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Comparison of AstraZeneca and sinopharm vaccines as boosters in protection against COVID-19 infection

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ABSTRACT

Background: As the global number of confirmed cases rises past 640 million, vaccination remains the most effective measure in controlling COVID-19. Studies have shown that two doses of vaccination can significantly reduce hospitalization and mortality rates among patients, but the effectiveness of booster doses is also important. We aimed to evaluate the role played by the type of the 3rd dose of vaccination by comparing the safety and efficacy of two common vaccination histories differing only in the 3rd received dose.

Methods: We conducted a cross-sectional study on patients with respiratory symptoms suspected of having SARS-CoV-2 infection using Real-time PCR. We also collected information on the age, gender, and type of vaccine received for the third dose.

Results: Out of 346 cases with respiratory symptoms, 120 cases tested positive for SARS-CoV-2 and had received two doses of Sinopharm and a different booster dose of either AZD1222 (AstraZeneca) or BIBP (Sinopharm). Among these 120 patients, vaccination with AZD1222 as a booster dose resulted in fewer symptoms compared to those vaccinated with three doses of BIBP.

Conclusions: Our study demonstrates that booster doses can help reduce hospitalization and the severity of infection, and it appears that a combination of different vaccines may be effective against severe COVID-19 infection.

1. Introduction

1.1. History of viral respiratory infections

Acute respiratory tract infections are a frequent occurrence among individuals of all ages and genders. These infections can be severe and persistent, with many such historical examples being caused by viruses [1]. Many types of viruses, including Orthomyxoviridae, Paramyxoviridae, Picornaviridae, Coronaviridae, and Adenoviridae, can cause respiratory infections. The most common means by which viruses enter the body is through aerosolized droplets or saliva [2] (see Tables 1–3, Fig. 7).

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Table 1
Demographic characteristics of patients.

characteristic	Age	Total positive SARS-CoV-2 cases	No[a] (%)
Age (Year)	18–30	30	32%
	30–50	64	68.00%
Type of vaccine received	SSS[b]	68	72.3%
	SSA[c]	26	27.7%

[a] Number.
[b] Patients who have received all 3 doses of Sinopharm vaccine.
[c] Patients receiving 2 doses of Sinopharm vaccine and 1 dose of AstraZeneca.

Table 2
Descriptive analysis of research divided by symptoms, age and type of vaccination.

Variable	N	N = 94
Shiver, n (%)	94	38 (40)
Cough, n (%)	94	94 (100)
Fever, n (%)	94	30 (32)
Rhinorrhea, n (%)	94	61 (65)
Sore throat, n (%)	94	68 (72)
Back.Ache, n (%)	94	40 (43)
Vaccination, n (%)	94	
SSA		26 (28)
SSS		68 (72)
Age, n (%)	94	
18–30		30 (32)
30–50		64 (68)

Table 3
Comparing clinical manifestation of patients divided by type of vaccination.

Variable	N	Vaccine		p-value[a]
		SSA, N = 26	SSS, N = 68	
Shiver, n (%)	94	6 (23)	32 (47)	0.034
Cough, n (%)	94	26 (100)	68 (100)	
Fever, n (%)	94	4 (15)	26 (38)	0.034
Rhinorrhea, n (%)	94	12 (46)	49 (72)	0.019
Sore throat, n (%)	94	10 (38)	58 (85)	<0.001
Backache, n (%)	94	4 (15)	36 (53)	<0.001
Age, n (%)	94			0.26
18–30		6 (23)	24 (35)	
30–50		20 (77)	44 (65)	

[a] Pearson's Chi-squared test.

1.2. Coronaviridae family

The family Coronaviridae belongs to the order Nidovirales and consists of two subfamilies: Coronavirinae and Torovirinae. Coronaviruses are enveloped viruses with a single-stranded, positive RNA genome that is nearly 30 kb in length, making it the longest genome among positive polarity RNA viruses [3,4]. The main evolutionary reservoirs for coronaviruses with zoonotic sources are cement bats, and these viruses can cause a variety of diseases in animals such as dogs, cats, pigs, and birds [5,6]. The subfamily Coronavirinae is further divided into four genera: α, β, γ, and δ-coronaviruses. The genus α-CoV includes two human species: hCoV-229E and hCoV-NL63. The β-coronavirus genus includes hCoV-OC43, hCoV-SARS, hCoV-HKU-1, and Middle Eastern respiratory syndrome (MERS). The γ-genus contains viruses that infect whales and birds, while the δ genus contains viruses isolated from animals such as pigs and birds [3,7,8].

