Original Article

Post-Vaccination Serological Evaluation of COVID-19 in the Population of Kenitra, Morocco

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ABSTRACT

Background

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is responsible for Coronavirus Disease 2019 (COVID-19) and is considered one of the most challenging pandemics of the 21st century. This complex situation has brought together scientists and healthcare professionals to develop new vaccines that are both safe and quick to produce.

Method

The present study aims to evaluate the effects of COVID-19 vaccination on the serology of 701 patients attending healthcare centers in the province of Kenitra (Rabat-Salé-Kenitra region) based on various demographic and clinical parameters. The types of vaccines administered (Sinopharm, AstraZeneca, Johnson & Johnson, Pfizer) and vaccination schedules were examined, highlighting variations in immune responses. Subsequently, logistic regression analysis was used to assess the contributions of variables such as age, gender, comorbidities, types of vaccines administered, and history of COVID-19 infection.

Results

Data analysis reveals a slight female predominance among participants (55.9%), a diverse age distribution ([55-60], 12.8%), and a significant prevalence of comorbidities, mainly diabetes and hypertension (49.9% with diabetes). The results showed that age and history of COVID-19 infection had a significant influence on serological responses.

Conclusion

This finding could help practitioners and public health professionals optimize vaccination strategies for future epidemics.

Keywords

COVID-19; COVID-19 vaccine; Serology, Humoral Immunity; Coronavirus

INTRODUCTION

COVID-19, caused by the novel coronavirus SARS-CoV-2, emerged as a global health crisis at the end of 2019[1]. Initially identified in Wuhan, China, the virus quickly spread worldwide, leading to a pandemic declared by the World Health Organization (WHO) on March 11, 2020. Since then, COVID-19 has caused significant morbidity, mortality, and disruption of daily life, affecting millions globally[2].

The COVID-19 pandemic has spurred an unprecedented mobilization of medical and scientific resources to develop effective

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vaccines. Vaccination is considered one of the key measures to control the spread of the virus and reduce associated morbidity and mortality[3]. However, vaccine efficacy can vary based on various factors, including the demographic and clinical characteristics of patients[4]. This study aims to evaluate the impact of COVID-19 vaccination on the serology of patients, considering parameters such as gender, age, comorbidities, types of vaccines administered, and intervals between doses, by analyzing the correlations between these parameters and serological responses.

MATERIALS AND METHODS

The study was conducted from January 14, 2022, to May 23, 2023; in health centers in Kenitra, Morocco, focusing on patients of both genders aged 18 or older who had received at least one dose of a COVID-19 vaccine. A total of 701 patient records meeting the inclusion criteria were selected, while those not meeting these criteria were excluded.

Blood samples were collected aseptically and analyzed using the Enzyme-Linked Immunosorbent Assay (ELISA) technique at the National Institute of Hygiene-Rabat to measure antibodies, with seropositivity defined as levels ≥33.8 BAU/mL per WHO guidelines[5].

Various ethical aspects were meticulously considered, including obtaining authorization, securing the free and informed consent of study participants, ensuring their rights to anonymity and confidentiality, and guaranteeing fair and equitable treatment. All participants were fully informed, without exception, about the nature, purpose, and duration of their participation in the study.

Statistical analyses, including ANOVA and logistic regression, were employed to evaluate the influence of demographic and clinical factors on immune response, considering variables like vaccine type, dosage intervals, and prior infection.

RESULTS

Gender Distribution of Patients

The study on the evaluation of the effects of COVID-19 vaccination on patient serology reveals a gender distribution among participants: 44.1% male and 55.9% female. This female predominance in the sample can be examined from several perspectives (Table 1).

Table 1: Gender Distribution of Patients

Gender	Percentage (%)
Male	44.1 a
Female	55.9 b
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Age Distribution of Patients

The analysis of age distribution among participants in the study on the effects of COVID-19 vaccination on serology reveals a varied pattern. Young adults (18-35 years) are underrepresented, accounting for 5.6%-7.7% of participants. In contrast, middle-aged groups (35-60 years) are predominant, with the highest participation observed in the 45-50 years group at 16.7% (Table 2).

