SUSCEPTIBILITY TO SARS-COV-2 INFECTION AMONG CHILDREN AND ADULTS: A SEROPREVALENCE STUDY OF FAMILY HOUSEHOLDS IN THE BARCELONA METROPOLITAN REGION, SPAIN

Pedro Brotons PhD [1,2,3], Cristian Launes MD[1,3,4], Elena Buetas MsC[1], Vicky Fumado MD[1,4], Desiree Henares MsC[1,3], Mariona Fernandez de Sevilla MD[1,3,4], Alba Redin MsC[1], Laura Fuente-Soro PhD[5], Daniel Cuadras PhD[1], Maria Mele MD[1,4], Cristina Jou MD[6], Pere Millat[7], Iolanda Jordan MD[1,3,4], Juan Jose Garcia-Garcia MD[1,3,4], Quique Bassat MD[3,4,5,7,8], Carmen Muñoz-Almagro MD*[1,2,3,9] on behalf of Kids Corona Study Group

1. Institut de Recerca Sant Joan de Deu, Esplugues, Barcelona, Spain
2. Department of Medicine, Universitat Internacional de Catalunya, Barcelona, Spain
3. Consorcio de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP), Madrid, Spain.
4. Pediatrics Department, Hospital Sant Joan de Déu, Universitat de Barcelona, Esplugues, Barcelona, Spain
5. Centro de Investigação em Saúde de Manhiça (CISM), Maputo, Mozambique
6. Department of Pathology and Biobank, Hospital Sant Joan de Déu, Esplugues, Barcelona, Spain.
7. ISGlobal, Hospital Clínic - Universitat de Barcelona, Barcelona, Spain
8. ICREA, Pg. Lluís Companys 23, 08010 Barcelona, Spain
9. Molecular Microbiology Department, Hospital Sant Joan de Deu, Esplugues, Barcelona, Spain

*Corresponding author:

Prof. Carmen Muñoz-Almagro, MD, PhD
Molecular Microbiology Department
Hospital Sant Joan de Deu
Pº Sant Joan de Deu, nº 2
08950 Esplugues
Barcelona

Mail: cma@sjdhospitalbarcelona.org

Brief summary: We report similar SARS-CoV-2 seroprevalence in children and adults in quarantined households in metropolitan Barcelona (Spain) during the pandemic period April-June 2020. Predominant children asymptomatic infection and weak adult antibody response at early convalescence and beyond 6 weeks post-infection are documented.

Abstract

Background Susceptibility of children and adults to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and persistence of antibody response to the virus after infection resolution remain poorly understood, despite their significant public health implications.

Methods A cross-sectional seroprevalence study with prospective recruitment of volunteer families that included at least one first-reported adult case positive by SARS-CoV-2 PCR and at least one child aged less than 15 years living in the same household under strict home confinement was conducted in the Health Region of metropolitan Barcelona (Spain) during the pandemic period April 28-June 3, 2020. All household members were tested at home by a rapid SARS-CoV-2 antibody assay in finger-prick obtained capillary blood.

Results A total of 381 family households including 381 first-reported PCR-positive adult cases and 1,084 contacts (672 children, 412 adults) were enrolled. SARS-CoV-2 infection seroprevalence rates were 17.6% (118/672) in children and 18.7% (77/335) in adult contacts (p=0.64). Among first-reported cases, seropositivity rates varied from 84.0% in adults previously hospitalized and tested within 6 weeks since the first positive PCR result to 31.5% in those not hospitalized and tested after that lag time (p<0.001). Nearly all (99.9%) positive pediatric contacts were asymptomatic or had mild symptoms.

Conclusion Children appear to have similar probability as adults to become infected by SARS-CoV-2 in quarantined family households but remain largely asymptomatic once infected. Adult antibody protection against SARS-CoV-2 seems to be weak at early convalescence and beyond 6 weeks post-infection confirmation, especially in cases that have experienced mild disease.

Keywords: SARS-CoV-2, COVID-19, prevalence, household, antibody, children

Introduction

Coronavirus Infectious Disease 2019 (COVID-19) has become a global public health problem since it emerged at the end of 2019 [1]. One of the countries most affected by the COVID-19 pandemic has been Spain, with over 778,000 cases and 31,900 deaths confirmed as of October 1, 2020 [2]. A state of emergency was declared by the national government on March 14, 2020, imposing strict confinement for the population and the closure of all educational, cultural and leisure places across the country. Although children were initially subject to the same stringent quarantine measures as adults, daily outdoor strolls of those under 14 years of age were allowed for no more than one hour on April 26, in parallel to the progressive containment of the disease. Population enforced lockdown concluded on June 21.

The extent to which children may be less susceptible than adults to infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiological agent of COVID-19, remains unclear [3]. A number of population-based studies [4-7] and clinical case series [8-10] have suggested that pediatric populations have comparatively lower probability of being infected by the virus. Contact-tracing studies show mixed evidences, with either reduced [11-13] or similar [14] infection rates in children compared to adults. Duration of antibody protection against the virus is unknown and some early findings have suggested that it might not persist long once the infection has been resolved [15,16].

