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Evaluation of Vaccines Adverse Events Reporting System (VAERS) Related to Childhood Vaccines in Kingdom of Saudi Arabia (2017–2020)

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اللقاح هو وسيلة فعالة للقضاء على الأمراض المعدية، لكن تعتبر ردود الفعل العكسية للقاحات شائعة أيضًا بين الأطفال. تقيم هذه الدراسة الآثار الضارة التي تتعلق عمومًا بلقاحات الطفولة من واقع بيانات نظام الإبلاغ عن الآثار الضائرة للقاحات.

أدخلت المملكة العربية السعودية برنامج التحصين الوطني (NIP) لمكافحة الأمراض المعدية مما أدى إلى انخفاض معدل الأمراض التي يمكن الوقاية منها بنسبة 90٪.

في حين أن لقاحات الوقاية من الأمراض تعود بالنفع، إلا أن لها آثار ضائرة تتراوح بين الخفيفة إلى الشديدة وهو ما يتضح من خلال الاستخدام الواسع للقاحات. أنشأت الهيئة العامة للغذاء والدواء السعودية (SFDA) نظام التيقظ الدوائي يعرف باسم المركز الوطني للتيقظ والسلامة الدوائية (NPC)، حيث يتولى المركز تقييم عوامل السلامة والمخاطر المرتبطة باللقاح والإبلاغ عن الفحوصات من خلال الأنظمة الوطنية للإبلاغ عن الآثار الضائرة (NAERS).

يتولى نظام الإبلاغ عن الآثار الضائرة للقاحات رصد وتجميع وتحليل والإبلاغ عن البيانات المتعلقة بالتفاعلات المحددة للقاحات لتحديد أي مخاوف تتعلق بسلامة اللقاح تختلف عن العقاقير العلاجية الأخرى. يضمن نظام الإبلاغ عن الآثار الضائرة للقاحات رصد التفاعلات السلبية للقاح في الوقت الحقيقي ويوفر علامات السلامة من خلال تحليل الأحداث المرتبطة باللقاح التي يقدمها طواعية المتخصصين في المجال الصحي الذين يشهدون الآثار غير المرغوبة المحتملة. يعتبر هذا التقييم للمخاطر المحتملة ضروريًا للحفاظ على ثقة الجمهور في برامج التطعيم.

يكمن الهدف الأساسي من هذه الدراسة في تحديد اتجاهات الآثار الضائرة التالية للتطعيم (AEFI) للأطفال حتى سن 6 سنوات وحساب معدل حدوثها، فضلاً عن تحديد الجنس، والمناطق، والجرعات المجمعة أو الفردية بوصفها عوامل خطر ولتقييم مدى شدة هذه العوامل.

قدم نظام الإبلاغ الالكتروني لبرنامج الآثار الضائرة للقاحات VAERS في المملكة العربية السعودية تقارير باستخدام برامج الإكسل لكافة الآثار الضائرة التالية للتطعيم التي تحدث للأطفال حتى سن 6 سنوات خلال الفترة بين 2017-2020. تألفت هذه البيانات من التاريخ الطبي، والعرق، والمنطقة،

والعمر، وتاريخ التطعيم، وظهور أول ردود الفعل، والنوع، والموقع، والمدة، والفاصل الزمني بين ظهور ردود الفعل والإبلاغ. يعد هذا هو التقييم الأول لنوع VAERS في المملكة العربية السعودية. كانت البيانات التي تم جمعها غير معلومة الهوية، حيث تم الحفاظ على سرية المشاركين وتسجيل أرقام بطاقات هوية المشاركين فقط. استخدمت الحزمة الإحصائية للعلوم الاجتماعية (SSPS) الإصدار 23 (إس بي إي اس إنك، شيكاغو، إلينوي، الولايات المتحدة الأمريكية) لإدخال البيانات والتحليل الاحصائي.

أفادت البيانات التي جُمعت خلال الفترة بين 2017 إلى 2020 عن 1270 من الآثار الضائرة التالية للتطعيم، بواقع 43 حدث في 2017، و181 في 2018، و672 في 2019، و374 في 2020. كانت الآثار الضائرة التالية للتطعيم شائعة وحادة عند الأطفال من الذكور مقارنة بالإناث. وعلى مستوى المناطق، سجلت القنفذة النسبة الأعلى (51.49%) يليها منطقة عسير (22.1%)، في حين سجلت منطقتي مكة والرياض النسبة الأقل ويعزى ذلك إلى الخدمات الصحية الأفضل المتوفرة في هاتين المنطقتين. أفادت دراسة عن اللقاحات الفردية مقابل اللقاحات المجمعة عن اعلى معدل للحدوث في لقاح المكورات الرئوية (10.9%) يليه اللقاح الثلاثي الخناق– الكزاز– السعال الديكي (DTP-HiB-HB) بنسبة (5.5%) في حين سجل لقاح التطعيم الثلاثي ضد الحصبة، والنكاف، والحصبة الألمانية (MMR) بنسبة (4.2%) ولقاح الدفتيريا والتيتانوس والسعال الديكي والتهاب الكبد ب وشلل الأطفال والمستدمية النزلية بنسبة (5.5%) (DTaP-IPV-HiB-HB). كانت الحُمى هي الأثر المتكرر الإبلاغ عنه (92، 7.2%) في مقدمة التفاعلات غير المذكورة في الدراسة. كانت الفئة العمرية الأكثر تضرراً هي الأطفال الذين تقل أعمارهم عن عام واحد.

