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Adverse Events Following Immunization (AEFI) in Children under 7- year of Age during 2014 in Hamedan Province, Iran

Salman Khazaei[1], Shahab Rezaeian [2], Mohsen Razani [3], Ali Zahiri [4], *Mohammad Saatchi [5] , Somayeh Khazaei [6], Abdolah Mohammadian Hafshjani [7], Mahfam Darvishi [8]

[1]Department of Epidemiology & Biostatistics, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran. [2]Social Development & Health Promotion Research Center, Gonabad University of Medical Sciences, Gonabad, Iran. [3]Faculty Member of Nursing Department, Broujerd Branch, Islamic Azad University, Broujerd, Iran. [4]Expert of Public Health, Deputy of Health, Hamadan University of Medical Sciences, Hamadan, Iran. [5]Department of Epidemiology & Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. [6] Expert of Operating Room, Rafsanjan University of Medical Sciences, Rafsanjan, Iran. [7] Social Determinants in Health Promotion Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. [8] Lorestan University of Medical Sciences, Khorramabad, Iran.

Abstract

***Background*:** The surveillance of adverse events following immunization (AEFI) is essential to improve high standard of vaccine safety, and maintain public trust in immunization programs. This study aimed to determine the AEFI and their related factors in children.

***Materials and Methods*:** This cross-sectional study including all children under 7- year of age, in Hamadan Province, the West of Iran, in 2014. All of the AEFI related with Bacille Calmette-Guérin (BCG), Diphtheria, Pertussis, and Tetanus (DPT), Measles, Mumps, and Rubella (MMR) vaccines were obtained from the documented record-based by Health Centers, in Hamadan province.

Results: From a total of 239,204 doses administered, 284 AEFI were notified (11.8 per 10,000 doses). The proportion of AEFI was more frequently reported from Health Houses than Health Centers (60.2 vs. 37.0, P<0.05). The most frequently AEFI reported was lymphadenitis (31.4%), followed by hyperpyrexia (17%), and severe local reaction (13.5%). Most frequently AEFI reported were related to vaccination reaction (74.7%) and programmatic errors (12.7%). Also, for incidence of lymphadenitis, the overall median time from vaccination to adverse event was 2 days (IQR: 2-15) and the highest median time was 15 days (IQR: 15-571).

***Conclusion*:** Our study shown, an increased risk of AEFI in the region and point out that the programmatic error still needs to be considered. Accordingly, the more activities need to be consolidated to reduce the adverse effect. This study assessed the different aspects of AEFI which may help policymakers to improve the immunization programs.

***Key Words*:** Adverse events, Children, Immunization Programs, Vaccination, Iran.

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Corresponding Author:

Mohammad Saatchi, Department of Epidemiology & Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.

Email: m.saatchi65@gmail.com

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1- INTRODUCTION

The main goal of immunization is the prevention of infectious diseases in the community (1). According to World Health Organization (WHO) reports, some important achievements such as a dramatic decline in childhood mortality, increase in life expectancy, reduction in mortality and morbidity of infectious diseases are associated with immunization (2-4). The national immunization program was established in 1981 in Iran. In the past decades, this program has played an important role in controlling, elimination, and eradication of vaccine-preventable diseases (5). In addition, Iran has achieved the immunization coverage of 90% as an essential issue to prevent childhood infections suggested by WHO (6-10).

Although immunization with modern vaccines has the incredible results in decreasing infectious diseases, there is no vaccine free from adverse effects. Accordingly, the surveillance of adverse events following immunization (AEFI) to improve high standard of vaccine safety, and maintain public trust in immunization programs has been suggested (11, 12).

AEFI are caused by some reasons including vaccine product, vaccine quality, immunization error or program error, and coincidental event (13). Sometimes there is no cause-specific reason for AEFI. Several studies have reported the AEFI in both developed and developing countries (12, 14). A study conducted a two-year project of post-marketing surveillance of AEFI and revealed the increasing of number of reported AEFI (11).

In Iran, AEFI surveillance system is performed to monitor the suspected adverse events related to immunization. The main objectives of an effective and efficient surveillance system are to reflect health related events based on time, place, and person. This study therefore aimed to determine AEFI and their related factors in Hamadan province, Iran.

