COVID-19 in Tunisia (North Africa): Seroprevalence of SARS-CoV-2 in the general population of the capital city Tunis

Ines Cherif, Ghassen Kharroubi, Sana Chaabane, Rihab Yazidi, Mongi Dellagi, Mohamed Ali Snoussi, Sadok Salem, Soumaya Marzouki, Wafa Kammoun Rebai, Samia Rourou, et al.

COVID-19 in Tunisia (North Africa): Seroprevalence of SARS-CoV-2 in the general population of the capital city Tunis

Ines Cherif
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Ghassen Kharroubi
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Sana Chaabane
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Rihab Yazidi
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Mongi Dellagi
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Mohamed Ali Snoussi
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Sadok Salem
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Soumaya Marzouki
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Wafa Kammoun Rebai
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Samia Rourou
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Koussay Dellagi
   Institut Pasteur

Mohamed Ridha Barbouche
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Chaouki Benabdessalem
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Melika Ben Ahmed
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Jihene Bettaieb (✉ bettaiebjihene@yahoo.fr)
   Institut Pasteur de Tunis, University of Tunis El Manar, Tunis

Research Article

Abstract

Background:

Monitoring the coronavirus disease-19 (COVID-19) pandemic is primarily based on Reverse transcription polymerase chain reaction (RT PCR) detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As this test is mainly applied on persons with symptomatic disease, it may overlook individuals with pauci- or a-symptomatic infection. Seroprevalence studies are thus essential to get an accurate estimate of the actual SARS-CoV-2 diffusion within the populations. We report on the findings of the first serosurvey conducted in the capital city of Tunisia prior to the implementation of mass vaccination and analyzed factors associated with seropositivity.

Methods:

A cross sectional survey was conducted among households living in two areas of the governorate of Tunis, the capital city of the country. The survey was realized between March and April 2021, spanning the end of the second wave and the beginning of the third wave of COVID-19 and prior to the implementation of mass vaccination in Tunisia. SARS-CoV-2 specific immunoglobulin G (IgG) antibodies to the spike (S-RBD) or the nucleocapsid (N) proteins were detected using an in-house ELISA test. Results were adjusted for test performance. Multivariate logistic regression analysis was performed to determine factors independently associated with SARS-COV-2 seropositivity.

Results:

The survey included 1676 individuals from 431 households. The mean age and sex ratio were 43.3±20.9 years and 0.6 respectively. The weighted and test-performance adjusted prevalence of IgG antibodies to the N and the S-RBD proteins were 26.6% [22.9-30.8] and 25.1% [22.2-28.4] respectively. The weighted seroprevalence of anti-N and/or anti-S-RBD IgG antibodies was equal to 38.0% [34.6-41.5]. In multivariate analysis, age under 10, no tobacco use, previous diagnosis of COVID-19, a history of COVID-19 related symptoms and contact with a COVID-19 case within the household, were independently associated with higher SARS-CoV-2 seroprevalence.

Conclusions:

After the end of the second epidemic wave, more than one third of people living in Tunis got antibodies to SARS-CoV-2. Further studies are needed to monitor changes in these figures as Tunisian population is confronted to the subsequent epidemic waves and to guide the vaccine strategy.

I. Background

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first detected in Wuhan city, China in December 2019 [1]. Since then, the virus has rapidly spread throughout the world causing 126 million cases of infection and nearly 2.8 million deaths by the end of March 2021 [2] . By mid-January

2022, the World Health Organization (WHO) has registered nearly 319 million cases worldwide with more than 5 million deaths [3].

In Tunisia, the first case of coronavirus disease-19 (COVID-19) was identified in March 2, 2020. The spread of infection in the country just has been slowed down by the strict measures imposed by the national authorities after this introduction, such as a nationwide lockdown and borders closure. As a consequence, the total number of cases and deaths registered between March and June 2020 was very modest (29 cases with no deaths and 1087 cases with 49 deaths until March 17, 2020 and June 7, 2020 respectively)[4,5].   However, after borders reopening, the number of COVID-19 cases and deaths has dramatically increased, shaping two COVID-19 waves: the first in August-December 2020 and the second in January-March 2021[6]. Until March 28, 2021, 251,169 cumulative cases and 8760 COVID-19 related deaths were reported in Tunisia [7].

The monitoring of SARS-CoV-2 infection is mainly based on laboratory confirmed symptomatic cases and contacts. Hence, the true number of infected people is certainly much higher than the official reported figures mainly due to the often-asymptomatic forms of the disease. A meta-analysis conducted by Chen et al at the global level which has included 404 serological studies published between December 2019 and December 2020, estimated that 8% of the world population was at that date immune to the SARS-CoV-2. The estimated serology detected infections to confirmed cases ratio was equal to 11.1, stressing the very large burden of unreported SARS CoV-2 infection. Besides, population-based seroprevalence surveys were recommended by the WHO to determine as accurately as possible, the extent of the COVID-19 infection in the population [8]. Such data will provide valuable information to health authorities to tailoring prevention strategies, including vaccination.

 As the extent of the SARS-CoV-2 dissemination in Tunisian communities was not sufficiently documented, we assessed the seroprevalence of SARS-CoV-2 infection among the general population in the governorate of Tunis after the second epidemic wave, just before the start of the vaccination campaign and analyzed factors associated with seropositivity.

I I. Methods

1. Study design and population:

A cross sectional household survey was conducted between March and April 2021 in anticipation of the start of mass vaccination among general population. This period coincided with the end of the second wave and the beginning of the third epidemic wave of COVID-19 in Tunisia and was dominated by the circulation of the alpha variant [6]. The study took place in the city of Tunis in the two urban areas of El Omrane (41,781 inhabitants) and La Goulette (57,660 inhabitants) that were characterized by contrasted incidence of COVID-19 (COVID-19 incidence in El Omrane was equal to 1213 per 100000 population which corresponds to a low to intermediate incidence and in La Goulette to 2289 per 100000 population

which corresponds to a high incidence) The two areas have similar socioeconomic characteristics, including mainly moderate-income communities.

Tunisia is located in Northern Africa at the southern shore of the Mediterranean sea. The country population is 11,747 million according to the estimates of the National Institute of Statistics for 2020 [9] with almost 10% located in Tunis the capital city.

The study included all persons who were permanent residents in the selected houses and who gave their consent to participate to the study. We excluded the households in which at least one member refused to participate to the survey or refused blood sampling and those for which it was not possible to include all members after three visits of the investigators. Nevertheless, for children younger than five years, blood test refusal was not considered as a reason for household exclusion.

