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A seroprevalence study of SARS-CoV-2 and seasonal coronaviruses after the first SARS-CoV-2 circulation in New Caledonia, Pacific region

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ABSTRACT

Objectives: This study aimed to determine the seroprevalence of immunoglobulin G antibodies targeting SARS-CoV-2 and other human coronaviruses after the first circulation of SARS-CoV-2 in New Caledonia, Pacific region.

Methods: Blood samples were collected to detect the presence of SARS-CoV-2 immunoglobulin G antibodies. The sampling took place between July 2021 and July 2022 but was interrupted after the first circulation of SARS-CoV-2 (September 2021-March 2022) in New Caledonia. Data on ethnicity, age, gender, main residence, and anteriority of COVID-19 and vaccination were collected and analyzed.

Results: A total of 747 participants, representative of New Caledonia's adult population, were included in the study. We found that 81% of the population had antibody responses to SARS-CoV-2 at the end of July 2022. The vaccination rate was 75%, whereas infections had affected 40% of the population. Individuals aged >45 years were significantly more vaccinated than those aged 18-44 years (80%, 95% confidence interval 74-84%). Oceanians were the most infected (50%, 95% confidence interval 42-57%).

Conclusion: In New Caledonia, we show a high immunity rate (81%) after the first waves of SARS-CoV-2 circulation and the vaccination campaign. The analyses showed spatial heterogeneities in the infection rate across the territory and revealed that Oceanians were the most infected. Our study also highlighted high exposure of New Caledonia's population to other human coronaviruses.

Introduction

Serosurveys are epidemiological studies estimating population-level antibody prevalence. Seroprevalence studies initially provide information about transmission magnitude, allowing to forecast the future course of an outbreak [1]. With vaccination, it is now important to differentiate seropositivity due to past infection, past vaccination, or both to maximize the value of serosurveys, which may have implications for protection from future infection. Furthermore, stratifying seroprevalence by geography, age, ethnicity, and other variables can illuminate how different factors shaped an epidemic's trajectory and identify future public health priorities [2].

Since its emergence in December 2019, SARS-CoV-2, the causative agent of COVID-19, caused hundreds of millions of known infections worldwide [3]. In addition to SARS-CoV-2, humans are also susceptible to at least six other viruses of the *Coronaviridae* family. Among these, Severe Acute Respiratory Syndrome Coronavirus 1 (SARS-CoV-1) and Middle East respiratory syndrome coronavirus (MERS-CoV) are pathogenic

viruses associated with elevated morbidity and mortality rates [4]. In contrast, there are four endemic human coronaviruses (HCoVs) (NL63, 229E, HKU1, and OC43), which usually cause mild-to-moderate respiratory diseases with a seasonal pattern. Initial infection usually occurs in childhood and, virtually, everyone is expected to have some immunity to HCoVs by adolescence. However, immunity to HCoVs decreases over time; reinfections are, therefore, common throughout life [5].

The Pacific region has a very specific history of SARS-CoV-2 circulation. Indeed, most Pacific Island Territories implemented a strict border closure at the beginning of the pandemic. As a result, the region was impacted late by COVID-19 [6].

New Caledonia is a French overseas territory of 270,000 inhabitants located in the Pacific region, where 41.2% of the population self-declare as Melanesian, 24% as European, 8.3% as Polynesian, and 26.5% as belonging to other communities [7]. Melanesians represent 95% of the population in the Loyalty Islands Province, 72% in the North Province, and 29% in the South Province. In contrast, over 90% of the Europeans live in the South Province [7].