SARS-CoV-2 may be identified through serological detection of antibodies in blood or serum samples once seroconversion has been completed after the first week of symptom onset [17] or viral RNA detection in upper respiratory or other samples by real-time reverse transcriptase polymerase chain reaction (RT-PCR) during the days immediately after symptom onset [18]. Household serological studies are suitable designs to provide strong evidences on susceptibility to SARS-CoV-2 infection, disease spectrum, and antibody protection in defined, stable, easy-to-follow clusters of confirmed primary cases and their close contacts [19]. Ultimately, such evidences prove essential to inform age-selective or indiscriminate home quarantine measures and for the re-opening of schools.

The primary objectives of this study were to assess seroprevalence of SARS-CoV-2 infection in children and adult contacts living with first-reported PCR-positive adult cases in quarantined family households and determine persistence of antibody response in cases, while identifying associated factors.

Materials and Methods

Study design

A cross-sectional seroprevalence study with recruitment of volunteer families that included at least one first-reported parent positive by SARS-CoV-2 Real-Time PCR and at least one child living in the same household was conducted by researchers of University Hospital Sant Joan de Deu Barcelona. Family households were identified within the Health Region of metropolitan Barcelona (Spain), a densely-populated geographical area that became one of the main focuses of the pandemic in Spain. The study period spanned from April 28 to June 3, 2020.

Definitions

A family household was defined as a household where at least one parent aged 18 years or older and one child under 15 years of age lived together. A COVID-19 first-reported adult case was defined as the parent in the household who had a first confirmed positive result for SARS-CoV-2 RNA detection in a nasopharyngeal swab. An infected contact was defined as a household child or adult, other than the first-reported case, who was found positive for SARS-CoV-2 by a rapid Immunochromatographic Lateral Flow Assay (LFA) detecting IgG, IgM, or both, in finger-prick obtained capillary blood at the household visit. LFA was selected as an appropriate test for the study for ethical considerations, so as to avoid extracting venous blood from healthy or asymptomatic children, and enabled simple and rapid testing at homes. The SARS-CoV-2 household seroprevalence rate was calculated as the proportion of family contacts who were confirmed to be infected by the rapid LFA. Lag time elapsed between the first positive RT-PCR and the rapid LFA was considered as a proxy measure of SARS-CoV-2 antibody response persistence in first-reported cases.

Family household identification

The study setting, a tertiary-level university children's hospital located in metropolitan Barcelona, deployed an open web platform named Kids Corona through which families were invited to participate in the study. A team of epidemiologist researchers screened eligible families according to their demographic characteristics, their residence location, and the documental validity of the first-reported RT-PCR-positive result.

Data and sample collection

Home testing teams, each of them composed of two research nurses, visited every selected household, collected finger-prick capillary blood from all family members, and performed rapid LFAs at homes. Additionally, all first-reported cases that accepted to donate samples to the biobank of the study setting were extracted venous blood specimens. Blood extraction was carried out in parallel to rapid LFA testing during household visits. Serum samples obtained from blood were biobanked at -80ºC in the study site. The epidemiologist researchers interviewed every first-reported case by telephone 24 hours after sample collection. Interviews followed a structured questionnaire to obtain relevant epidemiological and clinical data of family members. Families with any invalid test result or that were not able to answer the questionnaire were excluded from the study.

Microbiological methods for SARS-CoV-2 antibody detection

Rapid IgG/IgM Covid-19 tests (2019-n-CoV Ab Test, Innovita Tangshan Biological Technology Co, China) were performed according to manufacturer's instructions. A minimum lag time of 14 days between the first positive RT-PCR and the LFA was established to maximize detection of seroconversion in first-reported cases. Since sensitivity of the rapid LFA that we used has been reported to vary from 29.5% in the first 1-5 days after symptom onset to 83.3% after 20 days [20], a performance comparison was undertaken withpaired finger-prick capillary blood specimens already tested by rapid LFA and biobanked serum samples tested by an enzyme-linked immunoassay (ELISA) (Abbott SARS-CoV-2 IgG).

Statistical analysis

SARS-CoV-2 household seroprevalence and seropositivity rates were compared with the Chi-square test or the Fisher's exact test. Univariate logistic regression analyses were performed to study the associations of clinical and epidemiological variables with SARS-CoV-2 seroprevalence and antibody response, considering those variables that showed a relationship with these outcomes at a *p* value ≤0.10 for multivariate analysis. Statistical significance was set at a p-value of <0.05 and confidence intervals (CI) at 95% level. All statistical analyses were performed using Stata v.15 software (Stata Corp., TX, US).

Ethics statement

Every adult household member gave an informed consent to participate. Informed consents were obtained from parents/guardians of children that participated in the study, as well as assents from every children aged ≥12 years. The study was approved by the Ethics Committee of Hospital Sant Joan de Deu prior to start.

