Original Article

Active surveillance of adverse events following immunization in primary health care

Vigilância ativa de eventos adversos pós-vacinação na atenção primária à saúde

Observación activa de eventos adversos posvacunación en la Atención Primaria de Salud

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Abstract

Objective: To describe the active surveillance of adverse events following immunization, their incidence and associated factors in a municipality of Minas Gerais, Brazil.

Methods: This is a prospective cohort conducted in Primary Health Care between 2017 and 2018. A total of 384 individuals who received vaccines were followed up, excluding those who had previous adverse events. At baseline, sociodemographic, health and vaccination history information and, in follow-up, the characteristics of adverse events and epidemiological surveillance actions were collected. The incidence rate of adverse events was estimated, and the chi-square test, poisson regression and Hosmer-Lemeshow test were performed.

Results: The incidence of adverse events was 13.36 cases/100,000 doses of vaccines (95% confidence interval: 13.34-13.38), with a higher incidence in children under 5 years of age. The most frequent adverse events were local pain, redness, hardening, followed by fever and persistent crying. Among the factors associated with the occurrence of adverse events, receiving tetanus and diffrhyphria vaccine (relative risk: 7.9; 95% confidence interval: 2.77-12.46) and intramuscular administration were considered at risk (relative risk: 6.1; 95% confidence interval: 2.55-14.63). Nursing professionals' conduct, considering the guidelines on the vaccines received, increased adverse event reporting (relative risk: 3.4; 95% confidence interval: 1.53-7.68).

Conclusion: The study allowed to know factors that favor the occurrence of adverse events. There is evidence that conducts adopted by nursing professionals in immunization rooms may avoid underreporting of adverse events following immunization.

Resumo

Objetivo: Descrever a vigilância ativa dos eventos adversos pós-vacinação, sua incidência e fatores associados, em um município de Minas Gerais, Brasil.

Métodos: Coorte prospectiva realizada na Atenção Primária à Saúde, entre 2017 e 2018. Foram acompanhados 384 indivíduos que receberam vacinas, excluindo-se aqueles que tiveram eventos adversos prévios. Na linha de base, foram coletadas informações sociodemográficas, de saúde e histórico de vacinação e, no seguimento, as características do evento adverso e das ações de vigilância epidemiológica. Estimou-se taxa de incidência de eventos adversos, e realizaram-se o teste do qui-quadrado, a regressão de Poisson e o teste de Hosmer-Lemeshow.

Resultados: A incidência de eventos adversos foi de 13,36 casos/100 mil doses de vacinas (intervalo de confiança de 95%: 13,34-13,38), com maior incidência em crianças menores de 5 anos. Os eventos adversos mais frequentes foram dor local, vermelhidão, endurecimento, seguidos de febre e choro persistente. Dentre os fatores associados à ocorrência dos eventos adversos, recebimento da vacina contra tétano e difteria (risco

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relativo: 7,9; intervalo de confiança de 95%: 2,77-12,46) e administração por meio da via intramuscular foram considerados de risco (risco relativo: 6,1; intervalo de confiança de 95%: 2,55-14,63). A conduta do profissional de enfermagem, diante das orientações sobre as vacinas recebidas, aumentou a notificação de eventos adversos (risco relativo: 3,4; intervalo de confiança de 95%: 1,53-7,68).

Conclusão: O estudo permitiu conhecer fatores que favorecem a ocorrência de eventos adversos. Há evidências de que condutas adotadas pelos profissionais de enfermagem nas salas de vacinação podem evitar subnotificações de eventos adversos pós-vacinação.

Resumen

Observación: Describir la observación activa de los eventos adversos posvacunación, su incidencia y factores asociados en un municipio del estado de Minas Gerais, Brasil.

Métodos: Cohorte prospectiva realizada en la Atención Primaria de Salud, entre 2017 y 2018. Se realizó el seguimiento de 384 individuos que recibieron vacunas, excluyendo a aquellos que tuvieron eventos adversos previos. En la línea basal, se recopiló información sociodemográfica, de salud e historial de vacunación y, en el seguimiento, las características del evento adverso y las acciones de observación epidemiológica. Se estimó un índice de incidencia de eventos adversos y se realizó la prueba χ^2 de Pearson, la regresión de Poisson y la prueba de Hosmer-Lemeshow.

