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SARS-CoV-2 IgG Amongst Dental Workers During the COVID-19 Pandemic

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ABSTRACT

Objectives: Since the SARS-CoV-2 outbreak in 2019, special safety protocols have been introduced in dentistry. Dental professionals were determined to be mostly at risk for contracting the virus due to aerosol-generating procedures used. This preliminary study starts the cycle of the laboratory protocols describing the quality and efficacy of laboratory tests in the SARS-CoV-2 immunoglobulin G (IgG) detection in the serum of asymptomatic dental personnel during the last quarter of 2020.

Methods: IgG levels were measured with the use of a semi-quantitative enzyme-linked immunosorbent assay (ELISA) in vitro diagnostic kit in the serum of a study group that consisted of 127 employees of the dental clinic divided into 3 subgroups: SUB1: dentists (n = 67); SUB2: dental assistants, dental hygienists, nurses, laboratory workers (n = 40); SUB3: administrative workers (n = 20). Pearson analysis of results from the questionnaires attached to the study protocol were provided to assure that the results compare to the participants' impressions about their general health.

Results: Positive ELISA IgG results were found in 6% (n = 4) of the SUB1 group, 7.50% (n =3) of the SUB2 group, and 5% of the SUB3 group. The percentage of participants without work interruption from the beginning of the pandemic was 54% of dentists and 60% of chairside assistants.

Conclusions: Serum IgG prevalence with the use of a semi-quantitative test was low, and further research on the biobanked samples should follow to determine the levels of IgG with quantitative methods and/or to evaluate the presence of neutralising antibodies in dental personnel. Because of the low representation of seropositivity studies in this group, it will be crucial to confirm the risk of COVID-19 transmission in dental offices.

Introduction

Dentistry is a medical profession that has been strongly associated with a major risk of infection during the COVID-19 pandemic,[1,2] since it was established that the SARS-CoV-2 virus is transferred by salivary droplets and by bioaerosols generated from the respiratory tract.[3,4] Because of its availability, saliva represents a noninvasive specimen for COVID-19 research,[5,6] and the SARS-CoV-2 viral load in this biomaterial has been confirmed in various studies.[7,8] Special precautions in dental studies during the pandemic period were based on the risk of operating in the open oral cavity with the use of aerosol-generating procedures (AGPs).[1,9–11] Common AGPs in the dental office involve the use of such equipment as high-speed air turbines.[12,13] To avoid the potential spread of SARS-CoV-2 during dental AGPs, a high level of personal protective equipment (PPE) is required.[3] At the beginning of the pandemic, when the necessary PPE was scarce due to delays in shipments in the East Asia, Europe, and the US,

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anxiety about getting infected was common amongst medical workers, as in a study presented in Israel.[14–16] Similar fears prompted many dental surgeries around the world to close during the first wave of the pandemic.[2,17,18] As the pandemic progressed, many scientific groups reported that the rates of SARS-CoV-2 infection amongst medical doctors varied amongst countries. As presented by Iyengar et al, dentists were the medical group that was suggested to be more prone to acquiring COVID-19 in India (2 reported COVID-19–related deaths until the end of 2020, percentage not provided).[19] Researchers from Turin, Italy, evaluated the seroprevalence of COVID-19 antibodies amongst medical workers, but they excluded dentists. This research, however, described the group of clinicians who are in direct contact with patients as those who might create antibodies for SARS-CoV-2 with the higher probability (7.5% of the whole study group).[20] In addition, a study from Germany showed that dentists were getting infected by the virus at a rate of 0.2% of the whole medical sector.[21]

Additional problems arise if dental patients are treated in open-plan clinical environments, such as those in teaching hospitals, with multiple patients in dental chairs and operators in close proximity.[12,22] For this reason, protocols created at the beginning of the pandemic assumed that only urgent procedures such as those involving pain reported by the patient or the risk of loss of a tooth should be performed, but other dental procedures should be postponed.[23–25] However, with the advance of the pandemic, dental work became impossible to avoid, despite the dentists' apprehension about being infected with SARS-CoV-2.[25,26]

