Original Article

COVID-19 Vaccination Adverse Events in Children: An Investigation with a Control Group in Tabriz Metropolitan City

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ABSTRACT

The occurrence of adverse events following vaccination with the novel coronavirus disease 2019 (COVID-19) vaccine in children remains somewhat unclear, with only a limited number of population-based studies having been conducted in this age group. The objective of this study is to ascertain the short-term adverse events associated with the Sinopharm and Soberana (Pasto CoVac) vaccination in children between the ages of 5 and 12. This study employs an observational design with a control group. The cluster sampling method was employed to recruit the study samples, with healthcare centers and mass vaccination centers of Tabriz designated as clusters. The ratio of the vaccinated and unvaccinated groups was 2:1, respectively. Information was gathered via telephone interviews with the parents or guardians of the subjects. The data were analyzed using a mixed-effect logistic regression model. In this study, a total of 913 children were investigated, comprising 577 vaccinated and 336 unvaccinated children. The results demonstrated that the most frequent complication among the vaccinated children was injection site pain, occurring in 178 cases (30.8%, 95% CI:(27%, 35%)) The most frequently reported systemic adverse events among vaccinated and unvaccinated children were fever (9.0% vs. 3.6%, p = 0.003), fatigue (5.5% vs. 0.9%, p = 0.002), and headache (2.9% vs. 0.6%, p = 0.032). No serious adverse events, including myocarditis, multisystem inflammatory syndrome (MIS), or hospitalization, were reported. The odds of experiencing any symptoms in the vaccinated group, adjusted for potential confounding variables, were significantly higher than in the control group (adjusted OR = 4.71, CI 95%: (3.04, 7.26), with a p-value of less than 0.001. The results indicate that the Sinopharm and Soberana (PastoCoVac) vaccines did not have any serious adverse effects. Moreover, it appears that some of the reported adverse events in other studies may be overestimated due to the absence of a control group.