2. Sampling procedure:

Households were included based on a two stage cluster sampling. First, each study area was stratified by communities (El Omrane comprises 6 communities: France ville, Bir Atigue, Cité des oliviers, Ras Tabia, Jbel Lahmer and Oued el Sebai and La Goulette comprises 5 communities: La Goulette, La Goulette casino, Khaireddine, Cité Essalama and Taieb El Mhiri). Within each community, a variable number of clusters of about five households proportional to its population size, were randomly selected. In each cluster, households were chosen using systematic sampling of every fifth household after a random starting point and a random direction. Then all individuals in the selected household were enrolled after being properly informed.

3. Sample size:

Assuming a design effect of 2, a prevalence equal to 50%, a precision of 0.05, a population size of 40,000, and a 95% confidence interval, the calculated sample size was equal to 760 individuals in each area, which correspond to about 190 households with an average household size equal to 4.

4. Data collection:

A face to face standardized questionnaire was administered to participants by trained investigators. This questionnaire included questions related to sociodemographic characteristics, lifestyle habits and medical history, compliance with barrier measures, risk factors for exposure to the SARS-CoV-2, history of COVID-19 infection and COVID-19 related symptoms.

Blood samples of about one to two milliliters were taken on a serum tube from each person. The collected sera were used for serological analysis using two in-house SARS-CoV-2 ELISA tests developed and validated at Institut Pasteur in Tunis (IPT). The two tests detect immunoglobulin G (IgG) antibodies

to the receptor-binding domain of the spike protein(S-RBD) or the nucleocapsid (N) proteins of the SARS-CoV-2 respectively. N and S-RBD recombinant proteins were produced in E Coli and the eukaryotic expression system Sf9 respectively. ELISA assays were subsequently optimized and validated using 108 sera from COVID-19 patients and 72 prepandemic sera from the Tunisian population. Using a receiver operating curve, developed assays displayed have very high performances (AUC: 0.966 and 0.98, respectively, p< 0.0001). This resulted in a specificity of 93% and a sensitivity of 95% for the anti-S-RBD test and a specificity of 93% and a sensitivity of 94% for the anti-N test (Benabdessalem et al., submitted manuscript).

5. Data analyses:

Qualitative variables were summarized in terms of frequencies and percentages and quantitative ones in terms of means and standard deviation.

In order to facilitate data interpretation, we dichotomized the responses to the four-point Likert type scale questions related to compliance with preventive measures (namely, social distancing, hand hygiene and wear of facial mask). Hence, the responses « Always » and « Often » were grouped together on the one side, and «Never» and « Occasionally » on the other side.

Contact with a COVID-19 case within the household was defined as a contact with at least one member of the household who was previously diagnosed with COVID-19 or who was tested seropositive to the SARS-CoV-2 in the present study. COVID-19 related symptoms included respiratory symptoms, fever, chills, digestive symptoms, headache, conjunctivitis, weakness, myalgia, arthralgia, anosmia, agueusia, sore throat and loss of consciousness.

The overall seroprevalence was calculated on the basis of the detection of IgG antibodies to either the S-RBD or the N proteins of the SARS-CoV-2. This crude prevalence was afterwards weighted, using the post stratification weight method, for age and sex of the population in "El Omrane" and "La Goulette" using data published in the 2014 Tunisia population and housing census [10]. The prevalence of IgG antibodies against S-RBD and N proteins were also adjusted for ELISA test performance using the following formula [11]:

$$Adjusted\ prevalence = \frac{Crude\ prevalence + Specificity - 1}{Sensitivity + Specificity - 1}$$

The chi-square test for bivariate analysis and multivariable logistic regression for multivariate analysis were used to identify factors associated with SARS-CoV-2 anti-S-RBD IgG antibodies and/or anti-N IgG antibodies seropositivity prevalence.

A *p* value ≤0.05 indicates statistical significance for all analyses.

I I I. Results

Overall, 1676 individuals from 431 households (190 in "La Goulette" and 241 in "EL Omrane") were included in the survey. Most were female (62.5%). The mean age of participants was equal to 43.3±20.9 years ranging from 1 to 100 years. Nearly a quarter (25.3%) were aged 60 years and above and 22,4% were smokers.

More than half of surveyed individuals (53.9%) were either employees or students; 58.6% didn't have any underlying medical conditions and majority of them lived in an independent house (90.9%) (Table 1). The mean number of persons per room was equal to 1.4±0.7.

Table 1

Sociodemographic characteristics and lifestyle habits of the study population, Tunis, Tunisia, March-April 2021

Characteristics	El Omrane (%)	La Goulette (%)	Both (%)
Total	851 (50.8)	825 (49.2)	1676 (100.0)
Sex	**n=851**	**n=825**	**n=1676**
Male	327 (38.4)	301 (36.5)	628 (37.5)
Female	524 (61.6)	524 (63.5)	1048 (62.5)
Age	**n=851**	**n=825**	**n=1676**
<10	49 (5.8)	33 (4.0)	82 (4.9)
[10-20[	118 (13.9)	93 (11.3)	211 (12.6)
[20-30[	88 (10.3)	94 (11.4)	182 (10.9)
[30-40[	98 (11.5)	130 (15.8)	228 (13.6)
[40-50[	122 (14.3)	151 (18.3)	273 (16.3)
[50-60[	143 (16.8)	133 (16.1)	276 (16.5)
≥60	233 (27.4)	191 (23.2)	424 (25.3)
Occupation	**n=848**	**n=823**	**n=1671**
Without professional and educational activities	441 (52.0)	330 (40.1)	771 (46.1)
Employee/student	407 (48.0)	493 (59.9)	900 (53.9)
Comorbidities	**n=850**	**n=823**	**n=1673**
Yes	339 (39.9)	353 (42.9)	692 (41.4)
No	511 (60.1)	470 (57.1)	981 (58.6)
Tobacco use (n=1670)	**n=847**	**n=823**	**n=1670**
Yes	185 (21.8)	189 (23.0)	374 (22.4)
No	662 (78.2)	634 (77.0)	1296 (77.6)
Dwelling type (n=1642)	**n=849**	**n=793**	**n=1642**
Apartment	11 (1.3)	139 (17.5)	150 (9.1)
Independent house	838 (98.7)	654 (82.5)	1492 (90.9)

Nearly two thirds of participants (68.4%) reported that they frequently comply with preventive measures and around the third (37.2%) declared private cars as the mean of transport they usually use. More details are presented in Annex 1.

Among all included individuals, 10.1% (95% confidence interval [CI]: 8.8-11.6) reported they had already been tested for SARS-CoV-2, of whom, 42.9% [35.7-50.5] tested positive. Hence, only 4.4% [3.5-5.4] of all participants knew they have been already infected by the pandemic virus.

