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Original Article

Public Health Section

Association of Adverse Events Following Immunisation with COVID-19 Vaccine and Lifestyle of Individuals: A Cross-sectional Analytical Survey

POOJITA SANTOSH RAO[1], VASAVI SANTOSH[2], DEEPAK LANGADE[3]

ABSTRACT

Introduction: The Coronavirus Disease-2019 (COVID-19) pandemic, being an emerging world health issue, has led to the swift development of vaccines. Various lifestyles, health conditions, and behaviours affect the body's reaction to immunisation.

Aim: To evaluate the association of Adverse Effects Following Immunisation (AEFI) with different lifestyles and health patterns.

Materials and Methods: A cross-sectional online epidemiological analytical survey in study population across India was carried out in Mumbai, India, from 1st June 2021 to 21st June 2021, using Google form survey. It included a sample of 586 responders. A questionnaire consisting of 26 questions regarding lifestyle habits and AEFIs following COVID-19 vaccine administration was distributed. Questions about lifestyle were obtained using Simple Lifestyle Indicator Questionnaire (SLIQ) which includes questions regarding diet, activity/exercise, alcohol consumption, smoking, and stress. Association between the SLIQ score, number and duration of AEFI was determined. Measurement data was presented as means with standard deviation. The SLIQ scores and age were compared between the different groups (AEFI present/absent, number of AEFI and duration of AEFI) using one-way Analysis of Variance (ANOVA).

Results: The incidence of reported AEFI was 577 (76.4%). The most frequently reported AEFI was redness 328 (74.38%) followed by pain, 233 (52.83%), swelling 233 (52.83%) and fever 222 (50.34%). It was observed that those with a higher SLIQ score, had an increased number and duration of AEFI (p=0.001). With increase in age, number and duration of AEFI experienced decreased (p<0.0001).

Conclusion: Balanced diet, mild to moderate exercise, abstinence from smoking and alcohol, reduced stress and younger age increase the number of AEFI, indicating a robust immune response.

Keywords: Coronavirus disease-2019, India vaccination, Lifestyle behaviours, Severe acute respiratory syndrome coronavirus syndrome-2

INTRODUCTION

Tremendous turmoil and global impact caused by the COVID-19 pandemic has led to accelerated development of vaccines against the coronavirus. A total of 102 candidate vaccines on 10 platforms are in clinical development, and 15 vaccines have already been licenced or approved for emergency use [1]. COVID-19 vaccination programme in India was initiated on 16th January 2021, and by 18th July 2022, an estimated 200 million vaccinations were completed [2].

High expectations of the general population regarding a vaccine's safety and efficacy challenge the introduction of any vaccine in the public health system. Rise in inflammatory markers within hours of vaccination due to immune response leads to AEFI. These Adverse Events (AE) may be any unfavourable or unintended sign, abnormal laboratory finding, symptom, or disease ranging from mild to life-threatening events. The reactions may be caused by the vaccine itself, or may be related to immunisation errors, anxiety or be coincidental [3].

Studies have documented that health behaviours have a direct association with vaccine responses or may synergistically interact with stress to predict vaccine response [4-6]. Hence, it would be interesting to assess whether individual lifestyle and behavioural factors alter the response to COVID-19 vaccine. There have been no large scale research studies on AEFIs with COVID-19 vaccine in the domestic population or their relation to individual lifestyles.

The primary objective of this cross-sectional survey was to estimate the association between AEFI with COVID-19 vaccination and common lifestyle predictors (diet, exercise, smoking, alcohol, stress) in the general Indian population. Considering this objective, the authors hypothesised that lifestyle factors may affect immune response, thereby causing variations in AEFI. The present study discusses the influence of lifestyle and age on AEFI with COVID-19 vaccines in India. The variables of gender, vaccine type and co-morbidities have already been published in a previous article [7].

MATERIALS AND METHODS

A cross-sectional online epidemiological analytical survey in study population across India was carried out in Mumbai, India, over 20 days from 1st June 2021 to 21st June 2021. Informed consent from the responders was obtained through Google forms circulated for the study. This study was conducted after obtaining approval from the Institutional Review Board (No. IREB/2021/OMDR/01).

Inclusion criteria: People above 18 years of age of Indian origin who had taken either one or both doses of COVID-19 vaccine were enrolled in the study.