يساعد رصد والإبلاغ عن الآثار الضائرة التالية للتطعيم في تحسين السلامة والقضاء على المفاهيم الخاطئة المتعلقة باللقاحات، وفي أغلب الأحيان يتقيد ذلك بنقص الإبلاغ بسبب نظام التيقظ الدوائي السلبي. علاوة على ذلك، هناك حاجة لتصنيف الآثار الضائرة التالية للتطعيم لتحسين الخصوصية بجعلها شاملة. لذا، فإن المراقبة والرصد الكافيين للآثار الضائرة المتعلقة بالتطعيم من الأهمية بمكان لتجنب تكرارها وصياغة خطة عمل مناسبة لمكافحتها.

ABSTRACT:

Background: Vaccination-associated adverse events are common among children and need to be monitored for evaluating the safety profile of immunization programs. Ministry of Health (MOH) of the Kingdom of Saudi Arabia (KSA) has launched the Vaccines Adverse Events Reporting System (VAERS) for the same purpose.

Aim: This study aims to evaluate the adverse events related to childhood vaccines from VAERS data.

Methods: A record-based descriptive study was carried out for all the reported vaccine adverse events (AE) in MOH-VAERS during 2017–2020 among children under six years of age in KSA. Data were extracted from the electronic reporting system for medical history, age, region, date of immunization, reaction onset, type, duration, site, and impact w.r.t hospitalization.

Results: Our analysis showed fever as the most common AE in one-year-olds following a combination vaccine against measles, mumps, rubella (MMR). Overall, the three-year trend showed AE exhibiting gender-specific variation, with a slight male preponderance. These events were also more common in the

Saudis of the eastern region that are better equipped with health care facilities, showing a clear region-specific pattern.

Conclusion: Childhood vaccine-related AE are usually mild and treatable and are bearable compared to the risks associated with the infection. Our study demonstrated pyrexia following MMR as the most common AE in Saudi male children of the eastern region. The occurrence and patterns of these events are in concordance with international data. Analysis of this data combined with previously published reports on vaccine-related adverse events can help in an appropriate training of the medical staff.

Keywords: Vaccines, Adverse events, Immunization, Saudi Arabia.

INTRODUCTION:

At the helm of the 20th century, the most serious threat to human life and well-being was infectious disease. Outbreaks of diseases were common with significant child mortality: 160 in every 1000 children born at the turn of the century dying of an infectious disease before the age of 5 years (Ellenberg & Chen, 1997). With the advent of vaccines, parents in most developed countries

no longer dread these highly communicable diseases. Vaccines eliminate contagious diseases, protect vaccinated communities and individuals, improve antibiotic resistance, and save treatment costs. Immunization or vaccination has emerged as a sine-qua-non of modern public health programs and one of the most cost-effective medical interventions (Maayan-Metzger, Kedem-Friedrich, & Kuint, 2005).

LITERATURE REVIEW:

Expanded programs of immunization (EPI) were introduced globally by the respective governments as a tool in early childhood healthcare to combat deadly communicable diseases. In the Kingdom of Saudi Arabia (KSA), the EPI commenced as a National immunization program (NIP) in 1976, under the auspicious of a Royal Decree, managed by the General Directorate of Infectious Diseases. The Royal decree that all children must complete their immunizations before issuing their birth certificates led to an almost complete eradication of diseases that hitherto were very common (Tufenkeji & Kattan, 1994). Within a relatively short period of time, KSA made great strides in its program of childhood immunization. More than 90% of school-age children are completely immunized, and the incidence rates of vaccine-preventable diseases had dropped by more than 90% from peak levels. The current immunization

schedule was enacted in 1991 by the Ministry of Health (MOH). High levels of immunity among residents against infections, such as meningococcal disease, are maintained by timely & meticulously crafted campaigns carried out annually prior to Haj season (Abdo, Sanai, & Al-Faleh, 2012).

The optimal vaccine is administered timely, administration of which can only be postponed due to fever, severe illness, child on immunosuppressive drugs or treatment. Despite vaccines' proven effectiveness in managing risks of deadly diseases in children, they are not entirely risk-free. While most are minor and self-limiting, rarely some adverse effects could be serious. Such side effects,

however, lead to waning public confidence, especially that of risk-averse parents in the immunization programs, where they question whether vaccines cause more harm than is justified by their benefits (Damnjanović et al., 2018). Vaccine benefits indeed outweigh the temporary and mild side effects which do not require treatment. Vaccine adverse reactions can be dichotomized as local and systemic or mild and severe. Some examples of side effects are: sore, painful arm, rash, itchiness, or swelling at site of injection; fever, irritability, unusual sleep patterns, nausea, and very rarely severe anaphylaxis by

measles-mumps-rubella (MMR) vaccine at a rate of 1/20,000 to 1/1,000,000 doses distributed (White, Boldt, Holditch, Poland, & Jacobson, 2012).

Because such rare effects are often not evident until vaccines come into widespread use, governments around the world maintain ongoing surveillance programs to monitor vaccine safety. In KSA, the Saudi Food and Drug Authority (SFDA), an independent body since 2003 working to regulate food, drugs, and medical devices as well as set necessary regulations, established a pharmacovigilance system in the form of the National Pharmacovigilance and Drug Safety Center (NPC). The NPC efficiently conducts several pharmacovigilance activities, such as evaluations of adverse drug events, vaccine safety, assessment of risk as well as periodic safety update reports, and other oversight and inspections through the National adverse events reporting system (NAERS) (Alharf et al., 2018).

