Vol 4 | Issue 1 | January - March | 2024

ORIGINAL ARTICLE - PUBLIC HEALTH

SURVEILLANCE OF ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) FOLLOWING ROUTINE IMMUNIZATION (RI) IN TAMIL NADU

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Abstract

INTRODUCTION : Globally, 3.5- 5 million childhood deaths are averted every year and more than 15 million future deaths have been halved with increasing access to immunisation services. Vaccines are safe, but it's a fact that no vaccination is risk-free, and after vaccination, side effects may occur in some instances. A vaccine may naturally result in fever, erythema, localized discomfort, etc. during the immunity-building process. There is a remote chance that the vaccine's ingredients will cause a foreign body reaction, which may raise some concerns to parents and caregivers. Monitoring of Adverse Events Following Immunization (AEFI) is an essential strategy for ensuring the safety of vaccines and its administration. This article describes status of implementation, key aspects and challenges of AEFI Surveillance in Tamil Nadu.

METHODS : The program documents from 2008, minutes of AEFI committee meetings and all cases discussed in each of the meetings were analysed.

RESULTS : Minor AEFI reported in the state HMIS portal is 2,671 in 2011-12 and is 46,369 in 2023-24. The approximate vaccine doses administered is 95.56 and 146.42 Lakhs in in 2011-12 and 2023-24 respectively. The number of reported serious and severe AEFI cases increased from 92 in 2015 to 457 AEFIs in 2023. However, there was a slight reduction in AEFI reporting seen in 2020, 2021 which may be due to COVID-19 pandemic. Annual reporting ratio of AEFI per 100,000 surviving infants, designated as a performance indicator is 0.71 in 2015-16 and 4.71 in 2023-24. Of total 1,887 serious and severe AEFI cases reported from the year 2015, 1,684(89.3%) has been discussed and of those, 47.8% of AEFIs were classified as 'A1'- Vaccine product related reactions, 39.3% as 'C'- Coincidental events and there were Zero% of AEFIs due to "A2"- Vaccine quality defect related reactions.

CONCLUSION : Trainings, increasing awareness among field level staff, and monitoring should be done consistently to further improve AEFI surveillance in the State. Embracing future research opportunities in AEFI including descriptive analysis, and qualitative study among field workers can indeed help stakeholders enhance the effectiveness and transparency of AEFI surveillance systems. This in turn contribute significantly to maintain public confidence in vaccination programs and ensuring vaccine safety for all populations.

KEYWORDS : Passive surveillance, vaccine safety, Routine Immunization

INTRODUCTION

Vaccines are known to protect against Vaccine Preventable Diseases (VPDs), which lowers the frequency and severity of VPDs and saves lives of the children. By guaranteeing that every person receives all necessary vaccinations at the proper age and in time, Immunization per se offers protection not only for the individual against the VPDs but also to the community. Vaccines are safe, but it's a fact that no vaccination is risk-free, and after vaccination, side effects may occur in some instances. It is also critical to remember that the benefits of vaccinations have far more outweighed the risks related to or perceived to be due to the vaccines.[1] Vaccines have brought a significant reduction in deaths and morbidity associated with VPDs.[2–4] Globally, 3.5 - 5million childhood deaths are averted every year and more than 15 million future deaths have been halved with increasing access to immunisation services.[5] Vaccines administered to the healthy new-borns and youngsters are alien substances to human bodies.[10] A vaccine may naturally result in fever, erythema, localized discomfort, etc. during the immunity-building process. In addition, there is a remote chance that the vaccine's ingredients will cause a foreign body reaction, which may raise some concerns to the parents and caregivers. With more number of vaccines being introduced in the Expanded Programme on Immunisation in many Low- and Middle-income Countries (LMICs) it is necessary to establish a functional Surveillance systems for Adverse Events Following Immunization(AEFI).[6–8] Each vaccine has their own related minor, serious and severe reactions at a particular expected incidence.[1,14] The World Health Organization

