ORIGINAL ARTICLE

A comparison between alpha and delta waves of COVID-19, in Tunisia

Comparaison entre les vagues Alpha et Delta de la COVID-19 en Tunisie

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Abstract

Introduction: Several nations have seen an increase in COVID-19 cases in 2020, exhibiting a wave pattern. Different COVID-19 variants caused these waves. In this perspective, the aim of the study was to compare epidemiological, clinical and evolutive profile of COVID-19 infection during two waves of COVID-19.

Methods: This is a cross-sectional analysis study of cases of COVID-19 confirmed by antigen test or RT-PCR, between April 2020 and December 2021. To compare clinical symptoms and severity criteria between two waves, we identified two groups, G1 corresponding to the alpha variant wave (from October 2020 to June 2021), and G2 corresponding to the Delta variant pandemic (from July 2021 to December 2021). Data collection was carried out using a questionnaire self-administered in French and Arabic developed with Google Forms and shared online via social media during one month (February 2022) with weekly reminders. Duration of one month was enough to get the necessary number of participants calculated. The study included all Tunisians who were infected with COVID-19 at least once and agreed to participate in the study.

Results: In total, 1328 COVID-19 patients were included. Eight hundred eighty-three patients were infected during the Alpha wave (66.5%) and 445 were infected during the Delta wave (33.5%). The median age was 37 years (interquartile range (IQR): 30–41 years). Clinically, during delta wave, these symptoms were more frequent; fever (57.8% versus 51.9%, p= 0.042), loss of smell (75.1% versus 65.1%, p≤10- 3), vomiting (20.2% versus 14.3%, p=0.006) and loss of taste (68.5% versus 58.5%, p≤10-3). On the other hand, aches were more frequent during Alpha wave (65.2% versus 56.2%, p = 0.001) and the impact of health professionals was greater (27.6% versus 15.7%, p≤10-3).

Conclusion: The Alpha variant had more pronounced clinical symptoms than the Delta variant. This can be explained by the high vaccination coverage during the pandemic by the Delta variant.

Key words: COVID-19 infection; Variants; COVID-19 waves

Résumé

Introduction: Plusieurs nations ont observé différentes vagues de COVID-19 durant l'année 2020. L'objectif de l'étude était de comparer le profil épidémiologique, clinique et évolutif de l'infection COVID-19 entre les deux vagues.

Méthodes: Il s'agit d'une étude transversale analytique. Elle a inclus tous les citoyens tunisiens qui ont été infectés par COVID-19 une fois et qui ont accepté de participer. L'infection a été confirmée par un test antigénique et/ou RT-PCR, entre Avril 2020 et Décembre 2021. Deux groupes ont été identifiés: G1 correspondant à la vague du variant alpha (d'octobre 2020 à juin 2021) et G2 correspondant à la pandémie du variant delta (de juillet 2021 à décembre 2021). La collecte de données était réalisée via Google Forms et partagé via les groupes Facebook et les chaines télévisées et radio.

Résultats: Au total, 1328 patients atteints de la COVID-19 ont été inclus. Parmi lesquels 883 patients étaient infectés pendant la vague Alpha (66,5%) et 445 étaient infectés par le variant Delta (33,5%). L'âge médian était de 37 ans (intervalle interquartile (IQR): 30-41 ans). Les symptômes les plus fréquents durant la vague Delta étaient : la fièvre (57,8% contre 51,9%, p= 0,042), la perte de l'odorat (75,1% contre 65,1%, p≤10-3), les vomissements (20,2% contre 14,3%, p=0,006) et la perte du goût (68,5 % contre 58,5%, p≤10-3). En revanche, les douleurs étaient plus fréquentes durant la vague Alpha (65,2% contre 56,2%, p≤10-3). Concernant la vaccination contre la COVID-19, le groupe Alpha avait une fréquence significativement plus élevée que le groupe Delta (34,4% contre19,6%; p≤10-3).

Conclusion: Le variant Alpha était caractérisé par des manifestations cliniques plus marquées que le variant Delta.

