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Seroprevalence of SARS-CoV-2 antibodies among oral health care workers with natural seroconversion: a systematic review and meta-analysis

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Aerosol and droplet exposure makes oral health care workers (OHCWs) highly susceptible to transmissible infections, for example with SARS-CoV-2. Population-based screening is useful in understanding public health interventions in COVID-19. This systematic review with meta-analysis presents the prevalence of SARS-CoV-2 antibodies among OHCWs. An electronic search has been performed to identify records indexed in Medline, Web of Science, Scopus, and the Cochrane Library until December 2023. All observational studies providing data on SARS-CoV-2 antibodies in OHCWs with natural seroconversion were included. The quality of 722 records was evaluated using the Joana Brigg's Institute (JBI) critical appraisal tool. Finally, ten studies were considered as eligible encompassing point-seroprevalence data on 6,083 dental professionals (dentists, assistants, and administrative staff) from seven European countries and Brazil. The antibody seroprevalence was pooled by a meta-analysis performed with MedCalc® statistical software. Applying random effects model, the overall seroprevalence of immunoglobulin G antibodies among OHCWs was estimated at 13.49% (95% CI 9.15–18.52%). The data indicate a somewhat increased occupation-specific risk for COVID-19 but more studies are required, especially later in the pandemic and following vaccination.

Keywords COVID-19, Health personnel, Seroprevalence, SARS-CoV-2, Antibody

Globally, the COVID-19 pandemic has resulted in a significant number of infections and deaths. It is estimated that, due to occupational risks and lack of protective equipment, 11% (95% CI 7–15%) of healthcare workers worldwide were infected by the SARS-CoV-2 virus in 2020[1]. The results of a systematic review and meta-analysis of studies that had included over 1,000 health care workers (HCWs) before the era of vaccination indicated an 8% (95% CI 6–10%) seroprevalence rate of SARS-CoV-2[2].

Oral health care workers (OHCWs) are particularly vulnerable to contracting transmissible diseases due to the nature of their professional practice[3].The transmission of COVID-19 is primarily through the contact of the oral, nasal, and ocular mucosae with droplets produced when a sick person sneezes, coughs, or speaks[4]. Additionally, direct or indirect contact with saliva can also lead to transmission[5]. It is worth noting that the aerosol generated during healthcare procedures, particularly during dental interventions, can be a significant means of transmitting various pathogens, including the SARS-CoV-2 virus[6]. The COVID-19 pandemic has prompted a worldwide discourse on the occupational risks linked to dental practice[7]. Consequently, more focus has been put on the implementation of biosafety protocols, the reinforcement of physical barriers, the reduction of aerosol generation, the vigilant monitoring of patients for COVID-19 symptoms, and the testing of both dental personnel and patients[8].

To collect epidemiological data, antibody testing serves as cost-effective means of choice. Using enzyme-linked immunosorbent assays (ELISA), chemiluminescent immunoassays (CLIA), or rapid diagnostic testing (RDT), the immune system of an individual can be evaluated by measuring the reactivity of its antibodies,

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like immunoglobulin M (IgM) and immunoglobulin G (IgG)[9]. Furthermore, neutralization tests (NTs) quantify neutralizing antibodies that can bind to viruses and prevent them from replicating[10]. According to the manufacturer's evaluation, the tests' diagnostic specificity and sensitivity may vary. The utilization of purified or recombinant protein antigens, such as spike (S), envelope (E), membrane (M), nucleocapsid (N), or receptor binding domain (RBD) proteins, as well as the meticulous assay optimization, can affect the reliability of these tests[11,12]. The Food and Drug Administration (FDA) has approved more than fifty test systems (https://www.fda.gov). The FDA website reports test properties such as antibody isotype detected, sensitivity, specificity, and positive and negative predictive values[13].

The question whether OHCWs face a greater risk of infection compared to community transmission remains unresolved. Several studies have indicated that OHCWs had either a lower or a comparable risk of infection compared to the general population. Some of these studies reported a missing correlation between clinical practice and the occurrence of infection[3,14,15]. Currently, there is a lack of knowledge regarding the overall seroprevalence of SARS-CoV-2 antibodies among unvaccinated OHCWs and associated factors. Hence, the present comprehensive review and meta-analysis aimed at ascertaining the prevalence of SARS-CoV-2 antibodies among dental HCWs. Estimates on prevalence by population-based serological testing are crucial in shedding light on SARS-CoV-2 epidemiology and in understanding public health measures in response to COVID-19.