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New Caledonia enforced a “zero COVID-19 strategy” that resulted in nearly no circulation of SARS-CoV-2 until September 2021. Indeed, the first COVID-19 case was reported in March 2020, and the island entered a strict lockdown with rigorous border control and quarantine for new arrivals, placing the territory in a so-called sanitary airlock [8]. The lockdown consisted of the closure of all places of social life, a stay-at-home order for all persons not carrying out “essential work,” one outing for 1 hour per day authorized within a 1-km radius from home, and mandatory mask-wearing outside the home [8,9]. In March 2021, the detection of a new local COVID-19 case led to the implementation of another strict lockdown [9]. In both cases, the approach successfully eliminated SARS-CoV-2 circulation, and the territory was declared “COVID-19 free” with no particular control measures against COVID-19, except the sanitary airlock [10]. The first autochthonous cases of COVID-19 were, however, detected at the beginning of September 2021, with a first epidemic peak caused by the Delta variant, although a strict lockdown was implemented. The second and third epidemic peaks due to Omicron BA.1 and Omicron BA.4/5 followed at the beginning of 2022 and in July-August 2022, respectively. During these periods, all symptomatic persons were asked to test for SARS-CoV-2 infection. A total of almost 80,000 infections were diagnosed using either RT-PCR or antigenic tests, causing 314 deaths [10,11]. Vaccination rollout, involving almost exclusively the Pfizer BNT161b2 vaccine, was initiated in January 2021 (Figure 1). At the end of August 2021, 39% of the eligible population had received at least one vaccine dose [10]. As of December 31, 2021, 67% of the whole population received two doses and, as of 31 July 2022, 69% of the whole population received one dose, 66% received two doses, and 35% received a booster dose [11].

In the Pacific region, few serosurveys have been conducted; one in Fiji Islands showed 95% immunity at the end of 2021 [12] and one in French Polynesia highlighted that at the end of 2021, 56.8% of the population aged 18-69 years had been infected by SARS-CoV-2 [13]. In this study, we estimated the seroprevalence of SARS-CoV-2 in the adult population of New Caledonia after the circulation of Delta and Omicron variants and vaccination rollout. Furthermore, we also estimated the seroprevalence of HCoVs to establish the unknown exposure rate to these viruses in tropical areas, such as the Pacific region.

Methods

Study population

The current study is part of the 2021-2022 Adult Health Barometer, a cross-sectional descriptive survey on New Caledonia’s adult population, which follows the World Health Organization STEPwise approach. Sampling was carried out based on residential dwellings recorded as the main residence in the last 2019 census and using a three-stage stratified cluster sample design. At the first level, 228 districts were randomly selected throughout the entire territory of New Caledonia, with unequal probabilities, considering the size of the population living in these areas. At the second level, 5471 households were randomly selected proportionally to their size. Finally, at the third level, within each selected household, the choice of one individual (aged 18-64 years) to be surveyed was made through random sampling. This sample was designed to be representative of the distribution of the adult population (aged 18-64 years) by province and gender, as well as by age group in New Caledonia. For our seroprevalence study, a sub-sample of 1815 people was drawn from the 5471 individuals. Blood samples and questionnaire were collected. This sub-sample was drawn to be representative of New Caledonia adult population by gender only. Because of SARS-CoV-2 circulation [11], data and blood collection took place in two phases from July 20 to September 6, 2021 and from March 7 to July 31, 2022 (Figure 1).

Multiplexed coronaviruses immunoassay

We used multiplex microspheres immunoassay to detect immunoglobulin G antibodies against SARS-CoV-2 and HCoVs. This 9-plex assay allows the simultaneous detection of antibodies to five SARS-CoV-2 antigens (whole trimeric spike [S], its receptor-binding domain, S subunit 2, nucleocapsid protein [N], and a membrane-envelope fusion protein) and the four HCoV-NL63, HCoV-229E, HCoV-HKU1, and HCoV-OC43 seasonal coronaviruses (S proteins) in 1 µl serum or plasma samples, allowing the identification of individuals infected with SARS-CoV-2 with 98.8% (95% confidence interval [CI] 96.5-99.6) sensitivity and 99.3% (95% CI 97.6-99.8) specificity [14]. No cross-reactivity between

