Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Vaccine 40 (2022) 477–482

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Acute unsolicited adverse events following BNT162b2 vaccine in Saudi Arabia, a real-world data

Abdulellah M. Almohaya [a,*], Haya Alsubie [b], Bader Alqarni [b], Bashayer Alzayad [a], Ali Alghar [a], Khalid Alshahrani [a], Mazin Barry [c]

[a] Department of Internal Medicine, Ad-Diriyah Hospital, Ministry of Health, Riyadh, Saudi Arabia
[b] Department of Pediatrics, Ad-Diriyah Hospital, Ministry of Health, Riyadh, Saudi Arabia
[c] Division of Infectious Diseases, Department of Internal Medicine, College of Medicine, King Saud University, Riyadh, Saudi Arabia

ARTICLE INFO

Article history:
Received 5 May 2021
Received in revised form 30 November 2021
Accepted 1 December 2021
Available online 13 December 2021

Keywords:
Coronavirus
Novel
Covid-19
Vaccine
Adverse events
Safety
Anaphylaxis

ABSTRACT

Background: Acute adverse events and anaphylaxis were reported after the administration of coronavirus disease (COVID-19) mRNA vaccines. We aim to explore the nature and outcome of adverse events following BNT162B2 vaccine in a community vaccination center, Riyadh, Saudi Arabia.
Method: Within 30 min post vaccination, all acute adverse events (AAEs) that occurred before March 31st, 2021, and in people older than 16 years were reviewed (AAE group). We used the case definition of Brighton collaboration on vaccine safety to define anaphylaxis. Patients' demographics, comorbidities, allergy history, and outcome at disposition were collected. Observation duration after vaccination was short (<15 min) or extended (<3 h). Statistical analysis was performed to study AAEs association with the study variables and outcomes.
Results: Out of 71,221 vaccine recipients, 144 (0.002%) had developed 345 AAEs, at a rate of 48.4 events per 10,000 dose administered. The majority of cases in AAE group were first dose recipients (93.8%) and previously healthy (59%), while the minority had a previous history of allergy (6.3%) or a laboratory-confirmed COVID-19 (4.2%). We found a significant association between female gender and the occurrence of any AAE (p-value = 0.002). Per every 10,000 doses administered, non-anaphylactic AAEs were dizziness (17.8), headache (9.7), nausea (7.1), or syncope (3.2). Only one in every ten AAEs was considered serious and resulted in an extended observation (4.8 per 10,000 doses), but only 1/144 required hospitalization for non-anaphylaxis reasons (0.1 per 10,000 doses). According to the Brighton collaboration definition of anaphylaxis, no single case of high certainty anaphylaxis was recorded. No death was documented in this cohort.
Conclusion: Acute adverse events due to BNT162b2 vaccine were rare and mostly non-serious with a tendency to occur more in women. Further prospective studies on larger vaccine recipients to evaluate the incidence of anaphylaxis in the Saudi population are warranted.

1. Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has caused one of the most devastating pandemics which has affected tens of millions of people globally and resulted in millions of deaths [1]. In less than a year of the first reported case of coronavirus disease (COVID-19), several vaccines against SARS-CoV-2 have been granted emergency use authorization and have been rolled out in many countries, including Saudi Arabia [2].

BNT162B2, a lipid nanoparticle that encapsulates nucleoside modified mRNA that encodes the SARS CoV 2 full length spike (S) protein, demonstrated 95% efficacy in preventing COVID-19 disease, seven days following a two-dose regimen [3]. However, in phase III randomized clinical trial, one in four (26.7%) vaccine recipients had at least a single adverse event within two months following any dose of BNT162B2 administration, but only 1.2% had severe or a life-threatening event [3]. Early after vaccine rollout in the real world, the United States Centers for Disease Control and Prevention (CDC)has reported that the risk of

Abbreviations: COVID-19, Coronavirus Disease 2019; AAE, Acute Adverse Reactions.