The weighted and test-performance adjusted prevalence of IgG antibodies against the N or the S-RBD proteins were equal to 26.6% [22.9-30.8] and 25.1% [22.2-28.4] respectively. The overall weighted seroprevalence (i.e. reactivity with S-RBD and/or N) was equal to 38.0% [34.6-41.5]. At the level of each study area, it was equal to 41.9% [38.0-45.9] in "El Omrane" and to 34.0% [28.5-39.9] in "La Goulette" (More details are presented in Table 2). Applying these percentages to the total population of each study area, we found that the estimated number of infected individuals in "El Omrane" and "La Goulette" were by March 2021, 34.5 and 14.8 times higher than the reported cumulative COVID-19 cases in each area respectively.

Table 2

Prevalence of Immunoglobuline G antibodies in the governorate of Tunis Tunisia, March-April 2021

	El Omrane % [95% CI][a]	La Goulette % [95% CI]	Both % [95% CI]
Unweighted seroprevalence			
Anti-S-RBD IgG[b] antibodies	32.0 [28.9-35.2]	29.8 [26.8-33.0]	30.9 [28.7-33.1]
Anti-N IgG[c] antibodies	33.6 [30.5-36.8]	26.3 [23.4-29.4]	30.0 [27.9-32.2]
Anti-S-RBD IgG antibodies and Anti-N IgG antibodies	24.2 [21.4-27.2]	22.2 [19.5-25.1]	23.2 [21.2-25.3]
Anti-S-RBD IgG antibodies and/or Anti-N IgG antibodies	41.5 [38.2-44.8]	33.9 [30.8-37.2]	37.8 [35.5-40.1]
Weighted seroprevalence			
Anti-S-RBD IgG antibodies	30.8 [27.3-34.5]	27.4 [23.5-31.7]	29.1 [26.5-32.0]
Anti-N IgG antibodies	34.1 [30.3-38.1]	26.2 [20.7-32.6]	30.2 [26.9-33.8]
Anti-S-RBD IgG antibodies and Anti-N IgG antibodies	23.1 [19.9-26.6]	19.7 [16.4-23.5]	21.4 [19.1-24.0]
Anti-S-RBD IgG antibodies and/or Anti-N IgG antibodies	41.9 [38.0-45.9]	34.0 [28.5-39.9]	38.0 [34.6-41.5]
The weighted and test-performance adjusted seroprevalence			
Anti-S-RBD IgG antibodies	27.0 [23.1-31.2]	23.1 [18.7-28.1]	25.1 [22.2-28.4]
Anti-N IgG antibodies	31.1 [26.8-35.7]	22.1 [15.7-29.4]	26.6 [22.9-30.8]

[a]: 95% Confidence Interval

[b]: Immunoglobuline G antibodies to the receptor-binding domain of the spike protein

[c]: Immunoglobuline G antibodies to the nucleocapsid protein

Among all seropositive participants, more than three quarter (79.2% [75.1-82.8]) were asymptomatic.

In univariate analysis, seropositivity prevalence varied significantly according to age groups ($p<10^{-3}$). Indeed, participants younger than 10 years had the highest seroprevalence of SARS-CoV-2 infection: 51.1% [35.2-66.8] still, none of them was previously diagnosed as COVID-19 case and only 7.1%

developed COVID-19 related symptoms. A higher seroprevalence at 47.9% [41.2-54.6] was also characteristic of the group of adolescents 10-20 years old.

Seropositivity was higher among participants who were in contact i) with a COVID-19 case within the same household (OR= 2.3 [1.8-2.9]), ii) with those who had reported any symptom compatible with a COVID-19 infection (OR= 2.0 [1.5-2.6]) and with those who were previously tested positive for COVID-19 (OR= 4.3 [2.4-7.9]). In addition, tobacco smokers had lower SARS-CoV-2 seroprevalence than non-smokers (OR= 0.5 [0.4-0.6]) (Table 3).

Table 3

Seroprevalence to SARS COV2 according to study variables Tunis, Tunisia, March-April 2021

Variables	N	Anti SARS-CoV-2 positive	Seropositivity prevalence % [95% CI][a]	Weighted Seropositivity prevalence % [95% CI]	Crude OR_c[b] [95% CI]	P value
Sex						NS
Male	628	236	37.6 [33.9-49.4]	39.8 [33.4-46.5]	1.1 [0.9-1.4]	
Female	1048	397	37.9 [34.9-40.9]	36.9 [33.3-40.7]	1	
Age						$<10^{-3}$
<10	82	42	51.2 [40.6-61.7]	51.1 [35.2-66.8]	1.9 [1.2-2.9]	
[10-20[	211	101	47.9 [41.2-54.6]	46.0 [39.0-53.2]	1.4 [0.9-2.1]	
[20-30[	182	50	27.5 [21.5-34.4]	27.4 [21.4-34.4]	0.6 [0.4-0.9]	
[30-40[	228	73	32.0 [26.3-38.3]	32.2 [26.4-38.6]	0.9 [0.6-1.3]	
[40-50[	273	102	37.4 [31.8-43.2]	38.1 [32.4-44.1]	1.1 [0.7-1.6]	
[50-60[	276	108	39.1 [33.6-45.0]	37.7 [32.1-43.6]	1.1 [0.7-1.6]	
≥60	424	157	37.0 [32.6-41.7]	37.1 [32.6-41.8]	1	
Occupation						NS
Without professional and educational activities	771	293	38.0 [34.6-41.5]	39.7 [35.2-44.5]	1	
Employee/student	900	338	37.6 [34.4-40.8]	37.0 [32.5-41.8]	0.9 [0.7-1.1]	
Comorbidities						NS

Yes	692	263	38.0 [34.4-49.7]	36.5 [32.1-41.1]	0.9 [0.7-1.1]	
No	981	369	37.6 [34.6-40.7]	38.7 [34.2-43.3]	1	
Tobacco use						**<10^{-3}**
Yes	314	98	26.2 [22.0-30.9]	25.7 [21.2-30.8]	0.5 [0.4-0.6]	
No	1296	530	40.9 [38.2-43.6]	41.2 [37.2-45.3]	1	
Respect of preventive measures						**NS**
Frequently	1138	457	40.2 [37.3-43.0]	39.2 [36.1-42.4]	1	
Occasionally/ Never	525	169	32.2 [28.1-36.3]	35.7 [28.5-43.6]	0.9 [0.7-1.1]	
Travelling abroad since December, 2019						**NS**
Yes	12	3	25.0 [8.9-53.2]	31.1 [19.1-46.2]	0.7 [0.4-1.3]	
No	1664	630	37.9 [35.6-40.2]	38.2 [34.8-41.8]	1	
Contact with a COVID-19 case within the household						**<10^{-3}**
Yes	1198	510	42.6 [39.8-45.4]	42.7 [38.6-47.0]	2.3 [1.8-2.9]	
No	478	123	25.7 [22.0-29.8]	24.7 [20.5-29.4]	1	
Seeking care in a health facility since the beginning of the COVID-19 pandemic in Tunisia (Mars 2020)						**NS**
Yes	909	347	38.2 [35.1-49.4]	36.4 [32.8-40.2]	0.9 [0.7-1.1]	
No	758	281	37.1 [33.7-40.6]	39.5 [34.1-45.3]	1	
Means of transport used						**NS**