Testing for SARS-CoV-2–specific immunoglobulin G (IgG) proteins is not a laboratory procedure for the diagnosis of infection with the virus but rather a measurement tool for the immunological response to a previous infection or contact with the virus.[27] The World Health Organisation provides for the optional diagnostics of antibody detection with semi-quantitative serological assays as being suitable for diagnosis of SARS-CoV-2 antibodies, and this measurement tool was used in this research.[27]

The Academic Dental Polyclinic attached to the Wroclaw Medical University (Wrocław, Lower Silesia region, Poland) provides dental treatment for patients in the fields of conservative dentistry, oral surgery, periodontology, prosthodontics, and oral mucosal diseases and is also a teaching unit for around 450 dental students each year. It has been open to patients during the pandemic and performed all necessary procedures in the field of dentistry. The aim of this study was to perform a screening test for SARS-CoV-2 IgG antibodies with the semi-quantitative enzyme-linked immunosorbent assay (ELISA) in vitro diagnostic (IVD) technique amongst the dental workers of the Academic Dental Polyclinic, which provides a workplace for 180 dentists.

Materials

Bioethical statements and data safety

The study protocol in written form was approved by the appropriate Wroclaw Medical University Bioethics Committee before the research started (Decision no. 576/2020). Each of the participants provided informed consent to participate in the study and was able to ask questions regarding the survey, as required by Declaration of Helsinki.

Study group

Specimens were collected from healthy volunteers at the Academic Dental Polyclinic attached to the Wroclaw Medical University (Wrocław, Lower Silesia region, Poland). Healthy volunteers were considered to be individuals without any significant illness relevant to the proposed study, for this reason it has been considered – not undergoing any pulmonary infections by probable COVID-19 background. Volunteers were within the ordinary range of body measurements, were not hospitalised, and were attending the common working space at the Academic Polyclinic. A total number of 127 medical personnel workers from the clinic was included. Volunteers were divided into 3 subgroups:

- SUB1: dentists
- SUB2: dental assistants, dental hygienists, nurses, laboratory workers
- SUB3: administrative workers.

The reason for this kind of subgroup division was the time exposed to direct aerosol contamination (dentist having the most and administrative workers having the least). The inclusion criteria for the study group were working clinically during the COVID-19 pandemic and, for the administrative workers, working in direct collaboration with dentists and dental workers amongst the regional dental clinic's facilities. Exclusion criteria were symptoms of respiratory disease such as cough, fever, or dyspnoea or being under quarantine. Patients were asked to fill in the necessary documents and short questionnaire about the presence of flu-like symptoms, influenza vaccination, number of household members, and days off from professional work in the period from the beginning of the pandemic (15 March) to 28 September 2020. Concerning the subgroups' working hours in the clinic during the pandemic, professionals from SUB1 were working a minimum of 240 hours with patients during the students' clinical classes for a period of 10 months (from October to June). SUB2 and SUB 3 consisted mostly of full-time professionals working 40 hours per week. Most of the doctors in dentistry (SUB1) were working in more than one clinic during some period of the pandemic.

The safety procedures implemented in the Academic Dental Polyclinic and the study group description

All of the clinical groups working in the dental clinic facility who have direct contact with patients have been allocated a higher level of PPE. Triage procedures for patients attending the clinic have been implemented, and phone-only registration has been provided. In the case of suspected respiratory tract disease mimicking symptoms of COVID-19, patients were asked to postpone their dental appointment for 14 days. Enrolled patients have their temperature measured on entrance and are asked to sanitise their hands and fill out the

COVID-19 information sheet. Waiting rooms have been adapted with measured social distancing markers and cleared of flyers, and patients are asked to attend exactly at the time of their visit. In contrast to some dental hospitals that work with the dental chairs in an open plan,[22] the regional dental clinic consists of all closed and separate operating rooms. Additional UV flow lamps were purchased. Gravitational ventilation has been provided, and the equipment is disinfected after each patient.

