Title: Reporting Issues of Adverse Effect of COVID-19 Vaccine - What we know or don't know?

Abstract:

Vaccines for COVID-19 in India have been allowed to be administered among large pool of adult population. In-depth knowledge regarding adverse effect of vaccine is scarce till date, mainly due to lack of reporting, analyzing and making the data publicly available. Informed choice by the recipients is totally barred and further, compensation associated with the vaccination is also compromised. These important issues need to be highlighted in the public forum for greater awareness and action.

Main text:

Vaccines for COVID-19 has been allowed by the government for all adults (18 years and above) while looking at the spread, and chronic nature of the second wave of pandemic in India. The surge of COVID-19 cases in India has placed the country at second position in terms of absolute cases of infection. Statistics shows that around 120 million population (8.6% of total population in India[a]) has been inoculated by the end of 17th April, 2021. That includes those have been vaccinated with first and second dosage(s) in the age group of 45 and above since the inception, which is 16th January, 2021. Only 15 million populations received both dosages of vaccine till now. India is administering two kinds of vaccine; one is Oxford-Astra Zeneca's Covishield, and another is Covaxin by indigenous Bharat Biotech. Most of the population has received the Covishield vaccines, and the females are marginally lower in getting the vaccination till date (COWIN, GoI, 2021). Despite all the efforts, a massive under-reach of the vaccination can still be estimated if India aims to fully cover adult population by the end of this year at the current rate (month of September, 2021) which is nearly 8 million dosages per day. Moreover, a shortage in the vaccine has already been noted which led to approve Sputnik-V developed by Gamaleya Institute of Russia during late March, 2021. Therefore, a surge in the demand for vaccine would be seen along with a massive stress on the health care management system.

It must be mentioned that the post-effect of the vaccination has not been deciphered with confidence by the governing bodies. Beside the issue of under supply of the vaccines, the fear of After Effect (AE) of vaccine can be perceived among population which might affect the vaccination program at large. Despite the rigorous clinical trial of the vaccine to measure the efficacy, until March 31st, 2021, a recent evidence of 180 cases of death has been learned from post-vaccination individuals by National Adverse Event Following Immunization (AEFI) committee of India (The Hindu, April 9th 2021). A three-fourth of these death has occurred within three days of vaccination of Covishield. The effect of these vaccines,

whether mild or severe, is varying to a great extent with respect to age, sex, and associated co-morbid conditions. Research on application of different vaccines across demographics and social groups could generate more robust statistics for efficacy, and the plausible effect of vaccine. During the clinical trial of Astra-Zeneca Covishield vaccine, effect like fever, transverse myelitis etc. have been observed (Voysey *et al*., 2020); however, these have been proven to impart an independent effect claimed by the researchers. The possible inadversities of the vaccines might appear due to insufficient time employed at the third stage of the vaccine administration in the clinical trial. The recent deaths are the probable result of that phenomenon. However, we have limited knowledge regarding cases reported till date as mild to severe post-vaccination AE in India. The under-enumeration of the number of cases of infection, number of subject observed symptom after vaccination etc. can be reflected through that information.

A growing evidence of death and few other side effects like allergic reactions or anaphylaxis, thromboembolic events, capillary leak syndrome etc. have been recognized in the various part of the world (China Global Television News, 17th April, 2020; DW news, 15th March), which led to halt the administration of the vaccines like, Covishield in a handful number of countries. The mRNA based vaccines are using polyethylene glycol as a substance. Even though it shows a negative non-irritating skin testing, still it can't say that there won't be any evidence of allergies in the subject (Banerji *et al*., 2020). This AE of the vaccines are not statistically proven for COVID-19, and the scattered information consummates that substantial evidence of negative effect of vaccines administered for COVID-19 cases at this time. It is highly expected that the country which are under-reporting the cases of infection or showing a poor reporting for causes of death, they are very likely to under-report any AE of drug mainly due to the lack of awareness or non-adherence to the system, per se. Moreover, when a massive pool of population is aimed to be vaccinated at a shorter period of time, it is intriguing to jolt down the AE and its extent of impact, effectively.