Results

Selection of family households

A total of 2,412 families showed interest in participating in the study, of which 1,359 met inclusion criteria. Four-hundred and ten families documented a first RT-PCR-positive result for a household adult case, signed informed consents for participation, and were visited and tested by rapid LFA. Of them, 26 were excluded due to invalid LFA results in any family member, and three declined to answer the questionnaire and were also excluded. A final number of 381 family households were selected.

Demographic characteristics of family households

A total of 1,465 family members were identified in the selected households, including 381 (26.0%) first-reported adult cases, 672 (45.9%) children contacts (<15 years), and 412 (28.1%) adult contacts (≥15 years). Family households ranged from two to seven co-habitants. Women predominated among first-reported cases (n=237, 62.2%) whereas the majority of contacts (children: n= 357, 53.1%; adults: n= 235, 57.0%) were male. Mean age of adult cases was 41.0 years (SD 5.9). Children and adult contacts had a mean age of 5.9 years (SD 3.7) and 40.0 years (SD 10.2), respectively. Of note, 68.9% of cases were health workers (Table 1).

Clinical characteristics of first-reported cases and children contacts

Overall, 87 (22.8%) first-reported cases were hospitalized due to SARS-CoV-2 infection before being confined at home. Mean length of hospital stay was 8.1 days (SD 6.4). Co-morbidities were self-reported by 20.2% of cases and obesity (12.1%) was the most common co-morbid condition (Table 2). In a multiple logistic regression obesity (adjusted odds ratio aOR 4.07, 95% CI 1.76-9.39), male sex (aOR 3.13, 95% CI 1.73-5.65), and age ≥40 years (aOR2.28, 95% CI 1.25-4.16) were identified as risk factors for case hospitalization whereas being a healthcare worker was a protective factor (aOR 0.19, 95% CI 0.11-0.34) (Table 3). Nearly all children contacts (99.9%) were paucisymptomatic or asymptomatic, except for a positive female child who was

hospitalized due to multi-systemic inflammatory syndrome (Kawasaki-like) and evolved positively during and after her stay at the study site.

Verification of SARS-CoV-2 rapid LFA sensitivity

A total of 250 biobanked serum samples were tested by ELISA and results were compared with those of finger-prick capillary blood specimens processed by rapid LFA. Mean time elapsed between first positive RT-PCR and rapid LFA for the overall collection of 1,465 specimens was 51.2 days (IQR 42-61 days) whereas for the 250 paired samples additionally tested by ELISA it was 49.8 mean days (IQR 40-60 days). Seropositivity rates for rapid LFA were low at weeks 3-4 (46.2%), increased up to a peak at week 6 (70.6%) and then dropped markedly to a plateau (range 35.0-37.2%) within weeks 8-12. ELISA seropositivity rates showed a similar pattern: detection yield was moderate at weeks 3-4 (61.5%), peaked at week 6 (94.1%) and slowly stabilized in weeks 8-12 (range 77.5-87.2%). Overall, ELISA detection yield was 1.3 times higher than that of rapid LFA in the first 6 weeks after infection confirmation and doubled rapid LFA detection yield beyond that time threshold (Figure 1).

SARS-CoV-2 seropositivity in first-reported cases and associated factors

A positive result by SARS-CoV-2 rapid LFA (IgM, IgG, or both targets) was found in 175 (45.9%) of first-reported cases, including 32.3% IgG-positive, 11.0% IgG- and IgM-positive, and 2.6% IgM-positive. SARS-CoV-2 seropositivity rates in the collection of 381 samples showed the same inverted U-shaped pattern observed for the 250 paired specimens (Figure 2). In multiple logistic regression, hospitalization (aOR 5.59, 95% CI 2.99-10.46), and time of convalescence ≤6 weeks (aOR 2.15, 95% CI 1.30-3.56) were significantly associated with SARS-CoV-2 seropositivity (Table 4). Particularly, marked differences between seropositivity rates before and after the convalescence time threshold of 6 weeks were observed among health workers (aOR 2.40, 95% CI 1.31-4.38), women (aOR 2.39, 95% 1.24-4.62), and cases not hospitalized (aOR 2.35, 95% CI 1.36-4.08). Conversely, differences in SARS-CoV-2 antibody detection before and after this time threshold were not significant in cases other than health workers, males, and inpatients.

Seroprevalence of SARS-CoV-2 infection in household contacts and associated factors

Among the 1,084 household contacts, 195 (18.1%) were SARS-CoV-2-positive by rapid LFA, including 118 out of 672 (17.6%, 95% CI 14.8-20.7%) children and 77 out of 412 (18.7%, 95% CI 15.0-22.8%) adults. The difference in SARS-CoV-2 seroprevalence rates between children and adult contacts was not statistically significant (p=0.64). Contact age group, contact sex, smoking habits of family members, and household occupancy rate were not found to be significantly associated with SARS-CoV-2 seroprevalence (Table 5). A sub-analysis of seroprevalence rates in children did not show any significant differences by the presence or absence of respiratory (19.2 *vs.* 17.5%, p=0.82) or gastrointestinal symptoms (21.1 *vs.* 17.0%, p=0.31), or cutaneous lesions (19.8 *vs.* 17.2%, p=0.48), as reported by their parents in the previous four months. In contrast, the use of public instead of private transportation to go to school before home confinement came into force was strongly associated with children being seropositive (33.3 *vs.* 14.9%, p<0.001) (Supplementary Table 1).