Venous blood collection and safety procedures

Blood collection was carried out at 3 different time intervals during the third quarter of 2020: 28 September 2020 (day 1, N = 34), 22 October 2020 (day 2, N = 39), and 19 November 2020 (day 3, N = 54) by medical personnel equipped with double nitrile gloves; a disposable suit with long sleeves, legs, and a hood; and an FFP3 mask covered with a surgical mask and a protective medical visor. Blood samples were collected at designated time intervals for each subject to reduce the risk of exposure to exhaled aerosols. Venous blood samples (9 mL) were withdrawn using the Retractable Safety Wingset Steel Needle (Beckton and Dickinson) into coagulant tubes (Beckton and Dickinson). An hour after the collection, the blood samples were centrifuged at 2500 rpm for 20 minutes at room temperature, and the serum was kept at 4°C until analysis on the same day or at −20°C if the laboratory procedures were delayed.

Methods

ELISA serum serological analysis

The level of IgG in blood serum was determined using an IVD-certified ELISA kit for SARS-CoV-2 IgG (COVID-19 [SARS-CoV-2] IgG ELISA, Demeditec Diagnostics GmbH, Lot. COVG-009) according to the procedure recommended by the manufacturer.[28] The qualitative immunoenzymatic determination of specific antibodies was based on the ELISA technique. In accordance with the producer's manual, samples with a concentration of <9 U/mL were considered nonreactive, those ranging from 9 to 11 U/mL were considered equivocal, and samples >11 U/mL were considered reactive. In the case of equivocal sample results, it was recommended by the manufacturer to repeat the test with a fresh sample in 2 to 4 weeks.[28] The manufacturer provided a set of 3 calibrators and 3 levels of controls. Final absorbance values for each control and sample in the plate layout were taken at 450 nm with a correction absorbance at 620 nm using ELISA spectrophotometry (EPOCH).

For the evaluation of the assay, it is a precondition that the absorbance values of the blank should be <0.100; the absorbance values of the negative control should be <0.200 and should be smaller than the cutoff; the absorbance values of the positive control should be greater than the cutoff; and the absorbance values of the cutoff control should be within the limits of 0.150 to 1.300. The results of the level of IgG in units [U] were achieved by mathematical testing using the formula provided in the test insert.

Statistical analysis

Statistical analysis was carried out using 3 libraries: Python (version 3.9.2), Scipy (version 1.4.1), and Numpy (version 1.19.2). The one-way Chi-square test was used to compute the *P* value for the hypothesis test in the observed samples. The choice of statistical assay was dictated by sample sizes. The one-way Chi-square test allowed for the assessment of the independence of the different study subgroups. Chi-square statistical power was 0.85 with a significance level of .05, an effect size of 0.35, and degrees of freedom = 6. Pearson test was used to determine correlations between continuous and categorical variables from the data set. Significance level of the test was .05, with statistical power of 0.91, an effect size value of 0.4, and 7 predictors. Cramer's V test was performed to determine correlation amongst categorical variables obtained from the questionnaire. For Cramer's V statistical test, power was 0.85 with significance level of .05, an effect size of 0.35, and degrees of freedom = 6. Values were established using PWR and DescTools R packages.

Results

The total number of participants involved in the study was 127, and 7 (6.2%) of all volunteers had positive results for SARS-CoV-2 IgG antibody testing with the use of the semi-quantitative IVD test. Questionnaires about the prevalence of flu-like symptoms in the subgroups from the period of 15 March to 28 September 2020 were evaluated statistically. The group characteristics are presented in Table 1.

Table 1 – Study group characteristics in division to 3 subgroups.

Study group	SUB1 group (dentists)	SUB2 group (chairside assistants)	SUB3 group (administrative workers)
No. of participants	67	40	20
Mean age, y	33 (SD, 11.5)	48.5 (SD, 11.7)	44.5 (SD, 15.1)
Sex (male/female)	17/50	4/36	3/17
Percentage of participants without work interruption	54% (n = 36)	60% (n = 24)	50% (10)
Influenza vaccination in the group	16% (n = 11)	5% (n = 2)	0% (0)
BCG vaccination in the group	96% (n = 64)	98% (n = 39)	75% (15)
Positive ELISA IgG results	6% (n = 4)	7.50% (n = 3)	5% (n = 1)
Positive real-time PCR in questionnaire for SARS-CoV-2	9% (n = 6)	2.50% (n = 1)	0% (n = 0)
Average number of cohabiting members in the household	2.00	2.2	2.05

BCG, Bacille Calmette-Guérin; ELISA, enzyme-lined immunosorbent assay; IgG, immunoglobulin G; PCR, polymerase chain reaction.