Mots clés: Infection à CIVID-19 ; Variants COVID; Vagues

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Introduction

At the end of 2019, Wuhan, China gave rise to the severe acute respiratory syndrome coronavirus-2, which caused the coronavirus disease 2019 (COVID-19) (1). This virus spread quickly throughout the world and produced many peaks in waves (2,3). In fact, several nations have seen an increase in COVID-19 cases throughout the high peak months of 2020, exhibiting a wave pattern (4). Following this, the World Health Organization declared COVID-19 as a pandemic on March 11, 2020. Approximately 236 million cases of the coronavirus disease 2019 (COVID-19) had been confirmed globally as of October 10, 2021(5). As a consequence of this pandemic, many problems were faced for global social and economic activity as well as health services (1). This led to a nationwide lockdown on March 22, 2020 (6). The first cases in Tunisia began in March 2, 2020, followed by several preventative measures that were put into place to lower the population's transmission levels. Among these measures, use of masks, physical segregation, the closing of schools and universities, prohibitions on sports and cultural events, closing of borders, and, focused screening have been implemented. Then, on July 2020 nonpharmaceutical interventions measures have, however, been drastically scaled back. More powerful waves followed, starting in October 2020, and the Ministry of Health in Tunisia was forced to act quickly by reinforcing its resources, especially with regard to hospital administration. Concerning COVID-19 symptoms, over 50% of cases were asymptomatic. However, some people develop symptoms such as fever, cough, myalgia, and influenza-like episodes; pneumonia was also sometimes experienced, as well as respiratory distress and thromboembolic complications (7). These symptoms varied according to COVID-19 variants. These variants were classified in three categories. They were variants under monitoring (VUMs), variants of interest (VOIs), and variants of concern (VOCs) (8). VOIs have been linked to growing prevalence and/or significant community transmission with various foci across multiple nations. Increased surveillance is necessary due to the uncertain phenotypic or epidemiological consequences of VUMs (8). VOCs have been linked to decreased effectiveness of diagnostic procedures, vaccinations, or therapies, as well as increased transmissibility and pathogenicity. Among these VOCs, the Delta variation transformed the epidemiological infection landscape of this virus during 2021 and posed a greater risk to worldwide public health. It quickly replaced the dominant Alpha version internationally (9).

However, the dearth of information about the comparison of COVID-19 clinical features of different variants, as well as the knowledge gaps in low-income nations, underscore the need of carrying out this study in Tunisia.

The aim of the study was to compare epidemiological, clinical and evolutive profile of COVID-19 infection during two waves of COVID-19.

Methods

Study design

This is a cross-sectional survey of COVID-19 cases confirmed by antigen test and/or RT-PCR in the Tunisian population between October 2020 and December 2021. An online questionnaire via Google Forms was administered. Social networks such as Facebook were used." The questionnaire was published through the Jawhara FM and Hannibal TV groups and pages

Study periods

Two periods were considered for the present study: a 210-day period corresponding to the Alpha variant (subperiod 1: October 2020 to Juin 2021), and a 240 day period corresponding to the Delta variant (subperiod 2: July 2021 to Decembre 2021) according to the national observatory of new and emerging diseases (Figure1) (10).

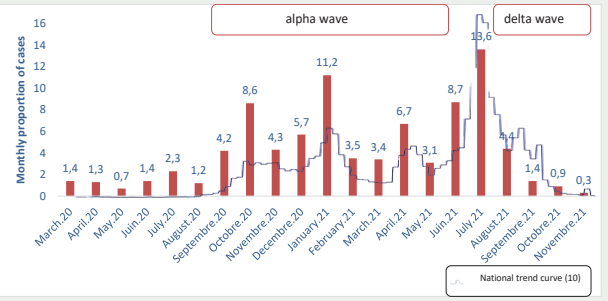

Figure1. Epidemic curve in Tunisia

Participants selection

All persons meeting the following criteria were included: Tunisian nationality, infected once with COVID-19 confirmed by PCR and/or rapid antigen test and having agreed to participate in the study. The participants who refused to participate were excluded from the study. They were excluded people aged under 18 years, Tunisians living abroad and non-Tunisians residing in Tunisia.

The required sample size was calculated using the formula: n=[(Zα/2)2 *p*(1-p)]/i2. The prevalence of COVID-19 varies between 5 and 40% (11). A proportion (p) of COVID-19 of 40% was chosen to maximize the sample size (11), a precision (i) of 5%, a risk error (α) of 5% and a loss of 30% due to non-eligible participants (not being a Tunisian, under 18 years of age, ect.) were considered, resulting in a required sample size of at least 404 participants.

Data collection

Initially, we carried out a pre-survey with 30 patients who were not included in the final study. This allowed us to assess the questionnaire's time and reformulate the order of the questions to make them clearer and more understandable.

Data collection was carried out using a questionnaire

self-administered in French and Arabic developed with Google Forms and shared online via social media during one month (February 2022) with weekly reminders. The one-month duration was sufficient to reach the number of subjects required as calculated at the beginning. Collection through social networks was chosen given that Facebook is the most used social media in Tunisia (12).
The questionnaire was composed of three parts: The first part was composed of questions, that described personal and sociodemographic characteristics of participants: age, gender, weight and size. In this part also participants were asked about their tobacco and alcohol status. The second part was about medical history: diabetes, respiratory disease, hypertension, dysthyroidism, immunodepression or other diseases. The third part was about COVID-19 symptoms.