Exclusion criteria: People who were not well versed with English language were excluded from the study.

Study Procedure

The study was in the form of Google forms questionnaire, with the link distributed through WhatsApp application. The data was collected based on passive reporting by the respondents. The questionnaire consisted of 26 questions, divided into two parts, and sought to examine socio-demographics, medical history, AEFI and lifestyle of individuals.

The first part consisted of basic information, including age, sex, and pre-existing co-morbidities, followed by information regarding vaccination, which included the vaccine's name and number of doses received. The AE as experienced by respondents were reported as either mild events like mild fever, chills, headache, tiredness, etc., or severe events like allergic reaction, fainting, hyperventilation, convulsions etc., which required medical attention. Duration of symptoms were also noted. Additionally, provision of free-text reporting allowed description of any other symptoms.

AEFIs were analysed in terms of number and duration of the event. The number of AEFIs reported were divided into four groups (No AE, 1-5 AE's, 6-10 AE's and >10 AEs); and the duration of AEFI into three groups (<3 days, 3-5 days and >5 days).

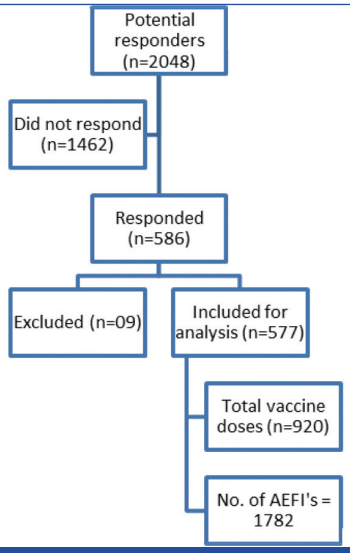
The second part was about participants' lifestyle and health status. SLIQ was used which has five components: diet (three questions), activity/exercise (three questions), alcohol consumption (three questions), smoking (two questions), and stress (one question). The dietary component includes consumption of green leafy vegetables, salad, fresh fruits and high fibre cereals; physical activity component consists of light, moderate and vigorous exercise; alcohol consumption includes type and frequency of consumption; smoking habits- yes/no, if no, whether they ever smoked; self-assessment of stress was on a Likert scale of 1 to 6. A level of 1 or 2 is considered very stressful, 3 or 4 moderate, while 5 or 6 were categorised as easy going. For each component, a raw score and a category score was calculated. To provide equal weightage for each component, overall SLIQ score was based on all the five category scores. Each component had a category score of 0, 1, or 2, so overall SLIQ scores can range from 0 to 10; higher the score, healthier the lifestyle [8].

STATISTICAL ANALYSIS

Measurement data was presented as means and Standard Deviation (SD) and 95% Confidence Intervals (CI), whereas categorical and nominal data were presented as numbers with percentages. The SLIQ scores and age were compared between the different groups (AEFI present/absent, number of AEFI, duration of AEFI) using one-way Analysis of Variance (ANOVA). Posthoc pair-wise comparisons were done using Bonferroni's method. Statistical significance was set at p-value <0.05 (95% CI). Statistical analyses were performed using the Statistical Package for the Social Science (SPSS) software version 25.0; (IBM Corp., Armonk, NY, US).

RESULTS

A total of 586 responders of Indian origin completed the AEFI questionnaire, of which nine responses were excluded due to incomplete information [Table/Fig-1]. Thus, the final cohort consisted of 577 respondents (231 male and 346 female) between age group 18 to 84 years. All respondents had received first dose of COVID-19 vaccination, whereas only 343 had received the second dose. The present article discusses a part of the results obtained from the survey.



[Table/Fig-1]: Flowchart of study responders.

The overall incidence of AEFI in the present study was n=577 (76.4%) with 337 individuals reporting 1-5 AEs (58.4% of the total respondents). The most frequently reported AEFI was redness present in 328 (74.38%) followed by pain in 233 (52.83%), swelling in 233 (52.83%), and fever in 222 (50.34%) cases.

The longest duration of any AEFI was considered as the number of days that AEFI was present. Most AEFIs were reported for <3 days, 358 (81.2%) followed by 3-5 days, n=58 (13.2%) and five days, n=25 (5.7%).