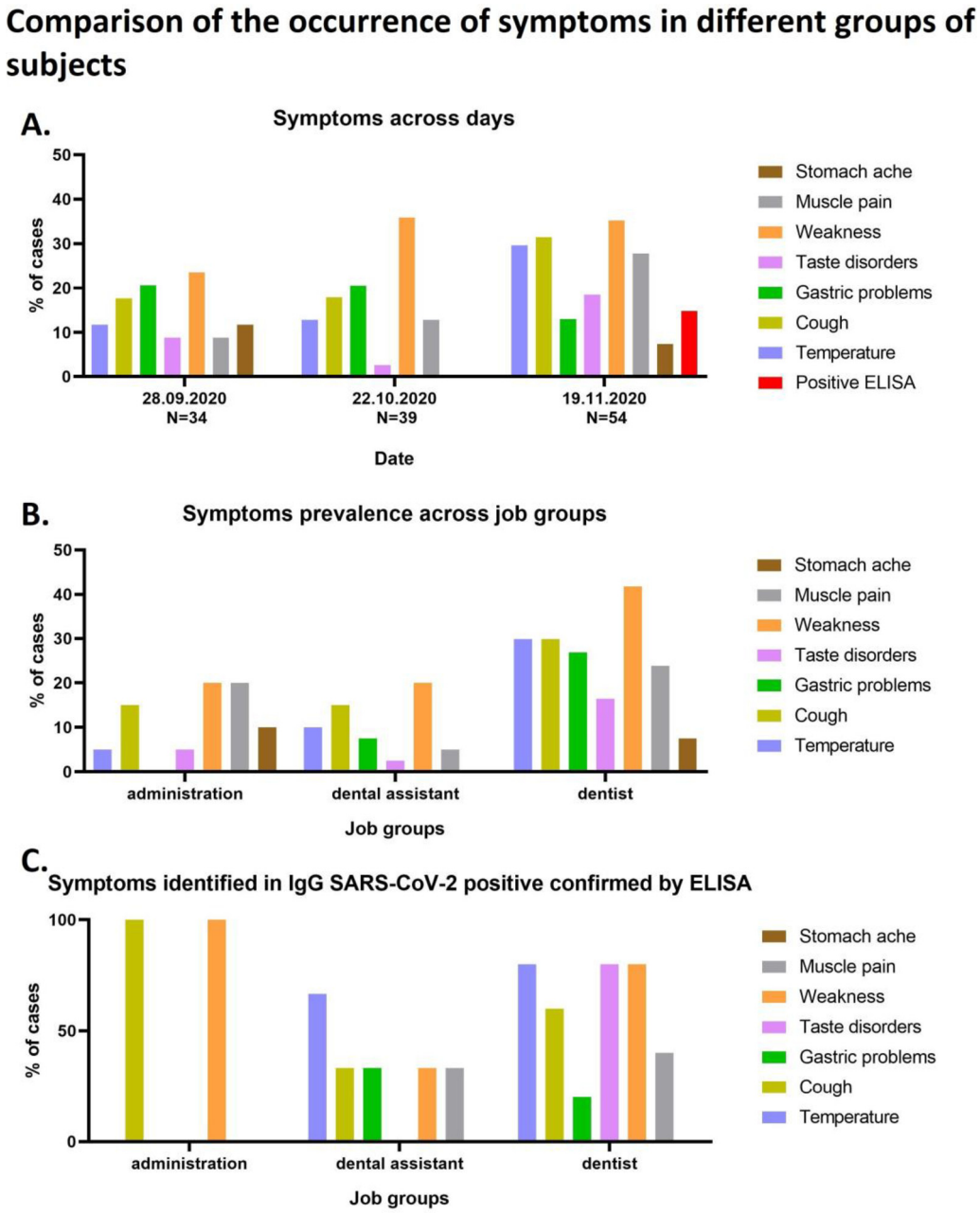

Fig. 1 – A, Prevalence of symptoms in participants on 3 different days in 3 months of blood collection. B, Prevalence of reported symptoms across 3 subgroups of the study: dentists, dental hygienists, and administrative workers. C, Classification of declared symptoms by 3 different subgroups: dentists, dental hygienists, and administrative workers, correlated with positive results of immunoglobulin G (IgG) for SARS-CoV-2.

Dividing the IgG results into subgroups, 6%[4] dentists had positive test results for SARS-CoV-2 IgG, along with 7.5%[3] from group SUB2 (chairside personnel) and 5%[1] from subgroup SUB3 (administrative workers). Collectively, 8 participants in the whole group had positive results for IgG SARS-CoV-2 (Table 1). The highest number of positive ELISA IgG results was observed on day 3 of blood collection (19 November 2020). The number of declared symptoms in all subgroups was also higher on this day (Figure 1, subfigure A).

Of the 8 cases that involved positive polymerase chain reaction (PCR) results for SARS-CoV-2 infection, positive ELISA results for IgG antibodies were only obtained in 4 cases. Although IgG antibodies were present in the other 4 cases, the PCR test result for SARS-CoV-2 was negative.

There were no significant statistical differences amongst the subgroups when the number cohabiting in the household was taken into consideration in light of a positive IgG ELISA value. Statistical analysis was performed using a Chi-square

Table 2 – Numbers of dental workers receiving positive and negative results in accordance with the number of people in the household.

No. of people in the household	Negative ELISA result (n = 119)	Positive ELISA result (n = 8)
0	16	3
1	10	2
2	43	1
3	25	0
4	20	2
5	4	0
6	1	0

ELISA, enzyme-linked immunosorbent assay.

test for independence of variables in a contingency table with $P = .2047$, a statistic value of 8.6, and degrees of freedom = 6; see Table 2.

