



VACCINE HESITANCY IN PREGNANT WOMEN DURING THE PANDEMIC IN BRAZIL AND SPAIN: A MIXED-METHODS STUDY

HESITAÇÃO VACINAL EM GESTANTES DURANTE A PANDEMIA NO BRASIL E NA ESPANHA: ESTUDO MISTO

VACILACIÓN VACUNAL EN EMBARAZADAS DURANTE LA PANDEMIA EN BRASIL Y ESPAÑA: ESTUDIO MIXTO

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RESUMO

Objetivo: analisar os fatores que levaram gestantes brasileiras e espanholas à hesitação vacinal durante a pandemia. **Método:** Estudo misto, realizado com 42 gestantes brasileiras e 40 espanholas, que responderam a um questionário online. No Brasil, a coleta de dados ocorreu entre julho e agosto de 2022 e, na Espanha, em março de 2023. Os dados quantitativos foram analisados por meio de estatística descritiva simples e as informações qualitativas foram categorizadas com base em análise temática. **Resultados:** A hesitação vacinal entre gestantes brasileiras e espanholas estava associada ao medo de efeitos adversos da vacina, à preocupação com o feto, ao questionamento sobre a origem e o rápido desenvolvimento das vacinas, à influência de informações acessadas pela internet e redes sociais e às divergências de opiniões e controvérsias entre os profissionais de saúde em relação à vacinação. **Conclusão:** Reduzir a desconfiança das gestantes em relação à vacinação, bem como estimulá-las para que estejam cada vez mais interessadas em utilizar todas as vacinas disponíveis, contribui para ampliar a cobertura vacinal. Assim, uma vigilância permanente nos serviços de saúde é necessária para fomentar segurança e garantir a defesa da vida.

Descritores: Hesitação Vacinal; Mulheres Grávidas; Pandemia Covid-19.

ABSTRACT

Objective: To analyze the factors that led Brazilian and Spanish pregnant women to vaccine hesitancy during the pandemic. **Method:** A mixed-methods study was conducted with 42 Brazilian and 40 Spanish pregnant women who answered an online questionnaire. In Brazil, data collection took place between July and August 2022, and in Spain, in March 2023. Quantitative data were analyzed using simple descriptive statistics, and qualitative information was categorized based on thematic analysis. **Results:** Vaccine hesitancy among Brazilian and Spanish pregnant women was associated with fear of vaccine's adverse effects, concern for the fetus, questions about the vaccines' origin and rapid development, the influence of information accessed through the internet and social medias, and differing opinions and controversies among health professionals regarding vaccination. **Conclusion:** Reducing pregnant women's distrust of vaccination, as well as encouraging them to be increasingly interested in using all available vaccines, contributes to expanding vaccination coverage. Thus, permanent surveillance in health services is necessary to promote safety and guarantee the protection of life. **Descriptors:** Vaccine Hesitancy; Pregnant Women; Covid-19 Pandemic.

RESUMEN

Objetivo: analizar los factores que llevaron a las mujeres embarazadas brasileñas y españolas a dudar en relación a vacunarse frente a la covid-19. **Método:** Estudio mixto parte de un proyecto más amplio del tipo websurvey. Participaron 42 mujeres embarazadas brasileñas y 40 españolas, que respondieron un cuestionario en línea. En Brasil, la recogida de datos se llevó a cabo en noviembre de 2022 y en España en marzo de 2023. Los datos cuantitativos se analizaron mediante estadística descriptiva simple y la información cualitativa se categorizó a partir del análisis temático. **Resultados:** La reticencia a la vacunación entre las embarazadas brasileñas y españolas está relacionada con el miedo a los efectos adversos derivados de la vacuna, la preocupación por la salud y desarrollo fetal, el cuestionamiento sobre el origen y desarrollo acelerado de las vacunas, la influencia de las informaciones accedidas a través de Internet y las redes sociales y las divergencias de opiniones y controversias profesionales ante el proceso de la vacunación. **Conclusión:** Reducir la desconfianza de las mujeres embarazadas hacia la vacunación, así como fomentar su interés por utilizar todas las vacunas disponibles, contribuye a ampliar la cobertura vacunal. Por lo tanto, es necesario mantener una vigilancia constante en los servicios de salud para promover la seguridad y garantizar la protección de la vida.

