

Evaluation of Side Effects Following COVID-19 Vaccination in Saudi Arabia's General Population

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ABSTRACT

Several regulatory bodies throughout the world have produced and approved several COVID-19 vaccines for use in emergencies. In addition to providing a centralised database of suspected adverse reactions and safety profiles for these vaccinations, the aim is to compare the safety and side effects of approved COVID-19 vaccines in Saudi Arabia. As part of this cross-sectional study, an online questionnaire was used to survey 633 vaccinated Saudi Arabian citizens. Their ages ranged from 15 to 85 years. According to the study, 33% of individuals had COVID-19 before immunisation, and 55% of participants had the virus. 10% of the study participants had two or more associated comorbidities, most commonly diabetes mellitus, respiratory issues, and hypertension. Fatigue, headaches, fever, myalgia, arthralgia, and injection site discomfort, tenderness, and swelling are the most common adverse effects of these vaccines, especially following the initial dosage. Systemic adverse effects were frequently observed in young female participants aged 15 to 30 years. According to age, gender, comorbidities, and vaccine type, this study makes assumptions about a database regarding the likelihood of experiencing COVID-19 vaccine side effects. Further research is needed to better understand the relationship between risk factors and developing negative outcomes.

Keywords: SARS-CoV-2, COVID-19 vaccines, Pfizer-BioNTech, Moderna, Oxford/AstraZeneca

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Introduction

The speed at which several vaccines were created and evaluated to protect against the 2019 coronavirus illness (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is astounding [1]. There are great hopes that the pandemic will soon come to an end because several of the vaccines that have been developed have performed better than expected. Globally, billions of doses of vaccines have been administered to date [2]. The United States authorised the first COVID-19 vaccines for use in emergencies in December 2020 [3, 4]. Delaying or forgoing vaccinations despite the availability of vaccine services is known as vaccine hesitation (VH) [5]. Misconceptions regarding the effectiveness and safety of vaccines exacerbate this expanding public health issue [6]. The majority of the information regarding the safety of the COVID-19 vaccine is derived from manufacturer-funded research that is carried out following standards set by the relevant drug regulatory bodies and supervised by impartial specialists. Injection site events (such as pain, erythema, or oedema) and systemic effects (such as fatigue, headaches, or aches in the muscles or joints) were among the adverse events reported in controlled trials using COVID-19 vaccinations, with infrequently serious adverse reactions [7–10]. Although the majority were minor, researchers calculated that between 50% and 90% of individuals had adverse reactions [8–10]. There is little real, patient-reported evidence of adverse outcomes after the COVID-19 vaccine, and who is

more likely to experience them, even though data on adverse reactions captured by government-sponsored monitoring systems has begun to emerge [11–13].

Some have created several possible COVID-19 vaccines for the biggest pharmaceutical companies in the world. On December 31, 2020, the Pfizer/BioNTech Comirnaty vaccine became the first coronavirus vaccine to be incorporated into the World Health Organization's (WHO) Emergency Use List (EUL). The Moderna coronavirus vaccine (mRNA 1273) was approved on April 30, 2021; the Johnson & Johnson Janssen Ad26.COV-2.S vaccine was approved on March 12, 2021, and the AstraZeneca AZD1222 and SII Covishield vaccines from AstraZeneca/Oxford were licensed for EUL on February 16, 2021. The Pfizer-BioNTech COVID-19 vaccine is the most well-known RNA vaccine. It is composed of a fat nanosphere that expresses the SARS-CoV-2 full-length spike (S) protein through nucleoside-modified mRNA [14–16]. The Saudi Food and Drug Authority (SFDA) of the Kingdom of Saudi Arabia (KSA) authorised this vaccine for emergency use on December 10, 2020 [17]. The vaccine's primary drawbacks include its incompatibility with other vaccines, the requirement for extremely low-temperature storage (it can only be kept at room temperature for two hours), and the fact that the only contraindication is a history of severe hypersensitivity reactions to any of its ingredients [18]. Moderna created mRNA-1273, a fat nanosphere containing mRNA, the second RNA vaccine. It is advised for persons over 18 and showed 94% efficacy in a phase III clinical research. Like the Pfizer-BioNTech BNT162b2 COVID-19 vaccine, it needs to be frozen, but at a higher temperature. It can be kept for up to 30 days at two to eight degrees Celsius. Its negative effects are similar to those of BNT162b2, with the most frequent being injection site soreness. Children and women who are pregnant or nursing shouldn't take it. Furthermore, it cannot be used in place of other immunisations, and a history of severe allergic responses to any of the vaccine's ingredients may be the main obstacle [19]. Several viral vector vaccines have been developed, such as Oxford/AstraZeneca's ChAdOx1 nCov-19 vaccine, which is vectored by chimpanzee adenovirus. When concerns about transverse myelitis surfaced on September 8, 2020, its Phase III study took a difficult turn. For seven days, the trial was halted. Both regimens demonstrated a 70% overall efficacy with a fairly sufficient safety requirement despite these variations [8, 20]. In addition to providing a database of the variations in the safety of these approved COVID-19 vaccines in Saudi Arabia, this study sought to evaluate the negative effects and reactions of the vaccination among the country's vaccinated population.