Car	607	229	37.7 [33.9-41.6]	38.6 [31.9-45.7]	1.0 [0.8-1.3]
Public transport	441	164	37.2 [32.8-49.8]	35.8 [30.4-41.5]	0.9 [0.7-1.2]
Bicycle/motorcycle	14	3	21.4 [7.8-47.6]	22.9 [7.0-53.9]	0.5 [0.1-1.7]
Different means of transport	176	71	40.3 [33.4-47.7]	43.1 [34.6-52.1]	1.2 [0.8-1.8]
None	394	150	38.1 [33.4-42.9]	38.3 [32.8-44.0]	1
Previous diagnosis of COVID-19 infection					$<10^{-3}$
Yes	73	56	76.7 [65.8-84.9]	71.6 [58.4-81.9]	4.3 [2.4-7.9]
No	1603	577	36.0 [33.7-38.4]	36.7 [33.2-40.3]	1
History of COVID-19 related symptoms					$<10^{-3}$
Yes	254	148	58.3 [52.1-64.2]	52.6 [45.5-59.6]	2.0 [1.5-2.6]
No	1408	481	34.2 [31.7-36.7]	35.5 [31.7-39.5]	1
Dwelling type					NS
Apartment	150	49	32.7 [25.7-40.5]	33.0 [25.2-42.0]	0.8 [0.5-1.2]
Independent house	1492	576	38.6 [36.2-41.1]	38.8 [35.1-42.5]	1

[a]: 95% Confidence Interval

[b]: Crude Odds ratio

In multivariate analysis, young age, previous diagnosis of COVID-19 infection, COVID-19 related symptoms, no tobacco use and contact with a COVID-19 case within the household were independently

associated with SARS-CoV-2 seropositivity (Table 4).

Table 4

Predictors of seropositivity among Tunisian participants as a result of multiple logistic regression analysis

Variables	OR_a[a]	$[CI_{95\%}]$[b]	P value
Tobacco use			
Yes	0.6	[0.5-0.8]	**0.001**
No	**1**		
Previous diagnosis of COVID-19 infection			
Yes	3.1	[1.6-5.8]	**<10^{-3}**
No	**1**		
History of COVID-19 related symptoms			**<10^{-3}**
Yes	1.8	[1.3-2.5]	
No	**1**		
Age			**0.03**
<10	1.9	[1.2-2.9]	
[10-20[	1.4	[0.9-2.1]	
[20-30[	0.6	[0.4-0.9]	
[30-40[	0.9	[0.6-1.3]	
[40-50[	1.0	[0.7-1.6]	
[50-60[	1.1	[0.7-1.6]	
≥ 60	**1**		
Contact with a COVID-19 case within the household			**<10^{-3}**
Yes	2.1	[1.3-2.5]	
No	**1**		

[a]: adjusted odds ratio

[b]: 95% Confidence Interval

I V. Discussion

In the present study, we conducted a cross sectional survey to assess the seroprevalence of SARS-CoV-2 in people living in two urban areas of Tunis: El Omrane and La Goulette. The two study areas were selected because they expressed contrasted incidence (intermediate to low versus high) of COVID-19, based on the cumulative incidence since the pandemic's onset. The weighted prevalence of seropositivity in the study population, defined by the detection of IgG antibodies against the N and/or the S-RBD proteins, was equal to 38.0% [34.6-41.5]. In multivariate analysis, we found that younger age, smoking status, previous confirmed COVID-19 infection, history of COVID-19 related symptoms and contact with a COVID-19 case within the household were independently and significantly associated with SARS-CoV-2 seropositivity.

Our study was conducted on March-April 2021 corresponding to the end of the second epidemic COVID-19 wave in Tunisia and the beginning of the third one. Hence and up to the study dates, the population has been exposed mainly to the wild original SARS-CoV-2 virus and to the alpha variant. Since then, the country was hit again by two additional much higher waves: the fourth wave on May-October 2021 mainly due to the circulation of the delta virus variant [6] (Figure 1) and the fifth wave starting in January 2022 due to the emergence of the Omicron virus variant.

Our results reveal that a large fraction (almost 40%) of the population of the study areas got infected after being exposed to just the second epidemic wave. In addition, the estimated seroprevalences were 34.5 and 14.8 times greater than the reported number of confirmed COVID-19 cases in "El Omrane" and "La Goulette" respectively. These figures stress the key role played by asymptomatic infection in SARS COV2 transmission and also illustrate the limits of case detection and contact tracing in the study areas. These shortcomes likely had severely jeopardised the impacts of individual preventive measures including isolation, in term of virus circulation. The prevalence figures also illustrate the high level of infection reached after an epidemic wave that was, all in all, relatively modest as compared to the fourth and fifth waves that hit the country in the following 12 months.

Noteworthy, as the cumulative COVID-19 incidence in the two studied areas was four times higher at the end of the fourth wave than after the second wave (Table 5), it seems intuitive that the proportion of individuals seropositive would by now exceed 100% if one consider high (>10) seroprevalence to incidence ratio revealed by our study as well as by others ; This means that many of the previously infected individuals will be re-infected (most likely silently) by SARS CoV-2 during the following waves, hence participating to maintaining high level of virus circulation and questioning the extent of the herd immunity in the exposed populations.

Table 5

COVID-19 incidence in the studied areas during the survey period and after the subsequent waves

Cumulative incidence*	End of the second wave (Survey Period)	End of the third wave	End of the fourth wave
El Omrane	1213	1843	5459
La Goulette	2289	2862	5338

*: per 100000 population

Surprisingly, we found that the SARS-CoV-2 seroprevalence was higher in the area of "low to intermediate" COVID-19 incidence ("El Omrane") compared to that in high COVID-19 incidence ("La Goulette"). One possible explanation could be that "La Goulette" is a seaside city and some Tunisians living abroad and other tourists came on summer 2021 after reopening of the borders, to spend holidays there. If they got infected in Tunisia during their temporary stay, they will be registered as cases by the regional health directorates. Still, they were not included in our survey as we only considered permanent Tunisian residents.

