Research Article

COVID-19 AFTER VACCINATION IN TLAXCALA, MEXICO

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ABSTRACT

Introduction: The COVID-19 pandemic has been variable, the application of vaccines has modified the behavior of the disease, persisting as a great threat to health. *Objective:* To describe the behavior of COVID-19 after vaccination in Tlaxcala, Mexico. *Methods:* Observational, descriptive, study. Prior approval by the local investigation committee, the record of patients with a positive rapid test or PCR for COVID-19 and at least one dose of the vaccine between March and October 2021 was reviewed. General data related to the disease and the vaccine were analyzed. A descriptive analysis and chi-square, Fisher's exact test, linear association, Mann-Whitney U test. SPSS program. *Results:* It included 2037 records, 50% women, median age 38 years, 17% had sudden onset of symptoms, 43% had a complete vaccination schedule, there were from 5 to 286 days between the first dose of vaccine and onset of clinical symptoms, 6% required hospitalization, 2% died (with a significant difference about comorbidities, the time between application and onset of symptoms and vaccination status). *Conclusions:* There is no difference in the behavior of COVID-19 with the vaccine brand, sex, or age, with a low frequency of hospitalization and mortality, associated with the number of comorbidities and vaccination schedule.

INTRODUCTION

The epidemiological behavior of the COVID-19 pandemic has been variable, the development of vaccines has modified the behavior of the disease, although they have good safety and effectiveness, severe cases continue to occur, persisting as a great threat to health (Ashktorab *et al*., 2021). COVID-19 is described more frequently in men, the most common symptoms are fever, followed by cough with expectoration, chest tightness, shortness of breath, and general symptoms such as fatigue, myalgia, headache, and anorexia (Zhu *et al*., 2020); severe pneumonia, pulmonary edema, and multiple organ failure are reported as the main causes of death (Qiu *et al*., 2020).

In January 2021, mass vaccination was approved (Xing *et al*., 2021), but the safety, duration of protection, interruption of viral transmission, and its effectiveness against variants of SARS CoV 2 are still being studied (Dabanch *et al*., 2021). Regardless of the type and dose, the vaccines against SARS CoV 2 have shown good effectiveness (51 to 95%), however, there are multiple factors involved in the immune response in the host, such as genetics, epigenetics, immunodeficiency, or chronic diseases (Diaz *et al*., 2021). In Latin America, there are six vaccines with emergency authorization: Pfizer/BioNTech from the United States/Germany, AstraZeneca/Oxford from the United Kingdom/Sweden, CanSino, Sinopharm, and Sinovac from China, and Sputnik V from Russia (Dreser, 2021). Vaccination began considering the population with the highest risk of infection, including health personnel and older adults and continued by age ranges, despite this, cases of COVID-19 with a positive test continue to be reported, after the administration of the first dose, with a less aggressive clinical behavior pattern than the conventional form (Ruiz *et al*., 2021). Therefore, in this study, we aim to describe the behavior of COVID-19 after vaccination in the Decentralized Administration Operative Organ in Tlaxcala.

METHODS

An observational, retrospective, cross-sectional, descriptive study was carried out at Instituto Mexicano del Seguro Social, Tlaxcala. Prior approval by the ethics and research committee, with registration R-2021-2902-032, an analysis of the records of all patients who requested medical attention in any of the family medicine units and hospitals between March and October of 2021 was carried out. This study included all individuals that met the operational definition of a suspected case and a confirmatory test for COVID-19, in addition, they must receive at least one dose of the COVID-19 vaccine. The main outcome considered was death or survival. According to the number of doses, they were classified as complete or incomplete vaccination. Concerning the time elapsed between the application of the vaccine and the onset of symptoms, they were classified as non-immunized, partially immunized, and fully immunized (Jara *et al*., 2021).

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The time elapsed between vaccination and the onset of symptoms, clinical manifestations, and comorbidities were measured. Descriptive analysis with frequencies and percentages was performed. Forage, the mean and standard deviation will be used if the distribution of the data is Gaussian (according to the Kolmogorov Smirnov test), otherwise the median and interquartile range. Inferential analysis: chi-square or Fisher's exact test and U Mann-Whitney. The statistical program SPSS version 24 was used.