Materials and Methods

On 10th August 2022, a cross-sectional survey was undertaken to analyse the adverse effects and reactions of the different COVID-19 immunisation kinds in Saudi Arabian residents. Before collecting data, the consent form was received from all participants electronically, and only those who agreed could complete the survey online. Taif University's Scientific Research Ethics Committee gave its approval to the project (Research number/44-014). 633 participants, ages 15 to 85 years, agreed to participate in this study and completed the online questionnaire. All participants lived in Saudi Arabia and had received the first dose or the full course of the vaccine (two doses) or booster in addition to the two doses at least 30 days before the trial. The questionnaire asked about the respondents' age, gender, weight, and comorbidities (hepatic, cardiovascular, respiratory, renal, hepatic, immunological, and endocrine diseases), as well as the type and quantity of vaccinations they received, their post-vaccination symptoms, and the duration of their symptoms. Therefore, the effectiveness of these vaccinations was evaluated by counting the number of people who contracted COVID-19 before and after vaccination. To ascertain which symptoms are most prevalent and which vaccination type may be linked to them, the incidence of these side events was assessed and investigated.

Statistical analysis: GraphPad Software, LLC's Prism 8 for OS X, version 8.4.3, was utilised in this investigation. One-way ANOVA, t-test, and chi-square were employed to compare continuous variables. A P-value < 0.05 was deemed statistically significant.

Results and Discussion

In Saudi Arabia, the COVID-19 vaccine's adverse effects and responses were assessed. A total of 633 individuals expressed interest in answering the survey. With a mean age of 27.6 ± 12.29 years, the majority of the study's 397 (62.7%) female participants and 236 (37.3%) male participants were between the ages of 15 and 85 years. Of the participants, 547 (86.4%) were either university graduates or enrolled students, and 566 (89.4%) did not smoke.

Of the subjects, 443 (70%) did not have a job. The majority of participants ($n = 308$) had a normal body mass index (BMI) of 48.7%, followed by 23.3% of overweight participants ($n = 147$) and 13.7% of obese participants ($n = 87$) (**Table 1**).

Table 1. Demographic characteristics of research subjects.

Variable	Characteristic	Total (n)	Total (%)
Gender	Female	397	62.7
	Male	236	37.3
Age	15-30	438	69.2
	31-45	125	19.7
	46-60	62	9.8
	61-75	6	1
	> 76	2	0.3
Smoking	No	566	89.4
	Yes	67	10.6
Education level	Primary	4	0.6
	Secondary	82	13
	University	547	86.4
Employment	Unemployed	443	70
	Employed	190	30
BMI	Underweight	84	13.3
	Normal	308	48.7
	Overweight	147	23.3
	Obese	87	13.7
	Extremely obese	7	1.1

According to **Figure 1a**, 292 respondents (46.3%) said they have contracted COVID-19 at some point. 9 participants (3%) had been exposed to the virus three times, 58 participants (19.9%) had been infected twice, and 225 persons (77.1%) had only been exposed once (**Figure 1b**). Moreover, over half ($n = 352, 55\%$) of the responders had COVID-19. About 30% of survey participants ($n = 104$) contracted COVID-19 following the second dose of vaccination, while roughly 33% of infected people ($n = 117$) had the infection before the first dosage. After the first dose, 50 participants (about 14%) contracted the infection, 78 participants (approximately 22%) contracted the infection after the third dose (the first booster dose), and only three participants contracted the infection after the fourth dose (the second booster dose) (**Figure 1c**).

