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Review

Population-based seroprevalence surveys of anti-SARS-CoV-2 antibody: An up-to-date review

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), has led to a global pandemic. However, the majority of currently available data are restricted to laboratory-confirmed cases for symptomatic patients, and the SARS-CoV-2 infection can manifest as an asymptomatic or mild disease. Therefore, the true extent of the burden of COVID-19 may be underestimated. Improved serological detection of specific antibodies against SARS-CoV-2 could help estimate the true numbers of infections. This article comprehensively reviews the associated literature and provides updated information regarding the seroprevalence of the anti-SARS-CoV-2 antibody. The seroprevalence can vary across different sites and the seroprevalence can increase with time during longitudinal follow-up. Although healthcare workers (HCWs), especially those caring for COVID-19 patients, are considered as a high-risk group, the seroprevalence in HCWs wearing adequate personal protective equipment is thought to be no higher than that in other groups. With regard to sex, no statistically significant difference has been found between male and female subjects. Some, but not all, studies have shown that children have a lower risk than other age groups. Finally, seroprevalence can vary according to different populations, such as pregnant women and hemodialysis patients; however, limited studies have examined these associations. Furthermore, the continued surveillance of seroprevalence is warranted to estimate and monitor the growing burden of COVID-19.

Introduction

Even though severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) only emerged at the end of 2019, the associated disease–coronavirus disease 2019 (COVID-19)–has spread rapidly to more than 180 countries/regions worldwide and has consequently led to a global pandemic (World Health Organization (WHO), 2020). As of September 7, 2020, nearly 27 million COVID-19 cases have been reported worldwide, causing 876,616 deaths, with an associated case fatality rate of 3.3% (World Health Organization (WHO), 2020; Lai et al., 2020a, b; Sheng et al., 2020).

Currently, the diagnosis of COVID-19 is confirmed by the detection of SARS-CoV-2 via real-time reverse transcription polymerase chain reaction (qRT-PCR) assays that target open reading frame-1 antibodies, envelope proteins, nucleocapsid proteins, RNA-dependent RNA polymerase genes, and the N1, N2, and N3 target genes, among suspected cases with an exposure history and signs/symptoms of SARS-CoV-2 infection (Lai et al., 2020c). However, the clinical manifestations of COVID-19 include both respiratory and extra-respiratory signs and symptoms and can range from an asymptomatic mild disease to severe disease/acute respiratory tract infections (Lai et al., 2020d, 2020e; Li et al., 2020a, b). Therefore, misdiagnosis of COVID-19 can occur in patients without a characteristic presentation, even for asymptomatic and mild infections, and in places where qRT-PCR is unavailable. These issues could limit our understanding of the extent of SARS-CoV-2 infection and further affect the implementation of infection control and prevention policies.

To resolve this issue, the use of a serological test to detect anti-SARS-CoV-2 antibodies could be a better way to estimate the burden of SARS-CoV-2 infection than the PCR method, and help improve understanding of the associated epidemiology (Lai et al., 2020c; Eckerle and Meyer, 2020; Ko et al., 2020; Lee et al., 2020a, Lee et al., 2020b). Hence, this review was conducted to provide updated and comprehensive information about the seroprevalence of the SARS-CoV-2 antibody in different populations.

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Population-based seroprevalence studies

Europe

Several large population-based studies have been conducted in COVID-19 hotspots (Pollán et al., 2020; Stringhini et al., 2020; Fiore et al., 2020; Vena et al., 2020; Gallian et al., 2020; Bogogiannidou et al., 2020; Silveira et al., 2020; Amorim Filho et al., 2020; Sood et al., 2020; Ng et al., 2020; Rosenberg et al., 2020; Havers et al., 2020; Nir et al., 2020; Sutton et al., 2020; McLaughlin et al., 2020; Naranbhai et al., 2020; Xu et al., 2020; Chughtai et al., 2020; Younas et al., 2020; Sam et al., 2020). In Spain, a nationwide, population-based sero-epidemiological study was conducted from April 27 to May 11, 2020 (Encuesta Seroepidemiológica de la Infección por el Virus SARS-COV-2 en España; ENE-COVID). In that study, 202,35,883 households were initially selected from the municipal rolls, using a two-stage random sampling method with stratification by province and municipality size. A total of 61,075 participants received the point-of-care test (Orient Gene Biotech COVID-19 IgG/IgM Rapid Test Cassette; Zhejiang Orient Gene Biotech, Zhejiang, China; reference GCCOV-402a), and among them, 51,958 further received a chemiluminescent microparticle immunoassay for the qualitative detection of IgG against SARS-CoV-2 nucleoprotein (SARS-CoV-2 IgG for use with ARCHITECT; Abbott Laboratories, Abbott Park, IL, USA; reference 06R8620). The seroprevalence was found to be 5.0% (95% confidence interval (CI) 4.7–5.4%) by the point-of-care test and 4.6% (95% CI 4.3–5.0%) by the immunoassay, with a specificity–sensitivity range of 3.7% (95% CI 3.3–4.0%; both tests positive) to 6.2% (95% CI 5.8–6.6%; either test positive) (Pollán et al., 2020).