Mean SLIQ score of the population was 6.61 (SD±1.2). The SLIQ scores were significantly higher for those who had experienced an AEFI (p-value <0.0001). Similarly, based on the number of AEFIs experienced by the responders, it was observed that those with a greater number of AEFIs had a higher SLIQ score (p-value=0.001) [Table/Fig-2]. Posthoc pairwise comparisons showed that SLIQ scores were significantly higher in responders with 1-5 AEFI's (p-value=0.006, 95% CI -0.72 to -0.08) and 6-10 AEFI's (p-value=0.003, 95% CI -0.97 to -0.14) than those without AEFI. Duration of AEFI experienced by responders increased with increase in SLIQ score (p-value <0.0001) [Table/Fig-2]. Posthoc pair-wise comparisons shows that SLIQ scores were significantly higher in responders with AEFI for <3 days (p-value=0.001, 95% CI 0.13 to 0.76) and 3-5 days (p-value=0.006, 95% CI 0.13 to 1.11) than those without AEFI.

Parameters	N	Mean	SD	95% CI for mean	Range	F-value, p-value
AEFI						
No AEFI	136	6.28	1.251	6.07 to 6.49	2-9	14.084, <0.0001
AEFI present	441	6.72	1.167	6.61 to 6.83	1-10	
Total	577	6.61	1.201	6.52 to 6.71	1-10	
Number of AEFI						
No AEFI	136	6.28	1.251	6.07 to 6.49	2-9	5.268, 0.001
1-5 AEFIs	337	6.68	1.175	6.55 to 6.80	1-10	
6-10 AEFIs	98	6.84	1.128	6.61 to 7.06	3-10	
>10 AEFIs	6	7.00	1.414	5.52 to 8.48	5-9	
Duration of AEFI (days)						
<3 days	358	6.72	1.192	6.60 to 6.85	1-10	6.767, <0.0001
>5 days	25	6.20	1.155	5.72 to 6.68	4-8	
3-5 days	58	6.90	0.949	6.65 to 7.15	5-9	
No AE	136	6.28	1.251	6.07 to 6.49	2-9	

[Table/Fig-2]: SLIQ scores and AEFI.
ANOVA test was used, p-value <0.05 considered significant

Age of respondents ranged from 18-84 years. Age was taken as a continuous dependent variable. Presence or absence of AEFI varied significantly with age (p-value <0.0001). Based on number of AEFI's experienced by responders, it was observed that those with more number of AEFI's were younger in age (p-value <0.0001) [Table/Fig-3]. Posthoc pair-wise comparisons shows that age was significantly lower in responders with 6-10 AE's (p-value=0.001, 95% CI 8.03 to 18.34) and >10 AEFI's (p-value=0.07, 95% CI 3.75 to 36.19) than those without AEFI.

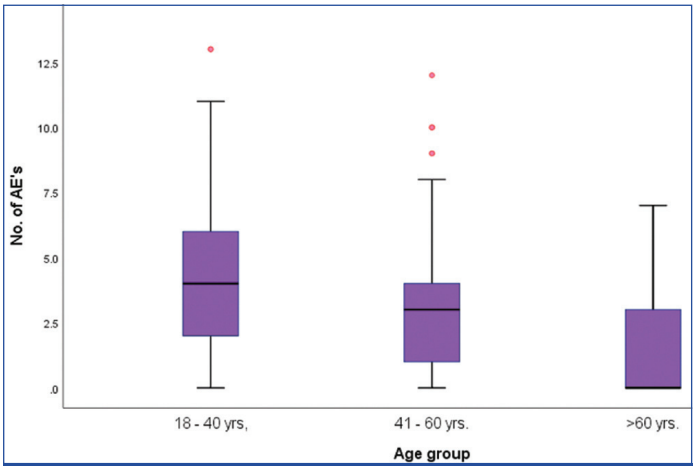
Additionally, age was significantly lower in responders with 6-10 AEFI's (p-value=0.001, 95% CI 4.35 to 13.27) than those with 1-5 AEFI's. Duration of AEFI experienced by the responders increased with decrease in age (p-value <0.0001) [Table/Fig-3]. Posthoc pair wise comparisons show that age has significant variation in responders with AEFI for <3 days (p-value=0.001, 95% CI 2.96 to 10.91) and

3-5 days (p-value=0.001, 95% CI 2.61 to 14.99) than those without AEFI. Additionally, age has significant variation in responders with AEFI for less than 3 days (p-value=0.002, 95% CI 3.10 to 19.43) and 3-5 days (p-value=0.002, 95% CI 3.69 to 22.57) than those with AEFI for more than five days. There is a significant negative association (r=-0.354, p-value <0.0001) between age of the individual and AEFIs reported.

