ORIGINAL ARTICLE

Association between demographic factors and side effects associated with COVID 19 vaccination

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ABSTRACT

Background: COVID vaccines were crucial in tackling the COVID 19 pandemic. However, they were also associated with side effects in the vaccinated population. These side effects included mild symptoms of COVID, fever, pain and swelling at the injection site. Hence, we evaluated the association between demographic factors and side effects in individuals following COVID vaccination.

Material and methods: A cross- sectional study was conducted in 93 participants for a period of 1 year, from January 2022 to January 2023. This was a retrospective study in which information regarding the side effects of two COVID vaccines was collected from the participants post-vaccination. Demographic data of vaccinated individuals and side effects associated with COVID vaccination were documented on a standardized proforma. Statistical analysis was performed to ascertain any association between the demographic variables and vaccination-associated side effects.

Results: Total 93 participants were evaluated during the study period. Our findings revealed higher frequency of vaccination-associated side effects in females and individuals above 20 years of age. The most common side effects included mild symptoms of COVID, fatigue and tiredness, fever, pain and swelling at the injection site and allergic reaction. None of these associations were found to be statistically significant.

Conclusion: Our findings suggested relatively higher frequency of vaccination-associated side effects in females and in individuals above 20 years of age which according to our inference, might be attributable to certain immune mechanisms in the affected population. In order to develop effective and safer vaccines, we recommend multi-center studies to explore the immunogenesis of such side effects.

Keywords: COVID, Demographics, Immunization, Vaccination-associated side effects

BACKGROUND

In 2020, when severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was rapidly proliferating throughout the world and was at its peak level of transmission, vaccines were most crucial in combating the COVID pandemic.[1-3] Various vaccines were developed and entered clinical trials by early 2020.[1,4,5] Owing to the situation many of these vaccines received emergency approval by FDA and governments worldwide launched vaccination campaigns to combat the spread of SARS-CoV-2.[1] There are four main categories of COVID vaccines viz. nucleic acid-based vaccines (DNA or mRNA), viral vector vaccines (replicating or non-replicating), live inactivated (or attenuated) virus vaccines, and protein-based vaccines.[6] Global vaccine safety studies have reported that recipients of the mRNA COVID vaccine typically experience local reactions more frequently than systemic ones.[1] While serious adverse effects have been rarely reported[1,7] in randomized clinical trials, most common vaccination-associated adverse effects include pain, redness and swelling at the injection site.[8,9] Systemic effects include fatigue, headache, muscle and joint pain.[8] While these adverse effects are mild and transient, studies have reported that approximately 50-90% of the participants experienced some form of adverse effect following vaccination.[8] In the Pfizer-BioNTech mRNA vaccine trial it was found that most

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frequently observed side effects included mild to moderate fatigue and headache.[1] AstraZeneca and Sputnik vaccine trails gave the same conclusion of mild to moderate side effects.[1] Some of the more severe effects of the vaccines, such as myocarditis and pericarditis, were later observed to occur almost exclusively after immunization with mRNA vaccines.[10] These rare vaccine related conditions could only be identified after the vaccines were authorized, as their low frequency made them undetectable even in large trials[10].

Among the COVID vaccines Sinopharm and Sinovac vaccines are both developed by growing SARS-CoV-2 virus in the lab and then chemically inactivating it.[11,12] Although inactivated, the virus has the active spike protein in its surface which serves as the primary target of the immune system.[11] Introduction of the inactivated virus leads to a cascade of events that triggers humoral and cellular immunity providing long term protection from the disease.[12] Both vaccines have same mechanisms of immunogenicity but variations in their efficacy have been reported.[13] Sinovac has reported efficacy of 50-84% compared to Sinopharm (79%).[13] The commonly reported side effects of both vaccines include pain at injection site, fatigue[14] ,headache, muscle and joint pain, fever, chills, redness at injection site and nausea.[14] Sinopharm trials have shown that the most commonly observed side effect is pain at the injection site followed by fever.[1] All the effects reported are mild, self-limiting and not requiring medical attention.[1]

Some preliminary studies have suggested that vaccination-associated side effects may vary based on gender and age.[15] Available evidence indicates that the innate, humoral, and cell-mediated responses to viral vaccines can vary between females and males.[16] A study reported that pain at the injection site was experienced more in males as compared to females.[17] In addition multiple studies reported an association of age with side effects of COVID vaccines.[18] Younger participants were were found to have symptoms of flu following vaccination[18] whereas other studies reported no such association.[19]

As a result, there has been growing interest in understanding the mechanisms behind these differences.[16] Hence we evaluated the association of gender and age with the development of side effects associated with COVID vaccines viz. Sinopharm and Sinovac vaccines.

