Post-vaccine adverse events in patients immunized against COVID-19 in a munici-pality in the south of Santa Catarina state in 2021

Henrique Guimarães Aires e Silva, Beatriz Ranson Margotti, Chaiana Esmeraldino Mendes Marcon

ABSTRACT

The mass availability of vaccines against the SARS-CoV-2 virus is the result of worldwide scientific efforts. However, insecurity and popular hesitation permeate the antivaccine movements. **Objective:** Analyze the profile of Post-Vaccine Adverse Events (PVAE) in the city of Tubarão, SC, Brazil, in 2021. **Methodology:** Cross-sectional epidemiological study with data from all standard PVAE notification forms in the city of Tubarão-SC in 2021. The variables analyzed were the epidemiological profile of the patient, the immunobiological administered, the type of event and the evolution of the cases. The incidence rate (IR) was calculated for 10,000 doses ap-plied. **Results:** The study population was 274 patients, 73% were female, with a mean age of 39.8±14.5 years. A total of 197,001 doses were applied in the year 2021, resulting in an overall IR of 13.9. There were 206 reactions reported in pa-tients immunized with AstraZeneca (IR=29.1), 43 with Pfizer (IR=5.1), 18 with Coro-navac (IR=4.8) and seven with Janssen (IR=13.8). There were only seven cases classified as severe (IR=0.3) and, of these, one patient died, with no causal rela-tionship established. **Conclusion:** The overall incidence of serious events was low, which corroborates the safety profile of available immunobiologicals against COVID-19.

Keywords: Coronavirus infection, Vaccination, Drug-related side effects and adverse Reactions.

INTRODUCTION

COVID-19 is an acute respiratory tract infection identified after increasing cases of patients with flu-like syndrome evolving to a severe acute respiratory syndrome, hospital admission and death in Wuhan, China, in late 2019[1]. The SARS-CoV-2 virus was identified as the etiological agent responsible for this disease of heterogeneous epidemiological and clinical presentation and responsible for the death of more than 680,000 Brazilians since the beginning of the pandemic[2,3]. To prevent the disease from advancing, social restrictive measures were instituted, such as lockdown and interpersonal distancing, which generated concern by limiting the social, economic, and routine health dynamics[4] - starting an unusual chapter in world history. Thus, there is great expectation that the implementation of vaccination programs against COVID-19 will control the pandemic's progress and allow the re-establishment of normal routines around the world.

Unlike what happens in other countries, there were no major social movements of resistance to vaccination in Brazil, except for specific episodes such as the Vaccine Revolt in 1904, which corroborates a "culture of immunization" in the country[5]. However, paradoxically, the diffusion of knowledge over the decades was not directly proportional to the increase in vaccination coverage. The factors related to the emergence of vaccine hesitancy may be of pseudoscientific, political, religious, ethical origin and/or the result of doubts about the safety and effectiveness of these immunobiologicals for COVID-19 - which reveals the need for a multimodal approach to combat it[6,7].

Despite being subjected to safety tests in clinical protocols, vaccines are not free of side effects related to their use, especially rare adverse events that may be underestimated in clinical trials before the pharmacovigilance phase. In Brazil, this monitoring is performed by the National System for Surveillance of Post-Vaccination Adverse Events (NSSPVAE), which

University of Southern Santa Catarina, Tubarão, (SC), Brazil.

https://doi.org/10.11606/issn.2176-7262.rmrp.2023.203651

values the continuous assessment of the relationship between risks, costs and benefits of the use of immunobiologicals, besides ensuring the credibility of the national immunization program since 1998. The action of NSSPVAE is essential in the context of the emergence of new immunobiologicals against COVID-19 since vaccines require a very high level of safety and even non-severe EAPVs can signal threats to biosafety[8].

The hesitancy to use vaccines in the context of the pandemic is strongly related to beliefs of no personal benefit and misgivings about their safety, occasioned by the rapidity of vaccine development[9]. Mild and moderate adverse events are the most common, such as fever, myalgia, fatigue and headache; however, severe reactions have been reported in the various COVID-19 vaccines currently available[10]. Thus, collecting data on these effects in the vaccinated population can add confidence in the hesitant population and increase vaccination coverage. Therefore, this study aimed to identify the main post-vaccinal adverse events of the COVID-19 vaccine in a municipality in southern Santa Catarina in 2021.

