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Coronavirus Pandemic

Geographic heterogeneity of SARS-CoV-2 circulation in Abidjan, Ivory Coast: a prospective study

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Abstract

Introduction: Few studies on SARS-CoV-2 seroprevalence in Ivory Coast have been conducted since the first case was reported on March 11, 2020. The main objective of this study was to observe and better understand the circulation of SARS-CoV-2 in Abidjan.
Methodology: This prospective study collected data concerning age, sex, vaccination status, municipality of origin, monthly income, frequency of malaria, and frequency of diarrheal diseases in persons who gave their informed consent. Venous blood samples were taken to test for anti-SARS-COV-2 antibodies (IgM and IgG) using the VIDAS automated system.
Results: A total of 1504 patients were recruited and tested for antibodies directed against SARS-COV-2. Data analysis revealed the presence of anti-SARS-CoV-2 in 53.5% of participants, 17.3% of the participants had a previous symptomatic infection, 31.4% had an asymptomatic infection, and 44.8% were never in contact with the virus. Seroprevalence of SARS-CoV-2 was higher in Marcory (70.9%) and Cocody (61.1%) than in the remaining townships (48.4%). Township rates of serologically confirmed SARS-CoV-2 infection correlated with poverty index ($p = 0.025$), children < 5 years' proportion in the township ($p = 0.026$), and levels of malaria ($p = 0.034$).
Conclusions: In the city of Abidjan, COVID-19 is strongly modulated by poverty, the proportion of babies and toddlers in the community, or exposure to malaria.

Key words: Geographic heterogeneity; SARS-CoV-2; Abidjan.

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Introduction

SARS-CoV-2 was first detected in December 2019 in Wuhan, China. Since March 15, 2021, more than 120.5 million confirmed cases with 2.6 million deaths were reported worldwide [1]. However, the gap between mortality observed in Africa (3.49%) and that observed in Asia (< 2%), America (4.57% north America; 3.87% south America), and Europe (3.74%) remains unexplained [2]. While several seroprevalence studies have given preliminary results in some African countries such as Zambia, Nigeria, Kenya, Ethiopia and Malawi [3-7] this was not yet the case in Ivory Coast where the first patient was reported on March 11, 2020, in the city of Abidjan the economic capital of Ivory Coast [8]. The population density in Abidjan is 3 times higher than anywhere else in the country according to the results of the General Population and Housing Census (RGPH) 2022 [9]. As of March 31, 2022, Ivory Coast had 81,741 confirmed cases, including 80,913 cured cases, 796 deaths and 23 active cases. The total number of samples collected was 1,471,872. On March 30, 127,548 doses of vaccine were administered, for a total of 11,742,302 doses from March 1, 2021 to March 30, 2022 [10]. During the period of study, the COVID-19 vaccines administered in Ivory Coast were coming from three different sources, AstraZeneca (Covishield), Pfizer (Comirnaty) and Sinopharm (BIBP-CorV) [11]. In February 2021, the different townships of Abidjan and its suburbs experienced different rates of confirmed COVID-19 cases ranging from Treichville-Marcory, 1915 cases per 100,000 residents to Adjamé with 300 cases per 100,000 residents [10]. To date, there is little data on the extent of the spread of COVID-19 in Abidjan and the immune status of the population after the various outbreaks and vaccination campaigns. The main objective of this study conducted on 1504 participants was to determine the levels of exposure to SARS-CoV-2 within the different townships of Abidjan and to relate them with demographic, socioeconomic, or epidemiological parameters.

Methodology

Definitions

Apparent COVID-19 was defined as a positivity for SARS-CoV-2 antibodies together with any of its known clinical manifestations, i.e., flu syndrome, fever, headache, anorexia, anosmia, ageusia, cough, nasal discharge, myalgia, shortness of breath. By contrast, inapparent COVID-19 was defined as a seropositive status without clinical manifestations at anamnesis.