Keywords: COVID-19, Adverse Reactions, Adverse events, Vaccination, Children

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1. Introduction

The ongoing Coronavirus Disease 2019 (Covid-19) pandemic represents a significant global public health threat. As of December 24, 2023, the World Health Organization (WHO) has documented over 773 million cases of coronavirus disease 2019 (Covid-19), with over 6.9 million associated deaths (2). In the same time period, more than 7.62 million cases and 146,751 cumulative deaths have been reported to the World Health Organization (WHO) in Iran (2). Moreover, over 13 billion doses of the SARS-CoV-2 vaccine have been administered globally, with over 155 million doses administered in Iran. The findings of the studies indicated that the hospitalization and mortality rates of patients with confirmed cases of SARS-CoV-2 infection who had not received the full vaccination regimen were significantly higher compared to individuals who had received the complete vaccination series, specifically two weeks after the administration of the second dose of the vaccine (4). The vaccination of children has been demonstrated to reduce the severity of infection and the mortality rate associated with the disease. Furthermore, it serves to prevent the spread of disease and to achieve herd immunity (5, 6). A large multi-country trial demonstrated that administration of two doses of the Sinopharm vaccine has an efficacy of 79% against symptomatic SARS-CoV-2 infection 14 or more days after the second dose. The vaccine has been demonstrated to be 79% effective in preventing hospitalization (2). PastoCovac (Soberana 02) is produced at the Pasteur Institute of Iran in collaboration with the Finlay Vaccine Institute of Cuba. It is a recombinant protein vaccine comprising a highly immunogenic region of the SARS-CoV-2 Spike (RBD) protein, conjugated to the tetanus toxin. Additionally, PasteoCovac Plus (Soberana Plus) serves as the booster dose of the candidate vaccine, comprising a dimer of RBD (50 µg) (7, 8). Sinopharm Beijing has developed an inactivated SARS-CoV-2 virus vaccine (Sinopharm BBIBP-CorV) utilizing the chemical β-propiolactone. The vaccine is treated with an aluminum-based adjuvant, which enhances its immunogenicity. It is recommended that two doses of the vaccine, administered 21 to 28 days apart, be administered to prevent SARS-CoV-2 infection. The vaccine should be stored at a temperature between 2 and 8 degrees Celsius (9). Iran has initiated a vaccination campaign targeting children between the ages of 5 and 12 with the Sinopharm and Soberana (PastoCoVac) vaccines. The vaccination regimen consists of two doses, administered with an interval of at least 28 days between each injection. Vaccination services in Iran are provided free of charge under the supervision of medical sciences universities and in healthcare centers and mass vaccination centers. The study examined the adverse events of the Sinopharm and Soberana (PastoCoVac) vaccines among individuals under the age of 18 in Tehran. The most frequently reported adverse events were pain at the injection site, fever, fatigue, and headache (10). The adverse events of the Soberana (PastoCoVac) vaccine in children have been investigated during two phases of the clinical trial. Following this, the vaccine was approved for emergency use in children and adolescents by Cuba's regulatory authority. However, it has not yet been approved by the WHO or the FDA. To date, the Soberana (PastoCoVac) vaccine has been approved for use in only four countries: Iran, Cuba, Venezuela, and Nicaragua (11). Notwithstanding considerable advancement in the administration of the SARS-CoV-2 vaccine and a notable decline in the incidence of severe illness, hospitalization, and mortality, the trajectory of the pandemic remains uncertain, and the road ahead is likely to be challenging. It is therefore imperative to sustain and enhance vaccination efforts, including the administration of booster doses, in accordance with the recommendations set forth by the World Health Organization (WHO). The dearth of empirical data concerning the potential adverse effects of currently available SARS-CoV-2 vaccines for pediatric populations in Iran may dissuade parents from participating in vaccination initiatives. Consequently, further well-designed studies are required to generate high-quality information regarding the side effects of the available COIVD-19 vaccines in children. The incidence of complications appears to vary between vaccinated and unvaccinated individuals. Accordingly, the present observational study with a control group was designed to determine the short-term adverse events attributed to the SARS-CoV-2 vaccination in children aged 5 to 12 years and to identify any differences between the two groups in Tabriz City.

2. Materials and Methods

2.1 Study Design

This observational study was conducted from March 2022 to September 2022 in the Tabriz metropolitan city (Iran) with the objective of evaluating the short-term adverse events associated with the administration of the SARS-CoV-2 vaccine in children aged 5 to 12 years. The present study compared children who received one or more doses of the SARS-CoV-2 vaccine (the exposed or vaccinated group) to children who did not receive any SARS-CoV-2 vaccine (the control or unvaccinated group) with respect to the occurrence of probable short-term adverse effects associated with the vaccine. The target population for this study was children between the ages of 5 and 12. However, to obtain the necessary data, parents or guardians of the children were interviewed via telephone. The Health Integrated Registration System (SIB), which is utilized for the documentation of all primary healthcare services and vaccinations in Iran, was previously employed for the recruitment of study participants at selected centers. Children aged 5 to 12 who had received the vaccination for the novel coronavirus (SARS-CoV-2) at the randomly selected centers (five healthcare facilities and one mass vaccination center) were invited to participate in the study as members of the vaccinated group. Children aged 5 to 12 who had not received the SARS-CoV-2 vaccine constituted

the control group for the study. The unvaccinated cohort was selected from the same health centers as the vaccinated cohort. The children in question were under the care of the health centers in question, and their contact information had been recorded in the SIB system. The selection of the control group was conducted in conjunction with the case group, with the objective of ensuring temporal alignment. One week following the administration of the vaccine, the selected cases were contacted for a follow-up interview. Concurrently, the parents or guardians of the selected controls who had consented to participate in the study were contacted via telephone for an interview. In calculating the sample size for the vaccinated and unvaccinated groups, a ratio of 2:1 was considered. The sample size formula for comparing two independent proportions was employed to estimate the requisite sample size. Considering a 3% prevalence of fever, the primary symptom, in the control group and an 8% prevalence in the vaccinated group (a 5% difference between the two groups), a 5% type I error, an 80% statistical power, and a coefficient of 1.2 for the design effect of cluster sampling, the sample size was estimated to be 617 in the vaccinated group and 309 in the control group. The cluster sampling method was employed for the purpose of recruiting the study sample. In consideration of healthcare centers and mass vaccination centers as clusters, five such centers and centers for mass vaccination for the treatment of patients with the novel coronavirus (2019-nCoV) were randomly selected.