Viral genomes consist of 5′ and 3′ terminals. The 3′ terminal region encodes structural proteins, including the spike protein (S), membrane protein (M), nucleocapsid protein (N), envelope protein (E), and haemagglutinin-esterase (HE) protein [6,9]. Human SARS-CoV-2 is transmitted through contact with infected individuals. The transmission of coronavirus between species and from human to human primarily depends on the binding affinity of the virus spike protein for the host cell receptor, ACE-2. ACE-2 is a receptor for coronavirus entry and plays a role in its pathogenesis, with high expression in alveolar cells of the lung, esophagus, kidney, colon, and bladder [6,10].

Coronavirus transmission has been primarily reported through respiratory droplets, but direct transmission from surfaces and oral-fecal transmission have also been observed during the COVID-19 pandemic [9]. In late 2019, a new β-Coronavirus called SARS-CoV-2 emerged in Wuhan, China, and rapidly spread worldwide, causing a range of respiratory illness from mild to severe. Common symptoms of COVID-19 include fever, cough, shortness of breath, muscle or body pains, headache, tiredness, loss of taste or smell, sore throat, nasal congestion or runny nose, and gastrointestinal symptoms such as nausea or vomiting, and diarrhea. In addition, neurological, renal, and gastrointestinal complications have been observed in a significant number of COVID-19 patients [11–14].

According to the World Health Organization (WHO), SARS-CoV-2 continuously mutates and changes in character. While most of these mutations are not dangerous, some can cause global concerns [15]. Coronaviruses are high-rate mutation RNA viruses that have relatively low rates of errors due to their polymerase-modifying enzyme, but naturally occurring mutations in the spike region during replication can lead to various variants. Several lineages have been identified globally, including the Omicron variant of this virus [16,17].

In November 2021, the Omicron (B.1.1.529) variant was detected in South Africa and quickly spread worldwide. Omicron has the highest number of mutation sites of all SARS-CoV-2 variants, with 33 mutations relative to the reference strain in Wuhan, China, and also has high transmission power. The WHO has identified this variant as a cause for concern [18–20].

To protect against SARS-CoV-2, the WHO implemented various strategies such as social distancing, travel restrictions, and mandatory masks in public places. Ultimately, it was determined that the most effective strategy was vaccination [21]. Clinical trials in animals and humans have demonstrated the safety and efficacy of certain vaccines, which have been granted approval by the WHO and the health organizations of various countries for use in different countries [22]. Since the emergence of the coronavirus, several vaccines have been developed using various platforms worldwide, including inactivated, live attenuated, recombinant protein, vectored, and mRNA-based vaccines [23,24].

Among proposed vaccines, DNA vaccines have the ability to stimulate both humoral and cellular immunity and possess several properties including proper folding of antigen proteins, economic efficiency, rapid production, and easy storage, suggesting its potential for effective protection against COVID-19 [25]. Previous experiments on the MERS-CoV vaccine (INO-4700) were utilized in the development of the coronavirus vaccine, as well as the design and technology of the Zika GLS-5700e vaccine, which received approval in less than 7 months [26]. Recent research on various coronaviruses indicates that SARS-CoV and MERS-CoV tend to elicit strong T and B cell immune responses [27].

1.3. Sinopharm vaccine

The Sinopharm vaccine, also known as BBIBP-CorV, is an inactivated vaccine developed by the Chinese state-owned pharmaceutical company Sinopharm and approved for use in the United Arab Emirates (UAE) [24]. It works by inducing the production of antibodies against the inactivated virus antigen [23]. The vaccine is administered in two doses within a month. Phase 1 and 2 human clinical trials in China were conducted on 640 participants and found that the vaccine elicited high-titer neutralizing antibodies with mild side effects, including fever and injection site pain [28]. Phase 3 clinical trials involving 60,000 participants were conducted in the UAE, Bahrain, Egypt, Jordan, Peru, and Argentina, and the vaccine was approved by the UAE on December 9, 2020, with an effectiveness of 86% [28]. The WHO also reported that the Sinopharm vaccine was tested in three clinical trials involving 16,

671 people and generally had mild to moderate side effects, including fatigue, headache, and injection site pain [23,28]. This vaccine works by inducing the production of antibodies to enhance the immune system against inactivated antigens [23,29].

