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Assessment of Causality, Severity and Seriousness of Adverse Event Following Immunization in Iraq: A Retrospective Study Based on Iraqi Pharmacovigilance Database

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Abstract

Immunization is one of the most cost-effective and successful public health applications. The results of immunization are difficult to see as the incidence of disease occurrence is low while adverse effects following the immunization are noticeable, particularly if the vaccine was given to apparently healthy person. There are High safety expectations of population regarding the vaccines, therefore they are more prone to hesitancy regarding presence of even small risk of adverse events which may lead to loss of public trust to the vaccination programs.

Vaccine safety monitoring is needed as they are now administered to the general population and also available to special categories such as pregnant women and patients with different diseases whom not subjected to clinical trials as well as the incorrect administration rout and the presence of rare or delayed onset adverse events make the presence of surveillance system necessary. The aim of the current study was to measure the distribution, percentage, and frequency of adverse reactions related to vaccines administration in Iraq and to assess the causality, severity, seriousness of these adverse reactions. This study is a retrospective descriptive study for surveillance of vaccine safety conducted using Iraqi pharmacovigilance centre database from 2014 till the end of 2018. This study conducted in period from 1st September 2018 till February 2019 and was in corporation with Iraqi pharmacovigilance center in Iraqi Ministry of Health. 2116 Adverse events were included and outcomes, severity, seriousness, and causality of adverse events were assessed. Majority of adverse events following immunization cases (90.97%) were mild, non-serious (94.47%) and recovered (94.23%). Most reports were for general disorders and administration site conditions and the majority were for elevated body temperature and injection site reactions.

Keywords: Vaccine, Pharmacovigilance, Adverse events following immunization, Iraqi pharmacovigilance center, immunization.

تقييم السببية ، شدة و جدية الاثار الجانبية بعد التطعيم في العراق : دراسة باثر رجعي بالاستناد لقاعدة بيانات مركز اليقظة الدوائي في العراق

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الخلاصة

يعد التطعيم من اكثر التطبيقات الصحية فعاليةً من حيث الكلفة . من الصعوبة ملاحظة نتائج عمليات التلقيح و ذلك لانخفاض نسبة حدوث الامراض في حين ان الاعراض الجانبية التي قد تحصل نتيجة اللقاحات تكون واضحة للعيان , خاصة و ان معظم اللقاحات تعطى لاشخاص سليمين . ان اتخاذ اقصى درجات السلامة و الحذر اهمية لضمان عدم فقدان المجتمع ثقته في حملات التطعيم و بالتالي قد تزيد من امكانية انتشار الامراض غير المرغوبة بها . قد تكون اعراض اللقاح الجانبية معروفة اثناء عمل التجارب الاولية لكن بعض الاثار لا يمكن معرفتها الا بعد فترة من الزمن , كاعطاء القاح بطريقة غير صحيحة او اعطائها للحوامل الذين قد يعانون من امراض مختلفة و قد تكون الاعراض الجانبية نادرة او تحدث بعد فترة زمنية و تكون متأخرة و من هنا تاتي اهمية متابعه اللقاحات من حيث الاعراض الجانبية التي قد تسببها . ان الهدف من الدراسة الحالية هو معرفة توزيع و نسب حدوث هذه الاعراض الجانبية و معرفة مدى سببية الاعراض الجانبية للقاحات شدتها و جديتها . يعد البحث بحثا وصفيا باثر رجعي بالاعتماد على قاعدة بيانات المركز العراقي لاليقظة الدوائي للتقارير الموجودة و التي هي من سنة ٢٠١٤ لغاية نهاية ٢٠١٩ , تم خلال البحث في الفترة من اول من سبتمبرسنة ٢٠١٨ لغاية فبراير ٢٠١٩ , تجميع ٢١١٦ عرض جانبي و تجميع المعلومات حول شدة , وخطورة , وعواقب الاعراض الجانبية و تحديد سببيتها . تبين النتائج ان معظم الاعراض الجانبية كانت بشدة بسيطة (٩٠,٩٧ %) و غير جدية بنسبة (٩٤,٤٧ %) و قد تعافت الاعراض الجانبية في (٩٤,٢٣%) من الحالات . معظم الاعراض الجانبية كانت تعود تحت تصنيف الاضطرابات العامة و الحالات التي تصيب مناطق اعطاء و زرق اللقاحات و التي معظمها تعود لارتفاع درجة حرارة الجسم و التفاعلات الحاصلة في مناطق التلقيح في الجسم .