Study design, patients' recruitment and data collection

This was a prospective study that enrolled 1504 participants who came to the Pasteur Institute of Ivory Coast for any other laboratory tests and who gave their informed consent from April 2021 to July 2022. The data of interest (age, sex, vaccination status, municipality of origin) were collected using a structured questionnaire. For the minors, the same questionnaire was administered, and the answers were collected from the parents and or the guardian present.

Blood samples were taken on EDTA at the bend of the elbow under rigorous aseptic conditions in both children and adults. Antibodies directed against SARS-COV-2 were detected by the VIDAS SARS-COV-2 with the VIDAS automaton (bioMérieux, Marcy-L'Etoile, France).

In addition, to get more insights about the serological variations of SARS-CoV-2 prevalence, we decided to correlate the data collected in this survey about the different townships with relevant previously published data (2012-2015). These data were pertaining to population density, percentage of the population < 5 years or > 50 years, index of poverty, modes of public transportation, healthcare facilities (health centers, maternal care facilities, Traditional medicine center), and mean prevalence of malaria and diarrheal diseases (Table 1) [12-16].

Ethical approval

The study was conducted in accordance with international ethical regulations for biomedical research involving human subjects [17]. Information and consent forms were read, approved, and signed by each study participant. It received approval from the National Ethics Committee for Health and Life Sciences (Ref no. 173-21/MSHP/CNESVS-kp).

Statistical analysis

Data entry and analysis were done using Excel software. They were performed using a Prism 8.0.2 statistical package (GraphPad, USA) and in case of very small p values ($p < 1.0\ E\text{-}04$) with the BiostaTGV online software (https://biostatgv.sentiweb.fr/?module=tests) to improve the appraisal of significance magnitude. Numerical variables comparisons between two groups were performed either by a Student's t-test or by a Mann-Whitney U test as appropriate. Categorical variables were summarized as frequencies that were compared by Fisher's exact test when two groups were compared or by the chi-squared test in the presence of more than two groups. Pearson's and Spearman's coefficients and corresponding p-values were calculated. The level of significance was set at $p < 0.05$.

Results

Patient socio-demographic data

A total of 1504 participants living in Abidjan and its suburbs have been enrolled in the survey. The general features of the population studied are summarized in Table 1. The median age of the population was 43.5 years i.e., much older than the age of the general population in Ivory Coast (median: 20.9 years, see Figure 1A). The M: F sex ratio was well balanced (0.94) and not significantly different from the one of the general population (M:F = 1.037). The place of habitation was known for 1392 persons. Most of them (n = 1341, 96.3%) came from the Greater Abidjan district (94.9%) or an immediately neighboring city (Grand-Bassam, 1.4%). The remaining (3.3%) was coming from more distant districts in Ivory Coast (Table 2).

Table 1. Features compared with Clinical and Biological outcomes of the COVID-19 survey conducted in 2021.

Features	Category
Population density (Hab/Km^2), 2015	Demographic
Percentage of habitants < 5 years (%), 2013	Demographic
Percentage of habitants > 50 years (%), 2013	Demographic
Number of habitants/Any Public transportation Station, 2015	Economic
Number of habitants/Bus Station, 2015	Economic
Number of habitants/Small Bus (Gbaka) station, 2015	Economic
Number of habitants/Collective taxi (Woro Woro) station, 2015	Economic
Poverty index (%), 2014	Economic
Number of habitants/Health center, 2012	Health
Number of habitants/Maternal Health Facility, 2014	Health
Number of Habitants/Traditional Medicine center, 2012	Health
Mean Prevalence of Diarrheal Diseases (%), 2014	Health
Mean Prevalence of Malaria (%), 2014	Health

