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Brief communication

Surveillance of adverse events associated with 145 000 doses of COVID-19 vaccines in a Brazilian municipality

Paulo Ricardo Martins-Filho,[1] Ricardo Ruan Rocha Santana,[2] Taise Ferreira Cavalcante,[3] Waneska de Souza Barboza,[4] Mércia Feitosa de Souza,[5] Marco Aurelio de Oliveira Góes,[2] Ângela Marinho Barreto Fontes,[5] Marcia Estela Lopes da Silva[5] and Diego Moura Tanajura[1]

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ABSTRACT There is a lack of real-world surveillance studies on reports of adverse events associated with COVID-19 vaccination, as well as comparative analyses of adverse events from vaccines with different platforms. This observational, descriptive, retrospective study based on secondary data describes the adverse events following immunization (AEFIs) related to the first 145 000 doses of COVID-19 vaccines delivered in Aracaju municipality, Sergipe state, northeast Brazil. Records of AEFIs were collected using the e-SUS Notifica database for January 19 to April 30, 2021. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for AEFIs and the type of COVID-19 vaccine, either CoronaVac (Sinovac–Butantan) or Oxford–AstraZeneca (Fiocruz). A total of 474 AEFIs (32.7 events/10 000 doses) from 254 individuals were reported and analyzed, and all of them were classified as non-serious. There was an association between the use of the CoronaVac vaccine and headache (OR = 2.1; 95% CI: 1.4–3.2), pain at the injection site (OR = 9.6; 95% CI: 3.9–23.8), lethargy (OR = 5.2; 95% CI: 1.8–14.8), fatigue (OR = 10.1; 95% CI: 2.4–42.3), diarrhea (OR = 4.4; 95% CI: 1.5–12.5) and cold-like symptoms (OR = 8.0; 95% CI: 1.9–34.0). However, the proportion of individuals reporting fever was higher among those who received the Oxford–AstraZeneca vaccine (OR = 3.1; 95% CI 1.5–6.4). This population-based observational study strengthens the evidence for the safety and tolerability of the CoronaVac and Oxford–AstraZeneca vaccines used against COVID-19.

Keywords COVID-19; SARS-CoV-2; COVID-19 vaccines; drug-related side effects and adverse reactions; injection site reaction.

Mass vaccination is the most cost-effective measure to control and prevent infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The available vaccines have 50–95% effectiveness in preventing severe outcomes from coronavirus disease 2019 (COVID-19) and have been shown to be safe in clinical trials (1–5). Despite adverse events following immunization (AEFIs) being well documented in vaccine trials, post-approval surveillance of these is critical to improve safety and maintain public confidence in a vaccination program (6). There is a lack of real-world surveillance studies of AEFIs associated with COVID-19 vaccination, as well as a lack of comparative analyses of adverse events from vaccines using different platforms.

This observational, descriptive, retrospective study based on secondary data describes the AEFIs related to the first 145 000

[1] Investigative Pathology Laboratory, Federal University of Sergipe, Aracaju, Sergipe, Brazil ✉ Paulo Ricardo Martins-Filho, prmartinsfh@gmail.com
[2] Department of Medicine, Federal University of Sergipe, Lagarto, Sergipe, Brazil
[3] Health Sciences Graduate Program, Federal University of Sergipe, Aracaju, Sergipe, Brazil
[4] Municipal Health Secretariat, Aracaju City Hall, Aracaju, Brazil
[5] State Health Secretariat, Government of Sergipe State, Aracaju, Brazil

doses of COVID-19 vaccines delivered in Aracaju municipality, Sergipe state, northeast Brazil. Aracaju is one of the poorest regions in the country, has an area of 182.2 km^2, and has an estimated population of 657 053 inhabitants. On March 14, 2020, the first case of COVID-19 was identified in a female patient who had traveled to Spain; on April 2, 2020, the first death from the disease was officially confirmed. At the time of writing this manuscript in 2022, SARS-CoV-2 had infected 150 303 individuals and resulted in 2558 deaths. In Brazil, CoronaVac (a Sinovac–Butantan product) was the first vaccine approved for use against COVID-19 and was delivered primarily to elderly people, health care workers and members of Indigenous communities, all of whom were considered priority groups for immunization at the beginning of the vaccination campaign. In Aracaju, the first doses of the vaccine were administered on January 19, 2021. In early February 2021, the first doses of the Oxford–AstraZeneca vaccine (produced in Brazil by Fiocruz) were administered.

Records of AEFIs were collected using the e-SUS Notifica database for January 19 to April 30, 2021. The e-SUS Notifica database was launched in Brazil on March 27, 2020, and it has been used as a passive surveillance system by public and private health professionals to notify AEFIs occurring within 30 days of vaccination. If an adverse event occurs, the patient is followed up until it resolves. For this study, information about age, sex, type of COVID-19 vaccine, and AEFIs was extracted. Adverse events were classified as serious or non-serious. Serious adverse events included death, life-threatening illness, hospitalization or prolongation of hospitalization, and permanent disability. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for associations between AEFIs and the type of COVID-19 vaccine (CoronaVac vs. Oxford–AstraZeneca). In the case of zero events, a continuity correction of 0.5 was used. Analyses were performed using JASP software version 0.13 (JASP, Amsterdam, the Netherlands).