A study in Switzerland reported the preliminary results of the surveillance of 2766 participants from 1339 households, with a demographic distribution similar to that of the canton of Geneva, between April 6 and May 9, 2020 (Stringhini et al., 2020). In that study, 12 weekly seroprevalence surveys, using a commercially available ELISA (Euroimmun; Lübeck, Germany; #EI 2606-9601 G) targeting the S1 domain of the spike protein of SARS-CoV-2 (serum diluted 1:101), were processed on a EUROLabWorkstation ELISA (Euroimmun) (SEROCoV-POP study). The results estimated the seroprevalence to be 4.8% (95% CI 2.4–8.0%; n = 341) in the first week, 8.5% (95% CI 5.9–11.4%; n = 469) in the second week, 10.9% (95% CI 7.9–14.4%; n = 577) in the third week, 6.6% (95% CI 4.3–9.4%; n = 604) in the fourth week, and 10.8% (95% CI 8.2–13.9%; n = 775) in the fifth week (Stringhini et al., 2020).

In Denmark, a total of 20,640 blood donations were given by 17–69-year-old donors from April 6 to May 3, 2020, which were then subjected to a plasma or whole blood lateral flow test, performed according to the manufacturer's recommendations (IgM/IgG Antibody to SARS-CoV-2 lateral flow test; Livzon Diagnostics Inc., Zhuhai, Guangdong, China) (Erikstrup et al., 2020). The overall unadjusted seroprevalence was 2.0% (95% CI 1.8–2.2%), and after adjusting for assay sensitivity and specificity (including their CI), the overall seroprevalence was 1.9% (95% CI 0.8–2.3%) (Erikstrup et al., 2020).

In Italy, 390 blood donors in the Lodi Red Zone were recruited from March 18 to April 6, 2020, for a study that utilized the SARS-CoV-2 microneutralization assay (Percivalle et al., 2020). A total of 91 (23%) participants were positive for SARS-CoV-2-specific neutralizing antibodies (≥1:10), while 299 (77%) tested negative (<1:10). In contrast, the seroprevalence was only 0.99% (n = 9) among 904 healthy blood donors in the Apulia region, South Eastern Italy (Fiore et al., 2020). Recently, one large series including 3609 adult volunteers from five administrative departments of the Liguria and Lombardia regions showed the seroprevalence was 11.0% (n = 389) (Vena et al., 2020).

In France, 998 samples collected from blood donors during the last week of March or the first week of April 2020 were tested for neutralizing antibodies against SARS-CoV-2, and the overall seroprevalence was found to be low (2.7%, n = 27) (Gallian et al., 2020). By contrast, a more updated surveillance conducted between May 4 and June 23, 2020 in France showed higher adjusted estimates of seroprevalence (positive anti-SARS-CoV-2 ELISA IgG result against the spike protein of SARS-CoV-2), with values of 10.0% (95% CI 9.1–10.9%) and 9.0% (95% CI 7.7–10.2%) in Ile-de-France and Grand Est, respectively–two regions with high rates of COVID-19–and of 3.1% (95% CI 2.4–3.7%) in Nouvelle Aquitaine–a region with a low rate of COVID-19 (Carrat et al., 2020). Moreover, they noted that confinement was associated with a higher seroprevalence, but that a lower seroprevalence was observed in smokers compared to non-smokers (Carrat et al., 2020).

During the early stage in Greece, the positive rate of anti-SARS-CoV-2 IgG was only 0.36% (n = 24) among 6586 serum samples, and the crude prevalence was 0.24% (5/2075) in March and 0.42% (19/4511) in April (Bogogiannidou et al., 2020).

America

In Brazil, three rounds of probability sample household surveys in the state of Rio Grande do Sul were conducted in nine large municipalities using the Wondfo lateral flow point-of-care test for IgM and IgG against SARS-CoV-2 (https://en.wondfo.com.cn/product/wondfo-sars-cov-2-antibody-test-lateral-flow-method-2/). The seroprevalence was estimated to be 0.048% (2/4151; 95% CI 0.006–0.174%) during April 11–13, 2020 (round 1), 0.135% (6/4460; 95% CI 0.049–0.293%) during April 25–27, 2020 (round 2), and 0.222% (10/4500; 95% CI 0.107–0.408%) during May 9–11, 2020 (round 3) (Silveira et al., 2020). Furthermore, a significant upward trend was observed throughout the surveys (Silveira et al., 2020).

