Severity of Covid-19 Cases in the Months of Predominance of the Alpha Variant and the Role of Vaccination

Dídac Florensa (✉ didac.florensa@gencat.cat)

University of Lleida

Jordi Mateo

University of Lleida

Radu Spaimoc

University of Lleida

Carme Miret

Epidemiology Service, Department of Health, Lleida

Sofia Godoy

Epidemiology Service, Department of Health, Lleida

Francesc Solsona

University of Lleida

Pere Godoy

Epidemiology Service, Department of Health, Lleida

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Abstract

The emergence of new variants of the SARS-CoV-2 virus may suppose a problem for public health to control the COVID-19 pandemic. The aim of this study was to assess and compare symptoms and severity of COVID-19 cases in the months with a predominance of the Alpha variant compared to the Delta variant, taking the effect of COVID-19 vaccination into account. A prospective epidemiological study of SARS-CoV-2 in the province of Lleida was done that aimed to search for differences between the predominance of the Alpha and Delta variants. The information analyzed was the symptoms, specific comorbidities, socio-demographic information and vaccination status. A bivariate and multivariate analyses were performed to estimate the adjusted odds ratio (aOR) and its 95% confidence interval (CI) in order to investigate relationships of symptoms and severity between variants. In the Alpha variant period there was an increased risk of ICU admission (aOR=2.0; 95%CI:1.2-2.3) and death (aOR=2.6; 95%CI:1.8-3.9) and cases were associated with those aged over 85 (aOR=2.1; 95%CI:1.7-2.6) and partially vaccinated (aOR=5.6; 95%CI:3.2-9.9) or unvaccinated (aOR=27.8; 95%CI:19.7-40.5). Regarding the symptoms, fever, cough and vomits gave significant results with aORs of 1.6 (95% CI: 1.5-1.7), 2.0 (95% CI: 1.9-2.2) and 2.5 (95% CI: 2.2-2.9). The results suggest that more severe cases appeared during the predominance of the alpha variant. The risk of ICU admission and the death was higher in the alpha period due to it affecting more elderly people and a lack of vaccination among cases. Fever, cough and vomiting were more frequent during the dominance of the alpha variant.

Background

The emergence of new variants of the SARS-CoV-2 has supposed a problem for controlling the COVID-19 pandemic. The COVID-19 variant of concern B.1.1.7, colloquially known as Alpha, was first identified in the United Kingdom (1). Then a new variant was discovered in India. The variant of concern B.1.617.2 was called Delta (2).

A previous study analysed the main symptoms of the Alpha variant by patient characteristics and the role of vaccination. Some studies (3, 4) found an association between the Alpha variant and an increase in hospitalization, ICU admission and mortality. However, Veneti and et al. (5) found no differences in the risk of hospitalisation between reported cases of the SARS-CoV-2 Delta and Alpha variants in Norway. And, Burki (6) concluded that the Delta variant was almost twice as likely to lead to hospitalisation as infection with the Alpha variant. Therefore, there are studies with different conclusions.

On the other hand, vaccination has had an important impact on virus transmission. Previous studies (7, 8) have demonstrated the effectiveness of the COVID-19 vaccine to prevent severe cases due to SARS-CoV-2. They conclude that effectiveness may decrease after 6 months of follow-up even though the vaccine remains highly efficacious in preventing serious cases of COVID-19 (9). Harder and *et al.* (10) compared the effectiveness of the vaccine between the Alpha and Delta variants. Their outcomes demonstrated that the strength of the vaccine was reduced by 10–20%, but maintained full effectiveness

against severe COVID-19. In Spain, the first doses of the vaccines were administrated at the beginning of January 2021. The first age groups to receive the vaccines were the ≥ 85 and 75–84 (11).

Related to the literature, a range of outcomes were obtained by different studies regarding the Alpha and Delta variants. However, they mostly concluded that the Alpha variant increased the risk of severe cases. Also, some of these studies worked on specific symptoms. In our case, we analyzed all of the symptoms seen in the patients registered and their vaccination status.