MATERIAL AND METHODS

After obtaining clearance from ethical committee of Sharif Medical Research Centre (Ref # SMDC/SMRC/270-22) a cross-sectional study was conducted from January 2022 to January 2023. Data collection was done after taking informed consent from the study participants. Sample size was calculated using an online[20] sample size calculator Scalex Sp 1.0.01.[20] Keeping the precision 5%, prevalence of COVID vaccination side effects to be 7%[21] and confidence interval 95%, the sample size was calculated to be 100. After data collection it was analyzed that individuals who had received PFIZER Biotech (2), Cansino (3) and Moderna (2) were very few in comparison to Sinopharm (47) and Sinovac (46). Therefore, only participants(n=93) administered with Sinopharm and Sinovac vaccines were included in the study as the major recipients of COVID vaccines during the study period. This study was a retrospective study in which information about the side effects of the vaccine was collected from the participants six months after they received the vaccination on a standardized proforma.

Participants who had received COVID vaccination irrespective of their age and gender were included in the study and those who refused to give consent to be included in the study, and those who had any illness and were on medication, were excluded. Data was collected using a pre-validated questionnaire with a Cronbach alpha value of 0.7.[22] Fisher exact test was used to assess any association between gender and age of the study participants with side effects due to Sinopharm and Sinovac vaccines. Chi-square test was used to ascertain any association between gender and age with pain and swelling at the injection site after sinovac injection. Statistical Package for Social Sciences 23 was used for data collection. A p value of ≤ 0.05 was taken as significant.

RESULTS

Regarding study participant, most were females (77.4%) compared to males (22.6%). More participants were above 20 years of age (78.5%) than those less than 20 years (21.5%). Sinopharm vaccine was received by 50.5% individuals while 49.5% received Sinovac.

The side effects experienced by individuals after administration of Sinopharm vaccine were not significantly associated with gender. A higher percentage of females developed symptoms of COVID,

fatigue, tiredness, fever, pain and swelling at the injection site, and allergic reaction as compared males (Table 1).

The association between age and side effects after administration of Sinopharm vaccine was not significant. A higher percentage of individuals above the age of 20 years developed symptoms of COVID, fatigue and tiredness, fever, pain and swelling at the injection site and allergic reaction as compared to those below 20 years of age (Table-II).

The association between age and side effects after administration of Sinovac was not significant. A higher percentage of females developed symptoms of COVID, fatigue and tiredness, fever, pain and swelling at the injection site and allergic reaction as compared to the males (Table-III).

The association between age and side effects after administration of Sinovac was not significant. A higher percentage of individuals above the age of 20 years developed fatigue and tiredness, fever, pain and swelling at the injection site and allergic reaction as compared to those below the age of 20 years. Symptoms of COVID infection were observed more in individuals less than 20 years of age (Table-IV).

Table-I: Association of gender with vaccination-associated side effects (Sinopharm).

Side effects after Sinopharm vaccination		Gender		Total	p value
		Male (n=10)	Female (n=37)		
COVID infection post vaccination	**Yes**	0 (0%)	3 (100%)	3 (100%)	1.00
	No	10 (23%)	34 (78%)	44 (100%)	
Tiredness and fatigue	**Yes**	3 (12%)	23 (89%)	26 (100%)	0.08
	No	7 (33%)	14 (67%)	21 (100%)	
Fever	**Yes**	0 (0%)	5 (100%)	5 (100%)	0.56
	No	10 (1%)	32 (76%)	42 (100%)	
Pain and swelling at injection site	**Yes**	5 (18%)	23 (82%)	28 (100%)	0.49
	No	5 (26%)	14 (74%)	19 (100%)	
Allergic reaction at the injection site	**Yes**	1 (33%)	2 (67%)	3 (100%)	0.52
	No	9 (21%)	35 (80%)	44 (100%)	

Table-II: Association of age with post COVID vaccine side effects (Sinopharm).

Side effects after Sinopharm vaccination		Age		Total	p value
		Less than 20 Years (n=7)	Above 20 years (n=40)		
COVID infection post vaccination	**Yes**	1 (33%)	2 (67%)	3 (100%)	0.39
	No	6 (14%)	38 (86%)	44 (100%)	
Tiredness and fatigue	**Yes**	5 (19%)	21 (81%)	26 (100%)	0.43
	No	2 (10%)	19 (91%)	21 (100%)	
Fever	**Yes**	0 (0%)	5 (100%)	5 (100%)	1.00
	No	7 (17%)	35 (83%)	42 (100%)	
Pain and swelling at injection site	**Yes**	4 (14%)	24 (86%)	28 (100%)	1.00
	No	3 (16%)	16 (84%)	19 (100%)	
Allergic reaction at the injection site	**Yes**	0 (0%)	3 (100%)	3 (100%)	1.00
	No	7 (16%)	37 (84%)	44 (100%)	

Table-III: Association of gender with post COVID vaccine side effects (Sinovac).