Data analysis

The statistical software IBM SPSS (IBM Corporation, Somers, NY, USA), version 26.0, was used for analysis. Tests were two-sided; statistical significance was set as $p < 0.05$. Numbers and percentages were calculated for qualitative variables. For quantitative variables, normality was tested by the Kolmogorov-Smirnov test. If the distribution is normal, they were presented by their means and their standard deviations otherwise by their medians and interquartile range. A univariate analysis was performed. The Chi-square test was used to compare percentages when the validity conditions allowed it (theoretical numbers per cell are ≥ 5), otherwise, the Fisher exact test was used. Student's t test was used for comparison of means.

Ethical considerations

Participation in the study was voluntary. Only participants who agreed to take part in the study were included. To ensure anonymity, full names were not collected, nor were email addresses. Anonymity and confidentiality were respected. The present study was carried out following ethical principles of the Declaration of Helsinki and was approved by the ethics committee of Farhat Hached University Hospital Center in Sousse.

Results

In total, 1328 COVID-19 patients were included. Eight hundred eighty-three patients were infected during the Alpha wave (66.5%) and 445 were admitted during the Delta wave (33.5%). The median age was 37 years (IQR: 30–41 years) and predominantly male, as only 11.1% are female. Approximately 23% of all patients had at least one comorbidity, and more than 25% of all patients had obesity. Notable symptoms include loss of smell (68.4%) and taste (61.7%), along with headaches (71.9%) and myalgia (62.2%). A significant proportion of participants are healthcare professionals (23.6%), highlighting their increased vulnerability to infection. The severity of the disease appears to be low, with only 6.0% requiring oxygen supplementation, 6.4% being hospitalized, and 1.1% admitted to intensive care. COVID-19 vaccination rate (16.9%) before infection was low (Table 1).

Table 1. Sociodemographic and medical characteristics

Characteristics	N=1328 (%)
Age, Median [IQR]	37 [31-42]
Gender N (%)	
Female	117 (11.1)
Smoking N(%)	231 (17.4)
Body Mass Index (BMI), Median (IQR)	25.7 [22.8-29.01]
Comorbidity N (%)	302 (22.7)
Specific comorbidities N (%)	
Asthma	85 (6.4)
Hypertension	79 (5.9)
Diabetes	53 (4.0)
Heart disease	11 (0.8)
Anemia	11 (0.8)
Infected healthcare professionals	314 (23.6)
COVID-19 vaccination before first infection	225 (16.9)
Fever	715 (53.8)
Headache	955 (71.9)
Sore throat	595 (44.8)
Myalgia	826 (62.2)
Chest pain	451 (34.0)
Loss of smell	909 (68.4)
Loss of taste	819 (61.7)
Vomiting	216 (16.3)
Diarrhea	490 (36.9)
Arthralgias	791 (59.6)
Breathing difficulty	292 (22.0)
Cough	34 (2.6)
Runny nose	506 (38.1)
Nausea	331 (24.9)
Oxygen supplementation	80 (6.0)
Hospitalization	85 (6.4)
ICU hospitalization	14 (1.1)

Univariate analysis revealed that anemia, COVID-19 vaccination before infection, fever, smell loss, taste loss, and vomiting were significantly more frequent in cases involving the Delta variant. On the other hand, infection of healthcare professionals, myalgia, oxygenation supplementation, hospitalization and ICU hospitalization were more frequent in the Alpha variant (Table 2).
Multivariate analysis revealed that anemia, fever and loss of smell were significantly more frequent in cases involving the Delta variant. In contrast, healthcare worker infection and myalgia were more frequent in the Alpha variant (Table 3). References

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3. Decreased Case Fatality Rate of COVID-19 in the Second Wave: A study in 53 countries or regions - Fan

Table 2. Comparison of Symptoms, Severity, and Sociodemographic Characteristics Between the Two COVID-19 Waves: Univariate Analysis