* Corresponding author at: Ad-Diriya hospital, Ministry of Health, Ar-Rihab, Ad-Diriyah, 13717, Saudi Arabia.
E-mail address: amalmohaya@moh.gov.sa (A.M. Almohaya).

https://doi.org/10.1016/j.vaccine.2021.12.001
0264-410X/

anaphylaxis from BNT162B2 vaccine was estimated to be as low as 11.1 events per million doses administered [4], and the only contraindication to the vaccine is an allergic reaction (of any severity) immediately after receipt of an mRNA COVID-19 vaccine or its components, including polyethylene glycol; or immediate allergic reaction (of any severity) to polysorbate [5]. The risk of such adverse events is not known in Saudi Arabia.

The BNT162B2 vaccine was granted emergency use authorization by the Saudi food and drug administration (SFDA) [6] on December 10, 2020 and rolled out to the public on December 17th, 2020 [2]. Another vaccine (ChAdOx1- AstraZeneca) was also rolled out on February 18, 2021 [7]. As of April 12, 2021, over six million vaccine doses have been administered from both types [8].

The Saudi national protocol [9] for vaccine administration recommends that persons who receive BNT162B2 must be observed after vaccination for 30 min for persons with a history of mild to moderate allergies or using anticoagulants or suffering from bleeding disorders, and for 10 min for all other persons.

While the mRNA vaccines have not been used outside of clinical trials before their worldwide rollout, we aimed to explore the nature and outcome of acute unsolicited adverse events following BNT162B2 vaccine during the observation periods in a community vaccination center in Riyadh, Saudi Arabia.

2. Method

2.1. Settings

2.1.1. Vaccine and vaccination center

A two-dose regimen of 30-μg of BNT162b2, a lipid nanoparticle–formulated, nucleoside-modified RNA encoding the SARS-CoV-2 full-length spike, were administered to each recipient at 3–6 weeks intervals. The community vaccination center located in a public hospital in Riyadh, Saudi Arabia is among the centers where BNT162B2 vaccine is administered at a rate of 1500–3000 doses per day. This center is equipped with the necessary medical, storage, and administrative support. The BNT162B2 vaccine is stored according to the manufacturer's recommendation.

2.1.2. Vaccination protocol

As part of the national campaign for mass vaccination against COVID-19, the Saudi Ministry of Health (MOH) has established an electronic system to book vaccination appointments, through which the vaccine recipient will choose a nearby center to receive the COVID-19 vaccine. Upon arrival at the vaccine center, the vaccine recipient will be evaluated by the vaccinator for any vaccine contraindications as per the vaccine manufacturer's recommendations. These contraindications include pregnancy or anaphylaxis to any of the vaccine components. If no contraindication, the vaccine is administered and followed by a 15–30 min observation period, according to the risk of anaphylaxis. In case the vaccine recipient is observed to have any adverse events, the necessary medical stabilization including, if needed, a transfer to critical care is provided, and a standard reporting sheet is completed by the vaccinator. If the patient's status is stabilized or the vaccine recipient did not develop any adverse events, he/she will be discharged home.

2.2. Study design and population

Between February 1st and March 31st, 2021, a retrospective review of all recorded adverse events following BNT162B2 vaccination was performed. During our inclusion period, those younger than 16 years of age were excluded from vaccination as per the manufacturer's recommendations. During the study period, the national phased approach for vaccination included all other age groups. The study analysis of adverse events was performed after the exclusion of reports with insufficient data. The form included (1) basic characteristics: demographic data, prior history of allergies, any comorbid conditions, previous laboratory-confirmed COVID-19, current regular medications, recent non-COVID-19 vaccination; (2) COVID-19 vaccine data: type, number of doses, date, locations. Data on adverse events included: symptoms, administration to adverse event duration, vital signs, as well as the final disposition and outcome.

2.3. Definitions

According to United States Food and Drug Administration (US-FDA) definitions, adverse events (AE) is any unwanted medical occurrence in an individual temporally following administration of the vaccine, either voluntarily reported by the vaccinated individual or observed by the health care provider, while serious adverse event (SAE) is defined as any adverse event that results in death, life threatening event, inpatient hospitalization, significant incapacity, or disruption to conduct normal life functions. Other important medical events that may not result in above states, but may require immediate intervention like allergic bronchospasm requiring intensive treatment, might be considered serious according to clinical judgment of physician in the scene [10]. For the purpose of this study, acute adverse event (AAE) and SAE that occurred 10–30 min following vaccination were included. Vaccine recipients who did not develop any adverse events were labeled as (no-AAE).

