Original Article

Comparative analysis of mRNA and inactivated COVID-19 vaccines: A study from Faisalabad district of Pakistan

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Abstract

Background: Pakistan has vaccinated over 122 million people. The two vaccines in widespread use are inactivated (BBIBP-CorV & Sinovac) and mRNA forms (BNT162b2 & mRNA-1273). The primary aim of this study was to compare these two forms of vaccines against unvaccinated individuals collectively and then to see which one is more efficacious.
Methods: Case–control study design was used to compare the efficacy of inactivated and mRNA vaccines against symptomatic infection, hospitalisations and mortality due to Severe Acute Respiratory Syndrome Coronavirus 2 between vaccinated and unvaccinated individuals. We derived recovery time from illness for both vaccines. Furthermore, we also compared the vaccines against similar parameters (symptomatic disease, hospitalisations and mortality). We calculated crude odds ratios for each dependent variable. p value of 0.05 or below was considered significant.
Results: Vaccinated individuals were significantly protected from hospitalisations and mortality compared to unvaccinated individuals ($p < 0.001$). There was no difference in protection from symptomatic disease ($p = 0.28$), hospitalisations ($p = 0.59$) and mortality ($p = 0.53$) between two forms of vaccines. mRNA vaccine had better recovery time than all other vaccines ($p < 0.001$).
Discussion: Our study showed that vaccinated individuals are at low risk of hospitalisations and mortality even without a booster and both vaccine forms are equally effective at preventing hospitalisations and mortality.

Keywords

COVID-19, mRNA vaccine, inactivated vaccine, Pakistan, infectious disease

Background

Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) has infected over 520 million people globally till date and over 6 million people have lost their lives due to COVID-19.[1]

South east Asia has reported over 58 million cases till date and 0.78 million deaths due to COVID-19 pandemic (World Health Organization (WHO) 2022).[2]

Pakistan has reported over 1.5 million cases of SARS-CoV-2 and till date more than 30,000 lives are lost.[3] Pharmacological and nonpharmacological strategies have been tried to lessen the mortality and morbidity burden. Vaccination remains the main tool in controlling this pandemic.

Worldwide over 11 billion doses of vaccine have been administered so far, which has played pivotal role in curtailing this pandemic (WHO, 2022).[4]

Pakistan has thus far vaccinated over 122 million people with different types of vaccines which include BBIBP-CorV (Sinopharm), Sinovac, CanSino, BNT162b2 (Pfizer), mRNA-1273 (Moderna) and Sputnik (Health Advisory Platform Ministry of National, 2022).[5]

This vaccination drive resulted in reduction of cases and deaths not only globally but also in Pakistan. Resultantly,

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by the end of 2021, most of the countries were lifting their lockdowns due to vaccine-derived immunity.

Two forms of vaccines which are most commonly used in Pakistan are inactivated type (Sinopharm and Sinovac) and mRNA type (Pfizer and Moderna) (NADRA, 2022).[6]

Faisalabad is the third largest city of Pakistan according to population criteria and is situated in the largest province Punjab. The total area of Faisalabad District is $5,857 \text{ km}^2$ (2,261 sq miles) and according to census of 2017, total population is 7,882,444 out of which 4,038,932 are males and 3,842,684 are females. Faisalabad is a major industrial and distribution centre because of its central location in the region with well-developed connecting roads, rails, and air transportation. Agriculture is also an important hallmark of this city.

The primary aim of this study was to compare these two forms of vaccines against unvaccinated individuals collectively and then to see which form (inactivated vs mRNA) is more efficacious during the time frame when Delta and Omicron were prevalent in Faisalabad district of Pakistan.

Methods

Study design

Efficacy of inactivated and mRNA form of vaccines against symptomatic infection with SARS-CoV-2 and its impact in preventing hospitalisations and mortality due to COVID-19 among vaccinated and unvaccinated individuals were assessed using a case–control study design.

We further compared mRNA and inactivated form of vaccines in preventing hospitalisation and mortality. Recovery time from COVID-19 infection was also calculated from the time patient reported to health facility till symptom free for 24 h which was transformed into two groups early (less than 14 days) and late (equal and more than 14 days) recovery time.

