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PREDICTOR ANALYSIS OF SMELL AND TASTE LOSS ONSET AND ITS SIGNIFICANCE IN COVID-19 DISEASE

ANALIZA PREDIKTORA ZA NASTANAK SIMPTOMA GUBITKA ČULA MIRISA I UKUSA I NJIHOV ZNAČAJ KOD COVID-19 BOLESTI

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Summary

Introduction. COVID-19 is defined as an infectious disease caused by the coronavirus. It manifests with various symptoms, including the loss of smell and taste. While the exact pathogenesis remains unclear, it is believed that these symptoms occur due to the virus's impact on angiotensin receptors. Post-COVID syndrome, which includes various long-term symptoms, can develop after the initial illness. This study aimed to identify predictors of taste and smell loss during COVID-19, evaluate their prognostic significance for disease outcomes, and explore their connection to the respondents' constitutional characteristics. **Material and Methods.** The research was conducted using an online questionnaire completed by 194 respondents who had recovered from COVID-19 disease (150 experienced taste and/or smell loss, and 44 did not). In January and February 2022, two versions of the questionnaire were distributed based on the presence or absence of these symptoms. **Results.** Significant predictors of sensory loss include profession requiring interaction with people, non-smoking status, absence of allergies, and experiencing mild respiratory infection more than once a year. The presence of sensory loss does not necessarily indicate a milder clinical course of the disease. Post-COVID symptoms (gastrointestinal, cardiovascular, skin lesions, and reactivation of herpes simplex virus) occurred significantly more often in the group that experienced taste and/or smell loss. **Conclusion.** While there are predictors for the development of taste and/or smell loss, they are not the guarantee of a better disease outcome. Post-COVID syndrome can manifest differently across various groups of respondents.

Key words. COVID-19; Taste Disorders; Olfaction Disorders; Anosmia; Ageusia; Post-Acute COVID-19 Syndrome; Angiotensin-Converting Enzyme 2; Receptors, Angiotensin; Taste Buds; Surveys and Questionnaires

Sažetak

Uvod. COVID-19 se definiše kao infektivna bolest uzrokovana virusom korona. Bolest se manifestuje mnogobrojnim simptomima, među kojima se nalaze gubitak čula mirisa i/ili ukusa. Patogeneza nastanka ovih simptoma nije u potpunosti razjašnjena, ali se smatra da nastaju delovanjem virusa na angiotenzinske receptore, prisutne u sluznici respiratornog trakta i usne duplje. Nakon preležane bolesti, može se javiti i tzv. postkovid sindrom koji obuhvata različite dugotrajnije simptome. Cilj rada podrazumevao je određivanje prediktora za nastanak simptoma gubitka čula mirisa i ukusa u toku COVID-19 bolesti i analiziranje njihovog uticaja na ishod bolesti i njihovu povezanost sa konstitucionalnim obeležjima ispitanika.

Materijal i metode. Istraživanje je sprovedeno putem online upitnika na ukupno 194 ispitanika koji su preležali COVID-19, od kojih je 150 imalo simptome gubitka čula mirisa i/ili ukusa, a 44 nije. Kreirane su dve verzije upitnika koje su dostavljane ispitanicima nakon prethodnog intervjuisanja o prisustvu ili odsustvu navedenih simptoma, tokom januara i februara 2022. godine. **Rezultati.** Značajni prediktori za nastanak gubitka čula su: profesija koja podrazumeva rad sa ljudima, nekonzumiranje cigareta, odsustvo alergija i prisustvo blage respiratorne infekcije više od jedanput godišnje. Prisustvo simptoma gubitka čula ne znači nužno i blažu kliničku sliku bolesti. Postkovid simptomi (gastrointestinalni, kardiovaskularni, kožne promene i reaktivacija herpes simpleks virusa), značajno češće su se javljali u grupi ispitanika koja je imala simptome gubitka čula mirisa i/ili ukusa. **Zaključak.** Postoje prediktori za nastanak simptoma gubitka čula mirisa i/ili ukusa, ali oni ne predstavljaju garanciju za povoljniji ishod bolesti. Postkovid sindrom može imati različite oblike kod različitih grupa ispitanika.