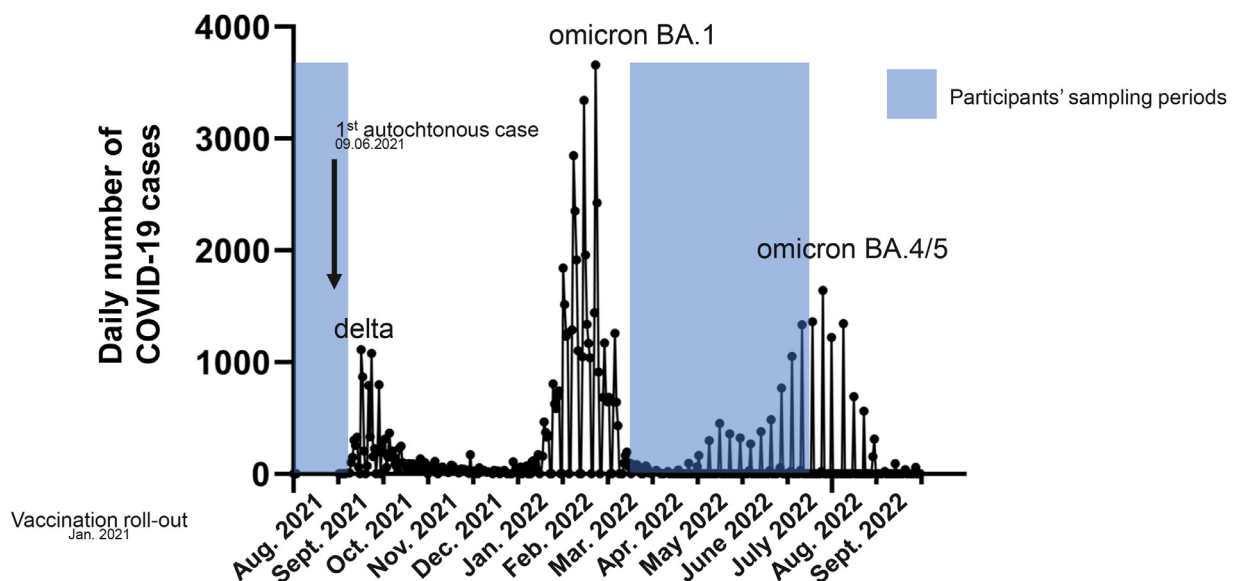


Figure 1. Participants’ sampling periods according to COVID-19 epidemiology in New Caledonia between August 2021 and September 2022. Daily number of COVID-19 cases are represented for the period between August 2021 and September 2022. The Delta, Omicron BA.1, and Omicron BA.4/5 epidemic peaks are shown. Participants were enrolled in the study and sampled from July 20 to September 6, 2021 and from March 7 to July 31, 2022 (blue-shaded periods).

Table 1
Participants characteristics and representativity according to the general adult population of New Caledonia.

		Sample size (n = 747)	% unweighted	% weighted	% in the general population ^a
Sex	Male	315	42,1	50,5	49,9
	Female	432	57,9	49,5	50,1
Provinces	North + Loyalty Islands	402	53,6	21,7	24,7
	South	345	46,4	78,3	75,3
Age	18-44	388	51,8	53,1	62,1
	45-64	359	48,2	46,9	37,9
Communities	Oceanians	391	52,1	42,2	52,4
	Other Communities	356	47,9	57,8	47,6

^a According to data from Institute of Statistics and Economic Studies of New Caledonia, 2019 census [7].

seasonal coronaviruses and SARS-CoV-2 infection was detected with the 9-plex assay [14]. Median fluorescence intensity was measured using a Luminex MagPix system. A 5-parameter logistic curve was used to convert median fluorescence intensity to antibody units, relative to the standard curve performed on the same plate to account for inter-assay variation. People are defined as vaccinated if they are anti-S–positive (regardless of their anti-N sero-status) or defined as infected if they are anti-N–positive (regardless of their anti-S sero-status). People are listed as having immunity if they are anti-S–positive or anti-N–positive. An individual that is anti-S seropositive and anti-N seropositive could have been infected or infected and vaccinated. With our serological assays, it was not possible to differentiate between these two possibilities.