	Alpha wave	Delta wave	p	ORc[CI95%]
Age, Median (IQR)	37.44[21-42]	36.9[30-42]	0.320	
Gender N (%)				
Female	704 (79.7)	352 (79.1)	0.789	-
Smoking N(%)	156 (17.7)	445 (16.9)	0.712	-]
Body Mass Index (BMI), Median (IQR)	26.6[23-29]	25.7[22.5-28]	**0.001**	**-**
Comorbidity N (%)	204 (23.1)	98 (22)	0.657	-
Specific comorbidities N (%)				
Asthma	56 (6.3)	29 (6.5)	0.902	-
Hypertension	58 (6.6)	21 (4.7)	0.179	-
Diabetes	38 (4.3)	15 (3.4)	0.412	-
Heart disease	6 (0.7)	5 (1.1)	0.522	-
Anemia	3 (0.3)	8 (1.8)	**0.009**	5.37[1.41-20.34]
Infected healthcare professionals	244 (27.6)	70 (15.7)	**≤10^{-3}**	0.48[0.36-0.65]
COVID-19 vaccination before infection	173 (19.6)	153 (34.4)	**≤10^{-3}**	2.15[1.66-2.78]
Fever	458 (51.9)	257 (57.8)	**0.042**	1.26[1.00-1.59]
Headache	631 (71.5)	324 (72.8)	0.606	-
Sore throat	403 (45.6)	192 (43.1)	0.388	-
Myalgia	576 (65.2)	250 (56.2)	**0.001**	0.68 [0.54-0.86]
Chest pain	304 (34.4)	147 (33)	0.613	-
Smell loss	575 (65.1)	334 (75.1)	**≤10^{-3}**	1.61[1.24-2.08]
Taste loss	514 (58.2)	305 (68.5)	**≤10^{-3}**	1.56[1.22-1.99]
Vomiting	126 (14.3)	90 (20.2)	**0.006**	1.52[1.13-2.05]
Diarrhea	320 (36.2)	170 (38.2)	0.484	-
Arthralgias	526 (59.6)	265 (59.6)	0.995	-
Breathing difficulty	193 (21.9)	99 (22.2)	0.871	-
Cough	22 (2.5)	12 (2.7)	0.823	-
Runny nose	346 (39.2)	160 (36)	0.253	-
Nausea	212 (24)	119 (26.7)	0.277	-
Oxygen supplementation	58 (6.5)	16 (4.9)	**0.020**	0.74[0.46-0.92]
Hospitalization	66 (7.4)	19 (4.25)	**0.024**	0.62[0.38-0.94]
ICU hospitalization	11 (1.2)	3 (0.6)	**0.025**	0.46[0.37-0.62]

COR: crude odds ratio, **CI**: confidence interval

Table 3. Comparison of Symptoms, Severity, and Sociodemographic Characteristics Between the Two COVID-19 Waves: Multivariate Analysis

	Univariate analysis		Multivariate analysis	
	ORc [CI]	**p**	**ORa[CI]**	**p**
BMI	-	0.001	-	≤10^{-3}
Anemia				
No	1		1	0.012
Yes	5.37[1.41-20.34]	0.009	5.87[1.48-23.26]	
Infected healthcare professionals				
No	1		1	≤10^{-3}
yes	0.48[0.36-0.65]	≤10^{-3}	0.48[0.35-0.65]	
Fever				
No	1		1	
yes	1.26[1.00-1.59]	0.042	1.47[1.15-1.88]	0.002
Myalgia				
No	1		1	
Yes	0.68 [0.54-0.86]		0.65[0.50-0.83]	0.001
Smell loss				
No	1		1	
Yes	1.61[1.24-2.08]	≤10^{-3}	1.62[1.25-2.11]	≤10^{-3}

COR: crude odds ratio, **AOR**: adjusted odds ratio, **CI**: confidence interval

Discussion

When comparing clinical presentation of hospitalized patients admitted in Tunisia during the Alpha and Delta waves of COVID-19, we noticed that Delta wave, which ran from May 2021 to December 2021, had a milder course of disease than the Alpha wave, which ran from October 2020 to April 2021. Research from Iran, Japan, and Spain supported our findings and showed that the Delta wave era observed a milder course of the disease (13–15). There are several plausible reasons for the Delta wave of COVID-19's milder illness progression than the Alpha wave. First, compared to wave 2, older and more vulnerable people were more likely to contract the virus at the start of the pandemic (16). Although not statistically significant, we observed a tendency to infect elderly patients with comorbidities admitted in wave 1 than in wave 2. That could be explained by the beginning in 2020, of various limitations, restrictions, and directives. They were implemented in Tunisia in an effort to prevent the disease's spread and safeguard the old and fragile people. Therefore, we presume that during the Alpha wave of COVID-19, a higher proportion of the population was at danger of catastrophic illness. On the other hand, there were no variation in sex. That was different in a similar study conducted in Iran which showed that in the Delta

wave of the disease, women were more unlikely than males to be affected, whereas in the Alpha wave, men exhibited greater susceptibility to the illness. Therefore, studies conducted in Tunis and a meta-analysis published that man were significantly more affected by COVID-19 than women (17,18). It could be caused by immune system malfunctions, lifestyle choices like smoking, self-care for one's health, or other elements that could alter how the epidemic affects different genders (19–21).