Ključne reči. COVID-19; poremećaji čula ukusa; poremećaji čula mirisa; anosmija; ageuzija; post-COVID sindrom; angiotenzin konvertujući enzim tip 2; angiotenzin receptori; kvržice na jeziku; ankete i upitnici

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Abbreviations

SARS-CoV-2 virus	– Severe Acute Respiratory Syndrome Coronavirus 2
n-CoV	– new strain of coronavirus
ACE2 receptors	– angiotensin-converting enzyme 2 receptors

Introduction

COVID-19 is defined as an infectious disease caused by the SARS-CoV-2 virus (Severe Acute Respiratory Syndrome Coronavirus 2) [1]. At the end of 2019, a new strain of coronavirus (n-CoV) emerged in China, causing a systemic infection in humans. This strain had not been previously identified in humans. On February 11, 2020, the World Health Organization announced the official name of the disease as COVID-19, caused by the SARS-CoV-2 strain [2]. The clinical presentation of COVID-19 varies in severity. Common symptoms include weakness, malaise, fever, muscle and joint pain, cough, shortness of breath, nausea, vomiting, diarrhea, loss of appetite, headache, and a reduced or complete loss of the sense of smell and/or taste. Unlike other upper respiratory infections such as the flu or a cold, COVID-19 can independently cause a reduced sensation or even a complete loss of smell and/or taste. This specificity suggests a different pathogenesis for these symptoms. The primary mechanism of action for SARS-CoV-2 involves binding to angiotensin-converting enzyme 2 (ACE2) receptors. These receptors are widely distributed in the membranes of epithelial cells of the skin, oral mucosa, nasal cavity, and endothelial cells of blood vessels [3,4]. ACE2 converts angiotensin II into a fragment called Ang [1–7], which dilates blood vessels and lowers local blood pressure. When the virus binds to numerous ACE2 receptors, it stimulates and subsequently dysregulates them, leading to an increase in the local concentration of angiotensin II, which can cause significant increases in blood pressure and tissue inflammation. The high concentration of ACE2 receptors in the mucous membranes of the respiratory tract indicates that area is the primary site of action for the SARS-CoV-2 virus. This also explains the taste disorders observed in COVID-19 patients, as ACE2 receptors are significantly present in the epithelial cells of the tongue and salivary glands [5–7]. Post-COVID symptoms, which can manifest across various organ systems, are increasingly common. Neurological/cognitive symptoms include brain fog, dizziness, impaired attention, confusion, speech disorders, forgetfulness, tingling or loss of sensation in extremities, and burning skin sensations. Cardiovascular symptoms include chest pain, palpitations, and arrhythmias. Gastrointestinal symptoms include diarrhea, abdominal pain, bloating, nausea, vomiting, anorexia, and loss of appetite. Respiratory symptoms include chronic fatigue, shortness of breath, cough, sore throat, and a choking sensation. Musculoskeletal symptoms include pain in muscles, bones and joints, and joint stiffness. Psychological symptoms include emotional instability, anxiety, depression, and insomnia [8].

Material and Methods

This research was conducted as an epidemiologic retrospective cross-sectional study using a custom-developed questionnaire. The questionnaire was created based on a literature review and existing knowledge about COVID-19. Data collection occurred via an online questionnaire, which participants completed independently, and through direct surveys conducted by the researcher. The survey took place in January and February 2022, targeting respondents residing in the Republic of Serbia. The inclusion criterion was a history of COVID-19 infection between March 2020 and December 2021. The sample comprised individuals who had experienced COVID-19, reached through acquaintances and informal groups or social media profiles. There were no age restrictions. Participants were divided into two groups: one with symptoms of loss of smell and/or taste, and a control group of individuals who had COVID-19 but did not experience these symptoms.

