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Safety and Side Effect Profile of Inactivated Sars-Cov-2 Vaccine, BBIBP-Corv in Pakistani Population

Muhammad Hammad Athar, Muhammad Shahbaz Shoaib, Usama Bin Zubair*, Hafiz Waleed Khan, Muhammad Asif Nadeem, Abdullah Bin Masood*****

Department of Medicine, Combined Military Hospital, Malir/National University of Medical Sciences (NUMS) Pakistan, *Department of Psychiatry, Foundation University Medical College, Rawalpindi Pakistan, **Department of Medicine, Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan, ***Department of Medicine, Combined Military Hospital, Multan/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To evaluate the short-term safety & side effect profile of inactivated SARS-CoV-2 vaccine, BBIBP-CorV in Pakistani population.
Study Design: Prospective longitudinal study
Place and Duration of Study: Combined Military Hospital, Malir Pakistan, from Feb 2021 to May 2021.
Methodology: In this study, a total of 5428 individuals aged between 18 to 60 years were vaccinated with 0.5ml of inactivated SARS-CoV-2 vaccine, BBIBP-CorV two doses each 21 days apart. The study participants were observed in vaccination center for 30 minutes post vaccination and then followed up for the next 5 days after each dose. Patients were observed for local & systemic side effects after the vaccine at the spot and on follow up.
Results: A total of 5428 individuals were vaccinated out of which 252(4.46%) experienced local side effects which include 236 (4.34%) with pain at injection site and 16(0.002%) individuals with local induration at site of injection. 258(4.75%) participants experienced systemic side effects which include 103(1.9%) individuals with nausea within 30 mins, 29(0.53%) individuals with fever in first 2 hours and 126(2.32%) individuals reported fatigue.
Conclusion: SinoPharm VeroCell vaccine has a relatively good safety profile as far as the short-term side effects are concerned. Most of the individuals who got vaccinated did not develop any side effects. Even those who did develop local or systemic adverse effects, they were mild and short lived.

Keywords: COVID 19; Safety; Vaccine.

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INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) since its outbreak in 2019 has transformed our lives completely and left us clueless about the future. Pakistan was amongst the relatively less affected countries in the world during the first wave of COVID-19.[1] The introduction of COVID-19 vaccine in 2021 proved to be a spearhead in this battle against COVID-19 which claimed over thousands of lives in just a short span.[2] Especially at a time when various new variants of COVID-19 were spreading like fire & testing the already crippled health care system of Pakistan in the second and third waves.[3] The much-awaited COVID-19 vaccine was approved for emergency use and the challenge ahead was the establishment of trust in this vaccine focusing mainly on its efficacy & side effects.[4]

Correspondence: Dr Muhammad Shahbaz Shoaib, Department of Medicine, Combined Military Hospital, Malir Pakistan
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Immune system of the body is responsible for thwarting any possible threat posed from disease producing microorganisms as well as eliminating cancer producing cells from the body.[5] A vaccine is a biological preparation that provides active acquired immunity to a particular infectious disease. The process of vaccination is responsible for the eradication of few life-threatening infectious diseases from the world such as smallpox and polio (near eradication) and proved to be the mainstay in the prevention of infectious disease.[6] Since Feb 2021, seven different COVID-19 vaccines from three platforms have been administered as part of the mass vaccination program. Several types of potential COVID-19 vaccines are under development which include inactivated or weakened virus vaccines, protein-based vaccines, viral vector vaccines, RNA and DNA vaccines.[7] BBIBP-CorV, also known as SinoPharm COVID-19 vaccine is an inactivated virus vaccine. The immunogenicity studies of mice, rats, guinea pigs, rabbits, monkeys and other animals have

confirmed that the candidate vaccine has good immunogenicity. Safety evaluation experiments in different species of animals have proved the safety of technical vaccines. As COVID-19 vaccine was manufactured on an emergency basis with trails and research still in progress, the public had access to limited information about the vaccine and public appeared to fear its credibilty.[8] Further adding fuel to the fire was the news regarding mortality associated with vaccine in older age groups around the world as seen in case of Pfizer vaccine.[9]

Keeping in view the apprehensions of the health care workers & the general population regarding the safety profile of the SinoPharm vaccine, trials carried out in Chinese population have demonstrated an excellent safety profile of this vaccine.[10] Limited work has been done in this region of the world with regards to the vaccine associated adverse effects. An effort was made to provide an insight into the side effects of the Sinopharm vaccine observed in Pakistani population. This data would help us in anticipation, identification, and prompt management of any of the reported adverse reaction related to this vaccine administered in different ethnic populations.