Descriptores: Indecisión Frente a la Vacunación; Pandemia Covid-19; Mujeres Embarazadas.

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What is already known:

- Vaccine hesitancy in pregnant women is a complex and multifactorial phenomenon.
- The development of new vaccines against covid-19 contributed to low vaccination coverage among pregnant women during the pandemic.
- Changes in institutional recommendations influenced the behavior of pregnant women regarding covid-19 vaccination.

What this article adds:

- Vaccine hesitancy persists even with recommendations from health authorities such as the WHO.
- Differences in age, education, and religion among pregnant women in Brazil and Spain, showed correlations with the variables of fears, doubts, and sources of influence on vaccine hesitancy, interfering in different ways in the behaviors in each country.
- Educational strategies based on up-to-date scientific evidence are essential to reduce vaccine hesitancy and promote informed decision-making.

INTRODUCTION

Immunization programs are recognized for effectively contributing to the collective vaccination process and the control of infectious diseases. In Brazil, the National Immunization Program is one of the largest public vaccination programs in the world, offering the entire population the possibility of broad immunological coverage. Regarding covid-19, institutions such as the Oswaldo Cruz Foundation in Rio de Janeiro, Brazil, and the Butantan Institute in São Paulo, Brazil, participated in various national and international fronts in the search for and development of vaccines⁽¹⁾. In Spain, the Ministry of Health promoted the investigation and production of vaccines, taking into account the experience of researchers from public institutions and the dedicated work of health professionals to achieve high vaccination coverage⁽²⁾.

Although the social and economic benefits of immunization programs are recognized, there have been questions and doubts that contribute to the reduction of vaccination coverage rates, opening space for divergent opinions among the world population. This process interferes with people's behavior, generating the possibility of vaccine hesitancy, which consists of delaying acceptance, resistance, or definitive rejection of the possibility of being vaccinated, even when immunization is possible in health institutions⁽³⁾.

The phenomenon of vaccine hesitancy, initially influenced by a movement characterized as anti-vaccination, continues to find fertile ground in various groups and interferes with the expansion of vaccination coverage⁽⁴⁾. In this context, the feeling of insecurity regarding vaccines has increased over the years. Faced with the scientifically proven risk and the risk subjectively perceived by the population, the vaccination process has been influenced by the accelerated dissemination of false information through the internet and social media, especially with the arrival of the pandemic, casting doubt on current scientific production⁽⁵⁾.

However, the introduction of new vaccines on the world stage has been supported by multicenter scientific research and epidemiological and sanitary surveillance systems that monitor possible adverse post-vaccination events, with the aim of increasing the population's sense of security⁽⁶⁻⁷⁾.

Pregnant women are more susceptible to complications arising from exposure to and risk of disease, as observed during the covid-19 pandemic, increasing the possibility of uncertainty, insecurity, and vaccine hesitancy⁽⁸⁾. Estimates of global acceptance of the covid19 vaccine and hesitancy

among pregnant women are still unknown. However, recent studies conducted with these women point to differences in behavior related to the vaccination decision, considering regional realities⁽⁹⁻¹⁰⁾.

Considering the differences between the Brazilian and Spanish realities, pregnant women in both countries may show greater hesitancy in getting vaccinated against covid-19 compared to the non-pregnant population. The objective of this study was to analyze the factors that led Brazilian and Spanish pregnant women to vaccine hesitancy during the pandemic.

METHOD

This is a mixed-methods study, part of a broader research project that aimed to analyze the decision of the community and workers linked to Primary Health Care regarding vaccination against covid-19 during the pandemic in Brazil. In Spain, it was part of a study that aimed to investigate the psychological effect of covid-19 on pregnant women.

The study was conducted under the influence of John Creswell, whose data were collected and analyzed, allowing the identification of quantitative and qualitative results through an online questionnaire with closed and open questions⁽¹¹⁾. The Mixed Methods Appraisal Tool (MMAT) instrument was adopted, being recommended in mixed-methods studies in the health field⁽¹²⁾.

The study included 42 pregnant Brazilian women and 40 Spanish women, whose selection was carried out by non-probabilistic sampling, with expansion through the snowball sampling technique. Chain sampling is organized so that existing study participants recruit future participants, soliciting referrals and successive participations⁽¹³⁾. The inclusion criteria were pregnant women over 18 years of age who were familiar with digital resources. Cognitive impairment was considered an exclusion criterion.

