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SHORT PAPER

Adverse events following immunization and vaccine perception in nursing students

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Parole chiave: Vaccini, vaccinazione, studenti universitari, Sicilia, percezione vaccinazioni, studenti infermieristica

Abstract

Introduction. *Vaccines are one of the most successful and cost-effective public health interventions of modern times. This cross-sectional study investigated the perception of vaccinations and potential risks of adverse events following immunization among nursing students.*

Materials and Methods. *An anonymous, self-administered questionnaire was distributed to students undertaking a nursing degree course at the University of Palermo. This questionnaire consisted of three sections: the first part focused on socio-demographic information; the second part contained one question regarding the terms associated with vaccination; and the third part posed a question regarding adverse reactions after immunization. A multivariable logistic regression model was used and adjusted Odds Ratios will be presented in this paper.*

Results. *The sample consisted of 403 students and the mean age was 22.0 years (±3.0). Having considered the dependent variable "Have you ever had adverse reactions after being vaccinated? Moderate-severe", the statistically-significant independent variables were: the second (adjusted Odds Ratios 0.32) and third (adjusted Odds Ratios 0.18) years of study, the nursing students perceiving their economic and health status to be low (adjusted Odds Ratios 3.52 and 15.92 respectively). The following items from questionnaire were found to be associated with the term vaccination: "I associate the term vaccination with fear" (adjusted Odds Ratios 4.98) and "I do not associate the term vaccination with fighting illnesses" (adjusted Odds Ratios 10.02).*

Conclusions. *Although vaccines are generally safe if used correctly, no vaccination is completely risk-free. There was a general awareness of adverse events following immunization among nursing students in this study. The future healthcare workers have been identified as the most important information source regarding potential solutions in a rapidly evolving health scenario in fighting vaccine hesitancy.*

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Introduction

Vaccines are one of the most successful and cost-effective public health interventions in modern times. However, no vaccine is completely free of adverse effects or risk of complications, and vaccines are often associated with local reactions (1). Vaccination programs have contributed to the decline in morbidity and mortality of many infectious diseases. Vaccination programs rely on a high uptake level to be successful in reducing the prevalence and incidence of vaccine-preventable diseases (VPD). In addition to direct protection for individuals, high vaccination coverage rates induce indirect protection for the overall community by decreasing the risk of infection among those who remain susceptible. In addition to screening programs, primary prevention is essential in continuing a reduction in VPD. A recent study conducted among a large cohort of university students in Italy identified university students as a possible target for HPV vaccination. It also defined specific areas, such as the health-care professionals, who could be initially targeted in order to encourage primary prevention and vaccine uptake (2). Despite the availability of safe and effective vaccines in preventing diseases, a significant proportion of the eligible population remains unvaccinated. Vaccine hesitancy and refusal have become an emerging public health challenge: many European countries are facing increasing difficulties in achieving and maintaining target vaccination rates due to low health literacy and a fear of adverse events following immunization (AEFIs). AEFIs are defined as any *untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the use of the vaccine* (3). AEFIs include pain, swelling, and erythema at the injection site. Systemic reactions, including fever, irritability, drowsiness, and a rash, may also occur. As a result, pharmacovigilance is the practice of detecting, assessing, understanding, responding and preventing adverse drug reactions, including reactions to vaccines. Reports of suspected AEFIs represent an important source of information for the Italian Drug Agency (Agenzia Italiana del Farmaco or AIFA), as they facilitate the detection of potential warning signs relating to the use of medicines in order to enhance their safety (4). It is, therefore, necessary to have tools available to ensure the appropriate investigation and communication after serious incidences of AEFIs. Indeed, pharmacovigilance is now an integral part of the regulation of drug and vaccine safety, and surveillance systems exist to monitor and supply prompt and effective response actions. The aim of the present cross-sectional study is to investigate the perception of vaccinations and of potential risks of adverse events following immunization in nursing students of the University of Palermo.

