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Collegium Medicum
im. Ludwika Rydygiera w Bydgoszczy

Bydgoszcz 2023 r.

UNIWERSYTET
MIKOŁAJA KOPERNIKA
W TORUNIU
Wydział Lekarski
Collegium Medicum w Bydgoszczy

Aleksandra Kwaśniewska

Ocena częstości występowania objawów otolaryngologicznych, ogólnych oraz miana przeciwciał anty-SARS-CoV-2 w przebiegu infekcji COVID-19.

Rozprawa na stopień doktora nauk medycznych

Promotor:
prof. dr hab. n. med. Paweł Burduk

Bydgoszcz 2023 r.

Podziękowania

Serdecznie dziękuję Panu prof. dr hab. n. med. Pawłowi Burdukowi
za opiekę merytoryczną, cenne uwagi, poświęcony czas
oraz motywację do pracy podczas przygotowywania rozprawy doktorskiej.

Dziękuję mojemu mężowi Krzysztofowi za ogrom cierpliwości, wsparcia
i motywacji podczas pisania pracy.

Spis treści:

Artykuły włączone do rozprawy

Rozprawę doktorską przygotowano w formie spójnego tematycznie cyklu publikacji, do którego włączono następujące artykuły:

I

Kwaśniewska A, Kwaśniewski K, Skorek A, Tretiakow D, Jaźwińska-Curyłło A, Burduk P. Correlation of ENT Symptoms with Age, Sex, and Anti-SARS-CoV-2 Antibody Titer in Plasma. J Clin Med. 2023 Jan 12;12(2):610. doi: 10.3390/jcm12020610. PMID: 36675539; PMCID: PMC9867427.
Udział: koncepcja i projekt badania, zbieranie danych, analiza piśmiennictwa, interpretacja wyników, napisanie i przygotowanie manuskryptu, graficzne przedstawienie wyników, korekta manuskryptu, ostateczne zatwierdzenie manuskryptu
Punktacja MNiSW: 140
Impact Factor: 4.964

II

Skorek A, Jaźwińska-Curyłło A, **Romanowicz A,** Kwaśniewski K, Narożny W, Tretiakow D. Assessment of anti-SARS-CoV-2 antibodies level in convalescents plasma. J Med Virol. 2022 Mar;94(3):1130-1137. doi: 10.1002/jmv.27433. Epub 2021 Nov 9. PMID: 34738646; PMCID: PMC8661642.
Udział: koncepcja i projekt badania, zbieranie danych, analiza piśmiennictwa, interpretacja wyników, **udział w przygotowaniu manuskryptu**, korekta manuskryptu, ostateczne zatwierdzenie manuskryptu
Punktacja MNiSW: 70
Impact Factor: 20.693

III

Bełdzińska K, **Romanowicz A**, Kwaśniewski K, Jaźwińska-Curyłło A, Tretiakow D, Skorek A: COVID-19 symptoms in the Pomerania region; Pol Otorhino Rev 2021; 10 (4): 9-14. DOI: 10.5604/01.3001.0015.6421

Udział: koncepcja i projekt badania, zbieranie danych, analiza piśmiennictwa, interpretacja wyników, **udział w przygotowaniu manuskryptu**, graficzne przedstawienie wyników, korekta manuskryptu, ostateczne zatwierdzenie manuskryptu
Punktacja MNiSW: 70

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Article

Correlation of ENT Symptoms with Age, Sex, and Anti-SARS-CoV-2 Antibody Titer in Plasma

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Abstract: Our objective is to evaluate the correlation between ENT symptom occurrence and antibody titer in convalescent plasma, as well as the influence of age and gender on ENT manifestations of COVID-19. We measured the levels of antibodies in 346 blood donors, who had PCR-confirmed previous infection and met the study inclusion criteria. We recorded otolaryngological symptoms during infection: dry cough, dyspnea, sore throat, smell/taste disturbances, vertigo, dizziness, nausea and vomiting, sudden unilateral loss of hearing, progressive loss of hearing, and tinnitus. In addition, we statistically analyzed the correlation between patients' antibody levels, symptoms, age, and gender using a chi-square test or Fisher exact test. A *p*-value less than 0.05 determined statistical significance. The mean age of the convalescents was 39.8 ± 9.56 SD and the median of the measured anti-SARS-CoV2 plasma antibodies was 1:368.5. The most common ENT symptoms were smell/taste disturbances (62.43%), dry cough (40.46%), sore throat (24.86%), and dyspnea (23.7%). Smell and taste disturbances were more frequent in younger patients and the marked antibody titer was lower, which was contrary to a higher antibody titer associated with dry cough, dyspnea, and dizziness. Occurrence of sore throat was not correlated with age, sex, or antibody level. There were no significant differences in otological symptoms in female patients. Gender does not affect the occurrence of ENT symptoms. The symptomatic course of SARS-CoV-2 infection is not always associated with higher levels of antibodies in the blood. The age of the infected patients, unlike gender, affects the occurrence of some ENT symptoms.

Keywords: COVID-19; convalescent plasma; SARS-CoV-2; ENT symptoms

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1. Introduction

Coronavirus disease 2019 (COVID-19) is an ongoing problem caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Initial infection appeared in Wuhan (China) in December 2019 and was declared a pandemic by the World Health Organization (WHO) in March 2020. According to the WHO, COVID-19 has infected over 600 million people and caused over 6.5 million deaths worldwide [1].

Symptoms of the disease are varied; besides general manifestations such as fever or chills, ear, nose, and throat (ENT) symptoms are also prevalent [2]. According to various authors, ENT symptoms associated with COVID-19 could include sore throat, headache, cough, dyspnea, pharyngeal erythema, nasal congestion and obstruction, rhinorrhea, nasal itching, upper respiratory tract infection, tonsil enlargement, sneezing, dysphagia, voice impairment, olfactory and taste dysfunction, dizziness, vertigo, tinnitus, and hearing impairment [2–5].

However, their frequencies differ in patients, as do anti-SARS-CoV-2 antibody levels in their plasma [6]. Treatment with convalescent plasma rich in anti-SARS-CoV-2 antibodies has proven effective in reducing the severe course and mortality of COVID-19 [7]. The correlation of demographic factors and the level of antibodies in relation to their effects on disease symptomatology has been evaluated previously [8–11]. However, only correlation with the severity of the disease was tested, without stratification by each symptom. Furthermore, it was investigated only for the general symptoms of COVID-19 infection, and not with a specific focus on otorhinolaryngological symptoms.

As has been shown by other authors, the severity of the disease affects anti-SARS-CoV2 antibody levels [12–14]. We aimed to analyze if particular otolaryngological symptoms could have a similar predictive value. Investigating the relationship between ENT symptoms and the level of antibodies may facilitate the prediction of the severity, duration and complications of COVID-19 based on the presence or absence of respective symptoms. This research may help otolaryngologists identify patients with COVID-19 infection, and, after further research, predict the course of infection. This could have both scientific and clinical significance.

This study aimed to show the frequency of ENT symptoms among COVID-19 patients, their occurrence depending on sex and age, and the correlation with IgG anti-SARS-CoV-2 antibody titers in convalescent plasma.

2. Materials and Methods

COVID-19 convalescents (n = 346) who donated blood at the Regional Center of Blood Donation and Treatment in Gdańsk (Poland) were enrolled in the study. The objective of blood donation was to acquire plasma rich in anti-SARS-CoV-2 antibodies to be used for the treatment of severe COVID-19 cases. SARS-CoV-2 infection was confirmed by polymerase chain reaction (PCR) testing of nasopharyngeal swabs. The convalescents' blood was donated from 10 to 120 days after a fourteen-day isolation period. None of the donors were vaccinated or hospitalized due to COVID-19. Patients were asked about otolaryngological symptoms of the disease: dry cough, dyspnea, sore throat, smell/taste disturbances, vertigo, dizziness, nausea and vomiting, sudden unilateral loss of hearing, progressive loss of hearing, and tinnitus. The inclusion criteria were confirmed SARS-CoV-2 infection, 18–64 years of age, and normal complete blood count, blood pressure, pulse, and body temperature. The exclusion criteria were autoimmune diseases, anti-HLA antibodies in the blood, active infection (including Treponema pallidum) or oncological illness, history of HIV, Hepatitis B or Hepatitis C infection, and being under the influence of psychoactive substances. The testing methodology of a study by Skorek et al. was replicated [11]. Blood tests were performed using the SARS-CoV-2 S-RBD IgG test of a MAGLUMI 800 device (Snibe Co., Shenzhen, China). Serological tests were performed using the in vitro chemiluminescent kit (Cat. No. SARS-CoV-2 S-RBD IgG122, Mindray, China) for the quantification of S-RBD IgG neutralizing antibodies (nAbs) against SARS-CoV-2. After collecting blood from the examined person, it was placed in test tubes with a separating gel or clot activator. After centrifugation (>10,000 RCF for 10 min), a sample (10 µL volume) containing no fibrin or other solids was collected. Subsequently, the sample, along with the buffer and magnetic particles coated with the recombinant S-RBD antigen, were mixed and incubated, resulting in the formation of immune complexes. After magnetic field precipitation, the supernatant was removed and washed. After the addition of ABEI-labeled anti-human IgG antibodies, the sample was subjected to another incubation and precipitation followed by washing to remove unbound proteins from the sample. Finally, the chemiluminescence reaction was initiated and the light signals were measured with a photomultiplier for 3 s in relative light units (RLUs), which are proportional to the SARS-CoV-2 S-RBD IgG concentration. In the case of a test performed 15 days after the onset of symptoms, the sensitivity of the test (according to the manufacturer) is 100.0% and its specificity is 99.6% (CE REF 30219017 M) [15]. Participation in the study was voluntary and written consent was obtained. The data collected were statistically analyzed

using the chi-square test or Fisher exact test when the chi-square test assumption was not fulfilled (theoretical values in each cell of the contingency table equal to at least 5) to derive *p*-values. A post hoc Bonferroni correction was applied. A *p*-value less than 0.05 (typically ≤ 0.05) determined statistical significance. Cohen's h effect size was calculated and classified as small (h = 0.20), medium (h = 0.50) or large (h = 0.80). These calculations were prepared using the Statistica 13.3 StatSoft PL software (Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz, Poland) and the R statistical package version 4.0.2. (Biostat, Warsaw, Poland).

The study was approved by the Regional Independent Bioethics Committee, Gdansk Medical University, Poland (NKBBN 199/2021).

3. Results

The study included 302 males and 44 females, whose mean age was 39.8 ± 9.56 SD (age range 18–64) (Table 1). The median of the measured plasma IgG anti-SASR-CoV2 antibody titers was 1:368.5. Median rather than mean antibody titer levels were calculated to minimize outlier values and for a more accurate predictive value. The FDA recommends 1:160–1:640 as the standard antibody level, which coincides with our work (the mean in the standard range is 1:400). Patients were divided into groups depending on sex and plasma antibody level.

Table 1. Demographic data.

Index	N
Mean age (95% CI)	39.80 (38.79–40.81)
Gender	
Male	302
Female	44
Antibody titer	
<1:368.5 (male:female ratio)	6:1
>1:368.5 (male:female ratio)	9:1
Clinical information	
Hypertension	9 (only males)
Familial hypercholesterolemia	1 (only females)
No comorbidities (male:female ratio)	7:1
Ethnicity	
Polish (%)	346 (100%)

The most common ENT manifestations of COVID-19 infection were smell/taste disturbances (62.43% of patients), dry cough (40.46%), sore throat (24.86%), and dyspnea (23.7%). Others included in the study were vertigo (11.85%), dizziness (8.09%), tinnitus (6.07%), nausea and vomiting (3.76%), sudden unilateral loss of hearing (1.73%), and progressive loss of hearing (0.58%).

We noted a statistically significant correlation between otolaryngological symptoms manifested during COVID-19 infection and measured antibody levels. The occurrence of dry cough, dyspnea, and dizziness was associated with higher antibody titers (Figure 1; Table 2). Additionally, in male patients there was a positive correlation between dry cough, dyspnea, dizziness, vertigo, and higher antibody titers ($p < 0.05$). Interestingly, smell/taste disturbances were correlated with lower antibody titers (Figures 2 and 3; Table 2).

Our study showed no statistically significant differences between sex and occurrence of any ENT symptom of COVID-19 (Table 2). An exception was seen in patients with lower antibody titers, whereby nausea and vomiting were more common in women than in men.