2- MATERIALS AND METHODS

This cross-sectional study including all children under 7-year of age was in Hamadan Province, the west of Iran, in 2014. Documented record-based on AEFI was done by Health Centers in the entire Province. In this regard, the rural primary health-care workers (*Behvarz* workers) in rural areas and the health technicians (known as the *Health Kardan*, with two years of college education) in urban areas report urgent (by 24 hours) and non-urgent (monthly) records which were addressed to those children who experienced any AEFI after immunization.

All cases of death due to result of vaccination, hospitalization, and adverse effects leading to tension in public opinion were considered as urgent and the rest of adverse effects as non-urgent reports. The data including gender, location, gestational age, hospitalization history, inoculation place, type of adverse effect, time between inoculation and incidence of adverse effect and its cause was collected using a check-list. In this study, we used information on AEFI after immunization with BCG, DPT, Measles, MMR vaccines. Descriptive analysis and also Chi-square test at the 5% significance level were used for data analysis using Stata 11 software (StataCorp, College Station, TX, USA).

3- RESULTS

A total of 239,204 doses of vaccine were injected; 31,943 doses were BCG, 146,322 DPT, and 60,939 doses were MMR. Totally, 284 (11.8 per 10,000 doses) AEFI have been signaled in 2014 year. The signaled AEFI of BCG, DPT, and MMR were 35.4, 10, and 2.5 cases per 10,000 doses, respectively. The incidence of AEFI was 12.9 in boys and 10.8 in girls per 10,000 doses. Also, the incidence by

residency was 15.5 in rural and 9.9 per 10,000 doses in urban.

Table.1 shows the frequency of AEFI by gender, residency, maturity, vaccination site, and type of vaccine. The proportion of AEFI was greater than boys (56.0%) compared to girls (44.0%) (Male to Female ratio: 1.3), without statistical significance (P=0.729). The proportion of AEFI was more frequently reported from Health Houses than Health Centers (60.2 vs. 37.0, P=0.001). Rural children and term ones, has been encountered with AEFI. The frequency of AEFI by type of reaction is shown in (**Figure.1**). Most frequently reported AEFI were: lymphadenitis (31.4%), hyperpyrexia (17%), severe local reactions (13.5%), redness and pain at the injection site (5.7%), abscess (4.2%), and seizures/convulsions (3.2%), respectively. The number of AEFI by types of immunization errors is shown in (**Figure.2**). Most frequently reported AEFI were related to vaccination reaction (74.7%) and programmatic errors (12.7%).

Table.2 shows the time from vaccination to the incidence of adverse events by type of AEFI. The overall median time from vaccination to adverse event was 2 days (IQR: 2-15). The highest median time of 15 days (IQR: 15-571) was seen for incidence of lymphadenitis.

Table 1: Frequency of AEFI by gender, residency, maturity, vaccination site, and type of vaccine in Hamadan, Iran, 2014

Variable	Subgroup	Type of vaccine				
		MMR	DPT	BCG	P-value	Total
Gender	Boy	7(4.4)	86(53.7)	67(41.9)	0.729	160(56.0)
	Girl	8(6.4)	64(51.6)	52(41.9)		124(44.0)
Residency	Urban	8(6.7)	46(38.7)	65(54.6)	0.001	119(42.0)
	Rural	7(4.2)	104(63.0)	54(32.7)		165(58.0)
Maturity	Term	12(4.6)	138(53.1)	110(42.3)	0.025	260(91.5)
	Preterm	3(12.5)	12(50.0)	9(37.5)		24(9.5)
Vaccination site	Health Houses	10(5.8)	109(64.0)	52(30.2)	0.001	171(60.2)
	Health Centers	5(4.8)	37(35.2)	63(60.0)		105(37.0)
Other*		0(0.0)	4(50.0)	4(50.0)	-	8(2.8)
Total		15(5.2)	150(52.8)	119(42.0)	-	284

*Other sites such as Hospitals and private system.