Methods

Study design, registration, and search protocol

The protocol for this systematic review and meta-analysis was submitted to the International Prospective Register of Systematic Reviews (PROSPERO) and received approval under the registration number CRD42023399599. The project was conducted in adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, as indicated by the completion of the PRISMA checklist (Supplementary file 1)[16]. A comprehensive search was performed to identify peer-reviewed articles indexed in Medline (via PubMed), Web of Science, Scopus, and the Cochrane Library until December 2023.

The applied search strategy included variations of the following terms: "SARS-CoV-2"," COVID-19", "coronavirus", "seroprevalence", and "oral healthcare worker". The terms and keywords were adapted for each database as required (Supplementary file 2). A thorough manual search was conducted covering the bibliographies of the original papers and review articles that had been included. Additionally, we searched grey literature sources, conference proceedings, and preprint repositories to ensure comprehensive coverage of relevant studies.

Eligibility criteria

We included all observational studies in our analysis. However, we only considered longitudinal studies if they had reported a point prevalence. Studies were excluded if they did not provide any information on dental personnel or if they reported the presence of SARS-CoV-2 antibodies in response to a vaccine. The studies had to investigate in a sample of OHCWs the prevalence of SARS-CoV-2 using a serological test capable of detecting IgG antibodies among unvaccinated OHCWs. All the studies obtained from various databases were consolidated in Endnote version 20, and duplicate references were identified and removed.

Study selection & data extraction

Two reviewers (ES and OF) independently examined the titles and abstracts as part of the initial article selection process. Subsequently, the authors obtained and thoroughly examined the full texts of all relevant studies. Any disagreements were resolved through discussion. Publications that did not meet the eligibility criteria were excluded, with the reasons for exclusion being documented. Subsequently, data was extracted and consolidated using a standardized data collection sheet. All data was classified in relation to year of publication, country, city/region, study timeline, setting, sample size, testing method, sensitivity, specificity, and outcomes according to the aims of the present study.

Quality assessment

In order to evaluate the methodological quality of each included study, two reviewers (ES and OF) independently employed the critical appraisal tool for prevalence studies created at the Joana Brigg's Institute (JBI)[17]. The other authors confirmed the evaluation results, and any significant inconsistencies were identified and addressed through discussion and verification. The tool has nine items, each of which can be answered with "yes", "no", "unclear", or "not applicable". The percentage of "yes" answers to the items in each study served as the basis for evaluation. A high (≥70%) proportion of "yes" responses referred to high-quality studies (with a low risk of bias), while a moderate (50–69%) and low (≤49%) proportion of 'yes' responses referred to moderate- and low-quality studies, respectively[17].

Statistical analysis

The meta-analysis was conducted using MedCalc® Statistical Software version 22.019 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2024) in order to pool seroprevalence of antibodies. For each trial, the seroprevalence of IgG antibodies with a 95% confidence interval (CI) was determined. The I^2 statistic was used to evaluate heterogeneity between the chosen studies. The I^2 statistic shows the proportion of overall study variation that can be attributed to heterogeneity rather than chance. In order to account for the significant heterogeneity observed in the results, a random effects model was utilized to estimate the pooled seroprevalence. The Forest Plot was employed to visually represent the calculated proportion from each study as well as the combined effect estimate with a 95% CI. Prevalence data were sorted in chronological order to consider the confounding factor time which is characteristic of a rapidly spreading epidemic. To assess publication bias, the symmetry of the funnel plots was visually evaluated and the results were further corroborated using Egger's test. A significance level of $P < 0.05$ for Egger's test was indicative of the presence of publication bias.