الكلمات المفتاحية: اللقاحات، اليقظة الدوائية، الاثار الجانبية بعد التلقيح، المركز العراقي لليقظة الدوائية، التطعيم .

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Introduction

Vaccine term is of broad meaning which refers to the biological product that enhances the immunity to prevent or sometimes treat diseases [(1)]. Based on the way of formulation and preparation, there are many types of vaccines given by different ways of administration. Monovalent vaccines are those with a single strain of antigen such as measles vaccine while polyvalent vaccines are those that contain more than one strain or serotype of the antigen such as of oral poliovirus vaccine (OPV). On other hand, combination vaccines are produced by combining more than one antigen in the single formula so the vaccine could protect from several diseases in the same time as well as reducing the need for multiple injections or administration [(2)]. Live attenuated vaccines are obtained through weakened organism that causes the disease to reduce their ability to be pathogenic, this kind of vaccine provides an immune response that mimics what happens when the infection that is caused by organisms such as OPV [(3)]. Inactivated vaccines are found using physical or chemical treatment so microorganisms get killed like inactivated polio vaccine (IPV) [(4)]. Toxoid vaccines are another type of vaccines in which the toxin of microorganisms isolated, purified then inactivated such as tetanus toxoid [(5)]. Subunit vaccines, like the inactivated vaccine, contain no live organism, but this type uses an antigenic portion of the microorganism instead of the whole killed microorganism such as Hepatitis B vaccine which use the surface antigen (HBsAg) [(4)].

Adverse events following immunization (AEFI) is defined as "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 (AE) may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease[(6)]. There are five known causes of AEFI: A. Vaccine product-related reaction, B. Vaccine quality defect-related reaction, C. Immunization error-related reaction, D. Immunization anxiety-related reaction, E. Coincidental event [(2,7)].

The most common systems that are widely used worldwide for data collection of adverse reactions is the Spontaneous reporting system (SRS) in national pharmacovigilance centres which is recommended by World Health Organization (WHO) [(9,10)].

Pharmacovigilance (PhV) according to WHO is defined as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related problems." The purpose of PhV is to improve medication safety and health care, it also acts as an indicator for clinical care standards[(2,10)]. Expanded Program on Immunization (EPI) was established in 1985 in Iraq which support the immunization services , it has strength points as it has good surveillance system and integration between authorities as well as coordination with WHO [(10)]. Vaccine safety monitoring is needed as they now are administered to the general population and also available to special categories such as pregnant women as well as incorrect administration rout and presence of rare or delayed onset adverse events make the presence of surveillance system necessary [(2)]. The aim of the current study was to measure the distribution, percentage, and frequency of adverse reactions related to vaccines administration in Iraq and to assess the causality, severity, seriousness of these adverse reactions.

Subject and Methods

This study is a retrospective descriptive study for monitoring of vaccine safety conducted using the Iraqi Pharmacovigilance database. Ethical approval was acquired from the Iraqi Ministry of Health as well as College of Pharmacy/University of Baghdad prior to conducting the study along with the approval of the Iraqi pharmacovigilance center to order an account for the access to the VigiFlow. The data of reports has been extracted from VigiFlow which is a management system for Individual Case Safety Report (ICSR) by Uppsala monitoring center (UMC) And VigiBase which is The WHO international ICSR database [(11)]. The study conducted between 1st of September 2018 rill February 2019. The data were reported from 2014 untill the end of the 2018 in corporation with Iraqi pharmacovigilance center in Ministry of Health.