Discussion

This study reported similar SARS-CoV-2 seroprevalence rates in children and adult contacts living with first-reported adult cases in family households under stringent home quarantine conditions. It also noted the predominance of asymptomatic presentations among infected children contacts and identified an inverted U-shaped pattern of weak antibody response against SARS-CoV-2 among adult cases in the early convalescence stage and beyond a post-infection time threshold of 6 weeks, particularly in those with mild disease that were not hospitalized. Interestingly, this pattern was not only observed in capillary blood samples tested by rapid LFA but also and more subtlety in serum samples tested by ELISA.

Our observation of similar rates of SARS-CoV-2 infection in children and adult contacts is in agreement with results from a study of 391 COVID-19 cases and close family and non-family contacts conducted in Shenzhen, China [14], which reported minor differences in infection rates between children (7.4% in those under 10 years of age, 7.1% in those aged 10-19 years) compared with adults (in the range 6.1-9.1% for subjects between 20 and 59 years). Notably, seroprevalence rates determined in our study exceed by more than 2 times those values. This difference could be related to the fact that identification of secondary cases in the referred study was done using RT-PCR in a single determination in a very acute scenario whereas we used serology assays at 3-12 weeks after first-reported case confirmation. In turn, a study with 105 cases and their household contacts in Hubei Province, China, identified a lower infection rate of 4% in children under 18 years of age in comparison with 17.1% in adults [21]. Similarly, age-gradient household prevalence rates ranging from 20.0% among children contacts younger than 5 years to 55.2% among adults aged 65 years or older were reported in a household prevalence study conducted in the New York State [22]. To be highlighted, these two studies used RT-PCR to identify cases, as opposed to our seroprevalence study. We speculate that age-related prevalence differences between serological and RT-PCR-based household studies could be originated by faster clearance of the virus in children than in adults, regardless of their similar susceptibility to infection, resulting in fewer children being identified as positive by RT-PCR than by serology. On the other hand, sex of households contacts, smoking habits of family members, and household occupancy rate were not associated with SARS-CoV-2 susceptibility to infection, as reported in other household studies [12,13,23,24].

Seropositivity rates against SARS-CoV-2 revealed to be markedly lower in first-reported adult cases that were tested in an early convalescence stage (≤4 weeks) and at a later post-infection stage (>6 weeks). This finding was observed in both the overall collection of 381 samples tested by rapid LFA and in the representative set of 250 paired samples also tested by ELISA. It raises concerns about reliability of results by rapid LFAs performed in the first weeks after infection and about long-term persistence of antibody response to the virus, since noticeable proportions from 12.8 to 22.5% of convalescent adults had negative results by ELISA 8-12 weeks after infection confirmation. To be highlighted, antibody protection was weaker in cases that were not

hospitalized, suggesting that infection severity may provoke a comparatively stronger response. The time-dependent SARS-CoV-2 antibody response pattern described in this study is in contrast with the observed persistence of antibodies in SARS-CoV-1, its closest-related human coronavirus, from 1 to 2 years [24]. However, it aligns with results recently reported on SARS-CoV-2 antibody decay during convalescence. A pre-print study describes loss of IgM antibodies in 31.4% of 1,470 adult patients hospitalized with COVID-19, after a median time of 41 days since symptoms onset, as well as loss of IgG antibodies in more than 10% of them, after 21 days post-symptom onset [15]. Another study with 37 asymptomatic but SARS-CoV-2 positive patients of all ages and equal number with severe symptoms found that 40% of asymptomatic individuals had undetectable levels of antibodies two months after infection, compared to 13% of those symptomatic [16].

While adults infected with SARS-CoV-2 and particularly the elderly are likely to experience serious disease and require clinical attention, children frequently present no or mild symptoms that resolve without medical intervention [25]. In agreement with previous literature, almost all infected children in our study were asymptomatic or had mild presentations. Interestingly, we did not find any significant difference in SARS-CoV-2 seroprevalence between children with or without respiratory or gastrointestinal symptoms, or cutaneous lesions, which confirms the unprecedent challenge of early diagnosis and transmission control of the virus in pediatric populations. SARS-CoV-2 infection in children contacts was positively correlated with the use of public transportation means to go to school, a risk factor presumably related with overcrowding. Similar risk factors of travelling together or sharing a vehicle have also been described in other studies [14,23]. Moreover, indoor air quality has previously been associated with transmission risk of the virus in closed settings [26] and World Health Organization guidelines have recently considered that airborne transmission may occur in crowded, poorly ventilated indoor environments [27]. However, we did not find any significant relationship between high household occupancy, a proxy for overcrowding, or smoking habits of family members, indicative of suboptimal indoor air quality, with SARS-CoV-2 household seroprevalence. A possible explanation for this could be that other behavior factors such as adherence of family members to hygiene measures, face mask use at home, and effective self-isolation of cases reported in the first place may have been more influential to minimize household virus transmission [23,28].