The aim of this study was to assess and compare the symptoms and severity of COVID-19 cases in the months when the Alpha variant predominated taking into account the effect of the COVID-19 vaccinations. We also compared the differing patient profiles and comorbidities between the Alpha and Delta periods.

Methods

This research is a prospective epidemiological study of SARS-CoV-2 in the province of Lleida aiming to search for differences between the periods of predominance of the Alpha and Delta variants. The information analyzed was the symptoms, specific comorbidities, socio-demographic information and COVID-19 vaccination status. The main sources of information were recorded cases from the Lleida and Alt Pirineu-Aran epidemiological service, which belongs to the Catalan Department of Health, in Spain. SARS-CoV-2 cases were detected by PCR (Polymerase Chain Reaction) and antigen tests. These cases were validated, studied and controlled by epidemiological professionals in order to monitor the disease and thus be able to observe the evolution of the pandemic in both outbreaks.

Data

The data collected correspond to new cases from two specific and consecutive waves of the pandemic with predominance of the Alpha and Delta variants. Data were collected by public health officials from the department of health by telephone interview with each patient and checking and/or reviewing clinical records, as is normal for data collection by the public epidemiological surveillance system. The first period comprises records from January 1, 2021 to March 31, 2021, with a predominance of the Alpha variant in the Lleida region. The second period, when the Delta variant was predominant, comprises records from April 1, 2021 to July 31, 2021 (10). In this second period, the government allowed mobility, social contacts and the opening of night clubs. The variables of the study were: **variant** (Alpha, Delta); **age group** (0–14, 15–34, 35–44, 45–54, 55–64, 65–74, 75–84, ≥ 85); **gender** (male, female); **asymptomatic** (yes, no); **hospitalized** (yes, no); **ICU** (yes, no); **death** (yes, no); **fever** (yes, no); **cough** (yes, no); **pneumonia** (yes, no); **sore throat** (yes, no); **shivers** (yes, no); **dyspnea** (yes, no); **vomiting** (yes, No); **diarrhea** (yes, no); **respiratory distress syndrome** (yes, no); **acute renal failure** (yes, no); **cardiovascular disease** (yes, no); **neurological disease** (yes, no); **vaccinated** (fully, half, non)

Statistics

We compared SARS-CoV-2 cases that appeared during the greater presence of the Alpha variant with those discovered during the greater presence of the Delta variant. We compared socio-demographic information, symptoms, the risk factors of the patients and the effect of vaccination. In the first analysis, crude odds ratios (OR) were used to compare the differences between positive cases between the variants.

A bivariate analysis was performed in order to investigate relationships between the dependent (the Alpha or Delta variants), and independent variables (UCI, death, socio-demographic data, symptoms, risk factors and vaccination status).

The patient profile of the Alpha variant comparing to the Delta wave as a reference category was analysed using a logistic regression to estimate probabilities, odds ratio (OR) and their corresponding 95% confidence intervals (CI).

The multivariable analysis was based on forward selection. This involves starting with no variables in the model, adding the variable (if any) whose inclusion gives the most statistically significant improvement to the fit, and repeating this process until none improve the model.

Results

The overall data set consisted of 27,011 SARS-CoV-2 cases confirmed by PCR and antigen tests. During the first period analyzed, when the Alpha variant was predominant, 13,037 cases were detected. The second period data set consisted of 13,974 cases. In this latter period, the Delta variant was predominant (Fig. 1).

Bivariate Analysis

Patient profiles, symptoms, comorbidities and the vaccination effect between the Delta and Alpha variants were analyzed and compared (Table 1). During the Alpha period, 6,645 (51%) women and 6,392 (49%) men were registered. However, in the Delta period the number of women was 6,727 (48.1%) and there were 7,247 men (51.9%) ($P < .001$). There were important differences between age groups in the results. During the presence of the Alpha variant, the number of cases in the 15–34 age group was 2,948 (23%) and during the Delta period, this increased to 5,308 (38%). However, from the 55–64 age range to the more elderly cohorts, the number of cases of the Delta variant decreased compared with the Alpha variant ($P < .001$).

