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Original article

Effect of COVID-19 booster vaccination on reducing mortality of patients hospitalized for COVID-19 at Sisaket Hospital

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Abstract

Background: Coronavirus disease 2019 (COVID-19) vaccines have the potential to decrease hospitalizations and mortality, regardless of the vaccine type. Toward the end of 2021, with the COVID-19 pandemic still ongoing, guidelines suggest the administration of booster shots once the primary vaccination series is completed.

Objective: This study aimed to investigate the efficacy of COVID-19 booster vaccinations and the timing between booster shots in terms of preventing mortality among patients with COVID-19 hospitalized at Sisaket Hospital.

Methods: A retrospective cohort study was conducted on individuals aged ≥18 years who were hospitalized with COVID-19 at Sisaket Hospital between January 1, 2022, and December 31, 2022. Data analysis was performed using descriptive statistics and multiple regression analysis techniques.

Results: The study included a total of 1,853 patients (women = 1,050, (56.7%)). The average age was 53.8 ± 20.4 years. Among them, 330 (17.8%) patients expired. According to vaccination history, the survival rates for those who did not receive any vaccination, received an incomplete primary vaccination series, and completed the primary series were 68.5%, 75.9%, and 85.6%, respectively. The survival rates of the groups that received one and two booster shots were 88.6% and 96.2%, respectively. Regarding the time interval between receiving booster shots, statistically significant differences were found among those vaccinated within 3, 3-6, and > 6 months.

Conclusion: COVID-19 booster vaccination has proven its efficacy in preventing fatalities among patients hospitalized for COVID-19, even after a single booster shot. In addition, a booster shot received > 6 months can still reduce the mortality rates compared with booster shots administered within 3 months, without significant difference.

Keywords: Booster shot, Covid-19 vaccine, hospital mortality.

The severe acute respiratory syndrome coronavirus 2 originated in Wuhan, China, at the end of 2019 and led to the coronavirus disease 2019 (COVD-19) pandemic in 2020.[1] Consequently, various vaccines types, including inactivated, protein-based, viral vector, and nucleic acid vaccines, were developed to prevent the disease.[2] The World Health Organization (WHO) certified the emergency use of vaccines. COMIRNATY® COVID-19 mRNA Vaccine (nucleoside modified) was the first vaccine approved on December 31, 2020, followed by COVISHIELD™ COVID-19 Vaccine (ChAdOx1-S [recombinant]) on February 15, 2021, and several others were certified subsequently. After vaccines had been in use for some time, studies confirmed that vaccines can effectively reduce disease severity, including hospitalizations and mortality rates, even when various vaccine types are used.[3] Toward the end of 2024, when the disease outbreak had not yet subsided, recommendations were made to administer booster shots after the completion of the primary vaccination series. This decision must consider various factors, such as age, type of the primary vaccine received, and time elapsed since the last vaccine dose.[4] Many discussions have been made regarding the appropriate interval, which varies from 2 months to 1 year, between the last dose and

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the booster shot.[5 - 7] In Thailand, in October 2021, recommendations were made to administer the third booster shot, and in January 2022, the administration of the fourth booster shot began. This rollout initially prioritized healthcare and public health personnel, frontline workers, and individuals in high-risk groups with chronic disease, who are at higher risk of severe illness, with an interval between the booster and the last dose of at least 3-6 months. This was done primarily to reduce severity and prevent mortality.

The effectiveness of each type of COVID-19 vaccine verified by the WHO for emergency use varies according to numerous reports. These variations primarily result from factors such as the vaccine type, studied population, and emergence of COVID-19 variants. In general, the WHO grants certification when the vaccine demonstrates an efficacy of not < 50.0% in preventing symptomatic disease and not < 70.0% in preventing severe illness. Thailand had imported and utilized all the vaccines validated by the WHO. Numerous studies have examined the effectiveness of COVID-19 vaccines worldwide, encompassing individuals who have not received any vaccines, who received a single dose, who had completed the primary vaccination series, and who received booster shots. The efficacy rates ranged from 54.0% to 85.0% [8], depending on the evaluation of infection prevention, severe illness prevention, or mortality prevention, as well as virus mutations or new variants.