Vaccine adverse events reporting system (VAERS) is a national vaccine safety surveillance program created as an outgrowth of the NAERS under MOH, geared to record and analyze data from reports of adverse events following vaccination. Data is collected for vaccine-specific reactions related to product, quality defect, immunization error or immunization anxiety, and coincidental events (Iskander, Miller, & Chen, 2004). By monitoring such

events, VAERS helps to identify any important new safety concerns that otherwise may not come to light before licensure.

The expected safety of routinely administered vaccines is quite different from other therapeutic products in that vaccines are given to healthy individuals before they could contract the disease. Moreover, they are administered to large populations of infants and children, whereas few drugs are recommended on such a mass scale. Post-marketing surveillance of safety relies on VAERS, which in essence is a safety signal detection and hypothesis-generating system (Shimabukuro, Nguyen, Martin, & DeStefano, 2015). Besides, VAERS is operated as a spontaneous reporting phenomenon, where real-time monitoring and analysis of spontaneous reports of adverse events following vaccination is carried out. This process begins with voluntary submission of reports of possible vaccine-associated events to VAERS by the astute health professional witnessing the first hint of a potential problem. One of the examples is that of

the investigation that resulted in the voluntary withdrawal of rotavirus (RV) vaccine, which was triggered by nine reports to VAERS of intussusception, eight of which occurred within one week of RV's first dose (Zhou & Ellenberg, 2003).

A sustained effort to monitor these data effectively and to develop more precise ways of assessing the risks of vaccines is mandatory to ensure public confidence in immunization programs.

This study aims to evaluate the VAERS in special context to childhood vaccines during the years 2017–2020 in KSA. We will thus calculate the incidence of AEFIs in children along with various risk factors that affects AEFI, such as gender, ethnicity, number of vaccines being administered simultaneously, and the regional difference. To the best of authors' knowledge, this is first-of-its-kind assessment of VAERS in KSA, which is formulated to determine the effectiveness of the reporting system and can also drive improvements to enhance its efficiency (Baker et al., 2015).

AIMS:

The study aims to evaluate the VAERS related to Childhood vaccines during the years 2017–2020 in KSA.

OBJECTIVES:

Primary objective

➢ To calculate the incidence & identify the trend of AEFI in children up to 5 years of age.

➢ To identify risk factors for AEFI, like gender, regions, or combined vs. single doses.

➢ To assess the most frequent & most serious AEFI & assess the outcome of VAERS.

Secondary objective

➢ To detect the defects in the VAERS and suggest improvements.

METHODOLOGY

1. Study Subjects and Study Design:

A record-based descriptive study design was applied, where excel extracted reports were retrieved from the electronic reporting system of the VAERS program in KSA for all AEFI in children aged up to 6 years during the study period between 2017–2020. Baseline characteristics were collected for each participant. Data points were extracted for medical history, age, region,

date of immunization, reaction onset, type, duration, site, and impact with respect to hospitalization. Data was also collected for the time lapse between onset & reporting.

Institution review board (IRB) approval was obtained from MOH and approved by the ethical committee of the research center at King Fahad Medical City, Riyadh (No. 20-662E). The purpose of the study, main objectives, and step-by-step procedure was clarified with NAERS Program. Potential benefits to participants and to the community from this research were elaborated. Possible risks that could be raised from this research were also discussed clearly.

Deidentified data: To assure anonymity, participant's names were not collected, and merely a patient's file number and ID were recorded. To maintain confidentiality, all data was collected directly in SPSS on the laptop with a personal password. All information obtained from reporting forms through a data collection sheet was used solely for research purposes.

2. Statistical Analysis:

Data entry and statistical analyses were performed using SPSS (statistical package of social sciences) version 23 (SPSS Inc., Chicago, IL, USA). The appropriate statistical tests were used. The normality of data was first tested by a one-sample K-S test. Basic descriptive statistics were computed as a baseline means, standard deviations (SD), and minimum and maximum range values for continuous variables, while categorical data were summarized as frequency & proportions. Independent t-test were used for the comparative analysis of parametric variables, while the Mann-Whitney U test (z) was used to compare nonparametric continuous variables in two different groups. Pearson Chi-square tests were applied for the comparative analysis of the categorical variables. They were presented in frequency tables and graphs as appropriate. *P*–value <0.05 was considered as statistically significant.

RESULTS

Data was extracted from the Vaccine Adverse Event Reporting System (VAERS) Health Electronic Surveillance Network (HESN) database comprising of subjects taking from 2017 through 2020. Out of 1270, overall reported Adverse Event Following Immunization (AEFI) were 43 (0.33) in 2017, 181 (1.42%) in 2018, 672 (5.42) in 2019, and 374 (2.97) in 2020. Region-wise figures are populated in Table 1.

Table 1: Year-wise incidence rate of Vaccine Adverse Events among 100,000 vaccinated children from 2017-2020 in KSA.

Year	Incidence Rate
2017	0.33 per 100,000
2018	1.423 per 100,000
2019	5.415 per 100,000
2020	2.972 per 100,000

In our data, the mean age of subjects was 8.9±12.5 months (range: 0–72). Out of the total 1270 reports for HESN-VAERS reported from 2017–2020, 621 (48.9%) were females, while 649 (51.1%) were males. Single vs. Combined Vaccines summary is illustrated in Figure 1. Pneumococcal had the highest reported incidents at 138 (10.9%), followed by 89 (7.0%) for DTP-Hib-HB combination doses. Whereas MMR incidence was for 54 (4.2%), and DTaP-IPV-HiB-HB incidence was reported in 70 (5.5%).

