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Short Communication

Prevalence of asymptomatic SARS-CoV-2 infection in an Austrian cohort

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first emerged at the end of 2019, causing the coronavirus disease (COVID-19). The main sources of infections are infected and asymptomatic persons. One major problem of the pandemic are the diverse symptoms and the varying manifestations of the illness. In this study, the IgG level recognizing the RBD of SARS-CoV-2 was determined within 336 volunteers from the environment of the University of Applied Sciences Wiener Neustadt. The aims of this study were to identify the estimated number of undiscovered COVID-19 infections and the corresponding antibody levels. In total, 11.3% of the non-vaccinated probands had a positive IgG antibody titer against SARS-CoV-2, whereas 4.0% did not test positive for SARS-CoV-2 or had never been tested at the time of sampling. Probands in this study reported tiredness (57,5%), ageusia/anosmia (55%) and headache (47,5%) as most frequent symptoms.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first emerged at the end of 2019, causing the coronavirus disease (COVID-19) [1]. Bats are thought to be the natural reservoir of SARS-CoV-2. XIao et al. were able to identify similarities of 90.5%, 100%, 98.6 and 97.8% of the S, E, M and N genes of a CoV strain found in pangolins and the SARS-CoV-2 strain, respectively [2]. SARS-CoV-2 is mainly transmitted through fomites and droplets during close, unprotected contact between infected and uninfected persons. Additionally, it can be transmitted indirectly through virus-contaminated droplets on hands and other surfaces. The main sources of infections are infected and asymptomatic persons. One major problem of the pandemic are the diverse symptoms and the varying manifestations of the illness, which can be incredibly severe, but also very mild in others [3, 4]. Symptoms appear approximately 2 to 14 days after virus exposure and include fever, muscle pain, headache, cough, sore throat and loss of taste or smell [4].

Currently, sampling of the upper respiratory tract through naso- and oropharyngeal swabs is the chiefly recommended method of testing for COVID-19. The detection of the virus should be carried out via real-time reverse transcription-quantitative polymerase chain reaction (RT-PCR) [5]. To estimate the exposure of the virus, the presence of antibodies specific to SARS-CoV-2 in blood samples can be determined. It is thought that the true number of infected persons is considerably higher than the official numbers suggest. Many infected people were not tested, especially at the beginning of the pandemic. Although testing is now very common, some mild or asymptomatic infections remain undiagnosed [5].

Antibodies produced against SARS-CoV-2 can typically be detected within 14 to 21 days of infection. Various tests exist to determine different types of antibody, using whole blood, serum or, plasma. These tests can also vary in the target antigen used (spike, membrane, or nucleocapsid proteins) [5].

In this study, the IgG level recognizing the RBD of SARS-CoV-2 was determined within 336 volunteers from the university's environment. The aims were to identify the estimated number of undiscovered COVID-19 infections and the corresponding antibody levels.

Method

Serum samples were collected through venipuncture from 336 participants between 15.2.2021 and 3.3.2021 and frozen in Eppendorf® tubes at -20°C until further procedure. The IgG level recognizing the RBD of the S protein of SARS-CoV-2 was determined through ELISA (DRG Instruments GmbH®). A questionnaire was completed to survey the COVID-19 anamnesis (e.g. if and how often the probands were tested, which tests were used, if they were tested positive, which symptoms they had etc.). Written, informed consent was obtained from all participants in accordance with the inhouse ethics committee. The data gathered was analyzed using Microsoft® Excel® and IBM® SPSS® Statistics 26.

Results

336 probands participated in this study; 107 (31,8%) were male, 229 (68,2%) female. 274 (81.6%) participants were tested at least once for SARS-CoV-2 with an antigen rapid test, 170 (50.6%) with PCR. 12