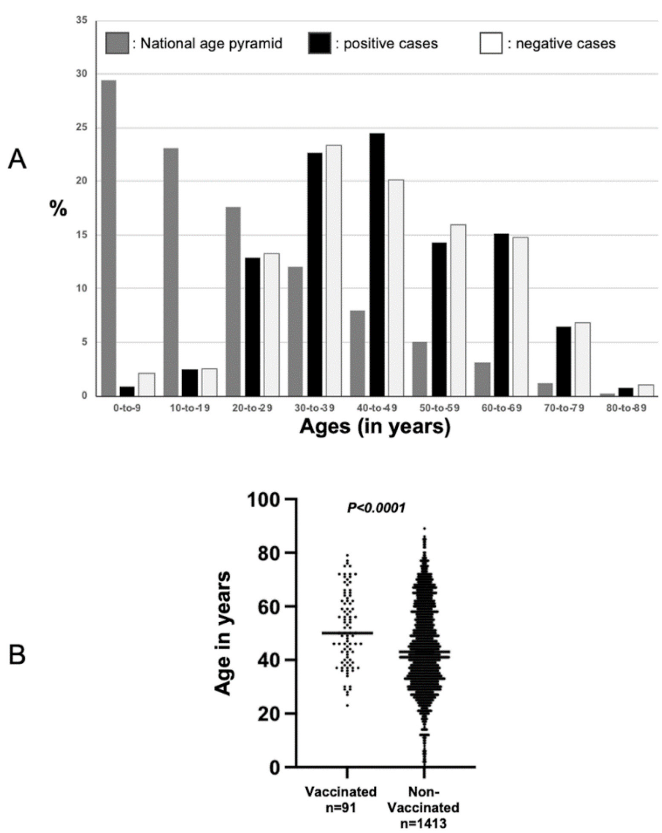
Self-reported symptoms

The 91 subjects (6.0%) who received the vaccine were significantly older than the rest of the participants (median, 50.0 years vs 43.0 years, $p < 0.0001$, Figure 1B). During the interview, 277 participants (18.4%) indicated having been previously affected by COVID-19. A vast majority (n = 1147, 76.2%) of the participants did not recall having suffered from any symptoms related to COVID-19 during this initial phase of the pandemic.

Serological data

We investigated immunity against SARS-CoV-2. Serological tests revealed the presence of IgM in 6.5% of cases while IgGs were found in 52.0% of cases for an aggregate proportion of 53.5%. Based on the serology, and considering only unvaccinated participants, 48.7% of them have been in contact with SARS-CoV-2. It includes 17.3% of seropositive participants who recovered from COVID-19 and 31.4% of the participants who had an asymptomatic infection. Finally, a large subset of participants (44.8%) was composed of the persons who, according to their serology, were either never in contact with the virus or did not keep a serological scar of a previous contact (Table 2 and Figure 2A).

Figure 1. A. Comparison of age distribution of the participants to the present survey with the age pyramid in Ivory Coast; **B.** Comparison of the age of Vaccinated and non-vaccinated participants to the survey.



According to the serological test 19 (20.8%) of the 91 persons who received the vaccine did not develop any antibodies against SARS-CoV-2 or develop only a weak and transient response to viral antigens. These possibly anergic patients tended to be younger (median, 46 vs 52 years) and more often women (68.4% vs 44.4, $p = 0.0752$) albeit none of these comparisons reached the level of significance.

Correlation between clinical and socio-demographic situation and serology

Concerning other clinical correlations, serologically positive individuals who developed symptomatic COVID-19 were similar in age to those who did not have symptoms (median, 45.0 vs 43.0 years, ns). Concerning the differences between sexes, among the seropositive participants, women were more

Table 2. Demographical, clinical and serological features of the participants.

