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Research Article

Covid 19 Vaccine Side Effects

The Severity of Covid-19 Infection and Vaccine Side Effects among the Saudi Population

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Abstract: COVID-19 first emerged in late 2019 in Wuhan, a city in the Hubie Province of China. Typical COVID-19 symptoms include fever, shortness of breath, and cough, whereas less common symptoms involve sudden onset of ageusia and/or anosmia, diarrhea, nausea, and vomiting. The primary objective was to compare the severity of symptoms among individuals infected with COVID-19 who have been vaccinated and those who have not. The second objective is to describe individuals' post-vaccination side effects and complaints to understand Saudis' aversion to vaccinations. This is a cross-sectional study among residents of Saudi Arabia including Saudis and non-Saudis. An online questionnaire was distributed via several social media channels. Univariate analysis was used to compare respondents' demographic, COVID-19 infection, and post-vaccination characteristics. Bivariate associations were assessed using Chi-square χ^2. Adjacent categories logit model was used to compare severity reported levels and COVID-19 related and demographic factors. A total of 1,432 respondents completed the survey. Most of the infected individuals were not immune at the time of infection and reported more than four symptoms. There was no significant association between vaccinated and non-vaccinated individuals in terms of reporting COVID-19 severe infection. On the other hand, there were several significant predictors of reporting severe COVID-19 infection level as number of symptoms, hospitalization, gender, marital status, and education attainment. Men are more likely to report severe COVID-19 complications. Participants who hold a higher degree are more likely to report severe COVID-19 infection. Local side effects included pain, swelling, itchiness, warmth, and bruising at the site of the injection. Systemic side effects included fever, headache, fatigue, period changes, and diarrhea. Allergic side effects include local rash, skin burning, and urticaria. Further research is needed to better understand the severity and side-effects of COVID-19 vaccines and even boosters.

Keywords: COVID-19; Signs And Symptoms; Vaccination; Side-Effects; Saudi Arabia

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1. INTRODUCTION

COVID-19 also known as Coronavirus Disease, first emerged in late 2019 in Wuhan, a city in the Hubie Province of China. It was only declared a pandemic in March of 2020 by the World Health Organization (WHO), and shortly after, classified as a respiratory virus. Typical symptoms of COVID-19 include fever, shortness of breath, and cough, whereas less common symptoms include sudden onset of ageusia and/or anosmia (loss of taste and smell), diarrhea, nausea, and vomiting [1]. As of November 30, 2021, the total number of cases and deaths in Saudi Arabia had reached over 500,000 and over 8,800, respectively [2]. Saudi Arabia was one of the leading countries to take COVID-19 precautionary measures to ensure the safety of its population [3]. The three main precautionary measures were regular hand washing, wearing a mask in public and crowded spaces, and maintaining a safe distance of six feet between individuals in public. The aforementioned measures have been put in place due to the virus's various modes of transmission from human-to-human which include aerosols and droplets from infected individuals through coughing, sneezing, or even talking. Such precautionary measures were the first armor against the spread of COVID-19; being effective, they are practiced until November 2021 [4]. COVID-19 vaccinations in Saudi Arabia are offered by the Saudi government free of charge for both Saudis and Non-Saudis since December 2020, as soon as the Pfizer-BioNTech vaccine was approved by the UK, making it one of the very first countries to roll out the Pfizer-BioNTech vaccine [5]. The Saudi Ministry of Health has opened an electronic portal called Sehhaty and Tawakkalna for citizens and residents of Saudi Arabia to book an appointment and receive their COVID-19 vaccine at their nearest center. This portal is also used for contact tracing as it monitors COVID-19 cases, schedules screening tests, and notifies residents if they were in the vicinity of a confirmed COVID-19 case [6]. The vaccination program in Saudi Arabia was in phases. First, individuals of age 65 and above and those with chronic medical conditions such as hypertension, diabetes mellitus, asthma, or other high-risk conditions were vaccinated with the Pfizer-BioNTech that was available at the time 5. Shortly after that, vaccination centers were open to all through an instant appointment booking system via Sehhaty app portal. Recently, vaccine centers began offering Pfizer-BioNTech and AstraZeneca vaccines to children and adolescents of age 12 years and above. Getting vaccinated has allowed the Saudi population to go back to a safe life. The Saudi government mandated vaccinations among adults on August 1, 2021, to enter any government or private entity, educational facilities, and any entertainment or sporting activity, such as malls and movie theaters [7]. Developing a vaccine against COVID-19 is considered a key strategy to end this pandemic. Although pharmaceutical companies, researchers, and scientists have worked hand-in-hand and tirelessly to develop vaccines that are safe and effective, there seems to be hesitancy among many individuals to get vaccinated which poses a barrier to the Saudi COVID-19 vaccination program [8]. With over 54% of the world's population being vaccinated with at least 1 dose, and over 47 million of them in Saudi Arabia, it has been shown that many vaccinated individuals, whether with one or two doses, were still unfortunate to contract the virus (vaccine breakthrough cases). Such cases add to the growing hesitancy among many individuals to get the COVID-19 vaccine. Furthermore, such cases also encourage further and aggressive research on COVID-19 infection and vaccine development, as vast amounts of information remain yet to be uncovered [9]. The primary objective of this study is to explore the severity of COVID-19 symptoms with a comparison between vaccinated and unvaccinated individuals. The secondary objective is to explore the side effects of COVID-19 vaccines to understand hesitancy towards COVID-19 vaccines among the Saudi population.