Data collection was carried out using questionnaires that were developed and answered through Google Forms. In Brazil, the research was conducted between September and November 2022, and in Spain, in March 2023. The form contained guidelines on the participation process and notes regarding the Informed Consent Form (ICF). The process allowed for continuation or refusal of participation, which occurred when the pregnant woman read, clicked, expressed interest, and proceeded in filling out the form. The research was disseminated on Brazilian and Spanish

social media, such as Facebook, and also sent via WhatsApp. The estimated time to complete the questionnaire was 15 to 20 minutes. To guarantee the anonymity of the participants, alphanumeric identifications were made according to the country. For example, women from Brazil were identified as Brazilian pregnant women GBR01, GBR02, etc.; and women from Spain as Spanish pregnant women GES01, GES02, etc. The instrument was initially developed in Brazil, requiring subsequent adaptations to the Spanish context.

The quantitative data were analyzed using simple descriptive statistics, and the qualitative information was categorized through thematic analysis. The development of thematic categories made it possible to understand the implicit meanings related to pregnant women's responses regarding vaccine hesitancy behaviors against covid-19, in addition to providing opportunities for comparative analyses between the groups from the two countries.

The study was approved by the Research Ethics Committee of Brazil (CAAE: 55406422.5.0000.5243 e nº 5.251.042/2022) and by the Research Ethics Committee of Spain (nº 1580/CEIH/2020). In Brazil, the study was conducted in accordance with the guidelines of Resolutions No. 466/2012 and 510/2016 of the National Health Council/Ministry of Health (CNS/MS). In Spain, Organic Law 3/2011, of December 5, on the Protection of Personal Data and Guarantee of Digital Rights (LOPDGDD) and the General Data Protection Regulation of 2016 (GDPR) were observed.

RESULTS

In Brazil, pregnant women were 27 years old on average, and the majority reported having minimum education's level and receiving a minimum wage. Skin color was identified by self-declaration, with 47.6% referring to being white and 50% black. More than half were evangelical religion (52%) and 97% reported being heterosexual. A significant part (40.5%) reported living with three people in the same household and 42.8% having only one child. Regarding vaccination, 52.8% of pregnant women reported immunization with more than two doses, 46.3% were immunized only with Biontech-Pfizer and only 4.8% of unvaccinated pregnant women.

In Spain, women were on average 38 years old, 92.5% declared themselves white, and 97.5% heterosexual. Regarding religion, 57.5% mentioned catholicism and 37.5% said they had no religion or were agnostic. As for education, 37.5% reported having a bachelor's degree. The majority (77.5%) reported having an income between two and four minimum wages. Regarding marital status, 90% were married/living with a partner and 92.5% in a biparental family, 52.5% indicated that they lived with three people in the same house and the same percentage had only one child. Regarding vaccination, 62.5% of pregnant women identified having been immunized with more than two doses, 70% with the BioNTech-Pfizer vaccine and 10% without vaccination.

Thus, it was possible to highlight differences related to profile, such as: age (Brazilian average of 27 years and Spanish average of 38 years), religion (Brazilians are

52% evangelical and Spanish women 57% Catholic and 37.5% without religion or agnostic), income (Brazilians with minimum wage and Spanish women between two and four minimum wages) and educational level (Brazilians with 45.2% elementary school and Spanish women with 37.5% higher education).

Among the factors associated with vaccine hesitancy in pregnant women in Brazil and Spain, it was possible to identify comparisons based on the following variables, as can be seen in Table 1.

Regarding the qualitative aspects, when analyzing the responses to the open questions, recurring themes were identified that allowed the creation of the following thematic categories: The fear of adverse effects after vaccination increases the possibility of doubting the vaccine; Questions related to the accelerated development and use of vaccines in pregnant women; Information sources and collective influence interfere with vaccine hesitancy. The main findings identified from the responses of the two groups of pregnant women can be seen in Box 1.

Fear of adverse effects after vaccination raises doubts about the effectiveness of vaccines. One of the factors associated with vaccine hesitancy, which generated the greatest discrepancy between pregnant women in the two countries, was the possibility of fear of suffering adverse events resulting from vaccination against covid-19. This factor was pointed out by 7.2% of Brazilian women and 30% of Spanish women. The fear of being infected by covid-19 after vaccination was mentioned by 4.8% of Brazilian women and 5% of Spanish women. Fear of needles was only mentioned by Brazilian pregnant women (14.2%). Another issue mentioned only by Brazilian pregnant women was the lack of time to get vaccinated (9.5%).

