Prevalence of overall side effects after COVID-19 vaccines

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ABSTRACT

Objective: The development of successful COVID-19 vaccines depends on both effectiveness and safety. Vaccine hesitancy is impacted by vaccine side effects. Therefore, this study aimed to evaluate the post-vaccination symptoms and adverse effects in the adult population who had received either one or two doses of the inactivated vaccines Sinopharm and Sinovac.

Methodology: This was a multicenter, cross-sectional study that was conducted in different hospitals, using a random sampling technique. The duration of the study was about six months, from July 2022 to December 2022, after receiving ethical approval. A total of 400 participants, aged 18 to 59 years, of both genders, who were able to give consent, were currently residing in Karachi, and had received at least one dose of the inactivated COVID-19 vaccines, Sinopharm and SinoVac, were included in the study. The frequency of the side effects following the first and second doses of COVID-19 vaccination was expressed in percentages, while demographics were shown as mean and standard deviation.

Results: The study findings showed that out of 400 participants, 262 (65.5%) were male and 138 (34.5%) were female, with a mean age of 41 years. Around 284(71.0%) participants received SinoVacvaccine and 116(29.0%)received Sinopharm, of whom 42(10.5%) received the first dose and 284(71.0%) received both doses of the inactivated vaccine. The most commonly reported side effect after 1st dose, fever, was reported by 212(53.0%) participants, and out of them, 52(24.5%) reported it to be severe. This was followed by pain, burning and swelling at the site of the injection in decreasing

order of frequency. Following the 2nd dose, fever was reported by 152(38.0%) participants, and in terms of severity, this was the only symptom reported as severe by the most participants.

Conclusion: This study concluded that both Sinopharm and Sinovac are generally safe to administer, and the overall side effects are mild, non-life threatening, and do not require hospital admission. The subjective level of most vaccine recipients was generally satisfactory.

Keywords: COVID-19 vaccines, Sinopharm and Sinovac, side effects, mild, moderate

INTRODUCTION

Novel coronavirus (COVID-19 or 2019-nCoV or SARS-CoV-2) emerged as a catastrophe in December 2019 and is still affecting the entire human populace in addition to the being a huge burden on the global healthcare, social, and economic systems.[1] The World Health Organization (WHO) declared a global emergency on January 30, 2020, when the virus broke out in the Chinese city of Wuhan.. Later, on March 11 2020, COVID-19 was declared a global pandemic, affecting more than 650 million people globally, including over 6.6 million deaths [2]. Pakistan also experienced the massive SARS-CoV outbreaks, with over 1.5 million confirmed cases of COVID-19 to date, and approximately 30 thousand people killed by the deadly virus.[3], [4] To limit its spread, global lockdowns were imposed, causing devastation of the livelihoods and crippling the global economy. [5]Despite the continued progress in the clinical research, the development of vaccines, and the advancement of treatment modalities, COVID-19 continues to wreak havoc across the world and poses a great threat to the entire human race,mainly due to the evolution of mutant strains of the virus. [6]

The development of vaccines against SARS 2-CoV has remarkably reduced the total number of newly detected cases, and the death toll has been significantly tapered down, with an estimated 0.7 million cases worldwide and almost 15 cases in Pakistan being reported each day. [7]

Coronavirus disease 2019 (Covid-19) is a highly contagious respiratory infection caused by an RNA virus, namely severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The main mode of transmission is airborne, caused by exposure to respiratory droplets/aerosols or closed contact with an infected individual. Transmission through fomites and contaminated surfaces has also been well described. [8] Individuals of all ages and genders are at equal risk of contracting the virus. However, the

severity of symptoms and prognosis of the disease are affected by the overall health status and patients with underlying comorbidities (diabetes, cardiovascular and renal diseases, chronic lung disease, and immune deficiencies) are at greater risk of developing complications. [9] In addition, patients aged 60 or older are more likely to progress to the morbidity and mortality of the infection. [10]