Between January 19 and April 30, 2021, 145 133 doses of COVID-19 vaccine were administered: 85 587 were CoronaVac and 59 546 were Oxford–AstraZeneca. A total of 474 AEFIs were reported (32.7 events/10 000 doses) from 254 individuals (mean age: 41 years; standard deviation: 9.8; 208/254 [81.9%] female) and analyzed, and all of them were classified as non-serious events. Of the 254 individuals with AEFIs, 221 (87%) received CoronaVac and 33 (13%) received Oxford–AstraZeneca. The most common AEFIs were headache (7.7 events/10 000 doses), pain at the injection site (5.1/10 000 doses), myalgia or arthralgia (3.3/10 000 doses), nausea or vomiting (2.6/10 000 doses), and fever (2.4/10 000 doses). We found an association between the use of CoronaVac and headache (OR = 2.1; 95% CI: 1.4–3.2; $P < 0.001$), pain at the injection site (OR = 9.6; 95% CI: 3.9–23.8; $P < 0.001$), lethargy (OR = 5.2; 95% CI: 1.8–14.8; $P = 0.002$), fatigue (OR = 10.1; 95% CI: 2.4–42.3; $P = 0.002$), diarrhea (OR = 4.4; 95% CI: 1.5–12.5; $P = 0.006$) and cold-like symptoms (OR = 8.0; 95% CI: 1.9–34.0; $P = 0.005$). However, the proportion of individuals reporting fever was higher among those who received the Oxford–AstraZeneca vaccine (OR = 3.1; 95% CI: 1.5–6.4; $P = 0.002$) (Table 1).

In this real-world surveillance study, we observed a rate of approximately 33 adverse events per 10 000 doses of COVID-19 vaccine during the first 3 months of the vaccination campaign in a Brazilian municipality. Despite the rate of AEFIs being lower than that shown in previous Phase 1 and 2, randomized controlled trials (7, 8), our findings also demonstrated that adverse events were mild and self-limited and included primarily headache and local pain at the injection site. Moreover, no life-threatening complications were reported, which indicates that these vaccines are well tolerated and have minor safety issues.

TABLE 1. Association between adverse events following immunization and type of COVID-19 vaccine, Brazil, 2021

Type of adverse event following immunization	Type of COVID-19 vaccine						OR (95% CI)	*P* value
	Both types (*N* = 145 133 doses)		CoronaVac (Sinovac–Butantan) (*n* = 85 587 doses)		Oxford–AstraZeneca (Fiocruz) (*n* = 59 546 doses)			
	n	No. of events/ 10 000 doses	*n*	No. of events/ 10 000 doses	*n*	No. of events/ 10 000 doses		
Headache	112	7.7	84	9.8	28	4.7	2.1 (1.4–3.2)	< 0.001
Pain at injection site	74	5.1	69	8.1	5	0.8	9.6 (3.9–23.8)	< 0.001
Myalgia or arthralgia	48	3.3	27	3.2	21	3.5	1.1 (0.6–2.0)	0.702
Nausea or vomiting	38	2.6	26	3.0	12	2.0	1.5 (0.8–3.0)	0.240
Fever	35	2.4	11	1.3	24	4.0	3.1 (1.5–6.4)	0.002
Drowsiness or lethargy	34	2.3	30	3.5	4	0.7	5.2 (1.8–14.8)	0.002
Fatigue	31	2.1	29	3.4	2	0.3	10.1 (2.4–42.3)	0.002
Diarrhea	29	2.0	25	2.9	4	0.7	4.4 (1.5–12.5)	0.006
Cold-like symptoms	25	1.7	23	2.7	2	0.3	8.0 (1.9–34.0)	0.005
Abdominal pain	20	1.4	16	1.9	4	0.7	2.8 (0.9–8.3)	0.067
Local reaction (erythema, induration, swelling)	16	1.1	10	1.2	6	1.0	1.2 (0.4–3.2)	0.774
Dizziness	9	0.6	8	0.9	1	0.2	5.6 (0.7–44.5)	0.106
Shortness of breath	2	0.1	2	0.2	0	0.0	3.5 (0.2–72.5)	0.421
Lymphadenopathy	1	0.1	1	0.1	0	0.0	2.1 (0.1–51.2)	0.652

CI: confidence interval; OR: odds ratio.

Although associations between specific vaccine platforms and adverse events are poorly understood, viral vector vaccines carry information that might be critical for the enhancement of proinflammatory cytokines, leading to an intense systemic response (9). In this study, immunization with Oxford–AstraZeneca – a replication-deficient chimpanzee adenovirus–vector vaccine encoding the SARS-CoV-2 Spike glycoprotein – was strongly associated with the occurrence of fever. This finding is in agreement with a previous study from Thailand that found a higher frequency of individuals reporting fever after vaccination with the chimpanzee adenovirus–vector vaccine compared with those receiving a whole-cell inactivated vaccine (10). However, in our study, individuals receiving the inactivated SARS-CoV-2 vaccine were more likely to experience headache, local pain, lethargy, fatigue, diarrhea and cold-like symptoms.