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(WHO) defines Adverse Event Following Immunization (AEFI) as "any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine".[9] Regardless of the reasons, an AEFI has the potential to deeply distress individuals to the point that they decide not to vaccinate their children and also inform their peer group about the same. This could result in vaccine denial/ hesitancy and the kids far more likely to contract a disease that can be prevented by vaccination, get gravely sick, become handicapped, and possibly even die. Thus, AEFI Surveillance contributes a lot to maintain a public trust about the immunization program being implemented in the country. However, the majority of AEFIs are moderate, resolve on their own, and don't require long-term care, extremely uncommon cases might result in substantial adverse reactions. Every time a vaccine is administered, the risk of AEFI is balanced against the danger of not immunizing a kid. A vaccination is only deemed safe when the advantages outweigh the disadvantages. However, even at a comparatively low incidence, there is a chance that the children who received the vaccination will experience a few major adverse effects due to the large absolute number of beneficiaries.

The way vaccination programs being implemented creates a "paradox," which means that the focus of attention changes with the implementation of immunization program when the vaccination coverage increases and disease burden reduces drastically, more cases of AEFI attract the attention of the people than the disease in the community.[11] The major objective of AEFI surveillance is early detection and analysis of adverse events and appropriate and quick response in order to decrease the negative impact on the health of individuals and the immunization programme. At least 10 AEFI per 100,000 surviving infants were reported in 2015 in 60% of the countries in the WHO Region of the Americas, 55% of the countries in Europe, 43% of the countries in the Eastern Mediterranean, 33% of the countries in the Western Pacific, and 27% of the countries in South-East Asia.[12] When novel vaccinations or vaccine combination products are introduced, monitoring AEFI is particularly crucial. AEFIs must be properly identified, reported, and handled. The vaccinators, healthcare specialists, and partners must collaborate well on this complicated activity that involves numerous interconnected and cross-disciplinary duties. Field-based healthcare personnel must identify and report all cases of AEFI occurring in their setting and expert AEFI causation evaluation and high-calibre AEFI field investigations should follow then. Sustaining the public's and healthcare professionals' faith in the vaccination program depends on timely and efficient internal and external communications. The program may be in jeopardy when AEFI reporting, investigation, causation evaluation, and communication are done poorly. This could have an impact on vaccination acceptance and uptake and expose communities to diseases that could be prevented by vaccination.[13] Assuring vaccine safety begins with efficient spontaneous AEFI reporting.[5]

Universal Immunization Program (UIP) under the Ministry of Health and Family Welfare, Government of India has been providing life-saving vaccines to approximately 27.4 million children and 30 million pregnant women, which benefits the largest cohort of beneficiaries in the world from Vaccine Preventable Diseases (VPDs).[14] In India, vaccinations administered as part of the Universal Immunization Programme (UIP) are voluntary.

With the introduction of the Universal Immunization Program (UIP) in 1985, AEFI surveillance was initiated in India in 1988. The World Health Organization, National Polio Surveillance Project India and other development partners provided technical help to Government of India in 2005–2006 to draft the National AEFI Surveillance and Response Operational Guidelines. The guidelines were revised in 2010, 2015 and latest by 2024. These guidelines, which were developed through consultation with a variety of stakeholders, including State Government program managers, academic institutions, independent subject experts, officials from the Drug Controller General of India (DCGI), development partners, and various government departments involved in the immunization program, are based on a framework suggested by the World Health Organization.[11]

In 2012, the Immunization Technical Support Unit (ITSU) established the AEFI Secretariat with the aim of establishing a team of committed staff at the national level, concentrating solely on vaccination safety surveillance. Any adverse event that occurs after receiving a vaccination—whether it is administered under the Universal Immunization Programme (UIP) or in the private sector, for adults or children, for travel abroad, etc. should be reported to the AEFI surveillance system.[15]

This article describes the status of implementation, key aspects and challenges of AEFI Surveillance in Tamil Nadu State.