Side effects after Sinovac vaccination		Gender		Total	p value
		Male (n=11)	Female (n=35)		
COVID infection post vaccination	**Yes**	0 (0%)	5 (100%)	5 (100%)	0.31
	No	11 (27%)	30 (73%)	41 (100%)	
Tiredness and fatigue	**Yes**	6 (19%)	25 (81%)	31 (100%)	0.46
	No	5 (33%)	10 (67%)	15 (100%)	
Fever	**Yes**	3 (21%)	11 (79%)	14 (100%)	1.00
	No	8 (25%)	24 (75%)	32 (100%)	
Pain and swelling at injection site	**Yes**	5(23%)	17 (77%)	22 (100%)	0.85
	No	6 (25%)	18 (75%)	24 (100%)	
Allergic reaction at the injection site	**Yes**	0 (0%)	1 (100%)	1 (100%)	1.00
	No	11 (24%)	34 (76%)	45 (100%)	

Table-IV: Association of age with post COVID vaccine side effects (Sinovac).

Side effects after Sinovac vaccination		Age		Total	p value
		Less than 20 years (n=13)	Above 20 Years (n=33)		
COVID infection post vaccination	**Yes**	3 (60%)	2 (40%)	5 (100%)	0.12
	No	10 (24%)	31 (76%)	41 (100%)	
Tiredness and fatigue	**Yes**	10 (32%)	21 (68%)	31 (100%)	0.49
	No	3 (20%)	12 (80%)	15 (100%)	
Fever	**Yes**	5 (36%)	9 (64%)	14 (100%)	0.49
	No	8 (25%)	24 (75%)	32 (100%)	
Pain and swelling at injection site	**Yes**	4 (18%)	18 (82%)	22 (100%)	0.14
	No	9 (38%)	15 (63%)	24 (100%)	
Allergic reaction at the injection site	**Yes**	0 (0%)	1 (100%)	1 (100%)	1.00
	No	13 (29%)	32 (71%)	45 (100%)	

DISCUSSION

The findings of this study reveal several important insights into the side effects experienced by individuals following the administration of COVID vaccines (Sinopharm and Sinovac) in relation to their demographic data.

According to our study, relatively higher percentage of females developed symptoms of COVID, fatigue and tiredness, fever, pain and swelling at the injection site and allergic reaction as compared to males. Similar results were seen in individuals who received Sinovac. However, no significant association between gender and side effects after administration of Sinopharm and Sinovac vaccines was found in our study. These findings are in accordance with existing literature, where female participants often reported higher rates of vaccination-associated side effects compared to males[23] A potential explanation for this could be hormonal differences between the two genders.[18] The influence of estrogen in females enhances their immune response making them more prone to vaccination-associated side effects.[24] However, it is important to note that the association between gender and side effects was not statistically significant, which suggests that while females may experience side effects more frequently, the difference may not be robust across populations or settings.[24] Another study reported similar results where higher percentage of females (19%) reported reaction at the injection site as compared to the males (7.9%). In contrast to our study, this association was significant (p=.018).[25] Similarly, higher incidence of immune reaction was seen in females (20%) as compared to males (10.9%) following vaccination though the association wasn`t statistically significant (p=0.066).[25]

A relatively higher percentage of individuals in our study having administered both vaccines and above 20 years of age developed symptoms of COVID, fatigue and tiredness, fever, pain and swelling at the injection site, and allergic reaction as compared to those below 20 years of age. With regards to Sinovac vaccine, symptoms of COVID were seen more frequently in individuals less than 20 years of age.

Ganesan et al suggested that older individuals may experience more pronounced immune response which could lead to more frequent or severe side effects.[8] Although in contrast to other studies, these findings corroborate our study results.[26] Another study reported that individuals above 24 years of age experienced more reactions at the injection site (20%) as compared to those younger than 24 years (13.3%),[25] similar to our study. However, in contrast to our study, individuals below 24 years of age (19.4%) experienced more immune reactions after vaccination as compared to those above 24 years (12%).[25]

Even though extensive literature exists on the side effects of COVID vaccines, specific vaccines have not been analyzed. In this regard we have made an effort in exploring the association of side effects related to specific COVID vaccines in terms of their participant demographics.

LIMITATION

Our study had few limitations. Majority of the participants received Sinopharm and Sinovac vaccines and hence, the study was based on the side effects of these two vaccines only. Furthermore, there might be a recall bias in our study as the study participants were investigated six months post-vaccination and therefore, may not have accurately recalled the development of immediate side effects following vaccination. With regards to these

limitations, we recommend a multi-center study with larger sample size and more defined timeframes post-vaccination for accurately investigating the safety of COVID vaccines on a wider population.

CONCLUSION

The prevalence of side effects of Sinopharm and Sinovac vaccines was higher in females as compared to males and in individuals above 20 years of age which according to our inference, might be attributable to certain immune mechanisms in the affected population. In order to develop effective and safer vaccines, we recommend multicenter center studies to explore the immunogenesis of such side effects.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Syed Muhammad Abdullah: Literature review and data collection, final approval, accountable for all aspects of the work

Dur E Shumyle: Manuscript write-up, final approval, accountable for all aspects of the work

Hina Rafiq Sheikh: Literature review and supervision

Noor Ul Huda: Data collection, final approval, accountable for all aspects of the work

Asma Shakoor: Data Collection, final approval, accountable for all aspects of the work

Hira Butt: Data Collection, concept and design, Manuscript write-up, statistical analysis critical revision, Supervision, final approval, accountable for all aspects of the work

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