In the questionnaire about declared flu-like symptoms, prevalence across the job groups was highest for dentists (Figure 1B).

Amongst the positive results for SARS-CoV-2 IgG antibodies obtained with the use of the ELISA technique were taste disorders, high temperature (>38.0°C), and feeling of weakness (Figure 1C).

In addition to the above, Pearson correlation statistics for entire group of participants were evaluated. The correlations for the whole group of participants worth noting were those with a low P value and high R coefficient. An R^2 coefficient >0.5 was interpreted as a strong correlation, increasing towards 1.0. The P value was used to determine the validity with which the above correlation can be interpreted as correct. Between positive real-time PCR and positive ELISA results, the observed coefficient was 0.505 with $P < .0001$.

Statistical descriptions of the values of the parameters determined during the research of the subgroups of dentists (SUB1) and chairside assistants (SUB2) based on the questionnaire were developed in the form of a heatmap (Figure 2). The correlation is presented by the use of colour: The darker the colour, the stronger the Pearson correlation and the higher the R index.

Discussion

In this study, dentists from all specialities (dental surgeons, periodontologists, orthodontists, conservative/restorative dentists, and prosthetic dental specialists) were included. We did not observe any variation in the results of SARS-CoV-2 amongst the dental specialisations. Similarly, there were no significant differences amongst the investigated subgroups of dentists, dental assistants, nurses, laboratory workers, and administrative workers who share common spaces and professional interests as well as sharing the same workspace (building). That is in concordance with Sarapultseva et al, who did not observe differences in the presence of IgG antibodies amongst chairside assistants and dentists.[29]