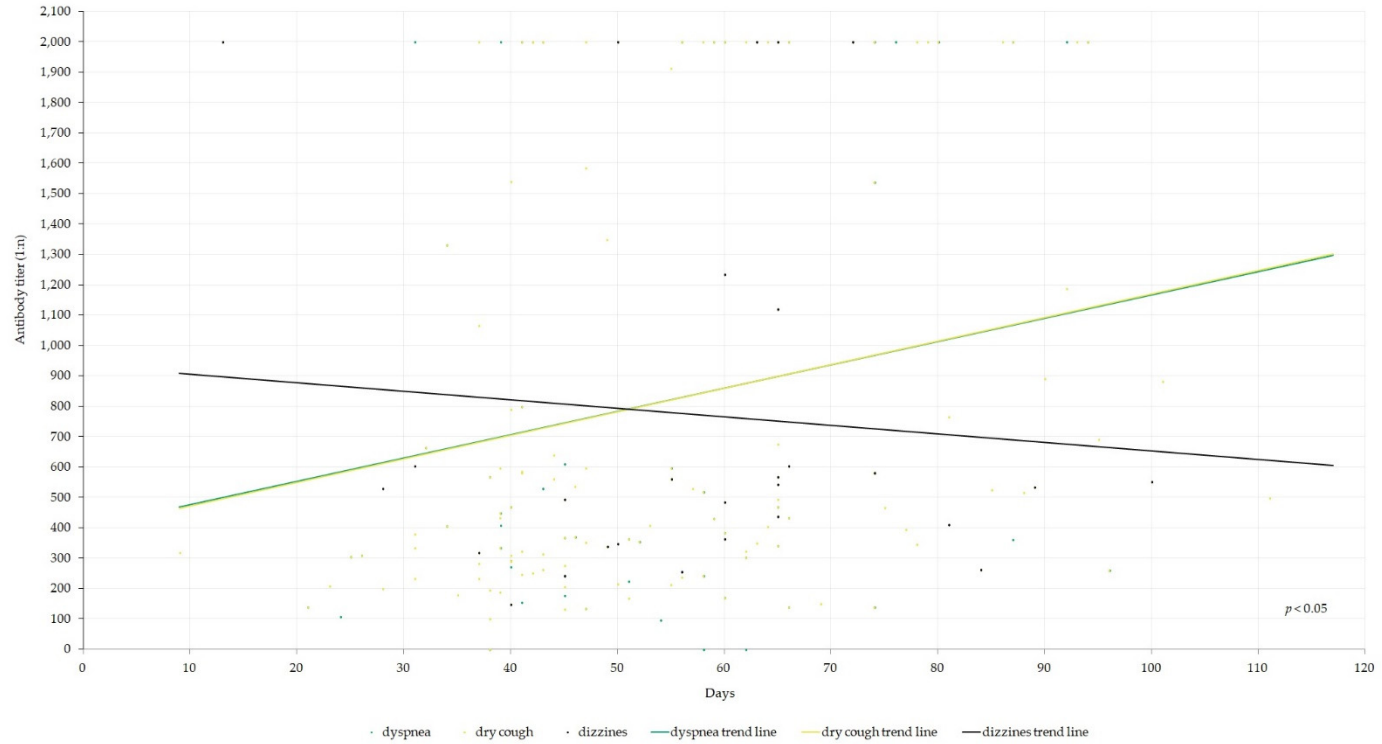

Figure 1. Anti-SARS-CoV-2 antibody titers depending on the symptoms of dizziness, dyspnea, and dry cough. Spots may represent more than one symptom. The chi-square test was used to derive the *p*-values.

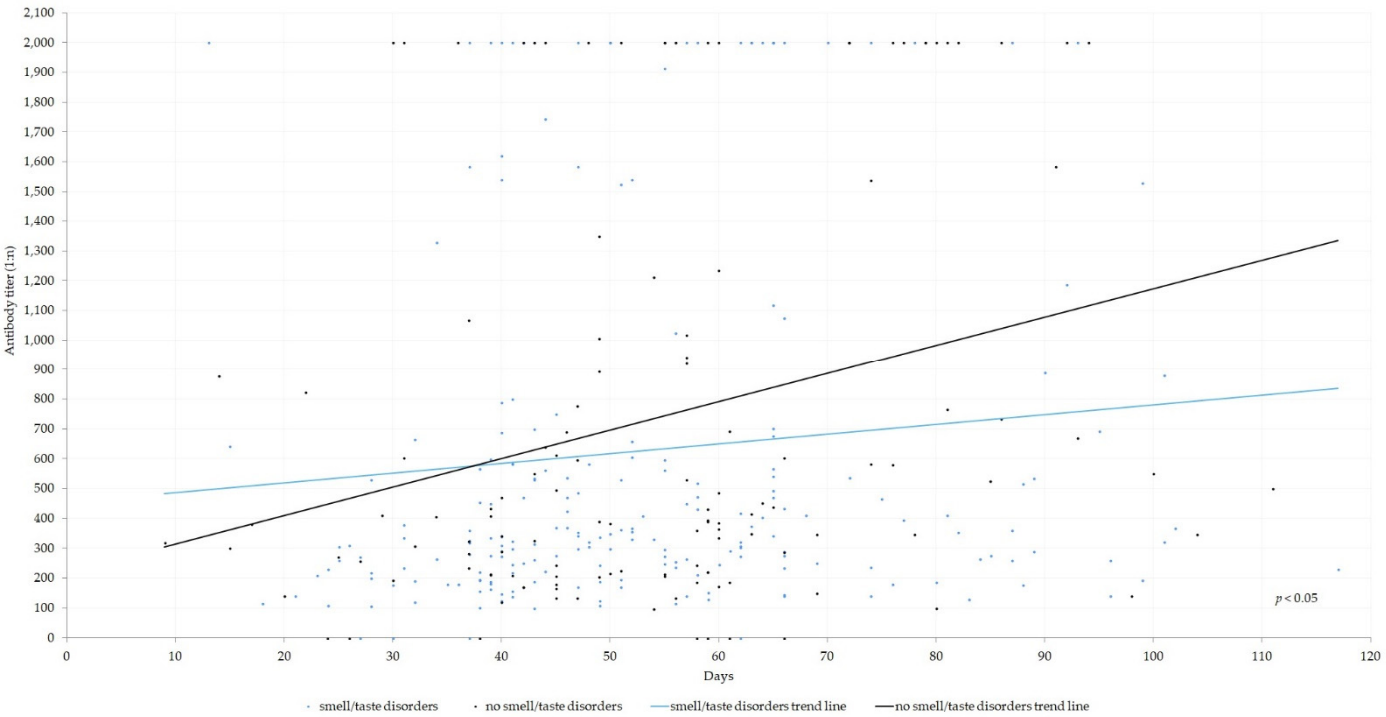

Figure 2. Anti-SARS-CoV-2 antibodies among patients depend on smell/taste disturbances. The chi-square test was used to derive the *p*-values.

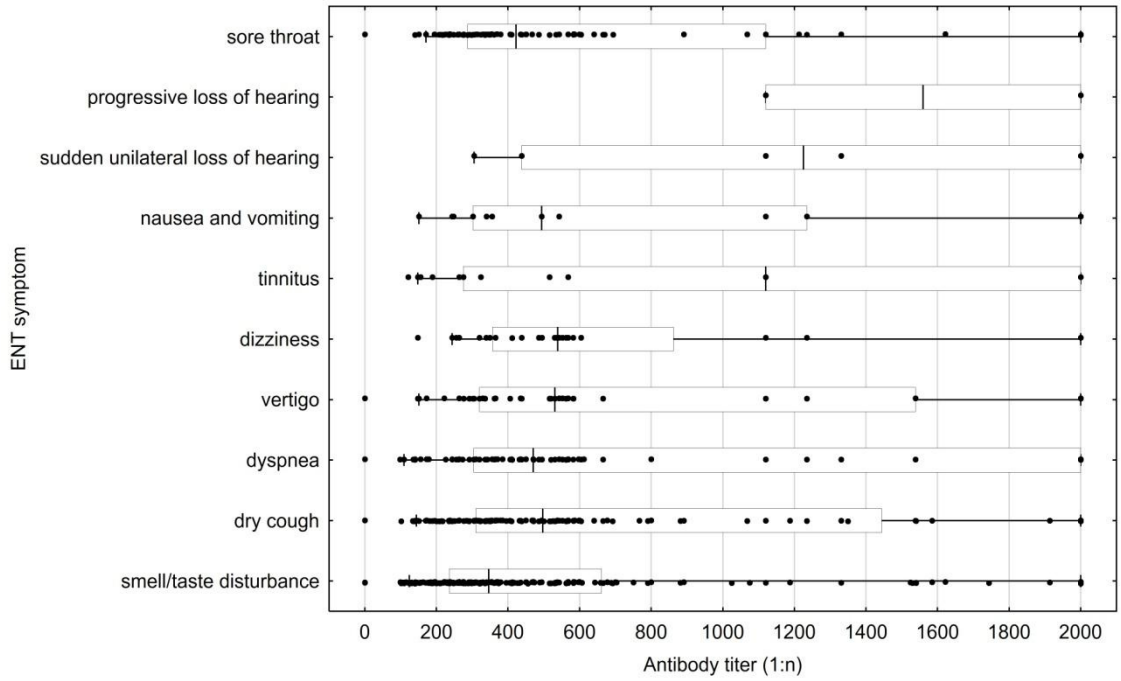

Figure 3. Antibody titer by reported ear, nose, and throat (ENT) symptom. Values for individuals with multiple symptoms are shown for each symptom individually. The center line denotes the median value (50th percentile), the box contains the 25th to 75th percentiles of the dataset, the whiskers mark the 5th and 95th percentiles, and values beyond these upper and lower bounds are considered outliers.

Patients were divided into younger and older groups based on mean age (under and above the age of 38.9). Smell/taste disturbances were more common in younger convalescents (statistically significant difference, $p < 0.05$) (Table 2). Likewise, this difference was maintained both within the male and female patient distributions ($p < 0.05$). There were no statistically significant correlations between sore throat and age, sex, or antibody level. In addition, there was no correlation between antibody titers and ENT symptoms in women ($p > 0.05$). Furthermore, there were no differences ($p > 0.05$) in otological symptoms (tinnitus, sudden unilateral loss of hearing, progressive loss of hearing) in female patients. Unfortunately, the proportion of female patients was too small to facilitate statistically significant results. According to Cohen's classification, the effect sizes observed in the statistically significant comparisons can be considered small effect sizes, which results from large disparity between group sizes.

Table 2. Statistical analysis of ear, nose, and throat (ENT) ENT symptoms by antibody titer; sex, and (age. The chi-square test and the Fisher exact test were used to derive the *p*-values; $p < 0.05$—outcome statistically significant (marked in bold); Cohen's h effect size was presented; 1:368.5—median antibody titer.

ENT Symptom	<1:368.5 (N = 173)	>1:368.5 (N = 173)	*p* Value	Cohen's h	Males (N = 302)	Females (N = 44)	*p* Value	Cohen's h	Age < 39.8 (N = 167)	Age > 39.8 (N = 179)	*p* Value	Cohen's h
smell/taste disturbance	117	99	**0.046** [a]	0.215	184	32	0.131 [a]	0.252	119	97	**0.001** [a]	0.355
dry cough	51	89	**<0.0001** [a]	0.452	125	15	0.357 [a]	0.151	65	75	0.573 [a]	0.061
sore throat	39	47	0.32 [a]	0.107	72	14	0.253 [a]	0.178	38	48	0.382 [a]	0.094
dyspnea	30	52	**0.005** [a]	0.302	72	10	0.871 [a]	0.026	45	37	0.17 [a]	0.148
vertigo	15	26	0.067 [a]	0.198	37	4	0.544 [a]	0.103	19	22	0.793 [a]	0.028
dizziness	8	20	**0.018** [a]	0.26	26	2	0.554 [b]	0.166	15	13	0.558 [a]	0.063
tinnitus	8	13	0.26 [a]	0.122	19	2	1 [b]	0.077	8	13	0.336 [a]	0.104
nausea and vomiting	6	7	0.786 [a]	0.03	10	3	0.221 [b]	0.162	6	7	0.885 [a]	0.017
sudden unilateral loss of hearing	1	5	0.215 [b]	0.189	6	0	1 [b]	0.283	2	4	0.686 [b]	0.081
progressive loss of hearing	0	2	0.499 [b]	0.215	2	0	1 [b]	0.163	1	1	1 [b]	0.005

[a] *p*-value calculated with chi-squared test, [b] *p*-value calculated with Fisher exact test.

4. Discussion

ENT symptoms were frequently observed in COVID-19 infection; however, much variability has been reported in the literature. El-Anwar et al. reported the most common manifestations to be cough (63.3%), dyspnea, (45%) sore throat (30%), nasal congestion (28.3%), nasal obstruction (26.7%), sneezing (26.6%), headache (25%) and smell/taste dysfunction (25%) [3]. However, another study by the same author presented sore throat (11.3%) and headache (10.7%) as the most frequently occurring symptoms [2]. Zięba et al. pointed out olfactory disorders (72%), taste disturbance (68%), and vertigo and dizziness (34%) [4]. Korkmaz et al. mentioned sore throat and smell/taste disturbances as prevailing symptoms [5]. We assume that results differed substantially between studies due to various factors influencing the tested groups. Possible factors might be age, comorbidities, research unit (blood donation center or ENT clinic), and geographical region, which could be associated with non-specific mutations of SARS-CoV-2. Furthermore, the ENT symptoms that the authors considered influenced the study results.

Our study showed no significant differences in ENT symptom manifestation in younger patients as compared with older patients, except for smell/taste disturbance, which occurred more often in patients under 39.8 years of age (Table 2). Elibol et al. report that otolaryngological symptoms are more frequent in the 18–30 age group, which is consistent with our smell/taste disturbance results **.** The authors noted that ENT manifestations of COVID-19 occurred more often in women [16]. Moreover, Takahashi et al. found gender differences in immune responses to SARS-CoV-2 and in prognostic factors for disease progression [17]. However, in our research, symptoms had different frequencies, e.g., sore throat occurred more often in women (31.82%) than men (23.84%), yet statistical significance was not achieved. As such, we are unable to conclude from our data that gender affects otolaryngological symptoms (Table 2). Furthermore, the female patient group in our study was small, probably caused by the exclusion criteria, as HLA antibodies in the blood appear after pregnancy. Therefore, statistical significance could be underestimated.

This study assessed otolaryngological symptom correlation with the level of anti-SARS-CoV-2 antibody titers; to the authors' knowledge, this is the first study to investigate this. This work may give rise to new considerations if ENT symptom occurrence could become a predictor of immune response; however, this requires further research with larger groups of people.

Plasma substance concentration could have a significant impact on the body's functioning; e.g., potassium disorders can lead to life-threatening conditions [18]. Zheng et al. measured serum albumin levels in patients with sudden sensorineural hearing loss (SSNHL) and proved low albumin levels to be associated with the worse SSNHL functional outcome [19]. We expect that plasma anti-SARS-CoV-2 antibody titer could contribute as a predictive factor for disease severity, duration, and complications.