Results

Selection of studies

The literature search process is depicted in a flowchart following the PRISMA format as illustrated in Fig. 1. The initial database search yielded 1,579 entries from which 857 duplicates were removed. The search in preprint databases showed no study reports that had not been published or whose publication was ongoing. Two more records were found and included after examining the reference lists. Altogether, 722 items were included in the title and abstract screening phases of the present study. Later, 15 articles remained to be appraised for eligibility based on the inclusion criteria. After full-text assessment, five more papers were excluded for the following reasons: no data reported on dental HCWs in two studies[18,19]; only seven cases (i.e. an insufficient number of participants) reported in one study which actually was a case series[20]; report on the Immunoglobulin-G (IgG) titer response of the SARS-CoV-2 mRNA vaccine (BNT162b2) but no data on the prevalence of COVID-19

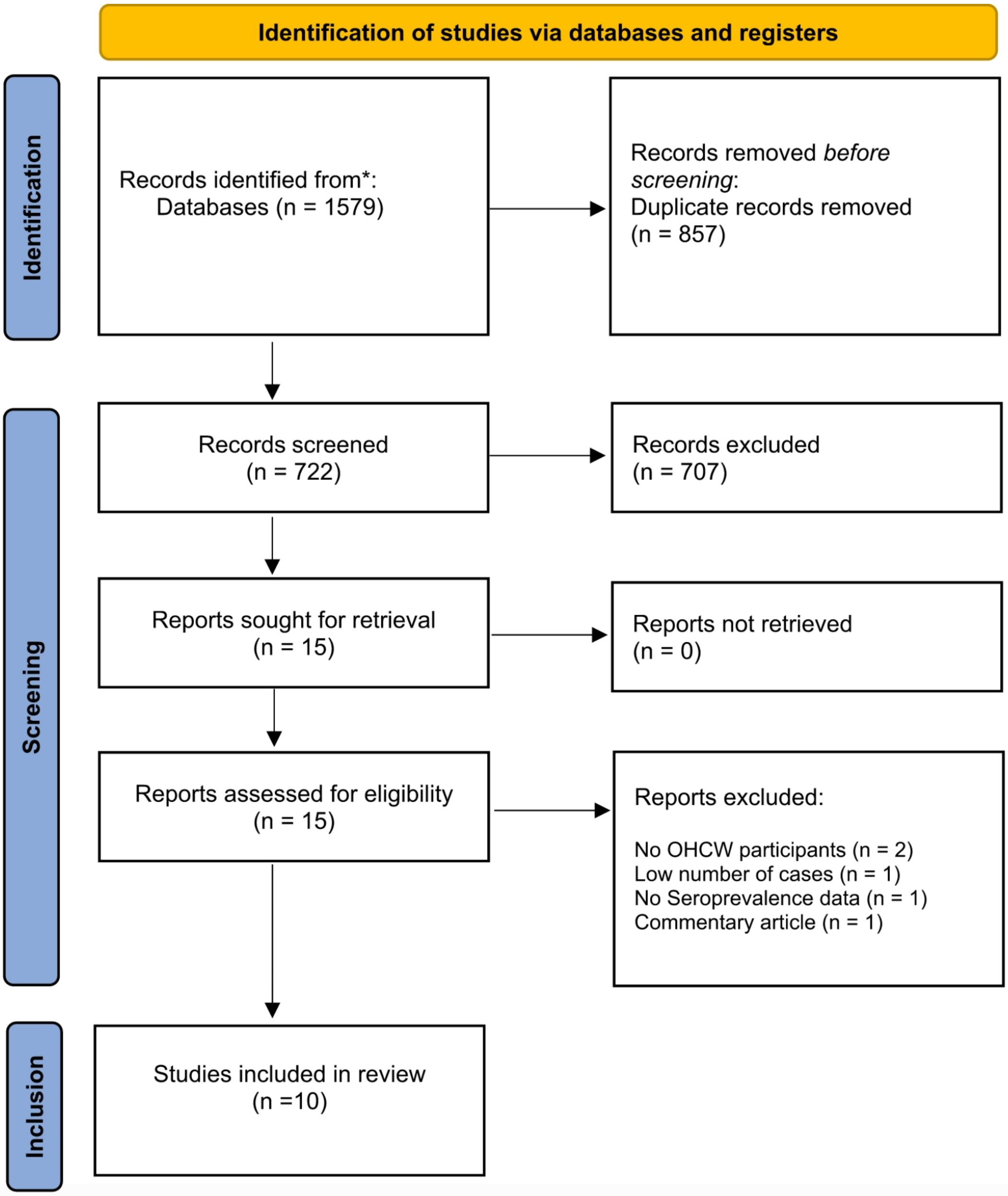

Fig. 1. Flow diagram for selection of articles.

infection in one study[21]; only a commentary on another work but no original data reported in one study[22]. Finally, ten studies were included in the current systematic review.

