The Effect of COVID-19 Vaccination on Reducing the Risk of Infection, Hospitalization, and Death in Isfahan Province, Iran

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Abstract

Background: We aimed to evaluate the effect of COVID-19 vaccines in preventing infection, hospitalization, and mortality due to COVID-19 in Isfahan Province, Iran.

Methods: Following a retrospective cohort design, data of all vaccinated individuals since the rollout of vaccination of the general population are analyzed, Mar 2020 to Aug 13, 2021. Moreover, the data of all non-vaccinated people were collected by the census method for this period. The two groups were compared concerning hospitalization and mortality using the Chi-square test. Kaplan-Meyer was also used to calculate the median interval between receiving a vaccine and outcome (hospitalization and death).

Results: Overall, 583434 people have received a second dose of a vaccine from Mar 2020 to Aug 2021, which 74% (n=433403) was Sinopharm, 18.2% (n=106027) AstraZeneca, 3.6% (n=21216) Sputnik, and 3.9% (n=22,788) Barekat. In contrast, 2,551,140 people living in the Isfahan Province did not receive a vaccine. The median interval between injection of the first dose and the hospitalization for those who received Sinopharm, AstraZeneca, Sputnik, and Barekat was 22, 61, 19, and 19 days, respectively. For unvaccinated cases, the rates of infection, hospitalization, and mortality (per 1000 population) were 69.7, 12.1, and 1.04, respectively. In contrast, for vaccinated individuals, these rates were 3.9, 1.08, and 0.09, two weeks after the second dose, respectively.

Conclusion: The highest and lowest reduction in relative risk was for those who received AstraZeneca and Sputnik, respectively.

Keywords: Vaccine; COVID-19; Hospitalization; Mortality; Iran

Introduction

In the nearly two years since the pandemic began, mass vaccination has been proposed as the most effective way to end the pandemic (1). The estimation of the percentage of the population that needs to be vaccinated to end the pandemic varies from one region to another and depends on the R0. For instance, for the Wuhan variant, most of the initial estimates range from 60% to 80% (2, 3). The Delta variant was first identified in India in Dec 2020 and soon spread to other countries. With an R0 of 5-8, the transmission power of this variant is higher than the alpha variant by 60%, resulting in significant increases in the number of
new infections, hospitalization, and mortality. Currently available vaccines are less effective against this variant, according to the estimates (4). Its R0 is about 6, which pushes the overall population herd immunity threshold to more than 85% (5). The incidence of COVID-19 infection after the breakthrough infections is a major challenge, as none of the currently available vaccines results in 100% protection against the disease. The first signs of this phenomenon were observed in health staff. A survey of 14,000 health professionals working in the health sector of Chicago, who were fully vaccinated, reported 22 cases of infection, most of which were asymptomatic or with mild symptoms (6). In another study conducted on Israeli health care professionals who received the biotech vaccine (messenger RNA platform), similar results are reported, i.e., 39 out of 1494 cases had mild symptoms or were asymptomatic. Their neutralization titer was lower in the pre-infection period than controls (those without infection) (7). In a case-control study on COVID-19 infected cases who some of them were vaccinated, compared to those vaccinated with BNT162b2 and ChAdOx1 vaccines, 116 out of 119 vaccinated people were only received the first dose. Two weeks after receiving the first dose, the relative risk of mortality was reduced by 69.3%. In addition, the hospitalization rate and its duration were significantly lower in those who only received the first dose (8).

In a preprinted article on the massive wave of the COVID-19 in India from Mar to Jun 2021, accompanied by a significant increase in the incidence of infection among vaccinated populations, genomic examination revealed that 86.69% of cases were new Delta variants. However, only 9.8% of vaccinated cases needed hospitalization, and the fatality rate was 0.4%, indicating the positive impact of vaccination on hospitalization and mortality (9).

A study in Bahrain, where approximately one million people (out of its 1.5 million population) have received two doses of COVID-19 vaccines, showed that all types of vaccines (e.g., Sinopharm, AstraZeneca, Sputnik V, and Pfizer/Biotech) have been effective in reducing infection, Intensive Care Unit Hospitalization, and mortality. Meanwhile, the Sinopharm vaccine is less effective than the Pfizer biotech, particularly in populations aged 50 yr or over and against the Delta variant (10).