Convalescent plasma is an accepted method of severe SARS-CoV-2 treatment [20,21]. Song et al. noted that the month after SARS-CoV-2 infection was the time of highest immunoglobulin titer [6]. Another study showed that the persistence of antibodies in plasma after COVID-19 infection was a minimum of 39 weeks [22]. Research has shown that administering convalescent plasma reduced mortality, the need for intubation, and the length of hospitalization [7,23]. However, complications of convalescent plasma immunotherapy, such as transfusion-related acute lung injury (TRALI), were reported [24]. After COVID-19 vaccination was introduced, it became the main method of prevention and thus also of fighting the virus. However, it did not completely eliminate the symptomatic course of the disease. Higher antibody titers post-vaccination were associated with worsening COVID-19 symptoms, which is likely due to an excessive immune response [25]. Every treatment has its side effects and possible complications, thus requiring an individualized approach and patient observation.

5. Conclusions

The most common ENT symptoms of SARS-CoV2 infection are smell/taste disturbances, dry cough, sore throat, and dyspnea. Smell or taste disturbances more often occur in younger patients and are related to lower anti-SARS-CoV-2 antibody titers in convalescent plasma. This study showed a statistically significant correlation between the occurrence of some otolaryngological symptoms and anti-SARS-CoV-2 antibody levels in convalescent plasma. Gender does not affect the occurrence of ENT symptoms during COVID-19 infection.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: No public database has been created. All data are available from the authors of the work.

Conflicts of Interest: The authors declare no conflict of interest.

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RESEARCH ARTICLE

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Assessment of anti-SARS-CoV-2 antibodies level in convalescents plasma

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Abstract

Despite extensive vaccination, the quantity of patients infected with the SARS-CoV-2 virus and its variants continues to grow worldwide. Treating patients with a severe course of COVID-19 is a difficult challenge. One of the generally accepted and specific therapy methods is the use of plasma rich in anti-SARS-CoV-2 antibodies. On the other hand, assessing the antibodies level depending on the time after infection allows for vaccine-decision. The study marked the level of anti-SARS-CoV-2 IgG antibodies in 351 COVID-19 convalescent residents of one geographical region in Poland. The study group included blood donors. The studies were cross-sectional and extended to a questionnaire to determine infection severity. These data were compiled statistically. The study considered epidemiological factors, the time from the end of the infection, and infection severity. The fastest increase of the antibodies level was observed up to 59 days after COVID-19, and it was statistically significantly higher among men. Higher levels of antibodies were found among people above the average age in both men and women. There was an increase in the level of antibodies since the onset of the disease in men, while in women, it decreased. The antibodies level was also found to depend on the severity of the course of COVID-19 infection. The optimal group of plasma donors in the studied geographical region is men and women above 39 years old. after a more severe infection. The titer of antibodies increases with time from the disease.

KEYWORDS

convalescent plasma, COVID-19, SARS-CoV-2, treatment

1 | INTRODUCTION

The plasma of COVID19 convalescents is rich in anti-SARS-CoV-2 antibodies, and its use in the treatment of a severe course of this infection is widely accepted. Passive increasing of the body's immune defense is based on multicenter observations of reduced mortality risk among transfused plasma patients with a high concentration of antibodies than those who received plasma with a low concentration of antibodies. Increased awareness of the health, society, and economy-connected harm caused by COVID-19 and an increasing sense of solidarity led to the growing number of donating blood COVID-19 convalescent patients.[1,2] Determining the optimal group of donors and the optimal period for donation have considerable significance for preparing the plasma specimen.

This study aims to determine the IgG anti-SARS-CoV-2 antibody titers in COVID-19 convalescents in the Pomeranian region of Poland, depending on the epidemiological factors, time since recovery (isolation), and the severity of the disease.

2 | MATERIALS AND METHODS

We recruited COVID-19 convalescents (infection was confirmed by Polymerase chain reaction [PCR] analysis of nasal swabs) who reported donating blood at the Regional Center of Blood Donation and Treatment in Gdańsk (Poland). The inclusion criteria were: confirmed SARS-CoV-2 infection, 18–56 years of age, normal complete blood count (hemoglobin, hematocrit, erythrocyte, and leukocyte formula, platelets), normal blood pressure, pulse, and body temperature. In addition, the IgG anti-SARS-CoV-2 antibody titers were measured, and a detailed survey was conducted regarding symptoms such as chills, dry cough, musculoskeletal pain, conjunctivitis, fever (defined as ≥38°C), fatigue, dyspnea, diarrhea, and smell/taste disturbances. The exclusion criteria were: autoimmune diseases, anti-HLA antibodies in the blood (postpregnancy or posttransfusion), active infection or oncological illness, history of viral disease (particularly HIV, Hepatitis B, and C), or infection with *Treponema pallidum*, being under the influence of psychoactive substances.

We divided the entire sample of participants into two subgroups depending on the severity of their COVID-19 illness. The severe course of COVID-19 was defined as ≥5 symptoms, whereas mild illness was defined as ≤4 symptoms.

Participation in our study was voluntary. It was conducted after the scheduled blood donation, whose purpose was to obtain plasma rich in anti-SARS-CoV-2 antibodies used to treat patients severely ill with COVID-19. Blood was collected 10–393 days after the 14-day isolation period. None of the participants had prior anti-SARS-CoV-2 vaccination, and none were hospitalized due to a severe course of COVID-19. Blood tests were performed using the MAGLUMI 800 device: test SARS-CoV-2 S-RBD IgG (Snibe Diagnostic; test result <1 AU/ml was nonreactive, whereas ≥1 AU/ml was reactive). Serological tests were performed using the in vitro chemiluminescent kit for the quantification of S-RBD IgG neutralizing antibodies (nAb) against SARS-CoV-2, intended for serum and plasma testing on automatic analyzers of the MAGLUMI series in accordance with the recommendations of the manufacturer of the SNIBE DIAGNOSTIC test. After collecting blood from the examined person, it was placed in test tubes with a separating gel or clot activator. After centrifugation (>10 000 RCF for 10 min), a sample (10 µl volume) containing no fibrin or other solids was collected. Then the sample, along with the buffer and magnetic particles coated with the recombinant S-RBD antigen, were mixed and incubated, which resulted in the formation of immune complexes. After magnetic field precipitation, the supernatant was removed and washed. After the addition of ABEI-labeled anti-human IgG antibodies, the sample was subjected to another incubation and precipitation followed by washing to remove unbound proteins from the sample. Finally, the chemiluminescence reaction was initiated and the light signals were measured with a photomultiplier for 3 s as a relative light unit (RLU) that is proportional to the SARS-CoV-2 S-RBD IgG concentration. All tests were performed after the manufacturer recommended calibration with quality control as well as precautions and safety measures for in vitro diagnostics. The sensitivity of the test (according to the manufacturer) in the case of a test performed 15 days after the onset of symptoms is 100.0% and its specificity is 99.6% (CE REF 30219017 M).[3] Our study protocol was approved by the local independent Bioethics Committee (NKBBN 199/2021). The obtained results were analyzed using the χ^2 test (Statistica 13.3 StatSoft Pl.). Statistical significance was accepted at $p < 0.05$. Excel software was used to illustrate the obtained results and determine the trends (Microsoft Corporation).

3 | RESULTS

We included a total of 351 COVID-19 convalescents in our study (305 males and 46 females), whose ages ranged from 18 to 63 (mean age 39). The obtained results were divided into four groups depending on the number of days since the isolation of the antibody titers (Table 1).

We noted an increasing trend in anti-SARS-CoV-2 antibody titers depending on the time since infection (Table 1, Figure 1). The highest increase in the average antibody titer was observed in convalescents from Group I versus II (increase by 82,4%). In addition, we noted an increase of 27.1% between Group II and III and between III and IV 6.4%. The total increase in antibody titer between Group I versus IV was 146.6%.

Based on the mean or median age, the group of convalescents was divided into two groups: <39 and ≥39 years of age. The results were illustrated in Figure 2. Participants who were at or above the mean age had higher antibody titers than those who were younger. Among the older (≥39 lat years of age) participants, the line of the trend was increasing, whereas it was horizontal among the younger (<39) ones. We noted a statistically significant difference between the minimum and maximum values of antibody titers depending on age.

A similar correlation was noted in terms of sex. Average antibody titers were lower among females than among males (statistically significant difference $p < 0.05$). In addition, among the female participants, we noted a decrease in the antibody titers depending on the time since infection. In contrast, among the males, this correlation was positive (increasing titers, Figure 3).

We noted higher antibody titers among the male and female participants above the mean age (statistically significant difference, $p < 0.05$). In addition, among the male participants, the difference between anti-SARS-CoV-2 antibody titers increased with time since

TABLE 1 Levels of IgG anti-SARS-CoV-2 antibody in the studied group of patients depending on the time after COVID-19

	<29 days	30–59 days	60–89 days	>90 days
Group size	27	204	95	25
Average antibody titer*	1:349 41	1:637 27	1:809 64	1:861 52

*Statistical significance $p < 0.05$.

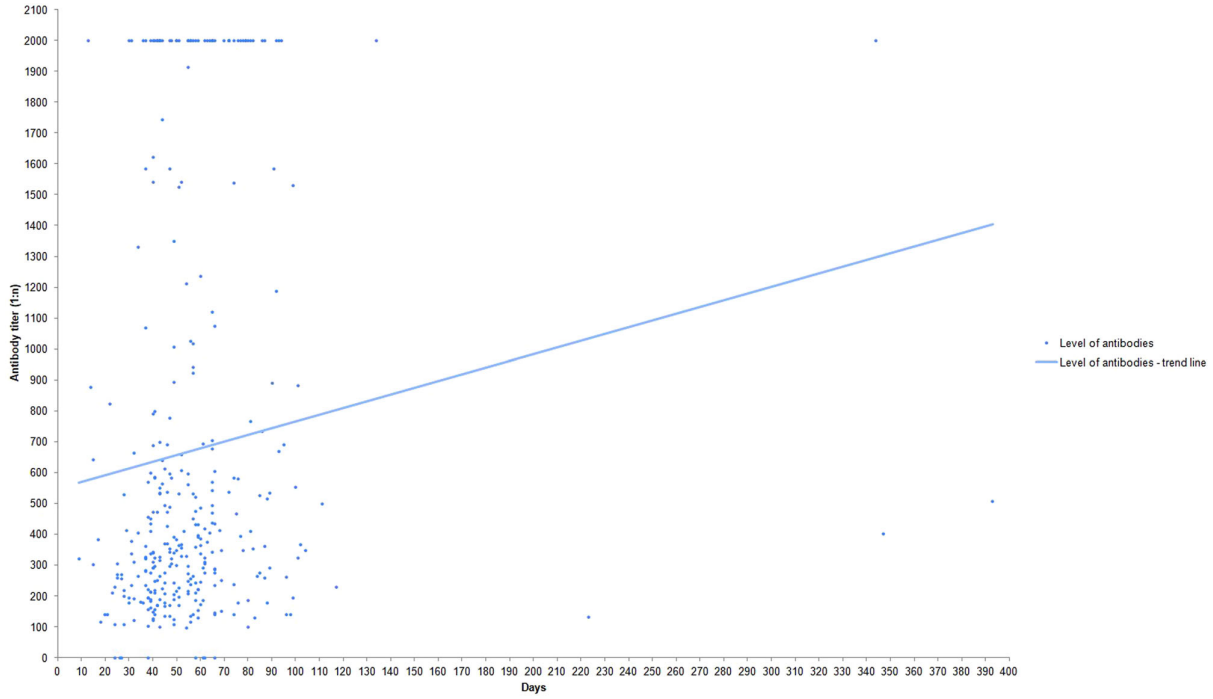

FIGURE 1 Anti-SARS-CoV-2 IgG antibodies among COVID-19 convalescents depending on the time since infection

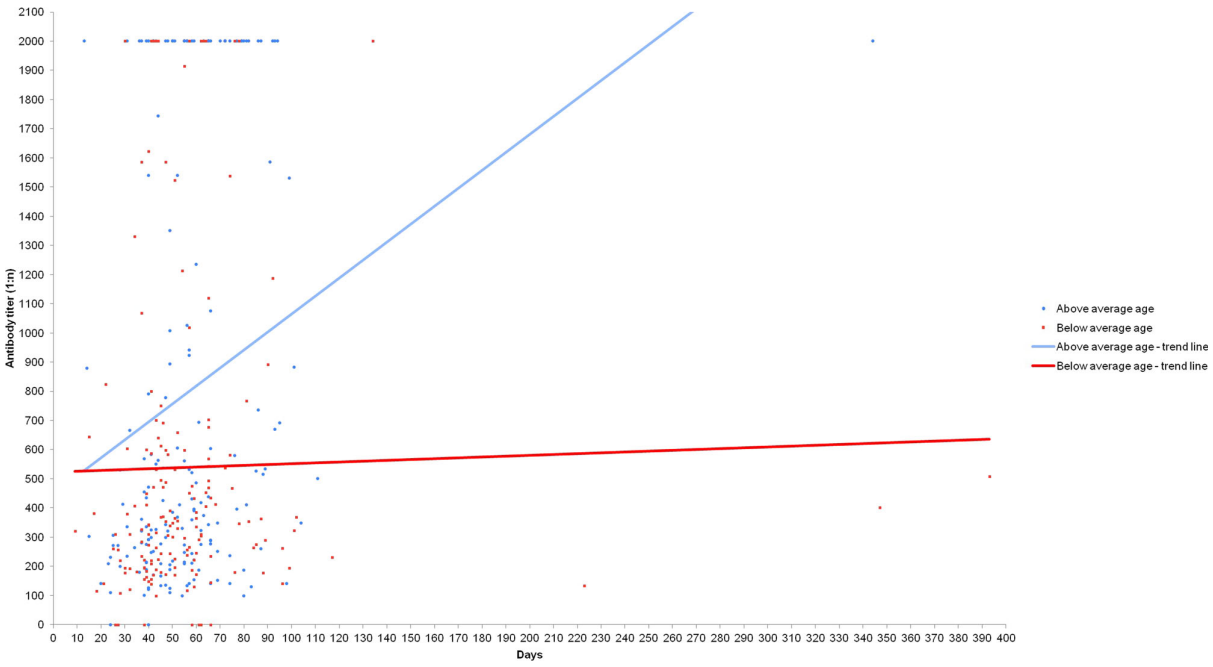

FIGURE 2 Anti-SARS-CoV-2 antibody titers depending on age

infection, whereas among the female participants, we observed an inverse correlation (Figures 4 and 5).

