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A Longitudinal Study on Adverse Events Following COVID-19 Vaccination among Healthcare Workers in a Tertiary Care Hospital in Tiruvallur District, Tamil Nadu

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ABSTRACT

Introduction: COVID 19 Vaccination which was started in January 2021 in India and is one of the major hopes for ending the pandemic. This study was done in a tertiary care hospital in India to understand the adverse events following COVID 19 immunization.

Methodology: This was a longitudinal study done in a tertiary care hospital in Thiruvallur district. By universal sampling, 1200 healthcare workers who got vaccinated in the hospital from January 20 to January 30, 2021 were study participants. Pre-tested semi structured questionnaire was used for data collection which was used for collecting data regarding socio-demographic details, adverse events immediately following vaccination and late adverse events which were followed up after 48 hours by telemonitoring.

Results: Around 3.7% of the study participants had immediate reactions, 6.3% developed reactions in waiting room and 50.4% developed late reactions which were mild to moderate in severity and got relieved on medication and rest. Female sex, previous COVID infection and age less than 30 years had statistically significant association with late vaccine reactions

Conclusion: The study shows that COVID vaccine adverse events though present were mild to moderate in severity and they should not be the reason to defer or refuse COVID vaccination.

Keywords: Vaccine, coronavirus, healthcare, Fever

INTRODUCTION

The outbreak of the 2019-novel-coronavirus-disease (COVID-19) caused by severe-acute-respiratory-syndrome-coronavirus-2 (SARSCoV-2) emerged from Wuhan in December 2019 and had been arousing great global health concern.[1–3] In spite of various preventive measures being taken all over the world, the cases and deaths are happening and vaccine seems to be one of the major tool to end the COVID Pandemic.

By December 2020 to January 2021, COVID Vaccination campaigns have started in countries like United States, United Kingdom, China, Israel and Russia[4]. In India, the COVID 19 vaccination campaign started on January 16. The vaccines used in India were COVISHIELD™ and COVAXIN. COVAXIN is being

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manufactured by local pharma company Bharat Biotech and is an inactivated vaccine. The controversy surrounding COVAXIN was that enough efficacy data was not available as vaccine started rolling out as "restricted use in emergency situations in public interest"[5].

COVISHIELD™ vaccine (ChAdOx1 nCoV-19 vaccine) was produced by Serum Institute of India in collaboration with Astrazeneca and Oxford University. It is made by using a weakened version of common cold virus (adenovirus) from chimpanzees which is made to look like coronavirus so that our body will produce antibodies against them. It is given as intramuscular injection of 0.5 ml in two doses 4 to 6 weeks apart. It is a well-studied vaccine. The vaccine efficacy rate based on preliminary studies were 73%. As stated by the manufacturer, the vaccine efficacy ranges from 62 to 90%. [6]

The interim data from the trial conducted among 23,000 participants in Brazil, UK and South Africa showed that, the common adverse reactions include tenderness; pain in injection site, headache and fatigue (> 50%), myalgia and malaise (>40%), chills and pyrexia (>30%); and arthralgia and nausea (> 20%). Most of the adverse reactions were mild to moderate in severity and got resolved within few days following vaccination. Uncommon side effects include dizziness, abdominal pain and rashes. Similar reactions were also observed in Phase II/III trial done in India but was done among only 1600 participants.[6]

The data on adverse reactions are limited especially in India, as with any vaccine in the early stages of initiation. In the first phase as announced by the Indian Government, all the health care staff are being vaccinated. Even among healthcare workers there was much vaccine hesitancy as many did not turn up for vaccination[7]. Because of the widespread infodemic on social media, in which all the adverse reactions were blown up out of proportions, anxiety was at large among healthcare staff and even general public. A survey done in India among 17000 participants showed the vaccine hesitancy rate to be 62%. The major reason cited for vaccine hesitancy was fear of adverse reactions and efficacy of the vaccines[8].

Since data on adverse reactions following COVID 19 vaccination is limited in India, the study was done with the objectives to understand adverse events following COVID 19 immunisation among healthcare workers and also to find out if there is any association between adverse reactions and sociodemographic factors and morbidity profile.

METHODS

This study is a longitudinal study done in a tertiary care hospital in Tiruvallur district, Tamil Nadu. All the Healthcare workers, staff and frontline workers who got vaccinated at the hospital were included as study participants. Vaccination drive was started in the hospital on January 20, 2021. Universal sampling technique was followed in which all the vaccine beneficiaries from Day 1 to Day 10 of the vaccination drive were included. Those who got vaccinated from other vaccination centers in the city were excluded from the study.