2.2 Data Collection

The data were collected using a checklist developed by the researcher and a telephone interview with one of the parents of the study population. The checklist was developed based on a comprehensive literature review and input from subject matter experts. It comprises the following items: Baseline characteristics (age, height, weight, parents' education, occupation, and place of residence), underlying diseases (type 1 diabetes, asthma, hemoglobinopathy, convulsion, immune system deficiency, allergy, and other diseases), history of SARS-CoV-2 infection and presentation of SARS-CoV-2-like symptoms, or short-term side effects of vaccine, including pain at the injection site (only in vaccinated children). The following symptoms were recorded: weakness and fatigue, headache, sore throat, cough, sneezing, runny nose, fever, chills, abdominal pain, anorexia, nausea, vomiting, diarrhea, skin rashes, shallow breathing, chest pain, muscle pain, bone pain, and joint pain. The date of presentation, medical visits, and medication taken during the seven-day follow-up period were also recorded for both the vaccinated and unvaccinated groups. As the data were collected via parental interviews with consent, and no sensitive personal, cultural, or socio-economic questions were posed, no missing data were encountered. In the case of recurrent events in a single individual following multiple doses, only a single occurrence was counted; thus, pooled adverse events occurring in all doses were reported. This study was approved by the ethics committee of Tabriz University of Medical Sciences (ethics code: IR.TBZMED.REC.1401.176). Telephone interviews were conducted with the consent of the parents or legal guardians of the children. Parents who did not consent to participate in the telephone interview were excluded from the study.

2.3 Data Analysis

The study findings are presented using descriptive and analytic statistics. The prevalence of adverse events/symptoms was reported for both groups, and the difference in the prevalence of the complication between the two groups was considered to be a complication attributed to vaccination. A comparison of the two groups with regard to the occurrence of adverse events and other qualitative and quantitative variables was conducted using a generalized mixed-effects linear model, which accounted for the cluster sampling design. To ascertain the impact of vaccination on adverse events while accounting for potential confounding variables, a multivariable model was constructed to analyze the data. Two-tailed tests with a significance level of 0.05 were conducted for the purpose of data analysis. The data were analyzed using the statistical software package SPSS 26.

3. Results

In this study, the reduction in the number of vaccinations permitted the collection of data from 913 subjects aged 5 to 12 years, of whom 577 (63.2%) had received at least one vaccination and 336 (36.8%) had not been vaccinated. Table 1 presents the background characteristics of the enrolled participants, classified according to the vaccine type. The mean age of the vaccinated cohort was approximately 8.9 years (standard deviation (SD) = 1.9), which was higher than that of the unvaccinated cohort (7.7 years (SD = 2.0)). The majority of vaccinated children had received the Sinopharm vaccine (444, 76.9%), followed by the Soberana (PastoCoVac) vaccine (133, 23.1%). Of the vaccine recipients, 241 (40.0%) had received their first dose, while 346 (60.0%) had received a second dose. There were no fatal or serious adverse events, including myocarditis and MIS-C, in either group. Table 2 presents a comprehensive account of all severe adverse events (respiratory) occurring within seven days post-vaccination. A total of 234 vaccinated participants (40.6%, CI95%: 36.5% to 44.7%) and 44 unvaccinated participants (13.1%, CI95%: 9.7% to 17.2%) reported at least one of the pooled adverse events occurring in all doses ($p < .001$). Thus, the attributable risk of the vaccine for experiencing at least one of the adverse events was 27.5% (95% CI: 22.11% to 32.89%). The multivariable mixed-effect logistic regression model revealed that the probability of experiencing any symptoms was significantly higher in the vaccinated group than in the control group, after adjusting for age, BMI, gender, underlying diseases, and previous infection with SARS-CoV-2 (adjusted OR = 4.71, CI 95%: (3.04, 7.26), p-value < .001).