RESULTS

A total of 2,037 patient records were evaluated, 50.5% (1,029) were female, age ranged from 18 to 96 years, median 38 years, and interquartile range (IQR) 17 years Confidence Interval 95 % (95% CI) 39.78 – 40.94. Eighteen patients (0.9%) were pregnant, between 5 to 40 gestation weeks (GW) with a median of 26 and IQR 14 GW. One patient in lactation, none in the puerperium.

Table 1 Occupation

Jobless	53 (2.6)	Teacher	16 (0.8)
Health worker	77 (3.8)	Student	43 (2.1)
Hausewife	236 (11.6)	Concierge	15 (0.7)
Formal worker	7 (0.3)	Retired	47 (2.3)
Informal worker	8 (0.4)	Other	1535 (75.4)
Frequency (percentage)			

Regarding occupation, 11.6% (236) are housewives, 4% (77) are health workers (Table 1). When evaluating the symptoms, 17% (351) had a sudden onset of symptoms, 81% presented headache, 82% cough, and no patient-reported nasal congestion or dysphonia (Table 2). Obesity, arterial hypertension, and diabetes mellitus were present in 9, 8, and 7% respectively (Table 3).

Table 2 Clinical manifestations

	n (%)		n (%)
Fever	1123 (55.1)	Headache	1653 (81)
Cough	1666 (81.8)	Odynophagia	1590 (78.1)
Chest pain	215 (10.6)	Myalgias	1165 (57.2)
Dyspnea	178 (8.7)	Arthralgias	996 (48.9)
Runny nose	1332 (65.4)	Anosmia	402 (19.7)
Coriza	37 (1.8)	Dysgeusia	335 (16.4)
Cyanosis	22 (1.1)	Postration	125 (6.1)
Polypnea	22 (1.1)	Shaking chills	640 (31.4)
Diarrhea	176 (8.6)	Conjunctivitis	251 (12.3)
Abdominal pain	167 (8.2)	Others	31 (1.5)
Attack on the general state	728 (35.7)		
Source: Clinical record, n Frequency, % percentage.			

Table 3 Comorbidities

	n (%)		n (%)
Hypertensión	159 (7.8)	Enfermedad cardiovascular	6 (0.3)
Obesity	187 (9.2)	Immunosuppression	3 (0.1)
Diabetes mellitus	142 (7)	HIV infection	4 (0.2)
Smoking	45 (2.2)	Chronic liver disease	1
Kidney disease	19 (0.9)	Cancer	2 (0.1)
Chronic obstructive pulmonary disease (COPD)	12 (0.6)	Neurologic disease	2 (0.1)
Asthma	9 (0.4)	Other	33 (1.6)
Frequency (percentage)			

43% (869) had a complete vaccination schedule, 57% (1168) had one dose. Regarding the brand of the vaccine, 35% (711) received the AstraZeneca vaccine, 10% did not remember the brand (Table 4).

Table 4 Vaccine Brand

	Frequency (percentage)
AstraZeneca	711 (34.9)
Sinovac	584 (28.7)
Pfizer BioNTech	345 (16.9)
Don't remember	212 (10.4)
CanSino	156 (7.7)
Sinopharm	12 (0.6)
Novavax	12 (0.6)
Sputnik V	3 (0.1)
Janssen	1 (0.0)
Convidencia	1 (0.0)

The time between the application of the first dose of the vaccine and the onset of the clinical symptoms was between 5 and 286 days with a median of 85 and IQR 71 days 95% CI 58.22 – 62.95; 26% started symptoms between 31 and 60 days (figure 1).