In Iran, 4,833,135 confirmed COVID-19 cases and 104716 deaths have been reported from Jan 3, 2020, to Aug 27, 2021. Moreover, as of Aug 23, 2021, 23,137,699 vaccination doses have been administered (11), including Sinopharm, AstraZeneca, Sputnik, and Barekat. Despite five courses of surges in the number of COVID-19 cases and high incidence and mortality in Iran, little information is available about breakthrough infections (infection after receiving the second dose) of various vaccines. Negative attitudes toward vaccines, low public trust in vaccines, and concerns about low effectiveness and safety are barriers to achieving herd immunity (12). Therefore, increasing public awareness through analyzing the efficacy of various administered vaccines would be of crucial importance. As various vaccines are available in Iran, comparing their efficacy in preventing severe consequences would be useful for making future decisions regarding vaccination programs. The Iranian healthcare system collects public health information through a system named SIB, which also contains information on side effects, new infections, hospitalization, and death due to COVID-19. Such information would be useful for increased transparency about the precise number of new cases, despite being vaccinated. According to Iran's COVID-19 vaccination program, all Iranians older than 18 yr must be vaccinated by the end of Jan 1400. Similar to many countries, in Iran, healthcare professionals, those working at nursing homes and mortuaries, as well as veterans, were first immunized against COVID-19, yielding about 1.5 million people. These groups were vaccinated from Mar 2020 until May 2021. Then, those older than 60 yr (about 8 million) and those with chronic diseases (aged 16 to 64 yr; about 4 million) were vaccinated, followed by those aged 75 and older, and 70 yr of old. Afterward, the age groups of 65-69 yr and 60 to 64 yr were vaccinated (13). The current study aimed to evaluate the effectiveness of COVID-19 vaccines in prevention, hospitalization, and mortality due to COVID-19.
in Isfahan province, Iran, from the beginning of the vaccination until Aug 15, 2021. To achieve this goal, the efficacy of different types of vaccines was calculated according to the hospitalization and death outcomes in young, middle-aged, and elderly age groups separated by the type of vaccine and compared with unvaccinated people.

Methods

Following a retrospective cohort design, data of all vaccinated individuals since the rollout of vaccination of the general population are analyzed, Mar 2020 to Aug 13, 2021. Moreover, the data of all unvaccinated people were collected by the census method for this period. All vaccinated and unvaccinated people were followed up until Aug 13, 2021, and data on positive PCR, hospitalization, and death were collected. This survey was part of a study on the vaccination campaign in Isfahan Province, central Iran confirmed by the Ethics Committee of the Isfahan University of Medical Sciences (code: IR.MUI.MED.REC.1400.345). All patients were told that their information would be reported in the articles and patients expressed their consent.

Data on the type of administered vaccines (i.e., Sinopharm, AstraZeneca, Sputnik, and Barekat), age group (young, middle age, and elder), number of doses (first and second), COVID-19 infection status (infected, hospitalized, and died), hospitalization status (discharged, died, and hospitalization during the study period), date of injection (first and second doses), date of hospitalization, and death were collected. Data were extracted from electronic records of patients (SIB system), syndromic registration system of acute respiratory diseases, and death registration system. The quality of all data was evaluated by the Information Technology Department of the Deputy for Public Health Affairs of the Isfahan University of Medical Sciences. Data analysis was administered using SPSS version 23 (Chicago, IL, USA). Frequency and percentage were used to describe quantitative data. The rates of infection, hospitalization, and mortality were calculated for both vaccinated and unvaccinated people. The relative risk (RR) of infection, hospitalization, and mortality were estimated for the vaccinated group compared to the unvaccinated group. The two groups were compared concerning hospitalization and mortality using the chi-square test. Kaplan-Meyer was also used to calculate the median interval between vaccine administration and outcome (hospitalization and death). Outcomes of hospitalization and death were compared between different vaccination groups and unvaccinated people using the log-rank test. Kaplan-Meyer was also used to calculate the median interval between vaccine administration and outcome (hospitalization and death). Statistical significance was considered when \( P \)-value<0.05.

Results

Overall, 583434 people have received a second dose of the vaccine from Mar 2020 to Aug 15, 2021, which 74\% (n=433403) was Sinopharm, 18.2\% (n=106027) AstraZeneca, 3.6\% (n=21216) Sputnik, and 3.9\% (n=22,788) Barekat. In contrast, 2,551,140 people living in the Isfahan Province did not receive a vaccine, who were categorized as the control group. Regarding the priorities published for COVID-19 vaccination, the elderly is the largest vaccinated group (61\% or n=356041), except for the health staff. The incidence of the disease was evaluated two weeks after receiving the first dose. Out of 324196 people who received the first dose, after two weeks, 4234 (1.3\%) had a positive PCR, of which 3460 were elderly. Comparison of the incidence, hospitalization, and death (per 1000 population), two weeks after receiving the first dose showed that the hospitalization and mortality were higher among unvaccinated people than their vaccinated counterparts by 2.6 and 4 times, respectively (Table 1).
Table 1: Comparison of the number and rate of infection, hospitalization, and death (per 1000 populations), two weeks after the first dose in the whole population