METHODOLOGY

Cross-sectional study design composed of the patients reported for post-vaccine adverse events (PVAE) after COVID-19 vaccination notified in the municipality of Tubarão, Santa Catarina, in the period between January 1, 2021, to December 31, 2021. All notification forms of EAPV not classified as immunization errors were included, and incomplete forms that impaired data analysis were excluded. This work was supported by a grant from the Institutional Program for Scientific Initiation Scholarships (PIBIC) of the National Council for Scientific and Technological Development (CNPq).

The Post-Vaccine Adverse Event Notification/ Investigation Forms are a standard document of the Health Surveillance Secretariat of the state of SC filled out during the investigation of a suspected case of HAPV which contain data on patient identification (age, sex, race/ethnicity, area of residence, pregnant or lactating woman), the immunobiological used and the vaccination act, the health unit where the immunobiologicals were administered/applied, the patient's previous pathological history, the medical care provided to the patient, the characterization of the VAS, the results of complementary tests, the final diagnosis, the programmatic errors (inadequate procedures) identified, the conclusion of the case, and other additional information. The immunobiologicals available at the time of this study were Coronavac from Sinovac and Butantan laboratories; Pfizer from Pfizer and BioNTech laboratories; AstraZeneca from AstraZeneca, Fiocruz and Oxford laboratories and Janssen from Johnson & Johnson laboratory. As for the severity and classification of PVAEs, data were collected regarding the need for medical care and the type of care provided (ambulatory/consultatory, observation for up to 24 hours, hospitalization with a length of stay longer than 24 hours, or no need for care) when available. Finally, data will be collected on the classification of the PVAE after the clinical outcome "Non-serious adverse event (NSAE)", "Serious adverse event (SAE)", "Immunization error (IE)" or "Not classifiable".

The present study was approved by the Research Ethics Committee of the Universidade do Sul de Santa Catarina under register number 5.033.420 on October 12, 2021. Data were collected and organized in a Microsoft Excel 2010 database. Descriptive and statistical inference analyses were performed in the SPSS software version 20.0 (SPSS Inc., Chicago, United States). The results were presented descriptively and in the form of tables and figures. Quantitative variables were described by means of measures of central tendency and dispersion of the data. Qualitative variables were described by absolute and percentage frequency.

RESULTS

In 2021, 197,001 doses of immunobiologicals against COVID-19 were administered in the municipality under study, and 294 patients with suspected Post-Vaccine Adverse Events (PVAE) were reported. Nineteen patients had their PVAE classified as immunization error and were not included in this descriptive analysis. Only one patient had a notification form without immunobiological data, which resulted in his exclusion. The study population consisted of 274 patients whose data were analyzed. The flowchart that summarizes the election of our sample is shown in Figure 1.

As for the identified immunization errors (6.4%), eleven patients had incorrect vaccine administration, six received inadequate doses of the administered vaccine, one patient had positive RT-PCR for COVID-19

at the time of vaccination, and one received the vaccine inadvertently for his age. Of these patients, there were no severe post-vaccine adverse events.

Regarding the study population, the majority was female (73%) and 267 patients were aged between 18 and 69 years (97.4%). Data such as area of residence and race/ethnicity were missing in almost all charts, which resulted in their non-evaluation in this study. Of the patients with PVAE, 17 were healthcare professionals. The mean age was 39.8 ± 14.5 years. The detailed profile of the study population is shown in Table 1.