When observing the open-ended responses, the fear associated with vaccine hesitancy was also mentioned by Brazilian and Spanish pregnant women. In the Brazilian women's responses, the fear was related to adverse reactions after vaccination reported by other people (pain, malaise, fever, etc.) and the possibility of developing pathologies such as thrombosis and heart attack, when superimposed on the gestational condition.

...many people where I live had a reaction, pain in the arm, fever. I was scared. (GBR28)

I was afraid of the third dose, afraid of thrombosis. (GBR20)

...cases of people who suffered a heart attack after being vaccinated. (GBR34)

Regarding Spanish women, in addition to the fear related to adverse effects, it was possible to highlight records directed at the fear of a possible miscarriage, as well as damage to fetal development.

A colleague told me that there were miscarriages. (GES02)

I had doubts about the impact on my pregnancy and on the normal development of the fetus. (GES14)

In my case, I waited until after the first trimester as a precaution, so that I could develop any secondary symptoms that could affect the fetus. (GES01)

Table 1 - Factors associated with Brazilian and Spanish pregnant women's hesitation of regarding vaccination against covid-19. Niterói, RJ, Brazil, 2022 (n=42) and Granada, Spain, 2023 (n=40)

Variables*	Brazil		Spain	
	n	(%)	n	(%)
Possibility of having adverse events from vaccination against covid-19	3	7,2	12	30
Fear of contaminating the fetus	5	11,9	14	35
Fear of contamination by covid-19 after vaccination	2	4,8	2	5
Fear of the needle	6	14,2	-	-
Lack of time	4	9,5	-	-
Regret not having been vaccinated at the right time or given the increase in the number of people contaminated by covid-19	3	7,2	1	2,5
Doubts and questions about the production of vaccines against covid-19	1	2,4	5	12,5
Questioning about the origin of vaccines against covid-19 and disbelief in effective/prolonged protection	2	4,8	7	17,5
Emergence of new strains/variants of covid-19	2	4,8	8	20
Rejection of vaccines like <i>Coronavac</i> and <i>Oxford-AstraZeneca</i>	2	4,8	2	5
Relatives	5	11,9	5	12,5
Health professional	5	11,9	3	7,5
Politicians and religious leaders	1	2,4	3	7,5
Friends	1	2,4	3	7,5
Information published on the internet/social networks (<i>Instagram</i> , <i>Facebook/Meta</i> , <i>WhatsApp</i>), radio, press and TV	7	16,7	10	25

*Note: The participant could select more than one option.

Source: prepared by the authors, 2023.

Box 1 - Issues associated with the hesitation among Brazilian and Spanish pregnant women regarding vaccination against covid-19. Niterói, RJ, Brazil, 2022 (n=42) and Granada, Spain, 2023 (n=40)

Records Units	Context Units	Thematic Categories
- Fear reaction. - Virus reaction in organism. - Pain in the arm - Fever - Thrombosis - Abortion - Myocardial infarction - Incomprehension of secondary effects. - Possible risks	Fear of post-vaccination adverse effects	The fear of adverse effects after vaccination increases the possibility of doubting the vaccine.
- Impact on pregnancy - Damage to the fetus - Impact on fetal development	Concern about the impact of vaccination on pregnancy and fetal development	
- Were made too fast - Creation speed - Precipitate use - Rushed use	Accelerated development of vaccines for emergency use	Questions related to the accelerated development and use of vaccines in pregnant women.
- Lack of research - Bit experiment - Lack of vaccination studies in pregnant women	Lack of research and testing of new vaccines in pregnant women	
- Read news - Saw the internet - Asked to a doctor - False information - Few information - Lack of information - Negative information - Harmful effects of vaccines - Unsafety - Fear - Rumor - Risky - Discrepancy of opinion - Different opinions - I did not see clearly - Criterion changes - Professionals' influence. - Nurse's recommendation - Doctor's recommendation - My family - Stories of friends - I wasn't vaccinated	- The search for information can lead to hesitation. - Insecurities regard to the false information about vaccines. - Divergence of information and changes in institutional programmatic criteria contribute to hesitancy. - Influence of professionals, relatives and friends that interfere in the individual decision process.	Information sources and collective influence interfere with vaccine hesitancy.