Questionnaire 1 - respondents with symptoms of loss of smell and/or taste

This questionnaire consisted of five sections. Section 1 consisted of questions related to constitutional characteristics and predictors, including gender, age, current profession, allergies, cigarette consumption, and tendency to experience mild respiratory infections annually. Section 2 consisted of questions regarding previous COVID-19 disease, including time of illness (month and year), symptoms, hospitalization and, vaccination status. Section 3 consisted of questions regarding symptoms of loss of smell and/or taste, such as intensity, onset, and duration of these symptoms, treatment, and olfactory training. Section 4 consisted of questions regarding Post-COVID consequences, the symptoms experienced in the six months following the illness, and diagnoses received during the same period. The last section required a photograph of the dorsal surface of the tongue, with precise instructions to ensure usability for analysis, aimed at minimizing direct contact due to the current epidemiological situation.

Questionnaire 2 - respondents without symptoms of loss of smell and/or taste

Questionnaire 2 was similar to Questionnaire 1, except it lacked the section concerning symptoms of loss of smell and/or taste. This alignment was necessary to compare the two groups of respondents effectively.

Responses concerning symptoms experienced during COVID-19 were classified by severity into mild, moderate, and severe clinical presentation. They were also categorized by predominant symptom type: respiratory, neurological, or other. Post-COVID symptoms were similarly categorized. Photographs of the dorsal surface of the tongue were analyzed to determine its anatomical characteristics and the number of fungiform papillae, which transmit taste sensations. Properly captured images showed these papillae as

distinct red nodules, enabling analysis. Fungiform papillae were counted visually on the anterior third of the dorsal surface. Each tongue was segmented into anterior, middle and posterior thirds, and measured using a ruler against the visible length of the dorsal surface in each photo. Data analysis was performed using the SPSS 21 statistical software. Results were presented as absolute frequencies and mean values in tabular format. Descriptive statistical techniques were used for result depiction. The chi-square test and t-test were employed to determine statistically significant differences between groups, with significance set at $p < 0.05$.

Results

The sample consisted of 194 respondents diagnosed with COVID-19. Of these, 150 exhibited symptoms of anosmia and/or ageusia during their illness, while 44 did not. Among the total respondents, 68 were male and 126 were female ($p < 0.05$). Additionally, 150 respondents were employed in professions involving direct interaction with others, while 44 were not. The average age of the respondents was 33.97 years, with ages ranging from 11 to 81 years. Statistical analysis revealed a significantly higher proportion of females, individuals employed

in people-centric professions, non-smokers, those without allergies, and those with recurrent mild respiratory infections among those experiencing symptoms of anosmia and/or ageusia during COVID-19 infection ($p < 0.05$). However, the number of fungiform papillae in the anterior third of the tongue did not show a significant association with the occurrence of these symptoms. Conversely, among respondents without symptoms of anosmia and/or ageusia, significant predictors were professions involving interpersonal interactions and non-smoking status ($p < 0.05$). Gender, presence of allergies, recurrent mild respiratory infections, and the number of fungiform papillae in the anterior tongue segment were not significant factors. The most prominent predictor distinguishing the two groups was the proportion of non-smokers ($p < 0.05$) (**Table 1**).

In the cohort of respondents experiencing symptoms of sense loss, a moderate clinical presentation characterized predominantly by neurological symptoms was observed, with no requirement for hospitalization ($p < 0.05$). Post-COVID symptoms, particularly respiratory and neurological manifestations, significantly prevailed in this group ($p < 0.05$). Conversely, among subjects without symptoms of anosmia and/or ageusia, a moderate clinical presentation marked by predominantly neurological symptoms

Table 1. Analysis of predictor significance within and between the two groups
Tabela 1. Analiza značajna prediktora unutar grupa i između dve grupe