1.4. AstraZeneca vaccine

Another vaccine that has been approved by many countries is The AstraZeneca vaccine [30]. The AstraZeneca ChAdOxnCoV-19 (AZD1222) vaccine, approved by the UK in November 2021, is a recombinant vaccine based on two decades of research and development on the chimpanzee adenovirus as vector, a non-replicating "ChAdOx1" vector developed by Oxford University and the Indian Serum Institute. The AstraZeneca vaccine encodes a complete, unchanged version of wild-type spike protein and induces a strong neutralizing antibody response as well as a CD8 + T cell response. The Oxford – AstraZeneca vaccine was approved in 170 countries in November 2021 [31,32]. Common side effects of the AstraZeneca vaccine include inflammation and pain at the injection site, fatigue, lethargy, headache, nausea, fever, and body aches that gradually improve over several days [33].

Studies have shown that while the AstraZeneca vaccine has numerous benefits, its observed safety is lower compared to Pfizer-BioNTech, and some cases of thromboembolic events have been reported following its use, leading some European countries to suspend its use. However, the European Medicines Agency, after reviewing the available evidence, concluded that the Oxford-AstraZeneca vaccine has a low risk of thromboembolic events and is still beneficial [34]. Among the other available vaccines, the AstraZeneca vaccine is considered economical and can be stored more easily than others in refrigerators [35]. Despite being approved by the WHO, the use of two doses of the AstraZeneca vaccine has been restricted in some countries due to severe thromboembolic complications in young women. Previous studies have shown that using a combination of vaccines is more effective at inducing both cellular and humoral immunity than using a single type of vaccine [36–38].

1.5. Objectives

In this study, we evaluated the symptoms of individuals with COVID-19 infection after receiving two doses of the Sinopharm vaccine and a booster dose of either Sinopharm or AstraZeneca.

2. Methods

2.1. Study design

This study was designed to assess the prevalence and severity of COVID-19 symptoms in individuals who received three doses of the vaccine but still contracted the infection. We also focused on the protection provided by the Sinopharm and AstraZeneca vaccines and analyzed symptoms by age and type of vaccine received at each dose.

2.2. Study population

From February to April 2022, 346 patients with respiratory symptoms who were referred to Besat Hospital were included in the study. Of these, 120 were positive for SARS-CoV-2 and 94 of these had received three doses of the vaccine. Relevant information was obtained from all individuals with respiratory symptoms and tested for SARS-CoV-2 using real-time PCR to examine the relationship between symptom severity and the type of vaccine received. Of the 346 cases with respiratory symptoms, 94 were positive for SARS-CoV-2. None of the studied cases had severe symptoms and quarantined themselves without being hospitalized. The sex, occupation, and place of residence of the patients were not considered in this study.

Of the 94 surveyed individuals, 31.9% (30 individuals) were between the ages of 18 and 30, and 64 individuals were between 30 and 50 years old. 26 of the 94 patients (27.7%) received the first and second doses of the Sinopharm vaccine and the third dose of the AstraZeneca vaccine, while 68 (72.3%) received all three doses of the Sinopharm vaccine. Of the 30 patients between the ages of 18 and 30, 24 received three doses of the Sinopharm vaccine and 6 received the first and second doses of the Sinopharm vaccine and the third dose of the AstraZeneca vaccine. Of the 64 patients between the ages of 30 and 50, 20 received the first and second doses of the Sinopharm vaccine and the third dose of the AstraZeneca vaccine, while 44 received all three doses of the Sinopharm vaccine. At least one month, but less than six months, had passed since the last vaccination dose in the study cases.

2.3. Collection and preparation of the samples

Nasal and nasopharyngeal swab samples were collected from each patient with respiratory symptoms who presented to the hospital. These samples, in viral transport medium (VTM), were transported to the laboratory for testing for SARS-CoV-2. The samples were stored at 2–8 °C and real-time PCR was performed within one day of sample collection.

