



ORIGINAL ARTICLE

Prevalence and predictors for adverse effects of Sinopharm and Sinovac COVID-19 Vaccines.

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ABSTRACT... Objective: To see the prevalence and potential predictors for side effects of Sinopharm and Sinovac COVID-19 vaccines among students of medical, and BS human nutrition and dietetics courses. **Study Design:** Cross-sectional Proforma-derived. **Setting:** Sialkot Medical College, Sialkot, Pakistan. **Period:** July and August, 2021. **Material & Methods:** Fifty students (MBBS = 30; Dietetics course = 20) with at least one dose of Sinopharm or Sinovac COVID-19 vaccine were recruited, purposively. The subjects were asked to report in an indigenously designed proforma on adverse effects using recall methodology for open time. **Results:** Forty nine subjects gave complete responses in the proforma. The rate of adverse effects increased from 75% (n = 3) against Sinopharm to 100% (n = 9) against Sinovac vaccine among 13 students of Dietetics who had only 1st dose. For rest of the 36 participants, the rate was found, as: 76.5% (n = 13) against each of the 1st and 2nd dose of Sinopharm; 78.9% (n = 15) against 1st and 68.4 (n = 13) against 2nd doses of Sinovac vaccine. The frequency of different adverse effects per individual ranged 1-3 (Sinopharm) or 1-4 (Sinovac). Whereas, lower rate of injection site pain was recorded on 1st dose of Sinopharm than Sinovac (52.9 vs 57.9%, respectively). None of the variables was noted as potential predictor for the side effects (p > .05). **Conclusion:** Sinopharm, and Sinovac COVID-19 vaccines exhibit almost similar prevalence of self-manageable side effects. Moreover, there is no predictor for the effects.

Key words: Adverse Effect, COVID-19 Vaccines, Injection Site, Medical Student, Prevalence.

INTRODUCTION

Misinformation on vaccine's safety, in terms of side effects encourages vaccine hesitancy.¹ The hesitant person is highly susceptible to the infection e.g. COVID-19. Unfortunately, this delaying attitude also prevails in medical students. Reporting of such attitude in them is surprising as they know about adverse impacts of the COVID-19 e.g. tongue ulcer.^{2,3}

At present, Pakistan is amongst the countries where triple mutant delta variant-mediated corona disease is on its peak. As per a reliable report on Aug 3, 2021⁴, the disaster hit 66 precious lives to death in last 24h with 6.0% case confirmation rate. Whereas, its vaccines are opposed through conspiracy theories on different issues including side effects despite of integrated productive

measures^{5,6} to neutralize the misperceptions. Fortunately, the adverse effects are predictable mild short term and self-manageable. The data on adverse effects become incredible when allergy-based adverse effects are misperceived with that of COVID-19 vaccines.

All the COVID-19 vaccines have side effects at each of the both stages i.e. clinical trials and field administration. An UAE-based study⁷ highlights incidence of injection site pain (ISP) and muscle fatigue after 1st, 2nd and/or both doses of Sinopharm COVID-19 vaccination. Similarly, females are more vulnerable to the effects than males. Similarly, there is risk of ISP and/or mild diarrhoea for 2-3 days⁸ on use of two doses of Sinovac COVID-19 vaccine with an interval of 28 days. Similarly, clinical and sociodemographic

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variables have potential to predict the effects in the human population.

Almost all the published studies on vaccines' adverse effects are manufacturer-funded and third party-monitored.⁹ However, there is acute scarcity of independent studies. This publication trend lowers the confidence of mass on vaccines' safety. On the other side, this confidence is necessitated for encouraging impacts on vaccine's acceptance¹⁰ in order to breach the sticky sphere of virus's variants. So, the objective of this study was to see the prevalence and potential predictors for side effects of Sinopharm and Sinovac COVID-19 vaccines among medical, and BS human nutrition and dietetics students. The findings will help this segment of students (in particular) and common man (in general) in developing an attitude for prompt vaccine acceptance clearing the misguided perception on the adverse effects.