METHODOLOGY

This Prospective longitudinal study was planned and conducted at Combined Military Hospital Malir from February 2021 to May 2021. Sample size was calculated using WHO sample size calculator by using population prevalence proportion of adverse effects with Covid-19 vaccine as 3.47.[11] Non-probability consecutive sampling was used to gather the data.

Inclusion Criteria: The participants included healthy individuals of either gender belonging to Pakistani origin aged between 18 to 60 years old without the history of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection established via on site inquiry & examination.

Exclusion Criteria: Individuals aged > 60 years, with fever at the time of vaccination, recent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, on high dose steroids, ongoing or recent chemotherapy, pregnancy/lactating mothers, individuals with known drug allergies and chronic diseases i.e., diabetes, heart failure, renal failure were excluded from this study.

Approval was taken from hospital ethical review committee certificate no. 60/2021/Trg/ERC & written informed consent from the participants of the study. Individuals included in the study were vaccinated with 0.5ml of SinoPharm VeroCell vaccine Intramuscular (IM) injection on deltoid muscle in two doses 21 days apart. Each of the vaccinated individual was observed for 30 minutes at the vaccination center and followed up via phone call and outdoor visits for the next five days post vaccination. Participants were inquired daily for the first five days if they had experienced any adverse effect post-vaccination. Any adverse effect reported was then verified by the clinician on the same day via outdoor visit.

Statistical analysis was done using Statistical Package for the social sciences (SPSS) version 22:00. Variables were defined for the data in separate spreadsheets. Frequencies and percentages were calculated by cross-tabulation analysis of the variables.

RESULTS

Vaccination drive of a total of 5428 individuals aged between 18-60 years was observed. Two doses each of SinoPharm VeroCell vaccine were administered 21 days apart & the recipients were observed for local and systemic adverse effects attributable to both the doses. Statistical analysis of the observed local and systemic side effects of the vaccine showed a total of 252(4.64 %) (Mean value 2.91, SD±0.411) individuals experiencing local side effects on administration of 1st dose as compared to 401 (7.38%) (Mean value 2.85, SD±0.518) on administration of 2nd dose. Whereas systemic side effects were experienced by 258(4.75%) (Mean value 3.91, SD±0.455) and 93 individuals (1.71%) (Mean value 3.96, SD±0.313) on administration of 1st & 2nd dose respectively. Injection site pain was observed in 236(4.34%) individuals on 1st dose and 390(7.18%) individuals on administration of 2nd dose. Local induration was observed in 16(0.29%) against 11(0.20%) individuals among both doses. Fatigue was observed in 126 individuals (2.32%) on administration of 1st dose versus 32(0.58%) individuals on the administration of 2nd dose. Vaccine administration leading to nausea within 30 minutes of inoculation was seen in 103(1.89%) individuals against a mere 53(0.97%) individuals on both doses respectively. Inoculum resulting in fever within 72 hours of administration was observed in 29(0.53%) individuals on administration of 1st dose against 08(0.14%) individuals on administration of 2nd dose. Cumulatively, 510(9.39%) against 494(7.38%) individuals experienced side effects on administration of both doses respectively, while 4,918(90.6%)

individuals versus 4,934(90.8%) individuals did not experience any side effects during the process of vaccination.

Table: Descriptive Statistics

Side Effects		n(%)			
		1st Dose	2nd Dose	Total with local side effects	
Local Side effects	Injection site pain	236 (4.34%)	390 (7.18%)	1st Dose	2nd Dose
	Local Induration	16 (0.29%)	11 (0.20%)	252 (4.64%)	401 (7.38%)
Systemic Side effects	Fatigue	126 (2.32%)	32 (0.58%)	Total with Systemic side effects	
	Nausea within 30 minutes	103 (1.89%)	53 (0.97%)	1st Dose	2nd Dose
	Fever within 72 hours	29 (0.53%)	08 (0.14%)	258 (4.75%)	93 (1.71%)
Total with side effects	1st Dose	510(9.39%)			
	2nd Dose	494(7.38%)			
Total without side effects	1st Dose	4,918(90.6%)			
	2nd Dose	4,934(90.8%)			
Total vaccinated		5,428			

DISCUSSION

It is well known that multiple variables such as genetic, environmental & demographic factors have a strong influence on the immune response generated in response to vaccination & infection by susceptible organism. Haralambieva *et al*., published a paper in April 2014 which demonstrated significant differences in the neutralizing antibody responses 2-6 years (median) after rubella vaccination in different racial groups with consistently higher titers observed in individuals of African descent, compared to individuals of European descent and/or Hispanic ethnicity (p<0.001).[12] Similarly, another study paper by Hsu LC *et al*. in April 1996 concluded that host factors pertaining to ethnic origin might be responsible for the hypo responsiveness to Hepatitis "B" virus (HBV) vaccine in the aboriginal populations in a serologic survey of,[1,812] fully vaccinated children residing in four aboriginal villages and four adjacent nonaboriginal Han Chinese rural villages in 1993.[13]