Resultados: La incidencia de eventos adversos fue de 13,36 casos/100.000 dosis de vacuna (intervalo de confianza de 95 %: 13,34-13,38), con mayor incidencia en niños menores de 5 años. Los eventos adversos más frecuentes fueron dolor local, enrojecimiento, endurecimiento, seguidos de fiebre y llanto persistente. Entre los factores asociados a la ocurrencia de los eventos adversos, la aplicación de la vacuna contra el tétanos y la difteria (riesgo relativo: 7,9; intervalo de confianza de 95 %: 2,77-12,46) y la administración por medio de la vía intramuscular fueron considerados de riesgo (riesgo relativo: 6,1; intervalo de confianza de 95 %: 2,55-14,63). La conducta del profesional de enfermería ante las instrucciones sobre las vacunas recibidas aumentó la notificación de eventos adversos (riesgo relativo: 3,4; intervalo de confianza de 95 %: 1,53-7,68).

Conclusión: El estudio permitió conocer factores que favorecen a la ocurrencia de eventos adversos. Hay evidencias de que las conductas adoptadas por los profesionales de enfermería en las salas de vacunación pueden evitar subnotificaciones de eventos adversos posvacunación.

Introduction

Immunobiologicals have excellent safety records, but are not exempt from causing adverse events following immunization, even if they are submitted to a rigorous clinical trial process, in which they are thoroughly tested and studied, to ensure maximum safety and efficacy for their users.[1]

An adverse event following immunization is characterized as any undesirable and unintentional event that an individual may develop when receiving a dose of some immunobiological.[2] Its occurrence may be related to the process of production and storage of these products, the physical and biological characteristics of vaccinated individuals and the process of administration of these immunobiologicals.[3,4] Adverse events following immunization are classified into two distinct types: severe adverse event and non-severe adverse event. They differ in their intensities and severities, in addition to the type of demand for clinical treatment.[3,5,6]

The occurrence of an adverse event following immunization can trigger rumors in the community, compromising the reliability of the Brazilian National Immunization Program (PNI - *Programa Nacional de Imunização*), with harmful consequences to public health, such as the reduction of vaccination coverage and the resurgence of immunopreventable diseases.[1] Thus, surveillance and monitoring of these adverse events or any other vaccination-related problems are essential so that the risks do not exceed the benefits achieved by PNI.[2] Most countries have surveillance systems, in which reporting of the occurrence of an adverse event following immunization can be performed spontaneously and actively by any individual, whether health professional or not.[4,5,7] In Brazil, reportings are made passively by health professionals when individuals, who received some immunobiological, had some adverse post-vaccination event in health services,[8] leading to underreporting.

Most studies are developed based on secondary data from the Brazilian Adverse Events Following Immunization Information System (SI-AEFI - *Sistema de Informação dos Eventos Adversos Pós-Vacinação*). However, the problems in filling out the reporting forms, especially with regard to the completeness of the fields, can interfere with information quality and, consequently, the actual situation of event occurrence.[9-11]

The proposal of this study advances knowledge by proposing to perform active surveillance of adverse events following immunization, with a direct search for data, allowing greater knowledge of these events in the community. This type of surveillance allows observing, knowing and identifying

an adverse event following immunization, planning health actions and improving communication between health professionals and users, enabling individuals to increase confidence in the immunobiologicals available in PNI.[12]

In Brazil, the nursing team occupies a prominent position regarding vaccination activities. Nursing is responsible for all stages of the vaccination process at the local health level, represented by immunization rooms, since users' reception; conservation and administration of immunobiological agents; management of the Information System of the Brazilian National Immunization Program (SI-PNI), in addition to surveillance of adverse events.

The present study aimed to describe the active surveillance of adverse events following immunization, their incidence and associated factors in a municipality of Minas Gerais, Brazil. Most studies conducted in Brazil are based on the database provided by SI-AEFI;[11] epidemiological cohort studies are essential to supplement such information in order to identify the incidence and factors associated with adverse events following immunization, contributing to safety in immunization rooms and, consequently, the maintainance of the reliability of PNI.

Methods

This is an observational epidemiological study of a prospective cohort, conducted in Primary Health Care (PHC) of a municipality of Minas Gerais, in southeast region of Brazil.

The research setting was composed of all 43 PHC units of the municipality, distributed in ten sanitary regions. For this study, these regions were grouped considering the population and territorial proximity, resulting in six sanitary regions. Subsequently, six PHC units were selected by a simple cluster sample, stratified by the six sanitary regions. The units were selected considering their strategic location because they presented a large flow of care, which eventually favored the opportunity to find individuals available for the study. Individuals were arranged proportionally to the size of each sanitary region.