The main strength of our study is that we analyzed information on SARS-CoV-2 prevalence and antibody response using a large number of family households located in a geographical area of high COVID-19 incidence during the study period. Additionally, the study was conducted in a situation of strict home quarantine that ensured similar exposure of all family contacts to infection irrespective of their age, thus avoiding biased assessment according to their different social interactions out of home. A limitation of the study was the imperfect sensitivity of the rapid LFA as well as the reduced number of antibody classes targeted by the test. Nevertheless, we consider that any potential bias derived from suboptimal test sensitivity would comparatively affect identification of infected children and adult contacts to the same extent. A second limitation that derived from the cross-sectional design was the impossibility to discern whether the cases initially identified were the first family members to become infected or not. The time elapsed between positive RT-PCR and rapid LFA (range 17-82 days) and evidences on the mean incubation period for SARS-CoV-2 (about 4-6 days with 95% of individuals presenting symptoms within 12 days) [29-31] point towards the plausibility that those first-reported cases were the primary vectors of infection in their homes. Indeed, a recent nationwide study undertaken in

South Korea reported that only 46 out of 1,248 (3.7%) household contacts were infected by children aged 0-18 years [32]. Likewise, a systemic review available in preprint describes that children are likely to be the source of infection in only 10% of households [33].

In conclusion, children appear to be as susceptible to SARS-CoV-2 infection as adults in family households under strict in-home quarantine but remain mostly asymptomatic once infected. Antibody response to infection of adults seems to be weak at an early convalescence stage and beyond 6 weeks post-infection confirmation, particularly among those who have experienced milder infection. Further household studies are needed to determine temporal patterns of antibody response against the virus in children and adults.

NOTES:

Contributions

Pedro Brotons, designed the study, analysed data, wrote the paper

Cristian Launes, collected data, analysed data, wrote the paper

Elena Buetas, collected data, performed experiments.

Vicky Fumado, collected data

Desiree Henares, collected data, performed experiments

Mariona F de Sevilla, collected data

Alba Redin, collected data, performed experiments

Laura Fuente-Soro, collected data

Daniel Cuadras, collected data

Maria Mele, collected data

Cristina Jou, collected data

Pere Millat, collected data

Iolanda Jordan, collected data

Juan J Garcia-Garcia, collected data

Quique Bassat, designed the study, collected data,

Carmen Muñoz-Almagro, designed the study, analysed data, wrote the paper, supervised the study

All authors and Kids Corona Study Group discussed the results and critically reviewed, discussed and accepted the final version of the manuscript.

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#KIDS-Corona Study Group

Cristina Adroher, Laia Alsina, Sara Ajanovic, Ainhoa Andueza, Sara Arias, Nuria Balanza, Barbara Baro, Elisenda Bonet-Carne, Joana Claverol, Marta Cubells, Claudia Fortuny, Aleix Garcia-Miguel, Eduard Gratacos, Maria Hernandez, Monica Morales, Felipe Pérez-Soler, María Ríos, Pere Millat, Gemma Pons, Francesc Torrents, Iris Uribesalgo, Anna Valls, Rosauro Varo

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Conflict of interests statement

Carmen Muñoz-Almagro reports grants to her organization from BioMèrieux, Roche Diagnostics, Qiagen, BioFire Diagnostics, Alere, and Genomica, outside the submitted work and personal fees from BioMèrieux, Roche Diagnostics, and Qiagen for presentations in satellite symposiums outside the submitted work. Pedro Brotons reports personal fees from Roche Diagnostics for a presentation in a satellite symposium outside the submitted work. The rest of authors declare no conflicts of interest.

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Figure 1.Seropositivity of SARS-CoV-2 antibodies detected by rapid antibody assay in first-reported cases according to time of convalescence (total samples n=381)

Figure 2.Seropositivity of SARS-CoV-2 antibodies detected by rapid antibody assay and ELISA in first-reported cases according to time of convalescence (total paired samples n=250)

Table 1. Demographic characteristics of study population

Variable	No. (%)
Total family households	381 (100.0)
Household mean surface area (SD), sqm	102.3 (43.0)
Total family members	1465 (100.0)
2	9 (2.4)
3	114 (29.9)
4	197 (51.7)
≥ 5	61(16.0)
Primary cases	381 (26.0)
Mean age (SD), yr	41.0 (5.9)
15-24 yr	1 (0.3)
25-34 yr	47 (12.3)
35-44 yr	246 (64.6)
45-55 yr	82 (21.5)
≥ 55 yr	5 (1.3)
Sex, female	237 (62.2)
Health worker	261 (68.9)
Children contacts	672 (45.9)
Mean age (SD), yr	5.9 (3.7)
< 1 yr	35 (5.2)
1-4 yr	297 (44.2)
5-14 yr	340 (50.6)
Sex, male	357 (53.1)
Adult contacts	412 (28.1)