Table 2: Age Distribution of Patients

Age	Percentage (%)
[18-25]	05.6a
[25-30]	07.7a
[30-35]	07.7a
[35-40]	09.7ab
[40-45]	12.1b
[45-50]	16.7bc
[50-55]	11.8b
[55-60]	12.8b
[60-65]	09.7ab
> 65	06.1a
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Distribution of Comorbidities within the Study Population

According to the data reported in Table 3, individuals without comorbidities represent only 7.1% of the participants. Diabetes is the most prevalent comorbidity, affecting 49.9% of participants, followed by hypertension (HTN), which is present in 35.7% of cases. Additionally, a combination of diabetes and hypertension is observed in 7.3% of participants,

highlighting the significant burden of these conditions within the study population.

Table 3: Distribution of Patients by Comorbidity

Comorbidity	Percentage (%)
No comorbidities	07.1 a
Diabetes	49.9 bc
Hypertension	35.7 b
Diabetes + Hypertension	07.3 a
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Distribution of Patients by COVID-19 Infection History

Analysis of the results indicates that among the surveyed patients, 32.7% reported having been previously infected with COVID-19, while 67.3% indicated they had never been infected. This distribution suggests that the majority of individuals included in the study had not contracted the virus by the survey date (Table 4).

Table 4: Distribution of Patients by History of COVID-19 Infection

History of COVID-19 Infection	Percentage(%)
Yes	32.7 a
No	67.3 b
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Administration of the First Dose of Vaccines and Distribution of Vaccine Types

The data show that 100% of participants received the first dose of the COVID-19 vaccine. (Table 5)

Table 5: Distribution of Patients by Administration of the First Dose of COVID-19 Vaccines

Administration of the First Dose	Percentage(%)
Yes	100 b
No	0.00 a
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

The distribution of types of vaccines administered for the first dose reveals a predominance of the Sinopharm vaccine, used by 59.5% of participants. AstraZeneca was the second most commonly administered vaccine, accounting for 26.5% of participants, while the Johnson & Johnson vaccine was given to 3.1%. Additionally, 10.8% of participants received the Pfizer vaccine, highlighting the varied use of different vaccine types in the study population. (Table 6)

Table 6: Distribution of Patients by Type of COVID-19 Vaccines Administered (First Dose)

Type of Vaccine Administered (First Dose)	Percentage(%)
Sinopharm	59.5c
AstraZeneca	26.5b
Johnson & Johnson	03.1a
Pfizer	10.8a
Total	100

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Administration of the Second Dose of Vaccines and Distribution of Vaccine Types

The data indicate that 90.7% of participants received the second dose of the COVID-19 vaccine, while 9.3% did not. (Table 7)

Table 7: Distribution of Patients by Administration of the Second Dose of COVID-19 Vaccines

Administration of the Second Dose	Percentage(%)
Yes	90.7b
No	09.3a
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Among participants who received the second dose, 56.6% were received the Sinopharm vaccine. The AstraZeneca vaccine was administered to 26.5% of participants, maintaining the same proportion as the first dose. The Pfizer vaccine was administered to 7.6% of participants for the second dose, showing a slight decrease from the first dose. Additionally, 9.3% of participants did not receive a second dose, which aligns with the proportion of individuals who reported not having received it. (Table 8)

Table 8: Distribution of Patients by Type of COVID-19 Vaccines Administered (Second Dose)

Type of Vaccine (Second Dose)	Percentage (%)
No Vaccine	09.3a
Sinopharm	56.6c
AstraZeneca	26.5b
Pfizer	07.6a
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Administration of the Third Dose of Vaccines and Distribution of Vaccine Types

The results show that 33.1% of participants received the third dose of the COVID-19 vaccine, while 66.9% did not. (Table 9)

Table 9: Distribution of Patients by Administration of the Third Dose of COVID-19 Vaccines

Administration of the Third Dose	Percentage (%)
Yes	33.1a
No	66.9b
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Among participants who received the third dose, 27.7% received the Sinopharm vaccine. The Pfizer vaccine was administered to 4.9% of participants for the third dose. While only 0.7% received the AstraZeneca vaccine. Additionally, 66.8% of participants did not receive a third dose, which reflects the high proportion of individuals who reported not having received it (Table 10).