	Group 1: with sense loss <i>Grupa 1: sa gubitkom čula</i>	Total <i>Ukupno</i>	χ^2 test within Group 1 χ^2 test u okvi- ru grupe 1	Group 2: wit- hout sense loss <i>Grupa 2: bez gubitka čula</i>	Total <i>Ukupno</i>	χ^2 test within Group 2/ χ^2 test u okviru grupe 2	χ^2 test between the two groups χ^2 test između dve grupe
Male/ <i>Muškarci</i>	48 (32%)	150	$p > 0.05$	20 (45.4%)	44	$p > 0.05$	$\chi^2 = 0.100$
Female/ <i>Žene</i>	102 (68%)	150	$p < 0.05$	24 (54.5%)	44	$p > 0.05$	$p > 0.05$
Work with people <i>Rad sa ljudima</i>	114 (76%)	150	$p < 0.05$	36 (81.8%)	44	$p < 0.05$	$\chi^2 = 0.418$
Work without people <i>Rad bez ljudi</i>	36 (24%)	150	$p > 0.05$	8 (18.2%)	44	$p > 0.05$	$p > 0.05$
Allergies <i>Alergije</i>	39 (26%)	150	$p < 0.05$	17 (38.6%)	44	$p > 0.05$	$\chi^2 = 0.104$ $p > 0.05$
Smokers <i>Pušači</i>	39 (26%)	150	$p < 0.05$	4 (9.1%)	44	$p < 0.05$	$\chi^2 = 0.018$ $P < 0.05$
Flu-cold more than once a year/ <i>Grip- prehlada više od jedanput godišnje</i>	96 (64%)	150	$p < 0.05$	25 (56.8%)	44	$p > 0.05$	$\chi^2 = 0.387$ $p > 0.05$
Fungiform papillae <100 <i>Broj pečurkastih papila <100</i>	44 (52.4%)	84	$p > 0.05$	12 (41.4%)	29	$p > 0.05$	$\chi^2 = 0.307$ $p > 0.05$
Fungiform papillae >100 <i>Broj pečurkastih papila >100</i>	40 (47.46%)	84	$p > 0.05$	17 (58.6%)	29	$p > 0.05$	

Table 2. Analysis of outcome significance within and between the two groups
Tabela 2. Analiza značajja ishoda unutar grupa i između dve grupe

	Group 1: with sense loss <i>Grupa 1: sa gubitkom čula</i>	Total <i>Ukupno</i>	χ^2 test with-Group 1/ <i>test u okviru grupe 1</i>	Group 2: with- out sense loss <i>Grupa 2: bez gubitka čula</i>	Total <i>Ukupno</i>	χ^2 test with- Group 2/ <i>test u okviru grupe 2</i>	χ^2 test between the two groups <i>test između dve grupe</i>
Clinical presentation- predominantly respiratory <i>Klinička prezentacija – dominantno respiratorna</i>	35 (23.3%)	150	p>0.05	12 (27.3%)	44	p>0.05	
Clinical presentation- predominantly neurological <i>Klinička prezentacija – dominantno neurološka</i>	69 (46%)	150	p<0.05	23 (52.3%)	44	p<0.05	$\chi^2=0.417$ p>0.05
Clinical presentation- other symptoms/ <i>Klinička prezentacija – ostalo</i>	46 (30.7%)	150	p>0.05	9 (20.4%)	44	p>0.05	
Clinical presentation-mild <i>Klinička slika – blaga</i>	36 (24%)	150	p>0.05	5 (11.4%)	44	p>0.05	
Clinical presentation- moderate <i>Klinička slika – umerena</i>	105 (70%)	150	p<0.05	37 (84.1%)	44	p<0.05	$\chi^2=0.164$ p>0.05
Clinical presentation-severe <i>Klinička slika – teška</i>	9 (6%)	150	p>0.05	2 (4.5%)	44	p>0.05	
Hospitalized <i>Hospitalizovani</i>	4 (2.7%)	150	p>0.05	3 (6.8%)	44	p>0.05	$\chi^2=0.194$ p>0.05
Non-hospitalized <i>Nehospitalizovani</i>	146 (97.3%)	150	p<0.05	41 (93.1%)	44	p<0.05	
Post-COVID-predominantly respiratory/ <i>Postkovid – dominantno respiratorni</i>	44 (29.3%)	150	p<0.05	10 (22.7%)	44	p>0.05	
Post-COVID- predominantly neurological/ <i>Postkovid – dominantno neurološki</i>	36 (24%)	150	p<0.05	13 (29.6%)	44	p>0.05	$\chi^2=0.001$ p<0.05
Post-COVID-other <i>Postkovid – ostalo</i>	47 (31.3%)	150	p>0.05	0 (0%)	44	p>0.05	
Without Post-COVID syn- drome/ <i>Bez Postkovid sin- droma</i>	23 (15.3%)	150	p>0.05	21 (47.7%)	44	p>0.05	