We divided the entire sample of participants into two subgroups depending on the severity of their COVID-19 illness. The severe course of COVID-19 was defined as ≥5 symptoms, whereas mild illness was defined as ≤4 symptoms. We noted a difference in antibody titers' minimum and maximum values depending on the severity of illness (Figure 6). These titers were higher among participants who

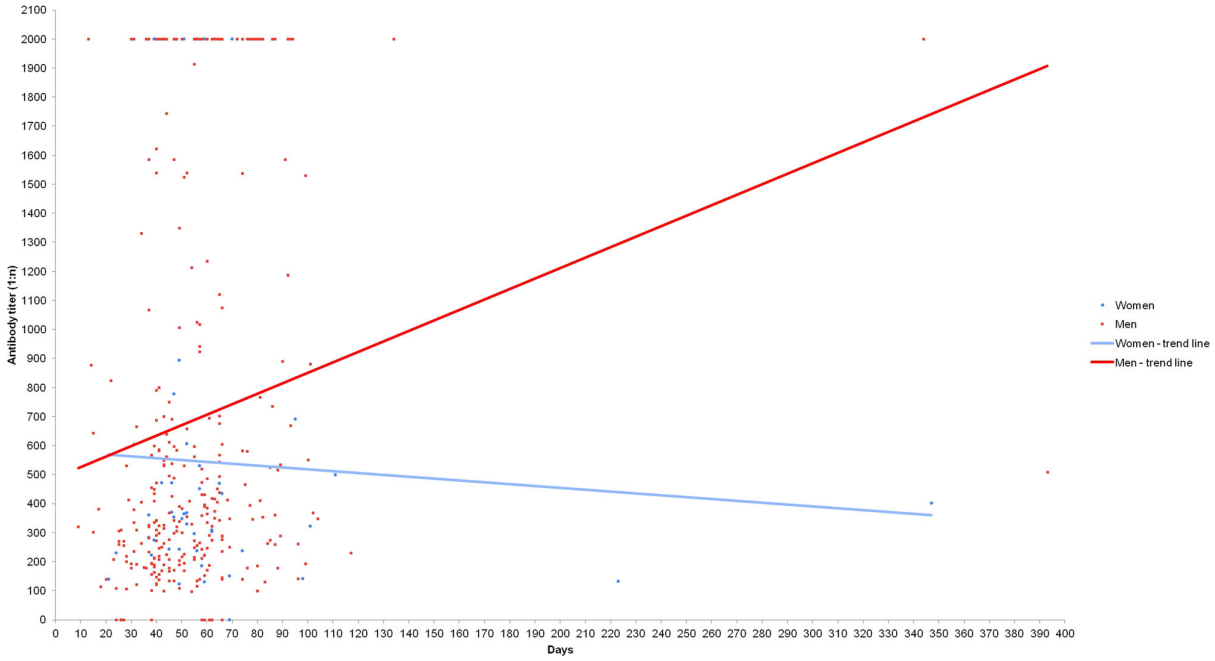

FIGURE 3 Anti-SARS-CoV-2 antibody titers depending on sex

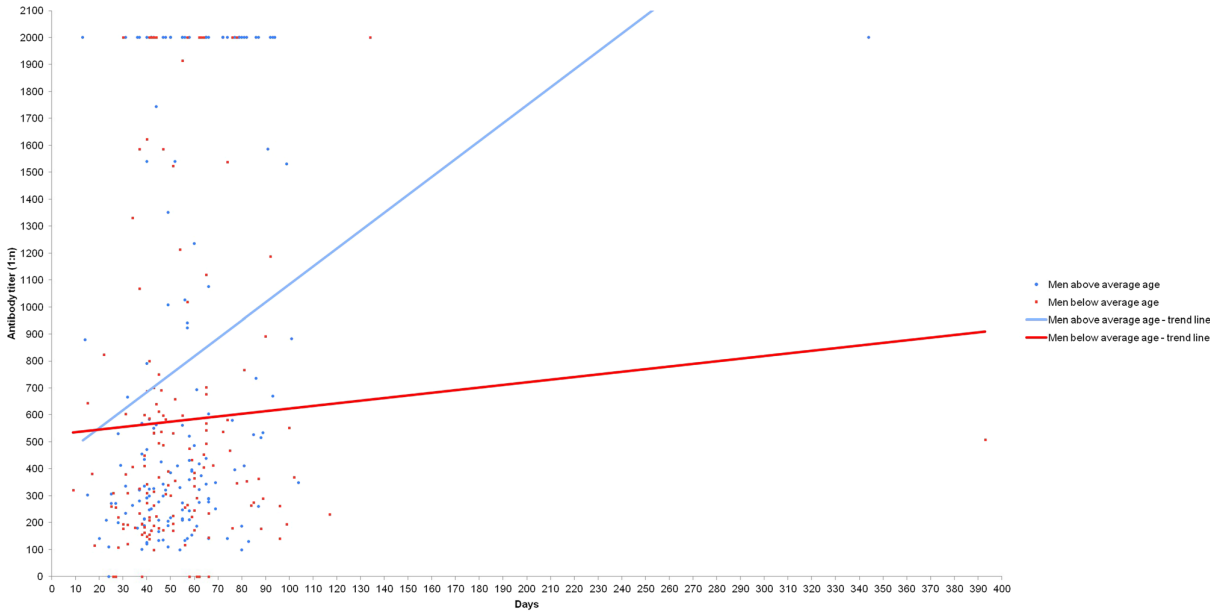

FIGURE 4 Anti-SARS-CoV-2 antibodies among males, depending on mean age

recovered from a more severe course of COVID-19 when measured early (<60 days since the end of isolation; statistically significant difference $p < 0.05$). However later, after 140 days, we noted an inverse correlation (higher antibody titers among participants after mild illness), which was not statistically significant and based on a small sample.

The anti-SARS-CoV-2 antibody titers were the highest in males and females above the mean or median age (≥39 years of age) and had a more severe course of COVID-19 (Figure 7). It is noteworthy that in female participants, we noted the higher antibody titers only in the early period (<2–3 months since the end of isolation; Figure 5).

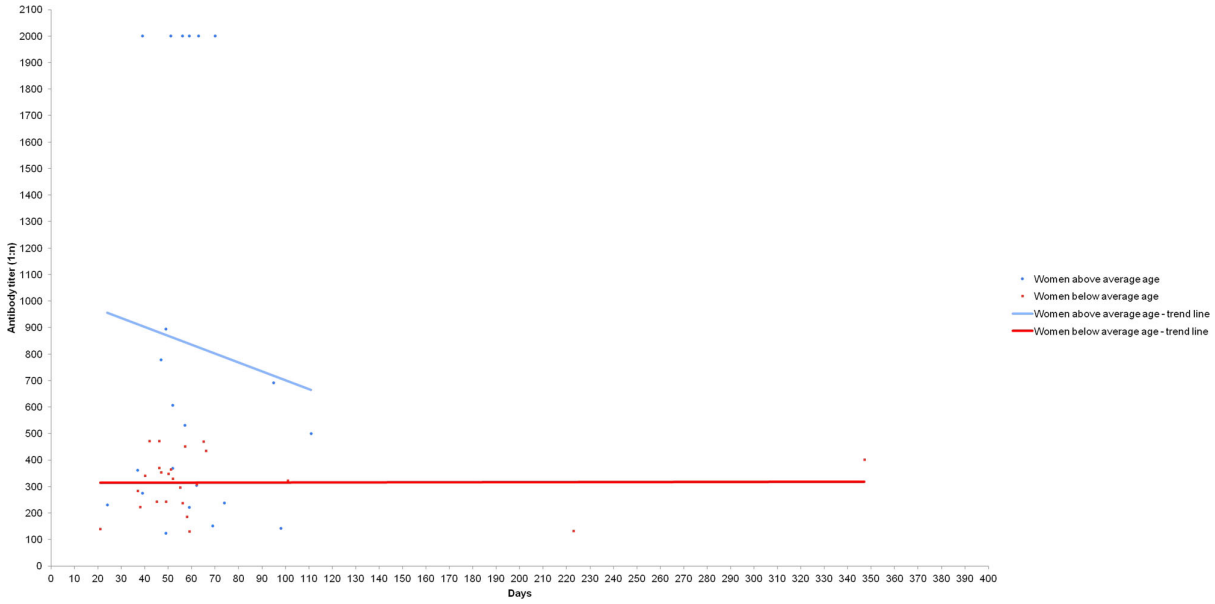

FIGURE 5 Anti-SARS-CoV-2 antibodies among females, depending on mean age

4 | DISCUSSION

Passive immunotherapy based on transfusing antibody-rich plasma obtained from convalescents is one of the strategies in treating infectious diseases. The effectiveness of plasma from convalescents has been demonstrated in treating hepatitis A and B, rabies, cytomegalovirus, and respiratory syncytial virus pneumonia.[4–7] In addition, this method helps treat patients with severe course of illness and postexposure prophylaxis.[4,5,8] Many authors confirm the effectiveness of convalescent plasma in preventing and treatment of a severe course of COVID-19. However, others did not find a statistically significant influence of it on mortality.[8–11]

In Poland, the supply, production, and storage of plasma are conducted by Regional Centers of Blood Donation and Treatment. Plasma donors are recruited from COVID-19 convalescents in whom high titers of specific anti-SARS-CoV-2 antibodies are expected. Flisiak et al. accepted antibody titer >1:500 as "high."[3] However, the salient questions about who the optimal donors are and when is the optimal time to collect their plasma remains unanswered. In their analysis of the *Spanish influenza* epidemic, Luck et al. noted that the plasma richest in antibodies was collected from convalescents 7–60 days after the end of infection symptoms.[4] Chen et al. reported a decrease in anti-SARS-CoV-2 IgG antibodies in the third month since recovery from COVID-19.[12] Klein et al. had similar results.[8] In our study, the convalescents had the recommended antibody titer (>1:500) after 30 days since the end of isolation. Our study participants donated plasma in various periods since recovery. Therefore, we had the opportunity to measure antibody titers for a long time, except for one male participant who donated blood 11 times within 6 months (due to continually high anti-SARS-CoV-2 titer, we could not obtain repeated antibody titer measurements in the same convalescent and asses individual trends. However, in this particular convalescent, it is not possible to exclude the possibility of reinfection. In available literature is no widely available and generally agreed-upon best test for measuring neutralizing antibodies, and the antibody titers in convalescent plasma from patients who have recovered from COVID-19 are highly variable.[13] The level of 27.4 AU/ml (the result is the same as the level 1:500) was defined on the basis of research conducted by the Polish Nationality Center for Blood and Blood Treatment - Maglumi and DiaSorin SARS-CoV-2 S-RBD IgG tests.

In our study, we noted higher antibody titers in convalescents who donated plasma later after infection, and these were mainly higher in those who were older and in males. These results are congruent with those published by Klein et al.[8] We first excluded anti-HLA antibodies (postpregnancy or post-transfusion) in all the collected blood samples, thus explaining the small number of female participants in our study. Furthermore, the weaker response to immunization, lack of anti-HLA antibodies despite a history of pregnancies might go hand-in-hand with low anti-SARS-CoV-2 antibody titers. Thus, as many as 60%–70% of female convalescents were excluded from our study due to the presence of anti-HLA antibodies.