Our results are in keeping with those reported at the global level in population surveys conducted among unvaccinated people and before the high circulation of the delta variant, which is known to be more contagious than previous variants [13] . Seropositivity rates reported worldwide [14–23], ranged from less than 2.6% in Sierra Leone [14] to 70.0% in Iquitos (Peru) [21](Annex 2). Such heterogeneity likely reflects differences in surveys design, dates of epidemic onset, the adherence of exposed populations to social restrictions and individual preventive measures applied in each country [24] and the type of laboratory test used.

Our result also corroborate previous studies mainly in the African continent in which a high underdetection and /or under-reporting of COVID-19 cases was noted [14,23,25–27]. This could be explained by the high percentage of COVID-19 asymptomatic cases. Indeed, we found that a large majority of seropositive participants (79.2%) didn't develop any kind of COVID-19 related symptoms. Such high percentage of asymptomatic COVID-19 cases was also found in some other studies [28,29]. Nevertheless, a memory bias, which can lead to an overestimation of asymptomatic forms, cannot be eliminated in this survey. Indeed, participants were asked about their symptoms since the beginning of the COVID-19 pandemic in Tunisia. Such a large gap between the true number of SARS-CoV-2 infected persons and the declared cases of COVID-19 can also be explained by limited testing, fear of the disease, infection related stigma and, in some cases, conviction that COVID-19 does not exists [29–31].This emphasizes the need of amplifying testing efforts, case finding and contact tracing [32] ,mainly with the circulation of the new Omicron variant characterized by a very high proportion of asymptomatic cases [33]. This is key to generating accurate data on SARS-CoV-2 in Tunisia and to implement evidence based public health measures to flatten the COVID-19 curve.

In this study, we found that age was independently associated with seropositivity. Indeed, children (age<10) had the highest percentage of IgG antibodies and the same trend is observed in the next age range (10-20). According to literature, youth are more likely to have social contacts than adults [34] and

may be less adherent to barrier measures such as masking, hand hygiene and social distancing [35]. Contacts in schools were also found to be more physical than those at workplace [34]. Another explanation could be that children seem to have higher and more sustainable immune responses than adults [36]. However, the findings of the present study do not support most of previous research surveys that found either a lower seroprevalence among youngest participants [26,37−39] or a non-significant difference according to age [29,40]. Such differences in results may be explained by the fact that most of the aforementioned studies that found a lower seroprevalence among youngest participants were conducted during the first wave of the pandemic, when majority of schools were closed unlike our study which was conducted in spring 2021 after schools' reopening. Previous longitudinal studies have found increased SARS-CoV-2 seropositivity among children along with the overall transmission of COVID-19 [41−43]. In addition, with the emergence of the Omicron variant, a rise in COVID-19 pediatric cases was noted [44]. This raises the concern of the potential influence of variants emergence on the transmission of SARS-CoV-2 among children.

We also found that none of seropositive participants aged under 10 years were previously diagnosed with COVID-19 which shows that the spread of SARS-CoV-2 among children and adolescents is extremely underestimated in Tunisia. Public health measures to decrease SARS CoV-2 transmission should thus include the entire population, and not only focus on adults [32]. Non pharmaceutical intervention, including masking, hand hygiene and ventilation of indoor settings, should also be strengthened mainly in schools [45] since the under 18 years old are still not a priority targeted group for COVID-19 vaccination in Tunisia.

 The Seroprevalence to SARS COV2 did not differ significantly according to sex in line with results of previous studies [18,40,46,47]. Moreover, our study together with previous ones [18,24,37,40,48], found a higher prevalence of antibody seropositivity among participants who report a history of COVD-19 like symptoms. Consistent with other studies [40,48], previous diagnosis of COVID-19 infection and contact with a COVID-19 case within the household were also independently and significantly associated with a higher percentage of SARS-CoV-2 IgG antibodies. However, surprisingly, we found that tobacco smokers had lower SARS-CoV-2 seroprevalence than non-smokers. A similar result was found by Alsuwaidi et al and Paleiron et al [18,49]. One hypothesis is that nicotine decreases the expression of the angiotensin converting enzyme 2 (ACE 2) which is a receptor of SARS-CoV-2. Another hypothesis is that SARS-CoV-2 and nicotine compete for binding to the nicotine acetylcholine receptor (nAChR) which is possibly involved in the physiopathology of COVID-19 infection [50]. However, our results should be interpreted with caution as we conducted an observational study. Also, participants may underreport their tobacco consumption introducing a social desirability bias to the survey. Indeed, a relationship between smoking and increased risk of COVID-19 infection was underlined by a British study that used mendelian randomization analysis [51]. In addition, evidence suggest that tobacco increases the risk of severe illness and deaths due to COVID-19 [52].

Finally, a non-significant association was found between seropositivity and the used means of transport. In accordance, an online survey conducted in France assessing factors associated with a higher risk to

COVID-19 contagion, found that public transport was not associated with a higher risk of virus transmission unlike restaurants and bars [53].

Strengths and limitations:

This is the first study in Tunisia that reports the extent of the COVID-19 infection among both children and adults. As well, our study is, to the best of our knowledge, the first seroprevalence survey reported from countries in North Africa Our study was conducted at the nadir of the second epidemic wave that peaked on January 4, 2021 and the start of the third epidemic wave that peaked on April 15 2021 (Figure 1) [6]. Importantly it took place just before the beginning of the COVID-19 vaccination campaign in Tunisia and hence the detected antibodies could be unequivocally attributed to natural SARS CoV-2 infection and not to vaccine administration. Also, the serum samples were tested using two in-house ELISA tests developed by IPT that detect with a high sensitivity and specificity anti-N and anti-S-RBD IgG antibodies, respectively. Indeed, anti-N IgG antibodies may appear before the anti-S-RBD [54] and the latter tend to wane at a slower rate than the anti-N antibodies [55]. In fact, Schoenhals et al found a decrease of more than 10% in the percentage of anti-N IgG antibodies among seropositive blood donors during a three months follow up in Toamasina (Madagascar) [56]. The detection in our study of antibodies to the two viral proteins gives a better chance to detect more infected cases than when using only one antigen.

Our study has some limitations. The ELISA tests detect SARS-CoV-2 antibodies which are known to be evanescent after natural infection and vaccination [57] In fact, the antibody decay after natural infection [55] may have minored the seroprevalence rates in our study population. Therefore, long term cohort longitudinal serological studies are warranted to assess the temporal dynamics of prevalence rates that integrate the opposing effects of natural antibody decay and the successive reinfections by different variants.

 Our study was conducted only in the capital city Tunis. Larger populational serosurveys including other regions in Tunisia, would best describe the actual dynamics of the epidemics in the country according to the diversity of local conditions (ie.in rural areas and in the various country eco-climatic stages, effect of transborder human movements, population density etc.). Besides, assessing in addition to serology, the protective virus neutralizing antibodies as well as the cellular immune responses to the COVID-19 infection, would certainly improve the estimation of the actual proportion of population immune to SARS-COV-2.