2.4. Extraction and real-time PCR test for detection

Viral RNA was extracted from 346 samples using the High Pure RNA Isolation Kit (Roche Manheim, Germany) according to the manufacturer's instructions. One-step Real-time PCR mastermix, which included enzymes, primers, and probes, was added to 5 μL of extracted RNA as template, along with positive and negative controls and an internal control (RNAse P gene). The mixture was subjected to real-time PCR using the Qiagen rotorgene q (Germany) according to the manufacturer's instructions. The thermal cycling conditions were as follows: one cycle at 50 °C for 15 min for RT activation, one cycle at 95 °C for 15 min for RT inactivation, and 45 cycles at 94 °C for 15 s, 57 °C for 30 s for E gene detection, and 58 °C for 45 s.

2.5. Statistical analysis

Categorical variables were summarized as n (%). The $\chi 2$ test or Fisher's exact test was used to compare differences between two independent groups, where appropriate. A two-sided α of less than 0.05 was considered statistically significant. Statistical analysis was performed using R version 4.1.3 (2022-03-10)."

3. Results

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has a range of symptoms that can vary from flu-like to acute respiratory syndrome. Common symptoms include a runny nose, stuffy nose, sore throat, headache, fatigue, sneezing, dizziness, muscle pain, loss or decrease of olfactory ability, chest pain, shivering, and fever. Our study included 94 patients with confirmed COVID-19 infection, confirmed by a positive PCR test for SARS-CoV-2, and vaccinated with three doses of vaccine. We divided these patients into two age groups: 18–30 years and 30–50 years (all subjects were vaccinated with two doses of Sinopharm vaccine) (Fig. 1).

The difference between the two age groups was in the third dose of vaccine, which was either given with Sinopharm or AstraZeneca. We also divided each of the two age groups into two subgroups: the first subgroup received the Sinopharm vaccine for the third dose, while the second subgroup received the AstraZeneca vaccine for the third dose (Fig. 2). We surveyed these individuals for symptoms including body aches, sore throats, runny noses, fever, shivering, and coughs. We have recorded the exact number of individuals with each of these symptoms (Fig. 3).

In the group of individuals who received three doses of the

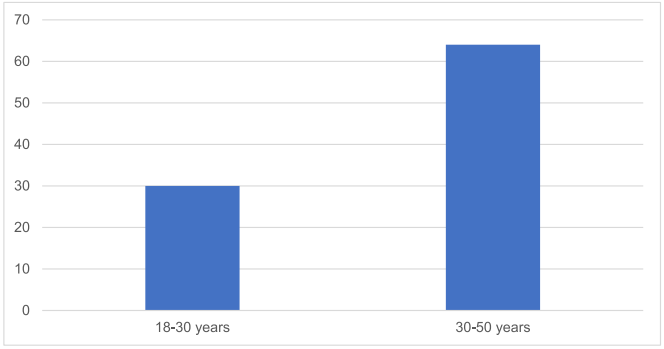

Fig. 1. Total number of patients by age.

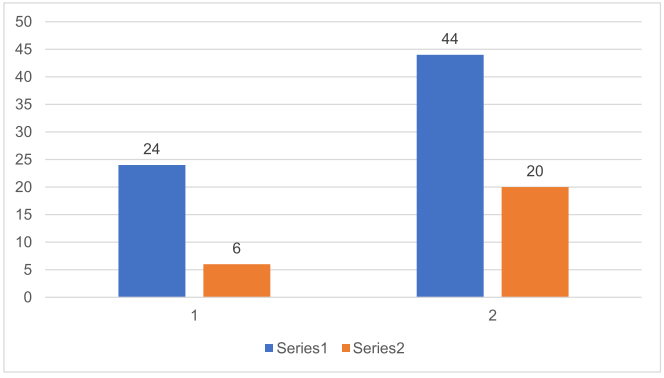

Fig. 2. Total number of patients by age and type of vaccination.

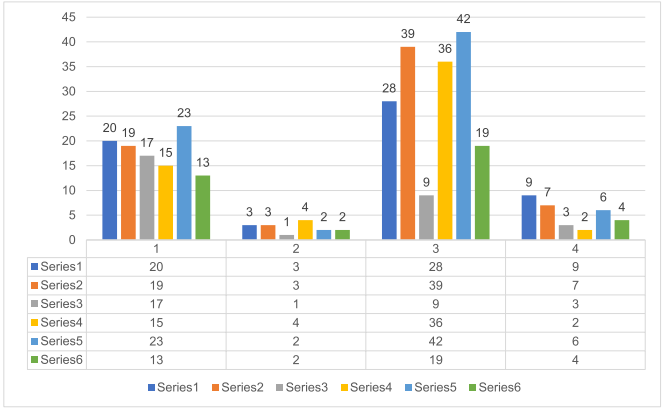

Fig. 3. Clinical manifestations of people by age and type of vaccination.