The cohort sample was calculated considering the population registered and assisted in the municipal public health system (n=187,030). We used the estimated proportion of 50% for a given characteristic, a value that provides the largest sample size for finite population, setting the significance level at 5% and the sampling error at 5%. The estimated sample for the composition of the cohort was 384 individuals.

The study included individuals who attended PHC units to receive some type of vaccine offered by the Brazilian PNI and had a telephone to help them follow up. The participation of public-target individuals of vaccination schedules contemplated in the Brazilian PNI was guaranteed. Individuals of any age who attended to receive special vaccines due to an adverse event prior to vaccination were excluded.

Data collection was performed between September 2009 and June 2010. The field research was prolonged due to the sample size, logistics and refusals (n=189) by the population to participate in the research. During this stage, six previously trained researchers collected the data at baseline, working on a relay scale in the selected units, for a period of 4 to 5 hours per day. Collection was performed in one health unit at a time. Telephone survey was conducted only by the main researcher.

A semi-structured questionnaire was used, adapted from the form of reporting/investigation of adverse events following immunization, standardized by the National Epidemiological Surveillance System.[2] The questionnaire consisted of a set of items related to: sociodemographic identification, health information and vaccination history, information on vaccines and adverse events following immunization, and guidance on vaccination.

At baseline, individuals who attended PHC units for vaccination and agreed to participate in the study were interviewed individually. The interview was conducted in a private room, in the Basic Health Unit itself, after vaccine administration, and lasted an average of 15 minutes. After the interview, participants were instructed regarding follow-up follow-up, to be performed by telephone contact after 72 hours of vaccination. Telephone interven-

tion is a contemporary, affordable and low-cost strategy for individual monitoring, which can increase bonding and access to health services.[13] The decision for the 72-hour follow-up period was due to the higher prevalence of adverse events following immunization in this period.[2]

In the follow-up, individuals were again interviewed regarding the presence or not of adverse events following immunization and, upon reporting the event, guidance was made regarding an event care and reporting. For individuals who were not found in the 72 hours of follow-up, new telephone contacts were made in an attempt to reduce sample loss. During the follow-up period, the search was also carried out in the municipal SI-AEFI, in order to identify the events reported and confirmed in the selected PHC units.

The outcome variable was the presence of adverse events following immunization with onset of symptoms up to 72 hours. The criteria for defining adverse events following immunization were: reports of local manifestations (pain, redness, hardening and edema) and systemic manifestations (thermometric fever, persistent crying, headache, vomiting, diarrhea, hypotonic-hyporesponsive episodes. For the hypotonic-hyporesponsive episodes, symptoms that identified hypotonia, hyporesponsiveness and cyosis were taken into consideration in individuals' report. For persistent crying, we considered the report of prolonged and inconsolable crying for more than 6 hours.[2] The vaccine composed of calmette-guérin bacillus (BCG), as it normally presents an adverse event after 72 hours, was excluded from the study.

The exposure variables were: sociodemographic identification (gender, age, date of birth, address and telephone contact); information on health and vaccination history (pre-existing diseases, known allergies, medications in use, clinical symptoms at the time of vaccination and presence of an adverse event following immunization in previous doses); current vaccination (date of vaccination, PHC unit, professional category of administrator and amount of vaccines administered); characteristics of the adverse event following immunization and epidemiological surveillance actions (date of identification and type of event, need for referral to other health services, health professionals' conduct, hospitalization, presence of systemic manifestations and receipt of information about vaccination guidelines and adverse events following immunization).

Stata software (version 14.0) was used for data analysis and processing. The distribution of relative frequencies for categorical and median variables for the variable age was calculated. The incidence of an adverse event following immunization was estimated considering the cases of events as numerator and the number of doses of vaccines applied during the study period in the denominator.[2] The municipal SI-PNI was used to survey the doses of vaccines applied during the study period.

