A STUDY TO ASSESS THE DISTRIBUTION OF SUSPECTED ADVERSE EVENTS FOLLOWING IMMUNISATION REPORTED IN A METROPOLITAN CITY IN INDIA

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ABSTRACT

Introduction: Adverse Events Following Immunization (AEFI) may be considered as major setback to our immunization efforts and can hinder the optimum utilization of the services provided. Around 14% of parents with a past history of facing a suspected AEFI in any of their children are hesitant to accept future immunizations. Our study aims to understand the distribution pattern of suspected AEFI cases during January 2017 and June 2018. **Methods**: We conducted a cross-sectional observational record-based study in a Metropolitan city in Maharashtra wherein all AEFI reporting forms namely Case Reporting Form (CRF), Preliminary Case Investigation Form (PCIF), and Final Case Investigation Form (FCIF) containing pertinent data on all AEFI cases that occurred from January 2017 to June 2018 were analyzed using Microsoft Excel 2013 and represented using tables and graphs. **Results**: The AEFI reporting rate was calculated as 5.8 per 100000 doses administered per year. The total number of AEFIs reported in the year 2017 and 2018 (up to June) were 71 and 58 respectively. 51.16% of the reported AEFIs were febrile seizures, 19.38 % were severe local reactions in the form of abscesses, and 9.3% were afebrile seizures. Twelve deaths were reported during the study period. Injectable Polio Vaccine (IPV) showed the highest rate of antigen-specific AEFI (13.2/100000 doses administered) while measles vaccine showed the lowest rate (2.7/100000 doses administered). **Conclusion:** Analyzing the distribution of suspected AEFI cases can aid in identifying causal links to known risk factors, inform the development of preventive measures, and enhance immunization coverage.

Keywords: AEFI, Vaccine, Reporting, India

INTRODUCTION

An Adverse event following immunization (AEFI) is any untoward medical occurrence that follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. (WHO,2016) The majority of the events reported are coincidental. However, some may be caused by the vaccine product or due to administration errors. Irrespective of the cause, AEFIs tend to stigmatize health providers and invite contempt of the general public. 14% of parents with a history of facing an AEFI in any of their children are hesitant to accept future immunizations. (Parrella,2012)

With Mission Indradhanush launched in December 2014 to increase immunization coverage and the introduction of new vaccines in the Universal immunization program including the pentavalent vaccine, IPV, rotavirus vaccine, PCV, and MR vaccine, India is confronted with the dual challenge of achieving both increased immunization coverage as well as immunization safety.

The credibility and reputation of the healthcare system are compromised when a suspected AEFI occurs.(Joshi 2018).

The effects of post-vaccination events are very minimally known and the assessment, and documentation of that Adverse events are minimal in the Indian population. Very few systematic studies have been conducted to assess vaccine safety. Some studies conducted in the southern part of India found that the adverse events were highest in pentavalent vaccines followed by the BCG vaccine. The most common adverse events were mild fever and swelling at the site of injection (Varun,2021). One similar study was conducted in North India which found out that the most common AEFI reported was fever (101, 47.6%), followed by swelling (53, 25.0%) and among the vaccines, Pentavalent and oral polio vaccine (OPV) (48.8 per 100 doses) was majorly responsible for AEFIs, followed by diphtheria pertussis tetanus (DPT) (Sneha,2023).

Based on the cause, AEFI is categorized into the following types namely Vaccine product-related reaction, Vaccine quality-related reaction, Immunization error-related reaction (program error), Immunization anxiety-related reaction, and Coincidental event. Serious reactions are those which result in death, have life-threatening consequences, and require inpatient hospitalization or require intervention to prevent permanent damage. Example: Anaphylaxis, thrombocytopenia. (WHO, 2016)

However, in the majority of cases, AEFI shows a temporal association between vaccination and adverse events and not a causal relationship between the two. Although most adverse events are minor (e.g. pain, swelling, redness at the injection site, fever), more serious reactions (e.g.seizures, anaphylaxis) can occur, though at a very low frequency (Immunisation,2023). This study was undertaken to understand the distribution pattern of suspected AEFI cases occurring in a given period of time.

METHODS

Study design – Cross-sectional observational record-based study

Study setting – Metropolitan city in India

Study sampling – Records of all suspected serious AEFI cases reported during the period of January 2017 to June 2018 were included in the study.