Figure 1: Single vs. Combined Vaccines in Vaccine Adverse Event Reporting System in KSA, 2017–2020.

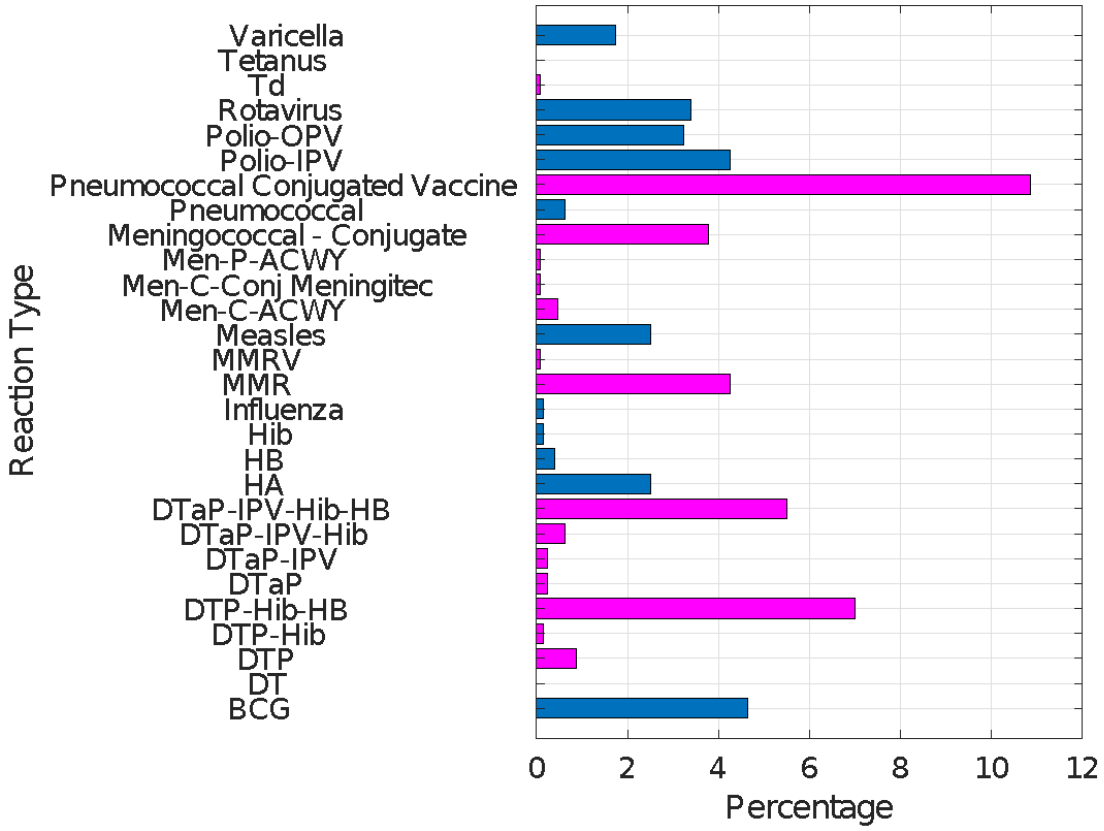


Table 2 shows the average onset time of reporting after adverse events and the vaccines that caused it. Overall mean onset time in days is 1.22 +2.77 (range: 0 – 150). Most of the other 1270 events, the onset time was the same day of vaccination.

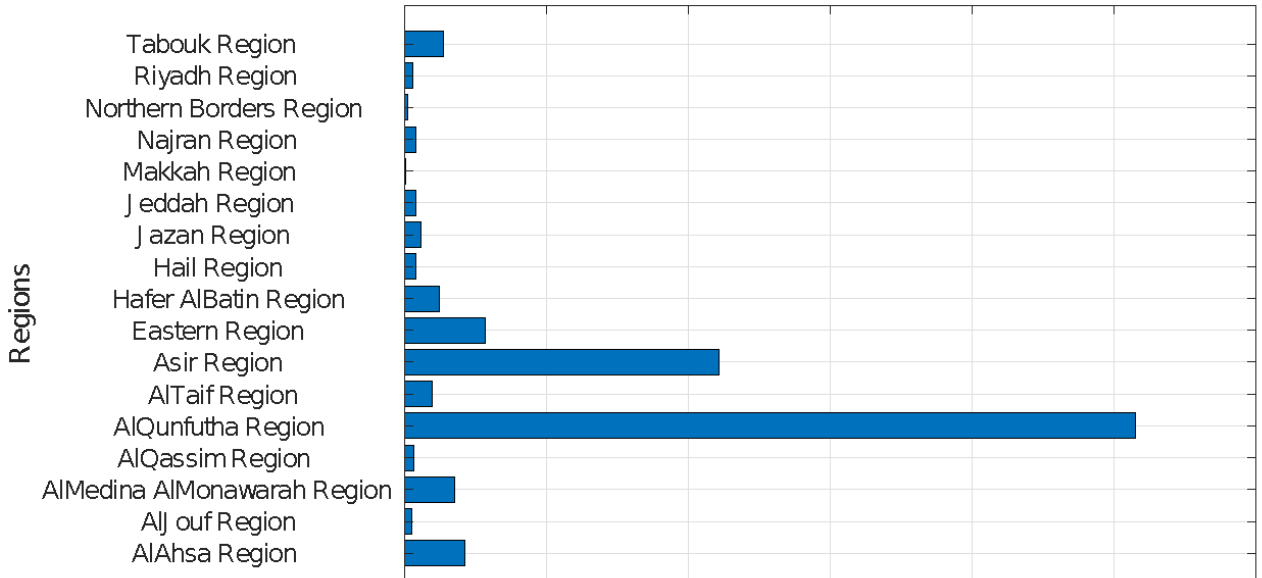
Table 2: Mean Onset time for vaccines causing an adverse event according to the Vaccine Adverse Event Reporting System in KSA, 2017–2020.