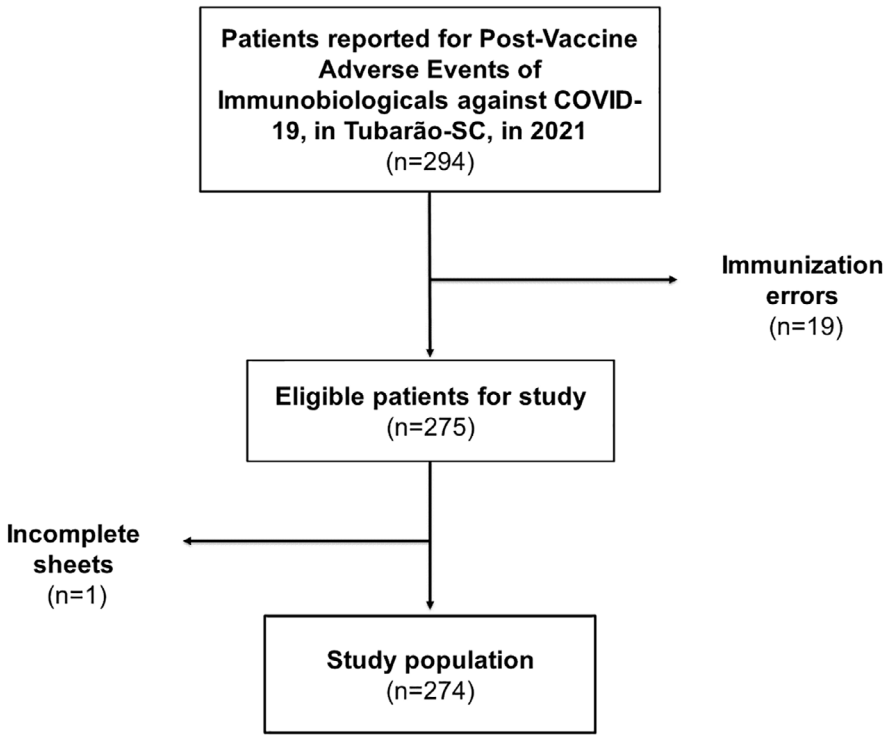

Figure 1. Flowchart of election of the study population

Table 1
Epidemiological characteristics of patients notified for post-vaccine adverse events of immunobiologicals against COVID-19 in 2021 in a municipality of Santa Catarina.

CHARACTERISTICS OF THE STUDY POPULATION	MEN		WOMEN		TOTAL	
	n	%	n	%	N	%
Age Group						
18-29 years old	18	23,7	58	76,3	76	27,7
30-49 years old	35	27,3	93	72,7	128	46,7
50-69 years old	21	33,3	42	66,7	63	23,0
70-89 years old	0	0,0	6	100,0	6	2,2
90 years and older	0	0,0	1	100,0	1	0,4
Health Professional						
Yes	3	17,6	14	82,4	17	6,2
No	71	27,6	186	72,4	257	93,8
TOTAL	**74**	**27,0**	**199**	**73,0**	**274**	**100**

The number of notifications per month was not homogeneous during the year 2021. There were no notifications in the month of January; however, the first half of the year accounted for 72.3% of all notifications, while in the following months, there were only 76 (27.7%). The average was 22.8 notifications per month. Regarding the distribution of immunobiologicals in the population and the occurrence rate of PVAEs, the main information is described in Table 2, while PVAEs are stratified by sex and age group of patients in Table 3.

At the time of this study, only five (1.8%) notifications were closed, while two (0.7%) were under evaluation and 268 (97.5%) were open, which is a limitation of the study concerning the use of notification forms. Despite this, 268 (97.5%) notifications were classified as not serious at the time of evaluation and seven (2.5%) as serious. The median for occurrence was 24 hours (2h-10 days) for the non-serious events and 8 days (1-15 days) for the serious events.

The main signs and symptoms presented by patients with PVAE varied according to the immunobiological used. The main signs and symptoms reported in the notification forms were arranged in order of frequency in Table 4. Other less common symptoms

Table 2
Immunobiologicals applied against COVID-19 and incidence rate of Post-Vaccine Adverse Events in a municipality of Santa Catarina in 2021

INDICATORS	IMMUNOBIOLOGICALS				TOTAL
	AstraZeneca	Pfizer	Coronavac	Janssen	
Doses applied	70.710	83.965	37.268	5.058	197.001
PVAE	206	43	18	7	274
Relative frequency	75%	15%	7%	3%	100%
SAE	3	3	1	0	7
Relative frequency	43%	43%	14%	0%	100%
Incidence of PVAE*	29,1	5,1	4,8	13,8	13,9
SAE* incidence	0,4	0,3	0,2	-	0,3

*Incidence rate per 10,000 doses applied.
PVAE = Post-Vaccine Adverse Events. SAE = Serious Adverse Event.