Case–control designs are considered powerful enough to estimate vaccine effectiveness (VE) and are used extensively for estimating effectiveness of influenza vaccines and vaccines against other respiratory viruses.[7,8]

Study time. Data included were from 15 July 2021 to 31 March 2022.

Data collection

Electronic record of all the individuals aged 12 and above, who were tested for COVID-19 during the above-mentioned time interval was analysed using the COVID-19 Dashboard of Faisalabad District. The COVID-19 dashboard is an integrated dashboard linked electronically with all hospitals and laboratories; both public and private, operating in district Faisalabad. Details of the all individuals who test positive for COVID-19 in any of these facilities are uploaded daily. Hospitals linked with this dashboard also upload the clinical status of all hospitalised COVID-19 patients and their outcomes, that is, intensive care admission, recovery, or death.

Individuals were divided into case and control groups depending on positivity of the COVID-19 test. The vaccination status of cases and control groups was compiled from National Database and Registration Authority (NADRA) of Pakistan.

During this period, totally 252,793 samples were taken. In all, 33,797 samples were drawn from symptomatic patients from OPDs of public and private hospitals in Faisalabad. In total, 734 samples out of 33,797 were rejected by the laboratory. Out of these, 53 were vaccinated with AstraZeneca, 117 with CanSino, 53 with sputnik and 42 with Pak-vac. In all, 1,716 were partially vaccinated and 6,673 had a booster dose. All of these were excluded from the study. In total, 15,579 were selected out of which 8,830 matched cases and controls were selected according to age and sex to minimise confounding.

To maintain the internal validity and quality of data, only those individual datasets were accepted in which all the information had been filled, that is, age, sex, COVID-19 results, vaccination status, vaccine type inoculated, clinical condition and hospitalisation status.

Inclusion and exclusion criteria

Inclusion criteria:

- All individuals, that is, males/females above the age of 12 years were included in the study
- All individuals fully vaccinated with inactivated or mRNA form were included.

Exclusion criteria:

- Individuals less than age 12 years were excluded.
- Partially vaccinated individuals were excluded.
- Individuals vaccinated with other forms of vaccines (AstraZeneca, Sputnik, Johnson and Johnson and CanSino) were excluded.
- Asymptomatic COVID-19 individuals were excluded.
- Individuals who received booster doses of vaccines were excluded.

Statistical analysis

Scale and categorical variables were identified. Age was divided into two groups: group 1 (12–44 years) and group 2 (45 years and above). Stratification of both male and female group was done into young (12–44 years) and old age (45 years and above) and was done to match cases with control group.

Recovery time was calculated from the time patient reported to health facility till symptom free for 24 h which was transformed into two groups early (less than 14 days) and late (equal and more than 14 days) recovery time.

Chi square and Fischer's Exact tests were applied to determine the odds of symptomatic disease due to SARS-CoV-2, hospitalisation and recovery after COVID-19 infection among vaccinated and unvaccinated groups. Recovery time

from illness was also calculated. We also calculated crude odds ratios for each dependent variable mentioned above. *p* Value of 0.05 or below was considered significant. Statistical analysis was done using SPSS version 21.

Ethical approval:. Formal ethical approval was granted before data collection commenced. The study was registered with the research department of district health authority, Faisalabad under the letter number *MIS/General/8151, dated 20*th *May, 2022.*

Results

The study sample included total of 8,830 individuals in which 4,745 were males (53.7%) and 4,085 were females (46.3%). Total cases with PCR-positive results were 4,069 (46.1%) and with negative results were 4,761 (53.9%). Total individuals found vaccinated against COVID-19 were 2,645 (30%) and unvaccinated were 6,185 (70%). Those who were vaccinated, 2,014 (76%) were vaccinated with inactivated virus vaccine and 631 (24%) with mRNA vaccine.

All individuals were stratified according to their gender (male and female) and age groups (12–44 years, 45 years and above). For each group and subgroups, odds ratios were calculated along with the *p* value using chi square and Fischer's Exact test.

Table 1 shows odds ratio for symptomatic COVID-19 infection in those who were vaccinated as compared to those who were not vaccinated. Overall, both types of

vaccines seem to be ineffective in preventing the symptomatic disease.

All vaccinated individuals were found to be protective against hospitalisation after COVID-19 as compared to unvaccinated individuals. Table 2 shows the full details.