Table 1. Background characteristics of the participants

Variable	Vaccinated Children with Soberana (n=133)	Vaccinated Children with Sinopharm (n=444)	Unvaccinated children (n=336)	P-value
Gender, n(%)				
Male	66 (49.62)	235(52.92)	155 (46.13)	0.79
Female	67 (50.38)	209 (47.07)	181 (53.87)	
Age, Mean (SD)	8.95 (1.88)	8.83 (1.93)	7.71 (2.02)	<.001
Weight, Mean (SD)	34.53 (12.23)	32.88 (11.28)	26.99 (9.93)	<.001
Height, Mean (SD)	136.44 (14.72)	134.54 (13.81)	126.8 (13.80)	<.001
History of Covid-19 (Yes), n(%)	57 (42.85)	139 (31.30)	58 (17.26)	<.001
Underlying Diseases, n(%)				
Nothing	118 (89.4)	404 (91.00)	282 (83.93)	0.16
Diabetes type 1	0 (0.00)	0 (0.00)	2 (0.60)	
Asthma	4 (3.00)	7 (1.60)	9 (2.68)	
Hemoglobinopathies	3 (2.30)	7 (1.60)	14 (4.17)	
Convulsion	2 (1.50)	7 (1.60)	4 (1.19)	
Immune System Deficiency	1 (.80)	9 (2.00)	0 (0.00)	
Allergy	4 (3.00)	10 (2.30)	16 (4.76)	

Table 2. Unsolicited pooled adverse events occur in all doses within 7 days after vaccination, overall safety set.

Adverse events	Vaccinated Children (n=577)	Unvaccinated children (n=336)	P-value*	p-value **
Having at least one adverse event	234 (40.55)	44 (13.10)	<.001	<.001
Having at least one respiratory adverse event	33 (5.72)	29 (8.66)	.05	.46

*p-value was calculated from the univariable mixed effect logistic regression model by considering healthcare centers as a random effect.
** p-value was calculated from the multivariable mixed effect logistic regression model by considering healthcare centers as a random effect adjusting for age, BMI, gender, Underlying Diseases, and Previous COVID-19 infection.

Among the vaccinated cohort, the most frequently reported adverse event was injection site pain, with 178 participants (30.8%, 95% CI:(27%, 35%)) experiencing this outcome. With the exception of injection site pain, all adverse events were reported by both vaccinated and unvaccinated groups (Table 3). Local reactions, particularly injection site pain, constituted the most prevalent reported complication. The most frequently reported systemic adverse events among vaccinated and unvaccinated children were fever (9.0% vs. 3.6%), fatigue (5.5% vs. 0.9%), and headache (2.9% vs. 0.6%). The incidence of these adverse events was significantly higher among the vaccinated cohort. It is noteworthy that, with the exception of nausea (1.6% of vaccinated individuals vs. 0% of unvaccinated individuals, p-value=0.030), the prevalence of the remaining gastrointestinal, respiratory, and musculoskeletal adverse events was comparable between the two groups. Approximately 3% of the vaccinated and 2% of the unvaccinated participants were referred to health centers due to adverse events associated with the vaccine or the disease. Approximately 25% of the vaccinated cohort and only 4.5% of the unvaccinated cohort took medication to prevent or alleviate the adverse effects of the vaccine or disease. No adverse events resulted in the need for hospitalization. The frequency of adverse events is presented in Table 4, stratified by the dose of vaccination.