Another study (Amorim Filho et al., 2020) included 2857 blood donors in Rio de Janeiro, Brazil from April 14 to April 27, 2020 and used MedTest Coronavirus 2019-nCoV IgG/IgM (MedLevensohn; Yuhang District, China), an immunochromatographic assay licensed by the Brazilian Health Surveillance Agency (ANVISA) in March 2020 (https://consultas.anvisa.gov.br/#/saude/q/?numeroRegistro=80560310056) that combines SARS-CoV-2 antigen-coated particles to qualitatively detect IgG and IgM antibodies. Overall, the seroprevalence without any adjustment was 4.0% (95% CI 3.3–4.7%), and the weighted prevalence was 3.8% (95% CI 3.1–4.5%). Lower estimates were found following adjustment for test sensitivity and specificity, at 3.6% (95% CI 2.7–4.4%) for the non-weighted prevalence and 3.3% (95% CI 2.6–4.1%) for the weighted prevalence (Amorim Filho et al., 2020).

In the USA, SARS-CoV-2-specific antibody testing using a lateral flow immunoassay test (Premier Biotech) was performed on the residents of Los Angeles County, California, or within a 15-mile (24-km) radius, between April 10 and April 14, 2020. Overall, 35 of the 863 adults included tested positive, with an unadjusted prevalence of 4.06% (exact binomial CI 2.84–5.60%). After adjusting for test sensitivity and specificity, the unweighted and weighted prevalence rates of SARS-CoV-2 antibodies were 4.34% (bootstrap CI 2.76–6.07%) and 4.65% (bootstrap CI 2.52–7.07%), respectively (Sood et al., 2020).

In the San Francisco Bay Area, the seroprevalence was tested using the Architect SARS166 CoV-2 anti-nucleocapsid protein IgG and was found to be only 0.1% in 1000 blood donors in March 2020 (Ng et al., 2020).

In New York, a total of 15,626 adult residents with complete data were tested from April 19 to April 28, 2020. Of the included residents, 15,101 (96.6%) had suitable specimens, of which 1887 (12.5%) were reactive and 340 (2.3%) were indeterminate. After

Table 1
Summary of population-based studies.

Author	Study site	Test	Period (all 2020)	Study subjects	Seroprevalence	Incidence (per 1,000,000 population) in indicated country (as of September 9, 2020) (World Health Organization (WHO), 2020)
Europe						
Pollán et al. (2020)	Spain (national and regional level)	Point-of-care antibody test, chemiluminescent microparticle immunoassay for IgG	April 27–May 11	35 883 households	5.0% (95% CI 4.7–5.4%) by the point-of-care test and 4.6% (95% CI 4.3–5.0%) by immunoassay	10 672.5
Stringhini et al. (2020)	Geneva, Switzerland	Anti-SARS-CoV-2-IgG antibodies using a commercially available ELISA	April 6–May 9	2766 participants from 1339 households	4.8% (95% CI 2.4–8.0%), 8.5% (95% CI 5.9–11.4%), 10.9% (95% CI 7.9–14.4%), 6.6% (95% CI 4.3–9.4%), and 10.8% (95% CI 8.2–13.9%) in weeks 1, 2, 3, 4, and 5, respectively	5066.5
Erikstrup et al. (2020)	Denmark	Commercial lateral flow test for IgG/IgM	April 6– May 3	20 640 blood donors aged 17–69 years	1.9% (95% CI 0.8–2.3%)	3029.4
Percivalle et al. (2020)	Lodi Red Zone in Lombardy, Italy	NA	April 6	390 blood donors	23% (n = 91)	4570.5
Fiore et al. (2020)	Apulia region, South Eastern Italy	Anti-SARS-CoV-2 IgG and IgM	May 1–31	904 healthy blood donors	0.99% (n = 9)	
Vena et al. (2020)	5 administrative departments of the Liguria and Lombardia regions in Italy	Anti-SARS-CoV-2 IgM or IgG	March 1–April 30	3609 adults volunteers	11.0% (n = 398)	
Gallian et al. (2020)	France	Antibodies neutralizing SARS-CoV-2	The last week of March, or the first week of April	998 blood donors	2.7% (n = 27)	4603.9
Carrat et al. (2020)	Ile-de-France (IDF), Grand Est (GE), and Nouvelle Aquitaine (NA) in France	Anti-SARS-CoV-2 ELISA IgG against spike (ELISA-S) and nucleocapsid (ELISA-NP), and anti-SARS-CoV-2 neutralizing antibody titers ≥40 (SN)	May 4–June 23	14 628 adults	Overall, 6.7% (n = 983) Adjusted estimates ELISA-S: IDF 10%, GE 9.0%, NA 3.1% ELISA-NP: IDF 5.7%, GE 6.0%, NA 0.6% SN: IDF 5.0%, GE 4.3%, NA, 1.3%	
Bogogiannidou et al. (2020)	Greece	Abbott SARS-CoV-2 IgG assay	March and April	6586 samples	0.36% (n = 24)	1092.4
America						
Havers et al. (2020)	10 regions in USA	SARS-CoV-2 spike protein ELISA	March 23–May 12	16 025 residents	1.0–6.9%	18 562.2
Sood et al. (2020)	Los Angeles County, California	Lateral flow immunoassay test (Premier Biotech)	April 10–14	1952 adult residents	4.06% (n = 35)	
Rosenberg et al. (2020)	New York	SARS-CoV-2 IgG testing was conducted using a microsphere immunoassay	April 19–28	15 101 adult residents	12.5% (n = 1887)	
Nir et al. (2020)	Indiana	Chemiluminescent microparticle immunoassay for SARS-CoV-2 IgG	April 25–29	3658 randomly selected persons	1.01% (n = 38)	
Sutton et al. (2020)	Oregon	SARS-CoV-2 IgG	May 11–June 15	897 participants	1.0% (n = 9)	
McLaughlin et al. (2020)	Blaine County	Abbott Architect SARS-CoV-2 IgG chemiluminescent microparticle immunoassay	May 4–19	917 adult residents	22.7% (n = 208)	
Naranbhai et al. (2020)	Chelsea	BioMedomics SARS-CoV-2 combined IgM/IgG LFA (BioMedomics, Morrisville, NC)	April 14–15	200 asymptomatic residents	31.5% (n = 63)	
Ng et al. (2020)	Two San Francisco Bay Area populations in the USA	Abbott Architect SARS-CoV-2 IgG (FDA, USA) and IgM (prototype) assays	March	387 hospitalized patients admitted for non-respiratory indications and 1000 blood donors	0.26% of 387 hospitalized patients admitted for non-respiratory indications and 0.1% in 1000 blood donors	19 255.0