Pearson's chi-square test was used for bivariate analysis. The explanatory variables, which obtained p-value less than 20% ($p<0.20$), were inserted by the backward method in the multivariate poisson regression model of robust variance, to verify the factors associated with adverse events following immunization. Those with the least meaning (higher value of p) were removed one by one from the model. The procedure was repeated until all variables present in the model presented statistical significance, with $p<0.05$. It is noteworthy that the multivariate model was controlled by the effect of individuals' age, categorized as: less than 1 year; 1 to 4 years; 5 to 19 years and 20 years or more. In this analysis, adults and the elderly were grouped into a single category due to the low occurrence of an adverse event following immunization observed in these age groups. The Hosmer-Lemeshow test was used to verify the adjustment of the final model. Relative risk (RR), with a 95% confidence interval (95% CI), was used as a measure of effect. For all analyses, a significance level of 5% was adopted.

The study was approved by an Institutional Review Board, under opinion 2,206,213.

Results

Of the total number of vaccinated individuals interviewed (n=384), more than half were female and white, aged between zero and 83 years, with

a median of 28.5 years. Regarding the age group, 32.3% were children under 5 years of age. In the sample, 2.6% of pregnant women were identified, but none of them presented an adverse event following immunization.

Regarding the history of information and health, more than half stated that they did not have any type of comorbidity. Among the self-reported comorbidities, the most cited were: heart diseases (18.5%) and diabetes (6.8%); consequently, the use of antihypertensivedrugs (14.3%) and antidiabetic (4.7%) were the most cited. Moreover, 2.9% of individuals reported having had at least one convulsive episode, 8.4% reported drug allergy and 1.8% lactose allergy.

Most vaccines were applied by nursing technicians (97.4%). Among those vaccinated, 78.1% reported that no vaccination screening was performed; more than half did not receive guidance about the vaccine administered, were not informed about the possibility of adverse events and did not receive guidance on the conduct if such an event occurred.

Among the individuals, 62.2% received only one vaccine, while the others ranged from two to three or more. The most used route of administration was intramuscular.

In the follow-up, there was a sample loss of 7.5% (n=29, due to the impossibility of contact with the vaccinated individual, according to the number or telephone address reported. Among the 355 vaccinated individuals followed, 35.8% (n=127) self-reported the presence of some type of adverse event following immunization.

Table 1 presents the clinical and epidemiological characteristics of vaccinated individuals who reported the presence of an adverse event following immunization (n=127). Local events were the most reported and included pain, hardening and redness at the vaccine administration site. Regarding systemic events, vaccinated individuals reported the presence of ≥37.5°C fever, headache and persistent crying. Other symptoms, such as diarrhea, hypotonic-hyporesponsive episode, nausea and vomiting, were also reported. It is emphasized that, in an analysis, more than one symptom was identified per vaccinated individual. Regarding the time of onset of an adverse event, 20.5% occurred less than 1 hour after vaccine administration; 40.2% in more than 1 hour, and 39.3% in more than 12 hours, not exceeding the follow-up time of 72 hours. Of the 127 vaccinated individuals who reported the presence of an adverse event following immunization, 26.0% sought health services, including immunization rooms in PHC units and hospitals. Only 17.3% were reported and investigated and, of these, 4.7% were hospitalized. Most of the reported adverse events following immunization were classified as non-severe (81.9%).

Table 1. Clinical and epidemiological characteristics of vaccinated individuals who reported presence of adverse events following immunization

Clinical and epidemiological variables	n(%)
Type of reported reactions	
Local events	71(55.9)
Simultaneous local and systemic events	39(30.7)
Systemic events	17(13.4)
Abdominal distension	
Local pain and redness	120(31.2)
Edema and hardening	36(9.3)
Systemic reactions	
Fever ≥37.5ºC	23(6.0)
Headache, nausea, and diarrhea	17(4.3)
Persistent crying and HHE	8(2.1)
Time of onset of symptoms	
1-12 hours	51(40.2)
12-72 hours	50(39.3)
15 minutes to 1 hour	18(14.2)
<15 minutes	8(6.3)
None	89(70.1)
PHC units immunization room	20(15.8)
Hospital	7(5.5)
Private physician's office	6(4.7)
Up to 72 hours of hospitalization	
No	121(95.3)
Yes	6(4.7)
AEFI reported and investigated	
No	105(82.6)
Yes	22(17.3)
AEFI classification confirmed	
AEFI not serious	18(81.9)
Severe AEFI	4(18.1)

HHE - Hypotonic-Hyporesponsive Episodes; AEFI - Adverse event following immunization; PHC - Primary Health Care.