Study tools – 1. Case Reporting Form (CRF)

2. Preliminary Case Investigation Form (PCIF)

3. Final Case Investigation Form (FCIF)

Study Procedure - Necessary permissions were sought from the concerned authorities of the metropolitan city civic administration. CRF, PCIF, and FCIF of all cases that occurred from January 2017 to June 2018 were obtained from the concerned authorities and studied for distribution of suspected AEFI cases.

Statistical analysis: The data obtained from records was compiled and analyzed using Microsoft Excel 2013 and represented in percentages using tables and graphs. The study began after Institutional Ethics Committee approval dated EC/241/2016.

RESULTS

It was found that the total number of AEFIs reported in the year 2017 and 2018 (up to June) were 71 and 58, respectively. There were 5 deaths among the 71 cases reported in 2017 and 7 among the 58 cases reported in 2018 (up to June 2018).

Table 1: Distribution of cases according to type of vaccine administered (N=129)

Vaccine administered	N	%
OPV	87	67.44
Pentavalent	72	55.81
DPT	43	33.33
IPV	40	31
MMR	21	16.28
BCG	9	6.98
Measles	6	4.65

Vitamin A	4	3.10
Hepatitis B_0	1	0.78
TT	1	0.78
Others	4	3.10

(Data not mutually exclusive)

Other vaccines administered were Varicella, Prevenar, Rotarix and Hexaxim.

According to the HMIS portal data on immunization, a total of 3624837 vaccine doses were administered in the period of 2017-2018. Hence the reporting rate was calculated as 5.8 per 100000 doses administered per year.

Specific AEFI reporting rates were calculated for individual vaccines. Following the pentavalent vaccine (9.1/100000 doses administered), DPT vaccine (8.4/100000 doses administered), MMR (7.6/100000 doses administered), OPV (7.2/100000 doses administered), BCG (3.3/100000 doses administered), and measles (2.7/100000 doses administered) was found to have the highest rate of antigen-specific AEFI.

A total of 288 vaccines were administered to 129 beneficiaries during the study period. It may be noted that more than one vaccine was administered to the beneficiaries at a time.

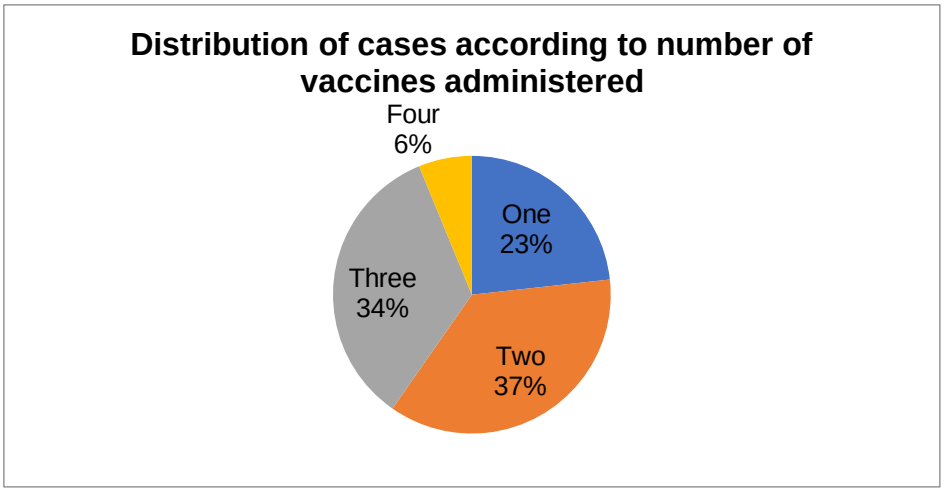

Figure 1: distribution of cases according to number of vaccines administered.

Table 2: Vaccine combinations administered (N=129)

Vaccine combinations administered	N	%
Penta + OPV + IPV	30	23.26
Penta + OPV	24	18.60
DPT	15	11.63
OPV + DPT	8	6.20
OPV + DPT + MMR	8	6.20
DPT + MMR	7	5.43
Penta + OPV + BCG + IPV	5	3.88
Pentavalent	5	3.88
Penta + IPV	4	3.10
OPV	3	2.33
OPV + DPT + MMR + Vitamin A	2	1.55
OPV + BCG	2	1.55
Measles	2	1.55
MMR	2	1.55

12 beneficiaries received vaccine combinations other than the ones mentioned in the above table.