2. MATERIALS AND METHODS

2.1 Study Sample

This is a cross-sectional study among adults above 18 years old residing in Saudi Arabia. The study inclusion and exclusion criteria included all Saudis and non-Saudis who live in Saudi Arabia during the data collection and excluded individuals under the age of 18. A total of 1,432 respondents completed the survey.

2.2 Questionnaire

Participants completed a self-reported online questionnaire that elicited three main sections. An online questionnaire was distributed via several social media channels, including WhatsApp, LinkedIn, Twitter, Facebook, and Instagram. The survey was created on the 4th of September 2021 and lasted for two weeks. The survey included three main sections. The first section covered demographics, including age, gender, employment status, income, marital status, and nationality. The second section included questions related to COVID-19 infection, signs and symptoms, vaccine, and related side effects. The third section covered health status related questions, including chronic medical conditions, height, weight, physical activity, and eating patterns[10].

2.3 Data Sources and Measurement

The survey was distributed in English and Arabic languages and validated by a language professional. A pilot study was carried out to ensure the study's reliability and validity [11]. No identifying information such as names or emails were collected. Access to the data was restricted to the authors only. Participation was voluntary and completing the survey was construed as consent from participants to be part of the study. Participants were able to withdraw at any time. Informed consent was obtained from all subjects involved in the study to conduct the research. This study is approved by the Institutional Review Board (IRB) at Alfaisal University (IRB # 20130).

2.4 *Statistical Analysis*

The authors first examined descriptive statistics to compare respondents' demographics. Then, univariate analysis was used to compare respondents' demographic, COVID-19 infection, and post-vaccination characteristics. Bivariate associations were assessed using Chi-square χ^2. We used adjacent categories logit models to compare severity reported levels and COVID-19 related and demographic factors. Proportionality assumption by each independent variable was examined and found that the log odds do not depend on the outcome category [12]. All analyses were performed using SAS 9.4 with a two-sided p-value (α=0.05).

3. RESULTS

Descriptive statistics were used to compare respondents' demographics. Univariate analysis was used to compare

respondents' demographic, COVID-19 infection, and post-vaccination characteristics. Bivariate associations were assessed using Chi-square χ^2 test. Adjacent categories logit model was used to compare severity reported levels and COVID-19 related and demographic factors. Proportionality assumption by each independent variable was examined and found that the log odds do not depend on the outcome category. All analyses were performed using SAS 9.4 with a two-sided p-value (α=0.05). A total of 1,432 respondents completed the survey. A large proportion of the respondents were individuals aged 18-29 (58.8%), females (60.75%), single (57.96), with normal weight (41.13%), holding bachelor's/diploma degree (47.56%), Saudis (72.97%), students (48.04%), with no reported chronic diseases (88.83%),and resided in the Central region of Saudi Arabia (60.48%) (Table 1).