Weisber et al. and Ko et al. noted that the antibody titers were higher in patients who had a more severe course of illness.[14,15] Our results were similar, with initial antibody titers 60% higher in participants who recovered from severe COVID-19 (≥5 symptoms) than those after mild illness (1:500 vs. 1:800). After 5–6 months since infection, the antibody titers in both groups became similar. Klein et al. noticed a similar trend: antibody titers were significantly higher in hospitalized patients (implying a more severe course of illness).[8] Robbiani et al. concluded that the observed difference in

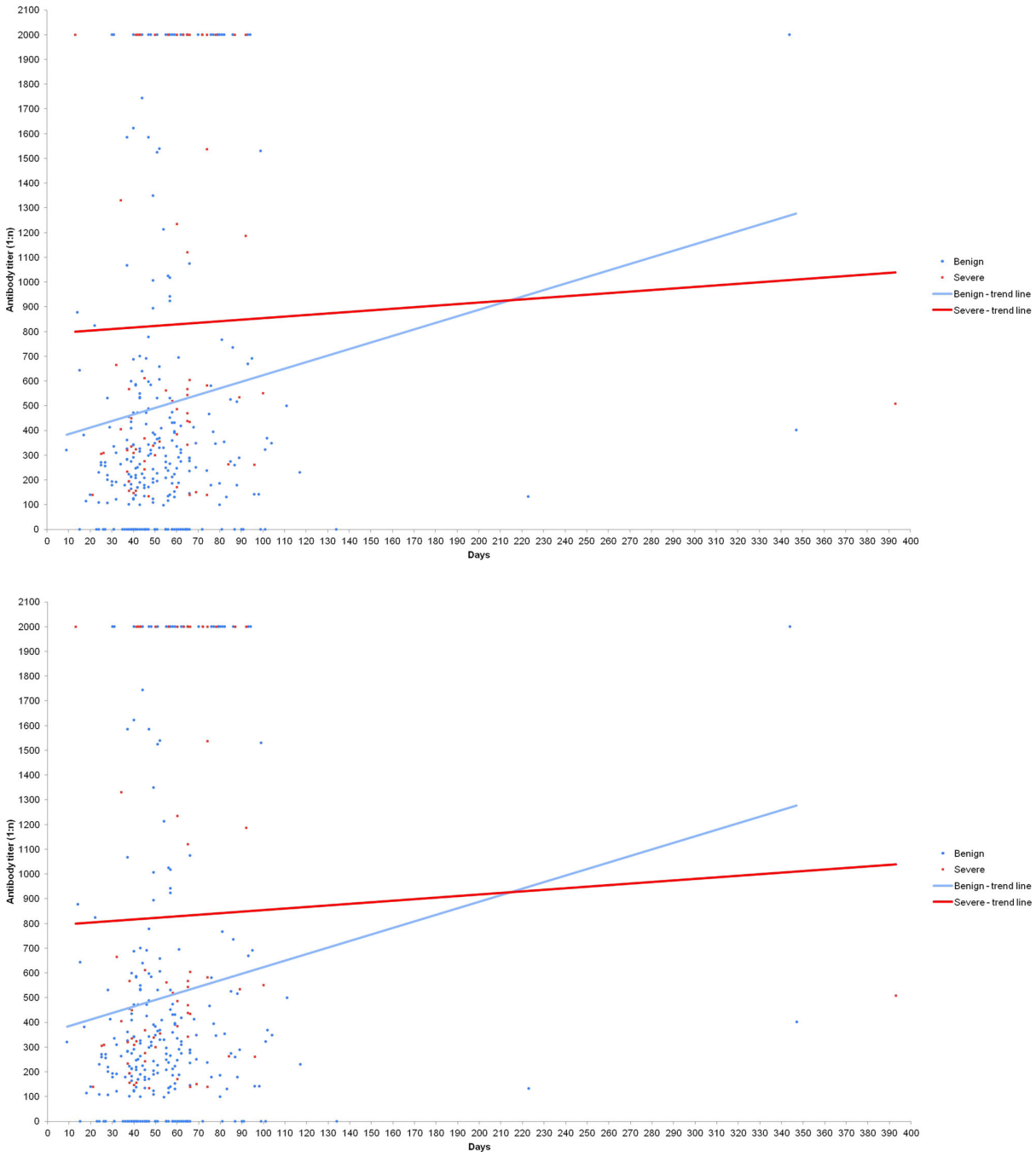

FIGURE 6 Anti-SARS-CoV-2 antibody titers depending on the severity of the disease

antibody titers is due to a more severe course of COVID-19 in older males and with higher mortality in that group.[16] Scully et al. sought to explain this difference via the influence of estrogen, testosterone, and progesterone on the immune response and the course of illness.[17] This correlation should also be considered as a possible explanation for the decreased antibody titers among older women in our study.

The presence of specific antibodies confirms past infection. However, it remains unclear how effective they will be in other patients. In their study about *Lassa fever*, Jahrling et al. assessed the quality of plasma via specific IgG antibody titers and the neutralizing test. The authors noted that the most effective plasma was obtained from convalescents after 8 months since recovery and had high antibody and neutralizing test titers.[18] Our study similarly observed the

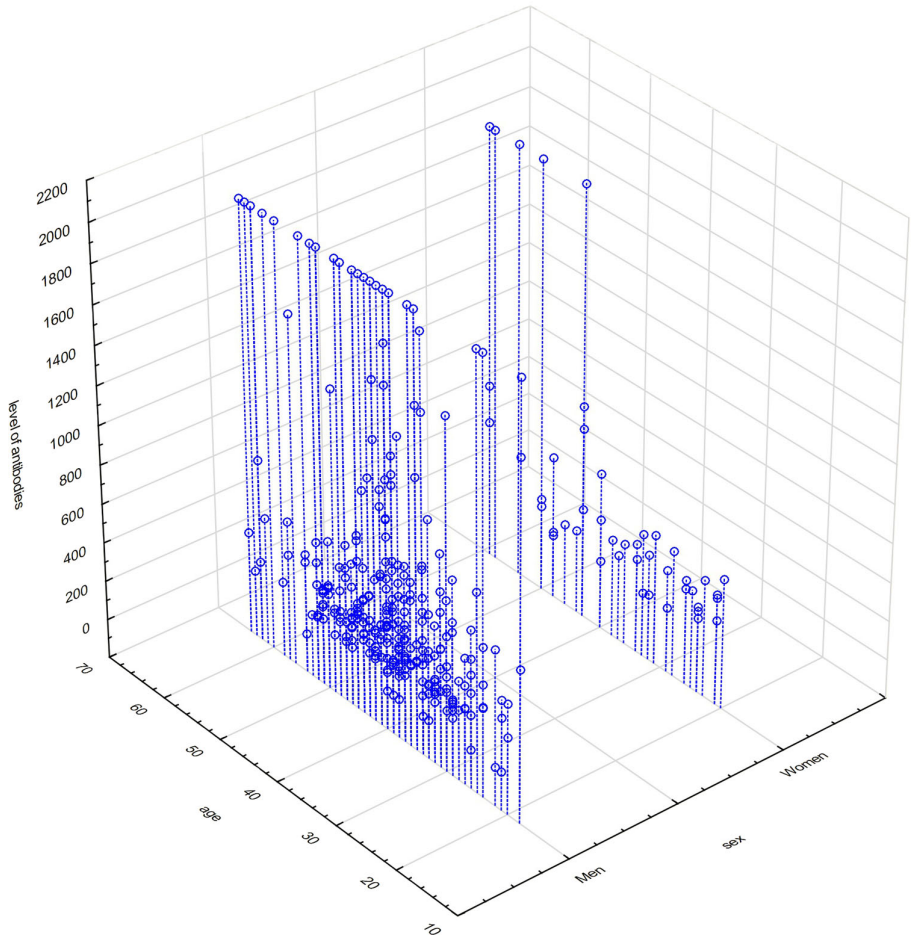

FIGURE 7 The anti-SARS-CoV-2 antibody titers depending on age and sex

most elevated specific IgG antibody titers in convalescents who donated blood over 90 days postrecovery. Klein et al. observed the effectiveness of convalescent plasma, which was assessed in terms of IgG anti-SARS-CoV-2 titer.[8] The poor quality of those antibodies might explain the poor efficacy of treatment using antibodies. It might be due to the titer of these antibodies and the low result of the neutralizing test, and the fact that the donor and recipient are not from the same geographical region. This factor might be of particular significance given the number of region-specific mutations of the SARS-CoV-2 virus. Therefore, plasma obtained from COVID-19 convalescents should be used to treat severely ill patients in the region closest to where the plasma specimen was collected and prepared.

5 | CONCLUSIONS

The anti-SARS-CoV-2 antibody titers increased together with time since infection. The later the convalescent donates blood, the greater the antibody titer. Therefore, the optimal plasma donors are older convalescents (≥39 years of age) who recovered from severe COVID-19.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ETHICS STATEMENT

The study protocol was approved by the Regional Bioethics Committee of Gdansk Medical University, Poland (approval nr. NKBBN 199/2021). The patient's written consent was obtained to use clinical data without disclosing personal data. All authors affirm that their study accepted the required ethical clearance and respected all ethical considerations.

AUTHOR CONTRIBUTIONS

Contributed to study concept and design, contributed to acquisition, drafted manuscript, critically revised manuscript, gave final approval: Andrzej Skorek. *Contributed to conception and design, data collection contributed to acquisition, critically revised manuscript gave final approval*: Anna Jaźwińska-Curyłło and Aleksandra Romanowicz. *Contributed to acquisition, analysis,*

and interpretation of the results; drafted manuscript; gave final approval: Krzysztof Kwaśniewski. *Contributed to conception, analysis, and interpretation of the results, critically revised manuscript, gave final approval*: Waldemar Narożny. *Contributed to conception, analysis, and results interpretation, drafted manuscript, critically revised manuscript, gave final approval*: Dmitry Tretiakow.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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INDEX COPERNICUS INTERNATIONAL

ORIGINAL ARTICLE

COVID-19 symptoms in the Pomeranian region

Objawy COVID-19 w rejonie pomorskim

Authors' Contribution
A–Study Design
B–Data Collection
C–Statistical Analysis
D–Manuscript Preparation
E–Literature Search
F–Funds Collection

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ABSTRACT:

Introduction: COVID-19 is a disease caused by pathogenic β-coronavirus. As a relatively new disease, diagnosis of COVID-19 is highly problematic and because of non-specific symptoms the infection must be confirmed with molecular tests.

Aim: Evaluation of the most common COVID-19 symptoms and statistical analysis of obtained data in order to confirm significant correlations between symptoms and age and sex of the examined patients.

Material and methods: A questionnaire has been carried out among 751 patients of Center for Blood Donation in Gdansk and the Department of Otolaryngology in Gdansk. The patients were convalescents after SARS-CoV-2 infection. The presence of virus was confirmed by a positive PCR test of RNA of the SARS-CoV-2 virus of each patent. The study has been carried out since the beginning of the presence of COVID-19 in Pomerania region till April 2021.

Results: Results of the questionnaires presented the most common general and otolaryngological symptoms of COVID-19. Collected data was statistically analyzed. Patients were divided according to age and sex. 30.2% of patients had severe clinical course of infection, 69.8% had mild clinical course. The most common general symptom associated with SARS-CoV-2 infection was fatigue, which was more common among women. Other common symptoms were loss of smell and taste, also more common among women, and muscle and joint pain. The most common other otolaryngological symptoms were sore throat and vertigo, all more frequent in men.

Conclusion: The study presents the correlation between incidence of COVID-19 disease symptoms and age and sex of patients. Fatigue, loss of smell and taste and muscle and joint pain were the most common symptoms of the infection. Presented data highlights the meaning of further research on COVID-19 symptoms.

KEYWORDS: COVID-19, general symptoms, otolaryngological symptoms

STRESZCZENIE:

Wstęp: Infekcja COVID-19 jest chorobą wywoływaną przez wysoko patogenny β-koronawirus, chorobotwórczy dla człowieka. Jako stosunkowo nowa jednostka chorobowa COVID-19 przysparza wciąż wielu trudności diagnostycznych. Z uwagi na nieswoistość objawów potwierdzenie zakażenia wymaga wykonania testów molekularnych.

Cel: Ocena najczęstszych objawów w przebiegu infekcji COVID-19 oraz analiza statystyczna uzyskanych danych w celu wykrycia istotnych zależności między występowaniem objawów a wiekiem i płcią badanych.

Materiał i metody: Przeprowadzono ankietę wśród 751 pacjentów Centrum Krwiodawstwa w Gdańsku oraz Kliniki Otolaryngologii w Gdańsku, ozdrowieńców po infekcji SARS-CoV-2 (drugi koronawirus ciężkiego ostrego zespołu oddechowego), u których obecność wirusa była potwierdzona dodatnim wynikiem badania PCR z nosa na obecność RNA wirusa SARS-CoV-2. Badania przeprowadzano od początku występowania schorzenia na terenie Pomorza do kwietnia 2021 roku.

Wyniki: Wyniki ankiety wskazały najczęstsze ogólne i otolaryngologiczne objawy zakażenia COVID-19. Zebrane dane poddano analizie statystycznej, grupę badanych podzielono według płci i wieku. Przebieg ciężki zakażenia zdiagnozowano u 30,2% pacjentów, zaś łagodny u 69,8% pacjentów. Najczęstszym objawem ogólnym, towarzyszącym zakażeniu wirusem SARS-CoV-2, było zmęczenie, częściej występujące u kobiet. Ponadto pacjenci zgłaszali wystąpienie innych objawów ogólnych, takich jak utrata węchu i smaku (częstsza wśród kobiet i osób młodszych) oraz ból mięśni i stawów. Do najczęstszych objawów otolaryngologicznych należały ból gardła i wirowe zawroty głowy, które częściej występowały wśród badanych mężczyzn.

Wnioski: Badanie wskazuje na zależność kluczowych objawów COVID-19 od wieku i płci. Zmęczenie, utrata węchu i smaku oraz ból mięśni i stawów są najczęstszymi objawami infekcji. Przedstawione wyniki podkreślają znaczenie dalszych badań nad symptomatologią infekcji.

SŁOWA KLUCZOWE: COVID-19, objawy ogólne, objawy otolaryngologiczne

ABBREVIATIONS

COVID-19 – coronavirus disease 2019
CNS – central nervous system
PCR – polymerase chain reaction
RNA – ribonucleic acid
SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2

INTRODUCTION

SARS-CoV-2 infection (or COVID-19 disease) is an infection caused by a pathogenic coronavirus, in which case early diagnosis and isolation is crucial. Because of its non-specific symptoms, the disease is still diagnostically challenging at its early stages. Varying clinical course and similarity to other viral upper respiratory infections led to attempts to unify and classify its clinical presentation since the pandemic started. Delayed diagnosis, massive infection or many risk factors of reduced immune response may lead to respiratory failure, multi-organ failure and death.

The clinical course of COVID-19 depends on the specific subtype of the virus (its mutations), and hence, there is geographical and temporal variability. Symptoms of SARS-CoV-2 infection include systemic symptoms and otolaryngological symptoms. In our study, we evaluated the symptoms of COVID-19 in a selected patient group in Pomerania since the outbreak of the disease to April 2021. Pomerania has 2.3 mln inhabitants [1]. Over that time, the dominant strain of SARS-CoV-2 was the alpha type [2–4]. The first infection was reported on March 14th, 2020 in this region [5]. Since then, 192 133 people got infected in Pomerania (as of July 21st, 2021) [6, 7].