There were 2141 adverse events for 1221 reports; some reports were excluded from the study based on the duplication of the reports and presence of identification number (ID) as well as missing of vital data for the assessment of the report. ID is a unique number is given for each report for facilitating their organization and tracking when needed. After exclusion, the included reports were 1209, which contains 2116 reported adverse events regarding vaccines. The data of adverse events collected and classified. Inclusion criteria included any report with available and valid data for the assessment of the case while some cases were excluded in the correlations as they have missing data. Adverse event following immunization were classified according to system organ class (SOC) which is the major category that AEFI belongs to , according to the medical dictionary for drug regulatory affairs (MedDRA) [(11)].

In order to assess the severity of the adverse events, the modified Hartwig and Seigel criteria have been used [(12)] as illustrated in table 1.

Table 1.The modified Hartwig and Seigel severity assessment scale for adverse drug reactions [12]

Mild	**Level 1**	An ADR occurred but required no change in treatment with the suspected drug
	Level 2	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in the (LOS)
Moderate	**Level 3**	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. And/or an antidote or other treatment requirement was required. No increase in LOS
	Level 4	Any level 3 ADR which increase LOS by at least 1 day. or the ADR was the reason for admission
Severe	**Level 5**	Any level 4 ADR which requires intensive medical care
	Level 6	The ADR caused permanent harm to the patient
	Level 7	The ADR either directly or indirectly led to the death of the patient

ADR: Adverse drug reactions; **LOS**: length of stay.

The outcomes of the AEFI were collected as they founded in ICSR of AEFI. The outcomes that the reporter would choose from according to WHO include: fatal, not recovered/not resolved, recovered / resolved , recovered / recovered with sequelae, recovering / resolving and unknown.The seriousness assessed according to six criteria that were adopted by WHO, same seriousness criteria are used in the Iraqi ICSR [13] and in Vigiflow reports [11] form as is shown in table 2.

Table 2. Seriousness assessment in the individual case safety report [13]

Do you consider the reaction to be serious? Yes No ☐ ☐	
If yes, please tick (✓) to indicate why the reaction is considered to be serious:	
☐ The patient died due to the reaction	☐ Involved or prolonged inpatient hospitalization
☐ Life threatening	☐ Involved persistent or significant disability or incapacity
☐ Congenital anomaly	☐ medically significant, please give details:

The revised WHO classification (second edition) was used for assessment of causality of AEFI which provided as a guideline for assessing the ICSR for causality [14] as shown in table 3:

Table 3. World Health Organization causality assessment algorithm for adverse event following immunization [14]

Adequate information available							**Adequate information not available**
Consistent with causal association to immunization				**Indeterminate**		**Inconsistent with causal association to immunization**	**unclassifiable**
A1 vaccine product related reaction (as per published literature)	**A2** Vaccine quality defect-related reaction	**A3** immunization error related reaction	**A4** immunization anxiety related reaction	**B1** temporal relation is consistence but there is insufficient definitive evidence for vaccine causing event (may be new vaccine linked event)	**B2** reviewing factors result in conflicting trends of consistency and inconsistency with casual association to immunization	**C** Coincidental Underlying or emerging condition(s) , or conditions caused by exposure to something other than vaccine	Specify Additional information required for classification :

Statistical analysis

The demographic parameters regarding the distribution of age, gender of patients as well as the type of vaccines and the year of the reports measured to show the distribution pattern of the reports using descriptive statistic using Microsoft Excel 2016. The relations were tested using Chi-square ,calculated by statistical package for the social sciences (SPSS) version 24.0.

Results

The reports of adverse events included in the study were 2116 from 2014 reports until the end of 2018 in which a number of reports were 77, 62, 213, 1080 and 684 for the years 2014, 2015, 2016, 2017 and 2018 respectively. The most age group of which adverse events (AEs) reported was infants by 1865 AEs (88.14%), while AEs for adults were 166 (7.84%), children 35 (1.65%), neonates 34 (1.61%) and adolescent 14 (0.66%). Two reports did not specify the age group of which they reported for as it demonstrated by table 4 .