METHODS

The AEFI Surveillance program documents from 2008 to till date were reviewed. All the AEFI meetings and the cases discussed in each of the meetings were compiled

and analysed. The Causality Assessment Report (CAR) of all cases were reviewed for the AEFI classification as per National AEFI Surveillance and Response Operational Guidelines. The approximate number of vaccine doses administered every year is calculated from the percentage of Fully Immunized (FI%) from the State HMIS data and the estimated infant target for the respective years were obtained from the program reports.

In Tamil Nadu, Routine Immunization (RI) sessions are planned on all Wednesdays of the month where the field staff who are the Village Health Nurses (VHNs) in rural areas and Urban Health Nurses (UHNs) in Urban areas vaccinate all their eligible beneficiaries both at the institutional (Facility) and field level (Outreach). Birth dose vaccinations are being given at all days in all Primary Health Centres, in all Secondary care hospitals such as District Hospitals, Sub district Hospitals and in all Tertiary care hospitals such as Medical College Hospitals. All the health field staff, identified vaccinators in secondary care and tertiary care centres have been trained in Immunization practises, picking up an AEFI and reporting. The reports from the Secondary and Tertiary care centres are being complied at their nearby Primary Health Centres by the designated surveillance health inspectors.

Government of India had developed an electronic web-based portal called SAFE-VAC (Surveillance and Action For Events following Vaccination) for AEFI database which serves as a dedicated Signal management system for vaccines, where all Serious and Severe AEFIs are reported from all over the nation and Tamil Nadu is updating the portal regularly.

RESULTS

AEFI cases reporting and Causality Assessment in Tamil Nadu is done according to AEFI Surveillance and Response Operational Guidelines by Government of India (1) . Once the field staff – Village Health Nurses (VHNs) in rural areas or Urban Health Nurses (UHNs) in Urban areas are informed about an AEFI, she immediately reports it to the Medical Officer who in turn classifies the type of AEFI reported. The minor AEFI are reported in the state Health Management Information System (HMIS). The serious/ severe type AEFI are reported to the District Health Officer (DHO) of the Public Health department who is the District Immunization Officer (DIO), in a Case Reporting Form (CRF) within 24 hours of reporting of AEFI, and the DHO in turn reports it to the State and national level authorities via the SAFE-VAC portal.

The Medical Officer then investigates the Serious and Severe event and collects the relevant records such as hospital case sheets, discharge summaries or preliminary post mortem reports in case of death and submit the documents along with the Case Investigation Form (CIF) within ten days of the reporting of the event. The final post mortem report wherever required should be submitted at the earliest. The Case Investigation Form (CIF) will be sent to the State only after thorough investigation by the District Health Officer (DHO) and the District AEFI committee via SAFE-VAC portal. The flow of reporting and processing of an AEFI till Causality Assessment Report (CAR) in Tamil Nadu is depicted in Figure 1. The AEFI surveillance for Serious and Severe AEFIs thus has five major steps such as Notification, Verification and Reporting, Investigation, Causality Assessment and Feedback.

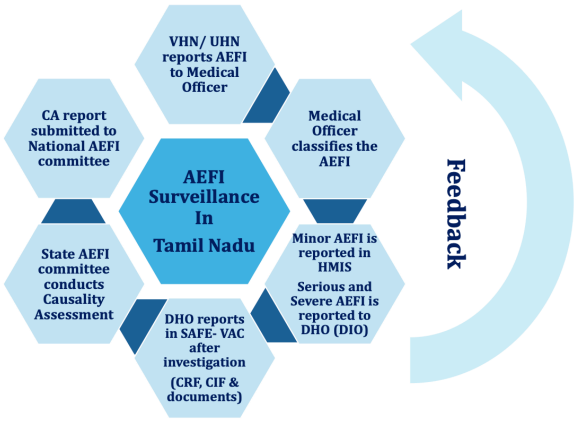

Figure 1: Flow chart depicting AEFI surveillance from reporting to Causality Assessment in Tamil Nadu.