MATERIAL AND METHODS

Into the study, 751 COVID-19 convalescents were enrolled, in whom the infection was confirmed by PCR testing of nasal swabs for SARS-CoV-2 RNA. It consisted of 599 males and 152 females. The participation was voluntary. The study was conducted among patients admitted to the Otolaryngology Department, University Clinical Center in Gdańsk, and individuals presenting to the Regional Blood Center in Gdańsk to donate plasma, so that plasma rich in anti-SARS-CoV-2 antibodies could be used in severe COVID-19 cases. The participants were asked to fill out a survey, where they were asked about systemic and otolaryngological symptoms. systemic symptoms included: shivers, dry cough, arthralgia and myalgia, conjunctivitis, fever >38°C, fatigue, dyspnoe, diarrhea, loss of taste and smell. Laryngological symptoms: sore throat, vertigo, dizziness, nausea and vomiting, sudden unilateral loss of hearing, progressive loss of hearing, tinnitus. In the survey, we also asked about the severity of infection (number of symptoms, oxygen therapy, hospital stay), its duration and comorbidities. Our study was approved by the Independent Bioethics Committee (NKBBN 199/2021). The data were statistically analyzed using the chi-squared test (Statistica 13.3 StatSoft PL software). The significance level was set at $P < 0.05$.

RESULTS

The studied group consisted of 751 individuals, including 599 males (79.8%) and 152 females (20.2%). The mean age was 38.0. Patients above the mean age (> 38.0) were considered senile, and patients at the mean age or younger (≤ 38.0) were considered young. There were 363 senile patients (48.3%) and 388 young patients (51.7%). Then, each age group was further subdivided by sex. There were 304 senile males (50.8%) and 295 younger males (49.2%). Among the women, there were 59 senile (38.8%) and 93 younger (61.2%) patients.

The most common systemic symptom was fatigue, which was reported by 488 participants (65.0%), including 377 males and 111 females. We also found a statistically significant difference between sexes – fatigue was more common in women. Also, fatigue was more common in younger than in senile women, and more common in younger men than in younger women (statistically significant differences). The second most common symptom was loss of taste and smell. It was reported by 486 participants (64.7%), including 370 males and 116 females. There was a statistically significant correlation between age and sex and loss of smell and taste – it was more common in women and in younger individuals. There was a statistically significant correlation between sex and dry cough as well as between sex and fever. Dry cough was reported by 282 participants (37.6%), including 243 males and 39 females, and fever was reported by 3000 individuals (40.0%), including 251 males and 49 females. Additionally, dry cough was statistically more common in younger men than in younger women, and fever was more common in senile men compared to senile women (statistically significant differences). We established a statistically significant correlation between sex and diarrhea in younger individuals (Fig. 1., Tab. I.). The studied group was further divided according to the course of the infection. Mild infection was defined as concurrence of 4 or less systemic symptoms, while severe infection was defined as 5 or more systemic symptoms and / or hospital admission. Severe infection was found in 227 patients (30.2%), while mild infection was observed in 524 patients (69.8%).

In addition to loss of taste and smell, the most common otolaryngological symptom was sore throat. It was present in 172 participants (22.9%), including 127 males and 45 females. We found a statistically significant difference between sex and sore throat as well as between sex and sore throat in senile participants. We found a statistically significant difference between sex and vertigo as well as between sex and vertigo in senile participants. This symptoms was present in 98 participants (13.0%) – in 68 males (including 35 senile males) and 30 females (including 13 senile women). Nausea and vomiting occurred in 30 individuals (4.0%) and were statistically more common in men than in women. There was a statistically significant difference between sex and nausea and vomiting in younger individuals. This symptom was reported by 7 young men and 8 young women. Tinnitus (de novo) was reported by 33 individuals (4.4%), and was statistically more common in senile participants (23 people) than in younger ones (10 people); it was also more common in senile men (18 people) than in younger men (7 people) (Tab. II.).

Tab. I. Statistical analysis of systemic symptoms of SARS-CoV-2 infection with respect to sex.

	M	K	ST	MŁ	MS	MM	KS	KM	MM	KM	MS	KS
Chills	26.38%	25.66%	24.52%	27.83%	24.01%	28.81%	28.81%	23.66%	28.81%	23.66%	24.01%	28.81%
	p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05	
Dry cough	40.57%	25.66%	42.98%	40.46%	43.42%	37.63%	45.76%	46.24%	37.63%	46.24%	43.42%	45.76%
	p < 0.05		p > 0.05		p > 0.05		p > 0.05		**p < 0.05**		p > 0.05	
Pain in muscles and joints	54.92%	58.85%	53.44%	57.73%	51.97%	57.97%	66.10%	53.76%	57.97%	53.76%	57.97%	66.10%
	p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05	
Conjunctivitis	5.51%	5.26%	6.34%	4.64%	6.58%	4.41%	5.08%	5.38%	4.41%	5.38%	6.58%	5.08%
	p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05	
Fever >38°C	41.90%	32.24%	40.77%	39.18%	43.42%	40.34%	28.81%	23.66%	40.34%	23.66%	43.42%	28.81%
	p < 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05		**p < 0.05**	
Fatigue	62.94%	73.03%	70.25%	67.78%	61.51%	64.41%	72.88%	73.12%	64.41%	73.12%	61.51%	72.88%
	p < 0.05		p > 0.05		p > 0.05		**p < 0.05**		**p < 0.05**		p > 0.05	
Dyspnoea	19.87%	21.05%	19.28%	20.88%	19.41%	20.34%	20.34%	21.51%	20.34%	21.51%	19.41%	20.34%
	p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05	
Diarrhea	11.02%	15.13%	12.40%	11.34%	12.17%	9.83%	13.56%	16.13%	9.83%	16.13%	12.17%	13.56%
	p > 0.05		p > 0.05		p > 0.05		p > 0.05		**p < 0.05**		p > 0.05	

Tab. II. Statistical analysis of otolaryngological symptoms of SARS-CoV-2 infection with respect to sex.

	M	K	ST	MŁ	MS	MM	KS	KM	MM	KM	MS	KS
Sore throat	21.20%	29.61%	24.24%	21.65%	22.04%	20.34%	30.88%	28.57%	20.34%	28.57%	22.04%	30.88%
	p < 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05		**p < 0.05**	
Loss of smell and taste	61.77%	76.32%	58.13%	70.88%	56.91%	66.78%	55.88%	92.86%	66.78%	92.86%	56.91%	55.88%
	p < 0.05		**p < 0.05**		**p < 0.05**		**p < 0.05**		**p < 0.05**		p > 0.05	
Vertigo	11.35%	19.74%	13.22%	12.89%	11.51%	11.19%	19.12%	20.24%	28.81%	20.24%	11.51%	19.12%
	p < 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05		**p < 0.05**	
Dizziness	7.01%	7.89%	7.16%	7.22%	7.24%	6.78%	5.88%	9.52%	6.78%	9.52%	7.24%	5.88%
	p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05	
Nausea and vomiting	2.84%	8.55%	4.13%	3.87%	3.29%	2.37%	7.35%	9.52%	2.37%	9.52%	3.29%	7.35%
	p < 0.05		p > 0.05		p > 0.05		p > 0.05		**p < 0.05**		p > 0.05	
Sudden-onset unilateral loss of hearing	1.34%	0.66%	1.65%	0.77%	1.97%	0.68%	0.00%	1.19%	0.68%	1.19%	1.97%	0.00%
	p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05	
Sudden-onset unilateral loss of hearing	0.67%	0.66%	1.10%	0.26%	0.99%	0.34%	1.47%	0.00%	0.34%	0.00%	0.99%	1.47%
	p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05		p > 0.05	
Tinnitus	4.17%	5.26%	6.34%	2.58%	5.92%	2.37%	7.35%	3.57%	2.37%	3.57%	5.92%	7.35%
	p > 0.05		**p < 0.05**		**p < 0.05**		p > 0.05		p > 0.05		p > 0.05	

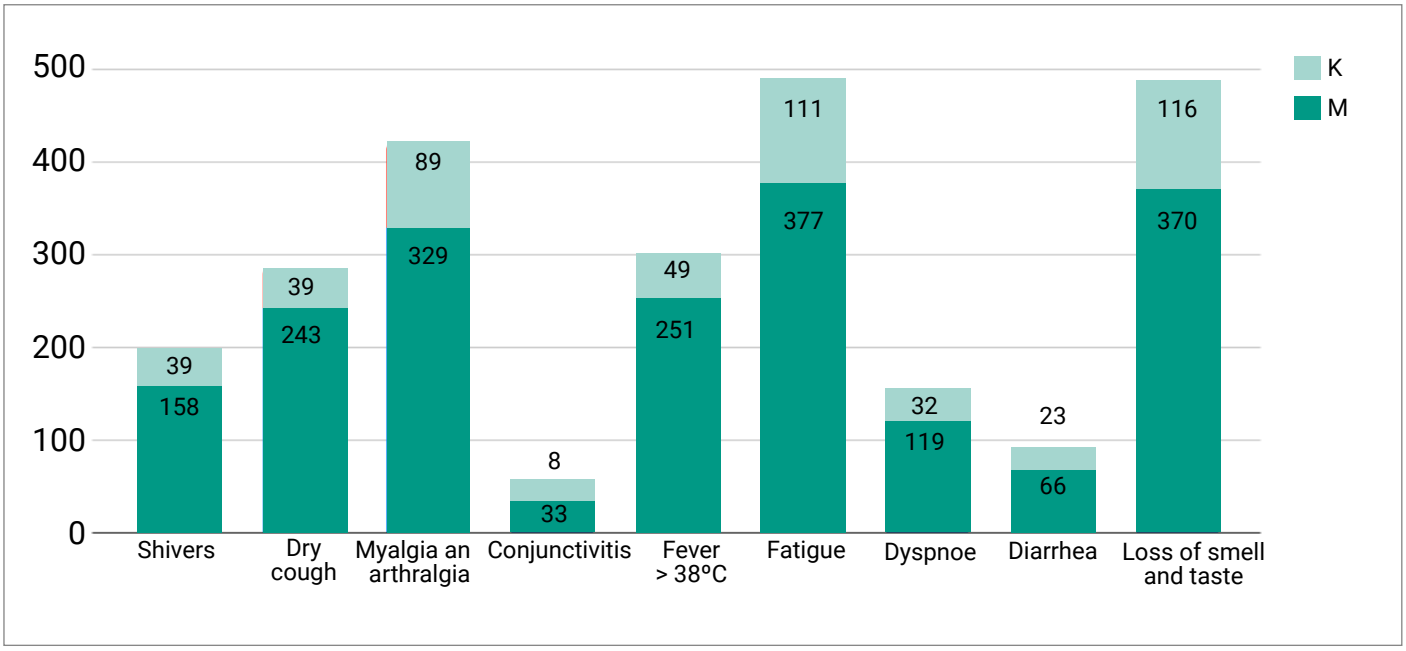

Fig. 1. Systemic symptoms of SARS-CoV-2 infection with respect to sex.

DISCUSSION

Confirmed SARS-CoV-2 infection in the past 15 months was diagnosed in 8.4% of the total population of Pomerania, which is the highest rate compared to other regions (e.g. Masovia – 7.2%; Silesia – 8.1%, Poland – 7.5%; Europe – 6.7%) [5, 8, 9]. The course and symptoms of COVID-19 varies between patients. According to the literature, 81% of SARS-CoV-2 infections are mild [10]. In our study, mild infection was diagnosed in 69.8%. However, many patients (over 30%) required more aggressive treatment, often at hospital. Usually, it was due to pneumonia, which may lead to acute respiratory failure. Severe COVID-19 infection can be associated with disseminated vascular pathology affecting heart, kidneys, liver, and CNS, which sometimes leads to multiorgan failure [11].

The non-specificity and variety of symptoms of SARS-CoV-2 infection in the absence of pathognomonic symptoms causes diagnostic problems. The use of molecular methods is the cornerstone of diagnosis [12]. The most common systemic symptoms of COVID-19 are cough, fever and fatigue [10, 13–15]. These symptoms are non-specific and are similar to flu symptoms. The possibility of co-infection with SARS-CoV-2 and influenza viruses should be considered [11, 12].

Approximately 70% of COVID-19 cases are accompanied by chemosensory pathology such as partial or total loss of smell and taste (hyposmia / anosmia, hypogeusia / ageusia) [12, 13, 15–20]. Smell and taste disorders are more common in women [12]. In our study, such pathologies were found in 64.9% of patients, mainly young people. Those symptoms stem from neurotropism of the SARS-CoV-2 virus to the tissues of the central nervous system [21]. The presence of olfactory and taste disorders is used to confirm the diagnosis of COVID-19 infection based on molecular tests. Said et al. reported an attempt to use the olfactory organ assessment as a screening test to detect COVID-19, finding the sensitivity and specificity of this method of 75% and 95% respectively [22]. Hyposmia and hypogeusia can also be thought of as distinguishing symptoms, mainly between influenza and COVID-19 [12]. Zayet et al. found an olfactory disorder in 17% of patients with influenza and 53% of patients with COVID-19, the differences being statistically significant. The authors also emphasized differences in the duration of those symptoms, i.e. 3 and 7 days respectively [23]. Other symptoms such as cough, fatigue or fever, due to their low specificity, cannot help distinguish between COVID-19 and other flu-like infections. SARS-CoV-2 infection can also be accompanied by other otolaryngological symptoms, such as sore throat, xerostomia, bitter taste, sore mouth [13, 19, 24]. Otolaryngological symptoms can sometimes be the first manifestation of an infection, or even the only symptoms of COVID-19.

It seems that neurotropism of SARS-CoV-2 virus is the cause of other otolaryngological symptoms such as vertigo, dizziness and tinnitus, which may be due to disruption of neural network responsible for hearing and equilibrium [25–27]. Experimental data show abundant expression of ACE2, TMPRSS2 and Furin receptors in a snail infected with SARS-CoV-2, which confirms its vulnerability [28]. Scarce number of report available in the literature makes it possible only to confirm the presence of equilibrium disorders accompanying COVID-19 [26–30].