As evidenced by the data presented in this table, there were no instances of recurrent events. The objective of this study was to assess the adverse events associated with the vaccination between recipients of the Sinopharm and Soberana vaccines, as well as those occurring after the first and second doses. The prevalence of symptoms and injection site pain among recipients of the Soberana vaccine was significantly higher than that among recipients of the Sinopharm vaccine (p-value <0.001). No statistically significant differences were observed in the incidence of other adverse events. Only fatigue and musculoskeletal adverse events following the initial dose were more prevalent than following the second dose. A greater proportion of vaccinated participants (90.3%) who experienced adverse events and a smaller proportion of unvaccinated participants (27.5%) reported that the complication(s) manifested on the first day following vaccination. On the second and third days or later post-vaccination, 3.9% and 6.0% of vaccinated participants, and 17.5% and 55.0% of unvaccinated participants, respectively, were reported ($p < 0.001$). The timing of adverse events did not exhibit a statistically significant difference based on the administered dose and vaccine type. Furthermore, the observed timing was consistent across both vaccinated and unvaccinated participants.

Table 3. Summary of unsolicited adverse events ≥0.1%, within 7 days after vaccination, overall safety set.

Adverse events, n (%)	Vaccinated Children (n=577)	Unvaccinated children (n=336)	Attributed risk% (CI 95%)	P-value*
Number of participants reporting at least one of the adverse events	234 (40.55)	44 (13.10)	27.46 (22.08, 32.58)	<.001
At least one of the systemic reactions	83 (14.38)	14 (4.18)	10.22 (6.64, 13.80)	<.001
Fever	52 (9.01)	12 (3.58)	5.44 (2.38, 8.51)	0.003
Fatigue	32 (5.55)	3 (0.90)	4.65 (2.53, 6.77)	0.002
Headache	17 (2.95)	2 (0.60)	2.35 (0.74, 3.96)	0.032
Appetite loss	6 (1.04)	0 (0.00)	1.04 (0.21, 1.87)	**-
Chills	3 (0.52)	1 (0.30)	0.22 (-0.60, 1.05)	0.963
Skin Rash	3 (0.52)	0 (0.00)	0.52 (-0.07, 1.11)	-
At least one of the respiratory adverse events	33 (5.72)	29 (8.66)	-2.91 (-6.46, 0.64)	0.054
Sore throat	11 (1.91)	5 (1.49)	0.42 (-1.29, 2.13)	0.706
Cough	12 (2.08)	13 (3.88)	-1.79 (-4.16, 0.57)	0.045
Sneezing	5 (1.49)	5 (0.87)	-0.62 (-2.12, 0.88)	0.286
Rhinorrhea	19 (3.29)	20 (5.97)	-2.66 (-5.58,0.26)	0.030
Shortness of breath and chest pain	3 (0.52)	0 (0.00)	0.52 (-0.07, 1.11)	-
At least one of the gastrointestinal adverse events	14 (2.43)	7 (2.10)	0.34 (-1.63, 2.32)	0.778
Abdominal Pain	7 (1.21)	3 (0.90)	0.32 (-1.03, 1.67)	0.601
Nausea	9 (1.56)	0 (0.00)	1.56 (0.55, 2.57)	-
Vomiting	6 (1.04)	2 (0.60)	0.44 (-0.72, 1.61)	0.589
Diarrhea	3 (0.52)	4 (1.19)	-0.67 (-1.97, 0.63)	0.307
At least one of the musculoskeletal adverse events	14 (2.43)	3 (0.90)	1.53 (-0.08, 3.14)	0.123
Muscle pain	12 (2.08)	3 (0.90)	1.19 (-0.35, 2.73)	0.209
Bone pain	1 (0.17)	0 (0.00)	0.17 (-0.17, 0.51)	-
Joint pain	1 (0.17)	0 (0.00)	0.17 (-0.17, 0.51)	-

*p-value was calculated from the univariable mixed effect logistic regression model by considering healthcare centers as a random effect.
** due to the zero number of events and invalid results, the p-value was not reported.