Table 1. Demographic characteristics of participants

Total	n (%)[1]
	1432
Age	
18 - 29	842 (58.8)
30 - 44	358 (25.00)
45 - 65	214 (14.94)
65+	18 (1.26)
Gender	
Male	562 (39.25)
Female	870 (60.75)
Marital status	
Married	570 (39.8)
Single	830 (57.96)
Divorced	25 (1.75)
Widowed	7 (0.49)
Body Mass Index (BMI)	
Normal	589 (41.13)
Underweight	103 (7.19)
Overweight	400 (27.93)
Obese	340 (23.74)
Education attainment	
Highschool or less	587 (40.99)
Bachelor's/ Diploma	681 (47.56)
Higher Degree	164 (11.45)
Chronic diseases status	
Yes	160 (11.17)
No	1272 (88.83)
Nationality	
Saudi	1045 (72.97)
Non-Saudi	387 (27.03)
Employment status	
Employed	488 (34.08)
Non-employed	191 (13.34)
Retired	65 (4.54)
Student	688 (48.04)
Monthly income in Saudi Riyals	
Less than 5000 SR	484 (33.80)
5,000 - 9,999 SR	171 (11.94)
10,000 - 20,000 SR	198 (13.83)
More than 20,000 SR	137 (9.57)
I prefer not to answer	442 (30.87)
Region of residency	
Central region	866 (60.47)
Eastern region	322 (22.49)
Northern region	67 (4.68)
Western region	87 (6.08)
Southern region	90 (6.28)

1 "n" sample size, % percentage

On an average, one out of four individuals reported previous infection with COVID-19 (25.63%). Most of the infected individuals were not immune at the time of infection (68.11%) and reported more than four symptoms (75.47%). Moreover, 9.81% reported severe infection and 11.17% were hospitalized. The majority (90.73%) of the respondents reported no complications during COVID-19 infection (Table 2).

Table 2. COVID-19 infection status and characteristics among participants	
Total	n (%)[1]
	367
Prior COVID-19 infection	
Yes	367 (25.63)
No	1065 (74.37)
Immunization status at the time of infection	
No, I wasn't immune	250 (68.11)
Yes, one and two doses	117 (31.88)
Number of symptoms during infection period prior to vaccination	
1 to 3 symptoms	90 (24.52)
More than 4 symptoms	277 (75.47)
Description of severity of infection	
Not too severe	205 (55.85)
Somewhat severe	125 (34.05)
Very severe	36 (9.81)
Hospitalizations during infection period	
Yes	41 (2.86)
No	325 (22.7)
Severe complications during infection period	
Bronchitis/Sepsis/Pneumonia	17 (4.63)
No complication	333 (90.73)
Missing	16 (4.35)
[1] "n" sample size, % percentage	

Respondents received predominantly the Pfizer-BioNTech vaccine for both their first and second doses (73.81% and 69.72%, respectively). Half of the respondents reported 1 to 3 systemic side effects after receiving the vaccine (50.77%), while (54.82 %) reported local side effects only (Table 3). Only few respondents reported allergic reactions (4.4%).

