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PANDEMIC INFLUENZA A/H1N1 VACCINATION COVERAGE, ADVERSE REACTIONS, AND REASONS FOR VACCINE REFUSAL AMONG MEDICAL STUDENTS IN BRAZIL

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SUMMARY

The aim of this cross-sectional study was to determine, among medical students at a public university in Rio de Janeiro, Brazil, the acceptance of the pandemic influenza A/H1N1 vaccine during the 2010 mass immunization campaign and the vaccine safety in this group and, among unvaccinated students, the reasons for refusing vaccination. Of a total of 858 students, 678 (79%) participated in the study. Vaccination coverage was 60.4% among students aged 20 to 39 years (an age group targeted for vaccination) and 43.8% among those who did not belong to this age group. The most frequent adverse reactions to the vaccine were pain at the injection site (8.7%) and fever (7.9%). There were no serious adverse reactions. Among students aged 20 to 39 years, the most common reasons for refusing the vaccine were "lack of time" (42.4%), "fear of adverse reactions" (41.9%), and "difficult access to the vaccine" (11.5%). Other reasons for vaccine refusal were "uncertainties about vaccine safety and efficacy" and "vaccination was not needed". To increase the acceptance of the influenza vaccine, a comprehensive immunization program should be offered to these students.

KEYWORDS: Vaccination; Influenza A/H1N1; Medical students.

INTRODUCTION

Influenza virus infection among health-care personnel can result in staff illness, absenteeism, and nosocomial transmission of the virus to patients at increased risk for influenza-related complications⁷. Thus, annual vaccination against influenza is recommended for health-care workers and students in the health professions^{8,21}. However, the vaccination coverage in both groups has been universally low, Brazil included^{5,11,16,20,25,29,33,35}. Among health-care workers, misconceptions about the seasonal influenza vaccine and the disease have been identified in review studies as significant barriers to the acceptance of the vaccine^{13,14}.

In April 2009, a new influenza A/H1N1 virus was identified in Mexico and, in a short time, spread to several countries. In June 2009, when more than 33,000 cases of the disease had been confirmed in 74 countries, the World Health Organization declared that the world was at the beginning of a new influenza pandemic³⁷.

In Brazil, there were 44,544 confirmed cases of pandemic influenza A/H1N1, with 2,015 deaths in the second half of 2009. The incidence rates of the disease were higher in children under two years of age and in individuals aged 20 to 29 years. The highest mortality rates were observed in persons aged 50 to 59 years and 30 to 39 years and in children younger than two years. Approximately 75% of the deaths occurred in individuals with underlying chronic diseases²⁴.

Pandemic influenza A/H1N1 vaccines were developed, and from September 2009 onward, immunization programs were implemented in several countries³⁶. In Brazil, the Ministry of Health conducted a mass immunization campaign against pandemic influenza A/H1N1 from March to May 2010, and target groups for vaccination in this campaign were health-care workers, the indigenous population, pregnant women, children aged six to 23 months, individuals with chronic diseases, and adults aged 20 to 39 years²². Unlike in other countries^{9,28}, in Brazil, medical students were not included in the health-care workers category in the definition of the target groups for vaccination against pandemic influenza A/H1N1²². However, most of these students are young adults, an age group for which vaccination was also recommended.

At the time of the mass immunization campaign against influenza A/H1N1 in Brazil, a study had already reported a low acceptance of the influenza A/H1N1 vaccine among health-care workers¹⁰. The knowledge about attitudes and behavior of medical students concerning immunizations can contribute to a better planning of future vaccination campaigns in medical schools.

In this context, this study aimed to determine the acceptance of the pandemic influenza A/H1N1 vaccine during the 2010 mass immunization campaign implemented by the Ministry of Health and the vaccine safety among medical students at a public university in Brazil and the reasons for refusing vaccination among unvaccinated students.

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MATERIALS AND METHODS

This cross-sectional study was conducted at the *Universidade Federal do Estado do Rio de Janeiro* Medical School. This medical school is one of the three public medical schools located in the city of Rio de Janeiro, Brazil, and offers a six-year course in medicine. Approximately one hundred forty students are admitted each year. Student training is held mainly at the university hospital, but also in other health-care facilities. All medical students enrolled at this school in the second semester of 2010 were eligible to participate in the study. The invitation to participate was made during mandatory classes for students on different occasions.

A self-administered questionnaire, with open- and closed-ended questions was used to collect the following data: age, sex, and the students' current year in medical school; vaccination status against pandemic influenza A/H1N1 after the mass vaccination campaign, which was conducted from March to May 2010; adverse reactions following vaccination, which the student considered as having a causal association with the vaccine and, among unvaccinated students, the reasons for refusing the vaccine. Most data were collected in November and December 2010, but some questionnaires were collected until April 2011.