Presence of neurological symptoms helps diagnose COVID-19, although sometimes it can only be the only manifestation of SARS-CoV-2 infection. For this reason, it is crucial to frequently perform PCR testing to detect the virus, maintain high hygienic standards and use personal protective equipment in order to limit spreading of the virus [25, 30].

CONCLUSIONS

COVID-19 infection has a broad spectrum of symptoms, which may be diagnostically challenging and require molecular testing to make the right diagnosis. Fatigue, loss of smell and appetite, myalgia and arthralgia are the most common symptoms. COVID-19 can also be accompanied by otolaryngological symptoms, the most common being sore throat and vertigo. The presented results and still scarce global data on COVID-19 symptoms emphasize the need for future studies.

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Wykaz skrótów:

SARS-CoV-2 - koronawirus ciężkiego ostrego zespołu oddechowego 2

COVID-19 - choroba koronawirusowa 2019

WHO - Światowa Organizacja Zdrowia

Wstęp

Wirus SARS-CoV-2 (koronawirus ciężkiego ostrego zespołu oddechowego) po raz pierwszy został wykryty w 2019 roku w Wuhan w Chinach i rozprzestrzeniając się stał się przyczyną ogólnoświatowej pandemii COVID-19. Światowa Organizacja Zdrowia (WHO) podaje ponad 750 milionów przypadków potwierdzonych infekcji COVID-19 i prawie 7 milionów zgonów z tego powodu (stan na dzień 16 sierpnia 2023) [1]. Pierwsze szczepienia przeciwko COVID-19 w Polsce pojawiły się w grudniu 2020 r. Przed pojawieniem się szczepień i nabyciem odporności populacyjnej jedyną metodą zapobiegania infekcji było przerwanie łańcucha epidemicznego. Zgodnie z WHO (ang. World Health Organization) do działań tych należy [2]:

- zachowanie co najmniej 1 metra odległości od innych osób
- noszenie odpowiednio dopasowanej maseczki, gdy zachowanie dystansu fizycznego nie jest możliwe lub w miejscach o słabej wentylacji
- wybieranie otwartych, dobrze wentylowanych przestrzeni; otwieranie okna w pomieszczeniu
- regularne mycie rąk mydłem i wodą lub preparatem na bazie alkoholu
- zakrywanie ust i nosa podczas kaszlu lub kichania
- pozostanie w domu i izolacja w razie złego samopoczucia

Poprzedzające pojawienie się szczepień przeciw COVID-19 próby pomocy osobom z ciężkim przebiegiem tejże infekcji obejmowały podaż osocza ozdrowieńców COVID-19. Zastosowanie tej metody sprawdziło się w przeszłości w leczeniu m. in. wirusowego zapalenia wątroby typu A i B, wścieklizny, cytomegalii czy gorączki krwotocznej Ebola [3]. Leczenie transfuzją osocza ozdrowieńców o bogatym w przeciwciała anty-SARS-CoV-2 opisywano jako skuteczne w zmniejszaniu ciężkości przebiegu i śmiertelności z powodu COVID-19, nie wszyscy autorzy jednak są zgodni co do tej zależności, a znaczenie tej metody zmalało na skutek wprowadzenia szczepień [4,5].

Światowa Organizacja Zdrowia przedstawia objawy COVID-19 zgodnie z podziałem [6]:

Najczęstsze objawy:

- gorączka
- kaszel

- zmęczenie
- utrata węchu i smaku

Objawy o mniejszej częstotliwości:

- ból gardła
- ból głowy
- bóle nieokreślone
- biegunka
- wysypka skórna, odbarwienia na palcach rąk i stóp
- zaczerwienienie lub podrażnienie oczu

Ciężkie objawy:

- duszność
- utrata mowy, mobilności lub dezorientacja
- ból w klatce

W dostępnych publikacjach stosuje się także inne klasyfikacje niż zastosowała Światowa Organizacja Zdrowia, a także wspomina się o innych mniej swoistych objawach infekcji wirusem SARS-CoV-2 takich jak nagła utrata słuchu, ostre uszkodzenie nerek, zakrzepica, zatkanie nosa czy wydzielina z nosa [7,8,9]. Rozważając COVID-19 jako stosunkową nową jednostkę chorobową i fakt pojawiania się mutacji wirusa, nie zaskakuje mnogość nowych, rzadkich symptomów czy odległych powikłań. Wiele z objawów infekcji SARS-CoV-2 są często spotykanymi w praktyce otolaryngologicznej. Spośród nich możemy wymienić m.in.: zaburzenia węchu i smaku, kaszel, ból gardła, wirowe zawroty głowy, uczucie niestabilności podłoża, nudności i wymioty, nagłą jednostronną utratę słuchu, postępującą utratę słuchu, szumy uszne [10,11]. Determinuje to znaczenie otolaryngologola w diagnostyce infekcji wirusem SARS-CoV-2. Przyczyną zaburzeń często klasyfikowanych jako idiopatyczne może być infekcja koronawirusowa. Przykładem jest anosmia, czyli całkowity brak węchu, która obecnie jest terminem powszechnie używanym, a przed pandemią COVID-19 była objawem rzadkim [12].

Występowanie danego objawu może różnić się z zależności czynników takich jak rejon geograficzny czy wariant wirusa [13,14], co może mieć znaczenie dla spójności wyników statystycznych.

Badania wykazały, że ciężkość przebiegu COVID-19 koreluje z wyższym mianem przeciwciał anty- SARS-CoV-2 w osoczu [15]. Najwyższe stężenie przeciwciał anty-SARS-CoV-2 opisywane jest około miesiąca po przechorowaniu, a utrzymywanie się przeciwciał w osoczu nawet do 39 tygodni [16,17]. Informacje te są istotne celem wyboru najlepszego dawcy osocza.

Nie opisano w literaturze korelacji danego objawu COVID-19 z poziomem przeciwciał anty-SARS-CoV-2 w osoczu ozdrowieńców, nie opisano również takiej korelacji w odniesieniu do objawów otolaryngologicznych. Określenie tych zależności może mieć znacznie dla lekarzy otolaryngologów w szybszej identyfikacji pacjentów z zakażeniem COVID-19, a w przyszłości przewidzieć przebieg zakażenia i pomóc w podjęciu decyzji o leczeniu.

Cele

Przeprowadzone badania zawarte w publikacjach mają na celu:

- wyodrębnienie najczęstszych objawów otolaryngologicznych w przebiegu COVID-19 u pacjentów w rejonie pomorskim
- ocenę miana przeciwciał anty-SARS-CoV-2 w odpowiedzi na infekcję COVID-19
- selekcję ozdrowieńców COVID-19 będącymi najlepszymi dawcami osocza
- ocenę korelacji objawów otolaryngologicznych COVID-19 z mianem przeciwciał anty-SARS-CoV-2
- określenie częstości występowania objawów otolaryngologicznych w zależności od wieku i płci
- ocenę korelacji ciężkości przebiegu infekcji COVID-19 z mianem przeciwciał anty-SARS-CoV-2 w osoczu

Potwierdzenie lub wykluczenie powyższych zależności może ułatwić pomoc chorym z ciężkim przebiegiem COVID-19, określić grupę ryzyka o największym narażeniu na wystąpienie danego objawu otolaryngologicznego i ciężki przebieg choroby. Dodatkowo wykazanie zależności objaw otolaryngologiczny - poziom przeciwciał - ciężkość infekcji pozwoliłoby na

szybką diagnostykę, podjęcie leczenia a po rozszerzeniu badań określenie wartości predykcyjnej danego objawu otolaryngologicznego.

I. W artykule “Correlation of ENT Symptoms with Age, Sex, and Anti-SARS-CoV-2 Antibody Titer in Plasma” (“Korelacja objawów laryngologicznych z wiekiem, płcią i mianem przeciwciał anty-SARS-CoV-2 w osoczu”) za cel obrano określenie częstości występowania objawów otolaryngologicznych wśród pacjentów chorujących na COVID-19, ich występowania w zależności od płci i wieku oraz korelacji z mianem przeciwciał IgG anty-SARS-CoV-2 w osoczu rekonwalescentów.

Badanych podzielono na dwie grupy względem trzech zmiennych: średniej wieku, mediany miana przeciwciał anty-SARS-CoV-2 w osoczu i płci, a następnie oceniono korelację objawów otolaryngologicznych ze zmiennymi w każdej z tych grup.

II. Celem publikacji “Assessment of anti-SARS-CoV-2 antibodies level in convalescents plasma.” (“Ocena poziomu przeciwciał anty-SARS-CoV-2 w osoczu ozdrowieńców”) było wyodrębnienie grupy ozdrowieńców z najwyższym mianem przeciwciał anty-SARS-CoV-2, którzy byliby najlepszymi dawcami osocza dla pacjentów z ciężkim przebiegiem infekcji SARS-CoV-2.

Pacjenci zostali pogrupowani w zależności od ciężkości przebiegu infekcji, wieku i płci, a następnie dla każdej grupy wyznaczono linię trendu miana przeciwciał w zależności od czasu jaki upłynął od infekcji SARS-CoV-2.

III. W artykule “COVID-19 symptoms in the Pomerania region“ (“Objawy COVID-19 w rejonie pomorskim”) celem pracy było określenie częstotliwości występowanie objawów ogólnych i otolaryngologicznych COVID-19.

Zastosowano podział badanych według kryterium wieku i płci. W kolejnym etapie określono częstotliwość danego objawu dla każdej z grup oceniając istotne statystycznie różnice otrzymanych wyników.

Podsumowanie

Choroba koronawirusowa 2019 (COVID-19) jest wciąż aktualnym problemem pomimo rozpowszechnienia szczepień ochronnych. Skuteczne zapobieganie, wykrywanie, potwierdzanie odpowiednimi testami i leczenie są istotnymi elementami walki z chorobą. Mimo znacznego rozszerzenia wiedzy na temat wirusa SARS-CoV-2, on wciąż mutuje i jest przyczyną zgonów na całym świecie.

Rozpoznawanie infekcji COVID-19 przez lekarzy pierwszego kontaktu jest niezmiernie istotne, jednakże wiele objawów tej choroby jest często spotykanych w praktyce otolaryngologa, toteż ważnym jest określenie roli lekarzy tej specjalności w wykrywaniu infekcji SARS-CoV-2. Szczególne znaczenie może mieć to w momencie, w którym testy na koronawirusa nie są wykonywane u wszystkich pacjentów przyjmowanych do szpitala. Dodatkowo poszerzenie wiedzy na temat zastosowanie osocza ozdrowieńców w leczeniu ciężkiego przebiegu infekcji wirusem SARS-CoV-2 może mieć znaczenie w przypadku nowych mutacji wirusa wobec których szczepienia okażą się nieskuteczne lub być punktem wyjścia dla badań nad innymi infekcjami wirusowymi.

Powyższe problemy badawcze determinują potrzebę określenia częstości objawów otolaryngologicznych, których przyczyną może być choroba koronawirusowa 2019. Dotyczy to nie tylko objawów najczęstszych jak ból gardła czy zaburzenia węchu i smaku, ale także tych mniej rozpowszechnionych w populacji ogólnej, a bardzo często spotykanych w praktyce otolaryngologicznej jak zawroty głowy czy szumy uszne. Co więcej, ocena korelacji danego objawu otolaryngologicznego z wiekiem, płcią badanych i poziomem przeciwciał anty-SARS-CoV-2 w surowicy rekonwalescentów COVID-19 może dać szansę na poprawę diagnostyki, leczenia i ocenę rokowania, a dalsze badania na wyodrębnienie objawu będącego czynnikiem prognostycznym choroby.

Udokumentowane w publikacjach zależności pozwalają na zdefiniowanie osób będących najlepszymi dawcami osocza bogatego w przeciwciała anty-SARS-CoV-2, określenie objawów otolaryngologicznych korelujących z mianem przeciwciał w osoczu ozdrowieńców, a także wpływu czynników takich jak wiek i płeć na przebieg choroby koronawirusowej 2019.

Wnioski

- Najczęstszym objawem ogólnym COVID-19 jest zmęczenie i ból mięśni i stawów.
- Najczęstszymi objawami otolaryngologicznym COVID-19 są zaburzenia węchu i smaku, suchy kaszel, ból gardła, duszność i wirowe zawroty głowy.
- Największy wzrost przeciwciał anty-SARS-CoV-2 obserwowano do 59 dnia po okresie izolacji.
- Zaobserwowano rosnący trend miana przeciwciał anty-SARS-CoV-2 w zależności od czasu od zakażenia.
- Zaobserwowano wyższe miana przeciwciał anty-SARS-CoV-2 w grupie powyżej średniej wieku badanych.
- Optymalnym dawcą osocza jest ozdrowieniec płci męskiej powyżej 39. roku życia, po ciężkim przebiegu infekcji COVID-19.
- Wiek badanych wpływa na występowanie zaburzeń węchu i smaku.
- Zaburzenia węchu i smaku częściej występowały u młodszych pacjentów, a oznaczone miano przeciwciał było niższe, co kontrastowało z wyższym mianem przeciwciał związanym z suchym kaszlem, dusznością i zawrotami głowy.
- Nie wykazano statystycznie istotnych różnic między płcią a występowaniem jakichkolwiek objawów laryngologicznych COVID-19.

Rozprawa doktorska pt.

“Ocena częstości występowania objawów otolaryngologicznych, ogólnych oraz miana przeciwciał anty-SARS-CoV-2 w przebiegu infekcji COVID-19.”