It was seen that 66 reported AEFIs (51.16%) were febrile seizures, 25 (19.38 %) were severe local reactions in the form of abscesses, and 12 cases (9.3%) were afebrile seizure. 12 deaths were reported (9.3%). Other cases reported included fever (5.42%), sepsis (2.32%), and Acute Flaccid Paralysis (2.32%).1.55% of the reported cases included jitteriness like involuntary movements, loss of consciousness, and breathlessness. Data was unavailable for 6.20 % of the cases.

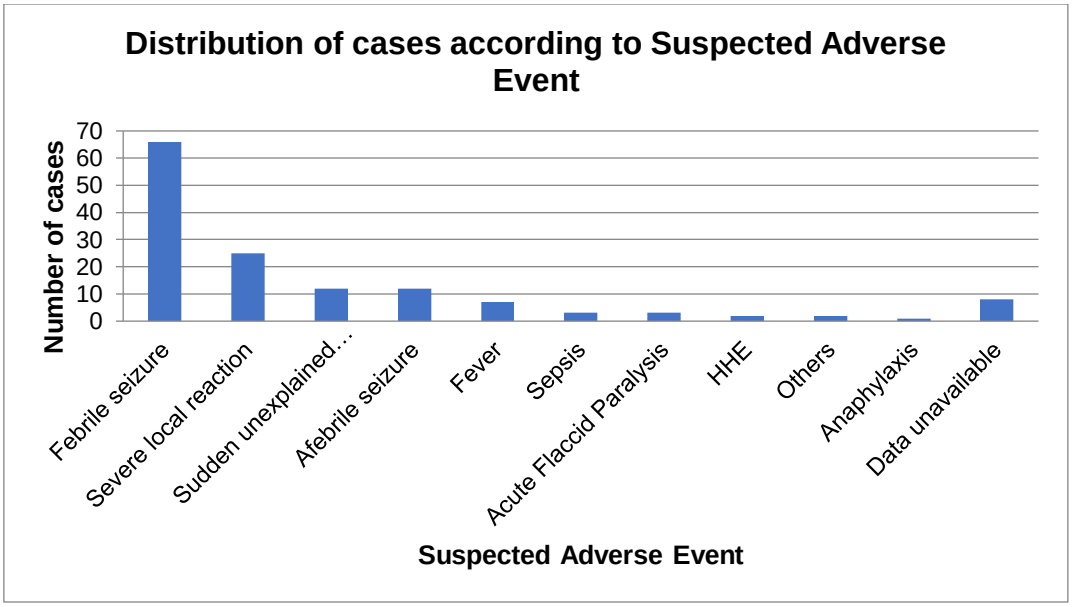

Figure 2: Distribution of cases according to suspected adverse event

Table 3: Distribution of AEFIs according to age and sex of patient

According to Age (N=129)		
Age (in months)	**N**	**%**
Less than or equal to 12	74	57.36
13 – 24	37	28.68
>24	16	12.40
Data unavailable	2	1.55
Total	129	100
According to Sex (N=129)		
Sex	**N**	**%**
Male	68	52.71
Female	61	47.29
Total	129	100

It was found that 104 AEFIs (80.6%) occurred during routine immunization while 10.8 % occurred during campaigns namely Intensified Mission Indradhanush or Intensive Pulse Polio Immunization. Data pertaining to this detail was unavailable in 12 case records (9.30%) It is also noted that among the 129 AEFI studied, 67 cases (51.94%) were vaccinated in a government facility, 60 (46.51%) were vaccinated in outreach sessions, 2(1.55%) were vaccinated in private set up.