Table 3. COVID-19 vaccines and characteristics among respondents	
Total	n (%)
COVID-19 vaccine - first dose	
Pfizer	1057 (73.81)
Oxford/ AstraZeneca	317 (22.14)
Moderna	1 (0.07)
Johnson (Johnson & Johnson)	1 (0.07)
Sinopharm	2 (0.14)
I haven't received the first dose yet	50 (3.49)
I don't know	4 (0.280)
COVID-19 vaccine - second dose	
Pfizer	992 (69.27)
Oxford/ AstraZeneca	209 (14.59)
Moderna	7 (0.49)
Sinopharm	2 (0.14)
I haven't received the second dose yet	222 (15.50)
Number of COVID-19 vaccine systemic side effects	
1 to 3 side effects	727 (50.77)
More than 4 side effects	692 (48.32)
None	13 (0.91)
Number of COVID-19 vaccine local side effects	
1 to 3 symptoms	785 (54.82)
More than 4 symptoms	640 (44.69)
None	7 (0.49)
Allergic side effects after COVID-19 vaccine	
Yes	63 (4.4)
I haven't received COVID-19 vaccine yet	90 (6.28)
I haven't experienced any allergic side-effects after	1279 (89.320
[1] "n" sample size, % percentage	
[2] Chi-square test for more than 5 frequency per cell	

In the multiple logistic regression model, there was no significant association between vaccinated and non-vaccinated individuals in terms of reporting COVID-19 severe infection (p-value = 0.24). On the other hand, there were several

significant predictors of reporting severe COVID-19 infection level as number of symptoms, hospitalization, gender, marital status, and education attainment (p-value <.0001, <.0001, 0.02, 0.04, and 0.04, respectively) (Table 4, Figure 1).

Table 4. COVID-19 infection severity among vaccinated and unvaccinated individuals

	AOR [1]	95% CI [1]	p-value[2]
Immunization status at the time of infection			
No, I wasn't immune	Ref	Ref	Ref
Yes, one and two doses	1.34	(0.82, 2.18)	0.24
Number of symptoms during infection period prior to vaccination			
1 to 3 symptoms	0.12	(0.11, 0.25)	<.0001
More than 4 symptoms	Ref	Ref	Ref
Hospitalizations during infection period			
Yes	0.16	(0.11, 0.33)	<.0001
No	Ref	Ref	Ref
Gender			
Male	Ref	Ref	Ref
Female	0.55	(0.33, 0.92)	0.02
Marital status			
Married	Ref	Ref	Ref
Single	1.67	(0.93, 2.97)	0.08
Divorced	2.17	(0.54, 8.67)	0.27
Widowed	0.11	(0.01, 0,91)	0.04
Education attainment			
High School or less	Ref	Ref	Ref
Bachelor's/ Diploma	1.23	(0.72, 2.13)	0.43
Higher Degree	2.52	(1.03, 6.17)	0.04

[1] Adjusted odds ratio (AOR), confidence interval (CI)
[2] Multiple logistic regression
Ref= Reference