Statistical analysis

All results presented were weighted, considering the survey design, and then adjusted for the population's gender distribution based on the 2019 census data. Therefore, the final weights were calculated for the participants based on the initial weights (from the sampling), the results of the data collection, and the known characteristics of the population. Margin calibration is the method used to obtain the final weights (i.e. an iterative process that matches the extrapolated sample to the population given characteristics) with the “icarus” package from R studio (R 4.2.1) software.

The seroprevalence of each virus was calculated as the weighted proportion of participants with detectable antibodies against the virus tested.

To carry out statistical analyses on comparable numbers, we divided our sample set into two age groups (18-44 and 45-64 years), two localizations (the North and Loyalty Islands Province vs the South Province), and two communities: the Oceanians (Melanesians and Polynesians) and the others (Europeans, Asians, etc.). We used the “Survey” package in R studio (R 4.2.1) software to calculate the proportion of SARS-CoV-2 vaccinated, infected, and immune population. Proportions were compared using the Pearson chi-square statistical test of independence for weighted data, applying the second-order Rao–Scott correction. Finally, we carried out multivariate analyses using a logistic regression model to identify the predominant factors influencing infections. A $P < 0.05$ was considered statistically significant. The 95% CIs were calculated using the Wald method.

Results

Participation

Of the 1815 selected volunteers, 750 were included, resulting in a participation rate of 41.3%. Of the 750, 747 samples were available for the SARS-CoV-2 serosurvey and 679 for other studies on infectious diseases in New Caledonia, including HCoV. A total of 78 participants were sampled before September 6, 2021 (beginning of SARS-CoV-2 circulation in New Caledonia) and the 669 remaining between March and July 2022. Our cohort was composed of individuals aged 18-64 years, 49.5%

of whom were women (Table 1). Of the 747 participants, the weighted repartition was as follows: 78% in the South Province, 16% in the North Province, and 6% in the Loyalty Islands Province. Of those, 42% self-declared as Oceanians (Melanesian and Polynesian) and 58% belonged to other communities (mostly European, Metis, and Asian) or preferred not to answer.

SARS-CoV-2 seroprevalence in New Caledonia

The detection of anti-S and anti-N antibodies and statistical analyses of weighted data showed that 81% (95% CI 76-85%) of the population was immune to SARS-CoV-2 at the end of July 2022. The vaccination rate (with 305 anti-S–positive and 270 anti-N– and anti-S–positive) was 75% (95% CI 71-80%). Previous infection (with 49 anti-N–positive and 270 anti-N– and anti-S–positive) was detected in 40% (95% CI 34-45%) of the population. No significant difference in the vaccination, infection, or immune status was observed according to gender (Table 2). Individuals aged >45 years were significantly more vaccinated than those aged 18-44 years (80%, 95% CI 74-84% vs 72%, 95% CI 65-78%) respectively. No difference in the infection and immunization rates were observed between the two age groups (Table 2). Interestingly, of the 78 volunteers sampled, before September 6, 2021, four had anti-N antibodies, indicating a recent COVID-19 infection.

Furthermore, there were significantly less infected people in the South Province, with 37% (95% CI 30-44%) participants who were previously infected in the South Province versus 49% (95% CI 44-55%) in the North or Loyalty Islands provinces. Immune and vaccinated status were similar between provinces. Interestingly, Oceanians were the most infected 50%, (95% CI 42-57%) vs 32% (95% CI 26-39%) among the other communities. There was no significant difference in the vaccination or global immune rate between Oceanians and all other communities (Table 2). A multivariate logistic regression model showed that Oceanians were significantly more infected independent of gender, age, and home province (OR 1.95, 95% CI 1.26-3.03, $P = 0.003$). Finally, the analysis of the questionnaire (Table 3) shows that of those questioned, 75% reported vaccination and 28% reported a recent SARS-CoV-2 infection mostly based on symptoms.

