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ORIGINAL ARTICLE

Evaluating the Factors Affecting the Occurrence of Symptomatic COVID-19 Illness after Vaccination

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ABSTRACT

Background: Vaccination against COVID-19 illness is mainstay of undertaking the pandemic. However, it has been frequently observed that many patients developed COVID-19 illness after vaccination.
Aim: To find out the factors other than the "mere chance" affecting the development of COVID-19 illness after vaccination so to identify high risk population and to suggest modify their vaccinations accordingly.
Study design: Descriptive, retrospective cohort study
Place and duration of study: Falahee Foundation Clinics of Shifa International Hospital, Islamabad from 1st February 2021 to 31st July 2021.
Methodology: Sixty health care workers (HCW) who got vaccinated were enrolled.
Results: 34 (58.6%) were male and 26 (41.4%) were females with mean age of 42±8.3 years. Twenty (33.3%) HCWs developed post vaccination symptoms, 12 of them got their COVID-19 PCR done. Seven (58.33%) had positive PCR and 5 (41.66%)had negative PCR. Female gender and co-morbid conditions affected the post vaccination symptoms and positivity of PCR significantly.
Conclusion: Female gender, hypothyroidism, hypertension and celiac disease patients proved high risk for vaccination in our limited cohort. So co-morbid condition need consideration regarding further inquiry and necessary vaccination modifications.
Keywords: Factors, Co-morbid, Post-vaccination

INTRODUCTION

In less than a year, an array of vaccines was developed to bring an end to the COVID-19 pandemic. As impressive as the speed of development was the efficacy of vaccines. Public vaccine hesitancy could still undermine efforts to combat the pandemic[1].

Large volumes of research show, however, that vaccine preferences hinge on specific vaccine attributes. Recent research considering the influence of attributes such as efficacy, side effects, and country of origin take a step toward understanding how properties affect individuals' intentions to vaccinate[2-6].

COVID-19 vaccine side effects have a fundamental role in public confidence in the vaccine and its uptake process[7]. Riad et al[7] further reported that overall prevalence of some local and systemic side effects was higher than the manufacturer's report. Above all, one of important reason of this hesitancy is the chance of post vaccination covid, which is evident from the research that some small proportion of the subjects develops COVID-19 few days after vaccination. Dooling et al[8] emphasized in their study that Coronavirus disease symptoms can be mistaken for vaccine-related side effects during initial days after immunization. Among 4,081 vaccinated healthcare workers in Israel, 22(0.54%) developed coVID-19 from 1-10 days (median 3.5 days) after immunization. They suggested that clinicians should not dismiss post vaccination symptoms as vaccine-related and should promptly test for coVID-19.[8]

There is substantial variation between individuals in the immune response to vaccination. These include intrinsic host factors (such as age, sex, genetics, and comorbidities) and extrinsic factors (such as pre-existing immunity, microbiota, infections, and antibiotics). Further, environmental factors, behavioural factors (such as smoking, alcohol, exercise, and sleep), and nutritional factors also influence how individuals respond to vaccines. Moreover, vaccine factors (such as vaccine type, product, adjuvant, and dose) and administration factors (schedule, site, route, time of vaccination, and co administered vaccines and other drugs) are also important[9].

Considering these facts as highlighted by the microbiologists, post vaccination coVID-19 is unlikely to be by chance only, so we decided this study to find out the factors including base line health factors which might influenced the occurrence of post vaccination coVID-19 in our community so to prevent this at the time of the next course of vaccination.

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MATERIALS AND METHODS

It was a descriptive, retrospective cohort study. Approval was taken from the IRB & Ehics Committee of SIH Islamabad. All medical and paramedical staff at Falahee Clinics of Shifa Foundation, who got vaccinated from February 2021 to July 2021, were asked for the consent of this study. Consisting of 160 subjects, was the expected cohort of the study, however only 63 subjects gave consent for this purpose. 3 subjects were excluded due to history of prior coVID-19 illness in them in recent 3 months. So finally, we recruited 60 subjects for this study. Research Performa were distributed to all the participants with full confidentiality (60 envelopes tagged with a serial number were put in a box containing research Performa. Each subject was asked to draw one envelope, fill it and put back in the box without showing the serial number on it to the researcher/ data collector, so their confidentiality remained intact). Performa included the demographic details, related to the vaccine and vaccination centre, post vaccination exposures and most importantly health and drug status of the subjects. Subjects who developed symptoms of coVID-19illness within the 2 weeks post vaccination, were labelled as having post vaccination symptoms and their PCR (if done) during this time period were accepted as evidence for post vaccination coVID-19 illness. After completion of data collection, all data was entered on SPSS 23 for analysis. Data was sorted out on the basis of post vaccination symptoms and coVID-19PCR results, and then their profiles were compared according to these two outcomes. Descriptive statistics were calculated for both qualitative and quantitative data and expressed as frequencies and percentages. Effect modifiers like gender, age groups, co-morbid, drug history, during and post vaccination exposure, were controlled through stratification and post stratification, chi square and Fischer's exact test was applied and p value <0.05 was considered statistically significant.