After the launching of Global Vaccine Safety Blueprint by World Health Organizations in 2011, the complaint against drug related adverse reporting system is quite strongly performing in many developing countries. Like the Vaccine Adverse Event Reporting Systems (VAERS) in the United States (US), Medicine and Healthcare Products Regulatory Agencies in the United Kingdom (UK) and other departments under wide range of ministries in advanced European, Asian nations are also not lagging behind to uptake such steps.The UK has a yellow card reporting system for adverse events which includes side effects, and fatal outcomes following COVID-19 vaccination. The yellow card reporting system is voluntary in nature where anyone encouraged to report irrespective of experiencing minor and major side effects post vaccination. It is found that 50 per one million populations have an incidence of AE in US. Majorly non-serious adverse effects have been found, and being females, at the age group of 18-49 years are very prone to report the AE (Gee *et al*., 2021). The UK provides weekly report of the reported infection from COVID-19 vaccination mentioning morbidity along with the nature of adverse events and mortality occurred, which depicts the promptness and sensitivity of the reporting, and healthcare system (MHRA, 2021).

India has adopted Pharma covigilence Programme under the aegis of Central Drug Standard Control Organization (CDSCO) for monitoring AEs due to drugs since 2010 to take necessary regulatory actions (Meher, 2019). In recent move to vaccination of adults in India, the Government has taken a step towards reporting the number of vaccination given that is represented by number of days, session, gender, types of vaccine etc. in the Co-Win Website across states. The adverse effect of vaccines is allowed to be reported through Co-Win, Arogya Setu App or reporting to the nearby medical facilities in the documents. Every block is assigned to identify a stipulated AEFI management center. That must be advertised for the public interest, so that they can reach out at the time of need. The Case Reporting Form to be filled to register a complain should be comprehensive, easy to fill, and illegible for the

masses. Still, too many doubts hover around active support system, and transparency in the reporting system delivered by the acting bodies.

Poor awareness, lack of active participation or negative attitude of the health care professionals, inadequate training, procrastination by the providers and consumers etc. might be major challenges represented by the system elucidated in the existing study (Mulchandani & Kakkar, 2018). Such has been again substantiated by the fact that Government has enlisted only 492 cases for severe and serious After Event Following Immunization (AEFI) which are fully documented as against 617 reported for AEFI reported by 29th March, 2021. While, 10 deaths out of 13 AEFI has been made public by the authority on March 17th, 2021. However, at least six of the cases do not hold any evidence for the post-mortem related facts (The Hindu, April 9th, 2021). Getting reported and releasing those reports are the priority at this time-point as the country is approaching towards severe scarcity in health services, and growing burden of death due to the pandemic.

Though, according to the existing vaccine safety surveillance mechanism, under the Universal Immunisation Programme (UIP) monitoring of post immunization AE is being carried out. But these information is not fully available in the public domain (IMTSU, 2021). Considering the poor educational achievement, low awareness, under reporting, improper system of dissemination, and compromised interest to highlight every bit of health system functionaries, it is imperative to suggest a robust, prompt, and public friendly design for grievance redressal arising from the vaccination. The important steps to reduce the adverse AEFI encompass a proper investigation which includes reporting and analysis, recognition of side effects, and further provide solution in each vaccination centres. From ethical point of view also its important to undertake an in-depth investigation, provide immediate medical care, and compensation to the victims. Despite the announcement made by WHO on No-Fault Compensation Programme in regards to covid-19 vaccination for 92 low and middle-income countries (WHO, 2021), a clarification for such compensation for AE of these

vaccines by the government is yet to come in the picture. Indian population need exceptional transparency related to drug, and vaccine specific AE, which builds trust in the health system, and also helps people to take an informed decision about uptake of vaccine. We must consider that while allowing the population to get the vaccines, we should not be leave out the socio-economically marginal section of the population to get the facility or addressing their grievance at any cost.

A great deal of effort is required to enlist data and to make it publicly available, foremost, to address right application of every vaccine. A serious emergency must be announced to tackle the wrath of the second wave of COVID-19 pandemic along with proper administration of the vaccine, so that we don't lose our near and dear one due to mere obdurateness of the system. Besides, a robust reporting system advanced technology would help to collate, and produce scientific decision-making system in this situation. Machine learning or artificial intelligence in that context has advanced the vaccine design in a considerable way through improved predicting capacity (Arshadi *et al.*, 2020; Mesko, 2017). Hence, advancement in the medical supremacy with the indigenous effort for artificial intelligence is highly recommended. It would help to gather information and to develop a decision-making system at the earliest towards AE of vaccine for the large, and diverse population like India.

N.B.

[a.] 11,99,37,641 total population vaccinated (Ministry of Health & Family Welfare). Total population in India 139,15,65,180 (Dash board- International Institute for Population Sciences (IIPS), Mumbai on 17th April, 2021.

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