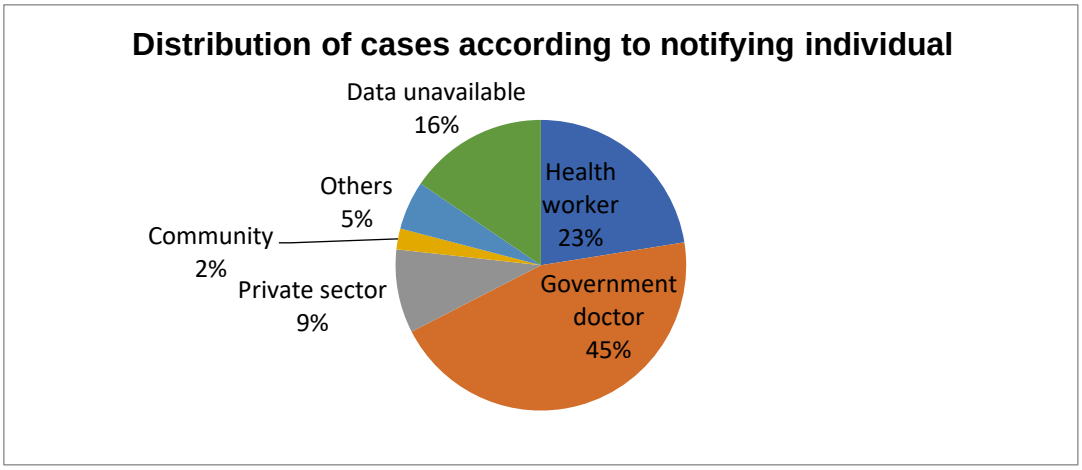

Figure 3: Distribution of cases according to notifying individual (N=129)

It may be noted that multiple responses were expected in this regard however records did not reveal so. It was seen that among the 129 AEFI studied, 91 cases were hospitalized and 37 cases were managed on an OPD basis. Out of the 91 that were hospitalized, 54(59.34%) were hospitalized in a government facility, and 30 (32.97%) were hospitalized in the private sector. The detail pertaining to place of hospitalization was incomplete in 7 case forms (7.69%).

DISCUSSION

The overall reporting rate was found to be 5.8 per 100000 doses administered per year. Similar studies were conducted in different regions of the world. The overall AEFI reporting rate was found to be 2.7 reports per 100000 distributed vaccine doses in Switzerland for the period 1991-2001(Schumacher,2010) , 9.2 per 100000 doses in Zhejiang province of China for the period 2008-2012(HU, 2013), 8.3 per 100000 doses administered in Oman during 2006-2015(Al Awaidy, 2010), 3.2 adverse events per 1000 antigens administered in Sri Lanka (WHO,2013) and 1.7 reported AEFI for 100 000 administered doses of vaccine in the period 2009–2012 in the Liguria Region(Alicino,2015).

However, it was difficult to compare and make interpretations about the reported AEFI rates as the exact number of children vaccinated annually was not known. In this study, 10.8% of the cases occurred during immunization campaigns, and 1.55% of the cases were immunized in the private sector. Hence the exact denominator could not be determined. The rates described in this study may be taken as estimates. Moreover, the information about the total number of reported AEFIs may be inaccurate due to gross underreporting (Singh ,2018) Such drawbacks in the assessment of reporting rates have been observed in other studies as well (Waldman, 2011)(Bonhoeffer,2009).

In this study, most cases received 2 vaccines during the immunization session (36.43%) and 34.11% had received a combination of 3 vaccines. Similarly, Clothier et al also found that three-quarters of vaccines were co-administered and a median of two vaccines were administered per AEFI case reported. (Clothier,2017) In a study conducted by Singh et al, it was found that 32% of AEFIs followed three vaccines used together (OPV-DPT-Hep B) and 22% followed two vaccines used together (OPV-pentavalent). Following injections of BCG (6.5%) and OPV (10.4%), AEFIs were greater among single-administered vaccinations (Singh ,2018)(Singh,2017).

Pentavalent and DPT vaccines were associated with reported AEFIs in studies conducted elsewhere. In a study conducted in Sri Lanka, the pentavalent vaccine (4.1/1000 doses administered) was found to have the second-highest risk of antigen-specific adverse events (AEFI), after the DPwT vaccine (10.9/1000 doses administered).[6] Hu et al in their study on AEFI surveillance in Zhejiang province of China found that the most frequently associated vaccine associated with the reports was DPT (30%) followed by MM, pH1N1, MR, and DT. (Hu Y,2013) Patel, Al-Rawahi et al. in their study conducted in Oman also found that the pentavalent vaccine (30%) was responsible for the highest number of AEFI reports followed by BCG and DPT. (Al Awaidy, 2010)

In previous studies, it was also stated that the introduction of new vaccines raised public concerns hence resulting in increased reporting, a phenomenon called Weber effect. (Littlejohn,2015)(Eberth,2014). Increased reporting rates of pentavalent and IPV vaccines could also be attributed to the above-mentioned phenomenon. Also, OPV was almost always given with pentavalent and IPV according to the immunization schedule; hence it may be seen to be associated with the highest number of cases.