Table 10: Distribution of Patients by Type of COVID-19 Vaccines Administered (Third Dose)

Type of Vaccine (Third Dose)	Percentage (%)
No Vaccine	66.8 c
Sinopharm	27.7 b
AstraZeneca	00.7 a
Pfizer	04.9 a
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Interval Between Vaccine Doses

Interval Between the First and Second Dose of COVID-19 Vaccines

The data reveal that the vast majority of participants received their second dose within a short interval after the first, with 49.1% within 30 days and 33.4% within 30 to 60 days. A small percentage of participants (3%) received their second dose between 60 and 90 days. Longer intervals, beyond 90 days, were much less common, with only 0.1% to 0.3% of participants receiving their second dose between 90 and 210 days after the first. Notably, 13.7% of participants did not receive a second dose, which is an important factor to consider. (Table 11).

Table 11: Interval Between the First and Second Dose of COVID-19 Vaccines

Interval Between the First and Second Dose	Percentage (%)
Not Vaccinated	13.7 b
≤ 30 Days	49.1 d
30-60 Days	33.4 c
60-90 Days	03.0 a
90-120 Days	00.1 a
120-150 Days	00.3 a
150-180 Days	00.1 a
180-210 Days	00.2 a
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Interval between the Second and Third Dose of COVID-19 Vaccines

The interval between the second and third doses shows a distinct pattern. A significant majority, 67.5% of participants, did not receive a third dose. Among those who did, the intervals vary widely. A small percentage received the third dose within 90-150 days, while larger proportions were observed in the 150-210 day range, with a notable peak between 180-210 days (9.3%). The most common interval after 180 days was 210-240 days (10%), likely reflecting updated booster

recommendations. However, intervals beyond 240 days saw a gradual decrease in third-dose uptake, with percentages ranging from 4.1% to 0.2%. (Table 12)

Table 12: Average Interval Between the Second and Third Dose of COVID-19 Vaccines

Interval Between the Second and Third Dose	Percentage (%)
Not Vaccinated	67.5
90-120 Days	00.3
120-150 Days	01.1
150-180 Days	03.9
180-210 Days	09.3
210-240 Days	10.0
240-270 Days	04.1
270-300 Days	01.9
300-330 Days	01.7
330-360 Days	00.2
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

Distribution of Serological Levels Among Patients

The serological results of participants in the study evaluating the effects of COVID-19 vaccination reveal a distribution of antibody levels with a significant majority having a robust immune response. The data show that 85.7% of participants have antibody levels above 33.8 BAU/mL, while 14.3% have levels equal to or below this value (Table 13).

Table 13: Serological Test Results of Patients Who Received COVID-19 Vaccines

Serology Level (BAU/mL)	Percentage (%)
≤ 33.8	14.3a
> 33.8	85.7b
Total	**100**

Means in the same column with the same letter do not differ significantly from each other at the 5% significance level.

DISCUSSION

The data indicates that women are often more inclined to participate in health studies and medical research initiatives[6], possibly due to greater concern for their health and higher receptiveness to public health recommendations. Women may also perceive the risk of contracting infectious diseases like COVID-19 differently and may be more proactive in seeking preventive measures such as vaccination[7]. However, the gender distribution could also reflect differences in accessibility and vaccine acceptance between men and women, influenced by socio-economic, cultural, or psychological factors. Some studies suggest that men are sometimes more hesitant to receive vaccines, which could explain their lower representation in this study[8].

The low representation of young adults may be due to their perception of COVID-19 as less severe or different vaccination priorities. In contrast, middle-aged adults are more aware of the risks, and their higher participation likely reflects prioritization in public health programs due to their increased risk of severe complications[9]. The underrepresentation of older individuals might stem from logistical challenges or prior vaccination coverage. However, given their vulnerability to severe COVID-19 outcomes, understanding their post-vaccination serological response remains crucial. This demographic diversity highlights the need for targeted vaccination strategies to ensure effective protection, especially for young adults and older individuals, and to achieve herd immunity against COVID-19[10].

The distribution of comorbidities in the study population highlights the importance of targeting high-risk groups in COVID-19 vaccination campaigns. Notably, only 7.1% of participants were without any comorbidities, and a significant portion had diabetes and/or hypertension—conditions known to increase the risk of severe COVID-19 outcomes. A combination of both diabetes and hypertension was present in 7.3% of participants, further emphasizing a particularly high-risk group. This underscores the need for an in-depth evaluation of vaccine efficacy in these populations, as they are particularly vulnerable to complications from COVID-19[11].