The clinical spectrum of the infection ranges from mild to critical, with patients suffering from trivial flu like symptoms to those progressing into severe pneumonia. [11] Fever, cough, and shortness of breath are the most commonly reported complaints; sore throat, anosmia, dysgeusia, anorexia, nausea, malaise, myalgia, and diarrhea are less commonly reported. Based on the severity of the presenting complaints, blood biochemistry, and radiological findings, the disease has been classified by the National Institutes of Health (NIH) into: asymptomatic infection**,** mild, moderate, severe and critical illness. Asymptomatic illness is when there is a positive SARS-CoV-2 test without any clinical features of COVID-19. Mild illness is described as positive SARS-CoV-2 test with flu like symptoms such as fever, cough, runny nose, anosmia, arthralgia, myalgia, headache etc, without dyspnea and abnormal chest radiology, while moderate illness is defined as clinical manifestations of COVID-19 with abnormal chest findings on radiology and ≥ 94% oxygen saturation (SpO2) on room air.Severe illness is defined as oxygen saturation (SpO2) on room air being ≤ 94%, position lung infiltrates being >50%, dyspnea with respiratory rate greater than 30 breaths/min, and critical illness being defined as individuals develop multiple organ dysfunction, acute respiratory failure, sepsis and shock [12]

Besides the respiratory manifestations, clinically evident involvement of other organ systems such as the renal, cardiac, gastrointestinal, hematologic, neurologic, and endocrine systems has also been reported. [13]

A wide variety of FDA approved therapeutics are currently indicated worldwide for the treatment of COVID-19 in symptomatic patients. These include antiviral drugs, (e.g., molnupiravir, paxlovid, remdesivir), anti-SARS-CoV-2 monoclonal antibodies (e.g., bamlanivimab/etesevimab, casirivimab/imdevimab,sotrovimab,bebtelovimab), anti-inflammatory drugs (e.g., dexamethasone), immunomodulators agents (e.g., baricitinib, tocilizumab). [14] Furthermore, azithromycin (a macrolide antibiotic) has shown promising results by greatly improving respiratory epithelial integrity and preventing lung fibrosis, thereby reducing the overall morbidity and mortality attributed to the COVID-19 infection. [15] At the emergence of the pandemic, anti-parasitic drugs such as Hydroxycholoquine, Chloroquine and Ivermectin were also proposed for the symptomatic patients, however, these agents are

no longer indicated for the treatment of COVID-19. [16], [17].For severe SARS-CoV-2 pneumonia in critically ill, watchful fluid management, lung protective oxygenation and ventilation, and intensive care are indicated. [18]

Several potential vaccines against SARS-CoV-2 have been introduced. The safety and efficacy of these vaccines have been well established after multiple successful clinical trials. There are mRNA based vaccines (Pfizer and Moderna), viral vector vaccines (AstraZeneca, Covaxin, Sputnik V), protein subunit based vaccines (Novavax) and inactivated vaccines (Sinopharm, Sinovac) among these.[1] According to the World Health Organization's current vaccination status, more than 13 billion vaccine doses have been administered globally as of December 2022. The development and administration of various vaccines against SARS-CoV-2 have significantly reduced the number of cases, hospitalizations, and deaths, and comorbidities associated with the infection. The vaccines are also substantially preventing the outbreaks, thus reducing the burden on the healthcare system and economy.[19]

On the other hand, numerous adverse effects of the vaccines have been reported. Adverse effects ranging from mild to severe occurred with mRNA vaccines. Pain at the injection site, headache, myalgia, chills, fever, itching, rash, and swelling at the injection site were the most commonly reported non-life threatening symptoms. [20] Several cases of myocarditis after the second dose of an mRNA vaccine in young males also became a cause of concern for the researchers. [21] With the ChAdOx1 nCoV-19 vaccine (AstraZeneca), rare but potentially fatal complications of immune thrombosis and thrombocytopenia, [22] cerebral venous sinus thrombosis, intracerebral and subarachanoid hemorrhage were reported in some individuals. [23] While the safety and efficacy of inactivated vaccines (Sinopharm, Coronavac, CanSino) have been well described, there are instances when the side effects of these vaccines were reported during the clinical trials as well as after the administration of these vaccines to the global masses. Commonly reported complaints were induration and pain at the injection site, and systemic reactions such as headache, fatigue, myalgia, diarrhea, coughing, and fever were revealed in the descending order of occurrence. [24] Despite the wide array of reported side effects of all these vaccines, the benefits of vaccination against COVID-19 have certainly outweighed the pitfalls.