Human coronaviruses seroprevalence in New Caledonia

Of the 747 samples, 679 were tested for the presence of anti-HCoV antibodies. All the individuals had already encountered HCoV-229E and HCoV-OC43. HCoV HKU-1 and NL63 circulated slightly less frequently, with 91% (95% CI 88-94%) and 81% (95% CI 77-85%) of the population being positive, respectively. No significant differences were observed according to the province, gender, or age groups. Conversely, Oceanians were significantly less exposed ($P = 0.027$) to NL63 (76%, 95% CI 68-83%) than the other communities (85%, 95% CI 80-88%).

Discussion

The current serosurvey targeting SARS-CoV-2 and seasonal HCoVs was conducted in a representative sample of the New Caledonian adult

Table 2

Distribution of anti-SARS-CoV-2 antibodies according to the different status (vaccinated, infected, immune) and class (sex, community, age, and localization).

	Vaccinated (anti-S seropositive)		Infected (anti-N seropositive)		Immune ^c (anti-S or anti-N seropositive)	
	% weighted (Obs) ^a	95% CI	% weighted (Obs) ^a	95% CI	% weighted (Obs) ^a	95% CI
Gender						
Women (n = 433)	75% (341)	69-80	41% (199)	35-48	81% (369)	75-85
Men (n = 314)	76% (234)	69-82	38% (119)	31-46	82% (254)	75-87
P-value ^b	0.9	-	0.5	-	0.8	-
Provinces						
North + Islands (n = 400)	76% (314)	70-82	49% (197)	44-55	84% (344)	79-88
South (n = 347)	75% (261)	69-80	37% (121)	30-44	81% (279)	74-86
P-value ^b	0.8	-	0.007	-	0.4	-
Age						
18-44 (n = 387)	72% (287)	65-79	43% (165)	36-50	80% (317)	72-85
45-64 (n = 360)	80% (288)	74-84	36% (153)	29-44	83% (306)	78-88
P-value ^b	0.039	-	0.2	-	0.4	-
Communities						
Oceanians (n = 389)	70% (290)	63-77	50% (202)	42-57	79% (323)	71-85
Others communities (n = 358)	79% (286)	73-84	32% (115)	26-39	83% (301)	76-87
P-value ^b	0.054	-	< 0.001	-	0.5	-
Overall (n = 747)	75% (575)	71-80	40% (318)	34-45	81% (623)	76-85

CI, confidence interval.

^a Obs: observation = n (unweighted)^b Chi-square test with Rao & Scott's second-order correction^c Immune status refers to someone that was infected (anti-nucleocapsid immunoglobulin G-positive) and/or vaccinated (anti-spike immunoglobulin G-positive).**Table 3**

Questions and answers of the questionnaires regarding SARS-CoV-2 vaccination or recent infection and correlation with antibody detection.

	Answer (%) ^b	Number of positive serology ^a
Infection question	Yes: 193 (28%)	127
	No: 554 (72%)	190
Vaccination question	Yes: 574 (75%)	524
	No ^c : 173 (25%)	52

Two questions regarding COVID-19 were asked to the volunteers: (1) Do you think you got COVID-19? (2) Are you vaccinated against COVID-19?

^a A positive serology is either anti-nucleocapsid and/or anti-spike immunoglobulin G.^b Percentage presented are weighted.^c No means here no or do not want to answer.

(18-64 years) population after the first waves of SARS-CoV-2 circulation (September 2021-March 2022) [10,11]. Participation in this study was moderate but in-line with other similar studies.

The Pacific region has a very specific history of SARS-CoV-2 circulation. Indeed, most territories implemented a strict border closure at the beginning of the pandemic. As a result, the region was more recently impacted by COVID-19. A serosurvey conducted in Fiji Islands at the end of 2021 showed 95% immunity [12]. Similarly, in New Caledonia, we show a high immunity rate (81%) after the first waves of COVID-19 circulation and vaccination campaign. Furthermore, a recent study in French Polynesia on 1120 participants highlighted a weighted SARS-CoV-2 seroprevalence of 56.8% for the population aged 18-69 years at the end of December 2021. The seroprevalence increased from 21.9% to 62.1% before and during/after the Delta wave. Of these infections, only 28.4% had been diagnosed by health care professionals [13]. We also show that at the end of July 2022, the vaccination rate was 75%, which is concordant with the data from the health authorities (69% of the whole population) [11]. We also found that the older age group (>45 years) was more often vaccinated, possibly owing to the fact that this age group is considered to be more at risk of developing severe forms of the disease and was, therefore, the most targeted and the most receptive to vaccination campaigns. Finally, according to the interviews, although 574 of the 747 participants declared anti-COVID-19 vaccination, only