Table 4. Frequency and percent of the adverse events according to the vaccine type and dose of vaccination

Adverse events, n (%)	Sinopharm (n=444)	Soberana (n=133)	P-value*	First Dose (n=231)	Second Dose (n=346)	P-value*
At least one adverse event	160 (36.04)	74 (55.64)	0.003	105 (45.45)	129 (37.28)	0.064
Pain at the sites of injection	117 (26.35)	61 (45.86)	0.001	82 (35.50)	96 (27.75)	0.037
At least one of the systemic reactions	62 (13.96)	21 (15.80)	0.400	38 (16.45)	45 (13.01)	0.187
Fever	38 (8.56)	14 (10.53)	0.363	22 (9.52)	30 (8.67)	0.621
Fatigue	24 (5.41)	8 (6.02)	0.794	19 (8.23)	13 (3.76)	0.022
Headache	15 (3.38)	2 (1.50)	0.385	9 (3.90)	8 (2.31)	0.174
Appetite loss	5 (1.13)	1 (0.75)	0.938	3 (1.30)	3 (0.88)	0.361
Chills	3 (0.68)	0 (0.00)	-**	2 (0.87)	1 (0.29)	-
Skin Rash	2 (0.45)	1 (0.75)	0.620	1 (0.43)	2 (0.58)	0.825
At least one of the respiratory adverse events	26 (5.86)	7 (5.26)	0.327	14 (6.06)	19 (5.49)	0.832
Sore throat	8 (1.80)	3 (2.26)	0.912	4 (1.73)	7 (2.02)	0.976
Cough	9 (2.03)	3 (2.26)	0.458	5 (2.16)	7 (2.02)	0.701
Sneezing	5 (1.13)	0 (0.00)	-	3 (1.30)	2 (0.58)	0.185
Rhinorrhea	13 (2.93)	6 (4.51)	0.743	8 (3.46)	11 (3.18)	0.897
Shortness of breath and chest pain	3 (0.68)	0 (0.00)	-	2 (0.87)	1 (0.29)	0.360
At least one of the gastrointestinal adverse events	9 (2.03)	5 (3.76)	0.141	7 (3.03)	7 (2.02)	0.293
Abdominal Pain	6 (1.35)	1 (0.75)	0.648	4 (1.73)	3 (0.87)	0.348
Nausea	5 (1.13)	4 (3.01)	0.064	5 (2.16)	4 (1.16)	0.188
Vomiting	3 (0.68)	3 (2.26)	0.157	4 (1.73)	2 (0.58)	0.174
Diarrhea	2 (0.45)	1 (0.75)	0.620	3 (1.30)	0 (0.00)	-
At least one of the musculoskeletal adverse events	12 (2.70)	2 (1.50)	0.593	10 (4.33)	4 (1.16)	0.012
Muscle pain	10 (2.25)	2 (1.50)	0.791	8 (3.46)	4 (1.16)	0.036
Bone pain	1 (0.23)	0 (0.00)	-	1 (0.43)	0 (0.00)	-
Joint pain	1 (0.23)	0 (0.00)	-	1 (0.43)	0 (0.00)	-
Physician visit	12 (2.70)	5 (3.76)	1.000	10 (4.33)	7 (2.02)	0.182
Using medicines for adverse events or prevention	107 (24.10)	32 (24.06)	0.585	62 (26.84)	77 (23.25)	0.162

*p-value was calculated from the univariable mixed effect logistic regression model by considering healthcare centers as a random effect.
** due to the zero number of events and invalid results, the p-value was not reported.