Short observation following vaccination is defined as less than 15 minutes following vaccine administration, while extended observation is labeled if lasted more than 15 minutes but less than 3 hours after vaccine administration.

We used Brighton Collaboration case definition criteria for anaphylaxis following vaccination [11]. The criteria are endorsed by the US CDC and classify post-immunization event into 5 levels of certainties, where the levels 1 and 2, 3 represent high, intermediate and low certainty of anaphylaxis, respectively, while level-4 and level-5 indicate unlikelihood of anaphylaxis.

2.4. Statistical analysis

Frequency, percentage, and median were used to present numerical variables. Further statistical analysis was carried out by using the SPSS software (version-23, IBM Corp., Armonk, N.Y., USA). A chi-squared test was used and all variables were subjected to calculate the odds ratio and 95% confidence interval, as needed.

3. Results

During the study period, a total of 71,363 individuals arrived for COVID-19 vaccination in our center. Out of those, 142 persons were not given the vaccine for variable reasons. [Fig. 1] Hence, the total number of vaccine recipients (VRs) were 71,221 individuals, ninety percent (91.17%) were younger than 55 years of age (n = 64,934) with a median age of 32 years (range: 16–109 years), 56% were male (n = 39.884), and 91% were Saudi nationals (64,811). Regarding adverse events, we found 144 (0.002%) vaccine recipients who had developed 345 acute adverse events (AAE group), while the remaining 71,077 vaccine recipients did not develop any adverse events (No-AAE group). A significantly larger percentage of female individuals were observed in the AE group compared to the no-AAE group (56.9% versus 44%) (p-value = 0.002) [Table 1].

The majority of cases in the AAE group had adverse events after the first dose of the two-dose regimen (93.8%). There were only

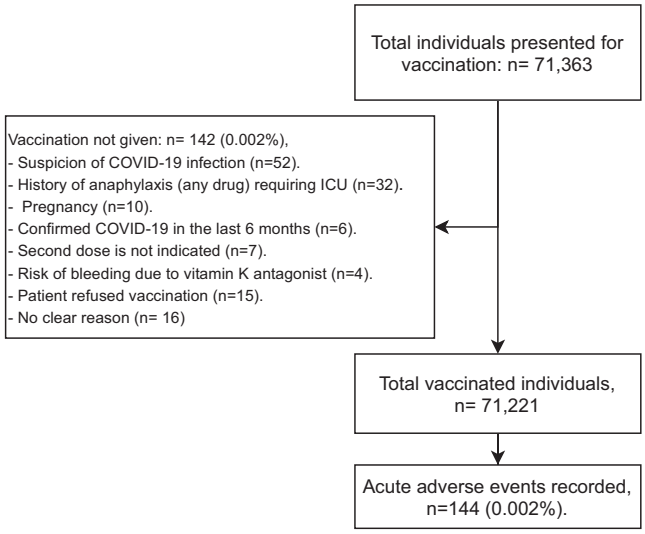

Fig. 1. Flowchart of individuals presenting for vaccination, total vaccinated individuals, and reported acute adverse events among BNT162b2 vaccine recipients in a community vaccination center, Riyadh, Saudi Arabia between February 18th - March 31st, 2021, COVID-19: coronavirus disease 2019; AAE: acute adverse events.

nine VRs (6.3%) who reported a previous history of allergy to food (n = 4), drug (n = 2), or non-specified (n = 3). Past medical history was non-revealing in 59% of the VRs, while the more frequently reported comorbid condition were cardiac disease (hypertension or ischemic heart disease, 11.8%) and/or diabetes mellitus (9%). Only six cases had a history of laboratory-confirmed COVID-19 [Table 2].

