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ADVERSE EFFECTS FOLLOWING IMMUNIZATION RELATED TO COVID 19 VACCINE

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ABSTRACT

COVID-19 is a disease caused by a virus named SARS- COV -2. Countries around the world are rolling out COVID 19 vaccines, and a key topic of interest is their safety. COVID 19 vaccines are crucial tools in the pandemic response and protect against severe disease and death. But they are also having risks or adverse effects which can be prevented. Adverse event following immunization is any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with usage of vaccine. Commonly reported AEFI include fever, myalgia, headache, pain at injection site. The older population with comorbidities are more prone to adverse effects. This review highlights the types of vaccines., ADR reported in WHO approved vaccines, causality assessment in AEFI and various studies detailing AEFI following COVID 19 vaccine.

Keywords: SARS-COV-2, VITT,VLP, TYPES OF VACCINE

Introduction

Nowadays, People are very concerned towards the risk involved with vaccines. AEFI is any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom or disease. Effective vaccines could produce few unwanted side effects mainly mild and clear up frequently. Many of the errors occurred is associated with vaccine administration and not due to vaccine. Therefore, a systematic data collection of all minor and major medical events occurred after vaccination, was performed in immunization program by WHO (1)

An infectious disease disaster in late 2019 and still contagious as on date occurred. One of the main reasons for decrease in the number of cases reported and mortality is Covid vaccine. There are few vaccines released into the market claiming that improve the immune response against SARS-COV-2. But the mechanism by which they act differs from one another.

Types of vaccines

Types of component viral vaccines

1. Protein sub unit: Contains isolated and purified viral proteins
2. Virus Like Particles (VLP): Contains viral proteins that mimic the structure of the virus, but no genetic material
3. DNA/RNA Based: Contains viral genetic material (such as mRNA) which provides instruction for making viral proteins
4. non-replicating viral vector: Contains viral genetic material packaged inside another harmless virus that cannot copy itself
5. Replicating viral vectors: Contains viral genetic material packaged inside another harmless virus that can copy itself. (2)

Table 1: - ADRs reported in WHO approved vaccines during clinical trials

Vaccine Name	Manufacturer	Vaccine Type	Commercial name	Adverse events
1.BNT162b2	Pfizer-BioNTech	COVID - 19 mRNA vaccine	COMIRNATY ®	Common: fever, fatigue, headache, pain at injection site. Serious: lymphadenop

				athy, CVA, myocardial infarction.
2. mRNA- 1273	Moderna	COVID 19 mRNA vaccine (nucleoside modified)	Not applicable	Common: tiredness, chills, underarm swelling, fever Serious; intractable nausea or vomiting and facial swelling
3.NVX- COV-2373	Novavax	COVID- 19 vaccine (SARS- COV -2rS recombinant, adjuvanted	NUVAXOVID ™	Common: tenderness, fatigue, malaise Serious; joint pain, nausea Rare: severe allergic reactions
4. AZD1222	Oxford/Astraz eneca	Non replicating viral vector	Vaxzevria	Common: arthralgia, nausea Serious; pyrexia, hemolytic anemia.
5.Covaxin	Bharat Biotech	COVID-19 vaccine (whole virion Inactivated corona virus vaccine)	COVAXIN ®	Common; fatigue, nausea and vomiting. Serious; not

				reported.
6.Covishield	Serum institute of India	COVID-19 vaccine (chAdOx1- S, recombinant)	COVISHIELD (™)	Common; fever, chills, shortness of breath., Loss of taste or smell.
7.Covovax	Serum institute of India	COVID 19 vaccine (SARS- COV 2- rS protein. Nanoparticle	COVOVAX (™)	Common: tenderness, headache, fatigue.
8.Ad26COV2S	Janssen	Non replicating viral vector	Johnson and Johnson vaccine	Common; myalgia, fever Serious; hypotension, worsening of multiple sclerosis.
9. BIBP Covid 19 vaccine	Sinopharm	Inactivated COVID 19 vaccines (Vero cell)	Covilo	Common: fever, headache
10.Corona vac	Sinovac	Inactivated COVID 19 vaccines (Vero cell)	Corona vac	Common; pain at injection site. Serious: urticaria

Causality Assessment in AEFI

Causality assessment is the relationship between two events (the cause and the effect), where the second event is a consequence of the first.