Materials and Methods

This cross-sectional study was approved by the Ethical Committee of the University Hospital "Paolo Giaccone" of Palermo, Minutes No. 07/2019 (No. 25) of 17 July 2019. An anonymous, self-administered questionnaire was distributed to the 409 students attending the 3-year nursing degree course at the University of Palermo, who were requested to fill it after having signed an informed consent form. The questionnaire had been prepared by the authors of this paper and consisted of three sections. The first section focused on obtaining socio-demographic information. The second part contained 8 possible answers to the question: "What term do you associate with vaccination?" (needles/syringes, uselessness, solidarity, fear, pharmaceutical business, fighting illnesses, protection and prevention), and students could indicate

their answers by ticking "Yes" or "No". The third part of the questionnaire contained the following question: "Have you ever had adverse reactions after having been vaccinated?" and the students could choose from the following responses: a) none; b) mild (localized skin reaction, low-grade fever, headache, tiredness); c) moderate (soreness arm, fever > 38.5° C, seizures caused by fever, temporary low platelet count); d) severe (difficulty in breathing, anaphylactic shock). The responses were subsequently aggregated and dichotomised into "none-mild" and "moderate-severe" categories.

The statistical significance level chosen for the entire analysis was 0.05 and absolute and relative frequencies were calculated for all the qualitative variables. Categorical variables were summarized as proportions and analyzed by Fisher's exact test. A multivariate logistic regression model was used. The results have been expressed as adjusted Odds Ratio (aOR) with 95% Confidence Intervals (CI). Each independent variable was adjusted for all the other independent variables. The data were analysed using the 14STATA statistical software version (5).

Results

Compliance in filling the questionnaire was 100% for the 1st and 3rd year, and 95.8% for the 2nd year students. Table 1 shows the descriptive characteristics of the sample. The 403 students (65.0% female and 100.0% born in Italy) were 22.0 years (±3.0) old. 38.0% reported attending the first year of study and 45.9% were in-site students. 17.1% reported a low economic status whilst 95.0% were enjoying a medium-high health status.

Statistically-significant differences were observed for *adverse reactions* following bivariate analysis, as reported

Table 1 - Sample description

		N (%)
Sex	Female	262(65.0)
	Male	141(35.0)
Country of birth	Italy	403(100.0)
	Other	0 (0.0)
Are you an off site, in-site or commuter student?	off site	112 (27.8)
	commuter	106 (26.3)
	on site	185 (45.9)
Year of study	First	153 (38.0)
	Second	115 (28.5)
	Third	135 (33.5)
Perceived economic status	Medium-high	334 (82.9)
	Low	69 (17.1)
Perceived health status	Medium-high	283 (95.0)
	Low	20 (5.0)
Have you ever had adverse reactions after being vaccinated?	None	290 (71.9)
	Mild	68 (16.9)
	Moderate	43 (10.7)
	Severe	2 (0.5)
Age	Mean (standard deviation)	22.0 (± 3.0)

Table 2 - Bivariate associations between reported adverse reactions and the questionnaire variables (Fisher's exact test deployed)