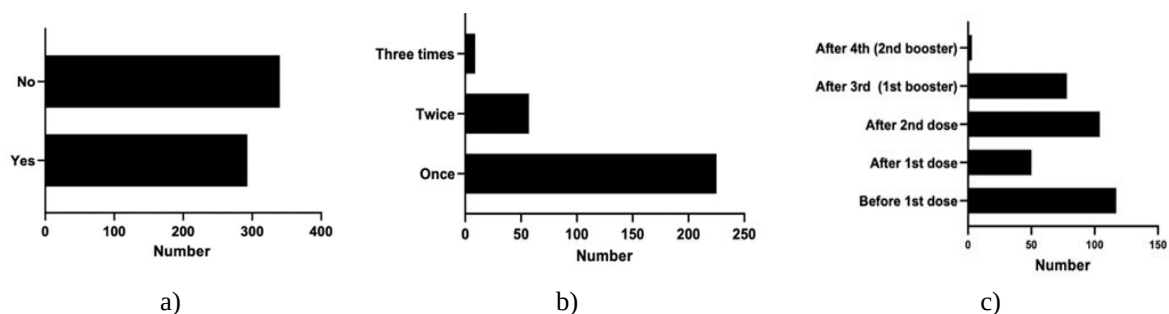


Figure 1. History and prevalence of COVID-19 infection among research participants: a) the number of people who had previously contracted SARS-CoV-2, b) the number of COVID-19 cases, and c) SARS-CoV-2 infected before or following immunisation.

When asked about their vaccination history, 504 (almost 80%) of the participants in our study received the first dose of Pfizer, 117 (18%) received AstraZeneca, and 12 (2%) received Moderna. Pfizer was the most widely used COVID-19 vaccine type in the second dosage, followed by Moderna and AstraZeneca, with 501, 72, and 60 people immunised overall, respectively. The initial booster dose was consistently given by Pfizer ($n = 451$), Moderna ($n = 104$), and AstraZeneca ($n = 34$). As a result, 589 (93% of the participants) received the first booster dose. 240 Pfizer, 28 Moderna, and 16 AstraZeneca were among the 284 (45%) participants in the second booster dose

(Figure 2). Since not all participants consented to receive the boosters, the number of participants who received them was smaller than that of the first and second doses, even though the first and second doses were required in Saudi Arabia.

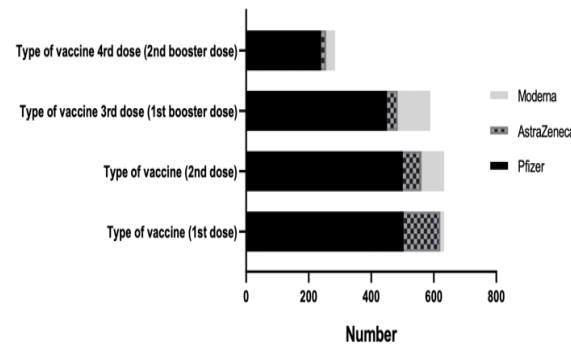


Figure 2. Types of COVID-19 vaccines in Saudi Arabia

About 77% of respondents ($n = 489$) in the current study reported having no allergies, while 23% ($n = 144$) had (Figure 3a). Furthermore, compared to 63 respondents (10%) who had comorbidities, 570 respondents (90%) had no relevant comorbid conditions (Figure 3b). About 34% of the study participants had hypertension, 22% had respiratory issues, 20% had diabetes mellitus, 13% had arthritis, and 11% had other illnesses (Figure 3c). There is no statistically significant difference between those who had coronavirus before vaccination and those who did not, according to Table 2.