Table 4 . Demographic distribution of the adverse events following immunization

Year	AEFI Count (%)
2014	77 (4%)
2015	62 (3%)
2016	213 (10%)
2017	1080 (51%)
2018	684 (32%)
Total	2116 (100%)
Gender	AEFI count (%)
Male	1012 (47.83%)
Female	932 (44.05%)
N/A	172 (8.13%)
Total	2116 (100%)
Age group	AEFI count (%)
Infant	1865 (88.14%)
Adult	166 (7.84%)
Child	35 (1.65%)
Neonate	34 (1.61%)
Adolescent	14 (0.66%)
N/A	2 (0.09%)
Total	2116 (100%)

N/A :not available

It was found that Hexavalent vaccines had the most number of reports by 977 (46.17%) followed by Pentavalent II 473 (22.35%). The third-most reports were for Pentavalent I vaccine 233 (11.01%) as shown below in table 5.

Table 5. Types of vaccines associated with adverse event following immunization .

Vaccines Administered	**AEFI Count (%)**
Hexavalent	977 (46.17%)
Pentavalent II	473 (22.35%)
Pentavalent I	233 (11.01%)
Tetanus	168 (7.94%)
BCG	103 (4.87%)
MMR	51 (2.41%)
Measles	40 (1.89%)
Hepatitis B	22 (1.04%)
Influenza	14 (0.66%)
Pneumococcal	13 (0.61%)
Rota Virus Vaccine	10 (0.47%)
OPV	6 (0.28%)
Hepatitis A	2 (0.09%)
Meningococcal	2 (0.09%)
Tick-borne encephalitis	1 (0.05%)
Pneumococcal & Hexavalent	1 (0.05%)
Grand Total	2116 (100%)

Hexavalent : (Diphtheria, Tetanus, acellular pertussis– Hepatitis B -inactivated polio-Haemophilus b **)** Vaccine**,**
Pentavalent I : (Diphtheria, Tetanus, acellular pertussis - inactivated polio-Haemophilus b**,) vaccine ,**
Pentavalent II : (Diphtheria, Tetanus whole cell pertussis -Hepatitis B-Haemophilus b) vaccine **,**
BCG: Bacillus Calmette- Guérin Vaccine,
MMR: Measles ,Mumps and Rubella vaccine,
OPV: Oral Polio vaccine

The most AEFI was related to general disorders and administer site conditions (57.75%), followed by skin and subcutaneous tissue disorders (29.11%). In addition, 8.65% of the reports were for immune system disorder as shown in table 6.

Table 6. Adverse event following immunization classified by system organ class

SOC	Count of SOC	%
General disorders and administration site conditions	1222	57.75%
Skin and subcutaneous tissue disorders	616	29.11%
Immune system disorders	183	8.65%
Infections and infestations	30	1.42%
Blood and lymphatic system disorders	29	1.37%
Respiratory, thoracic and mediastinal disorders	9	0.43%
Gastrointestinal disorders	9	0.43%
Nervous system disorders	6	0.28%
Vascular disorders	5	0.24%
Metabolism and nutrition disorders	2	0.09%
Musculoskeletal and connective tissue disorders	2	0.09%
Cardiac disorders	1	0.05%
Congenital, familial and genetic disorders	1	0.05%
Injury, poisoning, and procedural complications	1	0.05%
Grand Total	**2116**	**100.00%**

SOC: system organ class**.**

Regarding the severity assessment of AEFI, it was found that 90.97% of the reported AEs were mild, while 2.5% were of moderate severity, 0.14% were severe while the severeity class of 6.38% of the reports couldn't be specified as shown in table 7.