Comorbidities were present in 23% of patients during the Alpha wave and in 22% during the Delta wave. Our results were significantly closer to a meta-analysis where the overall frequency of patients with at least one comorbidity was equal to 31% (18). In our study, the most common comorbidities among infected patients with confirmed COVID-19 were asthma, hypertension, cardiovascular diseases and anemia. This result was also noted in a study conducted in Tunis (17) with a prevalence of 44.6% of hypertension and 4.4% of heart failure. Another study in Danmark revealed a prevalence of 32.8 % of hypertension and 7.7 % of asthma (16). Medical comorbidities, such as the presence of chronic respiratory disorders, have been linked to an increased incidence of serious events in patients with COVID-19, according to a recent meta-analysis (18).

Vomiting was more reported among patients infected in wave 2 than those in wave 1. Likewise, multiple studies support that gastrointestinal manifestations were more common in wave 2 (16,19). For that, recognizing gastrointestinal symptoms in adult and juvenile populations is crucial. As a counterpart, ignorance of these common manifestations in COVID-19 infection (22–24), may cause major problems by delaying the early diagnosis and treatment of COVID-19 patients (19). Taste and smell loss and fever were the more typically reported infection symptoms in the second group of patients, this indicates that Delta VOCs were more frequently linked to systemic infection symptoms than Alpha VOCs (25). But the progression was benign. This can be explained by vaccination against COVID-19. In fact, the vaccination was a protective factor during the wave 2 of COVID-19 (17).

Additionally, COVID-19 variants may have changed from wave 1 to wave 2, which may have affected patient severity of illness (16).

On the other hand, the improvement of the quality of patient care can explain the reduce in severity levels (17). Likewise, recent research has compared the severity features of COVID-19 patients from various waves. In our study, patients from wave 2 have experienced intensive care unit fewer than those from wave 1. A study from Danmark support our findings and reported that during the Delta wave, only six patients were admitted to the intensive care unit, while 25 patients were admitted during the Alpha wave (16). On the other hand, our results were similar to the literature in terms of hospitalization number (2,16,26,27). Accordingly, when the pandemic first started, there were a lot of COVID19 admissions (16). Therefore, some research explain that the disease's Delta wave, which started at the beginning of the year's comparatively warm months, was linked to a lower hospitalization rate; however, the disease's Alpha wave, which started at the beginning of the year's relatively warm months, saw a significant climb in the hospitalization rate (19). Furthermore, the Alpha wave of the epidemic began when no standard and comprehensive protocol was published for treatment of patients, worldwide; and scientific evidence was mainly the results of experiences from limited studies, usually in small sample size populations or small study areas, that presented various treatment approaches to health-care professionals which results in a higher number of hospitalization (19,28). Therefore, in the initial wave, more COVID-19 patients needed breathing assistance (19,29,30). Some studies explained this by the mean age which was lower in the Delta wave compared to the Alpha one. A systematic review and meta-analysis reported a median age of 46.2 years among the patients with a confirmed COVID-19 diagnosis (31). Although the exact cause for the difference of the patients' age between the two waves is unknown, it has been hypothesized that older adults have a further risk of COVID-19 infection, disease-related hospitalization and more severe complications (32–34). This can be associated to identify older adults in the alpha wave of the outbreak and younger adults in the later phases of the epidemic. Thus wave 2 had a more favorable evolution than wave 2.

This study's unique description of the two COVID-19 epidemic waves is by far its greatest strength. There have been relatively few studies up to this point that have detailed more than one wave of the COVID-19 outbreak (35). There are a number of limitations to this study that need to be considered. First, because the data was gathered via a survey, the veracity of self-reported information may be subject to recall or social desirability biases, potentially impacting the accuracy of responses. Furthermore, because social media sites were the only means of recruiting, selection bias might have had an impact on the participant pool. This strategy might have restricted participation to people with social media accounts and internet access, which could have excluded a portion of the population and impacted the results' ability to be applied broadly. Future research could improve the findings' representativeness and dependability by addressing these limitations.

Conclusion

This study highlights that the Alpha wave of COVID-19 was associated with greater severity compared to the Delta wave, including higher rates of hospitalization and ICU admissions. Common symptoms included headaches and loss of smell, with the latter being more prominent during the Delta wave. Increased vaccination coverage during the Delta wave likely contributed to the observed reduction in severity. Healthcare professionals were more frequently infected during the Alpha wave, and comorbidities, including obesity, remained significant risk factors.

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