In a search for SI-AEFI during the study period, eight vaccination errors were identified reported by the PHC units participating in the study. However, these errors did not cause adverse events and were also not part of the study. In addition, six adverse

events following immunization related to bcg vaccine were identified, but did not enter the study analysis because they started after 72 hours.

To calculate the incidence, only the cases of confirmed Adverse events following immunization (n=22) were analyzed, considering 164,640 doses of vaccines applied in the studied period, in the selected regions. The incidence was 13.36 cases/100,000 doses of applied vaccines (95%CI 13.34-13.38). The highest incidence was in children under 5 years of age (45.6%), and the most frequent events were pain, redness and hardening, followed by fever, edema, hypotonic-hyporesponsive episode, diarrhea and persistent crying.

In a bivariate analysis, the incidence of adverse events following immunization was higher among vaccinated individuals who received guidance on vaccines and those caused by them and on the conduct to be taken in the presence of these events. Intramuscular and oral administration routes were also associated with the presence of adverse events following immunization (Table 2).

Regarding the percentage distribution of adverse events following immunization, according to the vaccines received at the time of data collection, it was identified that hepatitis B and influenza vaccines were associated with a higher risk of adverse events (Table 3).

In a multivariate analysis, when adjusted for age, it was observed that the receipt of guidance on the vaccines administered increased 3.4 times the reporting of adverse events following immunization. The vaccine administered intramuscularly increased the risk of adverse events by up to 6.1 times. As for the vaccines received, the diffrhyphtheria and tetanus vaccine increased the risk of having an adverse event following immunization by up to 7.9 times, while the hepatitis B vaccine reduced this risk. The other variables did not present statistical significance, being excluded from the adjusted model, because they presented a value of p> 0.05 (Table 4).

Table 2. Confirmed Adverse events following immunization, according to sociodemographic characteristics and health history of vaccinated individuals, activities performed in immunization services and applied vaccines

Variables	Total n(%)	AEFI (%)		P value
		Yes	No	
Sex				
Female	209(54.4)	6.7	93.3	
Male	175(45.6)	4.5	95.5	0.372
Age group, years				
≥20	242(57.0)	5.0	95.0	
1-4	54(19.8)	6.6	93.4	0.915
<1	48(12.5)	6.3	93.7	
5-19	40(10.7)	7.3	92.7	
Ethnicity				
White	202(52.6)	6.4	93.6	0.530
Non-white	182(47.4)	4.9	95.1	
Pregnant women				
No	374(97.4)	5.8	94.2	
Yes	10(2.6)	-	100.0	0.430
Childlike				
No	323(84.1)	5.2	94.8	
Yes	61(15.9)	8.2	91.8	0.366
Guidance on the vaccine				
No	236(61.5)	3.4	96.6	
Yes	148(38.5)	9.4	90.6	0.013
Specific information about AEFI				
No	228(59.4)	3.5	96.5	
Yes	156(40.6)	9.0	91.0	0.024
Conduct in case of AEFI				
No	267(69.5)	3.7	96.3	
Yes	117(30.5)	10.6	89.8	0.012
Number of vaccines received				
One	239(62.2)	6.3	93.7	
Three or more	74(19.3)	4.0	96.0	
Two	71(18.5)	5.6	94.4	0.772
Intramuscular injection				
No	337(87.8)	4.4	95.6	0.004
Yes	47(12.2)	14.9	85.1	
Subcutaneous route				
Yes	290(75.5)	9.5	90.5	
No	94(24.5)	4.5	95.5	0.065
Oral route				
Yes	347(90.4)	16.2	83.8	
No	37(9.6)	4.6	95.4	0.004

*Pearson's chi-square test; AEFI - Adverse event following immunization.

Discussion

Although passive surveillance can maintain and feed an information system and is a low-cost service, it has the disadvantage of underreporting adverse events following immunization[9,12,14] and reducing sensitivity to identifynew cases, signs or even new types of adverse events.[15]

An observational study conducted in the Puglia region of Italy showed that health services that perform search and active surveillance of adverse events following immunization considerably increase the number of these reportings.[16] This proves the results evidenced in this study in relation to adverse

Table 3. Adverse events following immunization, according to the vaccines received