| Vaccine Status         | Population | Infection (PCR +) | Hospitalization | Death |
|------------------------|------------|-------------------|-----------------|-------|
|                        |            | Number            | Frequency (per 1000) | Number | Frequency (per 1000) | Number | Frequency (per 1000) |
| Unvaccinated           | 2551140    | 177879            | 69.7            | 30946  | 12.1              | 2657   | 1                  |
| Vaccinated (two weeks after the first dose) | 324196 | 4234 | 13.1 | 1510 | 4.6 | 82 | 0.25 |
| Sinopharm              | 132786     | 2113              | 15.9            | 738    | 5.5               | 44     | 0.33               |
| Sputnik v              | 2655       | 91                | 34.2            | 28     | 10.5              | 3      | 1.1                |
| Astrazeneca            | 149139     | 1909              | 12.8            | 733    | 4.9               | 35     | 0.23               |
| COVIran Barekat        | 39616      | 121               | 3.1             | 11     | 0.27              | 0      | 0                  |

The median interval between receiving a first dose and the hospitalization was 22, 61, 19, and 19 d, respectively, for Sinopharm, AstraZeneca, Sputnik, and Barekat vaccines. The comparative data of the unvaccinated and vaccinated people separated by the type of vaccine is provided in Table 2. For the above mentioned period, of 2,551,140 unvaccinated people, 177,879 had a positive PCR and 30,946 were hospitalized, and 2,657 died. Of 584,434 vaccinated people, 2,272 had a positive PCR, 635 were hospitalized, and 58 died. For unvaccinated people, rates of infection, hospitalization, and death (per 1000 population) were 69.7, 12.1, and 1.04 for non-vaccinated people, respectively; while for vaccinated people, these rates were 3.9, 1.08, and 0.09, respectively, which shows reduced relative risk (RR) for rates of infection, hospitalization, and death by 94.4%, 91.7%, and 91.3% compared to unvaccinated people. The highest and lowest reduction in RR was for those who received AstraZeneca and Sputnik, respectively, while the RR of Sinopharm was between these two vaccines (Table 2). While only accounting for 4% of all administered vaccines, 28% of all vaccine failures were for this vaccine. On the other hand, about 18% of all administered vaccines were AstraZeneca and had a failure rate of 3%. The median interval between receiving a second dose and hospitalization and death in people who were fully vaccinated is provided in Table 3 (for the AstraZeneca vaccine, there should be 28 d between the first and the second dose). Kaplan Meier curve for the interval between both doses of Sputnik and Sinopharm vaccines is provided in Fig. 1.

Table 2: Comparison of the relative risk of infection, hospitalization, and death (per 1000 population), two weeks after the second dose in the whole population

| Vaccine status | Population | Infection | Hospitalization | Death |
|----------------|------------|-----------|-----------------|-------|
|                |            | Frequency (Number) | Risk reduction rate | Frequency (Number) | Risk reduction rate | Frequency (Number) | Risk reduction rate |
| Unvaccinated   | 2551140    | 69.7       | -               | 12.1  | -               | 1.04  | -                  |
| Total vaccinated | 583434   | 3.9        | 94.4            | 1.08  | 91.07           | 0.09  | 91.3               |
| Sinopharm      | 433403     | 3.5        | 94.9            | 1.3   | 89.2            | 0.12  | 88.4               |
| Sputnik v      | 21216      | 25.6       | 63.2            | 2.8   | 76.2            | 0.18  | 82.6               |
| Astrazeneca    | 106027     | 0.67       | 99              | 0.07  | 99.4            | 0     | 100                |
| COVIran Barekat | 22788     | -          | -               | -     | -               | -     | -                  |

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Table 3: The interval between receiving a second dose and hospitalization and death in fully vaccinated people, separated by the vaccine type

| Vaccine Type | Hospitalization |  |  | Death |  |  |
|--------------|----------------|---|---|-------|---|---|
|              | Median         | Standard Error | 95% Confidence Interval | Median | Standard Error | 95% Confidence Interval |
|              |               |               | Lower limit | Upper limit | Lower limit | Upper limit |
| Sinopharm    | 45.000         | 1.267          | 42.517      | 47.483      | 46.000      | 2.449       | 41.199      | 50.801      |
| Astrazeneca  | 19.000         | 1.309          | 16.434      | 21.566      | -           | -           | -           | -           |
| Sputnik v    | 50.000         | 0.968          | 48.102      | 51.898      | 52.000      | 11.500      | 29.460      | 74.540      |
| Total        | 45.000         | 1.230          | 42.590      | 47.410      | 47.000      | 2.175       | 42.738      | 51.262      |

Fig. 1: Kaplan-Meyer curve for the interval between the receiving doses and death in vaccinated people

Discussion

In this study, conducted in Isfahan Province, the outcomes of COVID-19 disease in vaccinated people were compared with their unvaccinated counterparts for the period of Mar 2020 to Aug 2021 (about six months). The study outcomes included infection, hospitalization, and mortality. For unvaccinated people, the rates of infection, hospitalization, and mortality (per 1000 population) were 69.7, 12.1, and 1.04, respectively. On the other hand, two weeks after receiving a second dose, these rates were 3.9, 1.08, and 0.09, respectively, which shows reduced RR by 94.4%, 91.7%, and 91.3% for infection, hospitalization, and death in vaccinated people compared to unvaccinated people.