Features	
Age (in years)	
Mean ± SD	45.01 ± 16.23
Median (IQR)	43.5 (33-58)
Sex (n, %)	
Females	775 (51.5)
Males	729 (48.5)
Anamnesis (n, %)	
Previously affected by the COVID-19	277 (18.4)
Received vaccine	91 (6.0)
Immune Status (n, %)	
IgM (+)	98 (6.5)
IgG (+)	783 (52.0)
overall	805 (53.5)
Clinical Status (n, %)	
Seropositive	
Recovered	260 (17.3)
Inapparent infection	473 (31.4)
Recovered and Vaccinated	11 (0.7)
Vaccinated only	61 (4.0)
Seronegative	
Inefficient vaccination	19 (1.2)
Infected without seroconversion	6 (0.3%)
Not infected	674 (44.8)
Townships (n,%)	
Cocody	427 (28.4)
Abobo	266 (17.6)
Yopougon	224 (14.9)
Marcory	86 (5.7)
Adjame	76 (5.0)
Koumassi	59 (3.9)
Port Bouët	59 (3.9)
Bingerville	48 (3.1)
Treichville	28 (1.9)
Attecoube	23 (1.5)
Plateau	11 (0.7)
Anyama	13 (0.8)
Grand-Bassam	21 (1.4)
Provincial Districts	51 (3.3)
ND	112 (7.4)

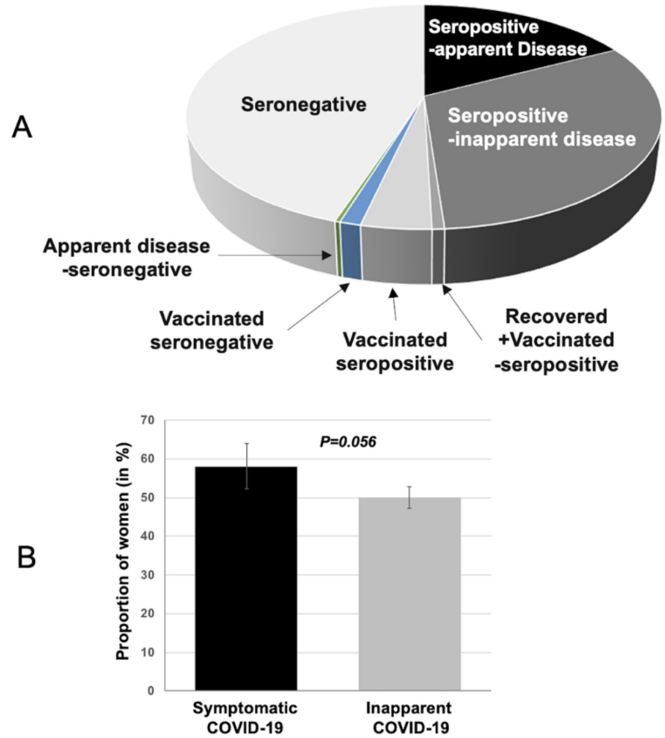
prevalent, albeit non-significantly, in the group with symptomatic forms of COVID-19 than in the group with asymptomatic disease (58.3% vs 50.9%, *p = 0.056,* OR = 1.34, 95% CI = 0.99-1.81, Figure 2B). This gender imbalance was, however, not observed at the serological level as the proportion of women was 51.2% in seropositive subjects and 53.6% in seronegative ones (*p = 0.36*).

We next examined the distribution of serological features between the different places of habitation within and around Abidjan. We observed that two townships of Abidjan displayed significantly higher rates of previous symptomatic COVID-19. It was Marcory (48.8%, *p = 3.04E-11*, OR = 4.79, 95% CI: 2.99-7.67) and Cocody (30.4%, *p = 3.76E-13*, OR = 2.76 95% CI: 2.09-3.65) while seropositivity rate was much lower in the other townships of the city taken all together (10.7%) (Figure 3A). Accordingly, the seroprevalence of anti-SARS-CoV-2 Ig was much higher in Marcory (70.9%, OR = 2.20, 95% CI: 1.34-3.71) and Cocody (61.1%, *p = 1.94E-04*, OR = 1.54, 95% CI: 1.21-1.94) than in the remaining townships (48.4%) (Figure 3B). By contrast the township of Abobo in the North of the Ivorian capital city was the area where participants in the survey presented the lowest seroprevalence of anti-SARS-CoV-2 Ig (44.8% vs 58.6%, *p = 6.46 E-7*, OR = 0.51, 95% CI: 0.39-0.68) (Figure 3C).