Type of Vaccine	Adverse Event	Mean Onset time (days)

DTP, DTaP, Pneumococcal based, Meningococcal, Polio, MMRV	High Fever	4.15
DTP, DTaP, Pneumococcal, Polio, MMRV, Meningococcal, Influenza	Hypotonic-Hyporesponsive Episode	0.5
DTP, DTaP, Pneumococcal based, Meningococcal, Polio, MMRV	High Fever	4.15
DTP, DTaP, Pneumococcal based, Polio, MMRV, Measles	Other serious events	2.6
DTP, DTaP, Pneumococcal based, Rotavirus, Polio, MMRV, Measles	Respiratory	0.2
DTP, DTaP, Pneumococcal based, Meningococcal, Polio, Hib,	Seizure	1.22

AlQunfutha region had the highest incidents reported with 654 (51.49%), followed by the Asir region with 281 (22.1%). Both regions reported approximately 73% of incidents. A summary of the frequency plot of reported incidents with respect to region is given in Figure 2.

Figure 2: Vaccine Adverse Events based on health regions in KSA, 2017–2020.



The highest reaction type was Other (no details given in the database, and after asking the NARSP person in charge, she said any other AE means other than the mentioned here), with 146 (11.5%) cases reported, followed by fever 92 (7.2%). Figure 3 shows in percentage all the adverse events reported from 2017 to 2020.

Figure 3: Vaccine Adverse Events based on reaction types, 2017–2020

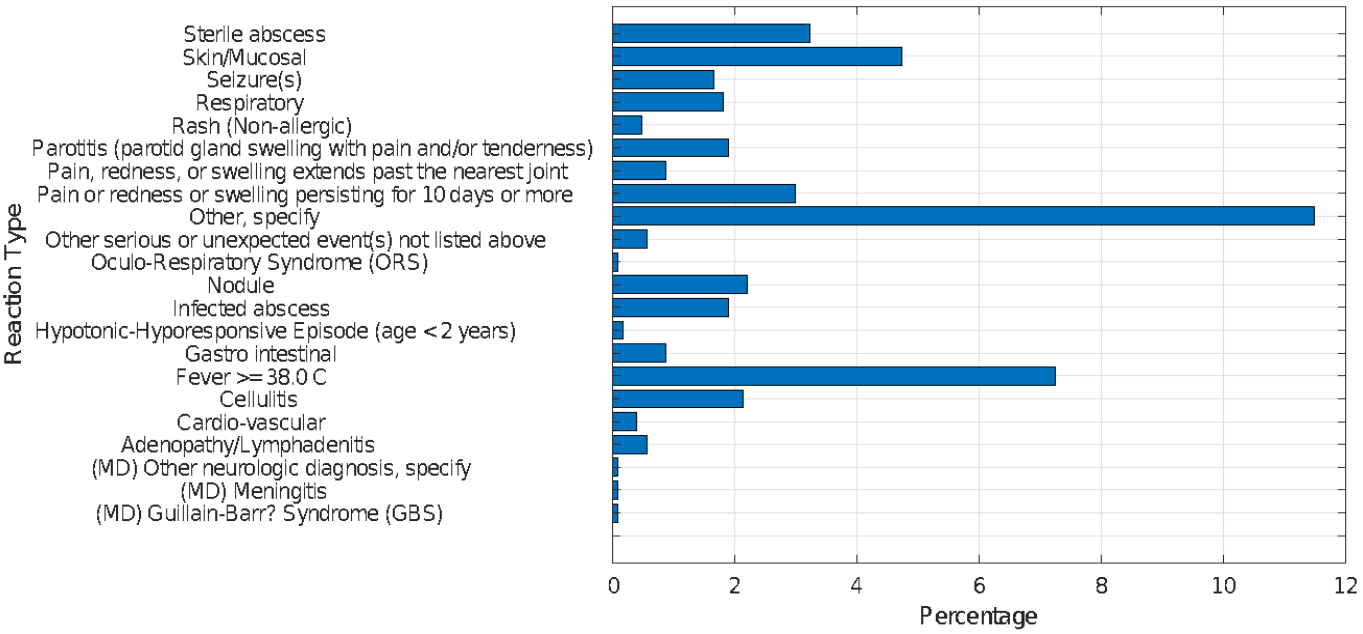


Figure 4 shows the count of events caused by a particular agent over time from 2017–2020, resulting in a trend graph. These agents caused more than ten serious events. The idea is to show the rate of incidents reported for a particular vaccine over the reporting history from 2017–2020.

Figure 4: Cumulative events of VAE for DTP-Hib, Pneumococcal, and Pneumococcal conjugates from 2017-2020. The agents caused more than ten serious events.