Study characteristics

The ten studies that had been included contained point seroprevalence data on 6,083 OHCWs from seven countries in Europe (Italy, United Kingdom, Russia, Spain, Poland, Germany, Sweden) and one country in South America (Brazil). Table 1 shows the main characteristics of the studies including seroprevalence rates, sensitivity, and specificity of the tests employed. Most of the studies had been conducted between May and November of 2020. One study from Brazil and one from Germany had been conducted from January to March 2021[14,23]. The lowest sample size was 50, the highest 2,784 [14,24]. All studies included had assessed the seroprevalence of IgG antibodies against SARS-CoV-2. All applied tests had targeted diverse spike-surface proteins, only the Swedish study had additionally detected vaccine independent nucleocapsid antibodies. Based on the manufacturers' data, the sensitivity of the tests ranged from 94.4 to 100% and the specificity from 85 to 99.6%, (Table 1). The main outcomes of the studies included are provided in Table 2.

Quality assessment

According to the JBI critical appraisal tool, studies were evaluated based on a scale between 1 and 9. In consequence, all of the studies showed a low risk of bias (Supplementary file 3). In this regard, nine studies achieved the highest JBI score while the study of Abo-Leyah et al. scored 7 as it had used a small sample size ($n=50$) and it had not reported the response rate[24].

Meta-analysis of the Seroprevalence

In a meta-analysis using random effects modeling, the seroprevalence of IgG antibodies among the 6,083 OHCWs in all studies was estimated to be 13.49% (95% CI 9.15–18.52%) (see Supplementary file 4 and Fig. 2). The prevalence of IgG seropositivity varied between the studies and ranged from 5.2 to 26%. The highest prevalence was observed in Scotland (UK)[24]. A thorough examination of the funnel plot symmetry, as supported by the Egger test and presented in Supplementary file 4, did not reveal clear evidence of publication bias. However, a meta-analysis to determine the factors influencing the prevalence could not be conducted due to significant heterogeneity in the measures and questionnaires employed across the studies included.

Discussion

This is the first systematic review and meta-analysis that estimates exclusively the global seroprevalence of SARS-CoV-2 antibodies among unvaccinated dental HCWs. In the present study, an effort was made to address the limitations of earlier systematic studies and to supplement their findings accordingly. A meta-analysis from 2022 had revealed a prevalence of 9.3% in OHCWs[3]. The research had combined population-based antibody measures and PCR based diagnosis of acute infections but did not take into account the inherent variability between the different types of measurements. Two studies had not separated OHCWs from other medical doctors and one study had collected data through an online questionnaire based on self-reported information[25]. Zooming in on