Levels of AEFI causality assessment and their scientific basis

Causality assessment of AEFI should be performed at several different levels. The first is the population level, where it is necessary to test if there is a causal association between the use of a vaccine and a particular AEFI in the population. Secondly, at the level of the individual AEFI case report, one should review previous evidence and make a logical deduction to determine if an AEFI in a specific individual is causally related to the use of the vaccine. The third level of assessment is in the investigation of signals.

Steps for causality assessment of an individual AEFI

Causality assessment has four steps, as follows:

Step 1: Eligibility. The first step aims to determine if the AEFI case satisfies the minimum
criteria for causality assessment as outlined below.

Step 2: Checklist. The second step involves systematically reviewing the relevant and available information to address possible causal aspects of the AEFI.

Step 3: Algorithm. The third step obtains a trend as to the causality with the information gathered in the checklist.

Step 4: Classification. The fourth step categorizes the AEFI's association to the vaccine or vaccination on the basis of the trend determined in the algorithm. (3)

WHO causality assessment scale and Naranjo probability scale are the widely used and commonly preferred in most of the practices.

Studies conducted in AEFI following COVID 19 vaccine

- Adverse events following immunization against COVID-19 among healthcare workers: An observational study in Haryana by Chintu Chaudhary et al. conducted a study over two series of COVID vaccination drive sessions.
  In the study, 68 individuals (9.5%) reported to have documented comorbidity, out of which 61 individuals had either hypertension or diabetes or both. Adverse events following Immunization (AEFI) were assessed and followed up in regular intervals with first reporting of AEFI within 30 min, then within 1 day (24 h) and then any AEFI within 7 days. The overall incidence of any AEFI reported including any major, minor with the first dose vaccination, and was found to be 136/1000 vaccination events , with most people experiencing any AEFI after 30 min but within 24 h following immunization . After the subsequent second dose of vaccination, only two persons (3/1000 vaccinations) experienced mild symptoms and remaining 609 did not experience any symptoms after the vaccination. The results shown in this study are from the first dose of COVID vaccination. Most of the adverse events were short-lived and reported in the first 24 h of vaccination.(4)

- Another study was conducted based on AEFI of COVAXIN vaccine in a tertiary hospital in India, by Swayam Pragyan Parida et al and it was found that no

severe adverse events were reported, and about 1.6% had moderate AEFI. Pain at the injection site (14.6%), fever (9.7%), and myalgia (5.9%) were the common adverse events reported by the participants. AEFI incidence was higher in the first dose (38.1%) when compared to the second dose (26.4%).The most significant finding was that the major factors associated with AEFI were female sex, history of an allergic reaction, presence of comorbidities, acute infection in the past 3 months, and intake of chronic medications.(5)

- A systematic review was done on AEFI during pregnancy and newborn period by T.Roice Fulton. A total of 240 adverse events were reported among all selected publications. A significant proportion of these described typical pregnancy complications and a variety of congenital abnormality. (6)

Table 2: - Top 10 adverse effects reported in pregnancy period.

Adverse event	Number of times reported
Miscarriage/spontaneous abortion	31
Preterm birth	31
Stillbirth	25
Fever, maternal	19
Pre-eclampsia	14
Site pain	12
Low birth weight	12
Elective abortion	11
Respiratory distress	11
Small for gestational age	11

- A study on incidence, Pattern and Severity of Adverse Events Following Immunization (AEFIs) Associated With Chadox1 nCOV-19 Corona Virus Vaccine (Recombinant) among the Healthcare Workers of a Tertiary Care Uttar Pradesh, India was done stating that only around 10% experienced any AEFI within the directly observed period. The most common AEFI was pain/tenderness at the injection site experienced by 59.3% of those who experienced any AEFI followed by headache/dizziness (35.3%), itching/rashes at the injection site (8.1%), nausea/vomiting (5.8%) and fever/chills (4.7%). The majority (95.3%) of the AEFIs observed were of minor severity with no serious AEFIs observed as per the WHO severity classification. Thus Coronavirus vaccine (recombinant) is proven to be safe based on these findings as the majority of AEFIs observed were of minor grade only. (7)