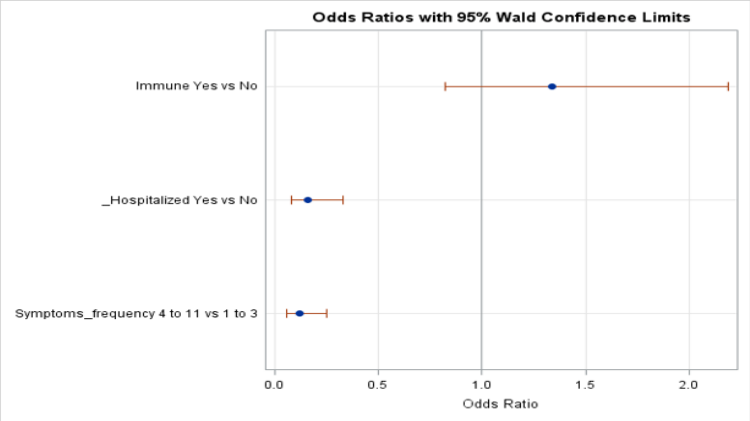

Fig:1 COVID-19 related predictors of severe COVID-19 infection

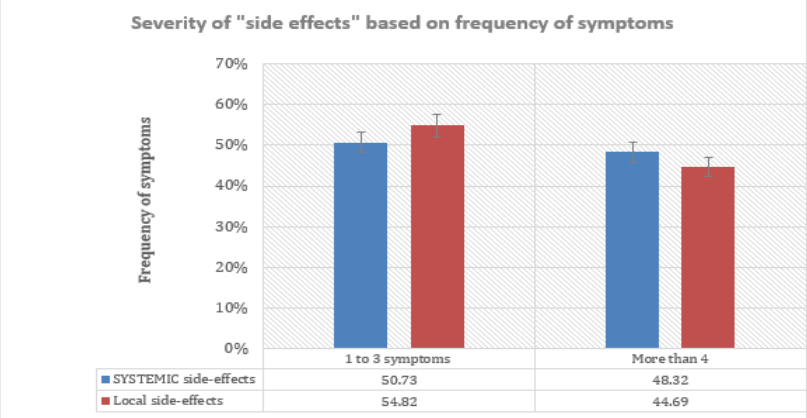

Fig 2 Severity of vaccine side effects

Respondents who reported 1 to 3 symptoms were less likely to report severe COVID-19 infection compared to those who reported more than 4 symptoms (Adjusted odds ratio AOR = 0.12; 95% CI = 0.11 - 0.25) (Figure 1). Similarly, respondents who reported hospitalization were less likely to report severe COVID-19 infection (AOR = 0.16; 95% CI = 0.11 - 0.33). Females and widowed respondents were less likely to report severe COVID-19 infection compared to males and married respondents (AOR = 0.55; 95% CI = 0.33 - 0.92, AOR = 0.11; 95% CI = 0.01 - 0.91, respectively). Respondents with higher education were two times more likely to report severe COVID-19 infection compared to those with high school or less (AOR = 2.52; 95% CI = 1.03 - 6.17) (Table 4). The symptoms of COVID-19 infection, the local, systematic, and allergic vaccine side-effects are presented in Table 5.