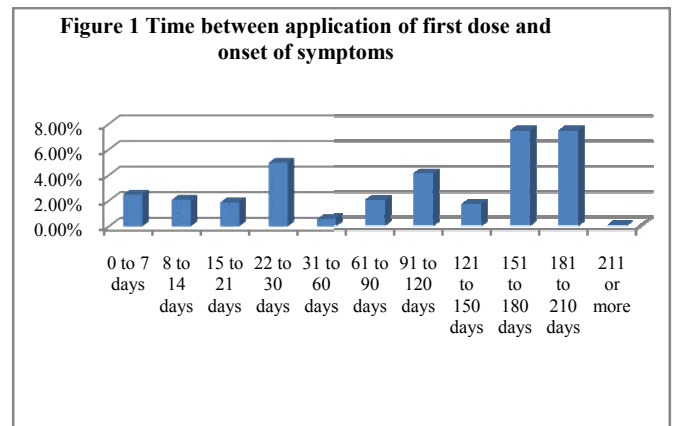**Figure 1** Time between application of first dose and onset of symptoms

Table 5 Death related factors

|	Survived 1996 (98)	Died 41 (2)	p*	OR	IC 95%
Incomplete vaccination	1153 (98.7)	15 (1.3)	0.006	2.37	1.24-4.50
Full vaccination	843 (97)	26 (3)			
Not COPD history	1988 (98.2)	37 (1.8)	0.000	26.86	7.74-93.16
COPD history	8 (66.7)	4 (33.3)			
Not HBP history	1849 (98.5)	29 (1.5)	0.000	5.20	2.6-10.4
HBP history	147 (92.5)	12 (7.5)			
Not DM history	1869 (98.6)	26 (1.4)	0.000	8.49	4.38-16.43
DM history	127 (89.4)	15 (10.6)			
Fischer's exact test*					

94% (1921) of the patients were managed on an outpatient basis, 6% (116) required hospitalization. Nine patients (0.4%) required ventilatory mechanical support, integrating clinical and radiographic diagnosis of pneumonia in 4% (75), five patients requested voluntary discharge, 93 (5%) were referred to another hospital unit with no report of a death, 41 (2%) died. No statistical difference was observed between death and sex, hospital management, occupation, vaccine brand, history of cardiovascular disease, history of kidney disease, neurological disease, asthma, immunosuppression, smoking, obesity, HIV, cancer, or pregnancy. A difference was observed between the number of comorbidities and death (p=0.000), in patients, without comorbidities, the percentage of deaths was 1.1% while with four comorbidities it increased to 33% (figure 2).
The comorbidities associated with death were chronic obstructive pulmonary disease (COPD), systemic arterial hypertension (HTN), diabetes mellitus (DM), and a complete vaccination schedule (Table 5).

A significant difference was observed between death and the days between symptoms and the first dose (p=0.026 95% CI -

43.69 to -2.997) (figure 1), but not so with age (0.641 95% CI -5.09-3.142) and days between the onset of symptoms and the second dose (p=0.410 95% CI -40.195-16.411).

Figure 2 . Number of comorbidities and death
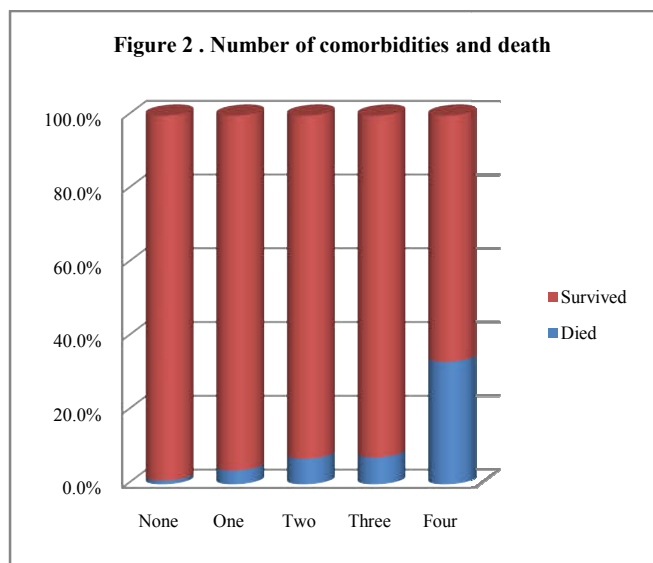
According to the immunization status, a significant difference was observed with death (chi-square 0.006) (figure 3).