MATERIAL & METHODS

The present cross-sectional proforma-based study was conducted between July and August 2021 in Sialkot Medical College (SMC), Sialkot, Pakistan recruiting students from MBBS and BS in HND (Human Nutrition & Dietetics) courses.

A sample size of 50 subjects was set considering recommended range (24-50)^{11,12} for any pilot study. The SMC – a private Institute was selected from a pool of three Colleges (one public and two private) located at city Sialkot, purposively. Within the SMC, all the levels of MBBS (1st to 5th Professional) and BS in HND (1st to 8th Semester) were considered before registering all students. The students (male/female), aged ≥ 18 years with at least one dose of vaccine (Sinopharm/Sinovac) were enrolled. However, all those who had previous report of COVID seropositivity, no COVID-19 vaccination or vaccine other than the understudy two vaccines, had autoimmune/chronic (e.g. nephrotic syndrome) disease, or less than 15 days since last shot of vaccine were excluded.

A proforma including segment on vaccination status, adverse effects, and history of illness was

designed by a team of Linguistic experts and epidemiologists and tested through pre pilot survey on 15 participants. There was a list of 15 different side effects including fever, cough, tiredness, sore throat and other against each of the two doses to tick the appropriate one. Whereas, history of illness included family history of known allergy, personal history of bronchial asthma, fit (febrile/epilepsy), dermatitis/eczema, and steroid intake in the past two months were followed by two options (Yes/No).

The proforma was administered to finally-recruited 50 subjects during College hours and asked to response it in open time and stress free mood. They were also advised to drop the same in a purpose-built paper box after complete fill in. The study was conducted after getting clearance from the ethics committee of the Research Centre vide a letter No. MRC-3-TPMB/2021 dated 15-06-2021. Similarly, participation consent of the subjects was obtained before recruitment.

The data from proforma were entered in the sheet of SPSS ver. 25.0. Independent sample t test was applied on continuous data to compare the mean age of MBBS and BS HND students. The prediction of various binomial variables for adverse effects was assessed using chi square test. A p value $\leq .05$ was taken as statistically significant for the tests.

RESULTS

Of 50 participants, forty nine i.e. 30 from medical and 19 (out of 20) from dietetics courses gave completely filled in proforma with female predominance: 95.9%, n = 47. Similarly, mean age of medical students (21.9) had significant difference with that of dietetics (20.5 years); $t(47) = -2.11$, $p = .04$. Compared to Sinopharm, higher dosing interval was recorded for Sinovac (M = 31.1 vs. 23.8 days, respectively).

Thirty six subjects had both the doses while 13 (all from dietetics course) had only 1st dose of vaccine. In only 1st dose taking participants, the rate of adverse effects was found, as: 75%, n = 3 (Sinopharm) and 100%, n = 9 (Sinovac). The rate situation changed for other 36 subjects, as: 76.5%,

n = 13 (Sinopharm) and 78.9%, n = 15 (Sinovac). Not a single variable was found as a predictor for the effects using chi square test Table-I (a). One subject reported intake of steroids while no one stated hospitalization in the past two months.

After 2nd dose, the rate of effects (76.5%, n = 13) against Sinopharm vaccine was noticed very close to that of 1st dose (75%). In case of Sinovac vaccine, it (68.4%, n = 13) was remarkably lesser than 78.9% of 1st dose. Like post 1st dose, there was no evidence of prediction for side effects by any of the variables as shown in Table-I (b). However, family history of known allergy (bronchial asthma, dust or food allergy) seemed to have inclination towards the prediction (95% CI: .845 – 3.087; p = .06).

