ABSTRACT

**Background:** The advent of a vaccine for COVID-19 has been a breakthrough to prevent infection from the virus. The objective of this study was to compare the frequency and severity of COVID-19 infection among vaccinated and non-vaccinated healthcare workers (HCWs).

**Methods:** This was a prospective cohort study conducted on HCWs at Liaquat National Hospital, Karachi. The participants n=2500 were recruited before (November 2020 to January 2021) and after vaccination (February 2021 to May 2021). A detailed history including vaccination status, from the patients, was taken by treating physicians. All recruited patients were followed up for three months for upper respiratory tract symptoms. Chi-square test/Fisher exact was applied for associations. Poisson regression was applied to compute the incidence rate. A p-value ≤0.05 was defined as statistically significant.

**Results:** The 2500 participants were included in each group of this cohort study. The median age of unvaccinated and vaccinated healthcare workers was 33 (27 - 42.5) years and 35(29 - 45) years respectively. During three months, 166 (6.64%) workers acquired COVID-19 infection yielding an incidence of 7.6 per 10,000 person-days. All the cases were mild and were managed at their home during their quarantine period. Within 3 weeks after the first dose, 2(0.08%) workers had COVID-19 infection with an incidence rate of 0.4 per 10,000 person-days. After administration of the second dose, 4(0.16%) found COVID-19 positive within 21 days with an incidence of 0.8 per 10,000 person-days.

**Conclusion:** Vaccine provides significant (p<0.001) protection against COVID-19 infection in healthcare workers in a highly infective environment.

**Keywords:** Health Care Worker; Immunization; Vaccination; COVID-19.

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INTRODUCTION
At the start of February 2021, Pakistan launched a nationwide immunization program against COVID-191. The priority was given to healthcare workers (HCWs) from the beginning of the pandemic as they were directly exposed. The advent of a vaccine for COVID-19 has been a breakthrough to prevent infection from the deadly virus. Different vaccinations have been offered by different countries to their populations, all of which have shown reasonable efficacy and adverse effect profile. The efficacy of the Chinese vaccine has been recently reported as 50%, while a 65% efficacy was reported from Indonesia and Pakistan in the general population2-3.

Healthcare workers (HCWs) have a critical element in teaching the overall public approximately the supply of the vaccine and its implications within the coming years4. In Pakistan, HCWs are being prioritized for an early primarily Chinese-based COVID-19 vaccination program4. This is being mandated at some point in the West, prioritizing high-hazard groups, and HCWs being diagnosed as such. Therefore, it is far critical to recall HCW attitudes in the direction of the COVID-19 vaccine because it will cause higher dissemination of expertise amongst the overall public. Given the paucity of statistics concerning vaccines in South-East Asia among HCWs, the study was carried out to mark the significance of the Sinopharm vaccine among HCWs.

Literature is available regarding vaccine effectiveness among healthcare workers5-6. Studies determining the incidence of post-vaccine among healthcare workers are limited in Pakistan6-7. Therefore, the study aimed to compare the frequency of COVID-19 infection among vaccinated and non-vaccinated healthcare workers regarding Sinopharm administration.

METHODS
This prospective cohort study was conducted in Liaquat National Hospital, Karachi. Approval was taken from the institutional ethical review committee. Healthcare workers from November 2020 to January 2021 were unvaccinated while healthcare workers from February 2021 to May 2021 were vaccinated. All employees were recruited and followed till 12 weeks after receiving the second dose of vaccination. Healthcare workers who resigned and died due to another cause except for COVID-19 infection within 3 months of study duration were excluded from the study.

HCWs were instructed to report symptoms they experienced during this period. The results of COVID-19 PCR were documented and the HCW was followed up for clinical outcome. Vaccine effectiveness was assessed on the following 4 parameters; decrease in overall incidence in the study population, the need for COVID-19 hospitalization, decrease in disease severity, oxygen requirement and decrease in mortality after vaccination.

Another study reported that the COVID-19 positive rate was 52% and 48% among unvaccinated and vaccinated healthcare workers respectively8. Taking a 95% confidence interval and 80% power, a sample of 2452 healthcare workers per group was required. Data were analyzed using Stata version 16. Frequencies/percentages were computed to summarize categorical variables. Numerical variables were expressed as median with an interquartile range after assessing the normality assumption. Chi-square test/Fisher exact was applied. Poisson regression was applied to compute the incidence rate. Effects of covariates were adjusted to calculate adjusted incidence. The exposure command was used to account for personal time in the model. A p-value ≤0.05 was defined as statistically significant.

RESULTS
A total of n=2500 participants were included in each cohort. The median age of unvaccinated and vaccinated healthcare workers was 33 (27 - 42.5) years and 35 (29 - 45) years respectively. Age groups were significantly different among the unvaccinated and vaccinated groups (Table 1). Figure 1 depicts gender distribution among the two groups which were significantly different (p<0.001). Risk exposure is displayed in Figure 2 among the two groups. The distribution of risk exposure was significant among the group (p<0.001).

Table 1: Comparison among unvaccinated and vaccinated healthcare workers.