Vaccinated individuals were found to be protective against mortality from COVID-19 as compared to unvaccinated individuals. Table 3 shows the full details.

While comparing the two forms of vaccines, our analysis showed that there was no significant difference between the two forms of vaccines in preventing symptomatic COVID-19 infection. Table 4 shows the details.

Hospitalisation rate and mortality were very low among vaccinated individuals; therefore, no significant association was found, and results showed no significant difference in both forms of vaccines. Tables 5 and 6 show the details of the results.

mRNA form of vaccine showed a mean recovery period of 4.9 ± 5.59 among all age groups as compared to Inactivated form of vaccine which showed mean recovery period of 5.7 ± 6.77 days. This mean difference in recovery period between two forms of vaccines was found to significant (*p* value 0.007).

Discussion

Our study showed the effectiveness of inactivated and mRNA vaccines in preventing hospitalisations and mortality. Moreover, it provides reassurance that there is no

Table 1. Symptomatic COVID-19 infection among vaccinated and unvaccinated individuals (odds ratio).

Gender of the patient	Age (years)	Vaccination status	PCR detected *n* (%) 4,069 (46.1)	PCR not detected *n* (%) 4,761 (53.9)	Odds ratio	95% CI		*p* Value
						Lower	Upper	
Male	12–44	Vaccinated	492 (48.6)	520 (51.4)	1.31	1.13	1.52	<0.001
		Not vaccinated	855 (42)	1183 (58)	Ref			
	45 and above	Vaccinated	253 (47.6)	279 (52.4)	0.87	0.71	1.07	0.19
		Not vaccinated	593 (51)	570 (49)	Ref			
Female	12–44	Vaccinated	304 (43.9)	389 (56.1)	0.91	0.76	1.09	0.31
		Not vaccinated	829 (46.1)	968(53.9)	Ref			
	45 and above	Vaccinated	176 (43.1)	232 (56.9)	0.83	0.66	1.04	0.11
		Not vaccinated	567 (47.8)	620 (52.2)	Ref			

Table 2. Hospitalisation with COVID-19 among vaccinated and unvaccinated individuals.

Gender of the patient	Age (years)	Vaccination status	Hospitalised N (%) 134 (3.3)	Not hospitalised N (%) 3935 (96.7)	Odds ratio	95% CI		*p* Value
						Lower	Upper	
Male	12–44	Vaccinated	2 (0.4)	490 (99.6)	0.38	0.08	1.78	0.23
		Not vaccinated	9 (1.1)	846 (98.9)				
	45 and above	Vaccinated	7 (2.8)	246 (97.2)	0.32	0.14	0.72	0.004
		Not vaccinated	48 (8.1)	545 (91.9)				
Female	12–44	Vaccinated	0 (0.0)	304 (100.0)	a	a	a	a
		Not vaccinated	13 (1.6)	816 (98.4))				
	45 and above	Vaccinated	4 (2.3)	172 (97.7	0.24	0.08	0.66	0.03
		Not vaccinated	51 (9.0)	516 (91.0)				

a: No statistics are computed because hospitalised or not is a constant (0).

Table 3. Mortality with COVID-19 between vaccinated and unvaccinated individuals.

Gender of the patient	Age (years)	Vaccination status of the patient	Current status of the patient		Odds ratio	95% Confidence interval		p Value
			Recovered N (%) 3,963 (99.2)	Dead N (%) 106 (0.2)		Lower	Upper	
Male	12–44	Vaccinated	491 (99.8)	1 (0.2)	3.47	0.42	28.91	0.27
		Not vaccinated	849 (99.3)	6 (0.7)				
	45 and above	Vaccinated	247 (97.6)	6 (2.4)	3.14	1.32	7.48	0.007
		Not vaccinated	551 (92.9)	42 (7.1)				
Female	12–44	Vaccinated	304 (100)	0 (0)	. a			
		Not vaccinated	820 (98.9)	9 (1.1)				
	45 and above	Vaccinated	173 (98.3)	3 (1.7)	4.26	1.3	13.96	0.014
		Not vaccinated	528 (93.1)	39 (6.9)				

a: No statistics are computed because hospitalised or not is a constant (0).

Table 4. Comparative analysis of symptomatic COVID-19 infection between inactivated and mRNA vaccines.