In our study, the prevalence of flu-like or COVID-19 symptoms was highest in the group investigated in November compared to the groups investigated earlier in September and October. Furthermore, the one day with the highest number of positive cases of IgG antibodies was 19 November. This time frame represented the peak of the second SARS-CoV-2 wave of infections, with 24.213 cases of SARS-CoV-2 infections confirmed by PCR in Poland, where these tests were performed.[31] Only 8 of all 127 investigated participants had a confirmed positive PCR result for SARS-CoV-2 infection prior to drawing blood for this study, and only 4 of them presented a positive IgG ELISA finding. However, 4 cases involved positive ELISA findings without any previous confirmation of SARS-CoV-2 infection reported by the patient. The reason for not registering the previous COVID-19 test results by the study group was that researchers were not responsible for the molecular SARS-CoV-2 tests, and for such it was not possible to gain information about the date and type of the test done by healthy volunteers participating in our research. In these last 4 cases, the participants could have had an asymptomatic infection, so they did not have the basic requirements for a PCR test. These cases of infection without obvious symptoms could possibly have involved many people and, without the assessment of IgG production, it is not possible to know more about this situation in the whole population.[30] In our study, administrative workers were also involved. Even if this group has no direct contact with patients, the study presented participants from all subgroups sharing the same workspace. Also amongst this group were support staff (cleaning personnel who are involved in cleaning of the dental surgeries and corridors). The results for IgG SARS-CoV-2 antibodies in this subgroup were relatively low (4.4%). A similar study provided results of the seroprevalence amongst dental workers in the UK, where also subject not involved in the direct work with patients have been included.[18] However, unlike in our study, the aim of researchers was to provide information about the seroprevalence amongst the group in time, also after vaccination against COVID-19.

Jackson et al reported 78% agreement with the statement that dental procedures generate aerosol.[3] However, it is important to underline that in the cited article, the authors did not divide dental procedures into subgroups according to the risk of generating bioaerosols, and their diversity presents a need for safety classification.[10] All the dental procedures were analysed as a uniform group, which might be a reason for the result discussed in their study.[3] In the research conducted by Abdelkarim et al, contaminated surface area proportion using a high-speed air turbine reached 77.3%, but use of dental lasers caused only 3.8% to 7.3% of surfaces to be contaminated.[13] The proportion of surfaces contaminated is shown to be strictly related to the dental technique used and, for this reason, in periodontology manual scaling and polishing were recommended instead of ultrasonic techniques,[24] but some of the contamination might have been caused even from the removal of impacted third molars or routine extractions.[11]

At the beginning of the risk assessment, the limitations of activities in dental offices were introduced.[23] The range of dental services provided in the office as part of general primary care, dental surgery, paediatric dentistry, and conservative dentistry was limited to procedures necessary in cases of urgent need for intervention: that is, pain, inflammation and purulent processes, injuries, cysts, and conditions with risk of complications in patients.[32,33]