The hospitalized cases decreased during the Delta period with 245 patients (1.8%) compared with the 491 (3.8%) patients in the Alpha period. 56 (0.4%) cases required ICU admission during the Alpha period

and 25 (0.2%) during the delta ($P < .001$). Death was also significant with 161 (1.2%) cases related to the Alpha variant. In the case of the Delta, the number of deaths was 36 (0.3%) ($P < .001$).

Regarding symptoms, the P-value was significant in all cases ($P < .001$). Major differences between variants were observed in the number of patients with fever and cough. There were also significant differences related to comorbidities. Finally, vaccination also was significant ($P < .001$) in all categories. The number of positive cases that they were fully vaccinated increased notably in the period dominated by the Delta variant.

Multivariate Logistic Regression Model

The socio-demographic information, symptoms and comorbidities of the patients were very different for the two variants (Table 2). Male gender was significant regarding female gender in the wave corresponding to the Alpha variant (aOR = 0.9; 95% CI: 0.9–1.0). The first significant age group was [15–34] (aOR = 0.5; 95% CI: 0.4–0.5). The [35–44] age group was also significant (aOR = 0.7; 95% CI: 0.7–0.8). Older people also obtained significant outcomes (aOR = 2.7; 95% CI: 2.2–3.2). Hospitalized did not obtain significant p-value, but the risk of ICU admission was higher during the Alpha variant wave (aOR = 1.7; 95% CI: 1.1–2.7). Also, the aOR for death was also significant with 2.7 (95% CI: 1.9–4.0).

Significant outcomes were obtained in case of symptoms. Fever and cough obtained significant results with aORs of 3.7 (95% CI: 3.4–4.0) and 4.3 (95% CI: 4.0–4.6). Sore throat was also significant with higher risk with the Alpha variant. The aOR obtained were 1.2 (95% CI: 1.1–1.2). The digestive symptoms also were significant. For vomits, the OR was 2.7 (95% CI: 2.4–3.2) and for diarrhoea, 0.6 (95% CI: 0.5–0.7). Acute renal failure also gave a significant aOR of 2.9 (95% CI: 1.4–7.3).

Regarding the comorbidities, respiratory and cardiovascular diseases were significant (aOR = 3.0; 95% CI: 1.7–6.3) and (aOR = 1.3; 95% CI: 1.1–1.5) respectively. Finally, vaccination also produced significant results. The aOR for the half-vaccinated cases was 5.6 (95% CI: 3.2–9.2) and the aOR for the non-vaccinated was 35.7 (95% CI: 25.7–51.3).

Discussion

The risk of ICU admission and death was higher in the period of predominance of the Alpha variant compared to the Delta wave, adjusting in the regression model for the importance effect of age and partial vaccination or lack of vaccination. In addition, in the cases in the period of the Alpha variant wave, there were certain clinical peculiarities such as a higher percentage of fever, cough and vomiting.

Our work was based on a previous study (12), which described the reported cases and identified disease severity risk factors on the first wave in Spain even though they did not compare this to waves caused by other variants. Another starting study was (13), which analysed the transmissibility and global spread of COVID-19 variants and their differences in terms of effects. In addition, Twohig and *et al.* (14) analyzed

the hospital admission risk from the Delta variant compared with Alpha variant. They found a higher hospital admission and emergency care risk for unvaccinated patients during the Delta wave compared with the stage with the higher presence of the Alpha variant. Finally, regarding the effectiveness of mRNA vaccines, it was shown that they reduced the risk of hospitalization and death significantly. Additionally, Bernal *et al.* (15) analyzed the effectiveness of COVID-19 vaccines against the Delta variant and suggested a lower degree of the protection than against the Alpha variant, even though they still guaranteed a high level of effectiveness.