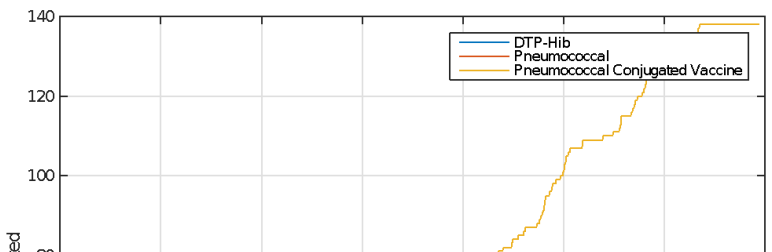


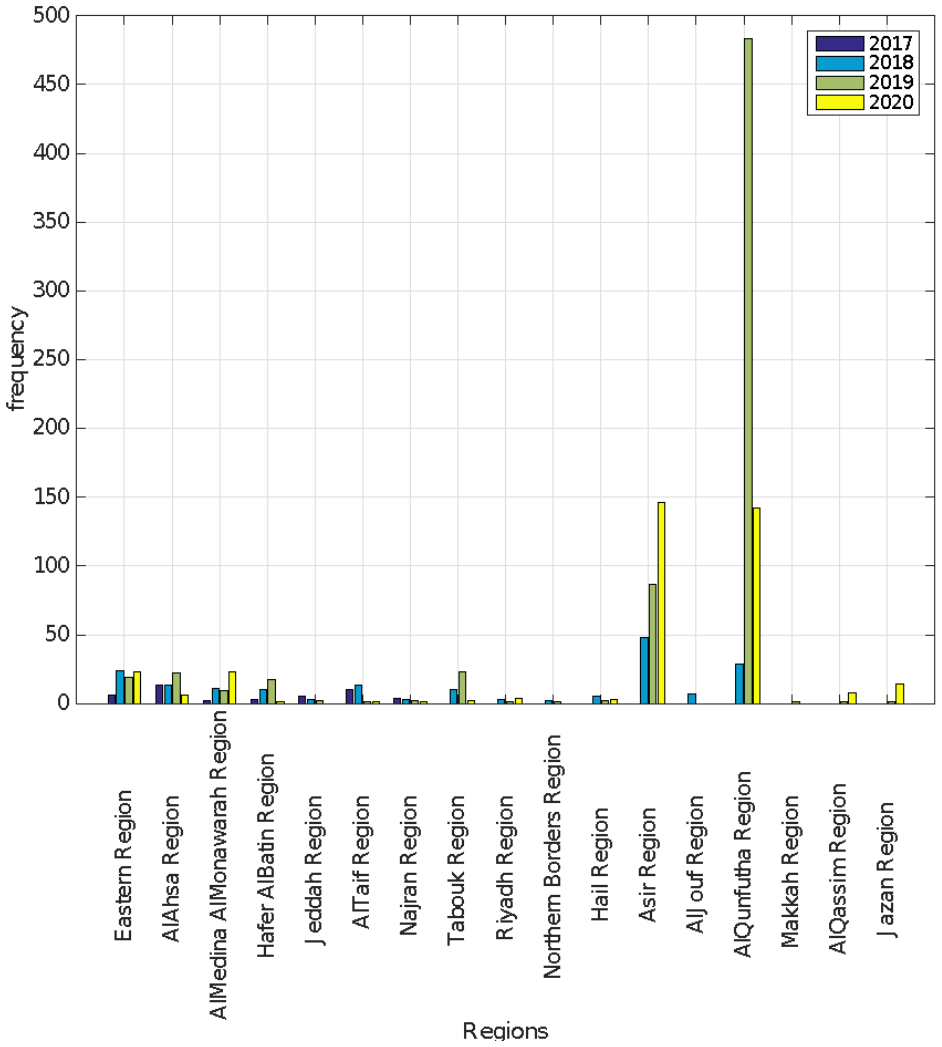
Table 3 and Figure 5 show the incidence rate per year per region for the HESN study. The number of years from 2017–2020 are color-coded, whereas the regions are on the x-axis. It is interesting to note that number of cases reported in AlQunfutha and Asir region is the highest, with 2019 being particularly of the highest incidents among all-region in all years.

Table 3: Region-wise incidence rate of Vaccine Adverse Events among 100,000 vaccinated children from 2017-2020 in KSA.

Regions	2017	2018	2019	2020	Total
Eastern Region	0.46	1.89	1.68	1.85	1.46
AlAhsa Region	2.36	2.40	4.05	1.00	2.42
AlMedina AlMonawarah Region	0.23	1.28	1.01	2.34	1.24
Hafer AlBatin Region	1.24	4.22	7.36	0.39	3.21
Jeddah Region	0.30	0.19	0.16	0.00	0.17
AlTaif Region	1.96	2.60	0.28	0.25	1.41

Najran Region	1.25	0.95	0.61	0.28	0.76
Tabouk Region	0.00	2.03	8.36	0.66	2.23
Riyadh Region	0.00	0.10	0.03	0.14	0.07
Northern Borders Region	0.00	1.01	0.56	0.00	0.39
Hail Region	0.00	1.57	0.64	0.87	0.77
Asir Region	0.00	6.11	10.20	15.56	8.32
AlJouf Region	0.00	3.06	0.00	0.00	0.72
AlQunfutha Region	0.00	17.83	621.14	166.01	132.93
Makkah Region	0.00	0.00	0.14	0.00	0.04
AlQassim Region	0.00	0.00	0.15	1.12	0.39
Jazan Region	0.00	0.00	0.17	2.13	0.64
Total	0.33	1.423	5.415	2.972	2.59