Table 7. Severity types of Adverse event following Immunization

Severity	Count	%
Mild	1925	90.97%
Moderate	53	2.50%
Severe	3	0.14%
Unknown	135	6.38%
Total	2116	100.00%

Outcomes of AEFI were collected according to the final result that seen by the reporter regarding the AEs where 94.23% of the AEs were resolved, 2.79% of AEs were with unknown outcome while not available data was found in 2.27% of reports as shown in table 8.

Table 8.Adverse event following immunization outcomes

The outcome in reports of AEFI	Count	%
recovered/resolved	1994	94.23%
Unknown	59	2.79%
N/A	48	2.27%
not recovered/not resolved	7	0.33%
recovering/resolving	5	0.24%
Fatal	2	0.09%
recovered/resolved with sequelae	1	0.05%
TOTAL	2116	100%

N/A: not available, **AEFI:** Adverse event following immunization The majority of cases were not serious cases (94.47%) while 1.47% of the reports were seen to increase hospitalization and 1.13% of total reports were life-threatening as shown in table 9. Regarding the six AEFI reported as led to disability (Table 9), two were for BCG due to lymphadenopathy, two for Hexavalent vaccine due to injection site swelling, one for measles for rash and one for polio vaccine due to weakness of the injected limb. The first five cases recovered while the polio AE were reported as not recovered. 25% of the life-threatening conditions were reported to measles vaccine and they were due to anaphylaxis and anaphylactoid responses.

Table 9. Seriousness of adverse event following immunization

Seriousness	count	%
Not serious	1999	94.47%
Increase Hospitalization	31	1.47%
Life threat	24	1.13%
Unknown	24	1.13%
Medically significant …	30	1.42%
Disability	6	0.28%

The two fatal cases were reported for BCG vaccine. Relation of gender with outcomes, severity and seriousness was tested and it showed no statistically significant relation of gender with each of these three parameters as shown in table 10

Table 10. Relation of the outcome , severity and seriousness of adverse event following immunization with gender

Parameter	**male**		**Female**		**Total**	**P. Value**
Outcomes	**No.**	**%**	**No.**	**%**	**No.**	
Recovered	952	95.97%	886	97.15%	1838	0.159 N.S
Others*	40	4.03%	26	2.85%	66	
Total	992	100.00%	912	100.00%	1904	
Severity	No.	%	No.	%	No.	
Mild	913	96.72%	860	97.40%	1773	0.656 N.S
Moderate	29	3.07%	22	2.49%	51	
Severe	2	0.21%	1	0.11%	3	
Total	944	100.00%	883	100.00%	1827	
Seriousness	No.	%	No.	%	No.	
Yes	947	94.89%	887	96%	1834	0.246 N.S
No	51	5.11%	37	4%	88	
Total	998	100%	924	100%	1922	

*others : Unknown, not recovered/not resolved, recovering/resolving, fatal, recovered/resolved with sequelae , NS : not significant , (P<0.05)

Regarding the relation of age group with each of outcome, severity and seriousness, there is a significant relationship between age group with each of these parameters. Recovery outcome was significantly lower in adolescent group compared to other age groups. Regarding severity, AEFIs of mild severity was significantly lower in child age group compared to other age groups (p-value <0.0001). With respect to seriousness, serious AEFIs was significantly higher in child age group compared to other age groups (p-value <0.0001) as shown in table 11.

Table 11. Outcome , Severity and seriousness of adverse events following immunization in respect to age group