The literature revised tried to analyze and compare the symptoms and effectiveness of the vaccine against the COVID-19 variants. Their results suggested some controversial differences. Some studies demonstrated that the Alpha variant may increase the risk of ICU admission and the mortality (3, 4). Other studies concluded that there were no significant differences (5). However, after reviewing earlier literature about the effectiveness of vaccines and the new variants, most studies suggest that vaccine protection was higher against the Alpha variant. However, their effectiveness for preventing severe cases caused by the Delta variant remained high.

In general, significant results were obtained in some aspects. One of the most significant was for the age group 15–34 (16). The number of cases among this cohort increased significantly during the wave of the Delta variant, which suggests that the risk from the Delta variant was higher in this group (aOR = 0.5) than it was for the period dominated by the Alpha variant. Similar results are seen with the 35–44 and the 65–74 age groups. The latter group started to receive the first doses of the vaccines just when the Delta variant started to be predominant (17). Therefore, they were still exposed to the virus. However, older people, specifically the ≥ 85 age group (aOR = 2.7), had a higher risk from the Alpha variant than in the period dominated by Delta variant because in the earlier period they had not received the two doses of the vaccine (18). During the wave caused by the Delta variant, these groups were fully vaccinated.

Regarding ICU admission and mortality, the number of cases was higher during the predominance of the Alpha variant (161 deaths) compared with the period with the Delta variant (36 deaths). The multivariate analysis confirmed the higher risk from the Alpha variant. The risk of ICU admission due to the Alpha variant was double the risk in the period dominated by the Delta variant (19, 20). Mortality was 2.7 times higher with the Alpha variant than with the presence of the Delta variant. This risk may be related to the fact that the Alpha may be more aggressive (3, 4).

The most significant symptoms observed during the Alpha period were fever, cough and vomits. Fever was 3.7 times higher ($P < .001$) and cough, 4.3 times ($P < .001$). These could be directly related as symptoms indicating a higher possibility of a case becoming severe (21). Regarding vomits, the incidence of this symptom was 2.7 times higher with the Alpha variant. However, this symptom may not be related to the risk of hospitalization, ICU admission or death (22). These differences suggest that symptoms could vary depending on the variant given that the genetic composition of the COVID-19 variants is different (23).

Finally, outcomes for half- and unvaccinated patients were also significant compared with the fully-vaccinated. Being half-vaccinated meant a higher risk (5.6 times) compared with the fully-vaccinated during the period dominated by the Alpha variant ($P < .001$). The unvaccinated also gave a higher risk from the Alpha variant. The risk for unvaccinated patients was 35.7 times higher ($P < .001$) than for the fully-vaccinated. These outcomes suggest high effectiveness of the current vaccines against severity and death (24).

This study has some limitations. The transition between the predominance of the Alpha and Delta variants may mean some cases are included in the wrong period, even though there were fewer at that time. Some asymptomatic patients may have developed symptoms after the interview and not been registered. Some symptoms could also have appeared after the interview and not been recorded. The logistic regression model took into account the main variables involved, such as vaccination and morbidities, but there could still be a residual confounding effect on the results.

In conclusion, the results help to suggest that more severe cases appeared during the predominance of the Alpha variant. This fact may demonstrate that this variant may be more aggressive than the Delta, depending on the case. The risk of ICU admission and the death was higher in the Alpha period. Moreover, fever, cough and vomits were more frequent during the presence of the Alpha variant. The lack of vaccination was the main risk factor when infected by the Alpha variant and this suggests that the vaccines are effective at avoiding UCI admission and death.

These results encourage us to move ahead with new studies into the effectiveness of the vaccines against new variants, go deeper into the effect of these vaccines and their importance for keeping protection high.