and a lack of hospitalization was noted. No statistical significance was observed regarding the type of Post-COVID symptoms. The most notable disparity between the two groups pertained to the presence of Post-COVID symptoms, including cardiovascular, gastrointestinal symptoms, skin changes, and reactivation of herpes simplex virus (p<0.05), which were significantly more frequently in Group 1 (**Table 2**).

When comparing the number of fungiform papillae with the onset day of taste loss symptoms, it was observed that a slightly higher proportion of subjects with fewer papillae experienced taste loss within the first to third day, whereas a slightly larger proportion of subjects with a greater number of papillae lost their sense of taste between the fourth and sixth day. However, these differences did not reach statistical significance (**Table 3**).

Additionally, when comparing the number of fungiform papillae in the anterior third of the tongue with the duration of taste loss symptoms, no statistically significant differences were found (**Table 4**).

Furthermore, comparing the number of fungiform papillae in the anterior third of the tongue with the intensity of taste loss symptoms revealed no statistically significant differences (**Table 5**).

Upon analyzing the intensity of the loss of the sense of smell and/or taste, it was revealed that 82% of respondents reported a complete loss of the sense of smell (anosmia), while 18% experiences a partial loss (hyposmia). Additionally, 54% indicated a complete loss of the sense of taste (ageusia), whereas 46% reported a partial loss (hypogeusia). Concerning the onset of symptoms, 46% of respondents reported experiencing sense loss within the first to third day period, while 45.3% marked the fourth to sixth day, and

Table 3. Comparison of the number of fungiform papillae with the day of taste loss onset
Tabela 3. Poređenje broja fungiformnih papila sa danom početka simptoma gubitka čula ukusa

Total 84 Ukupno 84	Number of fungiform papillae in the anterior third of the tongue < 100 <i>Broj pečurkastih papila u prednjoj trećini jezika < 100</i>	Number of fungiform papillae in the anterior third of the tongue > 100 <i>Broj pečurkastih papila u prednjoj trećini jezika > 100</i>	χ^2 test χ^2 test
Onset of symptoms of loss of taste in 1-3 days/Početak simptoma gubitka čula ukusa u okviru 1–3 dana	25 (29.8%)	16 (19%)	$\chi^2=0.286$ $p>0.05$
Onset of symptoms of loss of taste in 4-6 days/Početak simptoma gubitka čula ukusa u okviru 4–6 dana	15 (17.9%)	20 (23.8%)	
Onset of symptoms of loss of taste in 7-10 days/Početak simptoma gubitka čula ukusa u okviru 7–10 dana	4 (4.8%)	4 (4.8%)	

Table 4. Comparison of the number of fungiform papillae with the duration of taste loss
Tabela 4. Poređenje broja fungiformnih papila sa trajanjem simptoma gubitka čula ukusa