Parameter	**Age groups**											P-value
	Neonate		**Infant**		**Child**		**Adolescent**		**Adult**		**Total**	
Outcomes	No.	%	No.	%	No.	%	No.	%	No.	%	No.	
Recovered	29	90.6%	1761	96.6%	32	96.97%	8	72.7%	162	97.6%	1992	
Others*	3	9.4%	63	3.4%	1	3.03%	3	27.3%	4	2.4%	74	<0.0001
Total	32	100%	1824	100%	33	100%	11	100%	166	100%	2066	
Severity	No.	%	No.	%	No.	%	No.	%	No.	%	No.	
Mild	23	92.%	1711	97.44%	25	80.65%	8	100%	156	98.11%	1923	
Moderate	2	8.%	43	2.45%	6	19.35%	0	0.00%	2	1.26%	53	<0.0001
Severe	0	0.%	2	0.11%	0	0.00%	0	0.00%	1	0.63%	3	
Total	25	100%	1756	100%	31	100%	8	100%	159	100%	1979	
Seriousness	No.	%	No.	%	No.	%	No.	%	No.	%	No.	
Yes	8	23.53%	66	3.58%	10	30.3%	2	14.29%	7	4.22%	93	
No	26	76.47%	1779	96.42%	23	69.7%	12	85.71%	159	95.78%	1999	<0.0001
Total	34	100%	1845	100%	33	100%	14	100%	166	100%	2092	

*others : Unknown, not recovered/not resolved, recovering/resolving, fatal, recovered/resolved with sequelae

The results of causality assessment are shown in table 12 where the majority (95.98%) of AEFIs were of A1 classification which almost was for body temperature conditions and local adverse eventst.

Table 12. The Causality assessment of AdverseEvent Following Immunization

Causality	Count	%
A1	2031	95.98%
B1	25	1.18%
B2	23	1.09%
A3	16	0.76%
Unclassified	15	0.71%
A4	6	0.28%
TOTAL	2116	100%

The majority of the Causality classified as vaccine product related reaction (A1) , which count for 95.98% of the total 2116 AEFI , folowed by 1.18% for B1 and B2 with 1.09% . six cases reported and classified as A4 and they were mostly a psychological events . some reportes could not be classified in one of the categories due to unavailability or mising of some data in the reports therefore classified as "unclassified".

Discussion

In order to identify and assess adverse reactions and events of drugs, the Pharmacovigilance depends on collection of information regarding the post-marketing events in post-marketing or approval phase of medications by a system that relays on spontaneous reporting system (SRS) in order to detect any problems with the vaccines, vaccination program or emergence of new adverse events that not reported in the trials [(15)].

The results of the current study revealed that the percent of AEFI reports is increased during 2017 and 2018 compared with previous years which may be related to increased awareness of health care workers. On its establishment, the Iraqi pharmacovigilance center (IPhvC) has adopted the mission of sensitizing and raising the awareness of the importance of reporting ADRs in ensuring patient safety through face-to-face communication with all health care workers in Iraq, where the need to create a reporting culture will be an intense challenge [(16)]. Infants were of highest reporting AEs and it may be owed to the fact that they are the most targeted group regarding the immunization programs.

Regarding the type of vaccines associated with AEs (Table 5), in the current study the Hexavalent had 46.17% followed by Pentavalent II with 22.35% . In a study regarding vaccine surveillance in Oman showed that Pentavalent II vaccine was third most vaccine that AEs reported for and they mostly were minor local reaction [(17)]. In studies comparing combination versus separated administered vaccines, the reported adverse event indicate that combining antigens usually does not increase adverse effects-in fact, it can lead to an overall reduction in adverse events [(18)]. The combination vaccines development increase the compliance and rates of vaccination coverage [(19)] while , the disadvantage combination vaccines is that it may not always be clear which component is responsible for a particular adverse event [(20)].

As is shown in table 6, general disorder and administration site conditions followed by skin and subcutaneous tissue disorders both had the highest reported percent (57.75% and 29.11% respectively), in which the most reported AEFI were for body temperature conditions and different type of injection site reactions such as redness, swelling, and pain. In one study in Switzerland from 1991 – 2001, it was also reported that the majority of AEs were for general disorder and administration site conditions (47%) [(21)]. In the United States during 11 years of AEFI surveillance the most reported AEs were fever and injection site reaction (about one quarter for each) [(22)].