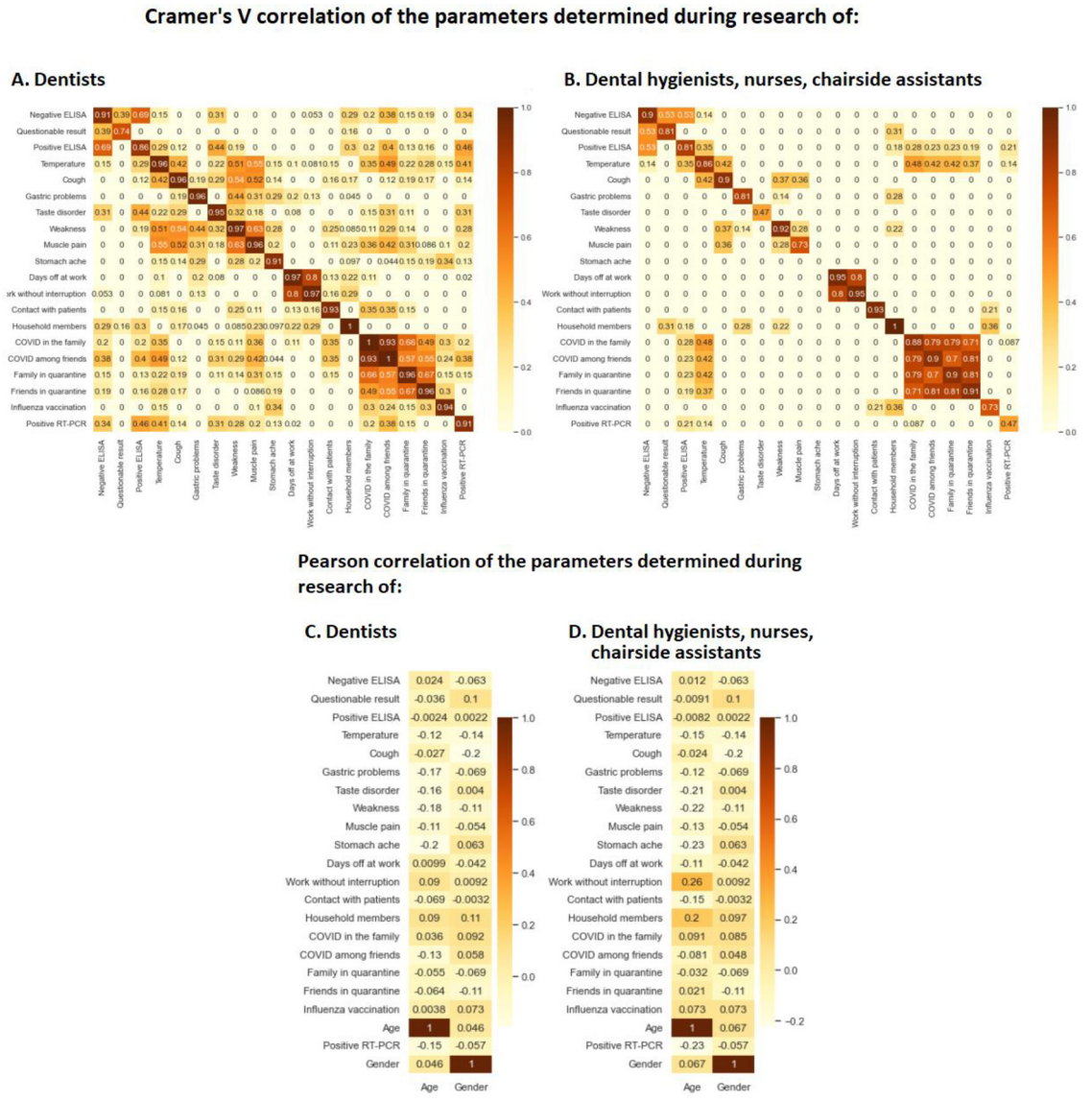

Fig. 2 – Cramer's V heatmap analysis (A and B) for the questionnaire answers regarding the flu-like symptoms reported by dentists and dental hygienists from the period of 15 March 2021 until 28 September 2020 compared with the enzyme-linked immunosorbent assay (ELISA) and real-time polymerase chain reaction (PCR) results. Continuous variables were tested for correlation with point-biserial coefficient (C and D). Values in A and B sections of the heatmap are values resulting from Cramer's V testing. Values in C and D sections of the heatmap are *R* values resulting from the Pearson correlation test. A and B, The colours correspond to the Cramer's B correlation values included in the heatmaps. The larger the value, the closer the colour is to brown, indicating a stronger correlation. The lower the value, the closer the colour is to yellow, which means a lower correlation. C and D, Colours correspond to Pearson correlation values. The higher the value, the higher the correlation between the 2 factors and the colour is more similar to brown. The smaller the value, the lighter the colour is, closer to yellow.

Conclusions and limitations

Limitations of the study include that the research did not cover all the dental workers from the Academic Dental Polyclinic. This issue has, however, been resolved by scheduling in parallel longitudinal research. Additionally, semi-quantitative ELISA might create discrepancies between the results and the actual concentration of the antibodies.

To our knowledge, this is one of the few available reports providing blood IgG results of all the coworking professionals in the dental area including dentists, chairside assistants, and administrative groups in one dental clinic. This research is in accordance with the latest statements that the risk of COVID-19 transmission in dental offices, even during AGPs and in the prevalence of asymptomatic patients, is low if safety measures and use of PPE are followed.

Conflict of interest

None disclosed.

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