The aim of this study was to evaluate the post-vaccination symptoms and adverse effects in the adult population aged 18-59 years in Karachi, Pakistan who had received either one or two doses of inactivated vaccines, Sinopharm and Sinovac.

METHODOLOGY

Study Design and participants:

A descriptive cross-sectional study based on a written questionnaire was conducted for 6 months, from July 2022 to December 2022 after taking ethical approval to assess the side effects associated with the COVID-19 vaccination, using a random sampling technique. The ethical approval was obtained from the Ethical Review Board. The study was multi-center and the data was collected from different hospitals in Karachi.A total of 400 participants, aged 18 to 59 years of both genders, who were able to give consent, were currently residing in Karachi, and had received at least one dose of the inactivated COVID-19 vaccines, Sinopharm and SinoVac, were included in the study. Pregnant women were not included in the study.

Survey tool:

The first part of the questionnaire included general demographics like age, weight, and gender. The second part of the questionnaire asked about vaccination status (1st or 2nd dose), type of vaccine received, comorbid conditions (Hypertension and Diabetes Mellitus) and previous exposure to COVID-19 infection. The third part of the questionnaire included a list of side effects of the inactivated vaccines based on the literature review [24, 25, 26] which were further categorized as mild, moderate and severe, as subjectively described by the participants. The local symptoms include pain, burning, redness, swelling at the injection site, and lymphadenopathy. The systemic symptoms include fever, headache, chills, myalgia, dyspnea, etc. Fever was classified into mild, moderate, and severe as 99-100°F, 101–103°F and above 103°F respectively. The last part of the survey was the subjective description of overall satisfaction of the respondents about their experience with the vaccination, which was classified as very satisfied, satisfied, slightly satisfied, and dissatisfied.

Statistical analysis:

The statistical analysis was done using SPSS version 26. The frequency of the side effects following the first and second doses of COVID-19 vaccination was expressed in percentages, while demographics wereshown as mean and standard deviation.

RESULTS

Of the 400 participants who consented to participate in the study, 262 (65.5%) were males and 138 (34.5%) were females, with a mean age of 41 years. Among the participants, 20(5.0%) reported a previous infection with COVID-19, while 380(95.0%) did not contract the infection. Hypertension and diabetes mellitus were found to be present as associated comorbidities in 88(22.0%) and 86(21.5%) participants, respectively.Around 284(71.0%) participants received SinoVac vaccine and 116(29.0%) received Sinopharm, of whom 42(10.5%) received the first dose and 284(71.0%) received both doses of the inactivated vaccine.The demographical details of all the participants are described in Table 1.

Side effects of vaccine after 1st dose:

A wide array of side effects were reported by the participants, the severity of which is further categorized into mild, moderate, and severe. The most commonly reported side effect, fever, was reported by 212(53.0%) participants, and out of them, 52(24.5%) reported it to be severe. This was followed by pain, burning and swelling at the site of the injection in decreasing order of frequency. Rash was also a notable side effect reported by 106(26.5%) participants, although only 6(5.7%) reported it to be severe. Joint pain, chills, sore throat, myalgia, and fatigue, were also reported by almost 130 participants; however, only a few reported them to be severe. The other side effects of mild severity were headache, anxiety, and lymphadenopathy, shortness of breath, cough, chest pain, diarrhea, flu, and nausea, in decreasing order of frequency. The tabulated form of these adverse effects is given in Table 2.