The data were entered into an electronic database using double data entry, and a descriptive analysis was performed for all study variables. The 95% confidence interval was calculated for the pandemic influenza A/H1N1 vaccination coverage and for the frequency of adverse reactions. The odds ratio was used to estimate the association between gender and acceptance of the pandemic influenza A/H1N1 vaccine. Epi Info (version 3.5.3 - 2011) was used for creating the study database and for analysis.

The study was approved by the ethics review committee of the Gaffrée and Guinle University Hospital at the *Universidade Federal do Estado do Rio de Janeiro*, and all students signed an informed consent before entering the study.

RESULTS

In the second half of 2010, 858 students were enrolled at the *Universidade Federal do Estado do Rio de Janeiro* Medical School, and 678 (79%) responded to the survey questionnaire. Response rate ranged from 63.0% among sixth-year students to 92.4% among fourth-year students (Table 1). The mean age of the students was 22.8 years \pm 2.8 (range: 17 to 49 years): 59.7% were female students, and 40.3% were male students. At the time of the vaccination campaign against pandemic influenza A/H1N1, 558 students (82.3%) were aged 20 to 39 years and, thus, belonged to an age group for which the vaccine was recommended. Information on age was missing for eight students.

Among students who were aged 20 to 39 years at the time of the immunization campaign, vaccination coverage was 60.4% (95% CI: 56.2% to 64.5%), and among those who did not belong to this age group, vaccination coverage was 43.8% (95% CI: 34.4% to 53.4%). In the whole group, vaccination coverage was 57.5% (95% CI: 53.7% to 61.3%), and being female was positively associated with vaccination against pandemic influenza A/H1N1 (OR = 1.62; 95% CI: 1.17 to 2.24). Vaccination status was missing for five students (0.7%) (Table 2). Vaccination coverage ranged from 44.3% among third-year students to 67.1% among sixth-year students (Table 1).

Table 1

Response rate and pandemic influenza A/H1N1 vaccination coverage among medical students according to student's year of medical school

Year of medical school	Response rate (%)	Vaccination coverage * (%)
First year	87.9	54.2
Second year	70.3	53.9
Third year	78.2	44.3
Fourth year	92.4	66.4
Fifth year	79.8	59.6
Sixth year	63.0	67.1

* *p* value: 0.002

Among vaccinated students (*n* = 390), the frequency of adverse reactions was 17.9% (95% CI: 14.3% to 22.2%). The most common adverse reaction was pain at the injection site (8.7%), followed by fever (7.9%), prostration (3.8%), myalgia (3.6%), headache (2.3%), malaise (1.5%), nausea (1.0%), and local erythema and/or edema and/or heat (1.0%). Other adverse reactions reported by the students were cold/flu-like symptoms (*n* = 4), pneumonia (*n* = 2), anorexia (*n* = 1), arthralgia (*n* = 1), leg pain and syncope (*n* = 1), pharyngitis (*n* = 1), acute gastroenteritis (*n* = 1), and laryngitis (*n* = 1). Serious adverse reactions were not reported. Information concerning adverse reactions was missing for three students (0.8%). The frequency of adverse reactions was 19.0% among women and 15.9% among men (*p* = 0.44).

All unvaccinated students reported one or more reasons for refusing the vaccine. Among students aged 20 to 39 years, the most frequently reported reasons for not being vaccinated were "lack of time" (42.4%), "fear of adverse reactions" (41.9%), and "difficult access to the vaccine" (11.5%). Among students younger than 20 years or older than 39 years, the most frequent reasons were "not belonging to a target group for vaccination" (66.1%), "fear of adverse reactions" (24.2%), and "lack of time" (22.6%). Several other reasons for not being vaccinated were reported, including doubts about the vaccine safety and efficacy and the perception that vaccination was not needed (Table 3).

DISCUSSION

In the definition of the target groups for vaccination against pandemic influenza A/H1N1 in Brazil, students of the health professions were not included in the health-care personnel category²². However, in this study, most of the students (82.3%) were in an age group targeted for vaccination: individuals aged 20 to 39 years. Nevertheless, among these students, we found a moderately low adherence to the vaccination campaign, and approximately 40% of them were not vaccinated. On the other hand, among students younger than 20 years or older than 39 years, the vaccination coverage was higher than expected (43.8%) because the vaccine was not formally recommended for them. In total, only 57.5% of all students were vaccinated, and a low vaccination coverage was found even among students in the clinical years of medical school who have more frequent contact with patients. Therefore, almost half of all students might have been at risk of acquiring the infection and of transmitting the influenza A/H1N1 virus to vulnerable patients with whom they have contact during their training.