Table 3
Post-vaccine adverse events of immunobiologicals used against Covid-19 stratified by age group and sex in 2021 in a municipality of Santa Catarina

AGE RATE	SEX	ASTRAZENECA		PFIZER		CORONAVAC		JANSSEN		TOTAL	
		n	%	n	%	n	%	n	%	n	%
18-29 years old	Men	13	21,7	3	33,3	2	33,3	2	0,0	18	23,7%
	Women	47	78,3	6	66,7	4	66,7	4	100,0	58	76,3%
30-49 years old	Men	24	26,1	6	26,1	3	42,9	3	33,3	35	27,3%
	Women	68	73,9	17	73,9	4	57,1	4	66,0	93	72,7%
50-69 years old	Men	17	32,7	3	33,3	1	50,0	1	0,0	21	33,3%
	Women	35	67,3	6	66,0	1	50,0	1	0,0	42	66,7%
70-89 years old	Men	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0%
	Women	2	100,0	2	100,0	2	100,0	2	0,0	6	100,0%
90 years and older	Men	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0%
	Women	0	0,0	0	0,0	1	100,0	1	0,0	1	100,0%
TOTAL		**206**	**75,2**	**43**	**15,7**	**18**	**6,6**	**7**	**2,6**	**274**	**100%**

reported were local erythema, tremors, pruritus, tachycardia, eye redness, local induration, fainting, local heat, ageusia, anosmia, tachypnea, pancreatitis, chest pain, paresthesia, dysarthria, angioedema, hoarseness, pallor, suppurated lymphadenitis, facial paralysis, and petechiae in descending order of frequency.

Regarding women, there were two pregnant women with reported PVAEs, one at 24 weeks gestational age and the other at 32 weeks, the latter having a PVAE classified as severe. Only one woman who was breastfeeding had reported PVAE, which was classified as not severe.

The seven cases initially classified as severe had their clinical histories reviewed and the outcome evaluated as to their status in the Santa Catarina State Department, as described in Table 5.

Table 4
Main signs and symptoms reported in the records of post-vaccine adverse events notification against Covid-19 by immunobiological in the year 2021 in a municipality of Santa Catarina

SYMPTOMS	ASTRAZENECA		PFIZER		CORONAVAC		JANSSEN		TOTAL	
	n	%	n	%	n	%	n	%	n	%
Myalgia	139	67,5	24	55,8	7	38,9	5	71,4	175	63,9
Headache	110	53,4	18	41,9	6	33,3	3	42,9	137	50,0
Fever	93	45,1	9	20,9	4	22,2	5	71,4	111	40,5
Nausea	54	26,2	6	14,0	5	27,8	2	28,6	67	24,5
Chills	53	25,7	3	7,0	1	5,6	1	14,3	58	21,2
Fatigue	28	13,6	1	2,3	7	38,9	1	14,3	37	13,5
Odynophagia	22	10,7	7	16,3	4	22,2	0	0,0	33	12,0
Local pain	27	13,1	3	7,0	1	5,6	1	14,3	32	11,7
Cough	16	7,8	9	20,9	4	22,2	0	0,0	29	10,6
Diarrhea	21	10,2	2	4,7	4	22,2	2	28,6	29	10,6
Abdominal pain	20	9,7	0	0,0	2	11,1	0	0,0	22	8,0
Coryza	10	4,9	6	14,0	3	16,7	0	0,0	19	6,9
Vomiting	15	7,3	2	4,7	1	5,6	0	0,0	18	6,6
Dyspnea	10	4,9	2	4,7	1	5,6	0	0,0	13	4,7
Arthralgia	10	4,9	0	0,0	0	0,0	1	14,3	11	4,0
Nasal Congestion	4	1,9	3	7,0	3	16,7	0	0,0	10	3,6
Sleepiness	8	3,9	0	0,0	0	0,0	0	0,0	8	2,9
Asthenia	4	1,9	4	9,3	0	0,0	0	0,0	8	2,9
Local edema	5	2,4	1	2,3	0	0,0	1	14,3	7	2,6
Dizziness	6	2,9	0	0,0	1	5,6	0	0,0	7	2,6
Sneezes	5	2,4	1	2,3	0	0,0	0	0,0	6	2,2
Sweating	4	1,9	1	2,3	1	5,6	0	0,0	6	2,2