The frequency of the adverse effects per subject was recorded, as: 0-3 (Sinopharm), and 0-4 (Sinovac). Whereas, one Sinopharm (5.9%) or three Sinovac-vaccinated subjects (18.5%) had

reported three effects. Injection site pain (ISP) was the most prevalent effect (same 52.9%) and (57.9 or 52.6% after 1st or 2nd dose) against Sinopharm and Sinovac, respectively; followed by body aches and tiredness. Furthermore other effects like fever, cough, headache, or dizziness were amongst the rare one. Surprisingly, there was no reporting for sore throat, skin problem, tastelessness, chest pain, short breathing or sudden shocks. Similarly, all the effects were mild short-term and resolved within couple of days.

Amongst 11 subjects with ISP on Sinopharm, two reported its occurrence after 1st dose, one after 2nd dose, and eight (72.7%) after each of the two doses. The bar diagram (Figure-1) developed considering the participants reporting the same effect after each of the two doses. The rate of ISP after Sinopharm immunization was found higher than that of Sinovac (72.7 vs. 61.5%, respectively). However, it decreased drastically for aches before inclination for tiredness.

Variable; Categories	Rate of Adverse Effects (% , n)	95% Confidence Interval	p Sig. (2-sided)
Gender			
Male	50 (1)		
Female	79.4 (27)	.690 – 1.190	.40
Age; years			
21 ≤	76.9 (10)		
>21	78.3 (18)	.532 – 1.778	1.00
Year of education			
2 ≤	72.7 (8)		
>2	80.0 (25)	.487 – 1.572	.68***
Vaccine			
Sinopharm	76.5 (13)		
Sinovac	78.9 (15)	.430 – 2.202	1.00
*Family history			
No	73.1 (19)		
Yes	90.0 (9)	.058 – 2.628	.40
**Personal history			
No	73.9 (17)		
Yes	84.6 (13)	.176 – 2.301	.68

Table-I (a). Predictors for adverse effects on 1st dose of Sinopharm or Sinovac Covid-19 vaccine

Total population = 36; *bronchial asthma, food or dust allergy; **bronchial asthma, food or dust allergy; fits (febrile/epilepsy), and/or skin problem (dermatitis/eczema); ***Fisher's Exact test

Variable; Categories	Rate of Adverse Effects (% , n)	95% Confidence Interval	p Sig. (2-sided)
Gender			
Male	50.0 (1)		
Female	73.5 (25)	.168 – 2.759	.48
Age; years)			
21 ≤	71.4 (10)		
>21	72.7 (16)	.646 – 1.493	.93
Year of education			
2 ≤	66.7 (8)		
>2	75.0 (18)	.560 – 1.411	.60
Vaccine			
Sinopharm	76.5 (13/17)		
Sinovac	68.4 (13/19)	.747 – 1.673	.59
Family history			
No	80.8 (21)		
Yes	50.0 (5)	.845 – 3.087	.06
Personal history			
No	78.3 (18)		
Yes	61.5 (8)	.786 – 2.057	.28

Table-I (b). Predictors for adverse effects on 2nd dose of Sinopharm or Sinovac Covid-19 vaccine

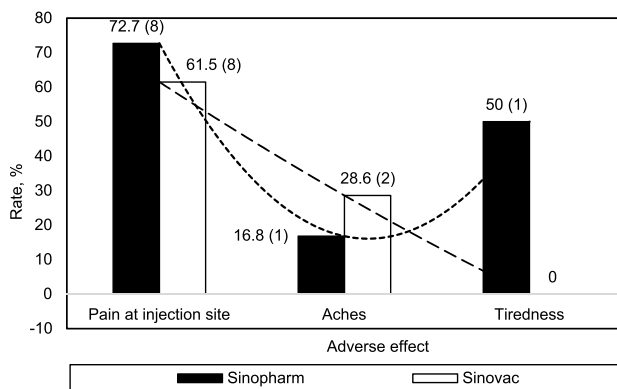


Figure-1. Rate of adverse effect appearing after both doses of COVID-19 vaccines (N = 36)

Frequency in parenthesis: The numbers of participants who had the side effect after each of the two doses (out of all those who had it after 1st, 2nd, and each of the two doses) of the vaccine; poly – polynomial trendline.