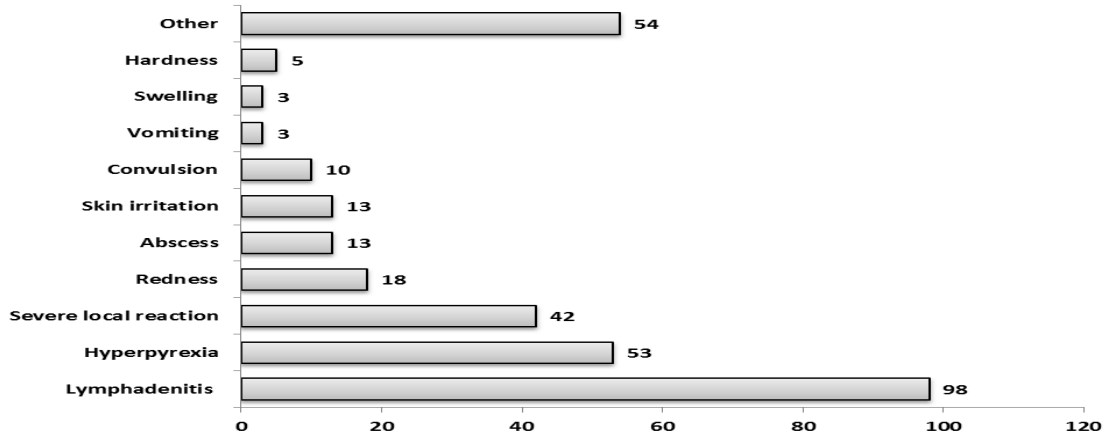

Fig.1: Frequency of AEFI reports by type of adverse reaction

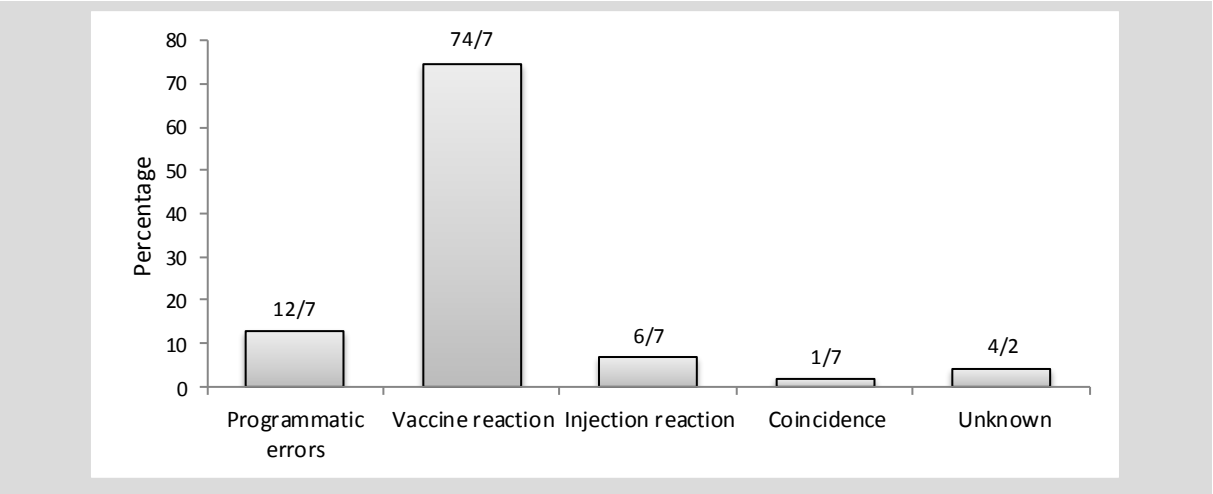

Fig.2: Percentage of AEFI by types of immunization errors

Table 2: Time to the incidence of adverse events by type of adverse events following immunization

AEFI type	Time from vaccination to report event								
	Median (IQR)	On time*	1st day	2nd day	3rd day	4th day	5th day	6th day	> 7days
Lymphadenitis	15(15-571)	9	5	4	5	4	3	0	68
Hyperpyrexia	0(0-1)	17	10	2	0	1	0	0	0
Severe local reaction	1(0-3)	18	21	2	1	0	0	0	0
Swelling and Redness	1(0-2)	2	11	2	2	1	0	0	0
Abscess	3(0-3)	3	3	0	1	0	0	0	5
Convulsion	0(0)	8	0	0	0	0	0	0	2
Skin irritation	1(1-3)	3	4	2	0	0	0	0	2
Vomiting	0(0)	2	1	0	0	1	1	0	0
Hardness	3(2-3)	0	1	1	1	1	1	0	1
Other events	3(0-152)	6	12	4	6	2	1	1	20
Total	2(2-15)	68	68	17	16	10	5	2	98

*The incidence time lower than 6 hours.