Table 5
Description of the main cases classified as serious post-vaccine adverse events in patients undergoing COVID-19 vaccination in a municipality of Santa Catarina in 2021.

IMMUNOBIOLOGICAL AND DOSE	GENDER AND AGE	CASE SUMMARY	MANAGEMENT
Pfizer D1	Female, 57 years old	Generalized pruritic rash with cough, headache, and the need for hospital admission for symptomatic control.	Contraindication with scheme substitution.

IMMUNOBIOLOGICAL AND DOSE	GENDER AND AGE	CASE SUMMARY	MANAGEMENT
AstraZeneca D1	Male, 59 years old	Influenza syndrome with signs of severity soon after the first dose, requiring hospitalization. He was diagnosed with COVID-19.	Scheme held with caution for inconsistent or coincidental causality.
Pfizer D1	Male, 20 years old	Patient with chest pain and dyspnea after 23 days of the first vaccine dose. There was an elevation of myocardial enzymes (ultrasensitive Troponin I 5.310 ng/ml), resting echocardiogram within normal range. Probable cause for post-vaccinal myocarditis.	Contraindication with scheme substitution.
Coronavac D1	Male, 22 years old	Probable immune thrombocytopenia with 8,000 platelets secondary to receiving immunobiologicals without bleeding and was discharged. Patient lost to follow-up after death from pulmonary focus sepsis two months after discharge.	Scheme closed.
AstraZeneca D1	Female, 38 years old	Pregnant woman 37 weeks and 3 days old, started with cough and palpitation, and a heart rate of 115 bpm. Test for COVID-19 was negative and she was discharged after clinical observation.	Adverse effect of the antiviral vaccine. Scheme maintained.
Pfizer D1	Woman, 88 years old	15 days after receiving immunobiologicals, the patient developed an acute ischemic stroke. Patient with previous high cardiovascular risk and documented atherosclerosis.	Scheme held with caution for inconsistent or coincidental causality.
AstraZeneca D1	Male, 20 years old	Patient with ventricular pre-excitation syndrome in follow-up since childhood, began with fever (38.7°C), fatigue, dyspnea, and tachycardia after vaccination, and heart rate control was performed in a hospital environment. Follow-up with an arrhythmologist physician.	Contraindication without substitution of the regimen due to risk of severe arrhythmia, despite the absence of a proven causal relationship.

DISCUSSION

The development of new immunobiologicals in the pandemic context of COVID-19 generated questions about their safety in the population, which was reinforced by the politicization of vaccines and dissemination of Fake News in social networks[11,12]. In a study by the Oswaldo Cruz Foundation[13], the prevalence of vaccine hesitancy for COVID-19 immunizers was 10.5% in January 2021 in Brazil, which is low when compared to a survey conducted in the United States of America in which 22% of the population stated that they would probably not receive the immunobiologicals[6]. In a report from the municipality of Tubarão-SC, vaccine adherence was 94% of the population older than 12 years for the first dose and 85% for the second dose at the end of the year 2021, which corroborates the trend of acceptance of COVID-19 vaccines in the country[14]. On the other hand, in the systematic review by Feikin and colleagues, a decrease of up to 30% in the efficacy of COVID-19 vaccines was observed after 6 months of follow-up[15]. Thus, the emergence of "non-vaccinator" individuals may threaten the vaccination coverage of various immunobiologicals in Brazil and demands guided strategies to ensure the health maintenance of the Brazilian population[16,17].