First author, year (ref. no.)	Country/ city/region	Study period	Setting	NO	AB	Method	Sensitivity	Specificity	Seroprevalence (IgG)
Fredriksson, 2023[1]	Sweden/ Stockholm	June 2020	public dental service	341	IgG	Luminex (immunoassay) and ELISA	99.4%	99.1%	$n=35$ (10.3%)
Cintora, 2022 [2]	Spain/ Madrid	May/ June 2020	University Dental Clinic	195	IgG IgM	2019-nCoV IgG/IgM Rapid Test Cassette	IgG: 100% IgM: 85%	IgG: 98% IgM: 96%	$n=39$ (20%)
Sarapultseva, 2021[3]	Russian Federation/ Ekaterinburg	May/ Aug. 2020	public & private dental settings	157	IgG IgM	enzyme immunoassay kits (VECTOR-BEST)	NR	NR	$n=19$ (11.5%)
Gallus, 2021[4]	Italy/ Lombardy region	May-Sept. 2020	public & private dental settings	499	IgM IgG	Ab-RDT immunochromatography test KHB® Diagnostic Kit (KHB, Shanghai, China)	95.1%	99.3%	$n=54$ (10.8%)
Abo-Leyah, 2021[5]	Scotland (UK)/Tayside	May-Sept. 2020	large teaching hospital	50	IgG	chemiluminescent immunoassay	95–100%	NR	$n=13$ (26%)
Shields, 2021[6]	UK/the West Midlands area	June 2020	dental settings	1507	IgG, IgA, IgM	IgGAM enzyme-linked immunosorbent assay (ELISA)	98.6%	98.3%	$n=246$ (16.3%)
Duś-Ilnicka, 2022[7]	Poland/ Wroclaw (Lower Silesia)	Sept.-Nov. 2020	University Dental Clinic	127	IgG	enzyme-linked immunosorbent assay (ELISA)	NR	NR	$n=8$ (6.2%)
Ribeiro, 2022[8]	Brazil/The Federal District	Oct.-Nov. 2020	private dental clinics	324	IgG IgM	OnSite COVID-19 IgG/IgM Rapid Test® (CTK, Biotech Inc, Poway, CA, USA)	97.1%	97.8%	$n=62$ (19.1%)
Miguita, 2022[9]	Brazil/Minas Gerais	Jan.-Mar. 2021	University Dental Clinic	99	IgG IgM	IgG/ IgM Rapid Test (732 – 10, Labtest Diagnóstica)	NR	NR	$n=16$ (16.2%)
Mksoud, 2022[10]	Germany/5 urban regions	Jan./ Apr. 2021	private dental clinics	2,784	IgG	anti-SARS-CoV-2-ELISA; Euroimmun, Lübeck, Germany	94.4%	99.6%	$n=146$ (5.2%)

Table 1. Characteristics of included studies. *NR* Not reported, *RDT* Rapid Diagnostic Test, *ELISA* Enzyme-linked Immunosorbent Assay.

First author/Year/Country	Conclusions
Fredriksson/2023, Sweden[1]	In conclusion, the Seroprevalence of SARS-CoV-2 infection in the dental staff of the Public Dental Service was approximately similar to that in a university hospital in the same region, and approximately equal compared to that the general population during the same time period.
Cintora/2022, Spain[2]	Among professionals at a dental clinic, SARS-CoV-2 was more prevalent in orthodontists than in the rest of dental sub-disciplines, with the lowest rates among the administrative staff.
Sarapultseva/2021, Russia[3]	Results showed that the prevalence of SARS-CoV-2 infection was not associated with sex ($\chi 2 = 0.394$, df = 1, $P = 0.53$, power = 0.09) or the role of the member in the dental team (dentist/dental assistant; $\chi 2 = 0.211$, df = 1, $P = 0.646$, power = 0.07). The most significant differences in the prevalence of SARS-CoV-2 infection were recorded between clinics A and C.
Gallus/2021, Italy[4]	Except the estimates for geographic area, none of the adjusted odds ratios (AORs) for other socio-demographic characteristics reached statistically significance. However, the authors found higher AORs in men, older subjects, participants living in relatively small municipalities (compared with subjects living in capitals of Lombardy provinces) and administrative personnel (compared to dentists).
Abo-Leyah/2021, Scotland[5]	Compared to both sets of population controls, HCWs had 3.6 times greater odds of a positive test compared to local controls (OR 3.4, 95% CI 1.85–6.16; $p < 0.0001$) and compared to Scotland-wide controls (OR 3.6, 95% CI 2.99–4.32; $p < 0.001$). Dental healthcare workers were the most frequently associated with a higher rate of SARS-CoV-2 antibody (26%).
Shields/2021, UK[6]	Natural SARS-CoV-2 infection leads to a serological response that remains detectable in over 70% of individuals 6 months after initial sampling and 9 months from the peak of the first wave of the pandemic. This response is associated with protection from future infection.
Duś-Ilnicka/2022, Poland[7]	There were no significant statistical differences amongst the subgroups (dentists, chairside personnel and administrative workers) regarding a positive IgG ELISA value.
Ribeiro/2022, Brazil [8]	The presence of antibodies was positively associated with confirmed diagnosis of COVID-19, loss of taste or smell, confirmed diagnosis of COVID-19 in a household member, but negatively associated with the treatment of patients with fever.
Miguita/2022, Brazil[9]	During this study, detection of antibody levels for SARS-CoV-2 was present in 16.2% dental health care workers. Half of the dental health care workers sustained the positive serology results during the 2 months of this research.
Mksoud/2022, Germany [10]	The results showed that the prevalence of SARS-CoV-2 antibodies among the dental team is comparable to the general population in Germany. However, the authors underpinned that these conclusions were based on weak evidence.