Figure 5: KSA's Regional Frequency of VAE based on incidents, from 2017-2020



DISCUSSION

Vaccination is one of the safest methods for the prevention of communicable diseases and has reduced morbidity and mortality over the past few decades (Spencer, Pawlowski, & Thomas, 2017). Several reactions to vaccines have been reported that are rarely adverse in nature (Shimabukuro et al., 2015). According to a 3-year prospective vaccine safety study, Sebastian *et*

al. reports the incidence of AEFIs as 13.7% (Sebastian, Gurumurthy, Ravi, & Ramesh, 2019). Adverse events that are caused by vaccines occur before and after licensure (Alomi, Alghamdi, & Alattyh, 2019). Appropriate monitoring and recording of such events is necessary to prevent their occurrence and devise a proper action plan (Khalil et al., 2003). Various factors influence the nature and severity of the AEFIs, including age, gender, and overall health status(Cassidy et al., 2016; Klein, Marriott, & Fish, 2015). This study has evaluated the data extracted from the VAERS program related to childhood vaccines during the years 2017–2020 in KSA. We have calculated the trends in AEFIs among children receiving vaccines in KSA and the various risk factors associated with these trends.

In total, 1270 AEFIs were reported during the study period. The number of AEFIs increased from 2017 to 2019 and then reduced significantly during 2020. The current vaccination schedule in KSA is in effect from 1st January, 2013 (Ministry of Health, 2021). Therefore, no significant changes have been made in the vaccination schedule during the study period to explain the trend of AEFIs. The number of births per annum has also not increased during the study period to explain the increase in reported AEFIs("Saudi Arabia - Number of births," 2021). The trends in the number of reported AEFIs therefore do not

correlate with the trends in birth rate or changes in the vaccination schedules. Various immunization errors related to vaccine preparation, handling, storage, or administration can lead to a cluster of the same events related in terms of time and place of vaccine administration. These errors are usually preventable, and their identification and correction can help in improving the vaccination program ((WHO), 2021). Such events could have accounted for the increase in the rate of AEFIs from 2018-19. However, the significant reduction in AEFIs during 2020 suggests that the errors were addressed appropriately as a result of improvement in NIP.

Region-wise incidence rate of VAEs among 100,000 vaccinated children during the period from 2017–2020 in KSA are lower in some regions such as Makkah (0.04) and Riyadh (0.07) as compared to other's including Asir (8.32) and AlQunfutha (132.93). According to MOH statistics, all the regions across KSA are not equipped with similar health facilities (Ministry of Health, 2012). Some regions, such as Makkah, have better health resources and services as compared to others. The availability of better health facilities and appropriate training of the medical staff can significantly reduce the number of AEFIs. The differences in the availability of health facilities, number of hospitals, and

availability as well as appropriate training of the medical staff can account for the observed variation in the incidence rate of observed VAEs across KSA.

Of all age groups, children less than one year of age are the most affected by AEFIs, with a study from Brazil documenting 80% of all the reported AEFIs as observed in this age group (Freitas et al., 2007), which might be due in part to the high doses of multiple vaccines being administered to the children that age. In our data, the mean age of subjects was 8.9±12.5 months (range: 0–72). AEFIs are usually more common and more severe among male children than female children (Adherkar, Deshpande, & Ghongane, 2016; Carrasco-Garrido, Gallardo-Pino, Jiménez-García, Tapias, & de Miguel, 2004; Khazaei et al., 2016). Our data was in concordance with previously published data, and AEFIs were relatively more common among males than in females.

In our study, the Pneumococcal vaccine had the highest reported AEFIs at 138 (10.9%) incidents. A retrospective analysis conducted between 1999 and 2003 before the introduction of the Pneumococcal vaccine found that the average annual incidence of invasive pneumococcal disease in children aged ≤five years was 17.4/100,000 population with four times increased risk during the first year of life than the following four years (Memish et al., 2010). This

suggests that the adverse events of this vaccine are negligible when compared to the high risk of infection among children.

In a pediatric study, the highest number of adverse reactions were associated with DTPa + Hib and MMR vaccines(Carrasco-Garrido et al., 2004). In another prospective 3-year study, Pentavac® was implicated in the majority of the reported AEFIs followed by BCG immunization(Carrasco-Garrido et al., 2004). In our data, second-and third- highest rates of AEFIs were associated with combination vaccines DTP-Hib-HB and DTaP-IPV-HiB-HB, respectively. Crowded vaccine schedules and simultaneous administration of vaccines against multiple antigens is an important cause for the adverse events related to vaccines. So inherent risk factors associated with these vaccines combined with combinatorial administration of these vaccines are probably associated with increased AEFIs.

According to a WHO report, fever is a common minor AEFI associated with Measles/MR/MMR vaccine (5-15%), Pneumococcal conjugate vaccine (~20%), and oral polio vaccine (up to 50%) ((WHO), 2021; Control, 2013). Fever is reported to be the most frequent AEFI with an incidence of 109.7 per 1000 doses of the administered vaccine, followed by persistent crying at a rate of 2.4 per 1000 vaccine doses and diarrhea at 2 per 1000 vaccine doses (M. S. Gold et