Discussion

In March 2022, the Iranian Ministry of Health and Medical Education granted approval for the Soberana (PastoCoVac) and Sinopharm vaccines to be administered to children under the age of 18 (10). Given the paucity of community-based studies examining the short-term adverse effects of the SARS-CoV-2 vaccination in children, the present study was designed to assess the prevalence of adverse events following vaccination in children aged 5 to 12 years. Given the similarity between the symptoms of common colds and those of the novel coronavirus disease (Covid-19), this study was designed and implemented as an observational study with a control group to accurately attribute the adverse events associated with the vaccination. The findings indicate that approximately 40.6% of vaccinated children and 13.1% of unvaccinated children experienced at least one adverse event. Thus, the attributable risk of the vaccine for at least one adverse event was 27.5%. A study revealed that the prevalence of at least one adverse event among 5–11-year-old Pfizer recipients was approximately 69% (12). Similarly, in a separate study, the prevalence of at least one adverse event among 10–18-year-old Sinopharm/Soberana recipients was reported to be approximately 67% (10). It appears that some of the adverse events documented in the aforementioned studies may be overestimated due to the absence of a control group. As anticipated based on the findings of nationwide studies and clinical trials, local reactions emerged as the most prevalent complication associated with the novel coronavirus disease (COVID-19). This report is presented irrespective of the type of vaccine studied (13, 14). Local reactions, particularly injection site pain, constituted the most prevalent reported complication among vaccinated participants in this study, occurring in 69.2% of cases. Moreover, the most commonly reported systemic adverse events among vaccinated children were fever, fatigue, and headache. The incidence of adverse events was markedly higher among the vaccinated cohort in comparison to the unvaccinated cohort. These findings align with those of other related studies. A review of the literature revealed that, following local adverse events (redness or pain at the injection site), systemic adverse events, including fever, fatigue, and headache, were the most prevalent adverse events (10, 13, 14). No statistically significant difference was observed between the two groups of participants with regard to appetite loss (1.0%), chills (0.1%), and skin rash (0.5%). In the study conducted by Capponi et al., the incidence of chills and rash was reported to be 6.2% and 1.8%, respectively (12). In the study conducted by Tavakoli et al., the incidence of chills, rash, and appetite loss was reported to be 2.8%, 3%, and 0.5%, respectively (10). These adverse events were classified as rare adverse effects, and it appears that these adverse effects are not regarded as the primary side effects of the SARS-CoV-2 vaccines. The higher prevalence of these adverse events in other studies compared to our study may be attributed to several factors, including potential overestimation and the absence of a control group. Additionally, differences in the vaccines utilized in the various studies may also contribute to the observed discrepancies. A statistically significant difference was observed in the incidence of nausea (1.6%) as a subset of gastrointestinal adverse events between the two groups. As reported in the clinical trial of the Sinopharm vaccine among children, the incidence of nausea was approximately 1.6%, which aligns with the findings of our study (14). The incidence of this adverse event among recipients of the Sinopharm vaccine has been reported to range from 0.5% to 2.7% in various studies. It appears that nausea is one of the infrequent adverse effects associated with the administration of the SARS-CoV-2 vaccine. No statistically significant difference was observed in the incidence of other subsets of gastrointestinal adverse events (0.3%), respiratory adverse events (3%), or musculoskeletal adverse events (1.5) between the two groups. The incidence of respiratory adverse events was higher among unvaccinated children than vaccinated children. The data demonstrate a high prevalence of respiratory illness, including colds, SARS-CoV-2 infection, and influenza, among children, particularly among unvaccinated children. This underscores the importance of the control group. The prevalence of these adverse events is reported to be 0.02% in gastrointestinal adverse events, 0.04% in respiratory adverse events, and 0.6% in muscle pain among 10–18-year-old Sinopharm/Soberana recipients (10). Among 5–11-year-old Pfizer vaccine recipients, joint pain and abdominal pain were reported to be the most prevalent at 6.7% and 10.8%, respectively. The prevalence of symptoms and pain at the injection site among recipients of the Soberana vaccine was significantly higher than that among recipients of the Sinopharm vaccine. However, the prevalence of other adverse events associated with both vaccines was similar and did not show any significant differences. In the study conducted by Tavakoli et al., the prevalence of fatigue, dizziness, and pain among recipients of the Sinopharm vaccine was significantly higher than that among recipients of the Soberana (PastoCoVac) vaccine (9). The adverse events associated with the Soberana (PastoCoVac) vaccine in pediatric patients have been examined during the two phases of the clinical trial, and no significant complications have been documented. The most frequently observed complication was injection site pain, while the most frequently reported systemic adverse events were discomfort, headache, and fever (11). The paucity of studies in this age group and with the Sinopharm and Soberana (Pasto CoVac) vaccines has rendered discussion on this topic challenging. Therefore, further population-based studies are recommended. A review of the literature indicates that the short- and long-term adverse effects associated with the SARS-CoV-2 vaccines are generally mild to moderate in severity (10, 12). In a single study, the efficacy and safety of the PastoCoVac vaccine were evaluated, and the incidence of serious adverse events was found to be less than 0.1%, with no vaccine-related deaths (7). In another study, no adverse effects were observed