All the healthcare workers, staffs and frontline workers who got vaccinated in the hospital were observed for a period of 30 minutes in the observation room as per the guidelines of Government of India.[9] For the study purpose those who developed any vaccine reactions immediately were classified as immediate reactions. The vaccine reactions if any, developed within the 30 minutes observation period were noted down and were classified as vaccine reactions within the observation period. After 48 hours of vaccination they were followed up through telemonitoring for any vaccine related adverse reactions. Those reactions were classified as vaccination reactions after the observation period. All those data were collected by a pre-tested semi-structured questionnaire. The questionnaire contained details regarding demography, any pre-existing morbidity, previous history of COVID infection, their height, weight and the details of medications taken for vaccine reactions. The vaccine reactions they developed were classified into mild, moderate and severe based on their perception of those symptoms and how far it affected their routine life and were included as part of the questionnaire. Severe reactions were those which required hospitalization. Based on their height and weight, Body Mass Index was calculated, and the participants were classified into underweight, normal, overweight and obese based on World Health Organization guidelines[10].

The data collected was entered in Microsoft Excel and analysed by using SPSS version 25. Descriptive statistics was used for data presentation in the form of tables and graphs. Bivariate and regression analysis was used to determine the predictor variables of vaccine reactions and reaction severity.

Ethical approval was obtained from the Institutional ethical committee of the tertiary care hospital. (SMC/IEC/2021/01/001)

RESULTS

Most of the study participants (57.8%) were found to be within the age group of less than 25 years and majority were females (60.1%). Doctors contributed to 35% of the participants, followed by nursing staff (24%), students (22.3%) and other hospital staff which includes hospital workers, administration staff and pharmacist contributed to 18.1%. (Table 1)

Regarding the morbidity details, 10% of the participants had suffered from a previous history of COVID-19, 4.5% had history of Hypertension, 3.2% Type 2 Diabetes Mellitus, 0.8% and 0.7% had suffered from previous history of respiratory diseases

like COPD, asthma and Cardiovascular diseases like myocardial infarction respectively. (Figure 1)

The vaccine reactions following observation period were more among females (57.4%) when compared to males, more among those aged less than 30 years (54%), were more pronounced in those who were underweight (62.7%) and those who had a previous history of COVID Infection (60%). On bivariate analysis, female sex, age less than 30 years, underweight, obesity and previous history of COVID 19 infection were found to have a statistically significant association with vaccine reactions after the observation period in the hospital. However, immediate reactions and reactions in observation room did not have any significant association with related factors. (Table 2).

On Multiple regression analysis, female sex (Adjusted Odds Ratio - AOR – 1.86), age less than 30 years (AOR – 1.33) and previous history of COVID Infection (AOR - 1.70) were found to be predictors of vaccine reactions following observation period with a statistically significant association (P<0.05). (Table 3)

Regarding the immediate reactions which were observed in the hospital setting, around 20% had headache and 30% had pain/tenderness at the injection site. Around 33% developed mild giddiness immediately following vaccination which was relieved on rest in the observation room. Among the late reactions which were enquired after the observation period, fever was the commonest (62.8%) followed by pain/tenderness at the injection site (40.8%), headache (36.5%) and body pain (29.7%). (Table 4)

The study participants were enquired on the perceived severity of reactions following COVID vaccination. It was found that, 3.7% reported immediate reactions among which 91.1% of them were found to be mild reactions.

Table 1: Socio-Demographic details of the study participants (N = 1200)

Variable	Participants (%)
Age	
<25 years	694 (57.8)
26-40 years	313 (26.1)
41-55 years	129 (10.8)
> 55 years	64 (5.3)
Sex	
Male	479 (39.9)
Female	721 (60.1)
Designation in Healthcare system	
Doctors	428 (35.7)
Nursing Staff	288 (24)
Other Hospital staff	217 (18.1)
Students	267 (22.3)

Table 2: Association between Immediate and Late Adverse Reactions following COVID Vaccination and related variables among study participants:

Variable	Reaction			Total (N = 1200) (%)
	Immediate (n = 45) (%)	Within 30 mins (n = 76) (%)	After Observation period (n = 605) (%)	
Female	29 (4%)	52 (7.2)	414 (57.4)	721 (60.1)
Male	16 (3.3)	24 (5.0)	191 (39.9)	479 (39.9)
	P = 0.54	P = 0.125	P = 0.000*	
Age < 30 years	36 (4.2)	59 (6.9)	464 (54.0)	859 (71.6)
	P = 0.202	P = 0.22	P = 0.000*	
Underweight	4 (3.6)	6 (5.5)	69 (62.7)	110 (9.2)
	P = 0.948	P = 0.69	P = 0.007*	
Obesity	25 (4.7)	39 (7.3)	249 (41.2)	537 (44.8)
	P = 0.137	P = 0.23	P = 0.012*	
Any Morbidity	3 (3.2)	6 (6.3)	40 (42.1)	95 (7.9)
	P = 0.752	P = 0.99	P = 0.09	
Previous COVID Infection	5 (4.2)	11 (9.2)	72 (60)	120 (10)
	P = 0.800	P = 0.18	P = 0.027*	

*P Value < 0.05, statistically significant at 95% Confidence Interval, $\chi 2$ – Chi-square

Table 3: Multiple Regression Analysis between symptoms observed after observation period and associated predictor variables among the study participants.