Thus, this study aimed to investigate the effectiveness of COVID-19 booster vaccinations and the interval between booster shots in preventing death among patients with COVID-19 hospitalized in Sisaket Hospital. The goal was to provide proper guidance and services to the population regarding the necessity of receiving booster shots and the recommended intervals between them to prevent severe illness or mortality.

Materials and methods

Study participants

This retrospective cohort study enrolled patients aged ≥18 years with COVID-19 who were hospitalized at Sisaket Hospital between January 1, 2022, and December 31, 2022.

The study protocol was approved by the Sisaket Hospital Research Ethics Committee (SSKH REC no. 012/2566).

Sample size estimation

For sample size calculation, a proportional comparison based on previous studies was performed.[9] The efficacy in preventing severe illness was approximately 52.0% in the group receiving two vaccine doses and 77.0% in the group receiving three vaccine doses, with a type one error (α) of 0.05 replacing the type two error (β) of 0.1, or a power of 90.0%. This calculation yielded a minimum sample size of 166 subjects for the study. Because this retrospective study does not affect personal data or patient rights, ensure the study's maximum accuracy, all data from 2022 were analyzed.

Data collection

Using the hospital information management professional program, data were collected from patients diagnosed with COVID-19, whether as a primary condition or a comorbid ailment, who were hospitalized during the specified period. All patients underwent testing for infection using real-time polymerase chain reaction throughout the study. Data collection included variables such as sex, age, treatment outcomes, and verification of COVID-19 vaccination history for all patients, sourced from the database within the Ministry of Public Health Immunization Center system.

Operation definition

"Nonvaccination" refers to individuals who have not received COVID-19 vaccination."Partial vaccination" refers to individuals who have received at least one vaccine dose but have not completed the primary vaccination series as recommended for each vaccine type or those who received the final dose of the series < 14 days before becoming ill. "Complete primary series" refers to individuals who have received the full recommended primary vaccination series for each vaccine type and received the final dose of the series at least 14 days before becoming ill. "Booster 1" refers to those who have received an additional vaccine dose beyond the primary series before becoming ill. "Booster 2" refers to individuals who have received two additional vaccine doses beyond the primary series before becoming ill. "Time interval" refers to the duration of time between receiving a booster shot and the onset of illness.

Statistical analysis

Descriptive statistics were utilized to elucidate the percentiles, including the minimum, maximum, mean, standard deviation, and median, between the first and the third quartiles, based on the characteristics of the data distribution. Inferential statistics were utilized with exact probability and the nature of the variable in relation to the survival of patients in proportion. The *t*-test or the Mann-Whitney U-test was employed to compare means based on the characteristics of data distribution. Univariable and multivariable logistic regression statistics were utilized to determine the effect of booster vaccines on reducing mortality in patients with COVID-19 at a 95% confidence interval (95% CI). $P < 0.05$ was considered statistically significant.

Results

In 2022, Sisaket Hospital treated a total of 2,426 patients with COVID-19, of whom 2,038 (84.0%) aged ≥18 years were eligible for analysis. Some patients were excluded because of voluntary withdrawal from treatment (n = 33) and unknown treatment outcomes, referrals, or incomplete data (n = 152). Therefore, a total of 1,853 patients were included in this study **(Figure 1).**

In 2022, a total of 1,853 patients with COVID-19 were treated as inpatients at Sisaket Hospital. Out of these, 1,050 were women (56.7%), with an average age of 53.8 ± 20.4 (range, 18 - 105) years. Unfortunately, 330 (17.8%) patients expired.

For this study, the vaccination history among inpatients was categorized by COVID-19 vaccination history before the infection. A total of 378 individuals (20.4%) had no history of vaccination. Among those who received vaccinations, 170 (9.2%) had received one or two vaccine doses but had not completed these 14 days before infection. Furthermore, 841 (45.4%) individuals had received two doses as per the primary series of each vaccine type and had no history of booster doses. In addition, 411 (22.2%) individuals had received one booster dose, whereas 52 (2.8%) had received two booster doses. Only 1 (0.1%) individual had received three booster doses.