within 30 minutes of the booster injections. The safety examination on day 7 revealed that pain at the injection site was the only local event observed in 15.9%, 11.3%, and 4.5% of the samples in the PastoCovac Plus, BBIBP-CorV, and PastoCovac groups, respectively. Additionally, systemic adverse events were observed in 19.4% of individuals in the BBIBP-CorV group, 14.3% in the PastoCovac group, and 4.5% in the PastoCovac-Plus group. Among these systemic adverse events, headache and weakness were the most prevalent. No adverse events were documented on day 21 during the three-week period following the injection (8). With regard to long-term adverse events, one study addressed some unsolicited adverse events during the 18-month follow-up period for PastoCovac and PastoCovac Plus. The combinational vaccine regimens consisted of AstraZeneca/PastoCovac Plus and Sinopharm/PastoCovac Plus. In total, unsolicited adverse events were documented for 3% of the study participants (15). The results of our study for children were comparable to those observed in adults for both vaccines. In this regard, the present study did not report any serious adverse events, including myocarditis and MIS-C. Approximately 3% of the vaccinated and 2% of the unvaccinated participants sought medical attention at health centers due to adverse events related to the vaccine or the disease. This figure was consistent with that reported by Tavakoli et al., who found that approximately 1.5% of participants (10) required further treatment. In light of these findings, it can be concluded that adverse events associated with the vaccination against the novel coronavirus are typically self-limiting. Approximately 24% of the vaccinated participants had utilized pharmaceuticals to prevent or alleviate vaccine-related adverse effects. The incidence of pain at the injection site, fatigue, and musculoskeletal adverse events was significantly higher among recipients of a single dose of the vaccine than among those who received two doses. The present study is one of a limited number of studies that has employed an observational study with a control group design to estimate the prevalence of short-term adverse events associated with the SARS-CoV-2 vaccination in children. This study design allows for the accurate estimation of the attributable risk associated with vaccination. In conclusion, the Sinopharm and Soberana (Pasto CoVac) vaccines are safe and have not been associated with any serious adverse events, including myocarditis, multisystem inflammatory syndrome (MIS), or hospitalization. Furthermore, it appears that the similarity between the adverse effects of the SARS-CoV-2 vaccine and those of a common cold may have led to an overestimation of the reported adverse effects in other studies due to the absence of a control group. The present study was conducted in the city of Tabriz; however, given the racial and genetic similarity between the two populations, the findings may be generalized to the country of Iran.

Limitations and Recommendations of the Present Study

The present study was conducted in an observational manner. Data were collected via self-report and via telephone interviews. It was not feasible to ascertain the severity of the reported adverse events, as they were subjectively reported and may have been influenced by a number of factors, including socioeconomic status, mood, sensitivity to adverse events, medical awareness, and other conditions. It appears that the implementation of a comprehensive registry system for the documentation of adverse events associated with vaccination may prove beneficial. Moreover, the lack of long-term follow-up in studies examining vaccination adverse events may result in the omission of unknown long-term adverse events. Therefore, studies with long-term follow-up are recommended.

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Authors' Contribution

PS and HA were the project's initiators. PS, NJ, HA, and SKH were responsible for the conceptualisation of the project. PS, NJ, and HN were responsible for the elicitation of knowledge, the collection of data, the analysis of data, and the interpretation of results. PS, NJ, and HA were responsible for the authorship of the manuscript. All authors have reviewed and approved the final manuscript for publication.

Ethics

All methods were conducted in accordance with the relevant guidelines and regulations. This project has been approved by the ethics committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1401.176). All participants provided informed consent prior to participation.

Conflict of Interest

The authors declare that they have no competing interests.

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Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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