Sinopharm vaccine (SSS) and were between the ages of 18 and 30, we observed a 8.2% increase in fatigue compared to individuals in the same age range who received a different third dose (SSA). Additionally, we found that in this group, other symptoms such as fever were almost 4.1% more prevalent compared to the group that received a different third dose. We present these findings in Figs. 4 and 5 which depict the percentage of each symptom among 18-30-year-old individuals who received the Sinopharm vaccine or AstraZeneca for their third dose (see Fig. 6).

Our findings show that individuals who received three doses of the Sinopharm vaccine experienced a higher prevalence of cough and fatigue compared to those who received two doses of Sinopharm and one dose of AstraZeneca. This suggests that symptoms were more severe in the group that received three doses of Sinopharm. On the other hand, those who received two doses of Sinopharm followed by one dose of

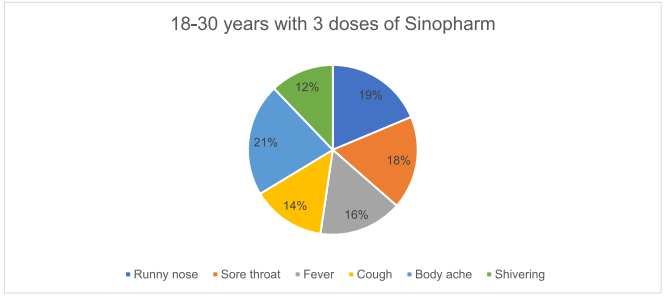

Fig. 4. Clinical manifestation in patients between 18 to 30 years old with three dose of sinopharm.

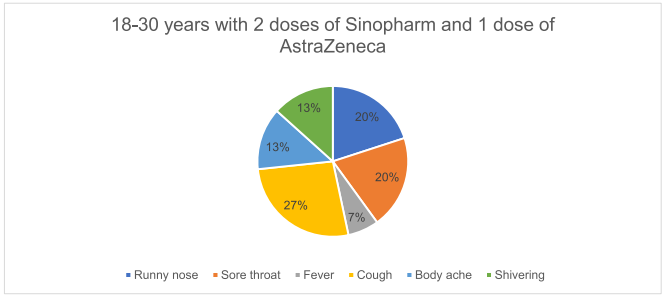

Fig. 5. Clinical manifestation in patients between 18 to 30 years old with three doses of astraZeneca.

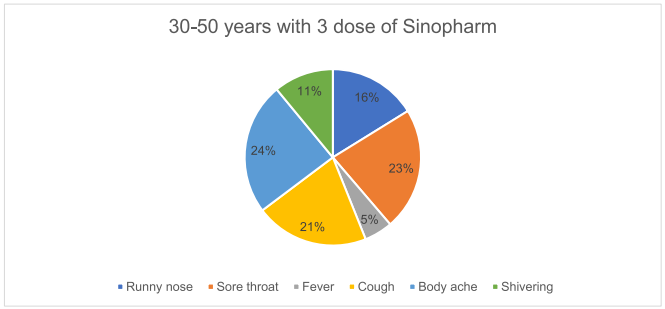

Fig. 6. Clinical manifestation in patients between 30 to 50 years old with three doses of sinopharm.

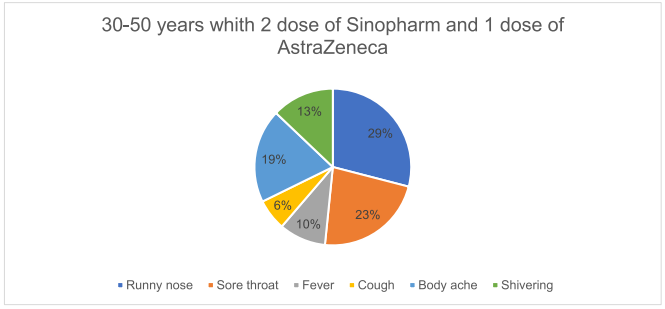

Fig. 7. Clinical manifestation in patients between 30 to 50 years old with three doses of astraZeneca.