Vaccines	Total (%)	AEFI (%)		P value*
		Yes	No	
Hepatitis B				
No	71.4	7.3	92.7	
Yes	28.6	1.8	98.2	0.037
dT				
No	76.3	4.8	95.2	
Yes	23.7	8.8	91.2	0.150
Penta				
No	93.2	5.8	94.2	
Yes	6.8	3.8	96.2	0.669
FLU3V				
No	70.3	7.4	92.6	
Yes	29.7	1.8	98.2	0.029
SCR				
No	88.5	5.0	95.0	
Yes	11.5	11.4	88.6	0.087
Yellow fever				
No	89.3	5.5	84.5	
Yes	10.7	7.3	92.7	0.643
VIP				
No	91.9	5.9	94.1	
Yes	8.1	3.2	96.8	0.532
Pneumo 10				
No	91.1	6	94	
Yes	8.9	2.9	97.1	0.464
Meningo C				
No	91.9	6.3	93.7	
Yes	8.1	-	100	0.152
DTP				
No	95.8	5.4	94.6	
Yes	4.2	12.5	87.5	0.234
Varc				
No	95.6	5.7	94.3	
Yes	4.4	5.9	94.1	0.978
HPV				
No	96.6	5.6	94.4	
Yes	3.4	7.7	92.3	0.757
VOP				
No	96.1	5.4	95.6	
Yes	3.9	13.3	86.7	0.196
ROTA				
No	94.8	5.2	94.8	
Yes	5.2	15	85	0.067
Hepatitis A				
No	98.7	5.4	94.6	
Yes	1.3	20	80	0.167
SCRV				
No	99.5	5.8	842	
Yes	0.5	-	100	0.727
dTpa				
No	98.4	5.8	94.2	
Yes	1.6	-	100	0.543

*Pearson's chi-square test. AEFI - Adverse event following immunization; dT - Diffrhyphthesis and tetanus vaccine (formulation for adults/adolescents); Penta - pentavalent vaccine (diffrhyphtheria + tetanus + pertussis + Haemophilus influenzae type B + hepatitis B); FLU3V - Inactivated and fragmented trivalent influenza vaccine; SCR - Measles vaccine + mumps + rubella; VIP - Inactivated Polio vaccine; Pneumo 10 - Pneumococcal vaccine 10-valent; meningo C - meningococcal type C vaccine; DTP - Diphtheria Vaccine + Tetanus + Pertussis adsorbed; Varc - Varicella vaccine; HPV: Quadrivalent human papillomavirus (HPV) [types 6, 11, 16, 18] recombinant vaccine; VOP - Inactivated poliovirus vaccine; ROTA - Human rotavirus vaccine G1P1[8]; SCRV- Measles vaccine + mumps + rubella + chickenpox; dTpa - Diphtheria vaccine + tetanus + pertussis

Table 4. Poisson's final regression model for factors associated with Adverse events following immunization

Variables	RR	95%CI	p-value†
Guidance on vaccines			
Yes	3.4	1.53-7.68	0.003
No	1	-	
Intramuscular injection			
Yes	6.1	2.55-14.63	<0.001
No	1	-	
Hepatitis B vaccine			
Yes	0.1	0.03-0.85	0.031
No	1	-	
dT vaccine			
Yes	7.9	2.77-22.46	<0.001
No	1	-	

*Model fit: quality fit = 1.00; †poisson multivariate regression (age-adjusted model). RR - relative risk; 95% CI - 95% confidence interval; dT - diffrhyphthesis and tetanus vaccine

events reported by individuals and those reported in PHC units. Even in the occurrence of adverse events following immunization, most vaccinated individuals did not return to the immunization rooms of PHC units for due reporting.

The results of this study demonstrate the incidence of adverse events following immunization consistent with that described in literature,[5,6,9] in which children under 5 years of age were more likely to develop this type of event. The high incidence may be associated with immaturity of the immune system and the high number of vaccines administered in this age group.[17-20]

Among the local and systemic events identified, pain and fever were the most common. Most Adverse events following immunization, local and systemic, are mild and self-limiting[8,9,17,21] and represent the area of activity of the nursing team, since, in brazilian public PHC units, it is the main responsible for vaccination activities.[14] The fact that local reactions are few and intense, in addition to being expected by the vaccinated individual, end up not being reported to PHC units.[5,8]