The Minor AEFI cases reported in the state HMIS portal is 2,671 in 2011-12 and is 46,369 in 2023-24 (up to Feb). The approximate no. of vaccine doses administered is 95.56 Lakhs in 2011-12 and 146.42 Lakhs in 2023-24 (up to Feb). The year wise Minor AEFI cases reported and the approximate vaccine doses administered from 2010 to 2024 is shown in Figure 2.

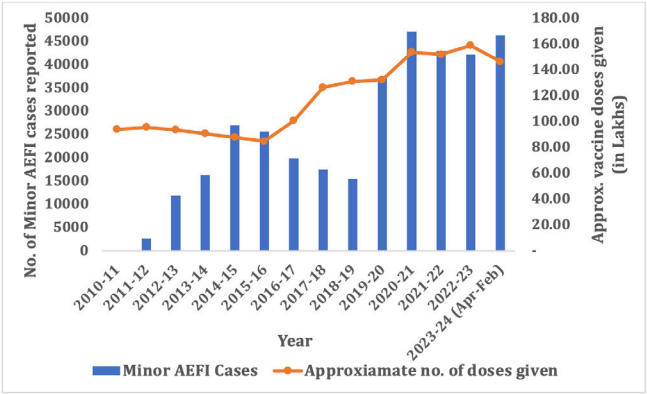

Figure 2: Trend of reported Minor AEFI in the state of Tamil Nadu from 2010 to 2023, (Source: tnhmis.org)

Global Advisory Committee on Vaccine Safety (GACVS) considered a number of principles in deriving a set of indicators for AEFI surveillance. Three types of indicators are proposed: (i) to monitor the volume of AEFI reports; (ii) to monitor the quality of those reports; and (iii) to monitor the quality of the response to serious AEFI. The proposed general indicator is the ratio of AEFI reports per 100,000 surviving infants per year and is designated as a performance indicator for tracking and monitoring progress in AEFI reporting by Global Vaccine Action Plan (GVAP).[16] The Annual AEFI reporting ratio of serious and severe AEFI per 1,00,000 surviving infants in the year 2015-16 is 0.71 and is 4.71 in 2023-24 (up to Feb). The year wise AEFI annual reporting ratio is shown in Table 1.

Table 1: Annual AEFI reporting ratio per 100,000 surviving infants from the year 2015 to 2024

Reporting year	Annual Infant target (in Lakhs)	Approx. vaccine doses given (in Lakhs)	AEFI reported (in Nos.)	Annual AEFI ratio per 100,000 surviving infants
2015-2016	10.22	84.63	73	0.71
2016-2017	9.95	100.7	75	0.75
2017-2018	9.70	126.35	164	1.69
2018-2019	9.44	130.82	90	0.95
2019-2020	9.54	132.16	228	2.39
2020-2021	9.32	153.61	186	2.00
2021-2022	9.21	151.85	190	2.06
2022-2023	9.15	158.7	296	3.23
2023-2024	9.16	146.41	432	4.71

AEFI Committees were established at the State and the district level in 2007 and at the National level in 2008. The Director of Public Health and Preventive Medicine (DPH&PM) is the Chairman of the AEFI Committee and Joint Director (Immunization) who is the State Immunization Officer (SEPIO/SIO) act as the convenor for the State AEFI Committee. District Health Officer in the districts who is the District Immunization Officer (DIO) heads the AEFI committee at the district levels.

The Committee also includes physicians, paediatricians, obstetricians-gynaecologists, neurologists and cardiologists, in collaboration with Indian Academy of Paediatrics (IAP) and Indian Medical Association (IMA).[17,18] The State AEFI committee also includes a National Consultant as a member. The State AEFI committee convenes at regular intervals discussing every AEFI reported in a hybrid mode of meeting including both in person and also a virtual mode so as to include all its members including the Government of India member (National consultant). The Causality Assessment is based on a detailed discussion of the cases reported followed by a Causality Assessment algorithm.