We next wondered whether these striking geographical differences could overlap with explanatory parameters linked to demography, socio-economic condition, or epidemiology. We decided to focus on population density, health structures, and public transportation facilities as these kinds of infrastructures participate either in the control or the spread of COVID-19. We added the data concerning malaria and diarrheal diseases that are regularly monitored in Abidjan (Table 1) [18].

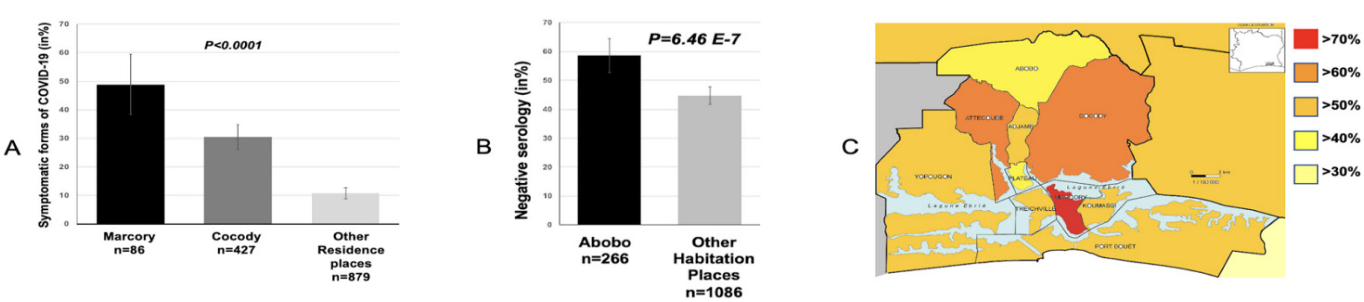
Among the different features examined only poverty index, population below 5 years, and levels of malaria or diarrhea were correlated either positively or negatively with clinical and or serological parameters.

Figure 2. A. Distribution of the different categories of participants according to serology, clinics, and vaccination; **B.** Proportions of women in the symptomatic/apparent and asymptomatic/inapparent forms of SARS-CoV-2 infections.



For a given township, the percentage of participants who declared a symptomatic form of COVID-19 together with a positive serological test (*bona fide* COVID-19) was in inverse correlation with the poverty index, the percentage of habitants below 5 years, or the rates of Malaria or diarrhea (Figure 4 A-E). By contrast, inapparent forms of the disease (seropositivity but absence of symptoms at anamnesis) were positively correlated with the same series of features (Figures 4 F-J).

Figure 3. A. Proportions of symptomatic/apparent forms of COVID-19 according to the township of origin; **B.** Proportion of participants with a negative serology in Abobo and other townships; **C.** Map of the different townships of Abidjan with their respective seroprevalence for SARS-CoV-2.



Discussion

An overall seroprevalence of 53.5% in a general population attending care at the hospital was observed in our study, a value much higher than the seroprevalence obtained in Gabon and the Democratic Republic of Congo about 17.2% and 16.6% respectively [19,20]. The higher seroprevalence observed in our survey was plausibly due to a bias of recruitment. All patients tested in our study were seeking care and thus mechanically more at risk of being contaminated by SARS-CoV-2. Alternatively, it might be due to climatic or demographic differences with Gabon being a country with a low-density of human population.

The 2021 IgG seroprevalence of 52% in Abidjan was nevertheless higher than the range of 5% to 40% found in three East-African countries (Malawi, South Africa, and Congo albeit in three studies conducted one year earlier at the very onset of the pandemic [7,21,22].