Our results should be interpreted with caution due to the inherent limitations of spontaneous (passive) surveillance and the lack of analysis of sex- and age-based differences regarding the adverse events. However, this population-based observational study reinforces the safety and tolerability of the CoronaVac and Oxford–AstraZeneca vaccines used against COVID-19.

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Vigilancia de eventos adversos asociados a 145 000 dosis de vacunas contra la COVID-19 en un municipio brasileño

RESUMEN Hay una carencia de estudios de vigilancia en el mundo real sobre la notificación de eventos adversos asociados a la vacunación contra la COVID-19, así como de análisis comparativos de los eventos adversos de vacunas con diferentes plataformas. En este estudio observacional, descriptivo y retrospectivo basado en datos secundarios se describen los eventos adversos supuestamente atribuibles a la vacunación o inmunización (ESAVI) relacionados con las primeras 145 000 dosis de vacunas contra la COVID-19 administradas en el municipio de Aracaju, estado de Sergipe, en la región Noreste de Brasil. Se recopilaron registros de los ESAVI del 19 de enero al 30 de abril del 2021 con la base de datos e-SUS Notifica. Se calcularon las razones de posibilidades (OR, por su sigla en inglés) y los intervalos de confianza (IC) del 95 % para los ESAVI y el tipo de vacuna contra la COVID-19 (CoronaVac [Sinovac-Butantan] o bien Oxford-AstraZeneca [Fiocruz]). Se notificaron y analizaron un total de 474 ESAVI (32,7 eventos/10 000 dosis) de 254 personas, y todos se clasificaron como no graves. Se encontró una relación entre el empleo de la vacuna CoronaVac y la cefalea (OR = 2,1; IC del 95 %: 1,4–3,2), dolor en el lugar de la inyección (OR = 9,6; IC del 95 %: 3,9–23,8), letargo (OR = 5,2; IC del 95 %: 1,8–14,8), cansancio (OR = 10,1; IC del 95 %: 2,4–42,3), diarrea (OR = 4,4; IC del 95 %: 1,5–12,5) y síntomas similares al resfriado (OR = 8,0; IC del 95 %: 1,9 a 34,0). Sin embargo, la proporción de pacientes que notificaron fiebre fue mayor entre los que recibieron la vacuna de Oxford-AstraZeneca (OR = 3,1; IC del 95 %: 1,5 a 6,4). Este estudio observacional poblacional refuerza la evidencia sobre la seguridad y tolerabilidad de las vacunas CoronaVac y Oxford-AstraZeneca empleadas contra la COVID-19.

Palabras clave COVID-19; SARS-CoV-2; vacunas contra la COVID-19; efectos colaterales y reacciones adversas relacionados con medicamentos; reacción en el punto de inyección.

Vigilância de eventos adversos associados a 145 mil doses de vacinas contra a COVID-19 em um município brasileiro

RESUMO Faltam estudos de vigilância no mundo real sobre relatórios de eventos adversos associados à vacinação contra a COVID-19, bem como análises comparativas de eventos adversos decorrentes de vacinas com diferentes plataformas. Este estudo observacional, descritivo e retrospectivo baseado em dados secundários descreve os eventos adversos pós-vacinação (EAPV) relacionados com as primeiras 145 mil doses de vacinas contra a COVID-19 entregues no município de Aracaju, capital do estado de Sergipe, na região Nordeste do Brasil. Os registros de EAPV foram coletados usando o sistema e-SUS Notifica com referência ao período de 19 de janeiro a 30 de abril de 2021. Razões de chances (*odds ratios*, ORs) e intervalos de confiança (IC) de 95% foram calculados para os EAPV e o tipo de vacina contra a COVID-19: CoronaVac (Sinovac-Butantan) ou Oxford-AstraZeneca (Fiocruz). Um total de 474 EAPV (32,7 eventos/10 mil doses) de 254 indivíduos foram relatados e analisados, e todos foram classificados como não graves. Houve uma associação entre o uso da vacina CoronaVac e cefaleia (OR = 2,1; IC 95%: 1,4-3,2), dor no local da injeção (OR = 9,6; IC 95%: 3,9-23,8), letargia (OR = 5,2; IC 95%: 1,8-14,8), cansaço (OR = 10,1; IC 95%: 2,4-42,3), diarreia (OR = 4,4; IC 95%: 1,5-12,5 e sintomas gripais (OR = 8,0; IC 95%: 1,9-34,0). Contudo, a proporção de indivíduos que relataram febre foi superior entre os que receberam a vacina Oxford-AstraZeneca (OR = 3,1; IC 95%: 1,5-6,4). Este estudo observacional de base populacional reforça as evidências da segurança e tolerabilidade das vacinas CoronaVac e Oxford-AstraZeneca usadas contra a COVID-19.

Palavras-chave COVID-19; SARS-CoV-2; vacinas contra COVID-19; efeitos colaterais e reações adversas relacionados a medicamentos; reação no local da injeção.