In this respect, it is important to emphasize the role of the nursing team in the surveillance of adverse events following immunization. The findings of this study identified that the fact that professionals provide guidance on vaccination increases the voluntary reporting of this type of event and, consequently, its incidence. However, more than half of vaccinated individuals reported that they

had not received basic information about the vaccines administered, what diseases they were preventing, and that possible adverse events could be caused by them. Health professionals with knowledge are able to inform individuals about the importance and benefits of vaccination and about the possible risks and occurrence of adverse events following immunization.[16,20] The provision of this information to the population, called vaccination screening, is recommended as a basic activity to be performed in immunization rooms. [10] Vaccination screening is a specific measure to avoid risks in vaccination, because, in addition to allowing monitoring individuals' vaccination status and health hisms, this is when health professionals have the opportunity to conduct advice on vaccines and their possible AEFI. [14]

When there is no clarification on the benefits of vaccination and possible adverse events following immunization, the population tends to withdraw from health services, compromising the next doses, both for fear of other reactions and for insecurity in the vaccine professional,[9] increasing the risk of acquiring immunopreventable diseases. With this, such diseases, which have already been controlled, can resurface.[8] Studies emphasize that adequate vaccination screening and health training and education are specific measures to increase the reporting of adverse events following immunization and ensure the quality and safety of vaccination. [17] In addition, knowledge about vaccines and their possible adverse events considerably increases the population's confidence in vaccination, since users feel welcome in immunization rooms, and this allows them to resolve existing doubts.

Diffrhyphthes and tetanus vaccine has been associated with an increased risk of causing an adverse event. This vaccine aggregates tetanus toxoids and diffrhyphtheria, as well as aluminum hydroxide and thurosal, considered one of the main responsible for causing local reactions. [22] The lack of knowledge of vaccine history in adults, due to the lack of evidence of vaccine administration, favors the development of adverse events following immunization due to revaccination in a shorter period than the recommended.[6,17]

Another finding refers to the lower reatogenicity of hepatitis B vaccine. [11,23] It is important to highlight that vaccines administered during this study, in general, had the same manufacturing origin, being largely produced in Brazilian laboratories, which demonstrates the quality of immunobiologicals produced nationally.

There was no significant association between the number of vaccines received and the presence of adverse events following immunization. A systematic review study indicated the absence of adverse events following immunization in the presence of administration of three or more doses of vaccines.[24] On the other hand, the intramuscular route of administration was associated with the presence of this type of event. This is due to the fact that most vaccines, because they are inactivated, require adjuvants, usually derived from aluminum, which increases the risk of local reactions. [15]

In this regard, health professionals need to have theoretical and practical knowledge for the administration of vaccines intramuscularly, so as not to incur errors that may generate adverse events following immunization and dissatisfaction of vaccinated individuals.[14,25] Certain precautions should be taken when administering a vaccine intramuscularly, considering the body composition of vaccinated individual, the size of the needle and the volume to be administered. [2]

The methodological quality of this study provided evidence-based data to estimate the incidence and risk of adverse events following immunization among vaccinated individuals. The cohort study provides better association estimates and allows for an accurate chronology between exposures and the event. However, it should be considered that the existence of a causal link between the event and possible exposure factors is complex and presupposes careful analysis of data quality and consistency. Cohort studies on Adverse events following immunization after vaccine licensing are still scarce, with most based on records of immunization information systems.[8,9]

With the results of this study, the importance of nursing professionals' conduct in the guidance in the immunization room is advanced in the

knowledge, to increase the reporting and investigation of adverse events following immunization and, consequently, the strengthening of their active surveillance.

As a limitation of this study, the inclusion of all age groups in the identification of adverse events following immunization made it difficult to compare the results with the scientific literature, since much of the research on this subject is carried out in children. Another limiting factor is the short follow-up period after vaccination (72 hours), which may have contributed to the non-observation of other possible events that occurred in the upper period of hours compared to that established for this cohort.

Conclusion

The study reinforces the importance of active surveillance of adverse events following immunization in Brazil and points to deficiencies in passive surveillance in the immunization rooms of PHC units, since it does not portray all cases of such events that occurred. The results evidenced contribute to highlight the underreporting of adverse events following immunization and the importance of nursing professionals' conduct in relation to vaccination guidelines. These findings may support the implementation of good practices in the immunization rooms of PHC units and be useful for future epidemiological studies related to immunization errors identified but not explored in this study.

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Collaborations

Batista ECC, Ferreira AP, Oliveira VC, Amaral GG, Jesus RF, Quintino ND, Viegas SMF and Guimarães EAA contributed to study conception, data analysis and interpretation, writing of the article, critical review of relevant intellectual content and approval of the final version to be published.

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