Figure 3 Vaccination status and mortality
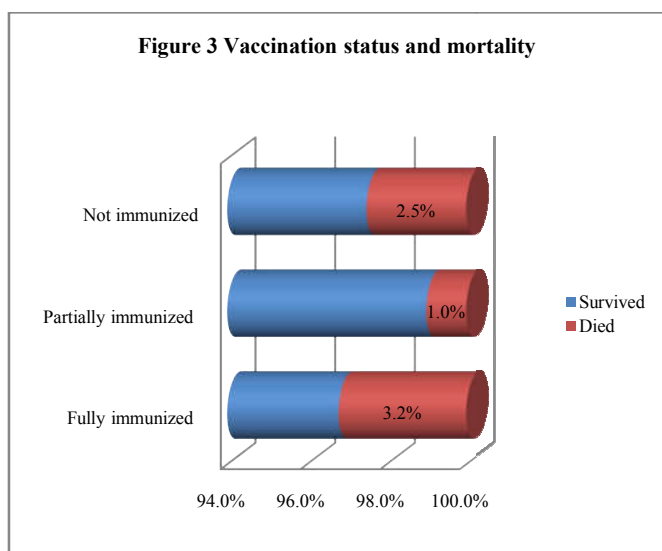
DISCUSSION

Sanitary conditions related to the pandemic have varied after vaccination, although in the present study no difference was shown with the outcome and the type of vaccine, almost half of the population had a complete schedule, only one being considered fully immunized. third of the population.

The symptomatology presented varies with that demonstrated before the vaccine, although the epidemiological behavior has varied in each region, respiratory symptoms have predominated, being described more frequently in men, within the clinical picture fever predominated, followed by cough with expectoration, chest tightness, and respiratory distress (Zhu *et al*., 2020), however in our patients after vaccination there was no difference in terms of sex, the most frequently reported symptoms were cough, headache, and sore throat, only half of the patients had to fever.

Although when comparing age, no statistical difference was shown with the outcome, the patients who died were in the

group between 18 and 60 years old, probably because most adults over 65 years of age had a complete vaccination schedule, most of them starting symptoms 14 days or more after the 2nd dose, which coincides with what was reported by Mazagatos *et al*., (2021), who demonstrated the efficacy of vaccines over time in geriatric patients, however, the vaccines evaluated were those of mRNA COVID-19 Comirnaty (Pfizer) and modern, while in the present study the vaccines that older adults had received were from the CanSino, AstraZeneca, Pfizer BioNTech, and Sinovac brands, not being able to assess asymptomatic infections since only patients with suspicious clinical symptoms were included and confirmed.

López Bernal *et al*., (2021). evaluated the effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines in patients with confirmed symptoms of COVID-19, in adults over 70 years of age, referring to a greater probability of testing positive for COVID in the first 9 days after vaccination, unlike from what was found in that the symptomatology in this age group began between days 0 and 24 after vaccination (95% CI 1.23-1.77 vs 3.81-5.13) coinciding with a similar effect between the vaccines.

Yoel Angel *et al*., (2021). in their study estimated the association of vaccination with the presence of asymptomatic and symptomatic infections in health workers, reporting symptomatic infection in eight vaccinated workers, with an incidence of 4.7 per 100,000 people per day, with a decrease in symptomatic cases in vaccinated patients, which may coincide with what was observed, with health personnel being only 5% of the population studied, with a low mortality rate.

Unlike what was reported in previous investigations, no difference was observed between the vaccines and mortality, the discrepancy was in whether or not they had a complete schedule, presenting more cases of death in those with a complete schedule.

Vaccine efficacy and vaccine coverage are different concepts; there are different ways to categorize the vaccination status of patients Yoel Angel *et al*., (2021) classify them as partially vaccinated (7-28 days after the first dose) and fully vaccinated late (> 21 days after the second dose), while Mazagatos *et al*., (2021) defines the COVID-19 vaccination status as Not vaccinated (no dose or 14 days or less since the first dose of the Moderna or Pfizer vaccine); partially vaccinated dose 1 (Vaccinated with the first dose of the Comirnaty or Moderna COVID-19 vaccine, and more than 14 days since vaccination), partially vaccinated - dose 2 (Vaccinated with two doses of the Comirnaty or Moderna COVID-19 vaccine, and less than 7 days from the second dose for Comirnaty or less than 14 days for the Moderna COVID-19 vaccine. Full immunity not achieved) and fully vaccinated (vaccinated with two doses and 7 days or more after the second dose for Comirnaty and 14 days or more for the Moderna COVID-19 vaccine (full immunity was achieved), while Jara *et al*., (2021),considered partial immunization (≥14 days after receiving the first dose and before receiving the second dose) and full immunization (≥14 days after receiving the second dose) to estimate vaccine effectiveness. In the present study, we used this categorization, observing a difference with mortality, with a greater number of patients dying with complete immunization. We took the data with reservation due to memory bias, since in some cases the exact date of vaccination could not be specified. vaccination, to calculate the vaccination status.