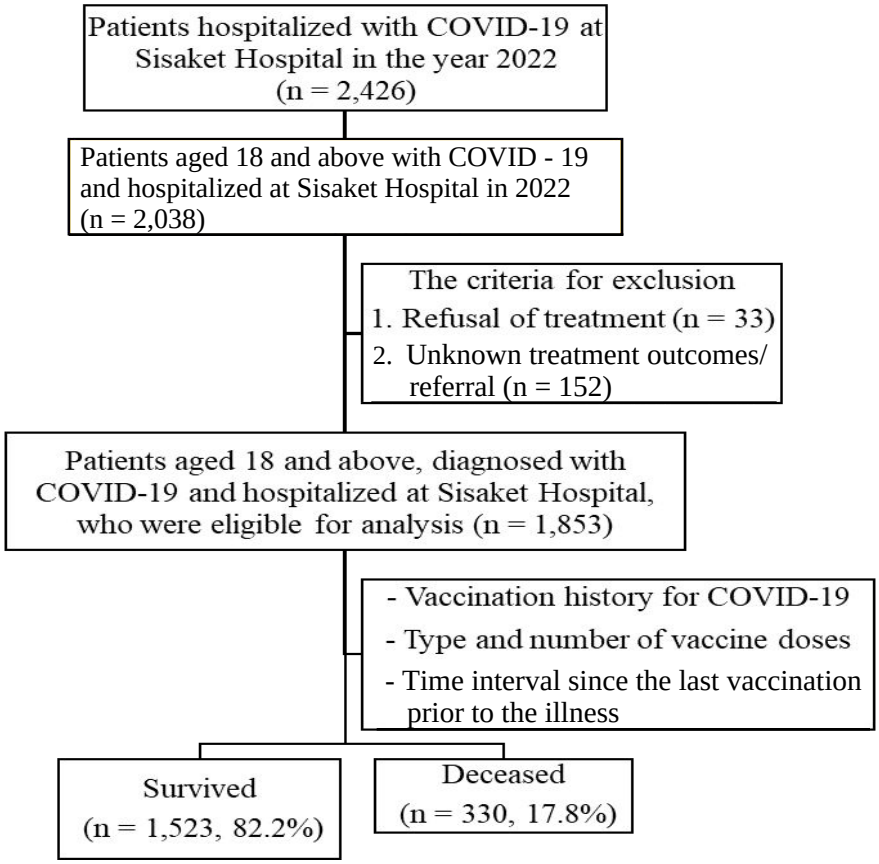

Figure 1. Study flow diagram.

Table 1. General characteristics of patients categorized by their COVID-19 vaccination history prior to this infection

	None vaccination (n = 378)	Partial (n = 170)	Complete primary series (n = 841)	Booster 1 (n = 411)	Booster 2 (n = 52)	Booster 3 (n = 1)	*P* - value
Sex, (n %)							0.08
Male	182 (22.7)	76 (9.5)	350 (43.6)	178 (22.2)	16 (3.4)	1 (0.1)	
Female	196 (18.7)	94 (9.0)	491 (46.8)	233 (22.2)	36 (3.4)	0	
Age (year), mean ± SD	60.6 ± 21.7	51.8 ± 21.9	50.8 ± 19.7	55.8 ± 18.4	43.7 ± 18.4	58.0 ± 0	< 0.001
Age group, (n %)							< 0.001
18 - 59 years	154 (15.0)	94 (9.2)	525 (51.1)	209 (20.4)	44 (4.3)	1 (0.1)	
60 - 69 years	69 (19.8)	34 (9.8)	146 (42.0)	96 (27.6)	3 (0.9)	0	
70 - 79 years	69 (25.6)	21 (7.8)	107 (39.6)	70 (25.9)	3 (1.1)	0	
≥ 80 years	86 (41.4)	21 (10.1)	63 (30.3)	36 (17.3)	2 (1.0)	0	
Underlying, n %	228 (24.3)	91 (9.7)	390 (41.6)	219 (23.4)	10 (1.1)	0	< 0.001
Health care worker	-	-	12 (26.1)	9 (19.6)	25 (54.4)	0	-

Table 2. The types of COVID-19 vaccines received by patients who had been vaccinated with a minimum of one dose.