During the study period, most of the vaccinated people were elderly. The highest and lowest reduction in RR was for those who received Astrazeneca and Sputnik, respectively. The findings of the present study concerning the reduction in RR are similar to a study conducted in Chile on inactive vaccines. In their study, the efficacy of vaccines in infection prevention, and reducing hospitalization and death is reported as 65.9%, 87.5%, and 86.3% (14). Moreover, in Brazil an efficacy of 100% was reported against severe COVID-19 infection (15).
In this study, further reduction of RR (positive PRC) for infection can be attributed to some problems in performing PCR tests to diagnose asymptomatic cases or those with mild symptoms, which translates into underestimation of new cases. The occurrence of several surges caused constant changes in policies related to the PCR test. For instance, for a while, asymptomatic relatives of patients were obliged to have a PCR test, and sometimes only high-risk cases were required to have a PCR test. In combination with the heterogeneity of the vaccination speed, this unstable trend resulted in problems for estimation of reduced incidence of COVID-19 in vaccinated people compared to their unvaccinated counterparts. In addition, it can be attributed to the gradual vaccination strategy in Iran. According to previous studies, the emergence of new variants, which vaccines may be ineffective against them, causes an increased incidence of COVID-19 (16). For vaccines that are based on inactive platforms, high antibody responses occur three weeks after, followed by a gradual decline (17). In addition, the six months’ cumulative incidence was calculated in this study, and the speed of vaccination has been significantly increased in recent months. Meanwhile, the incidence of COVID-19 infection among unvaccinated cases was calculated for six months. Hence, caution should be taken when interpreting the incidence of COVID-19 infection in vaccinated cases two weeks after receiving the second dose. The incidence of COVID-19 infection probably will increase in vaccinated people, and the efficacy of vaccines would be calculated with higher precision. Sputnik was the first administered vaccine in Iran; hence, the period is long enough to evaluate its efficacy. For the Sputnik vaccine, the risks of infection, hospitalization, and death were reduced by about 63.2, 76.2, and 82.6%, respectively. Therefore, it can be considered effective in the Isfahan Province.

For other vaccines, despite the long interval between doses, AstraZeneca has higher efficacy, meaning lower COVID-19 infection, compared to Sinopharm and Sputnik vaccines. Data related to the Barakat vaccine still are incomplete, due to the short period of its administration. For those who were fully vaccinated with Sinopharm, AstraZeneca, and Sputnik, the median interval between receiving a second dose and hospitalization was 45, 19, and 50 days, respectively. A study on those vaccinated using Pfizer and BioNtek reported that the median interval between vaccination and hospitalization was 39.5 (25.5-52) (18).

This study is one of the first of its kind at the provincial level in Iran. Since the beginning of the coronavirus pandemic, Iran has faced a pervasive crisis that engulfed the health system. International sanctions and some managerial shortcomings have caused problems for Iran's vaccination strategy. Furthermore, the diversity of vaccines and their different administration intervals have intensified problems related to the evaluation of their efficacy. Therefore, the present study tried to estimate the effect of vaccination on reducing the injuries and casualties of the COVID-19 by calculating the cumulative incidence during the early months of vaccination.

Herein, some limitations and challenges must be considered before the application of the findings. Firstly, data used in the present study are collected by systems that are not primarily designed for research purposes. In Iran, electronic data collection systems are nascent and require continuous modification and development. Secondly, most vaccinated people were either elderly or high-risk groups. Meanwhile, sufficient data were not available about the underlying disease(s) and demographic information (i.e., age and gender).

**Conclusion**

Finally yet importantly, this study shows the overall effect of all vaccines used so far in the prevention of infection, hospitalization, and death. Due to the rapid progression of vaccination in the last month, a periodic repetition of such studies (e.g., every three months), in combination with controlling confounders, would provide more comprehensive analyses to guide health policy-makers to make decisions regarding access to more effective vaccines as well as the booster dose in various population groups.
Ethical considerations

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Availability of data

Patient data will be provided to the applicant upon written request to the responsible author.

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Conflict of interest

The authors declare no conflict of interest.

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