			Author	Study site	Test	Period (all 2020)
Silveira et al. (2020)	Rio Grande do Sul, Brazil	Wondfo lateral flow point-of-care test for IgG/IgM	April 11– May 11	Household surveys	0.048% (95% CI 0.006–0.174%), 0.135% (95% CI 0.049–0.293%), and 0.222% (95% CI 0.107–0.408%) for April 11–13, April 25–27, and May 9–11, respectively	
Amorim Filho et al. (2020)	Rio de Janeiro, Brazil	NA	April 14–27	2857 blood donors	4.0% (95% CI 3.3–4.7%)	
Asia						
Xu et al. (2020)	Wuhan, China	IgM/IgG	March 9– April 10	17 368 residents	3.2–3.8%	62.9
Chughtai et al. (2020)	Pakistan	Chemiluminescence immunoassay method on Architect Ci8200 (Abbott)	May 20–30	154 young policeman	15.6% (n = 24)	1351.4
Younas et al. (2020)	Karachi, Pakistan	Electro-chemiluminescence immunoassay	June–July	380 healthy blood donors	21.4–37.7%	
Sam et al. (2020)	Kuala Lumpur and Selangor, Malaysia	In-house indirect ELISA detecting IgG to SARS-CoV-2 receptor binding domain	Main wave (January 29–April 14) and post-wave (April 15–June 6)	327 in main wave and 261 in post-wave	0.6% (n = 2) in main wave; 0.4% (n = 1) in post-wave	290.2
Noh et al. (2020)	Southwestern Seoul, Korea	Elecsys Anti-SARS-CoV-2 (Roche, Solna, Switzerland)	May 25–29	1500 residual serum samples from outpatients of two university hospitals	0.07% (n = 1)	413.1

CI, confidence interval; NA, not applicable; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

weighting, 12.5% were estimated to be reactive, and after further adjustment for test characteristics, the estimated cumulative incidence was 14.0% (95% CI 13.3–14.7%) (Rosenberg et al., 2020).

The largest study (Havers et al., 2020) was conducted in several regions, including San Francisco Bay Area, California, Connecticut, South Florida, Louisiana, Minneapolis-St Paul (St Cloud metro area), Minnesota, Missouri, New York, Philadelphia metro area, Pennsylvania, Utah, and Western Washington State from March 23 to May 12, 2020. A validated SARS-CoV-2 spike protein ELISA (Freeman et al., 2020) was used to test 16,025 persons, and the results showed that the adjusted estimates of seroprevalence ranged from 1.0% in the San Francisco Bay Area (collected April 23–27, 2020) to 6.9% in persons in New York City (collected March 23–April 1, 2020) (Havers et al., 2020).

In Indiana, the seroprevalence among 3658 randomly selected non-institutional participants was 1.01% (n = 38) between April 25 and April 29, 2020 (Nir et al., 2020). In Oregon, the overall seropositivity was 1.0% (n = 9) among 897 participants from 19 facilities participating in the Influenza-like Illness Surveillance Network (Sutton et al., 2020). In Blaine County, 208 out of 917 adult residents had positive anti-SARS-CoV-2 IgG and the overall seroprevalence was 22.7% between May 4 and May 9 (McLaughlin et al., 2020). The highest seroprevalence was found to be 31.5% among 200 asymptomatic residents in Chelsea, Massachusetts (Naranbhai et al., 2020).