V. Conclusions

Almost 40% of participants to our serosurvey had antibodies against SARS-CoV-2 after the second epidemic wave of COVID-19 in Tunisia. This figure illustrates the true proportion of individuals who got infected and as expected, was much higher than the reported number of confirmed COVID-19 cases. Our study calls for future larger seroprevalence surveys to monitor the impact of the successive epidemic

waves that hit the country as well as the effects of introducing mass vaccination to the COVID-19. This will inform on changes in the fraction of immune population and its impact on the evolving SARS-CoV-2 strains.

Abbreviations

Severe acute respiratory syndrome coronavirus 2: SARS-CoV-2

World Health Organization: WHO

Coronavirus disease-19: COVID-19

Institut Pasteur in Tunis: IPT

Immunoglobulin G: IgG

Receptor binding domain of the spike protein: S-RBD

Nucleocapsid protein: N

Declarations

Ethics approval and consent to participate:

The study protocol was approved by the Biomedical Ethics Committee (CEBM) of Institut Pasteur de Tunis (IPT) (2020/21/I/LR16IPT/V2). A written informed consent was obtained from participants aged 18 years and over. For minors or illiterate the consent was obtained from a legally acceptable representative.

Consent for publication:

Not applicable

Availability of data and materials:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Competing interests:

The authors declare that they have no competing interests

Funding:

Authors contribution:

IC: Data curation, Methodology, Formal analysis, Writing - original draft, GK: Data curation, Methodology, Investigation, Writing - original draft, SC: Project management and coordination, Investigation, Data curation, RY: Data curation, Investigation, MD: Data Curation, Investigation MAS: Data curation, investigation, SS: Data curation, investigation, SM: Investigation, validation WKR: Data curation, Investigation, SR: Data curation, Investigation, KD: Conception of the work, Resources, Funding acquisition, Supervision, Validation, Visualization, Writing - review & editing, MRB: Validation, review & editing CB: Supervision, Validation, Visualization, review & editing, MBA: Supervision, Validation, Visualization, review & editing, JB: Conception of the work, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing - review & editing.

All authors read and approved the final manuscript

Acknowledgments:

References

1. World Health Organization. Listings of WHO's response to COVID-19. https://www.who.int/news/item/29-06-2020-covidtimeline. [Accessed 30th November 2021]

2. World Health Organization. Weekly epidemiological update on COVID-19 - 30 March 2021.https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---31-march-2021. [Accessed 30th November 2021]

3. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. https://covid19.who.int. [Accessed 30th November 2021]

4. National Observatory of New and Emerging diseases.COVID-19 en Tunisie : Point de situation à la date du 07 juin 2020. https://www.onmne.tn/?p=10229. [Accessed 30th November 2021]

5. National Observatory of New and Emerging diseases.Point de situation sur l'épidémie d'infections au Nouveau Coronavirus « COVID-19 » à la date du 17 Mars 2020. https://www.onmne.tn/?p=10363. [Accessed 22th December 2021]

6. National Observatory of New and Emerging diseases.Bulletin de veille COVID-19 à la date du 12 Décembre 2021. https://www.onmne.tn/?p=15695. [Accessed 22th December 2021]

7. Ministry of Health.Point de situation en Tunisie – Coronavirus. http://coronavirus.rns.tn/point-de-situation-en-tunisie/[Accessed 10th January 2022]

8. World Health Organization. Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection. 17th March 2020.

9. National Institute of Statistics. Bulletin Mensuel de la Statistique, Septembre 2021. http://www.ins.tn/publication/bulletin-mensuel-de-la-statistique-septembre-2021.[Accessed 10th January 2022]

10. National Institute of Statistics. Recensement Général de la Population et de l'Habitat 2014. http://ins.tn/enquetes/recensement-general-de-la-population-et-de-lhabitat-2014.[Accessed 10th January 2022]

11. Sempos CT, Tian L. Adjusting Coronavirus Prevalence Estimates for Laboratory Test Kit Error. Am J Epidemiol. 2020;190(1):109–15.

12. Ritchie H, Mathieu E, Rodés-Guirao L, Appel C, Giattino C, Ortiz-Ospina E, et al .Coronavirus Pandemic (COVID-19). Published online at OurWorldInData.org. https://ourworldindata.org/coronavirus. [Accessed 23th January 2022]

13. Centers for Disease Control and Prevention. Delta variant: What we know about the science. https://www.cdc.gov/coronavirus/2019-ncov/variants/delta-variant.html. [Accessed 12th January 2022].

14. Barrie MB, Lakoh S, Kelly JD, Kanu JS, Squire JS, Koroma Z, et al. SARS-CoV-2 antibody prevalence in Sierra Leone, March 2021: a cross-sectional, nationally representative, age-stratified serosurvey. BMJ Glob Health. 2021;6(11):e007271.

15. Fryatt A, Simms V, Bandason T, Redzo N, Olaru ID, Ndhlovu CE, et al. Community SARS-CoV-2 seroprevalence before and after the second wave of SARS-CoV-2 infection in Harare, Zimbabwe. EClinicalMedicine. 2021;41:101172.

16. Reicher S, Ratzon R, Ben-Sahar S, Hermoni-Alon S, Mossinson D, Shenhar Y, et al. Nationwide seroprevalence of antibodies against SARS-CoV-2 in Israel. Eur J Epidemiol. 2021;36(7):727–34.

17. Le Vu S, Jones G, Anna F, Rose T, Richard J-B, Bernard-Stoecklin S, et al. Prevalence of SARS-CoV-2 antibodies in France: results from nationwide serological surveillance. Nat Commun. 2021;12(1):3025.

18. Alsuwaidi AR, Al Hosani FI, Al Memari S, Narchi H, Abdel Wareth L, Kamal H, et al. Seroprevalence of COVID-19 infection in the Emirate of Abu Dhabi, United Arab Emirates: a population-based cross-sectional study. Int J Epidemiol. 2021;50(4):1077-1090

19. Al-Abri SS, Al-Wahaibi A, Al-Kindi H, Kurup PJ, Al-Maqbali A, Al-Mayahi Z, et al. Seroprevalence of SARS-CoV-2 antibodies in the general population of Oman: results from four successive nationwide sero-epidemiological surveys. Int J Infect Dis. 2021;112:269–77.

20. Jeewandara C, Guruge D, Abyrathna IS, Danasekara S, Gunasekera B, Pushpakumara PD, et al. Seroprevalence of SARS-CoV-2 Infection in the Colombo Municipality Region, Sri Lanka. Front Public Health. 2021;9:724398

21. Álvarez-Antonio C, Meza-Sánchez G, Calampa C, Casanova W, Carey C, Alava F, et al. Seroprevalence of anti-SARS-CoV-2 antibodies in Iquitos, Peru in July and August, 2020: a population-based study. Lancet Glob Health. 2021;9(7):e925–31.