Source: prepared by the authors, 2023.

Questions related to the accelerated development and use of vaccines in pregnant women

Regarding covid-19 vaccines, insecurities and questions about their origin and development process, as well as disbelief in their long-term protection, were associated with vaccine hesitancy in 4.8% of Brazilian women and 17.5% of Spanish women.

In response to open-ended questions, the accelerated development of vaccines was reported by Brazilian pregnant women. However, Spanish women stated that there is little information about adverse effects in pregnant or breastfeeding women. In addition, questions arose about the lack of evidence related to covid-19 vaccines and the scant research on vaccination performed on pregnant women.

I think they were studied, I just thought they were done quickly. . . (GBR14)

I believe that the use of vaccines without sufficient information was too hasty. (GES26)

I found it very risky to get vaccinated during pregnancy with vaccines that have not yet been tested. (GES33)

Lack of studies on vaccination of pregnant women at the beginning of the pandemic. (GES24)

Sources of information and collective influence interfere with vaccine hesitancy

It was observed that 16.7% of Brazilian pregnant women and 25% of Spanish pregnant women identified information published on the internet or disseminated on social medias, radio, newspapers, and TV as relating to vaccine hesitancy.

Brazilian pregnant women identified their family members (11.9%) and healthcare professionals (11.9%) as groups that influenced vaccine hesitancy. Spanish women pointed to their family members (12.5%) as the group that exerted the greatest influence.

Regarding the descriptive part, it was observed in the responses of Brazilian pregnant women that the dissemination of negative and false information – when spread on the internet and social medias – collectively influenced behaviors related to vaccine hesitancy.

Circulation of negative information about the vaccine and its adverse effects. (GBR05)

I received several messages saying that the vaccine would not protect. (GBR36)

Furthermore, groups such as family, friends, and healthcare professionals were also identified in open-ended responses as potential influencers. As a possible to increase hesitancy, Brazilian women highlighted that healthcare professionals could also be associated with distrust and disbelief regarding the vaccination process.

My family also told me not to get vaccinated. (GBR29)

I saw doctors saying that other illnesses appear over the years, I saw this in Kwaia [...] I don't believe it, I saw it on the internet, I'm not getting vaccinated... I received reports from friends who got vaccinated and didn't get better [...] I had a friend who got worse, I think the vaccines aren't good. (GBR28)

In the appointments of Spanish women, statements re-

lated to insecurity, divergence of professional opinions, and doubts regarding changes in criteria during the vaccination process for pregnant women, on the part of the Spanish Ministry of Health, were highlighted.

I did not get vaccinated during pregnancy on the recommendation of my gynecologist and midwife. (GES10)

I didn't get vaccinated because of the change in vaccination criteria for pregnant women, as the criteria changed several times during my pregnancy and I didn't feel safe. (GES29)

I got vaccinated due to social pressure, because I didn't want to, but the government had already prohibited access to several places. I was informed and decided there wasn't much risk. (GES10)

DISCUSSION

The process experienced by pregnant women, from the decision to get vaccinated to the possibility of refusing vaccination, can be characterized by behaviors related to hesitancy. When women highlight fear, insecurities, and questions about the use of rapidly developed vaccines, for example, it becomes evident that the relationship between professionals and the population can be affected by situations influenced by political, economic, and cultural aspects. Considering the social context, people's decision-making power is influenced by multiple factors, such as gender, skin color, religion, profession, income, and level of education.

When identifying current scientific evidence on vaccination, analyses related to hesitancy can be observed, taking into account some variables that characterized the profile of the groups studied. Younger age was identified among pregnant women who presented hesitancy⁽¹⁴⁻¹⁵⁾. Lower economic income was also associated with vaccine hesitancy⁽¹⁶⁻¹⁷⁾. Religion, when influenced by traditional conceptions, can influence hesitancy behavior⁽¹⁸⁾. Similarly, lower levels of education were also correlated with resistance to vaccination⁽¹⁵⁾.