4- DISCUSSION

This study showed that during 2014, 284 children have experienced at least one complication of immunization. The frequency of side effects and complications were more in boys than girls, and in children who had vaccinated in rural Health Houses than those in Health Centers. Most complications were related to DTP vaccine. Seizure and high fever were more complications that occur after vaccination and adverse reactions to the vaccine response was determined the most common cause of complications after vaccination. The report of AEFIs is one of the main components of vaccine safety assessment that plays a great role in public health policies and led to enhance the credibility of immunization programs (15). Before marketing, efficacy and safety of vaccines basically were assessed by randomized clinical trials, but due to some restrictions, the effectiveness of the vaccines is not assessed in large populations or subgroups such as children, pregnant women and the elderly. Therefore always when entered the consumer market

there is occurred undercounting in vaccines' adverse effects (16, 17). So, epidemiological studies are the best tools for assessing the incidence of adverse effects and its associated factors in different populations.

In our study, the incidence rate of AEFI was 11.8 per 10,000 doses. This rate in a study to summarize passive surveillance data for AEFI in China for a 3-year period was 9.2 per 100,000 doses (18). In another study conducted in Singapore the incidence of AEFI for a two-year period was 4.4% (19). This rate in Cuba was 57.8 per 100,000 (20), the overall dose-based reporting rate for the 27 frequently reported vaccine types in the United States was 11,4 reports per 100,000 net doses distributed (21). It should be noted that different countries may perform various programs according to their epidemiological situation of vaccine-preventable diseases. On the other hand, difference in active or passive reporting of adverse effects, as well as differences in the incidence rate in terms of study period and study population could effect on comparing the results of different studies (22, 23) .

Our findings showed that about 60.2% of children with adverse effects had been vaccinated in rural Health Houses and 64% of them had DPT vaccine adverse effects. It, therefore, is necessary to more education of Health House workers for avoiding problems of injection safety and programmatic errors related to injection to improve safety and maintain public confidence in vaccines. In this study, 8 convulsions registered occurred following DPT vaccination. Some other studies reported the risk of febrile seizures following MMR vaccine (24, 25). In a study to determine the relation between DPT and MMR vaccinations and the risk of a first seizure concluded that the risks of febrile seizures on the day of receipt of DTP vaccine and 8 to 14 days after the receipt of MMR vaccine, were increased (24). In addition, hyperpyrexia and severe local reactions were the most common events following DPT vaccine, as reported in other studies conducted in different parts of Iran (26, 27). In other countries in China (18), Oman (28) and Brazil (29) DPT vaccine was also the most important factor of AEFI with more frequently of hyperpyrexia. We also found that convulsion and hyperpyrexia are the fastest adverse effects after vaccination that is 80% of cases have occurred in the first day, especially in the first 6 hours after injection. So, efforts to educate parents about the importance of vaccinations and its complications, for their children can be effective.

Our findings also showed that the 42% AEFI were related to BCG vaccine of which 82.3% of the adverse were lymphadenitis. The results of our study are consistent with other studies from Oman (28) and Poland (30) which reported that the 41% of AEFIs was related to BCG vaccine which. Various factors affected the complications of BCG vaccine including age of the vaccine recipient, doses of the vaccine, vaccine injection technique and vaccine manufacturer (31).

Regarding the high incident of lymphadenitis following BCG vaccine injection it is necessary to pay much more attention to first time immunization and retraining vaccinators especially in the field of BCG vaccine injection. The current study showed that 74.7% of AEFI are related to vaccine reaction which is concordance with results of other studies in Iran. But the incidence rate of programmatic error (12.7%) in our study was more than studies done in other regions in Iran (10, 27). On the other hand, the most common adverse (86%) events caused by programmatic error were lymphadenitis. Accordingly, health workers and policymakers should pay

more attention to preventing, controlling and monitoring the AEFI in the region.

4-1. Limitation

This study was associated with a limitation: According to the records of adverse effect the vaccine by health care providers based on parental reports. Therefore, mild adverse effects of the vaccine are prone to under-reporting.

5- CONCLUSION

Our study included an increased risk of AEFI in the region (Hamadan province) and the programmatic error still needs to be considered. Accordingly, the more activities need to be consolidated to reduce the adverse effect. Moreover, this study assessed the different aspects of AEFI which may help policymakers to improve the immunization programs. Knowledge about rate and common type of AEFIs facilitates improvement in the safety of vaccines and the vaccination process.

6- CONFLICT OF INTEREST: None.

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