In Navarro España Martinez *et al*., (2021), they demonstrated the effectiveness of the vaccine against COVID-19 by evaluating close contacts of patients with laboratory-confirmed COVID-19, reporting a higher incidence of infection in the unvaccinated compared to those vaccinated with one or more two doses (36% vs 23 and 12% respectively), however, even with two doses of vaccine there were positive cases, so the application of the vaccine does not guarantee the effect of the vaccination, which coincides with what was observed, that even though all the patients included had at least one dose of vaccination, they were positive for SARS CoV2 infection and even died from this cause, with a significant difference between those who had an incomplete to a complete schedule, although with a lower case fatality rate in the group. incomplete scheme.

The frequency of hospitalization and death due to SARS CoV2 in patients with at least one dose of vaccine was generally lower compared to that reported before starting vaccination, progressively decreasing at 60 days, then increasing at 210 days, unlike reported by Mateo *et al*., (2021), who calculated the rate of hospitalization, infection, and death in the period 0 to 14 days after the first dose and 15 days after the first dose to measure the impact of vaccination, reporting that the risk of infection gradually decreased until day 42-49 post first dose, after which they remained stable.

Vasileiou *et al*., (2021) associated hospital admission and the application of the first dose of COVID-19 vaccines in Scotland, excluding those who had previously tested positive, reporting an effect of the RNAmBNT162b2 vaccine of 91% for a decrease in hospitalizations between 28 and 34 days after vaccination, according to the results obtained, a similar effect was observed, with the percentage of hospitalizations being low, including all patients regardless of a history of COVID before vaccination.

In a prospective cohort study of approximately 10.2 million people over 16 years of age from February 02, 2021, to May 01, 2021, conducted in Chile, they looked for the effectiveness of the inactivated SARS CoV2 vaccine (CoronaVac) to prevent COVID-19, hospitalization, ICU admission, and death. They were divided into three groups, unvaccinated, partially immunized (>=14 days first dose), and fully immunized. Where the effectiveness of the vaccine was 65.9% (95% CI 65.2-66.6) to prevent COVID-19, 87.5% (95% CI 86.7-88.2) to prevent hospitalization, 90.3% (95% CI 89.1-91.4) to prevent ICU admission, and 86.3% (95% CI 84.5-87.9) for the prevention of death (Jara *et al*., 2021), with the same criteria we observed a significant difference with mortality, however the percentage of deceased patients was higher in the group of totally immunized, probably due to the staggered vaccination scheme, with the patients with the highest risk being those who were vaccinated as the first intention, including those with two or more comorbidities and age group.

This study has certain limitations such as the retrospective design, in which problems with data quality were observed, in addition to not considering some variables that could be of interest such as asymptomatic patients, the reason for referral to another unit, and the outcome of these patients. In addition to the staggering vaccination program (starting with older adults, health area and later for decades) as well as the times between the first and second dose and a different brand of vaccine. Not all physical examination parameters that could be

of interest, such as oxygen saturation, are available. It is unknown if the patients had any treatment through a private doctor and it is unknown if they received the same treatment either on an outpatient basis or hospitalization.

However, the results coincide with those reported in previous studies, they can be extrapolated to the adult population, with personal factors such as age and comorbidities being the ones that can influence the outcome in patients infected with SARS CoV2 who are still vaccinated.

CONCLUSIONS

The behavior of COVID-19 in patients who have received at least one dose of vaccine is similar with the brand of vaccine, with cough, headache, and odynophagia being the most frequent symptoms, with low frequency of hospitalization and mortality, being associated with the number of comorbidities (diabetes mellitus, COPD and arterial hypertension) and vaccination schedule.

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