The distance from the onset of the epidemics (March 2020 in Ivory Coast vs April 2020 in Congo) from the survey could not explain the difference between studies that were conducted almost simultaneously (April 2021 in Ivory Coast vs May 2021 in Congo)

In our study, 17.3% of the participants indicated having been previously affected by a clinically apparent form of COVID-19, a rate much lower than the 32% of symptomatic patients in a study conducted in similar settings but much earlier in the pandemic (March to August 2020) on 3464 patients in Gabon By contrast, it was higher than observations made in the Kenyan population exposed to SARS-CoV-2 (5.6% for Kenya, 8% for Mombasa, and 7.3% for Nairobi) Multiple explanations to such difference could be proposed such as social clustering [23], changing adherence to measures over time [24], seasonal effects on transmission [25], reopening of places of learning [26] but more importantly, the distance from the onset of the pandemics (3 months in Kenya, 12 months in Ivory Coast).

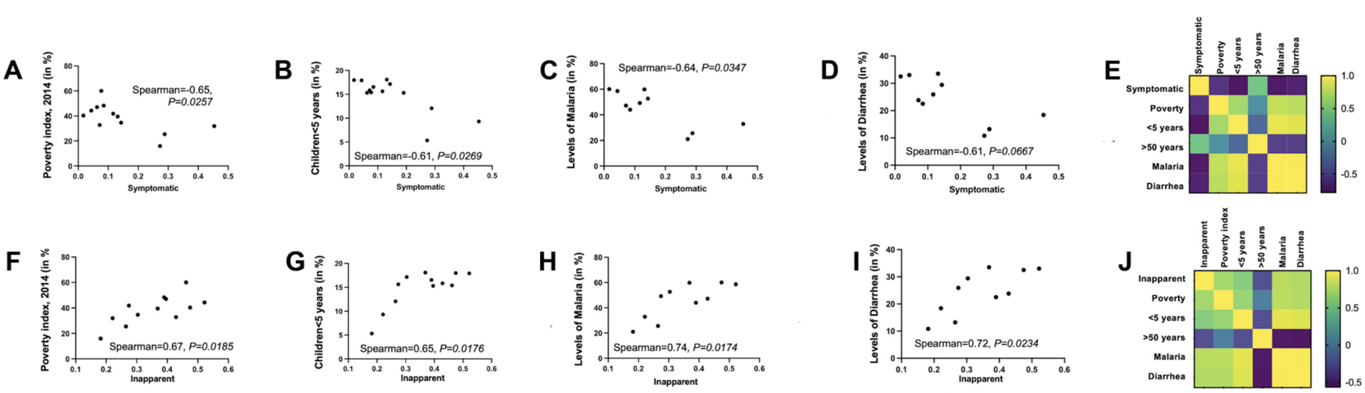
Only six persons who recalled having previously developed the disease did not develop any antibodies (n = 6/277, 2.1%). This could be explained by a genuine loss of immunity as already described on several occasions [27,28]. Another equally plausible explanation would be that these six participants did not develop COVID-19 but another respiratory infection.

In the current survey, 31.4% made an inapparent infection (n = 473). This rate was lower than the 64.2% of seropositive individuals who reported no symptoms in Cameroon [29]. The rate of asymptomatic COVID-19 observed in Abidjan was slightly above the threshold established in a meta-analysis conducted by D. Buitrago-Garcia *et al.* that reported rates ranging from 17.0 to 30% [30]. Symptomatic cases were often under-reported or misclassified as described by Angela *et al.* [31].

In our series, women (58%) were slightly more often clinically affected by the virus than men (50%). This observation was like that of Ogochukwu *et al.* in Anambra state, Nigeria [32]. This female predominance in symptomatic cases could be explained by the usually higher anxiety of women that prompts them to seek care more often than men in the presence of an unpredictable threat [33].