AstraZeneca experienced symptoms similar to a mild cold, resulting in a more manageable period of illness and recovery.

According to our statistical analysis, we suggest that the immunity induced by the AstraZeneca vaccine is more effective in preventing COVID-19 infection and reducing symptoms compared to the Sinopharm

vaccine. The third or booster dose is crucial in achieving stronger immunity.

Two approaches are available for administering a third vaccine dose: administering the same vaccine as the prior doses or administering a different vaccine. The latter approach, referred to as mixing and matching vaccines, may be beneficial in terms of avoiding the development of immunity against the vaccine. This is due to the fact that certain vaccines utilize modified viruses, which may elicit an immune response and potentially result in immunity against vector vaccines. The use of mixed vaccines for the booster dose may consequently decrease the probability of generating immunity against vector vaccines.

4. Discussion

As of December 2022, there have been over 640 million confirmed cases of COVID-19 and the disease has claimed over 6 million lives globally. Coronaviruses belong to the family Coronaviridae and are characterized by their enveloped, single-stranded RNA genome. Coronaviruses can be classified into four genera: alpha, beta, gamma, and delta. Alpha and beta coronaviruses infect mammals, while gamma and delta coronaviruses infect birds. Acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are examples of pathogenic coronaviruses.

One of the key goals of any vaccine is to reduce the severity of disease symptoms. In our study, we found that only 4.5% of individuals who received two doses of the Sinopharm and AstraZeneca vaccine experienced COVID-19 symptoms, and these individuals were in the age range of 18–30 years. In addition to reducing symptom severity, vaccines are also designed to induce immunity against the disease. Our study found that individuals who received the AstraZeneca vaccine demonstrated better immunity and fewer symptoms against COVID-19 infection compared to those who received the Sinopharm vaccine.

In a study conducted by Voysey et al. in Wuhan, China, the clinical symptoms of COVID-19 patients who were vaccinated were examined. The most common symptoms were fever (46%), fatigue (44%), headache (39%), and muscle pain (17%). Our study also found that individuals infected with omicron had similar symptoms, including sore throat, sneezing, runny nose, and chest pain [39]. The ChADOx1 nCOV-19 vaccine was tested in three different continents and was found to be highly effective, with 64.1% protection after one standard dose and 70.4% protection after two doses. No safety concerns were reported. Our study also found that the AstraZeneca vaccine may be more effective as a booster compared to the Sinopharm vaccine [40].

From December 14, 2020 to April 19, 2021, a total of 324,033 patients with respiratory symptoms were investigated, and 53,270 were found to be positive for SARS-CoV-2 infection. Of these, 2050 had a history of COVID-19 vaccination. The severity and mortality rate were lower in the vaccinated group compared to those without a vaccination history [41]. Sinopharm is classified as an inactivated vaccine, which has a high safety profile but may require booster doses to establish immunological memory. Our research found that COVID-19 infection severity is higher in people who were vaccinated with Sinopharm, suggesting a lower immunogenic potential of the vaccine [42].

In a study by Alqassieh et al., the efficiency of different vaccines was compared by examining positive IgG titer. The Pfizer-BioNTech vaccine had a positive IgG titer of 99.3%, while the Sinopharm vaccine had a titer of 85.7%, which may contribute to its lower efficacy as reported in our study [43]. The most important measure of vaccine efficacy is its ability to protect against severe disease and death. An effective COVID-19 vaccine should be able to reduce the severity of disease caused by SARS-CoV-2. To assess this, careful data collection is necessary to evaluate markers of severe disease, such as hospital admission, the need for respiratory support, and ICU admission [44].

The COVID-19 vaccine has been shown to be effective in reducing all SARS-CoV-2 infections by 76% within a few months of administration, hospitalizations for COVID-19 by 87%, ICU admissions by 92%, and mortality by 84%. This protection was found to decrease to 59% against the risk of SARS-CoV-2 infections, 52% against COVID-19-related hospitalizations, and 34% against mortality within 6 months after the primary vaccine cycle, but it remained high in preventing ICU admissions at 80% [45]. The protection offered by vaccines can occur in two ways: reducing susceptibility to disease or infection (direct protection) and reducing the number of infected individuals in a population or their infectiousness (indirect protection) [46].