This result has several implications for vaccination and pandemic management. Individuals previously infected with COVID-19 may have developed some natural immunity, though the duration and level of

protection can vary. This could influence vaccination strategies, potentially recommending a single dose or adjusting the vaccination schedule[12]. For those without prior infection, vaccination remains crucial to develop immunity against the virus, as vaccines are designed to stimulate a specific immune response, providing effective protection against severe disease and reducing community transmission[13]. Notably, 32.7% of participants reported a history of COVID-19 infection, which may impact vaccination strategies, as those with prior infection could have some level of natural immunity. Nonetheless, vaccination is essential for all, particularly to reduce illness severity and transmission.

All participants received the first dose of the COVID-19 vaccine, reflecting a high rate of acceptance. This could be attributed to effective awareness campaigns, the perceived urgency of protecting against the virus, and well-executed public health policies promoting vaccination[14]. The Sinopharm vaccine, an inactivated type, was the most commonly administered for the first dose (59.5%), followed by AstraZeneca (26.5%) and Johnson & Johnson (3.1%). Sinopharm's high usage can be attributed to its availability and logistical benefits, while AstraZeneca's widespread adoption is linked to its efficacy and relatively low cost.

The second dose was administered to 90.7% of participants, with vaccine distribution patterns similar to the first dose. This high adherence is crucial for ensuring complete and long-lasting immunity, as recommended by most vaccination protocols. However, nearly 10% of participants did not receive the second dose, possibly due to hesitancy, side effects, or logistical issues. Addressing these obstacles is essential for improving vaccination rates[15]. The high adherence to the second dose reflects the success of vaccination campaigns and effective management of vaccine resources. However, the significant minority not receiving the second dose underscores the challenges that must be overcome to achieve full vaccination coverage[16].

The third dose of the vaccine saw a significant drop in participation, with only 33.1% of participants receiving it. This sharp decline suggests several factors at play. First, the third dose, often considered a booster, may have been deprioritized by individuals and public health authorities due to perceptions that the initial doses provided sufficient protection or reduced urgency for additional doses. Additionally, factors like vaccine hesitancy, pandemic fatigue, or logistical constraints may have contributed to the low adherence[17]. The most common vaccine administered for the third dose was Sinopharm (27.7%), followed by Pfizer (4.9%) and AstraZeneca (0.7%). The limited uptake and vaccine diversity for the third dose highlight ongoing challenges in booster vaccination campaigns, influenced by factors such as vaccine availability, public health recommendations, and individual perceptions about the need for a third dose[18].

The interval between doses varied significantly, with the majority receiving their second dose within 30 to 60 days of the first. This concentration in shorter intervals reflects initial public health recommendations aimed at quickly completing the vaccination regimen to achieve optimal protection against COVID-19, ensuring rapid immunity in response to the pandemic's immediate threat. However, some participants received the second dose later due to logistical delays, medical complications, or variations in vaccination guidelines. While studies suggest that longer intervals between doses can enhance the immune response, the urgency of the situation typically favored faster schedules. The majority of participants who did not receive the second dose could benefit from targeted efforts to address barriers such as side effects from the first dose, vaccine hesitancy, limited access, or changes in health status[19].

For the third dose, most participants had intervals between 150 and 240 days, reflecting public health strategies to extend booster intervals. However, adherence to the third dose was much lower compared to the first two doses, highlighting persistent challenges in booster vaccine uptake[20].

The serological results revealed that 85.7% of participants had antibody levels above 33.8 BAU/mL, indicating a strong immune response and suggesting that the majority developed effective immunity against the virus post-vaccination. This robust immune response is essential for individual protection against severe infections and contributes to herd immunity, reducing virus transmission within the population. The high percentage of participants reaching this antibody level reflects the efficacy of the administered vaccines, including Sinopharm, AstraZeneca, Pfizer, and Johnson & Johnson. However, 14.3% of participants had antibody levels at or below 33.8 BAU/mL, indicating suboptimal protection. Several factors could explain these lower antibody levels, such as individual variations in immune response, comorbidities, advanced age, or extended

intervals between vaccine doses. This group may benefit from additional doses or boosters to improve their immune response, highlighting the importance of continued monitoring and personalized vaccination strategies, particularly for vulnerable individuals[21, 22].