Table 2
Pandemic influenza A/H1N1 vaccination coverage among medical students according to gender and age

Students	Vaccination against pandemic influenza A/H1N1						OR (CI) ¹
	Yes		No		Unknown		
	n	%	n	%	n	%	
Age: 20 to 39 years							
Male	128	54.0	107	45.1	2	0.8	
Female	209	65.1	110	34.3	2	0.6	
Total (n = 558)	337	60.4	217	38.9	4	0.7	
Age: < 20 or > 39 years							
Male	9	28.1	23	71.9	0	0.0	
Female	40	50.0	39	48.8	1	1.3	
Total (n = 112)	49	43.8	62	55.4	1	0.9	
All students: ²							
Male	138	50.5	133	48.7	2	0.7	ref
Female	252	62.2	150	37.0	3	0.7	1.62 (1.17–2.24)
Total (n = 678)	390	57.5	283	41.7	5	0.7	

¹ OR: odds ratio; CI: 95% confidence interval; ² Age was missing for eight students.

Table 3
Reasons for refusing the pandemic influenza A/H1N1 vaccine among medical students by age group

Reason for refusing the vaccine	Age group			
	20-39 years (n = 217) ¹		< 20 or > 39 years (n = 62) ¹	
	n	%	n	%
Lack of time	92	42.4	14	22.6
Fear of adverse reactions	91	41.9	15	24.2
Not belonging to a target group for vaccination	15	6.9	41	66.1
Difficult access to the vaccine	25	11.5	2	3.2
Uncertainty about vaccine efficacy, safety, "quality", benefits, or indications	12	5.5	-	-
Vaccination was not needed	9	4.1	-	-
Didn't want	8	3.6	2	3.2
Out of town/missed the deadline	6	2.7	-	-
Didn't want to stand in line/vaccine was not available at the health-care unit	2	0.9	-	-
Other reasons ²	8	3.6	3	4.8

¹ More than one answer was possible, and % does not sum up to 100%; ² Other reasons were as follows: trusted in herd immunity; lack of consensus among the professors; false positive for HIV; financial interests; does not agree with the campaign; medical advice because of the use of methotrexate and entanercept; vaccine may interfere with my treatment for chronic anemia; lack of studies with the vaccine; allergy; the campaign was to other groups; and did not care because it is the same as seasonal influenza.

According to a preliminary estimate of the Brazilian Ministry of Health in the 2010 mass immunization campaign, the pandemic influenza A/H1N1 vaccination coverage was more than 80% among target groups, including adults aged 20 and 29 years²³. In our group, vaccination coverage was lower than this estimate. To our knowledge, there are no other studies reporting on the pandemic influenza A/H1N1 vaccination coverage among subsets of target groups in Brazil. However, a review study reported that the seasonal influenza vaccination coverage among the elderly, in some Brazilian cities, was also lower than the estimates of health authorities for the entire group¹⁷. Additional studies could contribute to a better understanding of the acceptance of influenza

vaccination among different subsets of target groups in Brazil and to a better planning of future immunization campaigns.

In contrast, pandemic influenza A/H1N1 vaccination coverage in our group was higher than that reported by studies conducted in 2009/2010 among university students in other countries^{19,31,32}. In Athens, Greece, only 8% of 922 medical students had been vaccinated against pandemic influenza A/H1N1 by December 2009, and 67% of them reported that they would definitely or probably not accept the vaccine¹⁹. At a university in Texas, U.S. only 44% of 529 students interviewed were vaccinated against pandemic influenza A/H1N1 during a mass immunization campaign³¹. A

study conducted in India reported a vaccination coverage of only 12.7% among 802 university students³². In several countries, the pandemic influenza A/H1N1 vaccination coverage among health-care workers, including physicians, was also lower than the vaccination coverage observed among our students^{1-3,10,12,18,34,35}.

Different predictive factors for acceptance of the pandemic influenza A/H1N1 vaccine were identified among health-care workers, including gender, age, previous vaccination against seasonal influenza, and perceptions about the disease and the vaccine^{1-3,12,34}. In our group, female students were more likely to have received the vaccine, but we did not evaluate other factors that could confound this association. In India, pandemic influenza A/H1N1 vaccination coverage was also higher among female university students³². In contrast, among health-care workers in Italy, women had a higher risk of not being vaccinated². A study conducted with university students in the U.S. did not find an association between gender and acceptance of the vaccine³¹.

Among students in the age group targeted for vaccination (20 to 39 years old), the most common reasons for refusing the vaccine were "lack of time" (42.4%) and "fear of adverse reactions" (41.9%). Among students not belonging to this age group, "fear of adverse reactions" and "lack of time" were the second and third most frequent reasons, respectively. The lack of time could be justified by the student's daily schedule and by the fact that vaccination was not available to them at the university. However, the vaccine was available at no cost in many health-care facilities, and only about 15% of the students reported "difficult access to the vaccine" as a reason for not being vaccinated. Thus, the lack of time would probably not have been a significant barrier to vaccination if the students had considered this intervention an important strategy for preserving their health and the health of their contacts.