524 of them had anti-S antibodies, possibly owing to false declaration; however, we cannot rule out low vaccination response owing to incomplete vaccination scheme or other factors.

We detected recent SARS-CoV-2 infection in 40% of the adult population of New Caledonia in March-July 2022. Interestingly, according to the interviews, only 28% declared a recent infection (mostly based on symptoms). The North and the Loyalty Islands provinces and the Oceanian community were more affected by COVID-19. These two provinces are home to most of the Oceanian population who have a more traditional lifestyle, which may have favored, along with other social determinants, the circulation of the virus, as shown in other studies focusing on different ethnicities [15]. Furthermore, our serosurvey highlighted that four of 78 individuals sampled before the September 06, 2021 showed traces of recent infection. This could be owing to returning travelers previously exposed overseas or undetected SARS-CoV-2 circulation.

To the best of our knowledge, the seroprevalence of HCoVs has never been evaluated in the Pacific region so far. Our results emphasize the high circulation of these viruses in New Caledonia, as in other countries [5,16]. No specific differences were noted according to gender, age, and localization. NL63 was significantly less prevalent in Oceanians, although the seroprevalence was higher than 80%. These data are still in favor of a high circulation of this HCoV in this community.

Our study had some limitations. First, by focusing on the adult population, we could not include individuals aged under 18 years who have a role in COVID-19 transmission [17] and older individuals (65 years and older) who are considered as a population at risk of severe COVID-19. Older individuals account for 10% of the population, according to the last population census [7]. It is likely that the absence of representation of these older people may have led us to, at least, underestimate the vaccination rate because the vaccination coverage was more than 95% in this group [11]. Second, owing to study design, the statistical analyses were limited to groups of similar sizes. It would have been interesting to deepen our analyses according to communities and localization. Third, to ensure that everyone living in New Caledonia had the same probability of being drawn, households with a large number of people aged 18-64 years had a higher probability of being drawn. Because SARS-CoV-2 transmission is more likely in these larger households, the COVID-19 infection rate may have been overestimated in our study. Finally, with our

serological assay, it was not possible to distinguish between individuals who have been infected and individuals who had been infected and vaccinated. Because some individuals who were anti-S–positive may have received immunity through natural infection rather than vaccination, this may result in an overestimate of the vaccine coverage.

Overall, this study can inform the public health authorities about the level of SARS-CoV-2 immunity of the population of New Caledonia in July 2022. However, the duration of protection provided by hybrid immunity has not yet been determined. This immunity might wane in the absence of stimulation and might vary across age groups and/or individuals. As new SARS-CoV-2 variants emerge, prioritizing the use of COVID-19 vaccines will be helpful to achieve very high vaccination coverage rates in groups who are at risk of severe forms of the disease.

Declarations of competing interest

The authors have no competing interests to declare.

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Ethical approval

This study was approved by the “Comité de Protection des Personnes Ouest IV” (21.05.16.92458-avis_50_21_2 and avis_50-21_2MS1) and by the Consultative Ethics Committee of New Caledonia (Avis 2021-03 002). The study was recorded on *Clinicaltrials.gov* (ID: NCT05218304).

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Author contributions

CI, EM, PDM, and MDR conceived the study. PDM and MDR led the applications for funding. EM, AFG, and KH collected data. KH and EB

performed the experimentations. KH, MW, and MDR interpreted the data. KH, GB, EM, and MW implemented the statistical analyses. KH and MDR drafted the manuscript. All authors reviewed the manuscript and approved the final version before submission.

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