Confidence that the vaccine is safe and effective is an important predictor of vaccination intention[18]. In this study, most cases of PVAEs occurred in females aged 30-49 years, in line with data available from the "Epidemiological Report of

Santa Catarina"[19] and from Brazil[20]. In a large North American cohort[21], young and female individuals had an increased risk of having a PVAE. In the study by Xiong and collaborators[22], a higher probability of SAE occurrence was evidenced in patients aged 65 years or older and male. These findings reinforce the idea of Torjesen[23], which suggests careful evaluation of the vaccine benefit in elderly and frail patients since the occurrence of a PVAE could be the precipitating factor for the death of these patients, as was evidenced in the study by Silva and collaborators[24].

With the availability of the COVID-19 vaccine in Brazilian states, there was a significant decrease in the number of deaths and hospitalizations for the disease in all age groups in Brazil in the year 2021[25] and, with this, the post-vaccination adverse events. The proportion of occurrence of a PVAE in relation to the number of doses applied in the municipality in question was 0.13%, twice that observed in the state of Santa Catarina (0.07%)[19] and in Brazil (0.06%)[20], but one-third of that observed in a study in the state of Minas Gerais (0.45%)[24]. However, the incidence of a Serious Adverse Event (SAE) was 0.3 - very similar to the rates found in Santa Catarina (0.3), Minas Gerais (0.2) and Brazil (0.5). Therefore, we noticed a great variation in PVAE incidence in the different populations but not in SAE, which could be explained by the underreporting of mild PVAEs. There were no deaths directly related to these events in our study, which supports the idea of the safety of the use of these vaccines. Moreover, in Brazil, immunization errors accounted for 11.4% of PVAE notifications[20], approximately twice as much as found in our sample.

The clinical manifestations of non-severe PVAEs in the analyzed files were mostly mild (97.4%), especially myalgia, headache, fever, nausea and chills, which, in agreement with other studies, strengthens the idea of benignity associated with these events[20–22]. As in the national context[20], the main immunobiologicals related to the development of PVAEs were AstraZeneca and Janssen, which share similar mechanisms of action of adenovirus vectoring. The greater concern of the population with adverse events may have justified the higher number of notifications in the first half of 2021; however, these data may be influenced by at-risk populations that may be more susceptible to PVAEs.

Seven SAEs were reported in patients immunized in the municipality in southern Santa Catarina, where the present study was conducted. Although one patient developed thrombocytopenia, his clinical picture was not compatible with the thrombotic thrombocytopenic syndromes (TTS) reported in patients immunized with AstraZeneca and Janssen[20]. In a large case series of myocarditis after administration of messenger RNA-based vaccines against COVID-19[26], the prevalence of the disease was higher in males aged 12-24 years with a high-resolution rate with supportive clinical treatment, which is in line with the case reported in this study.

There was one case of SAE reported in a pregnant woman that required observation for less than 24 hours and hospital discharge. Despite the high risks regarding the use of drugs in relation to the maternal-fetal binomial, a US study of more than 3000 pregnant women did not identify patterns of adverse outcomes in these patients[27]. In the study by Menegali and collaborators[28], passive transplacental fetal immunization is suggested after vaccination of the pregnant woman in the third trimester, which requires further investigation of risks and benefits.

Because of the use of forms with secondary data, comorbidities and the outcome of the clinical cases studied were not included in most of the forms, which became a limitation of the study. Nevertheless, this work represents a synthesis of the profile of PVAEs in a population of Santa Catarina and a broad view of the most frequent signs and symptoms. Finally, when considering the results of this study, a low risk of developing HAE is suggested, which, associated with the benefit of effective vaccines[29], is paramount in maintaining the health of the Brazilian population.

CONCLUSION

Safety concerning the use of COVID-19 vaccines plays a unique role in maintaining vaccination coverage rates and perpetuating low rates of illness. Most cases of Post-Vaccine Adverse Events occurred in females aged 30-49 years immunized with AstraZeneca or Janssen. The main symptoms varied according to the age of the subjects and the immunobiologicals received, with myalgia, headache, and fever being the main symptoms reported. The overall incidence of serious events was low (3 per 100,000 doses administered), which corroborates the safety profile of available immunobiologicals against COVID-19 and reinforces their use as a control measure for SARS-CoV-2.