The State AEFI committee has convened 60 Causality Assessment meetings since 2014 till March 2024 (33 meetings from 2014 to 2020 & 27 meetings from 2021 to 2024). Totally, 1,887 serious and severe AEFI cases were reported from the year 2015. Of which, 1,684(89.3%) has been discussed in the State AEFI meetings and classification done and shared to the National AEFI Secretariat. The number of reported serious and severe AEFI cases increased from 92 in 2015 to 457 AEFIs in 2023 as shown in Figure 4., and the number of vaccine doses given also increased from 2015 to 2023. However, there was a slight reduction in AEFI reporting seen in 2020, 2021.

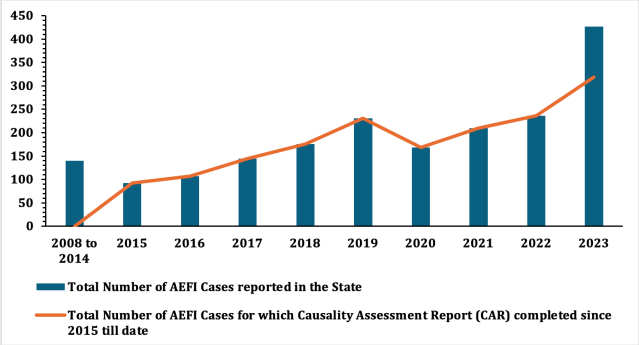

Figure 4 : Characteristics of AEFI reported and Causality assessment details done by State and submitted to National AEFI committee in Tamil Nadu, 2015 to 2024
(Source: O/o DPH&PM, Immunization Department)

The final classification has been adapted from definition and application of terms for vaccine pharmacovigilance Report of the CIOMS/WHO Working Group on Vaccine Pharmacovigilance.[19] The classification of "A. Consistent causal association to immunizatiown" and "C. Inconsistent causal association to immunization" (coincidental) are made clearer by the cause-specific definitions. When there is sufficient data on the AEFI but it cannot be placed into one of the aforementioned categories, the association is classified as "B. indeterminate." When there is a case without adequate information for causality conclusion, it is categorized as "D- Unclassifiable" and requires additional information for further review of causality. Of all the 1684 AEFIs discussed in the State AEFI meetings and classified, 47.8% of AEFIs were classified as 'A1'- Vaccine product related reactions, 39.3% as 'C'- Coincidental events which were emerging or emerged at the time of vaccination and there were Zero% of AEFIs due to "A2"- Vaccine quality defect related reactions.

The State Committee provides suggestions based on the discussions of the Causality Assessment in every meeting. These recommendations are then promptly communicated to all districts, aiding in raising awareness of the nature of the AEFI cases that occurred. The AEFI Secretariat in addition, does Causality Assessments at the National level. The

findings of the National Causality Assessment are regarded as final. The national level is using model 2, (1) in which all reported cases in the nation are categorized into serious and severe categories by a National sub-committee. The National AEFI Committee is presented with an overview of these situations as well as specifics of cases that require additional consideration. It should be mentioned that the National AEFI Committee meets every quarter, whereas sub-committee meetings occur more regularly at the national level.

Table 2 : Cause-specific categorization of AEFIs

Cause-specific type of AEFI	Definition
A. Consistent with causal association to immunization	
A1	Vaccine product-related reaction (An AEFI that is caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product)
A2	Vaccine quality defect-related reaction (An AEFI that is caused or precipitated by a vaccine due to one or more quality defects of the vaccine product, including its administration device as provided by the manufacturer)
A3	Immunization error-related reaction (formerly "programme error") (An AEFI that is caused by inappropriate vaccine handling, prescribing or administration and thus by its nature is preventable)
A4	Immunization anxiety-related reaction (An AEFI arising from anxiety about the immunization)
B. Indeterminate	
B1	Temporal relationship is consistent but there is insufficient definitive evidence for vaccine causing events.
B2	Reviewing factors result in conflicting trends of consistency and inconsistency with causal association to immunization
C. Inconsistent casual association to immunization	
C	Coincidental event (An AEFI that is caused by something other than the vaccine product, immunization error or immunization anxiety)
D. Unclassifiable	