DISCUSSION

The concerns on vaccine’s efficacy⁷ and safety (in terms of adverse effects) nourish attitude of vaccine hesitancy. Such attitude is also expected from medical or dietetics students. So, there is need of research to lessen the attitude in this

scholastic segment for confidence building towards vaccine acceptance¹⁰ highlighting prevalence of side effects and their potential predictors for COVID-19.

Quitting the study by one participant is unexpected as such practice is observed in interventional trials.^{13,14} However, female predominance is just on the basis of predominance of this gender in college roll. Coincidentally, females are more vulnerable to the effects than males.⁷ Similarly, time interval of two doses of COVID-19 vaccine (Sinopharm/Sinovac) has fairly good resemblance with that Pfizer-BioNTech and COVID-19 Moderna¹⁵ vaccine. Appearance of adverse effects in almost all the 16 participants (who had only 1st dose of vaccines) is just by chance. Like on exposure to 1st dose of Sinopharm⁷, mild side effects are somewhat indicators of immunity development. Moreover, the development of the effects endorses the findings of a published study^{16,17} associating the effects with all available COVID-19 vaccines. Steroid uptake for pain management has no link with the vaccine-mediated side effects.¹⁸

Decline in the rate of effects from 78.9 (post 1st dose) to 68.4% (post 2nd dose) of Sinovac is

in contrast to News Explanation¹⁹ on another vaccine Pfizer-BioNT that rate of side effects increases after 2nd dose. The difference in finding might be on account of different ethnicity cum life styles. Tendency of family history of past illness e.g. allergy to be predictor for the side effects is a threatening issue; so deserves due management. It can be addressed visualizing high mortality threat in the COVID-19 exposed - high risk diseases comorbid persons.^{20,21}

Emergence of comparatively high rate of injection site pain followed by tiredness on administration of the Sinopharm/Sinovac is in accordance with a published paper⁷ while contradicts a finding 'The rate of tiredness is followed by injection site pain'²² using Oxford-AstraZeneca and Pfizer-BioNTech vaccines. But, the controversy can be addressed considering predictors and effectiveness of the vaccines. In a Pakistani study²³, the ISP is 2nd to fever (56 vs. 69 out of total 205, respectively). The higher rate of muscular aches on each of the two doses of Sinovac vaccine shows its potential for developing some muscle-related problem²⁴ like myositis. Fortunately, the inactivated vaccines (Sinopharm/Sinovac) has less adverse effects than that of mRNA-based or aluminum-adjuvant vaccines.¹⁶

The study limited to small sample size with female predominance on account of constraints in financial and human resource. Similarly, a prominent number of students i.e. 13 reporting only 1st dose of the vaccines also make the study biased and infer-difficult.

CONCLUSION

Sinopharm, and Sinovac COVID-19 vaccines exhibit almost similar prevalence of mild short term self-manageable side effects in the students of MBBS, and dietetics of a single medical college. The injection site pain is the highly prevalent post-vaccination side effect followed by body ach. Surprisingly, none of the clinical and sociodemographic variables of the participants show prediction for the onset of the effects.

SUGGESTIONS AND RECOMMENDATIONS

The sample size (with significant balance in the

gender) should be increase to eliminate any chance of bias before generalization for mass. There is need of participants who have both the doses at accurate time to display the outcomes in a simple statistical way. Variables (other than in present work) are necessitated for screening as risk factors of the adverse effects.







Finding of not a single predictor for the effects needs a large scale study including all the possible predictors (clinical and sociodemographic). The outcomes will help the common mass (in general) and human health care professional (in particular) in perceiving that the side effects are just mild short-term to go for vaccine acceptance
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4	Hassan Osman Sultan	Literature review, data collection.	
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7	Mujahid Hussain	Statistical analysisinterpretation.	