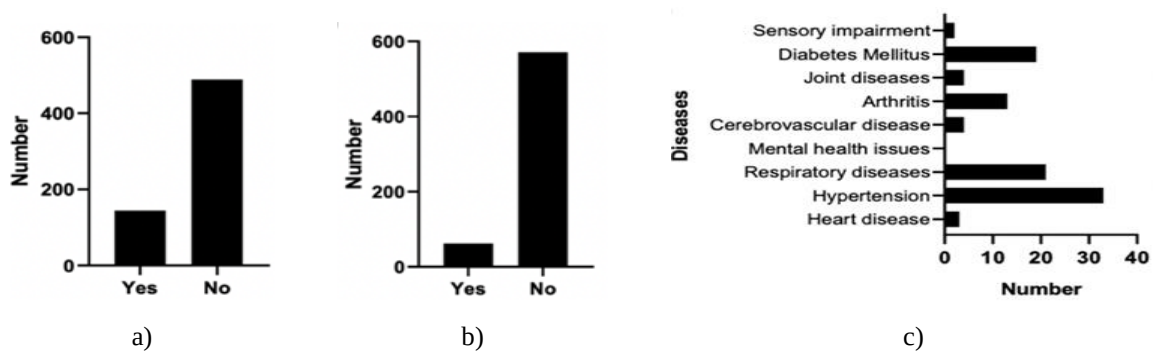


Figure 3. Comorbidity and allergy before COVID-19 immunisation; a) the number of people who suffer from allergies, b) the number of people who have comorbidities, and c) coexisting conditions.

Table 2. COVID-19 infection and comorbid disease

Comorbid diseases	COVID-19 infection		t-test	P-value
	Yes	No		
Hypertension	22	11	1.364	0.3057
Diabetes mellitus	9	10	0.3162	0.7676
Respiratory diseases	11	10	0.3111	0.7663
Arthritis	5	8	0.6000	0.6094
Cerebrovascular disease	2	0	1.000	0.4226
Joint disease	2	2	0.000	> 0.9999
Heart disease	1	2	0.4472	0.6985
Sensory impairment	1	1	0.000	> 0.9999

About 74% of respondents ($n = 466$) to our survey reported experiencing adverse reactions following COVID-19 injections. Following the first and second doses, as well as the initial booster doses, the most frequent systemic adverse effects of COVID-19 were fatigue, headaches, myalgia, fever, chills and shivers, and arthralgia (Figure

4a). For all research participants, the most frequent local side effects of the first, second, and booster doses were injection site pain, soreness, and swelling (**Figure 4b**). Using primarily Pfizer and/or AstraZeneca vaccines, it has been shown that the most serious adverse effects occurred after the first dose (43%), followed by the second dose (34%). The prevalence of the side effects was higher among youths aged 15–30 years ($n = 323$ out of 438) than among those aged 31–45 and 46–85 years ($n = 92$ out of 125 and $n = 51$ out of 70, respectively) (**Figure 5a**). Systemic adverse effects were more common in women ($n = 303$ out of 397) than in males (**Figure 5b**).

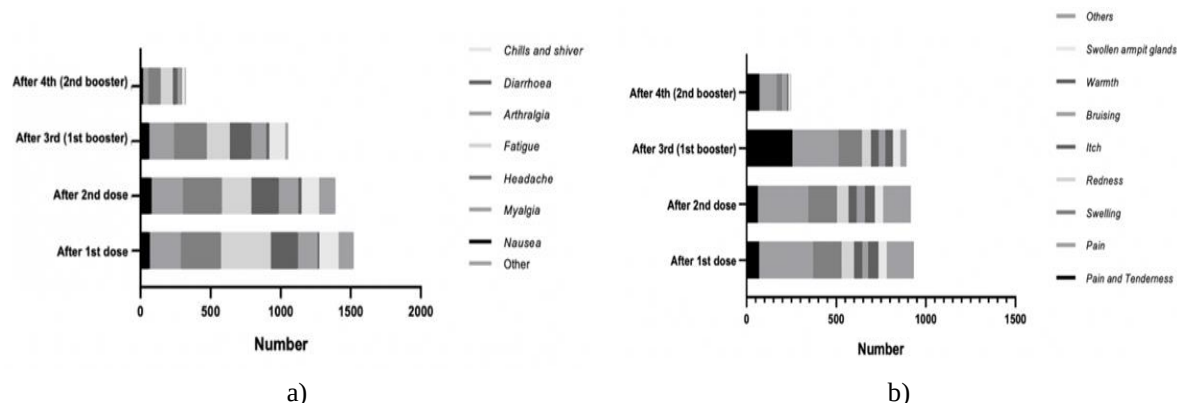


Figure 4. COVID-19 vaccine side effects: a) systemic side effects, and b) local side effects.