Side effects of vaccine after 2nd dose:

The side effects after the 2nd dose were found to be the same as those after the 1st dose; however, they slightly differ in frequency and severity. The most commonly reported side effect after the 2nd dose was pain at the site of injection 154(38.5%), however, none of the participants reported it be severe. Fever was reported by 152(38.0%) participants, and in terms of severity this was the only symptom reported as severe by the most participants, that is, 32(21.1%). This was followed by burning and swelling at the site of the injection, myalgia, rashes, joint pain, chills, and shortness of breath in decreasing order of frequency, and among these, the most commonly reported side effect of severe intensity was myalgia, reported by 16(12.5%) participants. Other notable side effects were headache and lymphadenopathy, although these were also of mild intensity. Other milder adverse effects were fatigue, diarrhea, flu, sore

throat, cough and redness at the site of injection. Nausea was reported by the fewest number of participants, 16(4.0%). The details of these adverse effects are given in table 3.

The overall subject level of satisfaction was found to be 216 (54.0%) participants were satisfied, 96 (24%) were very satisfied, 78 (19.5%) were slightly satisfied, and 10 (2.5%) participants were dissatisfied with the overall vaccination experience.

Table I: Table I: The participants' basic demographic characteristics (n=400).

Variable		**Mean±SD n(%)**
Age (years)		41.40±14.28
Weight (kg)		66.94±15.42
Hypertension Duration (years)		5.04±4.42
Diabetes Mellitus Duration (years)		4.04±4.00
Patency period days		13.68±14.21
Gender	**Male**	262(65.5%)
	Female	138(34.5%)
Hypertension	**Yes**	88(22.0%)
	No	312(78.0%)
Diabetes Mellitus	**Yes**	86(21.5%)
	No	314(78.5%)
	No	318(79.5%)
Previous COVID-19 Exposure	**Yes**	20(5.0%)
	No	380(95.0%)
Type of Vaccine	**Sinopharm**	116(29.0%)
	Sinovac	284(71.0%)
Vaccination status	**Partially Vaccinated**	42((10.5%)
	Fully Vaccinated	284(71.0%)
	Vaccinated with Booster Dose	74(18.5%)

Table II: Side Effects of Vaccination after 1st dose

Variable	Yes n(%)	No n(%)	Mild n(%)	Moderate n(%)	Severe n(%)
Pain at the site of injection	172(43.0%)	228(57.0%)	124(72.1%)	34(19.8%)	14(8.1%)
Swelling at the site of injection	154(38.5%)	246(61.5%)	94(61.0%)	56(36.4%)	4(2.6%)
Redness at the site of injection	70(17.5%)	330(82.5%)	54(77.1%)	14(20.0%)	2(2.9%)
Lymphadenopathy	90(22.5%)	310(77.5%)	54(60.0%)	30(33.3%)	6(6.7%)
Fever (temperature >37.8 ˚C)	212(53.0%)	188(47.0%)	80(37.7%)	80(37.7%)	52(24.5%)
Headache	92(23.0%)	308(77.0%)	54(58.7%)	36(39.1%)	2(2.2%)
Nausea	36(9.0%)	364(91.0%)	24(66.7%)	10(27.8%)	2(5.6%)
Rashes	106(26.5%)	294(73.5%)	76(71.7%)	24(22.6%)	6(5.7%)
Burning at injection site	166(41.5%)	234(58.5%)	158(95.2%)	6(3.6%)	2(1.2%)
Flu	62(15.5%)	338(84.5%)	38(61.3%)	18(29.0%)	6(9.7%)
Anxiety	90(22.5%)	310(77.5%)	84(93.3%)	6(6.7%)	0(0.0%)
Muscle pain (Myalgia)	114(28.5%)	286(71.5%)	92(80.7%)	16(14.0%)	6(5.3%)
Fatigue	106(26.5%)	294(73.5%)	48(45.3%)	40(37.7%)	18(17.0%)
Joint pain	130(32.5%)	270(67.5%)	82(63.1%)	38(29.2%)	10(7.7%)
Chills	126(31.5%)	274(68.5%)	68(54.0%)	68(54.0%)	68(54.0%)
Cough	76(19.0%)	324(81.0%)	54(71.1%)	20(26.3%)	2(2.6%)
Sore throat	114(28.5%)	286(71.5%)	86(75.4%)	86(75.4%)	86(75.4%)
Shortness of breath	90(22.5%)	310(77.5%)	60(66.7%)	30(33.3%)	0(0.0%)
Diarrhea	68(17.0%)	332(83.0%)	56(82.4%)	12(17.6%)	0(0.0%)
Chest Pain	76(19.0%)	324(81.0%)	28(36.8%)	44(57.9%)	4(5.3%)