Mean age (SD), yr	40.0 (10.2)
15-24yr	32 (7.8)
25-34 y.	48 (11.7)
35-44yr	230 (55.8)
45-55 yr	87 (21.1)
≥ 55yr	15 (3.6)
Sex, male	235 (57.0)

Values expressed as No. (%), unless otherwise stated

Abbreviations: SD, Standard Deviation; yr, year; sqm, square meter

Table 2. Clinical characteristics of first-reported cases

Variable	No. (%)
Hospitalization due to SARS-CoV-2 infection	87 (22.8)
Mean length of hospital stay (SD), days	8.1 (6.4)
Main comorbidities	77 (20.2)
Obesity	46 (12.1)
Hypertension	14 (3.7)
Immunocompromised	10 (2.6)
Diabetes	7 (1.8)
Autoimmune disease	27 (7.1)
Asthma	19 (5.0)
Past medical history	
Recent respiratory infection*	35 (9.2)
Recent gastrointestinal infection*	51 (13.4)
Previous invasive disease infection	25 (6.6)

Values expressed as No. (%), unless otherwise stated

Abbreviations: SD, Standard Deviation

* Since January 2020

Table 3. Factors for hospitalization of first-reported cases with SARS-CoV-2 infection

Variable	Group 1[a,b]	Group2[a,b]	Univariate analysis		Multivariate analysis	
	% Hospitalized	% Hospitalized	OR (95% CI)	*p* value	aOR (95% CI)	*p* value
Health worker *vs.*other professions	11.9	47.5	**0.15 (0.09-0.25)**	**<0.001**	**0.19 (0.11-0.34)**	**<0.001**
Sex, male *vs.* female	39.6	12.7	**4.52 (2.72-7.51)**	**<0.001**	**3.13 (1.73-5.65)**	**<0.001**
Age, ≥40 *vs.*<40 yr	31.5	13.6	**2.92 (1.74-4.90)**	**<0.001**	**2.28 (1.25-4.16)**	**0.01**
Hypertension, yes *vs.* no	57.1	21.5	**4.86 (1.64-14.42)**	**0.01**	2.28 (0.62-8.39)	0.21
Obesity, yes *vs.* no	37.0	20.9	**2.22 (1.15-4.27)**	**0.02**	**4.07 (1.76-9.39)**	**0.001**
Previous invasive disease infection, yes *vs.* no	40.0	21.7	**2.41 (1.04- 5.58)**	**0.04**	1.71 (0.64-4.55)	0.28
Immunocompromised, yes *vs.* no	20.0	23.0	0.84 (0.17-4.02)	0.83		
Autoimmune diseases, yes *vs.* no	22.2	22.9	0.96 (0.38-2.47)	0.94		
Asthma, yes *vs.* no	31.6	22.4	1.60 (0.59-4.35)	0.36		
Recent respiratory infection[c], yes *vs.* no	25.7	22.9	1.17 (0.52-2.60)	0.71		
Recent gastrointestinal infection[c], yes *vs.* no	29.4	22.1	1.47 (0.76-2.83)	0.25		

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; yr, year

[a] Group 1 refers to the variable group mentioned in the first place (i.e., health worker) and Group 2 refers to the variable group mentioned in the second place (i.e., other professions)

[b] Groups ≥10 observations

[c] Since January 2020

Table 4. SARS-CoV-2 seropositivity in first-reported cases and associated factors

Variable	Group 1[a,b]	Group2[a,b]	Univariate analysis		Multivariateanalysis	
	% Positive	% Positive	OR (95% CI)	*p* value	aOR (95% CI)	*p* value
Infection severity, patient not hospitalized *vs*. hospitalized	76.7	37.1	**5.68 (3.26-9.87)**	**<0.001**	**5.59 (2.99-10.46)**	**<0.001**
Time of convalescence, ≤6 *vs.* >6 weeks	58.8	41.0	**2.06 (1.30-3.26)**	**0.002**	**2.15 (1.30-3.56)**	**0.003**
Profession, health worker *vs.* others	40.2	59.0	**0.46 (0.30-0.72)**	**0.001**	0.76 (0.46-1.28)	0.31
Age, ≥40 *vs*. <40 yr	52.3	39.1	**1.70 (1.13-2.56)**	**0.01**	1.11 (0.70-1.75)	0.66
Sex, male *vs*. female	52.8	41.8	**1.56 (1.03-2.36)**	**0.04**	0.85 (0.52-1.39)	0.52
Recent respiratory infection[c], yes *vs.* no	31.4	47.9	0.49 (0.23-1.04)	0.06	0.43 (0.19-0.98)	0.05
Asthma, yes *vs.* no	63.2	44.9	2.09 (0.80-5.44)	0.13		
Previous invasive disease infection, yes *vs.* no	60.0	45.1	1.81 (0.79-4.14)	0.16		
Obesity, yes *vs.* no	53.3	44.8	1.47 (0.79-2.73)	0.22		
Hypertension, yes *vs.* no	50.0	45.6	1.18 (0.41-3.44)	0.76		
Autoimmune disease, yes *vs.* no	48.2	45.6	1.10 (0.50-2.40)	0.81		
Recent gastrointestinal infection[c], yes *vs.* no	47.1	46.2	1.03 (0.57-1.86)	0.92		