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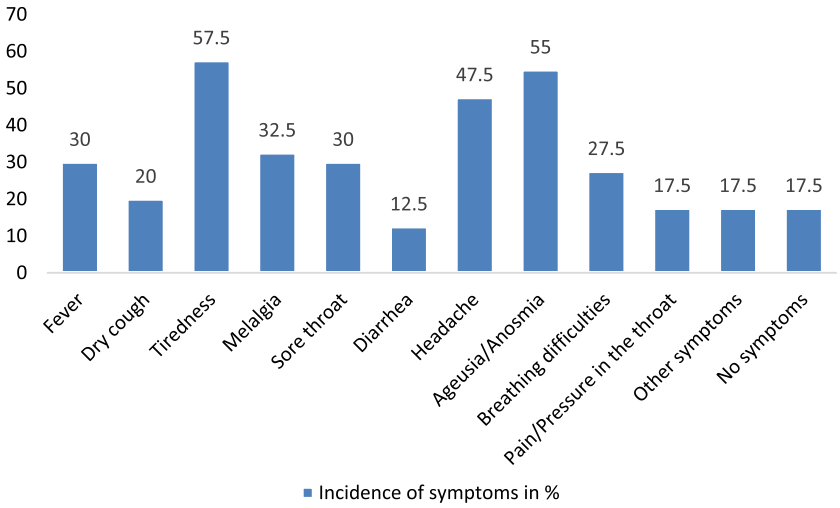

Fig. 1. Symptoms reported by probands in percent, who experienced an COVID-19 infection

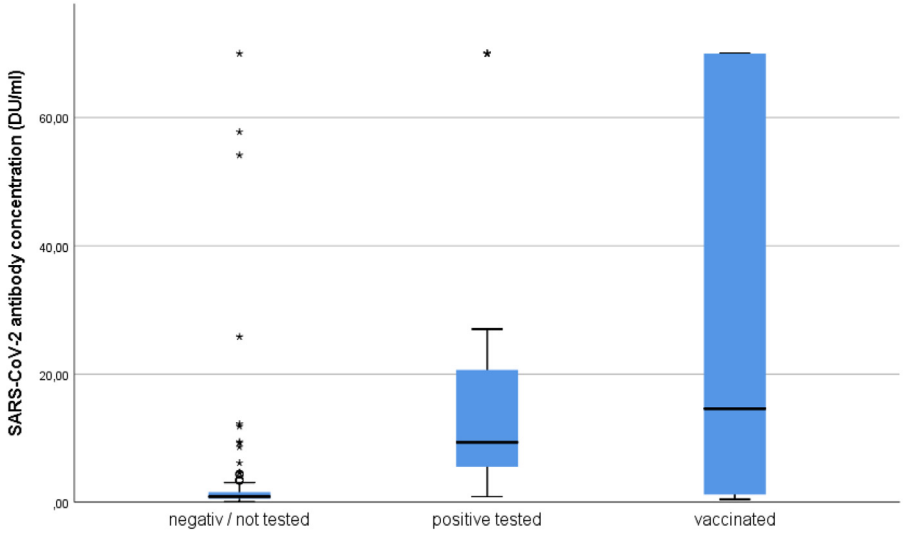

Fig. 2. Comparison of the SARS-CoV-2 IgG titer of probands tested positive, negative/not tested with PCR and vaccinated probands.

(4.4%) of the antigen rapid tests executed showed a positive test result, whereas 37 (21.8%) of the PCR tests carried out were positive for SARS-CoV-2. 275 (88.4%) of the non-vaccinated probands showed a negative, 1 (0.3%) person an intermediate and 35 (11.3%) a positive antibody level after the ELISA determination. 19 (5.7%) people were vaccinated with at least one dose at the time of sampling. 27 (8%) participants had never been tested for SARS-CoV-2 before. 4.0% of all probands showed a positive titer, even though they have never been tested positive with antigen rapid tests or PCR. 37 (11%) probands were tested positive for SARS-CoV-2 with PCR. No antibodies could be detected in 8 (21.6%) of them. Most of the participants who experienced an infection reported tiredness (57.5%) and ageusia/anosmia (55%) as the most frequent symptoms, followed by headache (47,5%) and melalgia (32.5%) (Fig. 1).

Comparing the titer of PCR positive, negative/not tested and vaccinated probands it could be shown that the vaccinated persons show a much higher titer than the ones who experienced an infection (Fig. 2). In the vaccinated group, probands are included where the time between vaccination and sampling was less than two weeks, which may influence the data.