In our study, the townships of Marcory and Cocody were those with the highest seroprevalence with respectively 70.9% and 30.4% of positive participants. The high socio-economic standards of the habitants of

Figure 4. A-D. Correlation curves of different economic (Poverty index, 2014), demographic (Proportion of children < 5 years old), and health (levels of malaria, or diarrheic diseases) variables according to the rate of symptomatic/apparent Sars-Cov-2 infection; **E.** Correlation matrix of these same parameters in participants who underwent a symptomatic infection by SARS-CoV-2; **F-I.** Correlation curves according to the same parameters according to the rate of asymptomatic/inapparent SARS-CoV-2 infection; **J.** Correlation matrix of these same parameters in participants who underwent an asymptomatic/inapparent infection by SARS-CoV-2.



these townships with the frequent necessity to travel could explain the high prevalence as air transport has been one of the fastest means of COVID-19 propagation, especially from Europe to Africa despite the closure of the airports as in other countries of the world [34]. By contrast, a lower seroprevalence of anti-SARS-CoV-2 Ig was observed for habitants in the most populated neighborhood of Abobo. This observation was counter-intuitive, as worldwide, poor people are more exposed to COVID-19 [35]. We hypothesized that the lockdown of poorer areas of Abidjan was stringently enforced preventing the circulation of the SARS-CoV-2. Investigations conducted on other continents suggested that poorer districts are more severely hit by COVID-19 [36]. Our data did not corroborate this view but provided rather a more balanced vision of the social impact of COVID-19. Indeed, in Abidjan, clinically apparent forms of COVID-19 tended to concern richer townships while asymptomatic forms seem to prevail in poorer areas. The rate of asymptomatic seropositive patients was positively correlated with the poverty index of townships. Such purely economic consideration had to be mitigated in Abidjan by the fact the proportion of < 5 years old is higher in townships with low socio-economic standards than in more affluent neighborhoods. Our observation is in keeping with the usual mildness of symptoms in children, adolescents, or young adults infected with SARS-CoV-2 [37]. However, as the age of participants in our survey was not significantly different between townships, we hypothesized that habitants of more affluent townships were more worried than dwellers of poorer neighborhoods by symptoms of respiratory diseases, or that the disease burden suffered by residents of wealthy neighborhoods being less than that of residents of poor neighborhoods, they could focus on COVID-19. In contrast, habitants from poor townships kept coming to our hospital to seek treatment for a more extensive diversity of diseases.

Our observation that the rate of symptomatic COVID-19 in each geographic location was in inverse correlation with the proportion of children in a given population was in keeping with the literature [38]. In a recent analysis of 47 countries from sub-Saharan Africa, we observed that the national proportion of the population below 15 years was in inverse correlation with the mortality from COVID-19 (Spearman r = -0.603*, p = 4.3 E-06)* [39].

Finally, we observed that symptomatic COVID-19 was inversely correlated with the level of malaria or diarrheal diseases while on the contrary inapparent COVID-19 was positively linked to the level of Plasmodium infestation and diarrhea. Several authors have suggested that malaria might confer some degree of protection against COVID-19 [40-42]. The elements underlying this hypothesis were concerning a putative cross-immunity between Plasmodium and SARS-CoV-2 or the antiviral activity of some anti-malarial drugs such as chloroquine. Young children were both non-immune to *Plasmodium* and thus more susceptible to developing a clinical form of malaria and intrinsically non-susceptible to the clinical forms of SARS-CoV-2 infections [43]. The proportion of < 5 years would be plausibly responsible for the contrasted picture of COVID-19 and pediatric diseases in Abidjan townships. To reinforce our hypothesis, we observed that the proportion of the population > 50 years was positively correlated with symptomatic COVID-19 in Abidjan townships *(p = 0.049).*

Our study presents, of course, some limitations. The first of them is that we did not have access to the vaccine type employed to immunize the patients because most of them did not know the brand name they had been given. In addition, they did not carry with them their vaccination card during interviews, and we cannot determine whether they followed the complete immunization procedure or not.

Conclusions

We observed that within the city of Abidjan and in its outskirts the seroprevalence of COVID-19 varied significantly from one township to another. The seroprevalence of SARS-CoV-2 was higher in the richest townships such as Cocody and Marcory while it was lower in the less affluent neighborhood. The most striking divergence between townships concerned however the clinical presentation of COVID-19. The disease was frequently symptomatic in more affluent townships where both the proportion of children below 5 years and clinical malaria are low while it took an inapparent form in poorer townships where both the proportion of children below 5 years and malaria were high.

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