Regarding the severity assessment of AEFI (Table 7), the majority of the AEFI cases (90.97%) were mild and it was mentioned in the supplementary information of vaccine safety , that the majority of vaccine reactions are "common", mild, settle without treatment, and have no long-term consequences [(23)].

regarding the outcomes of the AEFI (Table 8), the majority of cases were recovered with 94.23% percent,while With respect to seriousness (Table 9) the majority of AEFI cases were nonserious (94.47%) . In one study in 2016 in Switzerland regarding the AEFI summery, it was found that 55% of the reports were not serious adverse events [(24)].

In this study two cases were reported as fatal, both were reported for BCG vaccine as disseminated Bacillus Calmette-Guerin infection but there was no sufficient evidence to accuse the vaccine product. In fact, fatal dissemination of BCG infection is very rare to occur (up to 0.000159%) and almost in severe immunocompromised individuals [(25)] and the estimated rate of severe reaction occurrence with BCG is 1 in 1000 to 1 in 50.000 given doses [(2)] .

Among life threatening conditions, 25% of reports belonged to measles vaccine due to anaphylaxis and anaphylactoid responses in the results of this study and It is known that measles vaccine causes anaphylaxis in 1 per 100,000-million administered doses [(26)].

Regarding causality assessment of AEFI (Table 12), the majority (95.98%) of AEFIs were of A1 classification which almost was for body temperature conditions and local adverse events. In

Switzerland surveillance of AEFI from 1991 – 2001, it was found that 21.3% of the reported AEs were of very likely or certain causal relationship of which 86.6% related to local reactions [21]. Once vaccines are induce immune response by the vaccine antigen interaction with immune system which is essential in developing the immunity against the diseases, manifestation of mild adverse reaction is common such as redness, swelling at injection site. Fever as well is considered as inflammatory response associated with the immune response [14]. B1 classification as shown in table 13, was account for 1.18% of the AEFI. In B1 the temporal relation is established but the evidence to cause the vaccine is insufficient. It actually may be a new vaccine event and details of this events must retained. With time, if similar reports recorded so it may aid in suggestion a new potential causal relation [14] . If there is a conflicting trends between inconsistency and consistency with causality present, the AEFI will have B2 classification, despite of adequate information but it can not clearly classify the AE [14]. In this study it was found that 1.09% of the AEFI were classified as B2. In study performed in India regarding the causality assessment of AEFI it was found that B1 and B2 classifications accounted for 1% and 7% respectively among 1037 reports [27].

The A3 causality was seen in mostly for BCG vaccine, which counted for 75% for all A3 cases. It was reported and known that BCG vaccine cause a local reaction in 90-95% of patients, incorrect site of injection also leads to local reaction and abscess if BCG given by SC route, the incorrect injection site that lead to abscess for example ,was classified as A3 causality which refers to immunization error [2]. In a study conducted in India for AEFI, immunization error related was count for 13% of the reports and classified as A3 in one Indian study [27].

Six cases (0.28%) were classified as A4 causality as they were mostly a psychological event. Upon administering of Tetanus–diphtheria vaccine in 1998 in Jordan, 122 individual admitted to the hospital as they felt chest tightness, feeling faint, and dizziness and this accident was reported to be associated with mass psychogenic illness [28]. Adolescents, especially if immunized in mass clinical settings, are more prone to have anxiety-related vasovagal reactions resulting in fainting [29]. In a study conducted in India for AEFI, it was found that 17% of reports related to A4 classification (anxiety related) [27].

The current study is not without limitations, lack of some information in the reporting of adverse events due to absence of understanding or careless filling the data makes the assessment of severity and seriousness of the cases difficult as well as difficult or impossibility of tracking the machines that associated with the adverse events.

Conclusion and Recommendations

In general, the administered vaccines in Iraq were safe and the majority of them were mild and nonserious adverse events. Further investigation is required regarding the causality for unclassified category, some adverse events that reported and classified as B1 recommended to be tracked as they might be new adverse events of vaccines. It may be of benefit to share these results with the media in order to increase the trust of the public regarding the immunization programs.

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