- Another prospective study by Upinder Kaur et al on-safety analysis of Covishield vaccine use in healthcare workers was conducted. Primary outcome was safety and reactogenicity. Categories and outcomes of adverse events following immunization (AEFIs) were recorded, causality assessment was performed, and risk factors analysed.
  The results show that AEFIs following first dose were reported in 321. Among 730 participants who completed a 7-day follow-up post second dose, AEFIs occurred in 115. Majority of AEFIs were mild-moderate and resolved spontaneously. Serious AEFIs, leading to hospitalization was noticed in 1 (0.1%) participant with suspicion of immunization stress related response (ISRR). AEFIs of grade 3 severity were recorded in 4 participants (0.5%). No deaths were recorded. Regression analysis showed increased risk of AEFIs in younger individuals, two times higher odds in females, those with hypertension or with history of allergy; and three times higher odds in individuals with hypothyroidism.
  Thus, COVISHIELD carries an overall favorable safety profile with AEFI rates much less than reported for other adenoviral vaccines. Females, those with hypertension, individuals with history of allergy and hypothyroidism may need watchful vaccine administration. (8)

- A recent study done by Maryam Kakovan et al points out that various types of stroke including ischemic stroke, hemorrhagic stroke, as well as cerebral venous sinus thrombosis (CVST) occur after COVID-19 vaccination.Most of such patients were women under 60 years of age and who had received ChAdOx1 nCoV-19 vaccine.The most common symptom of CVST seen after COVID-19 vaccination was headache. It was found that low molecular weight heparin is commonly used in the treatment of CVST.The outcomes may worsen
  in CVST associated with VITT. (9)

<u>Vaccine - induced Thrombocytopenia in Covid 19 vaccination</u>

The discovery of the rare but significant and potentially fatal consequence of vaccine induced thrombocytopenia (VITT) aroused questions about the safety of

COVID-19 vaccinations, prompting many governments to reassess their vaccination strategy. Immune thrombotic thrombocytopenia caused by platelet-activating antibodies against PF4, which clinically mimics autoimmune heparin-induced thrombocytopenia, can occur after vaccination with ChAdOx1 nCov-19.

Oxford/AstraZeneca [ChAdOx1] (AZ) and Johnson & Johnson [Ad26.CoV2] were discovered by reviewing related papers to the condition above .S] Vaccine-induced Immune Thrombocytopenia and Thrombosis (VIITT) has been associated to significant thromboembolic events paired with thrombocytopenia (VITT). The pathophysiology of COVID-19 VITT is still a mystery, particularly the mechanisms that promote platelet activation, platelet factor (PF)4 release, complex formation, and PF4 antibody generation. This is a prospective study looking at the effects of several COVID-19 vaccines on inflammation (CRP, TNF-, IL-1, IL-6, IL-8, IL-10), vascular endothelial activation (syndecan-1, thrombomodulin, E-selectin, ICAM-1, ICAM-3, VCAM-1), platelet activation (P-selectin, TGF-, sCD40L) and aggregation.

The main findings were that both vaccines increased inflammation and platelet activation, but that AZ vaccination caused a more pronounced increase in several inflammatory and platelet activation markers than mRNA vaccination, and that post-vaccination thrombin generation was higher after AZ vaccination than after mRNA vaccination. There was no difference between the vaccine groups in terms of PF4 antibody levels or the proportion of people with positive PF4 antibodies. This is the first study to show that AZ immunization causes increased inflammation, platelet activation, and thrombin production when compared to mRNA vaccination. Specific components of the AZ adenovirus vector may operate as initial triggers of (hyper) inflammation, platelet activation, and thrombin production, thereby reducing the threshold for a cascade of events that results in death.