Table III: Side Effects of Vaccination after 2nd dose

Variable	Yes n(%)	No n(%)	Mild n(%)	Moderate n(%)	Severe n(%)
Pain at the site of injection	154(38.5%)	246(61.5%)	120(77.9%)	34(22.1%)	0(0.0%)
Swelling at the site of injection	142(35.5%)	258(64.5%)	76(53.5%)	66(46.5%)	0(0.0%)
Redness at the site of injection	40(10.0%)	360(90.0%)	28(70.0%)	0(0.0%)	12(30.0%)
Lymphadenopathy	100(25.0%)	300(75.0%)	76(76.0%)	24(24.0%)	0(0.0%)
Fever (temperature >37.8 ˚C)	152(38.0%)	248(62.0%)	80(52.6%)	40(26.3%)	32(21.1%)
Headache	100(25.0%)	300(75.0%)	54(54.0%)	44(44.0%)	2(2.0%)
Nausea	16(4.0%)	384(96.0%)	14(87.5%)	2(12.5%)	0(0.0%)
Rashes	126(31.5%)	274(68.5%)	110(87.3%)	14(11.1%)	2(1.6%)
Burning at injection site	146(36.5%)	254(63.5%)	124(84.9%)	8(5.5%)	14(9.6%)
Flu	64(16.0%)	336(84.0%)	36(56.3%)	26(40.6%)	2(3.1%)
Anxiety	92(23.0%)	308(77.0%)	80(87.0%)	12(13.0%)	0(0.0%)
Muscle pain (Myalgia)	128(32.0%)	272(68.0%)	78(60.9%)	34(26.6%)	16(12.5%)
Fatigue	90(22.5%)	310(77.5%)	44(48.9%)	38(42.2%)	8(8.9%)
Joint pain	116(29.0%)	284(71.0%)	80(69.0%)	28(24.1%)	8(6.9%)
Chills	116(29.0%)	284(71.0%)	60(51.7%)	44(37.9%)	12(10.3%)
Cough	44(11.0%)	356(89.0%)	20(45.5%)	18(40.9%)	6(13.6%)
Sore throat	60(15.0%)	340(85.0%)	48(77.4%)	8(12.9%)	6(9.7%)
Shortness of breath	114(28.5%)	286(71.5%)	74(64.9%)	40(35.1%)	0(0.0%)
Diarrhea	68(17.0%)	332(83.0%)	20(29.4%)	46(67.6%)	2(2.9%)
Chest Pain	92(23.0%)	308(77.0%)	68(73.9%)	24(26.1%)	0(0.0%)

Table IV: The prevalence of serious adverse effects and level of satisfaction for vaccine of participants.

Variable		n	%
1st doseAny serious Adverse Event (AE)	**Yes**	2	0.5
	No	398	99.5
2nd doseAny serious Adverse Event (AE)	**Yes**	6	1.5
	No	394	98.5
Overall subject level of Satisfaction for vaccine	**Very Satisfied**	96	24.0
	Satisfied	216	54.0
	Don't Know	78	19.5
	Dissatisfied	10	2.5

DISCUSSION

The emergence of COVID-19 pandemic across the globe posed a serious threat to international health care systems. The culprit took millions of lives and paralyzed the world economy. In order to control it, scientists, researchers, pharmaceuticals companies and governments took immediate measures to develop effective vaccines, which were made available at an unparalleled pace. The vaccinations available have proven to be highly effective against the virus and have saved millions of lives by not only hindering the transmission of the virus but also by significantly reducing the disease-induced mortality and morbidity [27].

Several vaccines have been developed by pharmaceuticals companies around the world with an established safety and efficacy profile. Among those are the Sinopharm and SinoVac vaccines, which have proven to be equally effective in combating the deadly virus. However, our study and several

others have demonstrated several potential, although non-lethal side, effects of these vaccines which are further discussed here.