One in every ten (9.9%) adverse events reported was considered serious adverse events (SAE). The most common of which was the acute transient loss of consciousness (n = 23), resembling in most instances a vasovagal response, which occurred at a rate of 3.2 per 10,000 doses. Other SAE that deemed by physician in the scene to be serious, were high blood pressure (n = 5), defined as systolic blood pressure above 140 mmHg and/or diastolic blood pressure above 90 mmHg, hypotension (n = 2), defined as a systolic blood pressure<90 mmHg, seizure (n = 3), hypoglycemia (n = 1), defined as a random blood sugar<70 mmol/dL. Meanwhile, non-serious adverse events occurred at a rate of 44.4 events per 10,000 dose administered, the most common of which were dizziness (127 events), headache (69 events), and/or nausea (51 events). When Brighton criteria were applied in this cohort, none qualified to level-1 certainty of anaphylaxis and only two cases had level-2 and level-3 certainty, both of which improved without a need for any anaphylaxis specific therapy. The data on the duration between vaccine administration to the occurrence of the first adverse event and the data on the vital signs were not analyzed due to the lack of data in the majority of this study cohort [Table 3].

Following any type of adverse events, three-quarters (75.7%) of vaccine recipients were observed for < 15 min and discharged in stable condition. However, the rate of extended observation (beyond 15 min) or hospitalization due to an SAE was estimated to be 4.9 per 10,000 doses administered [Table 3]. While an increasing number of adverse events in any single patient increased the likelihood of extended observation and/or hospitalization (*p*-value = 0.001), there was no statistical association between demographic, past medical history, and/or history of allergy with increased likelihood for extended observation and/or hospitalization [Table 4].

Table 2
Characteristics of individuals with at least one acute adverse event (AAE) among BNT162b2 vaccinated individuals in a community vaccination center, Riyadh, Saudi Arabia between February 18th - March 31st, 2021 (n = 144):

Parameters		n	%
History of allergy*	**Yes**	9	6.3
	No	135	93.8
Comorbid conditions	**Previously healthy**	85	59.0
	Cardiac disease	17	11.8
	Diabetes Mellitus	13	9.0
	Respiratory disease	7	4.9
	Myasthenia gravis	2	1.4
	Multiple sclerosis	1	0.7
	Other	12	8.3
History	**confirmed COVID-19**	6	4.2
	Other vaccines, last 6 months	5	3.5
Current medications	**None**	123	85.4
	Anti-hypertensive Drugs	7	4.9
	OHA or Insulin.	13	9.0
	Steroid	1	0.7
	Natalizumab	1	0.7
	Other medications	10	6.9
Number of doses	**First**	135	93.8
	Second	9	6.3
No. of AAE per person	**2–3 AAEs**	84	58.3
	>= 4 AAEs	37	25.7
The onset of adverse event	**<= 10 min after injection**	13	9
	11–30 min after injection	3	1.4
	Data not available	128	89.6

COVID-19: coronavirus disease 2019; AAE: acute adverse events. Cardiac diseases: hypertension, ischemic heart disease, heart failure. OHA: oral hypoglycemic agents.
* List of allergies reported to: beans or nuts (n = 3), penicillin (n = 2), fish (n = 1), unspecified (n = 3).

4. Discussion

In this real-world study from Saudi Arabia, acute adverse events within 30 min following administration of the BNT162b2 vaccine was found to be extremely low, at a rate of 48.4 events in every 10,000-dose administered, most of which required<15 min of

Table 1
Demographic data among BNT162b2 vaccinate recipients (VR) in a community vaccination center, Riyadh, Saudi Arabia between February 18th - March 31st, 2021 (n = 71,221), stratified by the number of those who developed acute adverse events (AAE) and those who did not (No-AE):

Parameters		Total n = 71,221 (%)	AE group n = 144 (%)	No-AE group n = 71,077 (%)	p-value	Odds ratio (OR) (95% CI)
Age	**Median (range)**	***32 (16–109)***	*29 (17–70)*	*32 (16–109)*	–	
	16–55 years	**64,934 (91.17)**	136 (94.4)	64,798 (91.2)	0.17	
	> 55 years	**6,287 (8.83)**	8 (5.6)	6,279 (8.8)		
Sex	**Female**	**31,337 (44)**	82 (56.9)	31,255 (44)	0.002	1.69 (1.21–2.34)
	Male	**39,884 (56)**	62 (43.1)	39,822 (56)		reference
Nationality	**Saudi**	**64,811 (91)**	136 (94.4)	64,675 (91)	0.15	
	Other	**6,410 (9)**	8 (5.6)	6402 (9)		

AE (adverse events) or no-AE, vaccine recipients who developed or did not develop adverse events.