22. Mattar S, Alvis-Guzman N, Garay E, Rivero R, García A, Botero Y, et al. Severe Acute Respiratory Syndrome Coronavirus 2 Seroprevalence Among Adults in a Tropical City of the Caribbean Area, Colombia: Are We Much Closer to Herd Immunity Than Developed Countries? Open Forum Infect Dis. 2020;7(12):ofaa550.

23. Wiens KE, Mawien PN, Rumunu J, Slater D, Jones FK, Moheed S, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Juba, South Sudan: a population-based study. Emerg Infect Dis.2021;27(6):1598-1606

24. Poustchi H, Darvishian M, Mohammadi Z, Shayanrad A, Delavari A, Bahadorimonfared A, et al. SARS-CoV-2 antibody seroprevalence in the general population and high-risk occupational groups across 18 cities in Iran: a population-based cross-sectional study. Lancet Infect Dis. 2021;21(4):473–81.

25. Mulenga LB, Hines JZ, Fwoloshi S, Chirwa L, Siwingwa M, Yingst S, et al. Prevalence of SARS-CoV-2 in six districts in Zambia in July, 2020: a cross-sectional cluster sample survey. Lancet Glob Health. 2021;9(6):e773–81.

26. Nkuba AN, Makiala SM, Guichet E, Tshiminyi PM, Bazitama YM, Yambayamba MK, et al. High prevalence of anti-SARS-CoV-2 antibodies after the first wave of COVID-19 in Kinshasa, Democratic Republic of the Congo: results of a cross-sectional household-based survey. Clin Infect Dis. 2021;ciab515.

27. Mwananyanda L, Gill CJ, MacLeod W, Kwenda G, Pieciak R, Mupila Z, et al. Covid-19 deaths in Africa: prospective systematic postmortem surveillance study. BMJ;372:n334.

28. Ing AJ, Cocks C, Green JP. COVID-19: in the footsteps of Ernest Shackleton. Thorax. 2020;75(8):693–4.

29. George CE, Inbaraj LR, Chandrasingh S, Witte LP de. High seroprevalence of COVID-19 infection in a large slum in South India; what does it tell us about managing a pandemic and beyond? Epidemiol Infect. 2021;149:e39

30. McGowan CR, Hellman N, Chowdhury S, Mannan A, Newell K, Cummings R. COVID-19 testing acceptability and uptake amongst the Rohingya and host community in Camp 21, Teknaf, Bangladesh. Confl Health. 2020;14(1):74.

31. McArthur L, Sakthivel D, Ataide R, Chan F, Richards JS, Narh CA. Review of Burden, Clinical Definitions, and Management of COVID-19 Cases. Am J Trop Med Hyg. 2020;103(2):625–38.

32. Byambasuren O, Dobler CC, Bell K, Rojas DP, Clark J, McLaws M-L, et al. Comparison of seroprevalence of SARS-CoV-2 infections with cumulative and imputed COVID-19 cases: Systematic review. PLoS ONE. 2021;16(4):e0248946.

33. Murray CJL. COVID-19 will continue but the end of the pandemic is near.Lancet. 2022; doi:10.1016/S0140-6736(22)00100-3

34. Mossong J, Hens N, Jit M, Beutels P, Auranen K, Mikolajczyk R, et al.Social contacts and mixing patterns relevant to the spread of infectious diseases. PLoS Med. 2008;5(3):e74.

35. Rumain B, Schneiderman M, Geliebter A. Prevalence of COVID-19 in adolescents and youth compared with older adults in states experiencing surges. PLoS ONE. 2021;16(3):e0242587.

36. Dowell AC, Butler MS, Jinks E, Tut G, Lancaster T, Sylla P, et al. Children develop robust and sustained cross-reactive spike-specific immune responses to SARS-CoV-2 infection. Nat Immunol. 2022;23(1):40–9.

37. Shakiba M, Nazemipour M, Salari A, Mehrabian F, Nazari SSH, Rezvani SM, et al. Seroprevalence of SARS-CoV-2 in Guilan Province, Iran, April 2020. Emerg Infect Dis. 2021;27(2):636–8.

38. Stringhini S, Wisniak A, Piumatti G, Azman AS, Lauer SA, Baysson H, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study.Lancet. 2020;396(10247):313–9.

39. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, Oteo J, Hernán MA, Pérez-Olmeda M, et al.Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study.Lancet. 2020;396(10250):535–44.

40. Murhekar MV, Bhatnagar T, Thangaraj JWV, Saravanakumar V, Kumar MS, Selvaraju S, et al.SARS-CoV-2 seroprevalence among the general population and healthcare workers in India, December 2020–January 2021. Int J Infect Dis. 2021;108:145–55.

41. Indenbaum V, Lustig Y, Mendelson E, Hershkovitz Y, Glatman-Freedman A, Keinan-Boker L, et al. Under-diagnosis of SARS-CoV-2 infections among children aged 0–15 years, a nationwide seroprevalence study, Israel, January 2020 to March 2021.Eurosurveillance. 2021;26(48):2101040.

42. Ulyte A, Radtke T, Abela IA, Haile SR, Berger C, Huber M, et al.Clustering and longitudinal change in SARS-CoV-2 seroprevalence in school children in the canton of Zurich, Switzerland: prospective cohort study of 55 schools. BMJ. 2021;372:n616.

43. Bundle N, Dave N, Pharris A, Spiteri G, Deogan C, Suk JE, et al. COVID-19 trends and severity among symptomatic children aged 0–17 years in 10 European Union countries, 3 August 2020 to 3 October 2021.Eurosurveillance. 2021;26(50):2101098.

44. Cloete J, Kruger A, Masha M, Plessis NM du, Mawela D, Tshukudu M, et al.Rapid rise in paediatric COVID-19 hospitalisations during the early stages of the Omicron wave, Tshwane District, South Africa (Preprint). 2021;doi: 10.1101/2021.12.21.21268108

45. World Health Organization. COVID-19 disease in children and adolescents: Scientific brief, 29 September 2021. https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-Sci_Brief-Children_and_adolescents-2021.1. [Accessed 23th January 2022]

46. Bobrovitz N, Arora RK, Cao C, Boucher E, Liu M, Donnici C, et al. Global seroprevalence of SARS-CoV-2 antibodies: A systematic review and meta-analysis. PLoS ONE. 2021;16(6):e0252617.

47. Hallal PC, Hartwig FP, Horta BL, Silveira MF, Struchiner CJ, Vidaletti LP, et al. SARS-CoV-2 antibody prevalence in Brazil: results from two successive nationwide serological household surveys. Lancet Glob Health. 2020;8(11):e1390–8.