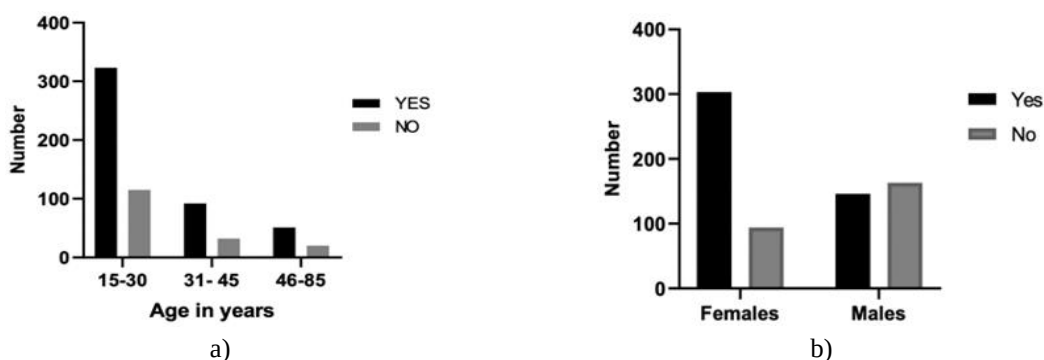


Figure 5. The COVID-19 vaccine's systemic side effects are contingent upon the participants' a) age and b) gender.

A serious health catastrophe was brought on by the COVID-19 pandemic, which spread swiftly around the world [21]. Most nations took preventive steps to stop the spread of SARS-CoV-2 when the COVID-19 pandemic started in early 2020, anticipating the availability of quickly produced, dependable, and efficient vaccinations [22]. When regulatory and medical decisions had to centre on determining priorities, estimating benefits and risks, and possible successes, the development of COVID-19 vaccines rapidly changed [23]. At least one government agency authorised the use of 18 vaccinations for emergency use in July 2021; 105 COVID-19 vaccine candidates were in clinical development, and 185 were undergoing pre-clinical testing [24]. As part of its early and remarkable efforts to stop the spread of SARS-CoV-2, Saudi Arabia has started an early immunisation campaign. The purpose of this study was to assess the prevalence of adverse reactions and side effects of COVID-19 vaccinations that have received Saudi Arabian approval. According to our research, over 55% of individuals had had one, two, or three COVID-19 infections. 33% of this group had previously contracted COVID-19. Nevertheless, 14% of participants received the vaccination following the first dose, 33% following the second dose, 22% following the first booster, and 1% following the second booster received the vaccination. 10% of research participants had two or more conditions at the same time, most frequently diabetes mellitus, high blood pressure, and respiratory disorders. These results may help explain how the immune system reacts to COVID-19 infection, which boosts humoral and cellular immunity [15, 25]. The probability and frequency of reinfection seem to be limited, even though it is possible to contract COVID-19 more than once. The intensity of the initial infection, the person's immune response, and the appearance of novel viral variations are some of the variables that may affect a person's risk of

contracting COVID-19 again. According to research, those who recover from COVID-19 have a robust immune response, which includes the development of antibodies, which may offer some degree of defence against reinfection. However, the length and intensity of the immune response may differ from person to person, and the precise duration of the protection against reinfection is still unknown. Consequently, it has been demonstrated that COVID-19 immunisation generates a robust immune response that can offer protection against the virus and its variations. The vaccinations are very successful in reducing the risk of COVID-19-related hospitalisation, serious illness, and death [15]. Numerous investigations confirmed that those with a history of COVID-19 infection have greater antibody concentrations [26–28].

Furthermore, 23% of the individuals experienced adverse reactions, such as rash, burning skin, and red welts on their lips and face. These people might have a higher chance of getting ill with COVID-19. Allergies can impair immunity and raise the likelihood of getting serious infections to eradicate the virus, even if they are not a direct risk factor for Covid-19 [29].