Variables		Have you ever had adverse reactions after being vaccinated?		
		none-mild (%)	moderate-severe (%)	p-value
Sex	Female	242 (92.4)	20 (7.6)	0.003
	Male	116 (82.3)	25 (17.7)	
Are you an off site, in-site or commuter student?	Off site	102 (91.1)	10 (8.9)	0.422
	Commuter student	96 (90.6)	10 (9.4)	
	On site	160 (86.5)	25 (13.5)	
Year of study	First	133 (86.9)	20 (13.1)	0.015
	Second	97 (84.4)	18 (15.6)	
	Third	128 (94.8)	7 (5.2)	
Perceived economic status	Medium-high	313 (93.7)	21 (6.3)	<0.001
	Low	45 (65.2)	24 (34.8)	
Perceived health status	Medium-high	354 (92.4)	29 (7.6)	<0.001
	Low	4 (20.0)	16 (80.0)	
What term do you associate with "vaccination"?				
	No	50 (94.3)	3 (5.7)	0.241
	Yes	308 (88.0)	42 (12.0)	
	No	351 (90.5)	37 (9.5)	<0.001
	Yes	7 (46.7)	8 (53.3)	
	No	119 (85.6)	20 (14.4)	0.138
	Yes	239 (90.5)	25 (9.5)	
	No	289 (94.4)	17 (5.6)	<0.001
	Yes	69 (71.1)	28 (28.9)	
	No	242 (92.7)	19 (7.3)	0.001
	Yes	116 (81.7)	26 (18.3)	
	No	4 (30.8)	9 (69.2)	<0.001
	Yes	354 (90.8)	36 (9.2)	
	No	3 (23.1)	10 (76.9)	<0.001
	Yes	355 (91.0)	35 (9.0)	
	No	2 (25.0)	6 (75.0)	<0.001
	Yes	356 (90.1)	39 (9.9)	

for the variables: "gender", "year of study", "perceived economic status", "perceived health status", and the question "What term do you associate with "vaccination"? for the terms "uselessness", "fear", "pharmaceutical business", "fighting illnesses", "protection", "prevention" (see Table 2). Table 3 shows the aOR where each independent variable has been adjusted for all other independent variables. Considering the dependent variable: "Have you ever had adverse reactions after being vaccinated? Moderate-severe", the statistically-significant independent, associated variables were: "second" (aOR 0.32, 95% CI 0.11-0.91) and "third" (aOR 0.18, 95% CI 0.06-0.55,) year of study, "low perceived economic status" (aOR 3.52, 95% CI 1.33-9.28) and "low perceived health status"(aOR 15.92, 95% CI 3.17-79.98), "I associate the term vaccination to fear" (aOR 4.98, 95% CI 2.01-12.34) and "I do not associate the

Table 3 - Multivariate logistic regression based on 403 observations (Adjusted Odds Ratio are presented and each independent variable has been adjusted for all other independent variable)

		Have you ever had adverse reactions after being vaccinated? Moderate-severe		
Independent variables		aOR	95% CI	p-value
Sex	Female	1		
	Male	1.09	0.44-2.72	0.853
Age	Unit increase	1.10	0.99-1.24	0.087
Are you an off site, in-site or commuter student?	Off site	1		
	Commuter student	1.50	0.48-4.71	0.488
	On site	0.97	0.32-3.04	0.965
Year of study	First	1		
	Second	0.32	0.11-0.91	0.033
	Third	0.18	0.06-0.55	0.003
Perceived economic status	Medium-high	1		
	Low	3.52	1.33-9.28	0.011
Perceived health status	Medium-high	1		
	Low	15.92	3.17-79.98	0.001
What term do you associate with “vaccination”?				
	No	1		
	Yes	1.09	0.27-4.38	0.905
	No	1		
	Yes	2.58	0.40-16.85	0.321
	No	1		
	Yes	1.04	0.43-2.50	0.930
	No	1		
	Yes	4.98	2.01-12.34	0.001
	No	1		
	Yes	1.01	0.41-2.43	0.994
	No	10.02	1.04-96.76	0.046
	Yes	1		
	No	1		
	Yes	0.48	0.03-6.99	0.590
	No	1		
	Yes	1.67	0.03-82.43	0.796

term vaccination to fighting illnesses” (aOR 10.02, 95% CI 1.04-96.76).