The mechanisms of vaccine associated adverse effects include immune-mediated reactions, viral activity, and injection-related reactions. For example, Anaphylaxis observed in individuals receiving COVID-19 vaccine is classic example of type I hypersensitivity reaction.[14] Example of viral activity attributed to live attenuated vaccine include death of a 15-month-old girl who developed varicella like rash 20 days after receiving varicella vaccine. She developed respiratory distress, sepsis & multi organ failure. Vaccine strain VZV was recovered from Bronchoalveolar lavage (BAL) samples.[15] Examples of injection related adverse effects include Complex regional pain syndrome, altered skin innervation, inflammation, psychogenic factors & syncope.[16] A case of acute myocarditis was reported in an otherwise healthy 56 year old male following the 2nd dose of Pfizer vaccine which raised suspicion whether the cardiac injury is due to host immune response to viral spike glycoprotein or due to non-specific inflammatory response secondary to vaccination.[17] Furthermore, European Medical Agency investigated a total of 325 cases which developed thrombotic thrombocytopenia, cerebral venous sinus thrombosis, splanchnic vein thrombosis & bleeding following immunization with Janssen, Astra Zeneca, Pfizer & Moderna vaccines.[18] Vaccine-induced thrombotic thrombocytopenia involves the production of antibodies against platelet antigens which in-turn triggers massive platelet activation, aggregation & consumption.[19] Limited data is available pertaining to the impact of genetic, environmental and demographic factors on adverse effects associated with COVID-19 vaccine. Therefore, we planned this study with the rationale to explore the spectrum of adverse effects related to the SinoPharm vaccine in Pakistani population with the view to assess the safety profile of the vaccine in Pakistani population in the light of trials conducted in Chinese population.

Keeping in view the vaccine-related adverse effects mentioned above, no such life-threatening adverse effects were reported in our study following the administration of SinoPharm VeroCell vaccine in Pakistani population i.e. anaphylaxis, myocarditis, COVID-19 infection & thrombotic complications.

Ethnic differences in response to vaccinations have been highlighted in the past.[20] As far as the adverse effects of the SinoPharm vaccine are concerned, Shengli Xia *et al*., published a study in which phase I & phase II trials demonstrated side effects of mild and moderate severity in 15% out of a total 320 participants who reported at least one adverse effect within 07 days of receiving the either vaccine and no serious adverse effects were reported within 28 days after vaccination with most common local adverse effect being pain at site of injection (4.3% in phase 1 & 6.5% in phase 2) & fever (0.6% in phase 1 & 2.5% in phase 2) being the most common systemic

adverse effect, Thus it can be concluded from this data that SinoPharm vaccine has illustrated an excellent safety profile in Chinese nation. Our study having a total of 5428 participants has also shown similar results with 9.1% & 10% individuals reporting non-life-threatening adverse effects following the 1st & 2nd dose respectively. Pain at injection site (4.3% on 1st dose & 7.18% on 2nd dose) was the most frequent local adverse effect reported following both the doses. However, fatigue (2.3%) was the most frequently reported systemic adverse effect following the administration of 1st dose while nausea (0.9%) was most frequently reported systemic adverse effect following the administration of 2nd dose. Adverse effects reported following 1st dose did not have a significant impact on developing adverse effects on 2nd dose.

Our study communicates the fact that SinoPharm vaccine has shown excellent safety profile in both Chinese & Pakistani population exposed to the same environmental factors. No major variation was noted in the adverse effects reported from both the ethnic groups. Although immune response generated in both the populations needs to be investigated for any differences. Genetics, environmental & demographic elements did not emerge as significant factors in modifying the severity & heterogenicity of the side effects already observed with the vaccine, which supports the fact that there is minimal interplay of SinoPharm vaccine with the host factors and it is relatively safe for immunization in racially diverse group of individuals with minimum hesitancy.

LIMITATIONS OF STUDY

The limitations to our study include short term assessment of the safety & side effect profile of inactivated SARS-CoV-2 vaccine, BBIBP-CorV as the participants were observed only up to five days following the 1st and 2nd dose of the vaccination. Therefore, the long-term safety & side effect profile could not be evaluated. In addition to above our study is based on symptomatic assessment of the participants thus laboratory investigations were not used to monitor the safety & side effects of the vaccine.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MHA & MSS: Data acquisition, data analysis, critical review, approval of the final version to be published.

UBZ & HWK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MAN & ABM: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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