al., 2020). High fever was associated with DTP, DTaP, Pneumococcal, Meningococcal, Polio, and MMRV vaccines in our data. The mean onset time for fever was 4.15 days. Hypotonic-Hyporesponsive Episode (HHE) has been documented as another AEFI linked with diphtheria, tetanus, *Haemophilus influenzae* type b, hepatitis B vaccines, and most commonly pertussis component vaccines (Braun et al., 1998; Cody, Baraff, Cherry, Marcy, & Manclark, 1981; DuVernoy, Braun, & Group, 2000). It is most frequently associated with primary immunization series, mainly after the first dose (Buettcher et al., 2007; DuVernoy et al., 2000; M. Gold, Kempe, & Osbourn, 1999; Goodwin, Nash, Gold, Heath, & Burgess, 1999; Greco et al., 1996; Gustafsson, Hallander, Olin, Reizenstein, & Storsaeter, 1996; Olin, Rasmussen, Gustafsson, Hallander, & Heijbel, 1997; Vermeer-de Bondt, Labadie, & Rümke, 1998). The median time for onset of HHE is 3-4 hours post-immunization but can range from immediately to 48 hours following immunization (Cody et al., 1981; DuVernoy et al., 2000; R. Gold et al., 1997; Goodwin et al., 1999). The mean onset time for HHE in our subjects was reported as 0.5 days that is slightly higher than the median range. In our study, respiratory events and other serious AEFIs were also reported to be associated with childhood vaccines.

In children, appropriate monitoring and reporting of AEFIs not only help ensure safety but also aids in clearing various misconceptions and reluctance among parents for the immunization programs. The expansion and maintenance of high immunization coverage are necessary to achieve disease prevention goals. The increased coverage results in vaccine administration in more individuals, in turn raising the probability of AEFIs. The accumulative analysis of these events can also help the NIP department to identify the most common and most serious AEFIs and the steps that can help in reducing these events. These include multiple measures, such as: the vaccine might be investigated for quality, product label and its use might be restricted partially or on a complete basis. The main goal with this is the well-being of the whole population, specifically infants, young children, and other vulnerable population groups that are primarily dependant on vaccines for protection from preventable communicable diseases.

Over the past decades, with a surge in vaccine administration, the common misconceptions surrounding EPI have also increased. These myths have led several parents to reconsider EPI, believing their child might be harmed with vaccination. A system like VAERS might help introduce greater transparency making it easier to build trust and determine myths from the

facts. Such a system can further help the policymakers and healthcare professionals to devise guidelines and awareness programs for the general public, paving the way for broader acceptance of the immunization programs and can pace the progress towards achieving the goals of wider herd immunity. The data from our study correlates with data previously reported from around the globe. This suggests that NIP can take the benefit from previously published reports on AEFIs to anticipate any adverse event and take appropriate steps for its prevention. Furthermore, the training of medical staff and improving the health services in the regions such as AlQunfutha and Asir region can also reduce the frequency of AEFIs in these regions.

CONCLUSION:

Vaccination is considered one of the safest modes for preventing communicable diseases. Childhood vaccination programs are designed and implemented across the globe and have helped in the significant reduction of childhood morbidity and mortality. However, some AEs have also been reported to occur as a consequence of childhood vaccines. MOH-KSA has designed a very effective immunization program. Active surveillance programs

can help in recording AEFIs that might go unreported otherwise. VAERS program has been designed for accurate and timely monitoring of AEFIs associated with immunization. In KSA, childhood AEFIs are more common among males as compared to females. The adverse events have been reported for almost all the childhood vaccines, fever being the most common. These AEFIs are usually mild and manageable. The serious events such as HHE and seizures might also occur and need to be addressed timely for preventing any life-long as well as life-threatening consequences. Region-wise trends show that some regions are not well-equipped for appropriate vaccine handling. Provision of better vaccine handling facilities and adequate training of the medical staff can help in reducing the incidence rate of AEFIs in these regions. Several improvements such as more specific case definitions can also help in an accurate reporting of these events that can help in designing programs that can reduce the occurrence of such events.

LIMITATIONS:

The study shows that VAERS surveillance provides an important complement to information related to NIP's benefits in the dramatic reduction of communicable diseases that have previously killed and disabled children. The

limitations of our study are those inherent to passive pharmacovigilance systems in vaccines, making them prone to a high rate of underreporting. Lack of infrastructure like internet and computers in some remote and far-flung healthcare centres, also contributes to underreporting in HESN programme. The current case definitions for AEFIs are usually non-specific and incomplete. They need to be more comprehensive and specific.

Fever, for instance, must include various categories to differentiate mild from severe forms. Further, the on going changes in the primary healthcare workforce have had a negative impact on the programme in terms of repeated reporting interruptions. These issues, if addressed, can help in the systematic training of physicians and nurses to prevent AEFIs associated with operational aspects of the program that can be easily controlled by vaccinators.

RECOMMENDATIONS:

VAERS serve as the nation's frontline post-licensure vaccine safety monitoring system. Despite limitations including reporting bias (e.g., over-or underreporting), inconsistent data quality and completeness, and generally the

inability to assess if a vaccine caused an AE, VAERS is a very useful resource for monitoring vaccine safety profiles. Several improvements can be made to enhance the efficiency of this system. Firstly, a proper case definition of an AEFI can help in more clear identification of the AE. Secondly, AEFIs related to inadvertent vaccination must be reported separately, as inadvertent vaccinations have been previously associated with increased AEFIs. Thirdly, increased reports of AEFIs from less-advanced areas in terms of medical facilities suggest increasing the number of vaccines centers and improving the staff training programs can reduce the AEFI reports. Fourthly, the report of any AEFI must be followed by an intensive investigation to ensure that the adverse event was a result of vaccination, **and that data entry must be precise with data properly annotated and not just lumped under 'other symptoms' label**. The factors that have led to any adverse event must also be identified to ensure the proper addressing of the issues to reduce any future AEFI. Together, these steps can enhance the efficiency of VAERs and reduce the number of AEFIs.

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