Gender of the patient	Age (years)	Vaccine form	PCR results		Value	95% Confidence interval		p Value
			Detected N (%) 1,225 (46.4)	Not detected N (%) 1,420 (53.6)		Lower	Upper	
Male	12–44	Inactivated form	346 (55.4)	278 (44.6)	2.06	1.59	2.67	<0.001
		mRNA form	146 (37.6)	242 (62.4)				
	45 and above	Inactivated form	204 (43.5)	265 (56.5)	0.22	0.12	0.41	<0.001
		mRNA form	49(77.8)	14(22.2)				
Female	12–44	Inactivated form	232 (41.7)	325 (58.3)	0.63	0.44	0.92	0.017
		mRNA form	72 (52.9)	64 (47.1)				
	45 and above	Inactivated form	139 (38.2)	225 (61.8)	0.12	0.05	0.27	<0.001
		mRNA form	37 (84.1)	7 (15.9)				

Table 5. Comparative analysis of hospitalisation with COVID-19 among individuals vaccinated with inactivated and mRNA vaccines.

Gender of the patient	Age (years)	Vaccine form	Admission status		Odds ratio	95% Confidence interval		p Value
			Hospitalised N (%) 13 (1.1)	Non-hospitalised N (%) 1,212 (98.9)		Lower	Upper	
Male	12–44	Inactivated form	2(0.6)	344 (99.4)	.a			
		mRNA form	0 (0.0)	146 (100.0)				
	45 and above	Inactivated form	4 (2.0)	200 (98.0)	0.31	0.07	1.42	0.135
		mRNA form	3 (6.1)	46 (93.9)				
Female	12–44	Inactivated form	0 (0.0)	232 (100.0)	.a			
		mRNA form	0 (0.0)	72 (100.0)				
	45 and above	Inactivated form	4 (2.9)	135 (97.1)	.a			
		mRNA form	0 (0.0)	37 (100.0)				

a: No statistics are computed because hospitalised or not is a constant (0)

difference in efficacy of mRNA and inactivated forms of COVID-19 vaccines.

Overview, Mechanism of actions, and Individual effectiveness of mRNA and Inactivated vaccines

Spike protein (S-protein) on the surface of SARS-CoV-2 has a key role in COVID-19 pathogenicity and its transmission. It is the fundamental structural unit that recognises and binds to angiotensin-converting enzyme receptors of host cells. Hence, it makes the S-protein an important target for neutralising antibodies and therefore for the development of vaccines.[9]

Genetic/nucleic acid or mRNA vaccines work on the principal of translation of an immunogenic protein by genetically engineered RNA/DNA.[10] A study involving 232,268 COVID-19 cases, found that two doses of the

Table 6. Comparative analysis of mortality with COVID-19 among individuals vaccinated with inactivated and mRNA vaccines.

Gender of the patient	Age (years)	Vaccine form	Status of the patient		Odds ratio	95% Confidence interval		p Value
			Recovered N (%) 1 215 (99.2)	Dead N (%) 10 (0.8)		Lower	Upper	
Male	12–44	Inactivated form	345 (99.7)	1 (0.3)	.a			
		mRNA form	146 (100.0)	0 (0.0)				
	45 and above	Inactivated form	200 (98.0)	4 (2.0)	2.13	0.38	11.96	0.329
		mRNA form	47 (95.9)	2 (4.1)				
Female	12–44	Inactivated form	232 (100.0)	0 (0.0)	.a			
		mRNA form	72 (100.0)	0 (0.0)				
	45 and above	Inactivated form	136 (97.8)	3 (2.2)	.a			
		mRNA form	37 (100.0)	0 (0.0)				

a: No statistics are computed because hospitalised or not is a constant (0).