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; wk, week; yr, year

[a] Group 1 refers to the variable group mentioned in the first place (i.e., health worker) and Group 2 refers to the variable group mentioned in the second place (i.e., other professions)

[b] ≥10 observations per group

[c] Since January 2020

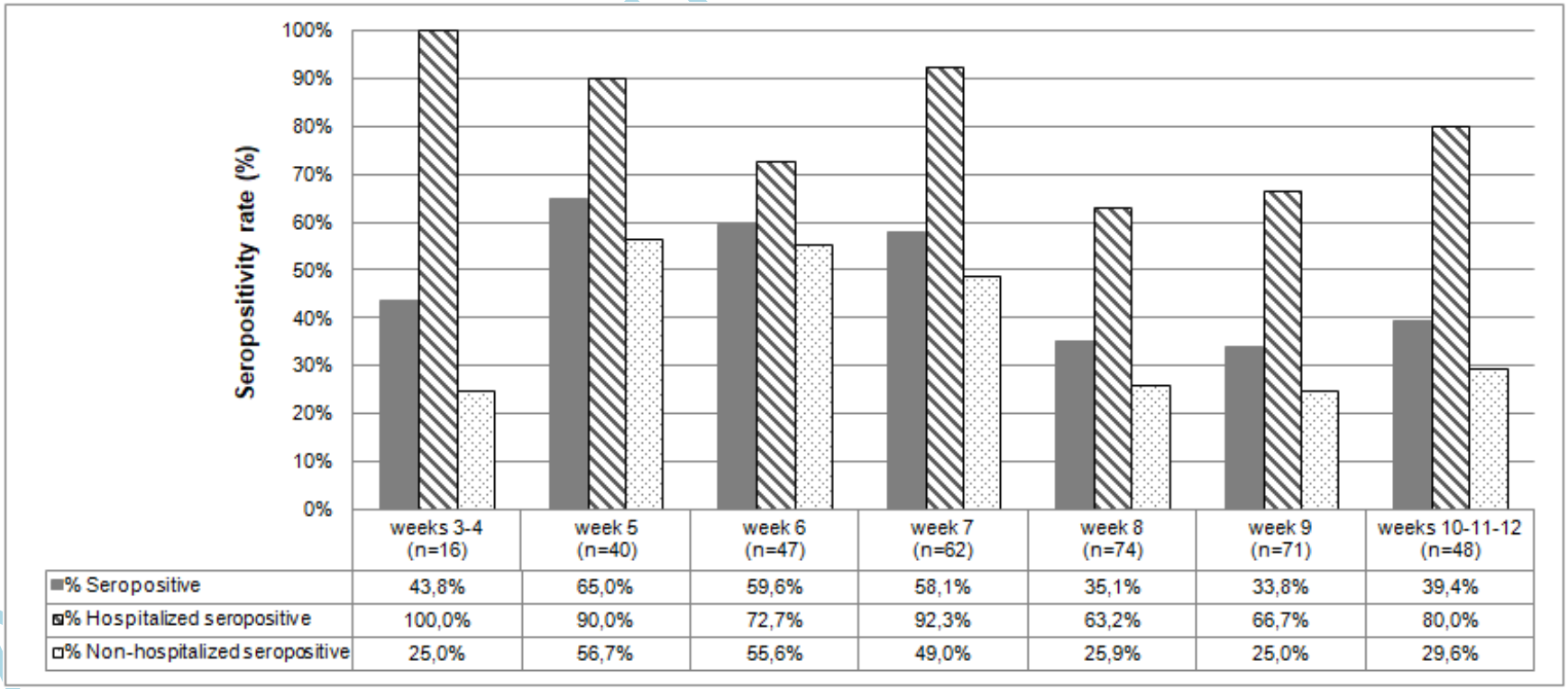
Table 5. SARS-CoV-2 household seroprevalence

Variable	Total No.	No. Positive	Prevalence rate (95% CI)	*p* value
Family households	381	127	33.3 (28.6-38.3)	
Contact groups				0.64
Children contacts (aged <15 yr.)	672	118	17.6 (14.8-20.7)	
Adult contacts (aged ≥18 yr.)	412	77	18.7 (15.0-22.8)	
Contact age groups				0.50
< 1 yr.	35	6	17.1 (6.6-33.6)	
1-4 yr.	297	57	19.2 (14.9-24.1)	
5-14 yr.	340	55	16.2 (12.4-20.5)	
15-24 yr.	32	5	15.6 (5.3-32.8)	
25-34 yr.	48	13	27.1 (15.3-41.8)	
35-44 yr.	230	36	15.7 (11.2-21.0)	
45-54 yr.	87	19	21.8 (13.7-32.0)	
≥ 55 yr.	15	4	26.7 (7.8-55.1)	
Contact sex				0.47
Female	492	93	18.9 (15.5-22.6)	
Male	592	102	17.2 (14.3-20.5)	
Smoking habits of family members				0.81
Yes	232	43	18.5 (13.8-24.1)	
No	852	152	17.8 (15.3-20.6)	
Household occupancy rate				0.13
< 20 sqm per person	374	77	20.6 (0.17-0.25)	
≥ 20 sqm per person	702	118	16.8 (0.14-0.20)	