Discussion and Conclusion

Many vaccines can be considered safe and effective if used correctly but no vaccine is completely risk-free, and adverse events will occasionally result after an immunization (6). In Italy formal recommendations regarding immunization are published by the Ministry of Health through the National Immunization Prevention Plan (6). This is a document concerning immunization policies, which lists all the vaccines offered free of charge to the general population and

to high-risk individuals, and their possible adverse events. The study outlined in this paper had a response rate of almost 100.0%, which underlines the importance given by nursing students of the University of Palermo regarding vaccination safety issues; 11.2% of the nursing students participating in this study reported that they had had moderate or severe AEFIs. As demonstrated in Table 2, those who answered reporting *a moderate or severe adverse event after immunization,* associated the term *vaccination* with "uselessness" (53.3%), "fear" (28.9%) and "pharmaceutical business" (18.3%). They did not consider vaccinations as a means of "fighting illnesses" (69.2%), "protection" (76.9%) and "prevention" (75.0%).

Similarly, as shown by a research group led by the authors of this paper in a 2016 study conducted on the general student population, a *moderate-to-severe* adverse reaction can negatively affect students' opinion on vaccines (7). However, due to the different target population studied, some important differences emerge. The general population of university students associates negative terms with "vaccination" as "needles / syringes" in contrast to nursing students who associate the term "fighting illnesses" in consideration of their study programme in the field of health. While science has almost invariably insisted that vaccines are safe and effective, many continue to express doubts and fears, and have often resisted the scientific perspective; therefore, effective risk communications strategies are critical to ensure confidence in immunization (8), especially given the absence of alarming safety data regarding reported AEFIs during recent years.

This study has its limitations. As a cross-sectional study, several independent variables could not be evaluated for cause and effect associations. Moreover, the use of a questionnaire aimed at students of a single University campus does not permit the generalisation of results in comparison with other universities in the Sicilian region or throughout Italy, despite the large sample size. Other limitations of the study may well include: the "recall bias", when students are asked to remember vaccinations which were administered at some point in the distant past; the "social desirability bias", when study participants may have incorrectly indicated having received certain vaccines to appear more health conscious; some reported confidence intervals were very wide and the aOR may not, therefore, be reliable. Other studies have confirmed that European Union healthcare providers have been identified as the most important and trusted source of information as to how to protect one's self from vaccine-preventable diseases (9). Much research has demonstrated that rigorously-designed, behaviour-based health communication activities can have a significant positive impact on health-related attitudes, beliefs and behaviours (9). Considering that the study sample in this research included university students, many of whom may well be the healthcare workers of the future, the authors of this paper consider it necessary to create a more efficient communication protocol, which underlines the ascertainable risks of vaccines and their verifiable benefits. By means of the continued reporting of adverse events after vaccination by public health professionals and the monitoring of these reported adverse events, public health systems will continue to be able to detect rare but potentially serious consequences of immunization. This knowledge will contribute to improving the safety of vaccines in the light of the fact that the scientific literature has highlighted the need to continue to refine our understanding of vaccine hesitancy, thereby working towards solutions in a rapidly evolving health scenario.

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Submission declaration and verification. This article has not been published previously, it is not under consideration for publication elsewhere, its publication has been approved by all authors and tacitly or explicitly by the responsible authorities, where the research was performed. Should it be accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically, without the written consent of the copyright-holder. The authors declare that the data in their paper are not the result of plagiarism, self-plagiarism or fraud, and that all data in the article are real, authentic and original.
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Riassunto

Eventi avversi da immunizzazione e percezione dei vaccini negli studenti del corso di laurea in infermieristica

Introduzione. I vaccini sono tra gli interventi di salute pubblica più efficaci dei tempi moderni. Questo studio trasversale ha lo scopo di indagare sulla percezione delle vaccinazioni e i dai potenziali rischi di eventi avversi a seguito di immunizzazione.

Materiali e Metodi. Un questionario anonimo è stato consegnato agli studenti che frequentano il corso di laurea in infermeria presso l'Università di Palermo. Il questionario era composto da tre sezioni: la prima parte si concentrava su informazioni sociodemografiche, nella seconda parte dovevano rispondere alla domanda relativa ai termini associati alla vaccinazione e nella terza parte veniva posta una domanda sulle reazioni avverse dopo l'immunizzazione. È stato utilizzato un modello di regressione logistica multivariabile e sono stati presentati gli Odds ratio aggiustati.