Pfizer vaccine had a VE of 97% against symptomatic infection, 97.2% against hospitalisation, 97.5% against intensive care unit (ICU) admission and 96.7% against death.[8] Two doses of the Moderna vaccine offer a VE of 93% against hospitalisation in post-marketing surveillance studies in the United States.[11]

Inactivated vaccines use enfeebled or inactivated coronavirus which itself does not cause illness but induce an immune response in the host. Sinovac and Sinopharm were developed on this principle.[9]

Sinovac showed a VE of 65.9% against symptomatic infection, 87.5% for hospitalisation, 90.3% for ICU admission and 86.3% for death in a large cohort of Chilean population.[12]

Sinopharm vaccine showed a VE of 94.3% (95% CI, 92.2–95.9%) for two doses of the BBIBP-CorV Sinopharm vaccine in the prevention of symptomatic SARS-CoV-2 infection, 60.5% (95% CI, 7.9–82.9%) in reducing hospitalisation with SARS-CoV-2 and 98.6% (95% CI, 94.2–99.6%) in preventing death from SARS-CoV-2 as compared to unvaccinated individuals in an elderly cohort of Pakistani population.[13]

All COVID vaccines are usually well tolerated, and adverse events associated with these vaccines are very rare and of mild severity.[14]

Comparison with previous literature and strengths and limitation of study

Age has been found to be a significant variable to determine the course of disease. This is in accordance with existing knowledge. Choi et al.[15] reported that mortality and length of hospital stay increase with increasing age and 18% mortality in patients of age 70 or above.

We observed no significant difference in protection from symptomatic disease between vaccinated and unvaccinated individuals possibly due to more than 6 months of time difference between two doses of vaccines and we excluded all individuals who had received booster doses.

We observed no significant difference in hospitalisation and in the final outcome (death or recovery) after having either mRNA vaccine or inactivated virus vaccine. Though, this is in contrary to, what Premikha et al.[16] had reported. They spotted that the individuals who had Sinopharm and SinoVac vaccine are 2.37 and 1.62 times more prone to contract COVID when compared with individuals who had Pfizer/BioNtech/Comirnaty vaccine.[16]

To our knowledge, no real-world study has shown direct comparison between two types of vaccines, that is, mRNA and inactivated in recovery time after contacting COVID-19. We observed that patients who received mRNA type vaccine had significant early recovery as compared to those having inactivated vaccines. This can provide basis to look for treatment for Long COVID. Thompson et al.[17] reported the reduction in viral load to 40% and shorter duration of illness with 2.3 less days spent on bed in individuals who had mRNA type vaccine as compared to unvaccinated.

Since the early days of vaccination programs to curtail COVID-19 Pandemic, there have been misleading news about better efficacy and outcomes of mRNA type vaccines over inactivated vaccines. Similarly, the effectiveness of these vaccines against different variants was questioned. Laboratory studies also reported minimal efficacy of inactivated vaccines as compared to mRNA. Furthermore, theoretically, experts were of opinion that inactivated vaccines have broader range of immunity as these can elicit response against viral proteins other than spike protein. To counter that, Singapore government published an article to clarify these myths. However, no real-time data in a large population cohort are available so far to give robust evidence by comparing these two vaccines.[18–20]

One of the strengths of our study is a large cohort size and we have effectively showed that both vaccines are equally effective in preventing severe disease from COVID-19 and had similar adverse events profile. The only difference was shorter time to recover in patients who had mRNA type vaccine.

Omicron virus was widely prevalent during the study period and was also detected in Pakistan,[21] so the effectiveness of both type of vaccines is same against Omicron as well. Due to the lack of access to genome testing, we were

unable to comment on effectives of both vaccines on every emerging variant.

Nonetheless, given the observational nature of this study, we may have missed SARS-CoV-2 cases which did not present for testing. It is possible that more individuals who were vaccinated did not get tests even if they had suggestive symptoms due to the false impression of total COVID immunity after vaccination. Moreover, given that a large population of Pakistan lives in rural areas, they may have struggled to access testing. Furthermore, we cannot predict about vaccine efficacy on asymptomatic transmission.

Another important limitation was the lack of genomic testing facilities which meant that although we can report this vaccines effectiveness for the strains commonly seen in Pakistan, we cannot comment on the protection it confers against all the variants of concern (B.1.351, P1).

Conclusion

Our study showed that both mRNA and inactivated form of vaccines are highly effective in preventing hospitalisations and mortality due to COVID-19 as compared to unvaccinated individuals even without a booster dose. Moreover, both forms of vaccines do not differ much in preventing hospitalisations and mortality due to COVID-19.

We observed no difference in protection from symptomatic disease due to COVID-19 between vaccinated and unvaccinated individuals and therefore it is necessary to get the booster dose to enhance the immunity. Early recovery from illness after getting vaccine will help researchers to look for the treatment of Long COVID.

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