Predictor Variable	Reaction after observation period			
	Beta Coefficient	P Value	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Female Sex	0.624	0.000*	2.033 (1.60-2.57)	1.867 (1.46-2.38)
Age < 30 years	0.286	0.040*	0.600 (0.46 – 0.77)	1.331 (1.01-1.75)
Underweight	-0.341	0.119	0.574 (0.38 – 0.86)	1.407 (0.91 – 2.16)
Obesity	-0.101	0.427	1.33 (1.06-1.68)	0.904(0.70-1.15)
Previous COVID Infection	0.531	0.008*	0.65	1.70 (1.14 – 2.51)

*P Value < 0.05, statistically significant at 95% Confidence Interval.
OR – Odds Ratio, CI – Confidence Interval

Table 4: Immediate and Late reactions observed after COVID Vaccination among study participants

Variable	Reaction (Multiple Responses)		
	Immediate (n = 45) (%)	Within 30 mins (n = 76) (%)	After Observation period (n = 605) (%)
Headache	10 (22.2)	15 (19.7)	221 (36.5)
Pain/Tenderness at Injection site	14 (31.1)	24 (31.6)	247 (40.8)
Giddiness/Dizziness	15 (33.3)	12 (15.8)	69 (11.4)
Fever	3 (6.7)	7 (9.2)	380 (62.8)
Swelling/Lump on site of Injection	2 (4.4)	0	6 (1.0)
Unwell/Tiredness	0	6 (7.9)	151 (25)
Body Pain	4 (8.9)	5 (6.6)	180 (29.7)
Stomach Pain	2 (4.4)	0	7 (1.2)
Nausea / Vomitting	0	6 (7.9)	44 (7.3)
Anxiety	0	1 (1.3)	7 (1.2)
Allergic reaction	0	1 (1.3)	7 (1.2)

Table 5: Reactions following COVID Vaccination with their severity and medication details

Reaction	Total (N = 1200)	Severity of reaction	
		Mild	Moderate
Immediate	45 (3.7)	41 (91.1)	4 (8.8)
Within 30 mins	76 (6.3)	56 (73.7)	20 (26.3)
After observation period	605 (50.41)	444 (73.4)	161 (26.6)

Medication following COVID Vaccination required in 304 (25.3) including Anti-Pyretic - 299 (98.3); Anti-Inflammatory 8 (2.6); Anti-Emetic 7 (2.1); Anti-Allergy – 3 (0.9) (Multiple responses)

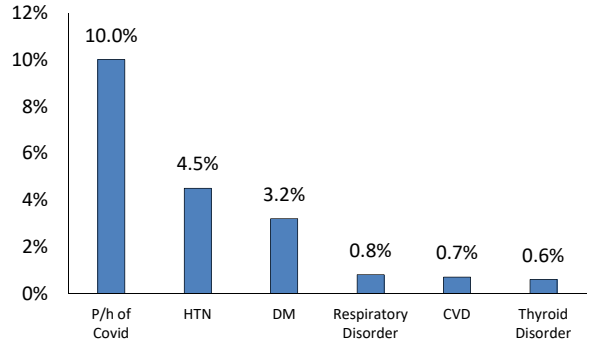

Figure 1: Morbidity Details of the study participants (n=1200)

Among the 6.3% who developed reaction in observation room, 73.7% were found to have mild reactions. Nearly half of the participants developed reactions after the observation period, among which, 73.4% were found to be mild reactions. Among those who developed reactions following vaccination, 25.3% took medication. The commonly used medicines were anti-pyretic like paracetamol (98.3%), Anti-inflammatory like Aceclofenac (2.6%) and anti-emetic like ondansetron (2.1%). (Table 5)

On Multiple regression analysis between vaccine reaction severity after observation period and related variables, age less than 30 years was found to be statistically significant (P<0.05) with AOR of 2.35. The other variables were not found to have significant association with immediate and late reaction severity among the study participants. (Table 6)

DISCUSSION

Vaccines have been used for the prevention of major infectious diseases since decades. Vaccines which are supposed to prevent diseases are now feared to cause diseases and complications due to the widespread infodemic regarding vaccines across social media and television[11]. COVID 19 has caused loss of lives of many people around the world and vaccine were meant to be one last ray of hope to reduce mortality and morbidity due to COVID 19 and develop herd immunity. But the misinterpretation regarding COVID 19 vaccines and fear of adverse reactions is preventing from attaining the expected results. The study done in Tiruvallur district to explore the extent of adverse events related to COVID 19 vaccination is discussed below.