In addition to these, it is possible to identify the existence of other factors that influenced behaviors related to vaccine hesitancy; in turn enabling comparisons between the behaviors of pregnant women in Brazil and Spain. Fear was one of the factors that intensely crossed people's lives since the beginning of the pandemic. For example, the possibility of infection or death from covid-19 led many people to seek vaccination as a survival measure⁽¹⁹⁾. In the case of this study, the fear of Brazilian and Spanish pregnant women seems to be correlated with adverse post-vaccination events and concern for the fetus, allowing the expansion of behaviors related to vaccine hesitancy⁽²⁰⁻²³⁾.

Pregnant women in both countries expressed concern about the accelerated development of covid-19 vaccines as a contributing factor to increased vaccine hesitancy⁽²⁴⁾. This rapid use of covid-19 vaccines raised doubts and questions regarding the efficacy and safety of the vaccines⁽¹⁴⁾.

Distrust in the vaccine safety process may be associated with general resistance related to rapid vaccination, questions about the scarcity of information, or the lack of specific studies on the development and efficacy of covid-19 vaccines in pregnant women⁽²⁵⁻²⁷⁾. Insecurity related

to vaccine development may also be associated with the dissemination and access to information that prioritizes highlighting adverse reactions or effects^(5,26) or the low level of education of people⁽²⁸⁾. In this study, the two groups of pregnant women showed differences in terms of education, with Spanish women reporting a higher level of education compared to Brazilian women. Lack of knowledge and formal education are factors that exert an important influence on the vaccine hesitancy/refusal process. The lower the level of schooling and knowledge, the greater the tendency towards vaccine hesitancy, the correlation of which can be identified in the following studies^(10,29-30). However, the higher the level of knowledge and the capacity for reflection and criticism, the lower the possibility of hesitancy regarding vaccination⁽³¹⁾.

Access to information from the media can influence hesitancy behaviors⁽¹⁶⁻¹⁷⁾, because when experienced without critical analysis, they can trigger collective rumors that generate insecurity and distrust about the effectiveness of vaccines⁽³²⁾. Such behaviors can be amplified considering the dissemination of false information on the internet and social networks. The irresponsible use of fake news and the lack of content monitoring on social media are associated with the possibility of vaccine hesitancy⁽⁵⁾. However, it is worth noting that access to information from the media can be used to clarify fake news about vaccination⁽³³⁾.

In a contradictory way, friends, family, and health professionals can also influence vaccine hesitancy processes, as can be identified in recent studies⁽³⁴⁻³⁶⁾. The lack or inadequacy of professional recommendations, for example, on the use of vaccines during prenatal care, may be associated with vaccine hesitancy⁽³⁷⁾. Thus, the role of health professionals is extremely relevant, whose actions must be committed to scientific processes based on scientifically proven information. Health professionals must be familiar with current vaccination recommendations so that they feel confident and can analyze the benefits and risks related to vaccination during pregnancy.

In this way, it is important to emphasize that pregnant women's confidence in scientific institutional, and professional guidelines is essential to continue ensuring a health education process that contributes to stimulating adherence to vaccination behaviors and expanding vaccination coverage⁽³⁸⁻⁴⁰⁾.

It should be noted that the results of this study do not allow for generalizations, and possible limitations include regionalization and the number of participants in each country. Expanding this research would enable the inclusion of pregnant women with different realities and contexts. Information on vaccine hesitancy among pregnant women can be useful for implementing health education actions and

specific communication strategies between health professionals and women, seeking to provide tools for informed decision-making regarding vaccination.

CONCLUSION

Based on the differences identified between pregnant women in Brazil and Spain, specificities related to the factors influencing vaccine hesitancy behaviors in each country are observed, such as correlations between age, education, and religion, and the variables of fears, doubts, and sources of influence on hesitancy.

A deep understanding of these factors is fundamental to reflecting on the importance of continuing the commitment to reducing distrust in vaccination, as the decision of pregnant women must be made responsibly, considering both individual protection and collective commitment.

Although the benefits of group vaccination have been scientifically validated throughout history, the need to disseminate information based on updated scientific evidence remains. Continuous vigilance by health professionals is important to ensure that pregnant women are increasingly interested in using the recommended vaccines and, in turn, contribute to expanding vaccination coverage. Thus, permanent surveillance in the health services of both countries becomes essential to promote safety and guarantee the defense of life.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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All authors are responsible for the writing of the manuscript and the critical review of the intellectual content, the final published version, and all ethical, legal, and scientific aspects related to the accuracy and integrity of the study.



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