Discussion

In this study, we attempted to evaluate the estimated number of asymptomatic SARS-CoV-2 infections by determining the IgG antibodies recognizing the RBD of the S protein of SARS-CoV-2 using ELISA.

In total, 11.3% of the non-vaccinated probands had a positive IgG antibody titer against SARS-CoV-2, whereas 4.0% did not test positive for SARS-CoV-2 or had never been tested at the time of sampling.

Worldwide, many studies have been carried out dealing with the seroprevalence of SARS-CoV-2, with varying results depending on the location, but with constantly higher true numbers than the officially reported number of confirmed cases. Ireland estimated in August 2020 that 1.7% of the Irish population between 12-69 years had experienced an infection, which was approximately three times higher than the total number of confirmed cases in this age group at this time [5]. In Geneva, Switzerland, a study investigated the seroprevalence of SARS-CoV-2 over the course of five weeks. They observed a seroprevalence from about 5% to 11% within the duration of the study. [6] . The slightly lower result in this study is probably due to the fact that all the study participants came from an academic environment and the majority from the health science sector.

In contrast to other studies, probands in this study reported tiredness (57,5%), ageusia/anosmia (55%) and headache (47,5%) as most frequent symptoms. In the study of Figueiredo-Campos et al. 60% of the hospitalized patients mentioned cough and fever as most frequent symptom, whereas in the present study only 6% and 9% of the probands suffered from these symptoms, respectively. Surprisingly, looking at healthcare participants, only similar results were obtained concerning the symptoms. In this group of participants, 37% indicated anosmia, 63% headache and 68% fever [7].

19 (1.78%) participants were already vaccinated at the time of sampling, around 58% had a positive titer. The reason why not all of the people vaccinated had an adequate titer can be the short duration of only two weeks between the vaccination and the sampling. It is likely that the immune system was not able to produce a sufficient number of antibodies. It was shown in other studies that IgG antibodies could be detected around day 14 after the onset of symptoms [8].

A study done by Pilz et al. investigated the potential of re-infection with SARS-CoV-2. It showed that the risk of re-infection is very low in the Austrian population. In the period of the second wave (September 1 to November 30) they recorded 40 (0,27%) tentative re-infections. Previous studies indicate a high correlation between neutralizing antibodies against SARS-CoV-2 and COVID-19 severity, suggesting that patients with a severe infection develop a stronger protective humoral immune response against the virus. This cannot be supported by the findings of the study, since several patients with tentative re-infections were already hospitalized during their first infection. The authors of this study also see a roughly similar protection against SARS-CoV-2 after natural infection and the vaccination, but mention that a direct comparison is difficult because of differences in the study designs and study populations [9].

The antigen used in the ELISA can be seen as a limitation of this study. Antibodies against the RBD of the S protein were detected. Using another method recognizing antibodies against the whole S protein or nucleocapsid proteins can result in divergent antibody values. However, a study has shown that the ability of antibodies binding the mono- and dimeric RBD protein is similar to the total protein fraction [7]. This indicates that this limitation has no tangible impact on the results of this present study.

Rostami et al. demonstrated in their article that the sensitivity of ELISA methods used for the detection of SARS-CoV-2 antibodies lies between 84-94%, whereas the Lateral flow immunoassay (66-80%) shows a lower and the Chemiluminescence assay (90-97%) a higher sensitivity. For all methods, a specificity of >95% could be calculated [10]. Consequently, it would be recommended to use Chemiluminescence assays as detection method in future projects dealing with SARS-CoV-2 antibodies.

An influencing factor concerning the proband collective is that the majority have a (healthcare-related) academic background. This leads to the assumption that they are better informed about the disease and the currently applied sanctions concerning the pandemic containment. This fact can influence the amount of people being infected with SARS-CoV-2. In their systemic review, Rostami et al. showed a pooled seroprevalence of 3.38% relating to about 264 million individuals worldwide. Their analysis suggests a higher seroprevalence in countries with a higher income and Human Development Index (HDIs). Reasons for that can include increased urbanization and population density, higher levels of social interaction and increased numbers of international travel. However, this data has to be interpreted carefully because of the lack of data in low income countries [10].

Declaration of Competing Interest

The authors have no conflict of interest to disclose.

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