Asia

In China, a serological survey (Xu et al., 2020) was conducted in seven cities, including Hubei Province (Wuhan, Honghu, and Jingzhou), Guangdong Province (Guangzhou and Foshan), Sichuan Province (Chengdu), and Chongqing between March 9 and April 10, 2020, and a validated serological test (Liu et al., 2020) for the presence of antibodies (IgM or IgG) against SARS-CoV-2 was tested in a total of 17 368 individuals. For 10,499 individuals in the community setting, the seropositivity ranged from 0.6% among 9442 community residents in Chengdu, Sichuan, and 1.4% among factory workers in Guangzhou, Guangdong, to 3.2% among 219 relatives of healthcare workers (HCWs), and 3.8% among 346 hotel staff members in Wuhan, Hubei (Xu et al., 2020). Moreover, seropositivity decreased progressively in other cities as the distance to the epicenter increased (Xu et al., 2020).

In Pakistan, 24 (15.6%) of 154 asymptomatic young policemen in high-risk areas of Lahore had positive anti-SARS-CoV-2 IgG (Chughtai et al., 2020), as did 21.4–37.7% of 380 healthy blood donors in Karachi (Younas et al., 2020).

In Malaysia, the seropositivity of anti-SARS-CoV-2 IgG was 0.6% (2/327) and 0.4% (1/261) based on serum samples collected for non-respiratory and respiratory infections during the pandemic and post-pandemic periods, respectively (Sam et al., 2020).

In Seoul, Korea, the seroprevalence was only 0.07% based on the surveillance of 1500 residual samples from outpatients of two university hospitals (Noh et al., 2020).

Summary

In summary, the reported seroprevalence ranged from <0.1% to more than 20% in the different regions and could increase with time (Table 1). Regular monitoring of the seroprevalence at each site should be indicated to establish the epidemiology of COVID-19.

Healthcare workers (HCWs)

Nosocomial transmission of SARS-CoV-2 is common within hospitals, and COVID-19 is a threat for HCWs, especially those without appropriate personal protective equipment (PPE)

(Houlihan et al., 2020; Hunter et al., 2020a, b; Kluytmans-van den Bergh et al., 2020; Lai et al., 2020f; Keeley et al., 2020; Wei et al., 2020). One population-based study demonstrated that the positive rate of anti-SARS-CoV-2 IgG or IgM in the hospital setting was 2.5% (170/6919), which was higher than that reported in the community setting (0.8%, 81/10,449) (Xu et al., 2020). In that study (Xu et al., 2020), the positive rate was highest for HCWs in Wuhan, Hubei (3.8%, 27/714).

Many studies had evaluated the seroprevalence among HCWs (Steensels et al., 2020; Martin et al., 2020; Korth et al., 2020; Stubblefield et al., 2020; Chen et al., 2020a, b; Pallett et al., 2020; Grant et al., 2020; Hunter et al., 2020a, b; Self et al., 2020; Moscola et al., 2020; Plebani et al., 2020). In Belgium, active screening was performed using a single-lane rapid IgG/IgM lateral flow assay directed to the nucleocapsid protein of SARS-CoV-2 (COVID-19 IgG/IgM Rapid Test Cassette; Multi-G), for 3056 staff in a tertiary center from April 22 to April 30, 2020 (Steensels et al., 2020). Overall, 197 staff (6.4%, 95% CI 5.5–7.3%) had IgG antibodies for SARS-CoV-2. In addition, household contacts of suspected or confirmed COVID-19 cases showed higher antibody positivity than those without exposure (81/593 (13.7%) vs 116/2435 (4.8%)), with an odds ratio (OR) of 3.15 (95% CI 2.33–4.25). Moreover, prior anosmia was associated with the presence of antibodies, with an OR of 7.78 (95% CI 5.22–11.53), as well as fever and cough (Steensels et al., 2020).

Another study in Belgium performed by Martin et al. (2020) reported on 326 staff from COVID-19 highly exposed units who received two rounds of serological testing (Euroimmun Anti-SARS-CoV-2 IgG; Medizinische Labordiagnostika AG, Lübeck, Germany). The IgG seroprevalence among those patients without a positive SARS-CoV-2 RT-PCR at baseline was 8.3% (n = 27) on day 1 and 9.5% (n = 31) on day 15 (Martin et al., 2020).

In Germany, 316 HCWs who had been in direct contact with COVID-19 patients underwent semi-quantitative ELISA testing (Euroimmun Medizinische Labordiagnostika, Lübeck, Germany) in a survey conducted from March 25 to April 21, 2020, and the seroprevalence was found to be 1.6% (n = 5) (Korth et al., 2020). Moreover, the seroprevalence was numerically higher in the

Table 2
Summary of the studies on healthcare workers (HCWs), children, and pregnant women.