Declarations

Contributors

D. Florensa, J. Mateo, F. Solsona and P. Godoy designed the study. D. Florensa and R. Spaimoc analyzed the data. D. Florensa wrote the manuscript. J. Mateo, F. Solsona and P. Godoy supervised the study and helped to interpret the data. C. Miret and S. Godoy collected data and helped to analyze them. All authors revised the manuscript and approved it for submission. The authors have read and approved the final manuscript.

Ethics approval and consent to participate

All data were anonymised to protect patient privacy and confidentiality. This study was part of the public health response to coronavirus outbreaks. This project was approved by the reference ethics committee (Committee of Ethics and Clinical Research of Lleida - CEIC). The patients were interviewed by telephone

to obtain the COVID-19 symptoms and vaccine information. They were informed about this study in this interview, and they provided informed consent during enrolment.

Data Availability

The dataset is available from the corresponding author upon reasonable request.

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Conflict of Interest

The authors declare that there no conflict of interest.

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Tables

Table 1. Bivariate analysis of COVID-19 cases between the predominance of alpha variant and the delta in Lleida region (Spain).

	Total		Alpha		Delta		Crude OR	95% CI	P-value
Gender	Count	%	Count	%	Count	%			
Female	13,372	49.5	6,645	51	6,727	48.1	Ref. group	-	-
Male	13,639	50.5	6,392	49	7,247	51.9	0.9	0.8 - 0.9	<.001
Age									
[0-14)	4,450	16.5	2,256	17.0	2,194	15.7	Ref. group	-	
[15-34)	8,256	30.6	2,948	23.0	5,308	38.0	0.5	0.5 - 0.6	<.001
[35-44)	3,975	14.7	1,970	15.0	2,005	14.3	1.0	0.9 - 1.0	0.2
[45-54)	3,841	14.2	2,076	16.0	1,765	12.6	1.1	1.0 - 1.2	.001
[55-64)	2,929	10.8	1,647	13.0	1,282	9.2	1.3	1.1 - 1.4	<.001
[65-74)	1,742	6.4	963	7.4	779	5.6	1.2	1.0 - 1.3	<.001
[75-84)	1,063	3.9	646	5	417	3	1.5	1.3 - 1.7	<.001
[85-)	755	2.8	531	4.1	224	1.6	2.3	1.9 - 2.7	<.001
Hospitalized									
Yes	736	2.7	491	3.8	245	1.8	2.2	1.8 - 2.6	<.001
No	26,275	97.3	12,546	96.2	13,729	98.2	Ref. group	-	-
ICU									
Yes	81	0.3	56	0.4	25	0.2	2.4	1.5 - 3.9	<.001
No	26,930	99.7	12,981	99.6	13,949	99.8	Ref. group	-	-
Death									
Yes	197	0.7	161	1.2	36	0.3	4.8	3.4 - 7.0	<.001
No	26,814	99.3	12,876	99.8	13,938	99.7	Ref.	-	-

group									
Fever									
Yes	5,614	20.8	4,511	35	1,103	7.9	6.2	5.7 - 6.6	<.001
No	21,397	79.2	8,526	65	12,871	92.1	Ref. group	-	-
Cough									
Yes	5,640	20.9	4,626	36	1,014	7.3	7.0	6.5 - 7.6	<.001
No	21,371	79.1	8,411	65	12,960	92.7	Ref. group	-	-
Pneumonia									
Yes	32	0.1	25	0.2	7	0.1	3.8	1.7 - 8.9	<.001
No	26,979	99.9	13,012	99.8	13,967	99.9	Ref. group	-	-
Sore throat									
Yes	3,665	13.6	2,232	17	1,433	10.3	1.8	1.7 - 1.9	<.001
No	23,346	86.4	10,805	83	12,541	89.7	Ref. group	-	-
Shivers									
Yes	3,259	12.1	2,049	16	1,210	8.7	2.0	1.8 - 2.1	<.001
No	23,752	87.9	10,988	84	12,764	91.3	Ref. group	-	-
Dyspnea									
Yes	1,104	4.1	745	5.7	359	2.6	2.3	2.0 - 2.6	<.001
No	25,907	95.9	12,292	94	13,615	97.4	Ref. group	-	-
Vomits									
Yes	2,119	7.8	1,604	12	515	3.7	3.7	3.3 - 4.1	<.001
No	24,892	92.2	11,433	88	13,459	96.3	Ref. group	-	-
Diarrhea									