	Inactivated	Viral vector	mRNA	Mixed
Partial	47 (27.7)	63 (37.1)	60 (35.3)	-
Complete				
Primary series	273 (20.9)	161 (12.3)	185 (14.2)	686 (52.6)
Booster 1	-	61 (13.2)	403 (86.9)	-
Booster 2	-	2 (3.8)	51 (96.2)	-
Booster 3	-	-	1 (100.0)	-

Table 3. General characteristics and vaccination history of COVID-19-infected patients treated as inpatients, categorized based on survival status.

Variables	Survivor (n = 1,523)	Non survivor (n = 330)	*P* - value
Sex (n %)			< 0.001
Male	623 (77.6)	180 (22.4)	
Female	900 (85.7)	150 (14.3)	
Age (year), mean ± SD	50.9 ± 20.2	67.1 ± 15.7	< 0.001
Age group (n %)			< 0.001
18 - 59 years	923 (89.9)	104 (10.1)	
60 - 69 years	274 (78.7)	74 (21.3)	
70 - 79 years	199 (73.7)	71 (26.3)	
≥ 80 years	127 (61.1)	81 (38.9)	
Underlying (n %)			< 0.001
No	771 (91.1)	75 (8.9)	
Yes	704 (75.1)	234 (25.0)	
Health care worker	46 (3.1)	0 (0)	< 0.001
Vaccination (n %)			< 0.001
None	259 (68.5)	119 (31.5)	
Partial	129 (75.9)	41 (24.1)	
Complete primary series	720 (85.6)	121 (14.4)	
Booster 1	364 (88.6)	47 (11.4)	
Booster 2	50 (96.2)	2 (3.9)	
Booster 3	1 (100.0)	0 (0)	

Table 4. The risk of mortality in hospitalized patients, categorized based on risk factors and vaccination status prior to this illness, which were analyzed using univariable and multivariable logistic regression.

	cOR (95% CI)	aOR* (95% CI)	*P* - value
Sex			
Female	(ref)	(ref)	
Male	1.7 (1.4 - 2.2)	1.9 (1.0 - 3.6)	0.047
Age	1.0 (1.0 - 1.1)	1.06 (1.0 - 1.1)	< 0.001
Underlying	1.1 (1.1 - 1.1)	0.94 (0.9 - 1.0)	0.08
Vaccination			
None / patrial	(ref)	(ref)	
Primary series	0.4 (0.3 - 0.5)	0.6 (0.4 - 0.7)	< 0.001
Booster 1	0.3 (0.2 - 0.5)	0.4 (0.2 - 0.5)	< 0.001
Booster 2	0.1 (0.0 - 0.4)	0.2 (0.4 - 0.7)	0.02

*Adjusted age gender and underlying disease and vaccination history.

Table 5. Interval duration of booster dose before infected.

Interval before infected*		
< 3 months	(ref)	
3 - 6 months	1.7 (0.9 - 3.4)	0.102
> 6 months	1.6 (0.7 - 3.7)	0.276

Based on the collected data, the individuals who did not receive any vaccines were on average older than other groups, that is, in the group aged ≥ 70 years, 25.0% - 1.0% did not receive COVID-19 vaccines (**Table 1)**.

Within the group that received a minimum of one vaccine dose or more, 37.1% received only one dose of viral vector vaccines, followed by mRNA vaccines (35.3%), and inactivated vaccines (27.7%). For those who completed the primary series, 52.6%, which was the highest percentage, received different vaccines. As for booster doses, nearly all were mRNA vaccines **(Table 2).**

In the analysis, the survival rate was higher in women (85.7%) than in men (77.6%) ($P < 0.001$). The surviving group was also on average younger than the deceased group (50.9 ± 20.2 *vs.* 67.1 ± 15.7 years, $P < 0.001$). Notably, the group aged ≥ 80 years recorded the lowest survival rate, at 61.1% ($P < 0.001$). In addition, concerning vaccination data, the non-vaccinated group exhibited the lowest survival rate at 68.5% **(Table 3).**