RESULTS

Thirty four subjects (58.6%) were male and 26(41.4%) were females with mean age of 42±8.3 years (34 to 52 years). We analyzed relationship of demographic and other factors with two outcomes that is; post vaccination symptoms and post vaccination PCR. Twenty (33.3%) HCWs developed symptoms i.e. fever±respiratory symptoms whereas 40(66.66%) didn't develop any symptom post vaccination. Among 20 symptomatic patients, only 12 got their covid PCR done, out of which 7 (58.33%) had positive covid PCR and 5(41.66%) had negative PCR.

Age group of our participant did not differ much, that's why we did not considered the results related to age. We found out the effect of gender on the outcomes. 7 out of 34(20.58%) males while 13 out of 26(50%) females developed post vaccination symptoms. Gender affected the post vaccination symptoms with statistical significance and positivity of PCR with border line significance with the female gender was affected more. (p value=0.017, 0.064 respectively). Effect of gender on post vaccination PCR is shown in figure 1.

The relationship of individual factors like post vaccination exposure, post vaccination gathering, Peri-vaccination stress and fever during one week prior to vaccination and the type of vaccination with post vaccination symptoms but none of these factors were found significant (Table 1).

The effect of different co-morbid condition on post vaccination symptoms, 41 among 60 HCWs had no known co morbid, 6 were hypertensive and 2 of them were diabetic, 5 HCWs were hypothyroid and four among them developed post vaccination symptoms. In addition, 5 of them had chronic gastrointestinal conditions (4 were of undiagnosed chronic dyspepsia, 1 of coeliac disease), out of which 3 (two dyspepsia and one coeliac disease patient) developed post vaccination symptoms while PCR was positive in patient with coeliac disease (Table 2).

On analysis of drug history, 11 out of 60 HCWs were found taking some medicines, among which, 3 of 4 HCWs who were taking thyroxin, 1 out of 3 on anti-hypertensive, while 3 out of 3 of miscellaneous medicine users developed post vaccination symptoms. The impact of drugs on post vaccination symptoms was found to be significant (p value = 0.008). Among these; four patients using thyroxin, one using antihypertensive, one from miscellaneous drug group and one non-drug user were tested coVID-19PCR positive. (p= 0.003)

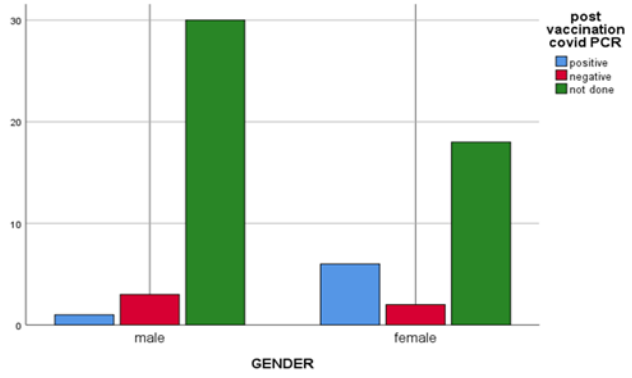
Table 1: Effect of non-demographic variables on post vaccination symptoms and coVID-19PCR

Variable	Post vaccination symptoms		P value	Post vaccination PCR		P value
	Yes	No		PCR done (total symptomatic)	PCR positive	
Post vaccination exposure with covid patients (n=21)	7(33.3%)	14(66.6%)	1.0	3(7)	2	0.79
Post vaccination attended gathering (n=21)	7(35%)	13(65%)	0.566	6(7)	4	0.377
Peri-vaccination stress (n=13)	4(30.7%)	9(69.2%)	1.0	1(4)	0	0.371
Fever during last one-week prior to vaccination (n=7)	0(0.00%)	7(100%)	0.084	0(0)	-	0.778
Congestion at vaccination centre (n=22)	9(33.3%)	13(66.6%)	0.344	4(9)	3	0.787
Time spent on vaccination centre >30 minutes(n=12)	4(33.33%)	8(66.66%)	0.37	1(4)	0	0.826
Type of vaccination(n=60)	20(33.33%)	40(66.66%)	0.769	12(20)	7	0.927

Table 2: Effect of co-morbid conditions on post vaccination symptoms and coVID-19PCR