AEFI	N	Mean	SD	95% CI for mean	Range	F-value, p-value
AEFI						
No AEFI	136	47.47	16.020	44.75 to 50.19	18-84	19.596, <0.0001
AEFI present	441	40.93	14.766	39.55 to 42.31	18-83	
Total	577	42.47	15.311	41.22 to 43.72	18-84	
Number of AEFI						
No AEFI	136	47.47	16.020	44.75 to 50.19	18-84	17.684, <0.0001
1-5 AEFIs	337	43.10	14.170	41.58 to 44.62	18-83	
6-10 AEFIs	98	34.29	14.594	31.36 to 37.21	18-80	
>10 AEFIs	6	27.50	12.755	14.11 to 40.89	19-52	
Duration of AEFI (days)						
<3 days	358	40.53	14.517	39.02 to 42.04	18-83	11.639, <0.0001
>5 days	25	51.80	13.118	46.39 to 57.21	19-80	
3-5 days	58	38.67	15.252	34.66 to 42.68	18-76	
No AE	136	47.47	16.020	44.75 to 50.19	18-84	

[Table/Fig-3]: Age (years) and AEFI.
ANOVA test was applied, p-value <0.05 considered significant

The mean (median, range) number of AE's reported in the age group 18-40 years was 4.20 (4, 0-13), whereas in age groups of 41-60 years and >60 years the number of AE's reported were 2.73 (3, 0-12) and 1.6 (9, 0-7) respectively. Thus, as the age increased, number of AEFIs decreased [Table/Fig-4].



[Table/Fig-4]: Age group and number of AEFI reported.

DISCUSSION

The society's expectations of high efficacy along with minimal AEFI make it a challenge [9]. Vaccines exploit the human immune system's ability to respond to pathogen's antigens via two mechanisms, innate and adaptive immune response [10]. Innate immunity is rapid, non specialised and first to act in response to an invading pathogen, resulting in inflammation, with signs such as redness, swelling, heat and pain [11].

The overall incidence of AEFI in the present study population was 76.4%. However, in an interim analysis on Healthcare Workers (HCW) in India by Kaur U et al., 40% were affected by AEFI after first dose and 15.7% after second dose. About 77% and 86% of them had systemic involvement [12]. A difference in age range of the study population could be the reason for difference in incidence of AEFI, as the youngest responder in the present study was 18-year-old, whereas Kaur U et al., study being on HCWs would imply an older age group [11]. Also, HCWs might have been exposed to these antigens previously and a larger percentage could be producing a secondary immune response, whereas the general population had lesser probability of exposure, could be majorly having a primary immune response.

In the study population, the most frequently reported AEFI were redness (74.38%), pain (52.83%), swelling (52.83%) and fever (50.34%). In comparison, higher incidence of AEFI among vaccinated Korean HCWs was reported by Jeon M et al., such as tenderness at the injection site (94.5%), fatigue (92.9%), pain at the injection site (88.0%), and malaise (83.8%) [13]. Lifestyle issues including physical activity, diet, smoking, alcohol consumption, and stress have all been shown to modify the immune system. A healthy, balanced diet and adequate nutrition is fundamental for a strong and optimally functioning immune system [14]. Specific nutrients may exert effects on immune functions through alterations of gut microbiota composition, cell activation and modification of both gene expression and production of signalling molecules [15].

Yang F et al., have also documented 20 functional food plants with immunomodulatory and antiviral properties, including liquorice, garlic, tea, ginger, turmeric, pomegranate and black pepper which would not only enhance the immune system but would also greatly impact overall health. They also advocated use of these in rapid recovery from SARS-CoV-2 infection. Probiotics, micronutrients and vitamins activate multiple immune mechanisms, boost immunological networks and enhance immune responses [16].

Western diet has also been shown to trigger reprogramming of innate immunity and lead to long-term changes in immune responses in mice [15]. Benefits of physical exercise depend on its nature, duration and intensity. It has been found that moderate exercise may boost immunity and lower risk of infections, while heavy exercise may dampen immunity and increase susceptibility to super infections. This forms as a J-shaped curve [15,17].