Streszczenie

Koronawirus SARS-CoV-2 po raz pierwszy pojawił się Chinach w grudniu 2019 roku, jego szybkie rozprzestrzenianie się spowodowało ogłoszenie pandemii COVID-19 przez Światową Organizację Zdrowia w marcu 2020 roku. W tym samym czasie pojawił się pierwszy przypadek infekcji Polsce. Wirus ten spowodował wiele strat demograficznych i gospodarczych, a jego obecność jest nadal aktualnym problemem zdrowotnym, dlatego potrzebne są badania usprawniające diagnostykę, prewencję i leczenie COVID-19. Wiele objawów infekcji SARS-CoV-2 jest objawami otolaryngologicznymi, a częstość ich występowania różni się między publikacjami. Podobna rozbieżność występuje w wynikach dotyczących poziomu przeciwciał anty-SARS-CoV-2 w osoczu ozdrowieńców COVID-19. Powodem tego może być mnogość czynników wpływających na wyniki jak płeć, choroby współistniejące czy szerokość geograficzna, a co za tym idzie, obecność innej mutacji wirusa. Badania przedłożone do rozprawy doktorskiej zostały przeprowadzone na populacji polskiej, nieobciążonej chorobami współistniejącymi, a poziom przeciwciał został oznaczony w różnym czasie od infekcji. Dane zostały zebrane w czasie przed pojawieniem się w Polsce szczepienia przeciwko koronawirusowi 2019, toteż przeciwciała w osoczu ozdrowieńców powstały wyłącznie w przebiegu przebytego zachorowania.

Cel pracy

Celem przeprowadzonych badań było określenie częstości występowania objawów otolaryngologicznych w przebiegu COVID-19 u pacjentów w rejonie pomorskim, ocena okresu od zachorowania w którym osocze ozdrowieńców zawiera największą ilość przeciwciał anty-SARS-CoV-2, selekcja ozdrowieńców COVID-19 będącymi najlepszymi dawcami osocza, badanie korelacji ciężkości przebiegu infekcji z poziomem przeciwciał anty-SARS-CoV-2 oraz określenie korelacji danego objawu otolaryngologicznego z mianem przeciwciał anty-SARS-CoV-2.

Materiał i metody

Metodologia przeprowadzonych badań, użyte materiały, grupa badawcza i metodyka analizy statystycznej została opisana w artykułach przedłożonych do rozprawy doktorskiej.

Wyniki

Publikacje wyodrębniły zmęczenie oraz bóle mięśni i stawów jako najczęstszy objaw ogólny, a zaburzenia węchu i smaku jako najczęstszy objaw otolaryngologiczny. Poziom przeciwciał anty-SARS-CoV-2 w osoczu ozdrowieńców najszybciej wzrastał do dwóch miesięcy po infekcji, a wyższe miana przeciwciał odnotowano u mężczyzn niż u kobiet, z ciężkim przebiegiem choroby koronawirusowej 2019 oraz u osób powyżej średniej wieku badanych. Przeprowadzone badania udokumentowały korelację występowania objawów otolaryngologicznych z poziomem przeciwciał, nie odnotowano jej natomiast w odniesieniu do płci.

Wnioski

- Najczęstszym objawem ogólnym COVID-19 jest zmęczenie i ból mięśni i stawów.
- Najczęstszymi objawami otolaryngologicznym COVID-19 są zaburzenia węchu i smaku, suchy kaszel, ból gardła, duszność i wirowe zawroty głowy.
- Największy wzrost przeciwciał anty-SARS-CoV-2 obserwowano do 59 dnia po okresie izolacji.
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- Optymalnym dawcą osocza jest ozdrowieniec płci męskiej powyżej 39. roku życia, po ciężkim przebiegu infekcji COVID-19.
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- Nie wykazano statystycznie istotnych różnic między płcią a występowaniem jakichkolwiek objawów laryngologicznych COVID-19.

Doctoral dissertation entitled

"Assessment of otolaryngological and general symptoms prevalence and the titer of anti-SARS-CoV-2 antibodies in the course of covid-19 infection."

Summary

The SARS-CoV-2 coronavirus first occurred in China in December 2019, its rapid spread resulted in the COVID-19 pandemic declaration by the World Health Organization in March 2020. First case of infection in Poland appeared at this time. This virus has caused many demographic and economic losses, and its presence is still a current health problem, which is why more research is needed to improve the diagnosis, prevention and treatment of COVID-19. Many symptoms of SARS-CoV-2 infection are otolaryngological symptoms, and their incidence varies between publications. A similar divergence appears in the results regarding the level of anti-SARS-CoV-2 antibodies in the plasma of COVID-19 convalescents. The reason may be a multitude of factors affecting the results, such as sex, comorbidities or geographical region which results in the presence of a different virus mutation. The research submitted for the doctoral dissertation was carried out on a Polish population free from comorbidities, and the level of antibodies was determined at different times from infection. The data was collected before COVID-19 vaccination appeared in Poland, thus the antibodies in the plasma of convalescents were formed only in the course of the SARS-CoV-2 infection.

Aims of the study

Study purpose was to determine the otolaryngological symptoms prevalence in the course of COVID-19 in patients in the Pomeranian region, to assess the period from the onset of illness in which the plasma of convalescents contains the highest amount of anti-SARS-CoV-2 antibodies, to select COVID-19 convalescents who are the best plasma donors, assess the correlation between the severity of the infection and the level of anti-SARS-CoV-2 antibodies, and to determine the correlation of each otolaryngological symptom with the level of anti-SARS-CoV-2 antibodies.

Materials and methods

The methodology of the research, the materials used, the research group and the methodology of statistical analysis were described in the articles submitted for the doctoral dissertation.

Results

The research defined fatigue, muscle and joint pain as the most common general symptom, and olfactory and taste disorders as the most common otolaryngological symptom. The biggest increase of anti-SARS-CoV-2 antibodies level in the convalescents' plasma was stated two months after infection, and higher antibody titers were recorded in men than in women, with a severe course of COVID-19 and in people above the mean age. The conducted studies documented the correlation of the otolaryngological symptoms occurrence with the level of antibodies, but it was not recorded in terms of sex.

Conclusions

- The most common general symptom of COVID-19 is fatigue and muscle and joint pain.
- The most common otolaryngological symptoms of COVID-19 are smell and taste disorders, dry cough, sore throat, shortness of breath and vertigo.
- The greatest increase in anti-SARS-CoV-2 antibodies was observed up to 59 days after the isolation period.
- An increasing trend in the titre of anti-SARS-CoV-2 antibodies was observed depending on the time from infection (in the whole group, while in the group of women an inverse correlation).
- Higher titers of anti-SARS-CoV-2 antibodies were observed in the group above the mean age.
- Optimal plasma donor is a male convalescent over 39 years of age after a severe course of COVID-19 infection.
- The age of the subjects affects the occurrence of smell and taste disorders.

- Smell and taste disturbances were more common in younger patients, and antibody titers were lower, in contrast to higher antibody titers associated with dry cough, shortness of breath, and dizziness.
- There were no statistically significant differences between sex and the occurrence of any ENT symptoms of COVID-19.

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I

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I

Kwaśniewska A, **Kwaśniewski K**, Skorek A, Tretiakow D, Jaźwińska-Curyłło A, Burduk P. Correlation of ENT Symptoms with Age, Sex, and Anti-SARS-CoV-2 Antibody Titer in Plasma. J Clin Med. 2023 Jan 12;12(2):610. doi: 10.3390/jcm12020610. PMID: 36675539; PMCID: PMC9867427.

Udział: koncepcja i projekt badania, analiza statystyczna, interpretacja wyników, graficzne przedstawienie wyników, przechowywanie danych, korekta manuskryptu, ostateczne zatwierdzenie manuskryptu

Punktacja MNiSW: 140

Impact Factor: 4.964

II

Skorek A, Jaźwińska-Curyłło A, Romanowicz A, **Kwaśniewski K**, Narożny W, Tretiakow D. Assessment of anti-SARS-CoV-2 antibodies level in convalescents plasma. J Med Virol. 2022 Mar;94(3):1130-1137. doi: 10.1002/jmv.27433. Epub 2021 Nov 9. PMID: 34738646; PMCID: PMC8661642.

Udział: analiza statystyczna, interpretacja wyników, graficzne przedstawienie wyników, korekta manuskryptu, ostateczne zatwierdzenie manuskryptu

Punktacja MNiSW: 70

Impact Factor: 20.693

III

Bełdzińska K, Romanowicz A, **Kwaśniewski K**, Jaźwińska-Curyłło A, Tretiakow D, Skorek A: COVID-19 symptoms in the Pomerania region; Pol Otorhino Rev 2021; 10 (4): 9-14. DOI: 10.5604/01.3001.0015.6421

Udział: koncepcja i projekt badania, analiza statystyczna, interpretacja wyników, graficzne przedstawienie wyników, ostateczne zatwierdzenie manuskryptu

Punktacja MNiSW: 70

Oświadczam, że udostępnienie trzech powyższych utworów nie narusza praw autorskich osób trzecich.

25.03.2023 r.

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prof. dr hab. n. med. Andrzej Skorek

Oświadczenie współautora o udziale w publikacji

I

Kwaśniewska A, Kwaśniewski K, **Skorek A**, Tretiakow D, Jaźwińska-Curyłło A, Burduk P. Correlation of ENT Symptoms with Age, Sex, and Anti-SARS-CoV-2 Antibody Titer in Plasma. J Clin Med. 2023 Jan 12;12(2):610. doi: 10.3390/jcm12020610. PMID: 36675539; PMCID: PMC9867427.
Udział: koncepcja i projekt badania, zbieranie danych, ostateczne zatwierdzenie manuskryptu
Punktacja MNiSW: 140
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Udział: koncepcja i projekt badania, zbieranie danych, przygotowanie manuskryptu, korekta manuskryptu, ostateczne zatwierdzenie manuskryptu
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Punktacja MNiSW: 70

Oświadczam, że udostępnienie powyższych trzech utworów nie narusza praw autorskich osób trzecich.

28.03.2023 Andrzej Skorek

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Oświadczenie współautora o udziale w publikacji

I

Skorek A, Jaźwińska-Curyłło A, Romanowicz A, Kwaśniewski K, **Narożny W,** Tretiakow D. Assessment of anti-SARS-CoV-2 antibodies level in convalescents plasma. J Med Virol. 2022 Mar;94(3):1130-1137. doi: 10.1002/jmv.27433. Epub 2021 Nov 9. PMID: 34738646; PMCID: PMC8661642.

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Punktacja MNiSW: 70

Impact Factor: 20.693

Oświadczam, że udostępnienie utworu nie narusza praw autorskich osób trzecich.

28.03.2023 .....

Data i podpis współautora

dr. n. med. Dmitry Tretiakow

Oświadczenie współautora o udziale w publikacji

I

Kwaśniewska A, Kwaśniewski K, Skorek A, **Tretiakow D**, Jaźwińska-Curyłło A, Burduk P. Correlation of ENT Symptoms with Age, Sex, and Anti-SARS-CoV-2 Antibody Titer in Plasma. J Clin Med. 2023 Jan 12;12(2):610. doi: 10.3390/jcm12020610. PMID: 36675539; PMCID: PMC9867427.
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Punktacja MNiSW: 70

Oświadczam, że udostępnienie powyższych trzech utworów nie narusza praw autorskich osób trzecich.

24.03.2023

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Data i podpis współautora

Dmitry Tretiakow

lek. Anna Jaźwińska-Curyłło

Oświadczenie współautora o udziale w publikacji

I

Kwaśniewska A, Kwaśniewski K, Skorek A, Tretiakow D, **Jaźwińska-Curyłło A**, Burduk P. Correlation of ENT Symptoms with Age, Sex, and Anti-SARS-CoV-2 Antibody Titer in Plasma. J Clin Med. 2023 Jan 12;12(2):610. doi: 10.3390/jcm12020610. PMID: 36675539; PMCID: PMC9867427.
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Punktacja MNiSW: 140
Impact Factor: 4.964

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Udział: koncepcja i projekt badania, zbieranie danych
Punktacja MNiSW: 70

Oświadczam, że udostępnienie trzech powyższych utworów nie narusza praw autorskich osób trzecich.

15.03.2023 A. Jaźwińska-Curyłło

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Data i podpis współautora

NIEZALEŻNA KOMISJA BIOETYCZNA DO SPRAW BADAŃ NAUKOWYCH
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*Uchwała nr NKBBN/**46**/2020* Gdańsk, 2020-04-06

Pan
Dr hab. med. Andrzej Skorek
p.o. Kierownika Katedry i Kliniki Otolaryngologii
Gdański Uniwersytet Medyczny

W odpowiedzi na zgłoszenie badań z dnia 30.01.2020r. na temat: **„Anosmia wrodzona i nabyta – wielopoziomowa analiza porównawcza"** *(praca studencka planowana do przeprowadzenia pod kierunkiem głównych badaczy: studentki Aleksandy Romanowicz i opiekuna dr n. med. Wojciecha Brzoznowskiego)* - Niezależna Komisja Bioetyczna do Spraw Badań Naukowych przy Gdańskim Uniwersytecie Medycznym na posiedzeniu w dniu 27 lutego 2020 roku zapoznała się z powyższym projektem pracy badawczej i – *po uzupełnieniu ww. wniosku przez badaczy zgodnie z zaleceniem Komisji w dniu 09.03.2020r.* - podjęła uchwałę o pozytywnym zaopiniowaniu tego projektu w zakresie przedstawionym we wniosku, gdyż są to badania poznawcze, nie budzące zastrzeżeń natury etycznej.

Niniejsza decyzja jest ważna do 31 grudnia 2020 roku, zgodnie z planowanym przez badaczy terminem zakończenia ww. badań.

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do Spraw Badań Naukowych
przy Gdańskim Uniwersytecie Medycznym
prof. dr hab. n. med. Bolesław Rutkowski