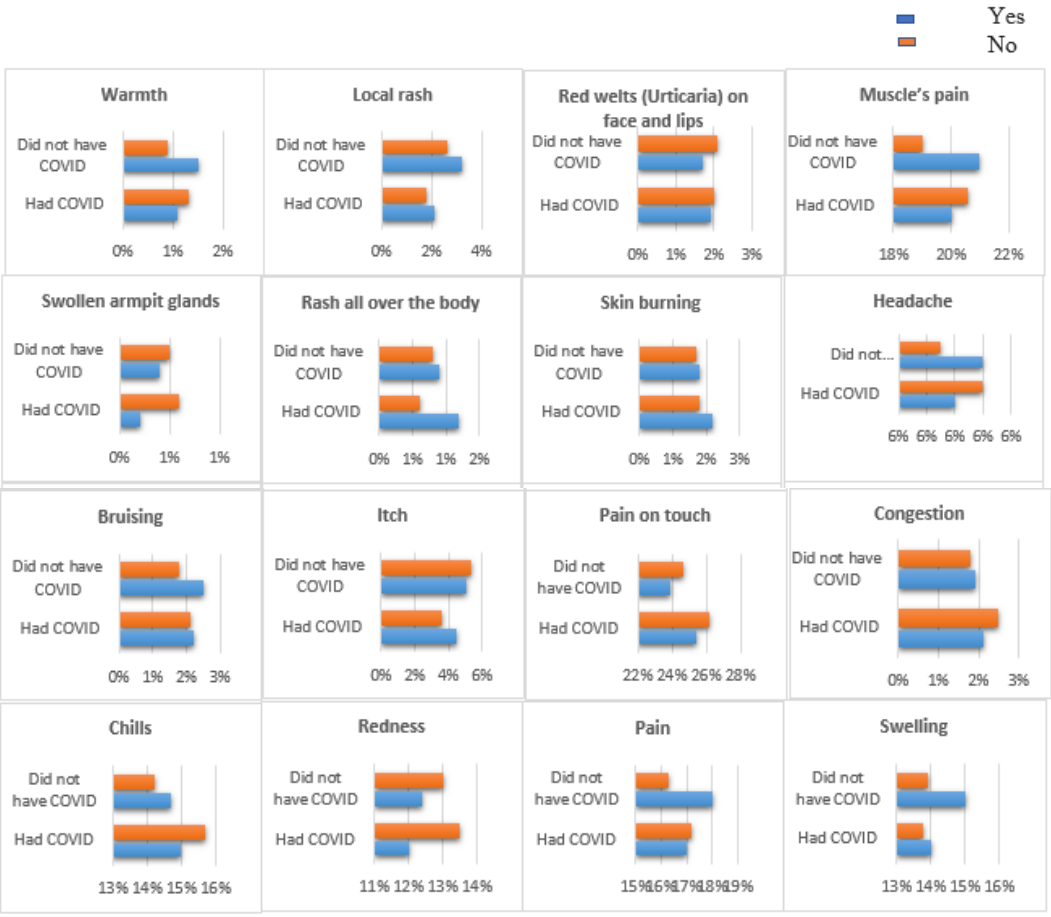

Fig 3: Severity of self-reported side effects after the first or second dose of the COVID-19 vaccine among participants who had or did not have a prior COVID-19 infection.

Prior COVID-19 infected individuals reported a slightly higher proportion of side effects such as pain in the injection site (25.4%) compared to (23.88%) among those without prior COVID19 infection. A slightly higher proportion of reported side effects for individuals with no prior COVID19 infection such as muscle's pain (21%) compared to (20%) prior COVID19 infection. Overall, in univariate analysis, as shown in figure1, there were no statistically significant differences in proportion of self- reported side effects after receiving the COVID-19 vaccines between previously COVID-19 infected individuals and those who were never infected.

Table 5. Symptoms and chronic diseases reported by respondents

Symptoms reported during infection period prior to vaccination	
Chills	Severe pain in the abdomen
Congestion	Elevation in the sugar levels
Muscle's pain	Severe mood changes
Cough	Vomiting (x2)
Sore throat	Hair loss (x2)
Headache	Sweating
Shortness of breath	Severe joints pain
Change of taste/smell	Allergy
Laziness	Nasal Allergy
Pain in the digestive system (x3)	Diarrhea (x2)
Severe pain in the eye (x2)	Memory loss
Redness in the eyes	Disturbance of perception and a coma state
Severe chest pain	

Local side effects reported after receiving COVID-19 vaccine	
Pain (at the site of injection	Redness (at the site of injection)
Swelling (at the site of injection)	Warmth (at the site of injection)
Pain on touch (at the site of injection)	Bruising (at the site of injection)
Itch (at the site of injection)	Swollen armpit glands after the first dose
Systemic side effects reported after receiving COVID-19 vaccine	
Headache	Rash around the neck region
Fatigue	Cold
Chills	allergy (x4)
Diarrhea	Heaviness in the hand
Fever	Severe itching
Joints	Swelling of the lymph nodes between the armpit and the breast (x5)
Muscles	Chronic urticaria flare
Nausea	Dizziness (x3)
Period changes	High cholesterol
Loss of vision	Pain in the abdomen (x2)
Shortness of breath from the first and second dose	Pain at the site of injection (x3)
Vomiting	Swollen lymph nodes by my chest area
Heart pain	chest pain
Hair fall (x3)	Excessive sleepiness
Lethargy and laziness (x4)	Pain in the shoulders
Allergic side effects reported after receiving COVID-19 vaccine	
Local rash	Skin burning after the first dose
Rash all over the body	Red welts (Urticaria) on face and lips