About 74% of respondents ($n = 466$) to our survey reported negative side effects from coronavirus vaccines. Following the first and second doses and the initial booster doses, the most frequent systemic adverse effects of COVID-19 were fatigue, headaches, myalgia, chills and shivering, and arthralgia (**Figure 4a**). However, for all research participants, the most frequent local side effects of the first, second, and booster doses were injection site discomfort, soreness, and swelling (**Figure 4b**). The innate immune system's mediation is to blame for this. Upon identifying vaccine proteins, neutrophils or macrophages release cytokines that trigger immunological responses, including fever, chills, nausea, and muscle pains. The majority of side effects are minor and go away in 24 to 48 hours. The variability depends on the dosage, age, and gender of the person [8]. These findings aligned with the findings of Alhazmi *et al.* [30], who found that 60–80% of adverse effects were linked to both Pfizer and AstraZeneca vaccinations. Additionally, recent studies found that people who received the identical immunisations experienced comparable side effects [31, 32]. The majority of our subjects (about 75–80%) received the Pfizer-BioNTech vaccine in the initial, second, and booster doses. Since younger people's immune systems are more robust and effective, the majority of our participants, who were between the ages of 15 and 30 years, were generally more likely to experience systemic adverse effects; nevertheless, this difference was not statistically significant. Similar results regarding systemic negative effects were reported by Alhazmi *et al.* [30]. This could be explained by the fact that most of the young individuals who developed systemic reactions received AstraZeneca's vaccination. According to some research, unpleasant effects are more likely to be reported by younger individuals than by older ones, which is in line with our findings [33–35]. In line with Menni and his group's investigation, which documented pain and soreness at the injection site, our subjects experienced local discomfort and tenderness at the injection site [32]. Additionally, a study conducted in Saudi Arabia by El-Shitany *et al.* [36] on a group of individuals who received solely the Pfizer-BioNTech vaccine revealed that 70–80% of their group experienced local pain.

Women were more likely than men to report side effects after immunisation in our study; 48% of females and 23% of males reported side effects after the first dose of the vaccine; this difference was statistically significant ($P < 0.0001$). Previous studies evaluating COVID-19 vaccines [36–39] have shown that women are more likely than men to experience side effects after vaccination. These side effects include influenza, the measles-mumps-rubella triple vaccine, attenuated Japanese encephalitis, and attenuated Dengue, which indicate that women have stronger immune responses and that side effects are more frequent and severe [23, 40].

We observed that the second immunisation dosage had an adverse event rate that was either somewhat greater or equivalent to the first. Regarding the negative side effects of the second dose of the vaccine, El-Shitany *et al.* [36] and Hatmal *et al.* [41] reached the same conclusion in their investigations. Since the immune system releases certain cytokines that produce inflammation in the vascular system, musculature, and numerous structures, in addition to common cold symptoms that persist for days after immunisation, this observation could be explained in terms of an immune system reaction [42]. According to our research, the first and second doses of the COVID-19 vaccination caused more severe adverse effects than the booster shots. The Centers for Disease Control and Prevention (CDC) report that the severity of side effects increases following the second dose, which contradicts this [18].

Our study has certain limitations, while being among the few in Saudi Arabia to examine the side effects of the three primary verified COVID-19 vaccinations. A self-administered web survey was used to collect the data, which may have introduced bias, particularly given the age category, as older people may find it challenging to access the internet. Additionally, evaluating thromboembolic profiles and other frequently reported symptoms

would be made easier by performing society surveys for the long-term side effects of these vaccines with a larger cohort of participants.

Conclusion

The short-term adverse effects of the Oxford-AstraZeneca, Pfizer-BioNTech, and Moderna COVID-19 vaccines were investigated in this study. Saudi Arabia has authorised the use of all three of these vaccinations. We observed several parameters affecting the severity, susceptibility, and mortality of COVID-19, including age, gender, and underlying comorbidities. In this study, the majority of vaccinated populations had fever, headache, injection site fatigue, discomfort, and redness; these symptoms were more prevalent in individuals who received the first and second doses of the vaccines. Furthermore, only a small number of patients needed medical care or hospitalisation because of the negative consequences of vaccinations. The Oxford-AstraZeneca vaccine was substantially linked to fever and exhaustion in comparison to the Pfizer-BioNTech vaccination. To assess the vaccines' ability to prevent and control SARS-CoV-2 infection as well as any long-term adverse effects, a comprehensive investigation is necessary.

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Conflict of Interest: None

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Ethics Statement: The study was approved by the ethical committee of Taif University (Research number/44-014), Taif University, Taif City, Saudi Arabia. All participants provided written informed consent before their enrolment in the study. Informed consent was obtained from all subjects involved in the study.

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