Values expressed as No. (%), unless otherwise stated

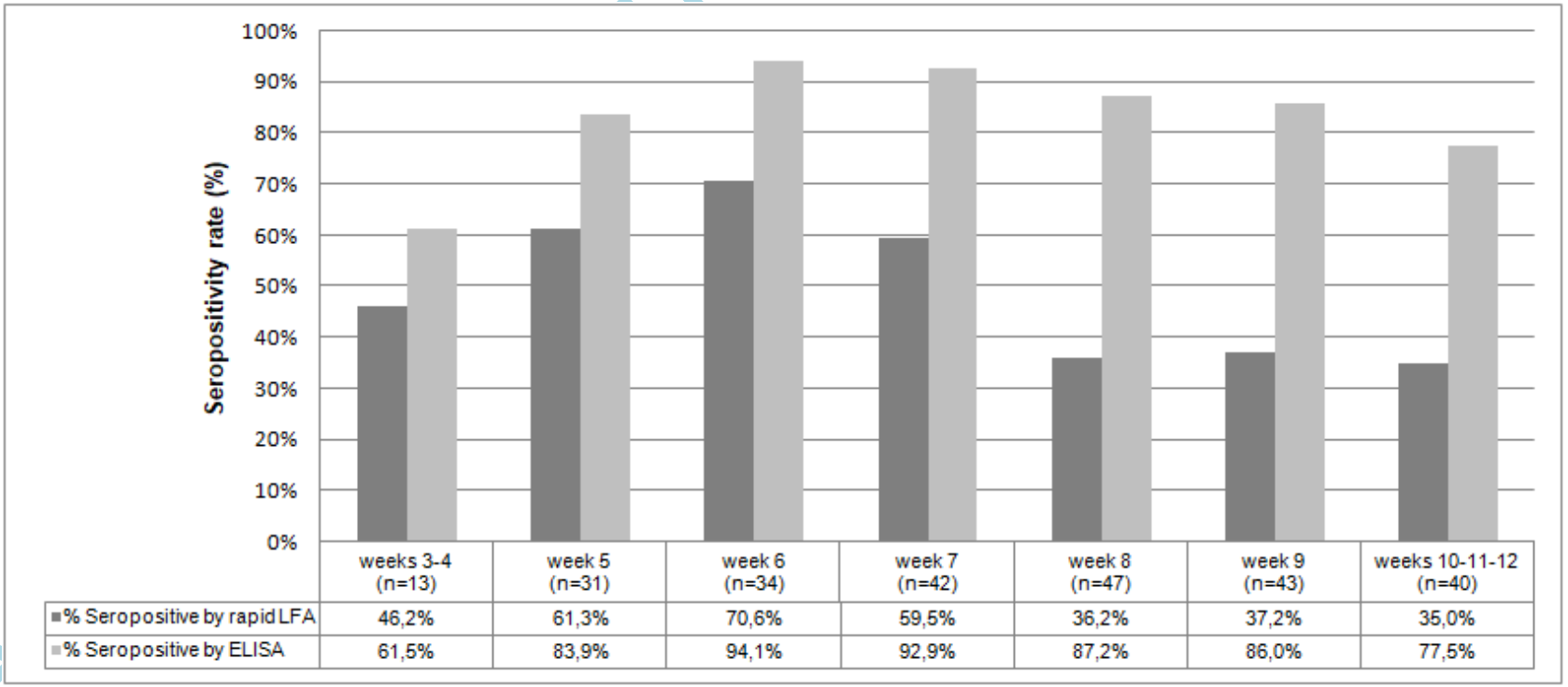
Abbreviations: CI, confidence interval; yr, year; wk, week; sqm, square meter

Figure 1



	weeks 3-4 (n=16)	week 5 (n=40)	week 6 (n=47)	week 7 (n=62)	week 8 (n=74)	week 9 (n=71)	weeks 10-11-12 (n=48)
% Seropositive	43,8%	65,0%	59,6%	58,1%	35,1%	33,8%	39,4%
% Hospitalized seropositive	100,0%	90,0%	72,7%	92,3%	63,2%	66,7%	80,0%
% Non-hospitalized seropositive	25,0%	56,7%	55,6%	49,0%	25,9%	25,0%	29,6%

Figura 2



	weeks 3-4 (n=13)	week 5 (n=31)	week 6 (n=34)	week 7 (n=42)	week 8 (n=47)	week 9 (n=43)	weeks 10-11-12 (n=40)
% Seropositive by rapid LFA	46,2%	61,3%	70,6%	59,5%	36,2%	37,2%	35,0%
% Seropositive by ELISA	61,5%	83,9%	94,1%	92,9%	87,2%	86,0%	77,5%