Total 84 Ukupno 84	Number of fungiform papillae in the anterior third of the tongue < 100 <i>Broj pečurkastih papila u prednjoj trećini jezika < 100</i>	Number of fungiform papillae in the anterior third of the tongue > 100 <i>Broj pečurkastih papila u prednjoj trećini jezika > 100</i>	χ^2 test χ^2 test
Duration of taste loss 1-5 days <i>Trajanje gubitka čula ukusa 1–5 dana</i>	7 (8.3%)	12 (14.3%)	
Duration of taste loss 6-15 days <i>Trajanje gubitka čula ukusa 6–15 dana</i>	20 (23.8%)	20 (23.8%)	$\chi^2=0.112$ $p>0.05$
Duration of taste loss more than 15 days <i>Trajanje gubitka čula ukusa više od 15 dana</i>	17 (20.2%)	8 (9.5%)	

Table 5. Comparison of the number of fungiform papillae with the intensity of taste loss
Tabela 5. Poređenje broja fungiformnih papila sa intenzitetom simptoma gubitka čula ukusa

Total 84 Ukupno 84	Number of fungiform papillae in the anterior third of the tongue < 100 <i>Broj pečurkastih papila u prednjoj trećini jezika < 100</i>	Number of fungiform papillae in the anterior third of the tongue > 100 <i>Broj pečurkastih papila u prednjoj trećini jezika > 100</i>	χ^2 test χ^2 test
Partial taste loss <i>Delimičan gubitak čula ukusa</i>	17 (20.2%)	19 (22.6%)	$\chi^2=0.412$ $p>0.05$
Total taste loss/Totalni gubitak čula ukusa	27 (32.1%)	21 (25%)	

8.7% indicated the seventh to tenth day. Regarding the duration of symptoms, 25.3% reported duration of 1-5 days, 45.3% experienced symptoms for 6-15 days, and 29.4% endured symptoms for more than 15 days. Among the various taste sensations, respondents most commonly reported the absence of pleasant taste perception (62%), followed by the inability to perceive salty (20%), sweet (8.7%), sour (6.7%), and bitter (2.7%) tastes. When questioned about experiencing unpleasant tastes without food or drink consumption, 18% of respondents answered affirmatively, though this was not statistically significant. Similarly, when asked about experiencing unpleasant tastes while consuming food or drink that should normally be enjoyable, 28.7% responded positively, also without statistical significance ($p>0.05$).

Discussion

The focus of this study was to comprehensively examine the clinical manifestation of COVID-19, particularly highlighting symptoms associated with loss of smell and/or taste. Emphasis was placed on identifying predictors based on the constitutional characteristics of the subjects. Our research revealed a higher prevalence of sensory loss symptoms among female subjects, consistent with findings from Lee et al., which noted a greater occurrence of anosmia and ageusia in younger females [9]. The observed higher susceptibility to COVID-19 in humans can be attributed to the increased ease of transmission through interpersonal contact. Interestingly, a substantial proportion of subjects in the anosmia and

ageusia group were found to be non-allergic, corroborating the findings of Licari et al., who suggested that the presence of allergies might act as a protective factor against anosmia [10]. This assertion is supported by the inverse relationship between allergic sensitization and ACE2 receptor expression, where natural allergen exposure significantly reduces ACE2 expression. Additionally, studies by Namiq Faiq et al. [11] and Iqbal et al. [12] highlighted the prevalence of smoking among respondents with loss of smell and/or taste in COVID-19 cases. Although our results confirmed a significant number of smokers among subjects with anosmia and ageusia, stratification by gender revealed a statistically significant difference in the number of non-smoking females experiencing these symptoms, aligning with the results of Talavera et al. [13]. While an association between recurrent influenza/cold episodes and anosmia in COVID-19 patients was anticipated, no statistically significant difference was found between these patients and those without symptoms. Similarly, no statistical significance was found when comparing the number of fungiform papillae with the presence or absence of taste loss symptoms and their intensity, onset, and duration. Tsuchiya et al. [14] and Sakaguchi et al. [15] explained the presence of ACE2 receptors in the papillae themselves, potentially elucidating the results, as the virus binds to these receptors, causing damage irrespective of their quantity. Regarding COVID-19 outcomes, attention was given to clinical imaging, hospitalization, and Post-COVID symptoms. Symptoms occurring in COVID-19 were categorized into three groups: primarily respiratory, predominantly neurological, and others, encompassing cardiovascular, gastrointestinal, and dermatological manifestations. Our findings indicated a significant number of subjects in both experimental and control groups exhibiting predominantly neurological symptoms during COVID-19, supported by Chen et al.'s confirmation of numerous neurological symptoms in COVID-19 patients [16]. Chen et al. confirmed that these neurological symptoms are not specific to this disease, highlighting multiple pathways of neurological damage, including direct neuropathogenic effects of the virus and indirect mechanisms such as hypoxia, dehydration, acute respiratory distress syndrome, and altered pH in the systemic state. Despite Zazhytska et al.'s assertion that anosmia and ageusia are neurological symptoms, our study did not find a significant difference between groups of subjects with and without loss of smell and/or taste [17]. In both