<table>
<thead>
<tr>
<th>Age in groups</th>
<th>Unvaccinated Frequency n (%)</th>
<th>Vaccinated Frequency n (%)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young (18-39 years)</td>
<td>1680 (67.2)</td>
<td>1519 (60.8)</td>
<td>**&lt;0.001</td>
</tr>
<tr>
<td>Middle (40-59 years)</td>
<td>709 (28.4)</td>
<td>847 (33.9)</td>
<td></td>
</tr>
<tr>
<td>Elderly (60 years and above)</td>
<td>111 (4.4)</td>
<td>134 (5.4)</td>
<td></td>
</tr>
</tbody>
</table>

**Significant at p<0.01.
During three months, out of 2500 unvaccinated healthcare workers, 6.64% of workers acquired COVID-19 infection. Among the unvaccinated group, 84.9% were symptomatic COVID-19 cases with the most frequent symptom of fever (70.9%) followed by cough (66%), muscle ache (53.2%), sore throat (37.6%) and shortness of breath (9.2%). All the cases were mild and did not require hospital admission and were managed at their home during their quarantine period. The median days to symptom resolution were 7 (3 – 10) days. Out of 166 (6.64%), 15 (9%) developed hypoxia. The incidence rate of COVID-19 infection among unvaccinated people is presented in Table 2. Within 3 weeks of the first dose, 2 (0.08%) workers came out to be COVID-19 infected. Both were female, symptomatic and directly involved in patient care. One of them had mild symptoms of cough and sore throat and the other had symptoms of shortness of breath and muscle ache. Symptoms of both were resolved within a week. Table 2 represents the incidence rate of COVID-19 infection within 21 days of the first vaccine dose. The incidence rate among sub-groups of other study variables is also represented in Table 2.
Crude incidence rate of COVID-19 infection was 99% lower in the vaccinated group than in the unvaccinated group. The incidence rate was also significantly lower in the vaccinated group as compared to the unvaccinated when effects of age, gender, risk exposure and person-days were adjusted (Table 3).

Table 2: Incidence rate of COVID-19 among healthcare workers.

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Unvaccinated</th>
<th>Vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Within 3 months</td>
<td>Within 21 days after dose 1</td>
</tr>
<tr>
<td>Frequency [n]</td>
<td>2500</td>
<td>2500</td>
</tr>
<tr>
<td>Events [n]</td>
<td>166</td>
<td>2</td>
</tr>
<tr>
<td>Person-days</td>
<td>217307</td>
<td>52483</td>
</tr>
<tr>
<td>Incidence rate per 10,000 person-days</td>
<td>7.6</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Age in groups

<table>
<thead>
<tr>
<th>Age group</th>
<th>Unvaccinated</th>
<th>Vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young age (18-39 years)</td>
<td>8.7</td>
<td>0.3</td>
</tr>
<tr>
<td>Middle age (40-59 years)</td>
<td>6.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Elderly (60 years and above)</td>
<td>7.3</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Gender

<table>
<thead>
<tr>
<th>Gender</th>
<th>Unvaccinated</th>
<th>Vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>7.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Female</td>
<td>8.8</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Risk Exposure

<table>
<thead>
<tr>
<th>Risk Exposure</th>
<th>Unvaccinated</th>
<th>Vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Directly exposed</td>
<td>8.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Indirectly exposed</td>
<td>6.9</td>
<td>0.0</td>
</tr>
</tbody>
</table>

#The incidence rate is expressed as 10,000 person-days.

Crude incidence rate of COVID-19 infection was 99% lower in the vaccinated group than in the unvaccinated group. The incidence rate was also significantly lower in the vaccinated group as compared to the unvaccinated when effects of age, gender, risk exposure and person-days were adjusted (Table 3).

After administration of the second dose, 4 (0.16%) were found to be COVID-19 positive within 21 days and all were males and young. 3 of them were directly involved in patient care and only one case was asymptomatic. One patient had only symptoms of fever which were resolved in three days. One had symptoms of fever, muscle ache and cough and the symptoms were resolved within a week. One case presented with symptoms of fever, sore throat, muscle ache and flu and within 5 days symptoms were resolved. None of them required hospital care nor developed hypoxia. The crude incidence rate and adjusted incidence rate for COVID-19 were significantly lower in the vaccinated group than in the unvaccinated group (Table 3).

Only 6(0.24%) were infected with COVID-19 within 6 weeks of administering the second dose of vaccine, 5 of them were belonging to a younger age group, male and symptomatic COVID-19 case. 2 of these 6, were not directly involved in patient care. Presenting symptoms were fever (83.3%), cough (50%), muscle ache (50%), sore throat (33.3%) and flu (16.7%) and symptoms were resolved within 7 days of onset. Hospital admission was not required and there was no reported hypoxia among these 6 infected workers. Adjusted COVID-19 incidence was 92% lower in vaccinated people than unvaccinated group (Table 3).
Within 12 weeks of injecting the second dose, 23 (0.92%) employees came out to be COVID-19 positive. Most of them were males (56.5%) and directly related to patient care (78.3%). 69.6% and 30.4% were young and middle-aged respectively. 17.4% of cases were ineffective, researchers have promoted herd immunity as a means of containing the present outbreak. A person can effectively and safely defend themselves against COVID-19 through vaccination. Even though the COVID-19 virus has been studied extensively since it was originally discovered, there are still many unanswered questions.