Table 3
List of the acute adverse events (n = 345) recorded in the 144 vaccine recipients and their outcome following the administration of BNT162b2 vaccination in a community vaccination center, Riyadh, Saudi Arabia between February 18th - March 31st, 2021, classified as per seriousness according to US-FDA criteria:

Adverse event			Freq*	% among adverse event group (n = 144)	Rate, per 10,000 doses.
Acute Adverse event (AAE)	**Serious AE (SAE), n = 34 (9.9%)**	**Syncope**	23	16.0	3.2
		Hypotension	2	1.4	0.3
		Convulsions	3	2.1	0.4
		Hypoglycemia	1	0.7	0.1
		High blood pressure	5	3.5	0.7
	Non-serious adverse events (NSAE), n = 316 (90.1%)	**Dizziness**	127	88.2	17.8
		Headache	69	47.9	9.7
		Nausea	51	35.4	7.2
		Fatigue	22	15.3	3.1
		Dyspnea	17	11.8	2.4
		Abdominal pain	6	4.2	0.8
		Numbness	6	4.2	0.8
		Vomiting	4	2.8	0.5
		Palpitations	4	2.8	0.5
		Wheezing	2	1.4	0.3
		Cold extremities	2	1.4	0.3
		Rash at the site of injection	1	0.7	0.1
		Hoarseness	1	0.7	0.1
		Injection site swelling	1	0.7	0.1
		Sweating	1	0.7	0.1
		Cough	1	0.7	0.1
		Chest pain	1	0.7	0.1
Brighton Collaboration criteria of anaphylaxis		**Level-1**	0	0	
		Level-2	1	0.7	
		Level-3	1	0.07	
		Level-4	0	0	
		Level-5	142	98.6	
Outcome		**Short observation**	112	75.7	15.3
		Extended observation	31	23.6	4.8
		Hospitalized	1	0.7	0.1

According to United States Food and Drug Administration (US-FDA) definitions, serious adverse event (SAE) is defined as any adverse event that results in death, life threatening event, inpatient hospitalization, significant incapacity, or disruption to conduct normal life functions. Other important medical events that may not result in above states, but may require immediate intervention like allergic bronchospasm requiring intensive treatment, might be considered serious according to clinical judgment of physician in the scene.
Hypotension: < 90 mmhg, Hypoglycemia: random blood sugar < 70 mg/dL, Hypertension: systolic blood pressure > 140 mmhg or diastolic blood pressure > 90, Short observation < 15 min, Extended observation > 15 min but less than 3 h.
* Frequency, a vaccine recipient may had more than one adverse event.

Table 4
Association of study variables with the acute need for extended observation and/or hospitalization among BNT162b2 vaccinated individuals in a community vaccination center, Riyadh, Saudi Arabia between February 18th - March 31st, 2021 (n = 144):

Parameters	Need for extended observation and/or hospitalization				p-value
	Yes n = 32		No n = 112		
	n	%	n	%	
Age above 55 years	2	6.3	6	5.4	0.846
Female gender	16	50.0	66	58.9	0.368
Saudi origin	30	93.8	106	94.6	0.846
Allergy	1	3.1	8	7.1	0.408
Medically free	22	68.8	83	74.1	0.548
Cardiac disease	5	15.6	12	10.7	0.448
Diabetes Mellitus	3	9.4	10	8.9	0.938
Autoimmune disease	0	0.0	1	0.9	0.592
Respiratory disease	0	0.0	7	6.3	0.147
Previous COVID diagnosis	1	3.1	5	4.5	0.738
Recent other vaccines	1	3.1	4	3.6	0.903
Number of adverse events per patient, mean	3.7	–	2.6	–	< 0.001
Number of adverse events per patient, > 3 AAEs	24	75	61	54.5	0.04

COVID: coronavirus disease. AAE: acute adverse event. Cardiac diseases: hypertension, ischemic heart disease, heart failure. OHA: oral hypoglycemic agents.

observation. Moreover, the rate of SAE that required extended observation and/or hospitalization was 4.8 events in every 10,000-dose administered. There was no single case of anaphylaxis nor death observed within the study. Compared to the fatality risk of COVID-19 in Saudi Arabia (1.24%, 124 deaths per 10,000 infected person) [12], such high safety profile during the immediate period post-vaccination is largely reassuring.