Co-morbid	Post vaccination symptoms		P value	Post vaccination PCR		P value
	Yes	No		PCR done (total symptomatic)	PCR positive	
No co-morbid (n=41)	10(24.39%)	31(75.6%)	0.014	4(10)	0(0%)	0.000
Hypertension (n=6)	2(33.33%)	4(66.66%)		2(2)	2(100%)	
Diabetes mellitus(n=2)	-	2(100%)		0(0)	-	
Hypothyroidism (n=5)	4(100%)	1(0.0%)		4(4)	4(100%)	
Chronic respiratory illness(n=1)	0(0.0%)	1(100%)		0(0)	-	
Chronic gastrointestinal illness (n=5)	4(75%)	1(25%)		2(4)	1(50%)	

Fig. 1: Effect of gender on post vaccination coVID-19 PCR



DISCUSSION

We observed that few of the health care workers developed coVID-19illness after vaccination in earlier times of 2021, while they were continuously working in hospital since the onset of the pandemic and did not develop the disease. This triggered the thought to inquire the factors affecting the occurrence of coVID-19 illness after vaccination so to better tackle the risk factors and to modify vaccination protocols in high risk population. Health care professional are the most exposed community regarding acquiring the coVID-19 illness, and further their health care records were likely to be more readily available then others, so we found this population most suitable for this study. This idea of research is reinforced by other authors as well like as Antonelli M etal. stated that to minimize CoVID-19 infection, at-risk populations must be targeted in efforts to boost vaccine effectiveness and infection control measures.[10]

Our study findings showed more female got symptoms after vaccination and most of them who were tested, were coVID-19 PCR positive. Though our study population is small but our results match the already published data like Tran VN and colleagues conducted a study on 1028 participants who were Vietnamese, only 40/1028 (3.9%) participants reported not having any AEFI, whereas 25/1028 (2.4%) reported to have severe symptoms. Data analysis showed that females complained about AEFI (adverse events following immunizations) symptoms more frequently than males[11]. Saeed and colleagues[12] and another study by Ahsan and colleagues[13] concluded in their studies that regarding vaccine related side effects, females were more likely to have the side effects than males.

Al Ghafri and colleagues[14] studied that factors causing post vaccination symptoms found out the proportion of participants with at least one adverse effect after vaccination was significantly more in individuals who were younger, females, with more than secondary education, and employed. Again these findings endorse our observations of development of post vaccination symptoms[15] and effect of female gender on it.

Co-morbid conditions affecting the post vaccination symptoms and positivity of coVID-19PCR was the most important outcome of our study. Abbas and colleagues[16] concluded that Malaise, headache and fever were observed to be the most common side effects of the vaccine and there was a linear

relationship between manifestations of adverse effects and history of co-morbid conditions.

We further found that thyroid disorder remained significant in causing post vaccination symptomatic coVID-19illness with positive PCR. Relationship of thyroid illness with coVID-19 illness and its vaccination is still undiscovered, however Hariyanto et al[17] conducted a meta- analysis and they concluded that thyroid disease seems to be associated with an enhanced risk of severe coVID-19infection. Most important reason for this can be that the thyroid hormones are very important in the regulation of innate immune response[18]. So in the light of this meta-analysis we can assume that this particular co-morbid can be affected with the vaccination as well.

Another indirect evidence in support of our results is that there are many published data on case reports of development of thyroid disease (often hyperthyroidism) after vaccination. Vera Lastra[19] presented the cases of two female health care workers who received a coVID-19 vaccine, and three days later developed clinical manifestations of thyroid hyperactivity, with increased thyroid hormone levels on thyroid function tests, suppressed thyroid-stimulating hormone, and elevated anti-thyroid antibodies. Jeeyavudeen[20] also shared a similar report.

Since our all thyroid patients are of hypothyroidism developing covid after vaccination while the case reports mostly we observed, were about hyperthyroidism after vaccination, so probably hypothyroidism is a risk factor for vaccine related covid infection while hyperthyroidism is after effect of vaccine. Peri vaccination thyroidal illness may be a risk factor and after effect for females only. So, the occurrence of coVID-19 illness after vaccination should not be considered a mere chance, rather risk factors should seriously be looked for.

Small data is weakness of our study and it couldn't represent the true /valid percentages of co- morbid associated with the development of coVID-19 illness after vaccination hence larger cohorts are required to validate this hypothesis.

CONCLUSION

Female gender, hypothyroidism, hypertension and coeliac disease may pose an important risk factor affecting the occurrence of symptomatic COVID-19 illness after vaccination and these populations need their vaccination schedules along with the doses, to be reviewed. Other co-morbid conditions also need to be trailed after vaccination.

Conflict of interest: Nil

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