The most frequent adverse events found in the study were febrile seizures (51.16%) followed by severe local reactions in the form of abscesses (19.38 %), afebrile seizures (9.3%), and 12 deaths (9.3%). This finding was similar to findings in other studies which found that fever and local reactions were the two most common reactions reported. In Australia, the most frequently reported adverse events were injection site reactions (26%) followed by pyrexia, rash, vomiting, headache, extensive swelling of the vaccinated limb, and diarrhea. (Aditi, 2015)In a study conducted in China, the most commonly reported adverse event was fever (46%) followed by injection site reaction (39%) and allergic reaction (7.2%). (Hu, 2013) In Oman, the most common adverse

events reported were local swelling and pain (49%) followed by BCG adenitis (23%) and abscess (8.4%). [5] Fever was the most commonly seen adverse event in Ghana, followed by urticaria (Ankrah,2018).

This study's reported cases revealed that, of those reported, 57.36% of probable AEFIs were observed in children under the age of one. Higher rates were reported in this age group in other studies as well. (Schumacher,2010),(Hu ,2013),(WHO,2013),(Aditi,2015) It was due to the large number of vaccines given to children of that age group. In this study, 80.6% of cases were vaccinated during routine immunization while 10.8 % were in campaigns namely Intensified Mission Indradhanush or Intensive Pulse Polio Immunization.

A total of 51.94% were vaccinated in a Government facility and 46.51% in outreach sessions. Only 1.55% were vaccinated in a Private setup. It was estimated that almost 20–30% of the pediatric and most of the adult immunizations were administered in the private sector, particularly in the urban areas. (Chiktara,2013) Moreover, vaccines not part of the Universal Immunization Programme were provided by the private sector only. Hence it was imperative that AEFIs from this sector were also reported and investigated as per national guidelines.

The results of this study showed that 44.96% of the instances were reported by government physicians, 22.48% by healthcare professionals, 12 cases (9.30%) by private sector providers, and roughly 8% by the child's parents, relatives, or neighbors. It should be mentioned that 15.5% of cases had an unidentified source.

According to an analysis of VAERS data, between 2012 and 2016, vaccine makers contributed 41% of the reports, vaccine providers submitted 32%, patients or parents submitted 13%, and 14% came from unidentified sources. (Miler ,2011) 88% of the AEFI reports, according to Clothier et al., were from medical professionals, with the remainder reports coming from vaccine recipients or guardians.(Clothier,2017) Out of 129 cases, 70.54% of cases had to be hospitalized. These findings were similar to the findings of the study by Singh et al which stated that most cases were vaccinated as part of routine immunization (61%) as compared to mass immunization campaigns (39%). Two thirds of them reported hospitalizations (65%). (Singh,2017)

Limitations

The results cannot be generalized to all districts due to inter-district variations. Exact denominators could not be determined due to inadequate data regarding total number of immunizations conducted in both private and public sectors.

CONCLUSION

While there is a system for AEFI reporting from the government sector in India based on the operational guidelines, there is limited awareness about the reporting system in the private sector resulting in inadequate reporting and incomplete data about the AEFI. There is, thus, a perceived need for improving AEFI surveillance in the private sector. a digital platform can be provided through which the immunisation sessions and AEFI data could be tracked. This is possible through information dissemination and better collaboration with professional bodies and Government of India. Further as mostly routine immunisation is being done in the government institutions a mandatory regular training of staff regarding the knowledge about the reporting system and process should be done. Staff must be encouraged to report adverse events without fear of penalty. The aim is to improve systems or provide further training, and not to blame individuals. Positive feedback to health workers is essential. The feedback should include the outcome of investigations or causality assessment when these are carried out, and recommendations on the management of the vaccinee, particularly with regard to the need for future vaccination. There must be an adequate supply of reporting forms. Also as the maximum number of AEFIs are being reported for the Pentavalent vaccine the health worker should be trained to ensure proper post-vaccination counseling of the parents to minimize the chances of AEFI and fear in their minds. By capacity building and increasing awareness among healthcare professionals' especially the field healthcare workers, about the AEFI surveillance methods, the AEFI surveillance program has facilitated the introduction of new vaccines. The improved AEFI surveillance and reporting system in India will go a long way to increase and retain the faith of the community in the existing and new vaccines and increase immunization coverage in India.

Conflicts of Interest

The authors declare no conflicts of interest.

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