Surveillance of COVID-19 vaccines after approval has revealed safety indications, including uncommon occurrences of thrombocytopenia with thrombosis observed in adenoviral vector vaccination recipients.

In study conducted by Nick Andrews et al .It was observed that greater waning in vaccine effectiveness against hospitalization was observed in persons 65 years of age or older in a clinically extremely vulnerable group and in persons 40 to 64 years of age with underlying medical conditions than in healthy adults.(10)

CONCLUSION

Even though vaccines have risks of adverse events, their advantages in disease prevention cannot be denied. Ongoing surveillance of AEFI and regular analysis revealed integral management of immunization programs. The above studies showed that most adverse events were short lived and reported in first 24 hr. of vaccination. The major factors associated with AEFI were female sex, history of allergic reaction and presence of comorbidities. The most common AEFI reported was pain/ tenderness at injection

site followed by headache, vomiting and fever. According to Johns Hopkins, the 2 mRNA vaccines, Pfizer and Moderna recommended by the Centre for disease control and prevention are safe and risks of serious adverse effects with these vaccines were minor.

Vaccine Induced thrombocytopenia occurred after vaccination with Oxford/ AstraZeneca and Johnson and Johnson was reported. Vaccination must not be done if there is history of severe allergic reactions to any ingredients of Covid 19 vaccine or you suspected Covid 19.
Every person should be made aware of common side effects and manage them confidently and take medications only when required. All AEFI should be reported using standard Covid 19 AEFI reporting form and followed by vigiflow, a management system for recording, processing of adverse effects. (3)

REFERENCES

1.Sharique Ahmad et al; "Adverse Event following Immunization (AEFI) and COVID-19 vaccination": A Review ,International Journal of Current Microbiology and Applied Sciences ISSN: 2319-7706 Volume 10 Number 06 Pg 555- 565 (2021).

2.Sutharson Lingadurai et al;" Adverse events following immunization (AEFI)for Covid vaccines approved by WHO- A short review". IP International Journal of Comprehensive and Advanced Pharmacology 2022;7(1): Pg40–43

3.WHO/HIS/EMP/SAV. JANUARY 2018; Causality assessment of an adverse event following immunization (AEFI): user manual for the revised WHO classification (Second edition) ISBN 978-92-4-151365.

4.Chaudhary, et al (2022). Adverse events following immunization against COVID-19 among healthcare workers: An observational study in Haryana, India. Asian Journal of Medical Sciences, 13(3), pg; 23–29.

5.SwayamPragyan et al "Adverse events following immunization of COVID-19 (Covaxin) vaccine at a tertiary care center of India" Journal of Medical Virology, Volume 94, Issue 6 Pg 2453- 2459

6. T. Roice Fultona, et al A systematic review of adverse events following immunization during pregnancy and newborn period. Vaccine 33 (2015) Pg6453–6465

7.Kamble B, Bashar M, Mishra C (February 02, 2022) Incidence, Pattern and Severity of Adverse Events Following Immunization (AEFIs) Associated with Chadox1 nCOV-19 Corona Virus Vaccine (Recombinant) Among the Healthcare Workers of a Tertiary Care Institute of Eastern Uttar Pradesh, India. Cureus 14(2): e21848. doi:10.7759/cureus.21848

8. Kaur U, Ojha B, Pathak BK, et al. A prospective observational safety study on ChAdOx1 nCoV-19 Corona virus vaccine (recombinant) use in healthcare workers-

first results from India. *EClinicalMedicine* . 2021;**38**:101038.
doi: 10.1016/j.eclinm.2021.101038

9.Maryam Kakovan, Samaneh Ghorbani Shirkouhi et al. A review article on stroke associated with Covid 19Vaccines,Journal of Stroke and Cerebrovascular Diseases, Vol. 31, No. 6 (June), 2022: 106440

10..Nick Andrews et al Covid-19 vaccine effectiveness against the Omicron (B. 1.1. 529) variant. New England Journal of Medicine 386 (16), 1532-1546, 2022