Author	Study site	Test	Period (all 2020)	Study subjects	Seroprevalence rate
Healthcare workers (HCWs)					
Steensels et al. (2020)	A tertiary center in Belgium	A single-lane rapid IgG/IgM lateral flow assay directed to the nucleocapsid protein of SARS-CoV-2 (COVID-19 IgG/IgM Rapid Test Cassette; Multi-G)	April 22–30	3056 staff	6.4% (n = 197)
Martin et al. (2020)	A tertiary referral hospital in Belgium	Euroimmun anti-SARS-CoV-2 IgG Medizinische Labordiagnostika AG, Lübeck, Germany	April 15–May 18	326 staff members working in COVID-19 highly exposed units	8.3% (n = 27) and 9.5% (n = 31) on days 1 and 15, respectively
Korth et al. (2020)	Germany	SARS-CoV-2-IgG	March 25–April 21	316 HCWs	1.6% (n = 5)
Stubblefield et al. (2020)	Nashville, Tennessee	A validated ELISA against the extracellular domain of the SARS-CoV-2 spike protein	April 3–13	249 HCWs who worked in hospital units with COVID-19 patients for 1 month	7.6% (n = 19)
Chen et al. (2020)	A hospital in China	Enzyme immunoassay and microneutralization assay	NA	105 HCWs exposed to 4 patients	17.1% (n = 18)
Pallett et al. (2020)	Multicenter in UK	EDI novel coronavirus COVID-19 IgG ELISA kit (Epitope Diagnostics, San Diego, CA, USA)	April 8–June 12	1299 symptomatic and 405 asymptomatic HCWs	10.6% in asymptomatic HCWs and 44.7% in symptomatic HCWs
Grant et al. (2020)	An acute integrated care organization in London, UK	Elecsys Anti-SARS-CoV-2 assay (Roche Diagnostics, Basel, Switzerland) for IgG and IgM	May 15–June 5	2004 HCWs	31.6%
Hunter et al. (2020)	An integrated healthcare system with 17 hospital in Indiana	Abbott Architect i2000SR chemiluminescent microparticle immunoassay for anti-SARS-CoV-2 IgG	April 29–May 8	734 HCWs	1.6% (n = 12)
Moscola et al. (2020)	52 sites in New York City	Seven different assays for anti-SARS-CoV-2 IgG	April 20–June 23	40 329 HCWs	13.7% (n = 5523)
Self et al. (2020)	13 medical centers in the United States	Enzyme-linked immunosorbent assay against the extracellular domain of the SARS-CoV-2 spike protein	April 13–June 19	3248 HCWs	6.0 (%) (n = 194)
Plebani et al. (2020)	Main hospitals of the Veneto Region of Italy	Maglumi 2000 Plus (New Industries Biomedical Engineering Co., Ltd (Snibe), Shenzhen, China)	February 22–May 29	8285 HCWs	4.6% (n = 378)
Children					
Torres et al. (2020)	A large school community in Santiago, Chile	The novel coronavirus (2019-nCoV) IgG/IgM Test Kit (Colloidal Gold) from Genrui Biotech Inc., China	May 4–19 (8–10 weeks after a school outbreak)	1009 students	9.9% (95% CI 8.2–11.8%)
Dingens et al. (2020)	Seattle Children's Hospital	Abbott SARS-CoV-2 IgG chemiluminescent microparticle immunoassay	March and April	1775 samples collected from 1076 children	1% (n = 10)
Pregnant women					
Flannery et al. (2020)	Two centers in Philadelphia	ELISA for SARS-CoV-2 IgG and IgM antibodies	April 4–June 3	1293 parturient women	6.2% (n = 80)
Crovetto et al. (2020)	Three university hospitals in Barcelona, Spain	VIRCLIA (Vircell Microbiologist, Granada, Spain) for anti-SARS-CoV-2 IgG, IgM, and IgA antibodies	April 14–May 5	372 women at 10–16 weeks of gestation and 502 during delivery	14% (n = 125)

CI, confidence interval; COVID-19, coronavirus disease 2019; NA, not applicable; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

intermediate-risk group than in the high-risk group (2/37 (5.4%) vs 3/244 (1.2%), $p = 0.13$) (Korth et al., 2020).

At Vanderbilt University Medical Center in Tennessee, 249 HCWs were investigated. These HCWs had regularly had direct contact with units housing adult COVID-19 patients in the month prior to undergoing testing with a validated ELISA against the extracellular domain of the SARS-CoV-2 spike protein (Stubblefield et al., 2020). Overall, 19 (7.6%) of the healthcare personnel tested positive for SARS-CoV-2 antibodies, and seropositivity was more common among those who reported not generally wearing PPE for all encounters when compared to those who reported always wearing PPE (15.8% vs 4.3%, $p = 0.07$) (Stubblefield et al., 2020).