The influenza A/H1N1 immunization campaign was implemented in Brazil when millions of doses of vaccines had already been administered worldwide and the World Health Organization had reported that no safety concerns had been identified for any of the pandemic influenza vaccines³⁶. Nevertheless, fear of adverse reactions was a significant barrier to the acceptance of the vaccine among our students. In studies conducted among university students^{19,32} and health-care workers in other countries^{1,3,10,34,35}, fear of adverse reactions was also one of the most common reasons for non-acceptance of the influenza A/H1N1 vaccine, and other reasons identified in these studies for non-acceptance of the vaccine were, in general, similar to the reasons reported by our group.

Altogether, the reasons for refusing the vaccine reported by our students demonstrate that they had an inadequate knowledge about the efficacy, safety, indications, and contraindications of the influenza vaccine. Misconceptions about influenza and the vaccine had already been identified as significant barriers to the acceptance of the seasonal influenza vaccine among health-care workers^{13,14}. Accordingly, the medical school should urgently provide educational activities regarding influenza and its prevention to these medical students.

Approximately 18% of our students reported adverse reactions to the vaccine, but there were no serious adverse reactions. In studies conducted among health-care workers^{2-4,12,26}, the frequency of adverse reactions following vaccination against pandemic influenza A/H1N1 ranged from 6.7% in Germany to 82.3% in Spain, and the adverse reactions reported by

our group were, in general, similar to those described in these studies. The adverse reactions also were similar to those typically observed after the administration of seasonal inactivated influenza vaccines⁶. The frequency of adverse reactions reported by different studies cannot be compared because of several factors, including the use of different vaccines.

Our study has several limitations. Although the response rate was relatively high (79%), a selection bias may have occurred. Additionally, we did not investigate why students decided to be vaccinated, especially those students who did not belong to an age group targeted for vaccination, and we also did not investigate other predictive factors for acceptance of the pandemic influenza A/H1N1 vaccine besides gender. However, the main limitation is that the results of this study cannot be generalized to other medical students in Brazil, as the context in which vaccination occurred in other medical schools might have been different. On the other hand, to our knowledge, there are no other studies reporting on influenza A/H1N1 vaccination coverage among medical students in Brazil, and our results can contribute to a better understanding of attitudes and behavior of medical students concerning influenza immunization.

In conclusion, we identified a moderately low adherence to the 2010 mass immunization campaign against pandemic influenza A/H1N1 among medical students in Brazil. The main reasons for vaccine refusal were lack of time, fear of adverse reactions, and misconceptions about the vaccine. The vaccine was well tolerated. To prevent the nosocomial transmission of influenza to vulnerable patients, mandatory vaccination of health-care personnel has been proposed or has been implemented in some settings^{27,30}. A recent study conducted in the U.S. reported that 77% of all medical schools offered influenza vaccines at no cost to students during the 2007/2008 season and suggested that annual influenza immunization of students could contribute to increase the acceptance of the vaccine among future health-care workers¹⁵. In Brazil, health authorities and medical schools should consider providing the influenza vaccine to medical students. However, a comprehensive immunization program is necessary to ensure a high vaccination coverage.

RESUMO

Cobertura vacinal para a influenza A/H1N1, reações adversas e motivos para a não aceitação da vacina entre estudantes de medicina no Brasil

O objetivo deste estudo transversal foi determinar, entre estudantes de medicina de uma universidade pública no Rio de Janeiro - Brasil, a aceitação da vacina contra a influenza A/H1N1 pandêmica durante a campanha de imunização em massa de 2010, a segurança da vacina neste grupo e, entre os estudantes não vacinados, os motivos para recusarem a vacinação. De um total de 858 estudantes, 678 (79%) participaram do estudo. Entre os estudantes de 20 a 39 anos de idade (um grupo etário alvo para vacinação) a cobertura vacinal foi de 60,4% e entre aqueles que não pertenciam a esta faixa etária a cobertura vacinal foi de 43,8%. As reações adversas à vacina mais frequentes foram dor no local da injeção (8,7%) e febre (7,9%). Não ocorreram reações adversas graves. Entre os estudantes de 20 a 39 anos, os motivos mais frequentes para recusarem a vacina foram "falta de tempo" (42,4%), "receio de reações adversas" (41,9%) e "difícil acesso a vacina" (11,5%). Outros motivos para a não

vacinação foram “incertezas sobre eficácia e segurança da vacina” e “vacinação não era necessária”. A fim de aumentar a aceitação da vacina contra a influenza, um programa de imunização abrangente deveria ser oferecido aos estudantes.

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AUTHOR CONTRIBUTIONS

Both authors participated in all study phases. EPS coordinated the study.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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