48. Tuells J, Egoavil CM, Pena Pardo MA, Montagud AC, Montagud E, Caballero P, et al. Seroprevalence Study and Cross-Sectional Survey on COVID-19 for a Plan to Reopen the University of Alicante (Spain). Int J Environ Res Public Health. 2021;18(4):1908.

49. Paleiron N, Mayet A, Marbac V, Perisse A, Barazzutti H, Brocq F-X, et al. Impact of Tobacco Smoking on the Risk of COVID-19: A Large Scale Retrospective Cohort Study. Nicotine Tob Res. 2021;23(8):1398–404.

50. Changeux J-P, Amoura Z, Rey FA, Miyara M. A nicotinic hypothesis for Covid-19 with preventive and therapeutic implications. C R Biol. 2020;343(1):33–9.

51. Clift AK, Ende A von, Tan PS, Sallis HM, Lindson N, Coupland CAC, et al. Smoking and COVID-19 outcomes: an observational and Mendelian randomisation study using the UK Biobank cohort. Thorax .2022;77(1):65-73

52. Patanavanich R, Glantz SA. Smoking is associated with worse outcomes of COVID-19 particularly among younger adults: a systematic review and meta-analysis.BMC Public Health. 2021;21(1):1554.

53. Pasteur Institute. Étude ComCor sur les lieux de contamination au SARS-CoV-2 : où les Français s'infectent-ils ? https://www.pasteur.fr/fr/espace-presse/documents-presse/etude-comcor-lieux-contamination-au-sars-cov-2-ou-francais-s-infectent-ils.[Accessed 20th January 2022]

54. Burbelo PD, Riedo FX, Morishima C, Rawlings S, Smith D, Das S, et al. Sensitivity in Detection of Antibodies to Nucleocapsid and Spike Proteins of Severe Acute Respiratory Syndrome Coronavirus 2 in Patients With Coronavirus Disease 2019. J Infect Dis. 2020;9;222(2):206-213.

55. Gallais F, Gantner P, Bruel T, Velay A, Planas D, Wendling M-J, et al. Evolution of antibody responses up to 13 months after SARS-CoV-2 infection and risk of reinfection. EBioMedicine. 2021;71:103561

56. Schoenhals M, Rabenindrina N, Rakotondramanga JM, Dussart P, Randremanana R, Heraud J-M, et al. SARS-CoV-2 antibody seroprevalence follow-up in Malagasy blood donors during the 2020 COVID-19 Epidemic. EBioMedicine. 2021;68:103419

57. Centers for Disease Control and Prevention. Science Brief: SARS-CoV-2 Infection-induced and Vaccine-induced Immunity. https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html. [Accessed 22th January 2022]
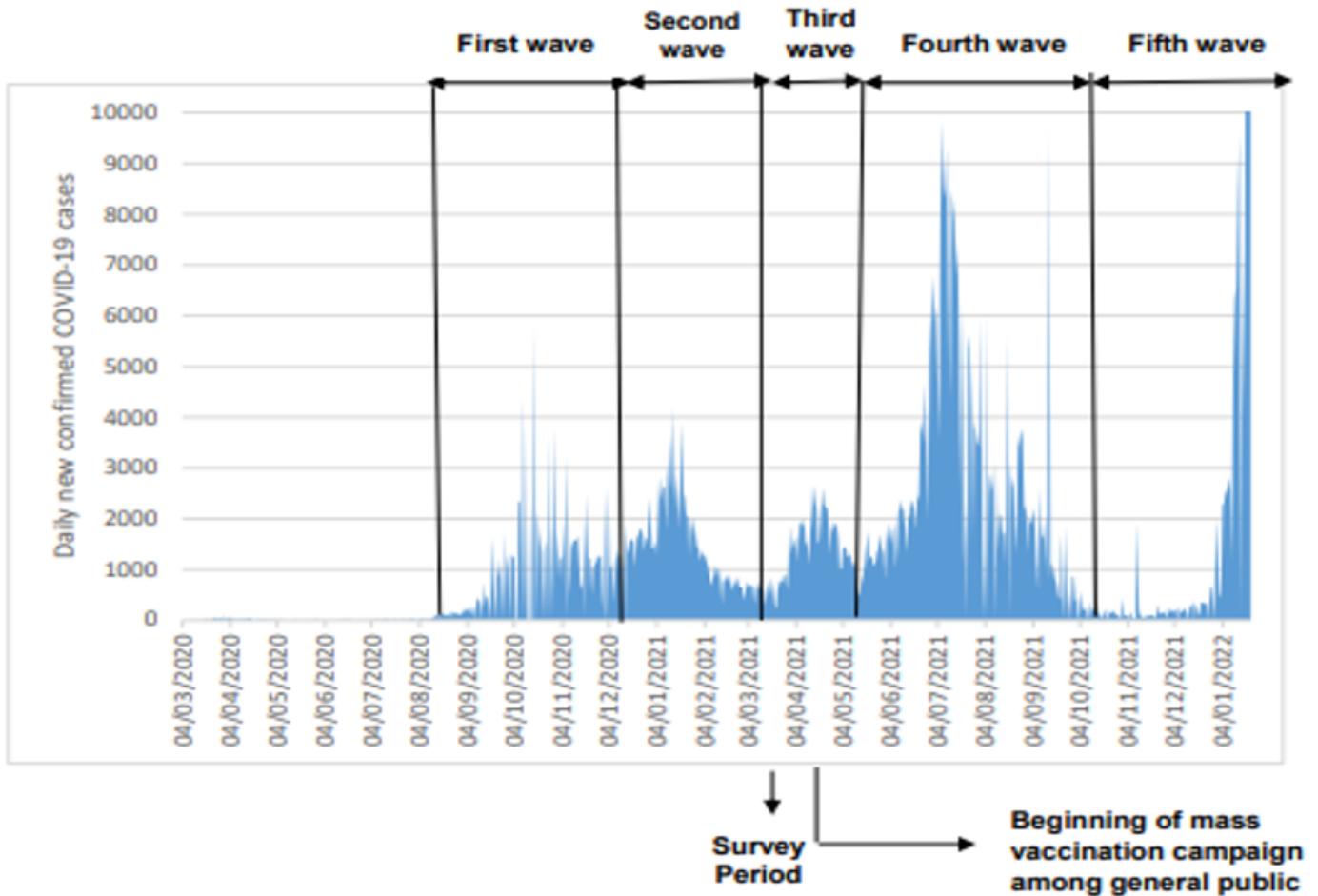
Figures

Figure 1

Epidemic curve COVID-19 cases in Tunisia expressed as daily new confirmed cases (Data source: [12])

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplementarymatvirology.docx