One important consideration in vaccine production is how the immune responses induced by the vaccine may affect SARS-CoV-2 transmission or the possibility of re-infection after vaccination [47]. Vaccinated individuals have been found to have a faster infection clearance time compared to unvaccinated individuals, with the median time for clearance of the virus from the body being 5.5 days for vaccinated individuals and 7.5 days for unvaccinated individuals. This shorter clearance time leads to a shorter overall duration of infection among vaccinated individuals [48].

According to a study by Zhu FC et al., approximately half of the recipients who received a second dose of the SARS-CoV-2 vaccine experienced headaches [49]. Randomized controlled trials in three countries have been conducted to investigate the relationship between age and vaccine side effects. One study, conducted on the ChAdOx1 nCoV-19 vaccine (AstraZeneca), found that older adults experienced lower intensity side effects [50]. The ChAdOx1 nCoV-19 vaccine has been found to have a higher rate of side effects after the first dose compared to the Sinopharm vaccine [51].

One potential side effect of the AstraZeneca vaccine that has been investigated is the occurrence of blood clots, which have been reported to occur in one in a million cases. This led the United States to limit the use of the AstraZeneca vaccine [52]. According to two studies by Ramasamy M et al., the majority of side effects seen after the second dose of both the Sinopharm and AstraZeneca vaccines were much lower than those reported after the first dose [53,54]. There is no scientific evidence to suggest that people who experience more severe vaccine side effects are better protected against COVID-19 than others [55].

In order to effectively induce antibody-mediated immunity, it is important for a vaccine to deliver a conformationally accurate protein. Ensuring the safety of vaccination is a top priority, and there is a potential risk that vaccinating individuals with acute infections could worsen SARS-CoV-2 infection [56]. The ChAdOx-1 nCoV-19 vaccine has been found to be safe and to have lower reactogenicity in older people compared to younger individuals. The immunogenicity after boost vaccination is similar across all age groups, and adverse effects and reactogenicity after boost vaccination were reported to be rare [57].

According to a study by Oguh CE, individuals aged 65–85 years old had lower neutralizing antibody responses compared to those aged 18–55 years old [47]. SARS-CoV-2 is highly contagious and can cause severe illness, particularly in crowded places like public transportation or indoor public spaces. To prevent or reduce the spread of the disease, it is important to adopt effective measures such as disinfection, environmental hygiene, and wearing masks [58].

It is worth noting that our study provided valuable insights into the necessity of booster doses and their role in reducing the severity and mortality rate of SARS-CoV-2 infection, as well as comparing the clinical manifestation of COVID-19 infection following vaccination with two different types of vaccines.

5. Conclusion

In this study, we compared the effectiveness of two vaccines, AstraZeneca (AZD1222) and Sinopharm (BIBP), as booster doses in individuals who had already received two doses of the Sinopharm vaccine. Our results showed that those who received the AZD1222 booster dose experienced less symptoms compared to those who received three doses of BIBP. These findings suggest that a booster dose may help reduce hospitalization and the severity of infection, and that using a

combination of vaccines may be effective in preventing severe COVID-19 infection. Further research should be conducted to evaluate the effectiveness of different vaccine combinations and to compare them with other vaccination strategies.

6. Recommendation

We recommend exploring the use of different vaccine combinations in the future, such as receiving two doses of the AstraZeneca vaccine followed by one dose of the Sinopharm vaccine, or being fully immunized with three doses of the AstraZeneca vaccine. Further research should be conducted to evaluate the effectiveness of these approaches and compare them with other vaccination strategies.

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Ethical guidelines

Written consent was obtained from all patients.

Authors contributions

Arash Letafati: Designed the study and conducted statistical analysis. Nooshin Eyvazzadeh, Niloofar Khakpoor, Benyamin Shamsodini: Wrote the manuscript. Fatemeh Melyani, Raha Taheri Bavili Olyaei, Elnaz Khodadoust Soufiani, Anahita Soleimani, Ayeh Khorshidian, Siavash Chalabiani, Amirhossein Garehkhani, Ghazal Mashhadi Hossein: Assisted in the research conducted in the hospital. All authors approved the final version of the manuscript.

Declaration of competing interest

The authors declare no conflict of interest.

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