In the present study, the incidence of adverse events following vaccination was found to be 3.7% immediately following vaccination, 6.3% experienced adverse reactions in observation room and nearly 50% experienced reactions after observation period. All the adverse reactions were found to be mild to moderate in severity and subsided one- or two-days following vaccination with adequate rest or with some medications.

Table 6: Multiple regression analysis of perceived severity of adverse events following COVID 19 immunization after observation period with associated variables.

Predictor Variable	Reaction after observation period (n = 605)			β Coefficient	P Value	AOR (95% CI)
	Moderate	Mild	Total			
Female Sex	115 (27.8)	299 (72.2)	414 (68.4)	-.101	0.626	0.903 (0.60-1.36)
Age < 30 years	137 (29.5)	327 (70.5)	464 (76.7)	.858	.001*	2.359 (1.39-3.99)
Underweight	18 (26.1)	51 (73.9)	69 (11.4)	-.118	.704	0.889 (0.48-1.63)
Obesity	67 (26.9)	182 (73.1)	249 (41.2)	.138	.497	1.148 (0.77-1.70)
Previous COVID Infection	24 (33.3)	48 (66.7)	72 (11.9)	-.389	.155	0.678 (0.39 -1.15)
Any Morbidity	12 (30.0)	28 (70.0)	40 (6.6)	.502	.190	1.65 (0.77-3.5)

Similar findings were obtained from studies done on ChAdOx1 nCoV-19 vaccine done in Brazil, UK and South Africa[12]. The most commonly reported adverse events were headache, fever/chills and myalgia. These findings were also found to be similar to ChAdOx1 nCoV-19 vaccine trial findings[12].

It was found that, the adverse reaction was found to be more prevalent among those less than 30 years of age and was less pronounced in the elderly and the association was found to be statistically significant. Similar results were obtained in study done by Voysey M et al in Brazil, UK and South Africa, where it was concluded that adverse events were less in number and intensity in older adults.[12]. Even in the Phase I/II trials in the UK it was observed that older tolerate the vaccine better compared to young people[12]. These results are encouraging that elderly being the most vulnerable for severe COVID infection and if they are vaccinated, it will help in reducing the mortality and morbidity related to the disease. The adverse reaction was also not influenced by any of the co-existing morbidity like diabetes, hypertension or any other diseases.

Participants who were found to be underweight and obese were found to have suffered more vaccine reactions compared to normal people. These findings would have been due to the decreased tolerance to the pain in these individuals and some nutritional deficiencies or health issues which would have been co-existing in them. Further research is needed to quantify these findings as people suffering from obesity tend to have a lower immune response to vaccines and causal association if any, exists, must be established[13].

One of the important reasons for vaccine hesitancy among people was that the COVID vaccines are produced in a shorter period without proper testing and validation. Adenovirus particles which are used in ChAdOx1 nCoV-19 vaccines have been tried and tested to be used as vaccine vectors and for gene therapies since a long time. Initially adenovirus was not chosen as ideal vaccine vectors as humans may have pre-existing immunity to adenovirus as evident from the failed adenovirus HIV STEP Trials[14-16]. But all that changed, when Chimpanzee adenovirus vectors were used in development of vaccines as evident by Ebola vaccines which provided high immunogenicity with good humoral and T cell mediated response in Sierra Leonean adults based on results of Phase 2 trials[17]. Since then, adenovirus vectors have been considered as the first candidate in development of vaccines for major emerging and re-emerging diseases as technology already exists for the same. These vectors have been proven that they can be manufactured at faster rate compared to other vaccine production methodologies like producing inactivated virus and mRNA vaccine technologies.[18,19]

The major fear among the population regarding vaccine uptake as evident from the survey done among 17000 participants found adverse reactions to be the main cause of concern among the 62% who were not willing to take the vaccine[8]. The present study shows that the adverse reaction though present, were mild to moderate in severity not affecting the daily routine and not life-threatening as many are believing due to the misinformation spread across various social media channels.

CONCLUSION

The findings from the study will help in alleviating the fears among both healthcare workers and general public and help in sensitization on vaccine uptake which will ultimately help in reducing the impact of COVID 19 Pandemic.

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