Table 2. Main outcomes of the included studies.

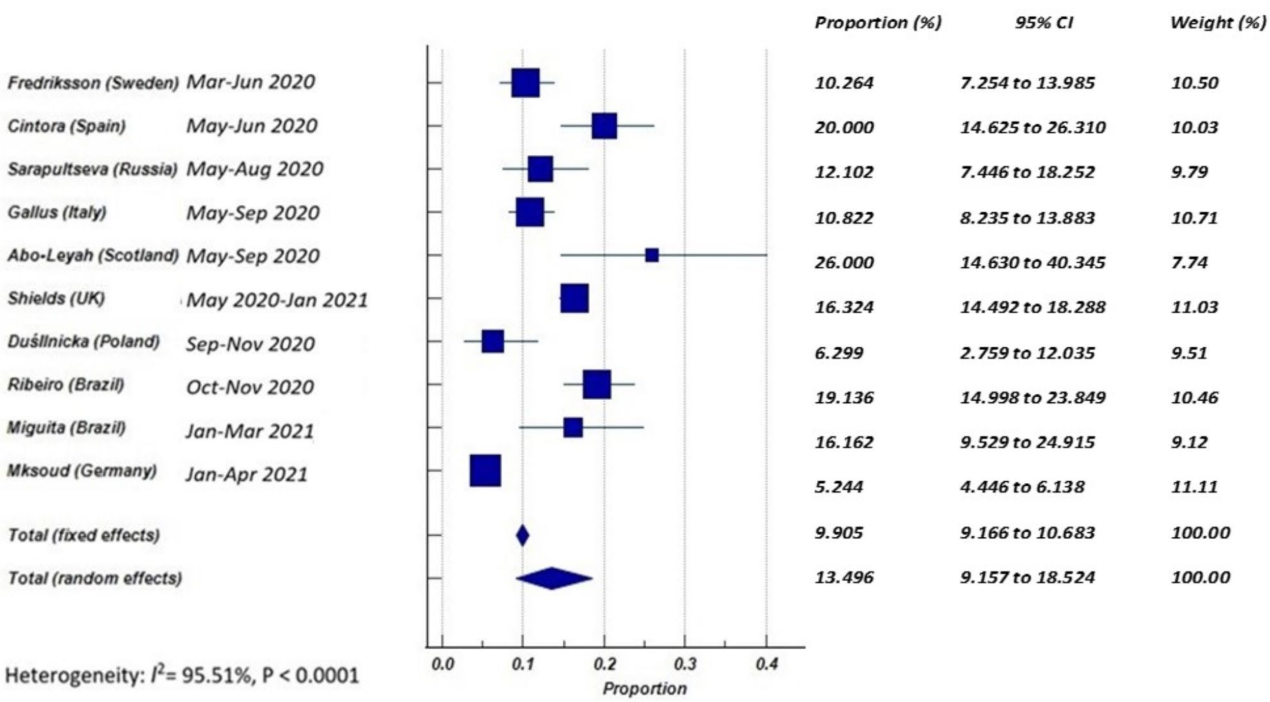

Fig. 2. Forest plot of seroprevalence of SARS-CoV-2 antibodies among oral health care workers.

inclusion and exclusion criteria for the present study, an outline is provided showing the cumulative incidence of SARS-CoV-2 infection based on IgG antibody detection among unvaccinated OHCWs.