Most studies done previously in Pakistan focused on the general population and include people who stayed at home during isolation. As the risk of infection was highest among the healthcare workers who have been the heroes of the pandemic; throughout the world and continued working and got high exposure during their work hours, the data from this group is important to determine the actual effectiveness of the vaccine in high contact scenarios. Hence this study determines the proportion and severity of infection among the vaccinated and non-vaccinated, high-risk group of healthcare professionals working on the frontline in one of the largest tertiary care hospitals in Pakistan.

In our study, 166 COVID-19 positive HCWs were identified during the pre-vaccination period whereas only 23 cases were COVID-19 positive following 3 months post-vaccination period (after the second dose). None of the patients required hospital admission and all had mild disease. Compared to COVID-19 data from the general population, 64.2%
of the cases were reported to be moderate to severe in nature. In this study, there were no mortalities reported in the pre or post-vaccination period in HCWs whereas data from the general population showed a mortality rate of 20.6% in COVID-19 positive patients. This difference in the severity of the disease and mortality may be because HCWs have quick access to hospital care and direct contact with doctors for their treatment compared to the general population.

Unvaccinated individuals have an 11 times greater risk of death from COVID-19 infection than those who are fully vaccinated. A study in the US reported that vaccinated people were 10 times less likely to be admitted to hospital and five times less likely to be infected than unvaccinated people. This study demonstrated significant effectiveness against COVID-19 infection, with a decrease in incidence rate from 7.6 per 10,000 person-days in the pre-vaccination period to 0.8 per 10,000 person-days following 21 days after the second dose of vaccination. This is consistent with the data gathered from another part of the US. In this study, the frequency of middle age and the elderly population was significantly higher among the vaccinated group even though this group of population is more vulnerable, a lower incidence rate was observed in the vaccinated group indicating the promised vaccine efficacy. Some studies showed a decline in the effectiveness of the vaccine in the elderly population whereas our study showed decreased incidence of COVID-19 cases in all vaccinated age groups, including the elderly population.

Not only with Sinopharm but all other vaccines showed a considerable decrease in the incidence rate of COVID-19 infection. A trial from the USA demonstrated 95% effectiveness of the Pfizer/Bio-tech vaccine in the general population. Comparable results were seen with Moderna Vaccine. Nation-based surveillance has high heterogeneity in populations with different exposure intensities to virus. Though a clear effect was seen after the vaccination in clinical trials data from high-risk subgroups is of great importance. Brazilian Double blinded RCT is being conducted where the effect of inactivating vaccine in HCW will be ground breaking and will demonstrate the real-world effectiveness of the vaccine in high-risk group. The severity of the disease was also decreased and symptoms were considered mild in vaccinated HCWs. Jara et al reported 87.5% prevention of hospitalization and 90.3% prevention of ICU admissions among a fully vaccinated population.

The decrease in the incidence rate of COVID-19 infection after 1st dose is around 90% in our study, pointing out the early effect of the vaccine and is consistent with international data. Hence, the impact of vaccination on our HCWs was evident even before the application of the second dose, but the data demonstrated a gradual increase in the incidence rate of COVID-19 from 0.8 per 10,000 person days at 21 days after the second dose to 1.2 per 10,000 person days at 84 days after the second dose of vaccination. The number of cases increases after 3 months of the vaccine when compared to 3 weeks, which shows a possible progressive fall of protection and need for a booster. That was also seen in other studies.

Our study has a few limitations. Healthcare workers were first randomly divided into two groups. One group was studied for COVID-19 status in the pre-vaccination period while the other group was studied after receiving the vaccination, hence, due to this random split, the frequency of directly exposed workers was significantly higher in the unvaccinated group. Although we have paid special attention and conducted several classes for staff to perform nasal PCR inappropriate techniques can alter the estimate of vaccine effectiveness. Moreover, during the period of study, only one vaccine type was available and no comparison with other vaccines was performed.

CONCLUSION
Two doses of the Sinopharm vaccine are effective among Health Care Workers, in decreasing incidence levels and the severity of disease including hospitalization and oxygen demand.

ACKNOWLEDGMENTS
The authors would like to acknowledge the colleagues and para-medical staff for their assistance.

CONFLICT OF INTEREST
The authors declared no conflict of interest.

ETHICS APPROVAL
Approval was taken from the Liaquat National Hospital ethics committee.

PATIENT CONSENT
Informed consent was taken from the patients.

AUTHORS’ CONTRIBUTIONS
FA conceptualized the study. SA and FA designed the study protocol. AA, KA and ND were involved in data collection. AA and ND performed data analysis, result write-up and interpretation. AA, KA and SS wrote the initial draft of the study. FA and SA critically reviewed and revised the initial draft. All authors read and approved the manuscript.

REFERENCES