REFERENCES

1. Islam MA, Kundu S, Alam SS, Hossan T, Kamal MA, Hassan R. Prevalence and characteristics of fever in adult and paediatric patients with coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis of 17515 patients. Hirst JA, organizer. PLoS ONE. April 6, 2021;16(4):e0249788.
2. Chua PEY, Shah SU, Gui H, Koh J, Somani J, Pang J. Epidemiological and clinical characteristics of non-severe and severe pediatric and adult COVID-19 patients across different geographical regions in the early phase of pandemic: a systematic review and meta-analysis of observational studies. J Investig Med. June 16, 2021;jim-2021-001858.
3. Ministry of Health. Panel of cases of coronavirus disease 2019 (COVID-19) in Brazil by the Ministry of Health [Internet]. 2021. Available from: https://covid.saude.gov.br/
4. Mari J de J, Oquendo MA. Mental health consequences of COVID-19: the next global pandemic. Trends Psychiatry Psychother. september 2020;42(3):219-20.
5. Hochman G. Vacinação, varíola e a cultura da imunização no Brasil. Ciênc saúde coletiva. february 2011;16(2):375-86.
6. Khubchandani J, Sharma S, Price JH, Wiblishauser MJ, Sharma M, Webb FJ. COVID-19 Vaccination Hesitancy in the United States: A Rapid National Assessment. J Community Health. April 2021;46(2):270-7.
7. Razai MS, Chaudhry UAR, Doerholt K, Bauld L, Majeed A. Covid-19 vaccination hesitancy. BMJ. May 2021;n1138.
8. Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Imunizações e Doenças Transmissíveis. Manual de vigilância epidemiológica de eventos adversos pós-vacinação - 4ª edição [Internet]. 2020. Available from: http://bvsms.saude.gov.br/bvs/publicacoes/manual_vigilancia_epidemiologica_eventos_vacinacao_4ed.pdf
9. Freeman D, Loe BS, Yu LM, Freeman J, Chadwick A, Vaccari C, et al. Effects of different types of written vaccination information on COVID-19 vaccine hesitancy in the UK (OCEANS-III): a single-blind, parallel-group, randomised controlled trial. The Lancet Public Health. May 2021;S2468266721000967.
10. Kaur RJ, Dutta S, Bhardwaj P, Charan J, Dhingra S, Mitra P, et al. Adverse Events Reported From COVID-19 Vaccine Trials: A Systematic Review. Ind J Clin Biochem [Internet]. 27 March 2021 [cited 19 May 2021]; Available from: http://link.springer.com/10.1007/s12291-021-00968-z
11. Galhardi CP, Freire NP, Fagundes MCM, Minayo MC de S, Cunha ICKO. Fake News and vaccine hesitancy in the COVID-19 pandemic in Brazil. Ciênc saúde coletiva. may 2022;27(5):1849-58.
12. Freitas MBA de, Oliveira M de S, Maciel IME. COVID 19 VACCINE ADHERENCE BY THE UNIFUNEC ACADEMIC COMMUNITY. Unifunec Ci Health and Biol. june 15, 2021;4(7):1-14.
13. Moore DCBC, Nehab MF, Camacho KG, Reis AT, Junqueira-Marinho M de F, Abramov DM, et al. Low COVID-19 vaccine hesitancy in Brazil. Vaccine. October 2021;39(42):6262-8.
14. Nery N, Ticona JPA, Cardoso CW, Prates APPB, Vieira HCA, Salvador de Almeida A, et al. COVID-19 vaccine hesitancy and associated factors according to sex: A population-based survey in Salvador, Brazil. Kumar S, organizer. PLoS ONE. January 21, 2022;17(1):e0262649.
15. Feikin DR, Higdon MM, Abu-Raddad LJ, Andrews N, Araos R, Goldberg Y, et al. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. The Lancet. March 2022;399(10328):924-44.
16. Sato APS. What is the importance of vaccine hesitancy in the decline of vaccine coverage in Brazil? Rev Saude Publica. 2018;52:96.
17. Succi RC de M. Vaccine refusal - what we need to know. J Pediatr (Rio J) [Internet]. 2018Nov;94(J. Pediatr. (Rio J.), 2018 94(6)). Available from: https://doi.org/10.1016/j.jped.2018.01.008.
18. Padamsee TJ, Bond RM, Dixon GN, Hovick SR, Na K, Nisbet EC, et al. Changes in COVID-19 Vaccine Hesitancy Among Black and White Individuals in the US. JAMA Netw Open. Jan 21, 2022;5(1):e2144470.
19. MONITORING POST-VACCINATION ADVERSE EVENTS (PAPV) AGAINST COVID-19 IN SANTA CATARINA [Internet]. 2022. Available from: https://www.dive.sc.gov.br/phocadownload/doencas-agravos/COVID%2019/boletim-EAPV-2022-2.pdf
20. Ministry of Health. SPECIAL EPIDEMIOLOGICAL BULLETIN - New Coronavirus Disease - COVID-19 [Internet]. 2021. Available at: https://www.gov.br/saude/pt-br
21. Beatty AL, Peyser ND, Butcher XE, Cocohoba JM, Lin F, Olgin JE, et al. Analysis of COVID-19 Vaccine Type and Adverse Effects Following Vaccination. JAMA Netw Open. 22 December 2021;4(12):e2140364.
22. Xiong X, Yuan J, Li M, Jiang B, Lu ZK. Age and Gender Disparities in Adverse Events Following COVID-19 Vaccination: Real-World Evidence Based on Big Data for Risk Management. Front Med. July 19, 2021;8:700014.
23. Torjesen I. Covid-19: Pfizer-BioNTech vaccine is "likely" responsible for deaths of some elderly patients, Norwegian review finds. BMJ. May 27, 2021;n1372.
24. Silva RB da, Silva TPR da, Sato APS, Lana FCF, Gusmão JD, Souza JFA, et al. Post-vaccination adverse events against SARS-CoV-2 (covid-19) in the state of Minas Gerais. Rev saúde pública. October 22, 2021;55:66.
25. Oswaldo Cruz Foundation. Covid-19 Observatory [Internet]. 2021. Available at: https://portal.fiocruz.br/observatorio-covid-19
26. Oster ME, Shay DK, Su JR, Gee J, Creech CB, Broder KR, et al. Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the US From December 2020 to August 2021. JAMA. January 25, 2022;327(4):331.