In the expanding corpus of scholarly literature that examines the frequency of SARS-CoV-2 infection among healthcare professionals, it is imperative to ascertain if specific occupations exhibit elevated rates of infection. At 13.4%, the seroprevalence in the present meta-analysis is somewhat higher than the rates reported in previous systematic reviews of HCWs from other disciplines (7% and 8.7% in the studies conducted by Gómez-Ochoa et al. (2020) and Galanis et al. (2021), respectively)[1,26]. The results of another meta-analysis also showed that the worldwide SARS-CoV-2 seroprevalence in the general population was 9.47% (95% CI 8.99–9.95%) during the pre-vaccination era[27]. Notable variations in SARS-CoV-2 seroprevalence across different countries and at various times were observed. These variations could be attributed to an array of factors, such as cultural practices, policies, mitigation efforts, health infrastructure, and the efficacy of implementing preventive and control measures[28]. Moreover, the study setting should be considered when interpreting the results. Overall, dentists employed by hospitals that treated patients with confirmed COVID-19 could be at a higher risk for infection than those who work at independent dentistry clinics or in private offices. Notably, the highest rate of infection was reported for OHCWs employed within the National Health Service in the East of Scotland (UK)[24]. Nevertheless, this elevated infection rate should be viewed with caution considering the low participation rate of dental staff in the study. In that study, 50 OHCWs had been included of which 13 with potential mutual dependency tested positive[24]. Even when comparing results obtained from hospitals, that can be considered as reference centers for confirmed cases, highly divergent epidemiological results were observed. While dental personnel in university settings in Madrid (Spain) and Minas Gerais (Brazil) displayed rates above average, the sample at the Wroclaw Medical University had the lowest rate of 6.2% [23,29,30].

The presented data allow for a very limited comparison between different subgroups due to significant variations in study design and lab methods, and due to a lack of reported data on strata within the studies included in the present analysis. Two studies reported no significant statistical differences between the subgroups (dentists, chairside personnel, and administrative workers) regarding a positive IgG ELISA value[30,31]. However, another study showed that the seroprevalence of SARS-CoV-2 was higher among orthodontists compared to other dental sub-disciplines, with the lowest prevalence observed among the administrative staff[29].

The literature search for the present work covered the papers from the start of the epidemic until the end of 2023. With the application of the afore-mentioned inclusion and exclusion criteria, only ten studies remained of which all refer to the pre-vaccination era. SARS-CoV-2 infection leads to antibody production against the spike and nucleocapsid proteins, whereas mRNA SARS-CoV-2 vaccines target the spike protein exclusively[32,33]. It is possible to differentiate between antibodies produced during a natural infection and those generated after mRNA vaccination by seeking out anti-N antibodies[34]. In the present meta-analyses, the Swedish group analyzed nucleocapsid antibodies as evidence of natural infection but, in the first months of the pandemic, this critical distinction had no relevance, because the mRNA vaccination was not yet on the market.

Some of the reviewed studies have mitigated bias by including a large number of participants; however, there is potential selection bias due to some investigators recruiting from a limited number of healthcare centers. Another limitation is the lack of data from a diverse range of countries, which could have provided a more comprehensive estimate of the global seroprevalence of anti-SARS-CoV-2 IgG antibodies among OHCWs. Importantly, the majority of studies had been conducted in Europe with sufficient access to personal protective equipment. However, the studies lacked specific information on local infection control practices. An additional limitation was the significant level of heterogeneity across the different studies. We addressed this issue by using a random effects model analysis when presenting the results. Also, the analysis of potential factors influencing seroprevalence rates was limited. Since most of the studies focused on healthcare workers as a whole, specific demographic characteristics within OHCW groups could not be extracted. Furthermore, various immunoassays had been utilized. Although most of the studies reported sensitivities and specificities above 90%, there were still variations possibly affecting seroprevalence rates.

Conclusion

Considering the limitations of the included studies, the overall seroprevalence of anti-SARS-CoV-2 IgG antibodies among OHCWs with natural seroconversion was estimated to be 13.49% (95% CI 9.15–18.52%). These findings from a selection of European and Brazilian dental teams indicate that the seroprevalence of SARS-CoV-2 antibodies based on natural seroconversion may be higher compared to other healthcare professionals (7-9%) and the general population (9.5%). The present study is the only systematic review summarizing exclusively the IgG results of OHCWs with natural seroconversion from all subtypes of professions such as dentists, assistants, and administrative staff.

Data availability

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

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Author contributions

E.S: Conceptualization, Investigation, Methodology, Formal Analyses, Writing-original draft, Review& & Editing,Project administration. M.L: Methodology, Writing- Original Draft Preparation. H.H.K: Investigation, Writing- Review and Editing. N.J: Investigation, Writing – Review, Institutional support. O.F: Supervision, Validation, Methodology, Formal Analyses, Writing-original draft; and Writing - Review & Editing. All authors reviewed the manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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