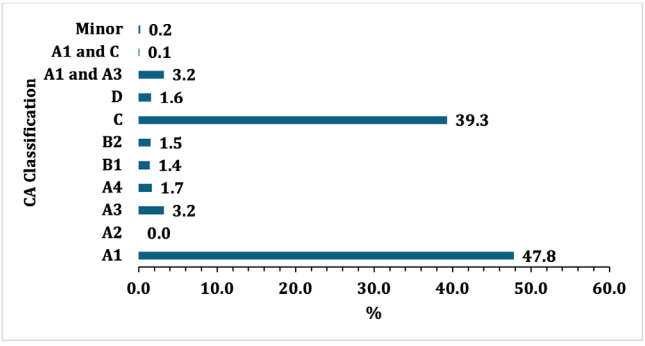

Figure 5 : Classification of AEFI following Causality assessment by State AEFI Committee in Tamil Nadu, 2015 to 2024 (Source: O/o DPH&PM, Immunization Division)

The State Committee provides suggestions based on the discussions of the Causality Assessment in every meeting. These recommendations are then promptly communicated to all districts, aiding in raising awareness of the nature of the AEFI cases that occurred. The AEFI Secretariat in addition, does Causality Assessments at the National level. The findings of the National Causality Assessment are regarded as final. The national level is using model 2,[1] in which all reported cases in the nation are categorized into serious and severe categories by a National sub-committee. The National AEFI Committee is presented with an overview of these situations as well as specifics of cases that require additional consideration. It should be mentioned that the National AEFI Committee meets every quarter, whereas sub-committee meetings occur more regularly at the national level.

Though AEFI reporting and management are in better progress in the state, there are also few challenges such as there are silent districts which report zero AEFI for the year. Those districts need to be focussed and ensured of adequate capacity building, refresher trainings and review of the processes of the surveillance system. Some of the districts were given with refresher trainings and once in a month, review of district level reporting. Apart from reporting, there are some challenges in obtaining the few documents for causality assessment like final post mortem report with chemical and visceral analysis which are usually delayed since all AEFI deaths are not necessarily being labelled as Medico Legal Cases. Another major challenge observed based on the minutes of the State AEFI Committee meetings is the poor quality of CIF and CRFs from the investigating officials in the districts which impedes / delays the Causality Assessment activities.

DISCUSSION

The state's reporting of AEFI cases including Minor cases in the state HMIS portal had improved over period of time. AEFI reporting ratio suggested as the performance indicator by GVAP criteria, also showed consistent increase and this may be due to better reporting of AEFI, in addition to increase in the number of doses administered to the children over period of time. The increasing trend in reporting reflects persistent efforts at state and district level including training and monitoring. Although COVID-19 pandemic had caused a hindrance in the reporting of AEFI cases, the state has rebounded with better performance in subsequent years.

At the District and State levels, the State has its own AEFI committees that were established in compliance with GOI guidelines. The Causality Assessment of each AEFI in the State is carried out by the State AEFI committee and the National AEFI committee. In order to improve communication between the National and State committees and to provide an outside perspective to the Causality Assessment, the National Consultant's involvement in the State AEFI committee is also beneficial. Most AEFIs occurred were due to innate nature of the vaccine itself or due to other coincidental events following Immunization.

It is strongly felt that still there is a lot of scope for

improvement in silent districts. It is a known fact that human resource-related issues are crucial to the reporting process of any programs / activities. All health staff should be reoriented at regular intervals on the importance of reporting of AEFI at the field level and on newer guidelines. Regular trainings and refresher trainings, increasing awareness among field level staff, and monitoring should be done in order to improve AEFI surveillance in the State.

Embracing future research opportunities in AEFI including descriptive analysis, detailed surveillance evaluation, and qualitative KAP method study among field workers can indeed help stakeholders enhance the effectiveness, efficiency and transparency of AEFI surveillance systems. This in turn contribute significantly to maintain public confidence in vaccination programs and ensuring vaccine safety for all populations.

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