Risultati. Il campione è composto da 403 studenti e la loro età media è di 22,0 anni (± 3,0). Considerata la variabile dipendente: "Hai mai avuto reazioni avverse dopo essere stato vaccinato? Moderato-grave" le variabili indipendenti statisticamente significative associate sono: il secondo (Odds ratio aggiustato 0,32) e il terzo (Odds ratio aggiustato 0,18) anno di corso di laurea, basso stato economico percepito (Odds ratio aggiustato 3,52) e basso stato di salute percepito (Odds ratio aggiustato 15,92), associare il termine vaccinazione alla parola "paura" (Odds ratio aggiustato 4,98) e non associare il termine vaccinazione alle parole "combattere le malattie" (Odds ratio aggiustato 10,02).

Conclusioni. Sebbene tutti i vaccini siano sicuri nessuna vaccinazione è completamente priva di rischi. In questo studio c'era una consapevolezza generale sugli eventi avversi a seguito di immunizzazione tra gli studenti infermieri. I futuri operatori sanitari sono identificati come la più importante fonte di informazioni per potenziali soluzioni in uno scenario sanitario in rapida evoluzione e le conoscenze miglioreranno la sicurezza dei vaccini combattendo l'esitazione vaccinale.

References

1. Spencer JP, Trondsen Pawlowski RH, Thomas S. Vaccine Adverse Events: Separating Myth from Reality. Am Fam Physician 2017; **95**(12): 786-94. Review. PubMed PMID: 28671426.
2. Baldovin T, Bertoncello C, Cocchio S, et al. Perception and knowledge of HPV-related and vaccine-related conditions among a large cohort of university students in Italy. Hum Vaccin Immunother 2019; **15**(7-8): 1641-9. doi: 10.1080/21645515.2018.1564432. Epub 2019 Feb 20. PubMed PMID: 30689506.
3. World Health Organization (WHO). Causality assessment of adverse event following immunization (AEFI): user manual for the revised WHO classification. 2nd ed. Geneva: WHO, 2018. WHO/HIS/EMP/SAV.JANUARY 2018. Available on: https://www.who.int/vaccine_safety/publications/aefi_manual.pdf [Last accessed: 2020, Mar 10].
4. Rapporto vaccini Agenzia Italiana del Farmaco (AIFA). Available on: https://www.aifa.gov.it/documents/20142/241056/Rapporto+Vaccini+2018.pdf/62975a0e-a836-da32-f7b9-1e39196374dd [Last accessed: 2020, Mar 10].
5. StataCorp 2015. Stata Statistical Software. Release 14. College Station, TX: StataCorp LP.
6. National Immunization Plan 2017-2019 [Piano Nazionale Prevenzione Vaccinale 2017-2019], (2017). Available on: http:// www.salute.gov.it/imgs/ C_17_pubblicazioni_2571_allegato.pdf [Last accessed: 2020, Mar 10].
7. Provenzano S, Santangelo OE, Lanza GLM, Raia DD, Alagna E, Firenze A. Factors associated with reporting adverse reactions after immunization, study in a sample of university students. Ann Ig 2018; **30**(5): 436-42. doi:10.7416/ai.2018.2244. PubMed PMID: 30062372.

8. Gidudu JF, Shaum A, Habersaat K, et al. An approach for preparing and responding to adverse events following immunization reported after hepatitis B vaccine birth dose administration. Vaccine 2019 Jul 20. pii: S0264-410X(19)30932-6. doi: 10.1016/j.vaccine.2019.07.041. [Epub ahead of print] Review. PubMed PMID: 31337590.

9. European Centre for Disease Prevention and Control (ECDC). Let's talk about protection. Stockholm: ECDC, 2016. Avaible on: https://ecdc.europa.eu /sites/portal/files /media/en/publications/Publications/lets-talk-about-protection-vaccination-guide.pdf [Last accessed: 2020, Mar 10].

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