The risk of anaphylaxis following vaccine administration is repeatedly reported to be low with various types of vaccines [13]. The current vaccine, BNT162b2, was expected to cause vacci-

nation hesitancy given its extraordinary rapid development and relatively new manufacturing technology. Phase III clinical trial of BNT162b2 vaccine did not show a significant risk of acute adverse events including anaphylaxis [3]. However, the United States centers for disease control and prevention (US CDC) reported a risk of anaphylaxis in 11.1 cases per million doses administered [4], especially among those with a history of documented allergy. This could suggest that the anaphylaxis incidence following BNT162b is 8.5 times the incidence reported in 2016 following other vaccines (1.31 per million doses) [14], though this is still considered extremely low. Among the current study participants, the absence of anaphylaxis can be explained by few factors. First, in our 71,221-dose cohort, the rate of occurrence of anaphylaxis as per the US CDC rate is expected to occur in less than one case (0.7 case), which lead to the absence of anaphylaxis in our cohort. Second, the exclusion of those with a known history of severe anaphylaxis (n = 32) might have prevented the occurrence of anaphylaxis.

The nature of post-vaccination syncope is not clearly understood. Recently, the World Health Organization (WHO) has proposed a new term, immunization stress-related response (ISRR), which is described as a spectrum of anxiety-related symptoms and signs that may develop before or after immunization. The symptoms may vary from mild feelings of worry to tachycardia, palpitations, dyspnea, syncope, or hyperventilation [15]. Such a term can apply to most of the symptoms reported in our cases. Post-vaccination syncope occurrence in our cases was as low as 3.2 per 10,000 vaccines administered. Reassuringly, such a rate falls within the range reported in the medical literature for other vaccines, 1.4 per 10,000 doses [16] – 8.8 per 10,000 doses [17]. However, in its phase III clinical trial, post-vaccination syncope was less observed in the BNT162b2 vaccine recipients compared to placebo. These altogether might hint toward that the observed syncope in our cohort was part of ISRR rather than other medical causes of syncope, especially that all of the study cohort spontaneously recovered.

Compared to males, female vaccine recipients were 69% more likely to experience acute adverse events, including allergic and/or non-allergic types of events. This has been previously documented in multiple reports that showed gender difference (more to females) in the hypersensitivity reactions following exposure to different allergens [18], including H1N1 vaccines [19] and BNT162b2 [4,20]. It is unclear whether this association is due to reporting bias or due to specific biological reasons, further studies are needed to explore this association. There was no significant association between age and the likelihood to develop AAEs. This is in contrast to the reported findings in the BNT162b2 phase III trial on acute and non-acute adverse events, in which those older than 55 years were less likely to develop any adverse events.

Overall, non-anaphylaxis adverse events in this cohort were mostly systemic and were considered non-serious, i.e., dizziness, headache, nausea, vomiting, fatigue. These events were all documented in the phase III trial of the BNT162b2 vaccine but with a higher frequency, mostly due to longer follow-up in the trial.

The medical management of post-vaccination adverse events is largely based on symptomatic treatment, as per the current recommendation by the US CDC as well as the Saudi MOH. No single patient within the cohort needed an epinephrine injection or invasive ventilation, and/or resulted in an immediate complication that led to death. This might be due to the exclusion of patients with any history of significant anaphylaxis from receiving the vaccine.

Although this study included a large number of vaccination doses, the current study has few limitations. Being retrospective, especially with the lack of control subjects could limit the generalization of its conclusion. Besides, lack of objective evaluation of these adverse events (i.e., laboratory and other diagnostics) might limit underlying cause identifications.

5. Conclusion

Acute adverse events due to BNT162b2 vaccine were rare and mostly non-serious with a tendency to occur more commonly in women. Further prospective studies on larger vaccine recipients to evaluate the incidence of anaphylaxis in the Saudi population are warranted.

Disclosure

All authors have read and agreed on the final version of this article. All authors have contributed to this research work.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

We acknowledge the distinct and significant contribution of all health care providers in the vaccination center who helped in the data collection.

Ethical approval

Approved by the institutional review board with an IRB log number: KFMC-21-146E.