In China, 105 HCWs exposed to four laboratory-confirmed COVID-19 patients received testing with an enzyme immunoassay (EIA), as well as a microneutralization assay, to assess the seroprevalence on day 14 of quarantine, in which 17.14% ($n = 18$) of HCWs were seropositive (Chen et al., 2020a, b). A higher risk of seroconversion was found for doctors exposed to COVID-19 patients (OR 346.837, 95% CI 8.924–13479.434), while a lower risk of seroconversion was closely related to direct contact with COVID-19 patients wearing face masks (OR 0.127, 95% CI 0.017–0.968) (Chen et al., 2020a, b).

Based on the above findings (Table 2), HCWs are at high risk of acquiring SARS-CoV-2 infection, and adequate PPE could help protect them from COVID-19.

In the UK, a multicenter investigation showed that the seroprevalence was 10.6% among 405 asymptomatic HCWs and 44.7% among 1299 symptomatic HCWs (Pallett et al., 2020). In another investigation in the UK, an overall seropositivity rate of 31.6% among HCWs was found, which was highest among staff working in a clinical environment with direct patient contact (34.7%) and lowest among those working in non-clinical environments without patient contact (22.6%) (Grant et al., 2020).

In contrast, a study in the USA showed that employees with heavy COVID-19 exposure had antibody prevalence similar to those with limited or no exposure and suggested that PPE use seems effective in the prevention of COVID-19 infection in HCWs (Hunter et al., 2020a, b). Another study showed similar findings, i.e. that seroprevalence was lower among personnel who reported always wearing a face covering while caring for patients (6%), compared with those who did not (9%) (Self et al., 2020). In the largest cohort study enrolling 40,329 HCWs in New York City, the overall seroprevalence was 13.7% ($n = 5523$); however, only 9.0% ($n = 3077$) among 34 251 without PCR testing were seropositive (Moscola et al., 2020).

Male and female population

Several population-based studies have demonstrated differences in seroprevalence rates among male and female subjects (Pollán et al., 2020; Stringhini et al., 2020; Amorim Filho et al., 2020; Sood et al., 2020; Rosenberg et al., 2020).

In New York, the weighted seroprevalence rate in males was 14.8% (95% CI 13.8–15.8%), which was numerically higher than that in females (13.3%, 95% CI 12.4–14.2%) (Rosenberg et al., 2020). In Switzerland, the rate of positive SARS-CoV-2 serology tests among males was 9.0% (118/1312), which was higher than that among females, at 6.9% (101/1454) (Erikstrup et al., 2020). In Los Angeles, the unweighted portion of the population positive for IgM or IgG among males was 5.18% (95% CI 3.10–8.07%), which was numerically higher than that among females (3.31%, 95% CI 1.94–5.24%) (Sood et al., 2020). In Brazil, males had a higher seroprevalence, after adjustment, than females (4.1% vs 3.5%, respectively), but the difference was not statistically significant (OR 1.20, 95% CI 0.82–1.76) (Amorim Filho et al., 2020). A similar trend was observed in a French study, in which the seroprevalence was higher in males than in females, but it did not differ significantly (2.82% vs 2.69%) (Gallian et al., 2020).

However, in Spain, the seroprevalence among males and females was similar, as assessed by the point-of-care test (5.0%, 95% CI 4.7–5.5% vs 5.0%, 95% CI 4.6–5.4%) and immunoassay (4.6%, 95% CI 4.2–5.0% vs 4.6%, 95% CI 4.2–5.0%) (Pollán et al., 2020). In the USA, there was no clear association between seroprevalence and sex across sites (Havers et al., 2020).

Overall, these findings indicate that the seroprevalence does not differ significantly between males and females.

Children

Four population-based studies have demonstrated a lower seroprevalence in children (Pollán et al., 2020; Stringhini et al., 2020; Havers et al., 2020; Sutton et al., 2020). Compared to subjects aged 20–49 years, children aged 5–9 years had a significantly lower seroprevalence of 0.8% (1/123) (relative risk 0.32, 95% CI 0.13–0.63) in a Swiss surveillance study (SEROCoV-POP) (Stringhini et al., 2020). In Spain, the ENE-COVID study showed that the seroprevalence rates in subjects aged 0–19 years were 3.4% using the point-of-care test and 3.8% by immunoassay, which were lower than the rates reported for any other age group (4.4–6.0% using the point-of-care test and 4.5–5.0% by immunoassay) (Pollán et al., 2020). In the USA, the seroprevalence in subjects aged 0–18 years ranged from 0.7% (95% CI 0–2.5%) in Western Washington State to 5.8% (95% CI 0–14.3%) in Minneapolis-St Paul-St Cloud metro area (Minnesota) (Havers et al., 2020). Moreover, the seroprevalence in this age group was numerically lower than that in other age groups in Western Washington State, New York, Louisiana, Missouri, and Connecticut (Havers et al., 2020).