The results of the univariable and multivariable logistic regression analyses are presented in **Table 4.** In the multivariable analysis, variables such as sex, age, underlying health conditions, and vaccination history were included to control for confounding factors in the equation, represented as adjusted odds ratios (aOR). Men had a 1.9 times higher mortality risk than females ($P = 0.047$). The risk increased by 6.0% for every additional year of age ($P < 0.001$). When comparing vaccination history with those who were not vaccinated or did not complete the primary vaccination series, the mortality risks were reduced to 55.0%, 35.0%, and 16.0%, respectively ($P < 0.001$). Having underlying health conditions did not significantly increase the mortality risk ($P = 0.084$) when controlling for sex, age, underlying health conditions, and vaccination history in the equation.

Regarding the timing of booster vaccination after the complete primary series, the mortality risk of the groups that received a booster shot in 3–6 months or after 6 months increased by 1.6–1.7 times compared with the group that received a boost shot within 3 months. However, these differences were not statistically significant ($P = 0.102$ and $P = 0.276$, respectively) **(Table 5).**

Discussion

This study revealed that COVID-19 booster vaccinations significantly reduce the mortality rates among patients hospitalized for COVID-19. In the comparison between individuals who received a single booster shot and those who did not receive any vaccines or did not complete the vaccination series,

the mortality rate decreased by 65.0%. Furthermore, the mortality rate was reduced by 84.0% among individuals who received two booster shots, showing statistical significance after adjusting for sex, age, and underlying health conditions.

However, in this study, only 25.0% of patients hospitalized for COVID-19 had received at least one booster dose within the data collection period. As indicated by a systematic review and meta-analysis, this discrepancy could be attributed to the effectiveness of the vaccine in reducing the disease severity among hospitalized patients [5, 10] or to low public acceptance of booster vaccinations, particularly in the southeast region where acceptance rates were as low as 52.0% compared with 77.0%–89.0% in other regions. [3, 11] In the older population, which is particularly vulnerable to severe illness, this study revealed an escalating vaccine refusal rate as age increased, particularly among individuals aged ≥ 80. Similar patterns were also noted in the acceptance of booster vaccinations among older adults.[12] In this demographic group, the main reasons for vaccine refusal likely stemmed from concerns about vaccine safety and uncertainty about its efficacy.[13]

This study, which provides actual evidence of the effectiveness in reducing mortality rates based on data from demographically similar regions, may bolster confidence among recipients, particularly the older group, to receive both primary vaccination series and booster shots. In addition, a significant concern was the appropriate timing for booster vaccinations. The results indicate that administering a booster shot after 6 months continues to significantly decrease mortality rates among patients hospitalized for COVID-19, displaying no statistical difference when compared with vaccinations given within 3 months after the primary series. Consequently, patients are deemed eligible to receive booster shots within 6–12 months, aligning with Thailand's annual influenza vaccination policy for high-risk individuals. These compelling findings not only endorse the existing policy but also enhance public confidence and acceptance of timely booster vaccinations.

The primary strength of this study lies in its highly reliable and minimally biased collection of vaccination data from each patient. The study evaluates survival and mortality rates without bias, and the analysis incorporates essential confounding factors to ensure that the results are likely due to the actual effects of the vaccines.

However, this study has limited ability to verify historical data for certain variables because of incomplete recording of information, such as the onset date of illness, presence of multiple underlying diseases, contracting COVID-19 before the current test, and intake of immunosuppressive medications that could affect the disease immunity status.

Conclusion

The results reveal that booster vaccinations effectively reduce mortality among patients hospitalized for COVID-19. Furthermore, a booster shot administered after a 6-month interval demonstrates comparable efficacy in reducing mortality to vaccinations given within a 3-month timeframe. Consequently, the dissemination of information about the effectiveness and appropriate timing of booster vaccinations, particularly among older adults, helps instill confidence within the population.

Conflicts of interest statement

All data generated or analyzed during the present study are included in this published article and the citations herein. Further details, opinions, and interpretations are available from the corresponding author on reasonable request.

Data sharing statement

All data generated or analyzed during the present study are included in this published article and the citations herein. Further details, opinions, and interpretations are available from the corresponding author on reasonable request.

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