References

[1] COVID-19 Map - Johns Hopkins Coronavirus Resource Center n.d. https://coronavirus.jhu.edu/map.html (accessed July 3, 2021).
[2] Barry M, Bahammam AS. COVID-19 vaccine in the Kingdom of Saudi Arabia: A true operation warp speed. J Nat Sci Med 2021;4:92–8. https://doi.org/10.4103/jnsm.jnsm_8_21.
[3] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med 2020;383(27):2603–15. https://doi.org/10.1056/NEJMoa2034577.
[4] Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine, United States, December 14 - 23, 2020. {MMWR} Morb Mortal Wkly Rep 2021;70:46–51. https://doi.org/10.15585/mmwr.mm7002e1.
[5] Center for Disease Control and Prevention. Interim Clinical Considerations for Use of COVID-19 Vaccines | CDC n.d. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html (accessed July 3, 2021).
[6] Saudi Food & Drug Authority Allows the Import and Use of Covid19 Vaccine | Saudi Food and Drug Authority n.d.
[7] Saudi Arabia approves AstraZeneca's COVID vaccine, state TV reports | Reuters n.d. https://www.reuters.com/article/us-health-coronavirus-vaccine-saudi-idUSKBN2AI1PU (accessed April 28, 2021).
[8] More Than 832 Million Shots Given: Covid-19 Vaccine Tracker n.d.
[9] Ministry of Health SA. COVID-19 Vaccination Program Clinical Guidelines. n.d.
[10] Food and Drug Administration. Safety Reporting Requirements for New Drug Applications Studies. 2020. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/safety-reporting-requirements-inds-investigational-new-drug-applications-and-babe (accessed April 29, 2021).
[11] Rüggeberg JU, Gold MS, Bayas J-M, Blum MD, Bonhoeffer J, Friedlander S, et al. Anaphylaxis: Case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine 2007;25(31):5675–84. https://doi.org/10.1016/j.vaccine.2007.02.064.
[12] Boretti A. COVID-19 fatality rate for Saudi Arabia, updated 8 August 2020. J Glob Antimicrob Resist 2020;23:329–30. https://doi.org/10.1016/j.jgar.2020.10.007.
[13] Bohlke K, Davis RL, Marcy SM, Braun MM, DeStefano F, Black SB, et al. Risk of anaphylaxis after vaccination of children and adolescents. Pediatrics 2003;112(4):815–20. https://doi.org/10.1542/peds.112.4.815.
[14] McNeil MM, Weintraub ES, Duffy J, Sukumaran L, Jacobsen SJ, Klein NP, et al. Risk of anaphylaxis after vaccination in children and adults. J Allergy Clin Immunol 2016;137(3):868–78. https://doi.org/10.1016/j.jaci.2015.07.048.

[15] McMurtry CM. Managing immunization stress-related response: A contributor to sustaining trust in vaccines. Canada Commun Dis Rep 2020;46:210–8. , https://doi.org/10.14745/ccdr.v46i06a10.
[16] U.S. Armed Forces AFHSC. Syncope, active and reserve components, U.S. Armed Forces, 1998-2012. Med Surveill Mon Rep 2013;20:5–9.
[17] Duffy J, Johnsen P, Ferris M, Miller M, Leighton K, McGilvray M, et al. Safety of a meningococcal group B vaccine used in response to two university outbreaks. J Am Coll Heal 2017;65(6):380–8. https://doi.org/10.1080/07448481.2017.1312418.
[18] Brown AFT, McKinnon D, Chu K. Emergency Department anaphylaxis: A review of 142 patients in a single year. J Allergy Clin Immunol 2001;108(5):861–6. https://doi.org/10.1067/mai.2001.119028.
[19] Halsey NA, Griffioen M, Dreskin SC, Dekker CL, Wood R, Sharma D, et al. Immediate hypersensitivity reactions following monovalent 2009 pandemic influenza A (H1N1) vaccines: Reports to VAERS. Vaccine 2013;31(51):6107–12. https://doi.org/10.1016/j.vaccine.2013.09.066.
[20] Almohaya A et al. Early solicited adverse events following the BNT162b2 mRNA vaccination, a population survey from Saudi Arabia. Preventive Medicine Reports 2021;24: 101595. https://doi.org/10.1016/j.pmedr.2021.101595.