In this study, we assessed the side effects of the vaccine after the first or second dose, the intensity of which was further categorized into mild, moderate, and severe. For Sinopharm and SinoVac almost 30% participants experienced local and systemic adverse effects. The findings of our study suggest that the frequency and severity of the adverse effects were overall milder with both doses of the Sinopharm or SinoVac vaccine. The most common adverse effects were fever, pain, and burning at the site of injection, rash and joint pain, myalgia, and fatigue etc, while the less common were shortness of breath, cough, chest pain, diarrhea, flu, and nausea.

The frequency of the reported side effects in our study differs between the first and second doses. In one of the cross-sectional survey studies conducted in UAE, the overall frequency of side effects was higher for the second dose than for the first dose with none requiring medical attention [28]. This is inconsistent with our study, where a greater number of respondents experienced the side effects after 1st dose of vaccination, however no treatment was required for any side effect. Like-wise, a cross sectional study conducted among the general population of Iran deduced that the undesirable effects were more prevalent after the first dose than the 2nd dose with overall side effects found to be mild and self-limiting [29].

In the study conducted by Saeed et al. 2021 [28], the most commonly reported side effects were localized; like pain, tenderness and redness at the site of injection. In contrast, our study reported fever as the most commonly reported complaint, followed by the localized symptoms including pain, swelling, and redness at the injection site. Fever was also the most frequently reported severe symptom among the other adverse effects. This could be attributed in part to differences in ethnicity among the respondents in both study groups and to individual inflammatory responses to the vaccination. Additionally, Babaee et al, (2022) [29] discovered fever to be the most frequently occurring side effect in the 30 to50 year old age group. These findings are in accordance with our study. Saeed et al. 2021 [28]in their study also reported nausea, diarrhea and cough as undesirable side effects of the vaccines after both doses. They discovered these side effects to be less frequent, with only 36 participants out of the total of 1080 mentioning these complaints after receiving the first dose, and 28 participants reporting these symptoms after the second dose. Similarly, another study showed a much lower frequency of these symptoms [30].

These findings are inconsistent with our study, where these symptoms have been reported in much greater numbers. One possible explanation for this could be attributed to recall and information biases.

A cross-sectional study conducted in the Pakistani cities of Rawalpindi and Islamabad found fatigue (lethargy) and myalgia to be common among 168 and 99 respondents, respectively. This is on par with our study, where these symptoms are reported at almost similar frequencies. Additionally, the occurrence of headache after 1st and 2nd jab of the inactivated vaccines was also a remarkable finding in both the studies [31].

Several other vaccines, including Pfizer, Moderna, and AsteraZeneca, which have been administered in Pakistan on a vast scale and have shown promising results in both decreasing the transmissibility of the virus and reduction in the disease related complications and mortality. Despite being unquestionably effective against COVID-19, these vaccines have demonstrated more frequent moderate to severe side effects in comparison to Sinopharm and SinoVac. Likewise, Ganesan et al. [32] in their study have illustrated more side effects with the Pfizer vaccine than with the Sinopharm vaccine. Additionally, another cross-sectional study conducted in Bangladesh has demonstrated that the side effects were more prevalent and pronounced in the recipients of Pfizer and Moderna vaccines, while the least common were found in the recipients of Sinopharm and SinoVac[33].

Thus, the findings of our study have shown that both Sinopharm and SinoVac have a better safety profile, and this statement can be further supported by the research of Talukder et al. [34] who in their study demonstrated a comparison of the safety profiles of different vaccines and found Sinopharm and SinoVac to be the safest among the others.

CONCLUSION

To conclude, our study has deduced that both Sinopharm and Sinovac are generally safe to administer, and the overall side effects are mild, non-life threatening and do not require hospital admission. The subjective level of most vaccine recipients was generally satisfactory. However, the limitations of the study could have been minimized by asking about the severity of the side effects on a rating scale rather than relying on subjective descriptions by the participants. Additionally, the side effects of the booster dose have also been inquiredabout. The comorbidities should also have been taken into account. Lastly, a rigorous follow-up of the participants after both doses of the vaccine was crucial to consider.

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