The logistic regression results provide the coefficients (B), standard errors (S.E.), Wald values, degrees of freedom (df), significances (Sig.), and odds ratios (Exp(B)) for each variable included in the model.

Gender did not show statistical significance ($p = 0.35$), suggesting it does not strongly influence post-vaccination serology. Age, however, was a significant factor ($p < 0.05$) with a B coefficient of -0.373, indicating that an increase in age decreases the likelihood of having serology > 33.8 BAU/mL, with an odds ratio of 0.688. This means each additional year reduces the probability of a high serological response by 31.2%.

Comorbidity did not show statistical significance ($p = 0.74$), indicating it does not significantly affect serology. Similarly, the type of first dose vaccine was not significant ($p = 0.507$), nor was the second dose administration ($p = 0.274$) or the type of second dose vaccine ($p = 0.85$). The administration of the third dose also did not show statistical significance ($p = 0.135$), nor did the type of third dose vaccine ($p = 0.108$).

However, a previous COVID-19 infection was a significant factor ($p < 0.05$) with a B coefficient of -1.278. This means that patients with a prior COVID-19 infection are less likely to have serology > 33.8 BAU/mL, with an odds ratio of 0.279, suggesting a 72.1% reduction in the probability of a high serological response post-vaccination.

The intervals between doses, i.e., the interval between the first and second dose ($p = 0.801$) and the interval between the second and third dose ($p = 0.906$), did not show statistical significance, indicating they do not have a notable impact on serology.

The identified correlations highlight important relationships between vaccination parameters and serological responses. The results indicate that age and previous COVID-19 infection influence the immune response, which is expected and supported by previous research[23;24].

The intervals between doses, while showing weak to moderate correlations with certain vaccine types, emphasize the importance of following optimized protocols for each vaccine[25, 26].

Table 19: Coefficients and Statistics for Variables Included in the Model at Step 1

Variable	B	S.E.	Wald	df	Sig.	Exp(B)
Gender	0.225	0.241	0.874	1	0.35	1.253
Age	-0.373	0.061	37.757	1	0	0.688
Comorbidity	-0.059	0.177	0.11	1	0.74	0.943
Type of first dose vaccine	0.159	0.239	0.441	1	0.507	1.172
Administration of the second dose	-0.851	0.778	1.196	1	0.274	0.427
Type of second dose vaccine	-0.053	0.282	0.036	1	0.85	0.948
Administration of the third dose	-1.957	1.309	2.236	1	0.135	0.141
Type of third dose vaccine	-0.403	0.25	2.585	1	0.108	0.668
Previous COVID-19 infection	-1.278	0.316	16.349	1	0	0.279
Interval between first and second dose	0.008	0.03	0.064	1	0.801	1.008
Interval between second and third dose	0.02	0.173	0.014	1	0.906	1.021
Constant	10.546	2.856	13.639	1	0	38024.285

B: Regression Coefficient; S.E.: Standard Error; Wald: Wald Test Value; df: Degrees of Freedom; Sig.: Significance; Exp(B): Odds Ratio

CONCLUSION

The present study highlighted the interplay between various factors, including age, gender, comorbidity presence, history of COVID-19 infection, administration of COVID-19 vaccine doses, the interval between administered vaccine doses, and patients' serological responses. The conclusions suggest that age and COVID-19 infection history are determining factors for a positive serological response. These results are essential for understanding the underlying mechanisms of immune responses and could guide public health professionals in optimizing vaccination strategies, not only for COVID-19 but also for future epidemics.

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This study did not receive any external funding.

Conflict of Interest

The authors assert that there are no conflicts of interest associated with this research.

Ethical clearence

There was no need for ethical clearance for this research.

Authorship Contribution

Sara El Fellaq: Acquisition of data, data analysis, interpretation of results, writing-original draft and submitting manuscript, Badreddine Dahou, Amine Rkhaila: involved in writing, reviewing, Amina Bouziani, Mohammed Chahboune: supervision and writing-review, Mohammed Chahboune: supervision and writing-review, Sara El Fellaq, Sara Ait Lachguer, Amina Bouziani, Mohammed Chahboune: interpretation of results, writing-original draft, reviewing and editing. All authors have read and agreed on the final version of the manuscript

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