Impaired host defence after alcohol exposure appears to be linked to a combination of decreased inflammatory response, altered cytokine production, and abnormal reactive oxygen intermediate generation. Furthermore, cellular immunity, particularly antigen-specific immune response, is impaired by both acute and chronic alcohol use. Although T-lymphocyte functions can be directly affected by ethanol, decreased antigen presenting cell function appears to be a key element in the ethanol-induced decrease in cell-mediated immunity. In addition, a preferential induction of Th2 vs Th1 immune response has been suggested based on the increased immunoglobulin levels seen in chronic alcoholics [18].

The influence of cigarette smoke on the immune system however, is diverse and of dual nature-pro-inflammatory and immunosuppressive. Cigarette smoke promotes inflammation by inducing the production of pro-inflammatory cytokines, such a Tumour Necrosis Factor-α (TNF-α), IL-1, IL-6, IL-8 and Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF), Nicotine has shown to decrease IL-6, IL-8, and IL-10 production. Cigarette smoke has a profound impact on activity and function of adaptive immune cells, namely T helper cells (Th1, Th2, Th17), CD4+CD25+ regulatory T cells, CD8+ T cells, B cells and memory T and B lymphocytes [19].

Psychological, social and behavioural factors can substantially affect the immune system's response to vaccines. Chronic stress is associated with dysregulated immunity. Psychological stress also increases circulating IL-6. Studies showed reduction in stress helped reduce extent of side-effects [20,21].

Measuring all these human behaviours is not an exact science and in health research, a measure that is short and easy, especially in a

clinical setting where responders are busy and patients may be ill is preferred. SLIQ is a short, easy-to-use instrument to measure all these lifestyle characteristics as a single construct [22].

The SLIQ score in our study showed a mean of 6.61 with a standard deviation of 1.2. The SLIQ score had a highly significant variation with the number and duration of AEFIs in the responders. A higher SLIQ score correlated with an increase in the number and duration of AEFIs. A significant negative association was seen between age and AEFIs experienced both in terms of duration and number of AEFIs. As the age increased, duration and number of AEFIs decreased. This is similar to previous studies done on HCWs by Kaur U et al., and Jeon M et al., [12,13]. They showed increased risk of AEFIs in younger individuals, and the severity and number of AEFIs were less in the older age group [12,13].

An impacting factor could be immunosenescence, which is the decline in immune function as age advances. With advancing age, thymic involution, decreased thymic output, as well as, micro nutrient deficiency result in declined T-cell function, which ultimately leads to reduced immune response [11]. Simpson RJ et al., in their review, have summarised some of the known effects of exercise on immunosenescence, and provide potential mechanisms by which exercise may help rejuvenate the aging immune system [17].

Vaccine platforms and age groups of vaccine recipients could account for much of the heterogeneity in safety profiles between COVID-19 vaccines. Reporting rates of AE from postauthorisation observational studies have been similar to results from clinical trials [1]. However, according to Wu Q et al., reporting rates of AE from postauthorisation safety monitoring (passive surveillance) were lower than in clinical trials and varied between countries [1].

Limitation(s)

The present study was an interim analysis. Large-scale and long-term population-level surveillance with diverse ethnicities is highly recommended to assess the safety profile of COVID-19 vaccines.

CONCLUSION(S)

Balanced diet, mild to moderate exercise, abstinence from smoking and alcohol, reduced stress and younger age are factors which increase the number of AEFI. AEFIs indicate a robust immune response. Hence, experiencing an AEFI should not be a factor for non acceptance of COVID-19 vaccine.

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PARTICULARS OF CONTRIBUTORS:
1. 3rd Year Student, HBT Medical College and RN Cooper Hospital, Mumbai, Maharashtra, India.
2. Professor, Department of Oral Medicine and Radiology, School of Dentistry, DY Patil University, Navi Mumbai, Maharashtra, India.
3. Professor and Head, Department of Pharmacology, School of Medicine, DY Patil University, Navi Mumbai, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Vasavi Santosh,
Flat No. 701, Gurusamridhi Heights, Plot No. 2, Sector-14, Sanpada,
Navi Mumbai, Maharashtra, India.
E-mail: sanvas72@yahoo.com

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