Yes	2,684	9.9	1,767	14	917	6.6	2.2	2.1 - 2.4	<.001
No	24,327	90.1	11,270	86	13,057	93.4	Ref. group	-	-
RDS*									
Yes	50	0.2	42	0.3	8	0.1	5.6	2.6 - 12.0	<.001
No	26,961	99.8	12,995	99.7	13,966	99.9	Ref. group	-	-
Acute renal failure									
Yes	39	0.1	34	0.3	5	0	7.3	2.9 - 18.7	<.001
No	26,972	99.9	13,003	99.7	13,969	100	Ref. group	-	-
Cardiovascular dis.									
Yes	581	2.2	401	3.1	180	1.3	2.4	2.0 - 2.9	<.001
No	26,430	97.8	12,636	96.9	13,794	98.7	Ref. group	-	-
Neurological dis.									
Yes	226	0.8	171	1.3	55	0.4	3.3	2.5 - 4.6	<.001
No	26,785	99.2	12,866	98.7	13,919	99.6	Ref. group	-	-
Vaccinated									
Fully	796	2.9	26	0.2	770	5.5	Ref. group	-	-
Half	172	0.6	29	0.2	143	1	6.0	3.4 - 10.5	<.001
None	26,043	96.5	12,982	99.6	13,061	93.5	29.4	19.9 - 43.5	<.001

RDS. Respiratory Distress Symptom

CI. Confidence Interval

OR. Odd Ratio

Table 2. Multivariate logistic regression analysis.

	Adjusted odds ratio	95% CI	P-value
Gender Female	1.0	Ref. group	-
Gender Male	0.9	0.8 - 0.9	.001
Age [0-14)	1.0	Ref. group	-
Age [15-34)	0.4	0.4 - 0.5	<.001
Age [35-44)	0.7	0.6 - 0.8	<.001
Age [45-54)	0.9	0.8 - 0.9	0.007
Age [55-64)	0.9	0.8 - 1.0	0.2
Age [65-74)	0.8	0.7 - 0.9	0.04
Age [75-84)	1.2	1.0 - 1.4	0.02
Age [85-)	2.7	2.2 - 3.2	<.001
Hospitalized	1.0	0.8 - 1.1	0.7
ICU	1.7	1.1 - 2.7	0.04
Death	2.7	1.9 - 4.0	<.001
Fever	3.7	3.4 - 4.0	<.001
Cough	4.3	4.0 - 4.6	<.001
Pneumonia	0.8	0.3 - 1.6	0.5
Sore throat	1.2	1.1 - 1.2	<.001
Shivers	0.9	0.8 - 1.0	0.1
Dyspnea	1.1	1.0 - 1.2	0.2
Vomits	2.7	2.4 - 3.2	<.001
Diarrhea	0.3	0.3 - 0.4	<.001
Respiratory distress syndrome	3.0	1.6 - 6.3	0.001
Acute renal failure	2.9	1.4 - 7.3	0.03
Cardiovascular disease	1.3	1.1 - 1.5	0.01
Fully-vaccinated	1.0	Ref. group	-
Half-vaccinated	5.6	3.2 - 9.2	<.001
None-vaccinated	35.7	25.7 - 51.3	<.001

Figures

Figure 1

Epidemiologic curve from 01-01-2021 until 31-07-2021. The grey colour represents the predominance of alpha variant. The red represents the predominance of delta variant.