4. DISCUSSION

4.1 COVID-19 Severity

This study highlights important aspects of COVID-19 pandemic among the population of Saudi Arabia. It sheds light on the severity of coronavirus and the side-effects of the vaccines. Our study indicates that (68.11%) of positive COVID-19 cases were not immune at the time of infection, this finding is in line with Menni et al. that suggested Pfizer-BioNTech (BNT162b2) and the Oxford-AstraZeneca (ChAdOx1 nCoV-19) vaccinations reduce the probability of SARS-CoV-2 infection [13]. In addition, the US Food and Drug administration issued an Emergency Use Authorization about the effectiveness of COVID-19 vaccines [14]. A study in New York among 8,690,825 adults found that the median effectiveness of the vaccine against Covid-19 was 91.3% for BNT162b2, 96.9% for mRNA-1273, and 86.6% for Ad26.COV2.S [15]. A meta-analysis review that evaluated 41 studies found that patients who were males, with advanced age, obesity, with a history of smoking, hypertension, diabetes, malignancy, coronary heart disease, chronic liver disease, chronic obstructive pulmonary disease (COPD) or chronic kidney disease (CKD) are more likely to develop severe COVID-19 symptoms [16]. Moreover, according to a study published by Zhang JJ et al. in China that consisted of 140 patients, ninety patients (64.3%) had at least one chronic disease such as hypertension and diabetes 17. Also, a retrospective study based in Saudi Arabia by Yousef M AlSofayan et al. found that 54.1% of the patients were males and 20.1% had comorbidities 18. Another study conducted in Italy found a higher severity of COVID-19 among older age groups as well as among males [19, 20]. Our results as well showed that females are less likely than men to report severe COVID-19 infection. A systematic review and meta-analysis based on 109 articles, found the severity of infection and risk of mortality to be associated with increasing age, male gender, dyspnea, diabetes, hypertension, and congestive heart failure. This article supports our finding of females being less likely to report severe infections, and further supports that chronic diseases play a role in severity of infection 21. The severity of infection also varied by educational attainment in our study; participants who hold a higher degree are more likely to report severe COVID-19 infection.

4.2 COVID-19 symptoms

Our findings revealed several reported symptoms during COVID-19 infection such as chills, congestion, muscle pain, sore throat, shortness of breath, joints pain, allergy, and mood changes. Based on the study by Zhang JJ et al.in China,out of the 140 patients, the most commonly experienced symptoms were fever (91.7%), followed by cough (75%), fatigue (75%), and chest tightness or dyspnea (36.7%). 39.6% of them complained about gastrointestinal symptoms, including nausea, diarrhea, poor appetite, abdominal pain, belching, and emesis [17]. Moreover, a retrospective study based in Saudi Arabia by Yousef M AlSofayan et al. focusing on COVID-19 signs and symptoms found that the most common symptom was cough (89.4%), followed by fever (85.6%), and sore throat (81.6%). As for the signs, 20.3% had a temperature above 38 C, 1.6% had a heart rate higher than 125 beats/min, and 4.7% had a respiratory rate above 24 breaths/min 18. However, another systematic review and meta-analysis found that the most common symptom was fever (81.2%), followed by cough (58.5%), fatigue (38.5%), dyspnea (26.1%), and lastly sputum (25.8%) [22]. Furthermore, according to a comprehensive review study by Ochani et al. the most common complaints are also fever, cough, and dyspnea, and less frequent gastrointestinal symptoms like diarrhea [23]. In addition to that, several studies

including a cross sectional study by Giacomelli et al. found that there have been reports and documentations of olfactory disturbances (anosima) as well as taste alterations during a COVID-19 infection 24.A study by S. Recalcati claimed that several infected patients have also developed cutaneous manifestations like erythematous rash, widespread urticaria as well as chickenpox-like vesicles [25].

