections. The odds ratio was used to measure the effect of vaccination status on breakthrough infections.

CONCLUSION

The study contributes to the evaluation of the COVID-19 vaccine and its efficacy against emerging variants since it suggests that vaccination status did not have a statistically significant association with breakthrough infections among the UST-FMS students during the study period. Majority (99.94%) of the UST-FMS students had received the complete primary COVID-19 vaccination series and only 6.61% of this population developed breakthrough COVID-19 infections, all of them occurring in those who received the complete primary COVID-19 vaccination series. According to statistical analysis, breakthrough infections were more likely (1.76 times) for those with booster shots than those without booster shots. The possible reason for this was the emergence of the Omicron variant. To improve the

study, external exposures and individual behaviors must be considered as potential factors influencing infection rates. Comprehensive surveillance may be enhanced by integrating additional questions, accounting for external exposure factors in the ThoMedSS when collecting data. Strict safety protocols should also be implemented continuously despite the high number of vaccinated students within the university premises. Additionally, adherence to these safety protocols should not be limited to the school premises, but also be practiced outside campus to mitigate breakthrough infections.

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Author's Contribution

Legends:

1. Research Project: A. Conception, B. Organization, C. Execution;
 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique;
 3. Manuscript Preparation: A. Writing the First Draft, B. Review and Critique
- Abustan 1.A., 1.B., 1.C., 2.C., 3.A.; Abundancia 1.C., 3.A.; Accad 1.C., 2.A., 2.B., 3.A.; Advincula 1.C., 3.A.; Afafe 1.C., 3.A.; Agraviador 1.C., 3.A.; Tabangay-Lim 1.A., 2.A., 2.C., 3.B.

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