groups, various other neurological symptoms were observed. Consistent with Talavera et al.'s findings, anosmia and ageusia were predictors of a favorable disease outcome, with affected patients exhibiting better immune responses [13]. However, our results suggest that the appearance of sensory loss symptoms may not necessarily indicate a milder clinical course, warranting further investigation to address potential sample size disparities. Post-COVID symptoms represent an extension of the disease, emerging after the acute phase. We proposed a classification of acute (lasting up to 4 weeks), continuous (lasting from 4 to 12 weeks), and post-COVID (symptoms developed during or after infection and lasting longer than 12 weeks) phases, in line with Sivan and Taylor's definition of post-COVID symptoms [18]. Our study supported the presence of post-COVID symptoms in both treatment groups, with respiratory and neurological symptoms predominating, as confirmed by Wijeratne et al. [19, 20].

The limitations of the study include the need for more detailed results, which could be obtained by increasing the number of participants in both samples and by comparing the results with those related to newer strains of the coronavirus. Additionally, in the future, employing a different method for counting fungiform papillae could potentially enhance the accuracy of the results.

Conclusion

Based on the conducted research, the following conclusions can be drawn:

1. Potential predictors for symptoms of loss of smell and/or taste during COVID-19 include working in professions involving interpersonal contact, non-smoking habits, absence of allergies, and experiencing mild respiratory infections more than once a year.
2. The severity of the clinical course of COVID-19 does not differ significantly between subjects with sensory loss symptoms and those without. However, there is a notable distinction in the types of post-COVID symptoms. Gastrointestinal issues, cardiovascular complications, skin changes, and reactivation of the herpes simplex virus were significantly more prevalent in the group experiencing loss of smell and/or taste.
3. There is no confirmed correlation between the number of fungiform papillae on the anterior third of the dorsal surface of the tongue and the onset time, duration, and intensity of taste loss symptoms, nor with the occurrence of various types of taste disturbances.

References

1. World Health Organization. Coronavirus [Internet]. [cited 2022 Jan 11]. Available from: https://www.who.int/health-topics/coronavirus?fbclid=IwAR3M7Bs_sVpW02MLDuQq5zNBuK-G-0KyIKkcg9Hp_dqtgAQGfDrEPnstinHjF0#tab=tab_1
2. Korona virus COVID-19: informacije, najčešća pitanja i odgovori [Internet]. 2021 [cited 2022 Jan 29]. Available from: <https://www.beo-lab.rs/korona-virus/?fbclid=IwAR1DEFgY6XR4VjPr8S--JqZrLRLqvRcx0712LBwGbbA1Bs-0n6MRMHV1uIU>
3. Živković-Marinkov EM, Milisavljević DR, Stanković MD, Filipović GL, Bojanović MR, Nikolić ND, et al. Oral manifestations in patients infected with COVID-19. *Acta stomatologica Naissi*. 2021;37(84):2334.
4. Mullol J, Alobid I, Mariño-Sánchez F, Izquierdo-Domínguez A, Marin C, Klimek L, et al. The loss of smell and taste in the COVID-19 outbreak: a tale of many countries. *Curr Allergy Asthma Rep*. 2020;20(10):61.
5. Klein S, Cortese M, Winter SL, Wachsmuth-Melm M, Neufeldt CJ, Cerikan B, et al. SARS-CoV-2 structure and replication characterized by in situ cryo-electron tomography. *Nat Commun*. 2020;11(1):5885.