4.3 Vaccine Side-effects

Overall, our findings confirm that the COVID-19 vaccine has several side effects. These side effects are unique based on the different variables used in the study. COVID-19 vaccine's body reaction is usual as the introduction of foreign substances in the body triggers an immune system response. There were local side effects such as pain, swelling, itchiness, warmth, and bruising at the site of the injection. Reported systematic side effects included fever, headache, fatigue, period changes, and diarrhea. Allergic symptoms such as local rash, skin burning, and urticaria were also reported. The literature also suggests similar findings. Comparable results are presented in a cross-sectional study among healthcare workers in the US (n=1245). The study found out that most of them have received the vaccine and reported one or more side effects post-vaccination. Most of those who reported side effects were able to perform daily activities, however, some of them took days off from work. Only a small number of people were required to visit the hospital. Commonly reported side effects include: soreness, fatigue, myalgia, headache, and fever [26]. Another cross-sectional study among Jordanians (n=2213) also confirms our findings as it indicated that many individuals experienced post-vaccine side effects. In this study, the majority of participants reported mild to moderate symptoms, while the minority reported severe symptoms. The study also reported that several factors such as the type of vaccine and number of vaccine doses play a role in increasing the severity of the vaccine side effects [27]. A Saudi local study among 455 individuals found similar findings as the most common side effects after the vaccine were site pain, flu-like symptoms, fever and tiredness. However, less common side-effects were chills, difficulty breathing, and joint pain. El-Shitany et. al found that females in Saudi Arabia had significantly more side-effects after vaccinations than males [28]. Moreover, a study in the United Arab Emirates found that vaccine post side-effects were common among those under 49 years old, with pain on the vaccine site, fatigue and lethargy were the most common reported side-effects [29]. According to a study in Australia, COVID-19 vaccines from AstraZeneca and Pfizer BioNTech can produce delayed-onset, local allergic responses after vaccination 30. Another cross-sectional study among adults in Czech Republic (n=922) found that the most commonly reported COVID-19 vaccine side effects were injection site discomfort (89.8%), fatigue (62.2%), headache (45.6%), muscular soreness (37.1%), and chills (33.9%) 31. A local study among Saudi residents found that injection site pain, headaches, flu-like symptoms, fever, and exhaustion were the most prevalent complaints after COVID-19 vaccine [28].In another study conducted in Jordan by Hatmal et al., the authors found that the most common post-vaccination effects were fatigue, headache, sleepiness, fever, chills, myalgia, and injection site pain [27]. The results also showed that 50.77% of the participants had three systematic side effects after receiving the COVID-19 vaccine, and 54.82% had local side effects. According to a study published in the UK by Menni et al., systemic side effects were more common after the first dose among individuals with previous SARS-CoV-2 infection than among those without known past infection (for both Pfizer-BioNTech and the Oxford-AstraZeneca vaccines). Local effects were similarly higher in individuals previously infected than in those without known past infection [32].

4.4 Limitations

There are several limitations to our study that should be noted. The cross-sectional nature of the study prohibits any causal inferences. Selection bias is a major limitation since the survey was distributed online, which prevents generalizability. We also relied on participants' responses solely with no clinical validation of healthcare providers. Additionally, some respondents have received the COVID19 vaccine long before he or she participated in the study, thus a potential recall bias might be expected.

5. CONCLUSION

In conclusion, this cross sectional study among residents of Saudi Arabia demonstrated that females are less likely than men to report severe COVID-19 complications. Participants who hold a higher degree are more likely to report severe COVID-19 infection. There were several COVID-19 vaccine side effects. Local side effects included pain, swelling, itchiness, warmth, and bruising at the site of the injection. While systemic side effects included fever, headache, fatigue, period changes, and diarrhea. Participants also reported allergic side effects such as local rash, skin burning, and urticaria. As literature on COVID-19 continues to develop, further research on the topic is warranted to fully understand the severity of COVID-19 infection and vaccines on the population.

6. AUTHORS CONTRIBUTION STATEMENT

Dr. Noara Alhusseini conceptualized the research idea. Dr.Noara Alhusseini, Dr. Aya Ismail, Dr. Hani Alaswad, Dr. Fawzy Abodahab, Dr. Shahdad Almutahhar, and Dr. Majd Khader collected and gathered the data with regard to this work. Dr. Majed Ramadan and Dr. Ismail Shakir analyzed these data and necessary inputs were given towards the designing of the manuscript. Dr. Alaa Alabadi-Bierman wrote parts of the introduction and discussion sections. All authors participated in writing the introduction and discussed the methodology, results and contributed to the final manuscript.

7. CONFLICT OF INTEREST

Conflict of interest declared none.

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