In addition, a cross-sectional study using the novel coronavirus (2019-nCoV) IgG/IgM Test Kit (Colloidal Gold; Genrui Biotech Inc., China) was conducted 8–10 weeks after a school outbreak, and the results showed antibody positivity rates of 9.9% (95% CI 8.2–11.8%) for 1009 students (Table 2). Moreover, the positivity was associated with a younger age ($p = 0.01$), lower grade ($p = 0.05$), prior RT-PCR positivity ($p = 0.03$), and history of contact with a confirmed case ($p < 0.001$) (Torres et al., 2020). In another study (Dingens et al., 2020), the seroprevalence in children who had visited Seattle Children's Hospital during the initial Seattle outbreak was determined using the Abbott SARS-CoV-2 IgG chemiluminescent microparticle immunoassay, and only eight children were found to be seropositive, with a seroprevalence of 0.7% (Table 2).

Overall, children seem to have a lower seroprevalence than adults, which is consistent with previous epidemiological findings of laboratory-confirmed COVID-19 cases (Lee et al., 2020a, b; Wang et al., 2020; Huang et al., 2020; Li et al., 2020a, b).

Other populations

Pregnant women can be infected by SARS-CoV-2, although data in this population are limited (Ashraf et al., 2020; Barbero et al., 2020; Sahin et al., 2020; Chen et al., 2020a, b; Schmid et al., 2020; Yu et al., 2020). Recently, 1293 parturient women were tested for SARS-CoV-2 IgG and IgM antibodies to the spike receptor-binding domain antigen using an ELISA at two centers in Philadelphia from April 4 to June 3, 2020. The results demonstrated that 80/1293 (6.2%) parturient women possessed IgG and/or IgM SARS-CoV-2-specific antibodies (Table 2) (Flannery et al., 2020). Another study at three university hospitals in Spain showed that 54/372 (15%) women in the first trimester of pregnancy and 71/502 (14%)

women in the third trimester had anti-SARS-CoV-2 IgG, IgM, or IgA using the VIRCLIA test (Vircell Microbiologist, Granada, Spain) (Crovetto et al., 2020).

A previous study of 187 COVID-19 patients showed that the risk of COVID-19 was higher for patients with blood group A than for those with a blood group other than A (OR 1.544, 95% CI 1.122–2.104; p = 0.006), while patients with blood group O had a lower risk of COVID-19 than patients with non-O blood groups (OR 0.649, 95% CI 0.457–0.927; p = 0.018) (Wu et al., 2020). Furthermore, Gallian et al. observed that the proportion of seropositivity was significantly lower in group O donors than in other donors (1.32% vs 3.86%, p = 0.014) (Gallian et al., 2020).

Patients undergoing hemodialysis are also at risk of COVID-19 transmission due to the need for frequent hospital stays, and therefore the difficulty in maintaining physical distancing (Yau et al., 2020; Tang et al., 2020; Arslan et al., 2020). The seroprevalence in hemodialysis patients ranged from 2.8% (16/563) to 3.6% (35/979) in a study in China (Xu et al., 2020). Another study showed the overall SARS-CoV-2 seroprevalence to be 36.2% (129/356) in hemodialysis patients, and 40.3% (n = 52) of them were asymptomatic or had negative PCR results (Clarke et al., 2020).

Association of seroprevalence rates with the country's incidence of COVID-19

In this review, no significant association was found between the incidence of COVID-19 cases and the associated seroprevalence (Table 1). Even within the same country, the seroprevalence ranged from 0.1% to 12.5% in the USA, and from 0.05% to 4.0% in Brazil (Amorim Filho et al., 2020; Havers et al., 2020; Ng et al., 2020; Rosenberg et al., 2020; Silveira et al., 2020; Sood et al., 2020). These findings may be due to the fact that anti-SARS-CoV-2 antibody seroprevalence varies according to the different study countries/regions, study populations, timing during the period of the COVID-19 pandemic, and methods used for serology testing. Therefore, the seroprevalence reported in this article can only reflect the situation of the time and place in which the surveillance investigation was performed and with the specific test method used. In fact, the number of COVID-19 cases is still growing rapidly, and given the time-sensitivity, a true estimation of the epidemiology of SARS-CoV-2 infection remains a great challenge. Therefore, such seroprevalence surveillance should be continued and is necessary to estimate the burden of COVID-19.

Conclusions

The seroprevalence of anti-SARS-CoV-2 antibody can vary across different regions and can increase over time during longitudinal follow-up. Although HCWs, especially those caring for COVID-19 patients, are considered a high-risk group, the seroprevalence in this group may not be higher than that observed in other groups if they wear adequate PPE. Regarding sex, no statistically significant difference was found between male and female subjects. Some studies have shown that children have a lower risk than other age groups, while others have not. Finally, the seroprevalence can vary according to different populations, such as in pregnant women and patients undergoing hemodialysis; however, relevant studies are limited. Therefore, further continued surveillance of seroprevalence is warranted to estimate and monitor the growing burden of COVID-19.

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We declare no conflict of interest.

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