27. Moro PL, Olson CK, Clark E, Marquez P, Strid P, Ellington S, et al. Post-authorization surveillance of adverse events following COVID-19 vaccines in pregnant persons in the vaccine adverse event reporting system (VAERS), December 2020 - October 2021. Vaccine. May 2022;40(24):3389-94.

28. Menegali BT, Schuelter-Trevisol F, Barbosa AN, Izidoro TM, Feurschuette OHM, Marcon CEM, et al. Vertical transmission of maternal COVID-19 antibodies after CoronaVac vaccine: A case report. Rev Soc Bras Med Trop. 2021;54:e0385-2021.

29. Ssentongo P, Ssentongo AE, Voleti N, Groff D, Sun A, Ba DM, et al. SARS-CoV-2 vaccine effectiveness against infection, symptomatic and severe COVID-19: a systematic review and meta-analysis. BMC Infect Dis. December 2022;22(1):439.

All authors contributed equally to all stages of this manuscript: design, submission to the Research Ethics Committee, data collection, analysis, writing of the final arti-cle, and review.

The study was carried out at the Universidade do Sul de Santa Catarina (UNISUL). This study received funding from the Institutional Program of Scholarships for Scien-tific Initiation (PIBIC) of UNISUL linked to the National Council for Scientific and Technological Development. We declare no conflicts of interest.

Corresponding Author:
Henrique Guimarães Aires e Silva
henriqueimbituba@hotmail.com

Editor:
Ada Clarice Gastaldi

Received in: oct 18, 2022
Approved in: mar 02, 2023