6. Hikmet F, Méar L, Edvinsson Å, Micke P, Uhlén M, Lindskog C. The protein expression profile of ACE2 in human tissues. *Mol Syst Biol.* 2020;16(7):e9610.
7. Ghafouri-Fard S, Noroozi R, Omrani MD, Branicki W, Pośpiech E, Sayad A, et al. Angiotensin converting enzyme: a review on expression profile and its association with human disorders with special focus on SARS-COV-2 infection. *Vascul Pharmacol.* 2020;130:106680.
8. Fernández-de-las-Peñas C, Palacios-Ceña D, Gómez-Mayordomo V, Cuadrado ML, Florencio LL. Defining post-COVID symptoms (post-acute COVID, long COVID, persistent post-COVID): an integrative classification. *Int J Environ Res Public Health.* 2021;18(5):2621.
9. Thakur K, Sagayaraj A, Prasad KC, Gupta A. Olfactory dysfunction in COVID-19 patients: findings from a tertiary rural centre. *Indian J Otolaryngol Head Neck Surg.* 2021;74(Suppl 2):2840-6.
10. Licari A, Votto M, Brambilla I, Castagnoli R, Piccotti E, Olcese R, et al. Allergy and asthma in children and adolescents during the COVID outbreak: what we know and how we could prevent allergy and asthma flares. *Allergy.* 2020;75(9):2402-5.
11. Faiq TN, Ghareeb OA, Ghaleb AA, Salahaldeen MS. Incidence of hyposmia and hypoguesia in COVID-19 patients in Kirkuk. *Journal of Research in Medical and Dental Science.* 2021;9(10):204-8.
12. Iqbal M, Khan SF, Khan S, Ahmad W. Prevalence of anosmia and ageusia in confirmed COVID-19 patients at teaching hospitals of District Bannu and Swat, Pakistan. *International Journal of Endorsing Health Science Research.* 2021;9(2):217-22.
13. Talavera B, García-Azorin D, Martínez-Pías E, Trigo J, Hernández-Pérez I, Valle-Peñacoba G, et al. Anosmia is associated with lower in-hospital mortality in COVID-19. *J Neurol Sci.* 2020;419:117163.
14. Tsuchiya H. Oral symptoms associated with COVID-19 and their pathogenic mechanisms: a literature review. *Dent J (Basel).* 2021;9(3):32.
15. Sakaguchi W, Kubota N, Shimizu T, Saruta J, Fuchida S, Kawata A, et al. Existence of SARS-COV-2 entry molecules in the oral cavity. *Int J Mol Sci.* 2020;21(17):6000
16. Chen X, Laurent S, Onur OA, Kleineberg NN, Fink GR, Schweitzer F, et al. A systematic review of neurological symptoms and complications of COVID-19. *J Neurol.* 2020;268(2):392-402.
17. Zazhytska M, Kodra A, Hoagland DA, Frere J, Fullard JF, Shayya H, et al. Non-cell autonomous disruption of nuclear architecture as a potential cause of COVID-19 induced anosmia. *Cell.* 2022;185(6):1052-64.e12.
18. Venkatesan P. Nice guideline on long COVID. *Lancet Respir Med.* 2021;9(2):129.
19. Wijeratne T, Crewther S. Covid-19 and long-term neurological problems: challenges ahead with Post-COVID-19 Neurological Syndrome. *Aust J Gen Pract.* 2021;50.
20. Nešković I, Vujkov S, Bradić Vasić M, Blagojević D, Komšić J. Oral manifestations of COVID-19 infection in children: a case report. *Med Pregl.* 2021;74(5-6):187-90.

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