Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 365-372 | ISSN:2251-6727

A Cross-Sectional Study on Covid Positive Patients (Vaccinated and Non-Vaccinated) Eliciting the Prevalence and Characteristics of Anosmia and Dysgeusia

Dr. Adithya. V[1], Prof Dr. Priya K[2*], Dr Balaji.D[3], Dr Ramya Shree[4]

[1]Junior Resident, Department of ENT, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu.,

[2]Professor, Department of ENT, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu.,

[3]Assistant Professor, Department of ENT, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu.,

[4]Senior Resident, Department of ENT, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu.,

*Corresponding Author: Prof. Dr Priya K

M.S ENT, Professor, Department of ENT, Chettinad Academy of Research and Education,
Chettinad Hospital and Research Institute, Mobile No: 9094402823,

(Received: 07 October 2023 Revised: 12 November Accepted: 06 December)

KEYWORDS
COVID-19; Anosmia; Dysgeusia; Mitral cells; Olfactory epithelium.

ABSTRACT:

Introduction: Anosmia and dysgeusia are frequent symptoms of COVID-19. SARS-CoV-2 is an RNA corona viridae virus with a single strand. The loss of mitral cells and the absence of dendrites from surviving mitral and tufted cells in the glomerular layer diminishes the bulb's trophic support for sensory neurons in the olfactory epithelium, thereby reducing neuronal longevity. It is possible that the virus will destroy the olfactory bulb instead of the epithelium.

Objectives: The present study aims to examine the effects of COVID-19 immunization on the incidence and remission of anosmia and dysgeusia, two unique sensory symptoms commonly associated with the condition.

Methods: This was a cross-sectional study which was conducted on 300 patients in the department of otorhinolaryngology from Feb 2022 to May 2023

Results: The results of our study demonstrate an association between vaccination and a decreased occurrence of anosmia and dysgeusia in individuals with COVID-19. Additionally, vaccinated individuals exhibited a significant expedited recovery from these symptoms.

Conclusions: This study highlights the need for worldwide vaccination initiatives as a complete approach for not only reducing the spread of diseases but also mitigating the sensory challenges associated with COVID-19.

1. Introduction

The COVID-19 infection has been frequently associated with the manifestation of anosmia and dysgeusia symptoms. Dysgeusia and anosmia have been observed in COVID-19 patients without concomitant nasal obstruction or other rhinitis symptoms. The etiology of this manifestation is likely attributed to the virus's direct impact on the olfactory and gustatory receptors.

STRUCTURE OF THE COVID VIRUS:

SARS-CoV-2 is a member of the family Coronaviridae and possesses a genome consisting of a single-stranded RNA molecule. The pathogen infiltrates host cells through the employment of a transmembrane spike glycoprotein (S).(Fig 1) This glycoprotein is comprised of two subunits, namely S1 and S2. S1 is responsible for binding to host cell receptors, while S2 facilitates the fusion process with the host cell membrane. The cleavage of the S protein by host proteases leads to its activation for membrane fusion. The ACE2 receptor, which serves as a functional receptor for the SARS-CoV-2 virus, is widely distributed throughout the human body, with particularly elevated expression in the

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(6), 365-372 | ISSN:2251-6727

nasal mucosa, lung parenchyma, and gastrointestinal tract.(1,2)

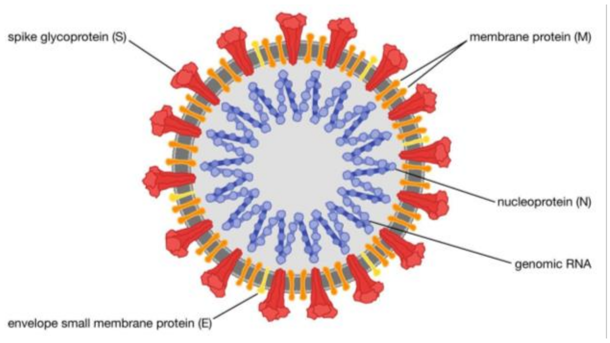

Fig 1 shows the structure of corona virus

2. Objectives

The aim of this cross-sectional study is to investigate and compare the prevalence and characteristics of anosmia and dysgeusia in COVID-19-positive patients who have been vaccinated (with Covishield or Covaxin) and those who have not been vaccinated. The study also seeks to assess the impact of vaccination on the resolution of these symptoms

INCLUSION CRITERIA:

- Patients diagnosed with COVID-19 infection
- Patients between the age of 18 yrs and 70 yrs

EXCLUSION CRITERIA:

- Patients who are not stable
- Patients aged < 18 yrs and > 70 yrs
- Patients with a history of anosmia/dysgeusia before the episode of COVID-19 infection

3. Methods

The present investigation was carried out at the Department of Otorhinolaryngology . The study was conducted in accordance with the guidelines set forth by the Institutional Human Ethical Committee and spanned from Feb 2022 to May 2023. This cross-sectional study was performed on a total of 300 patients.

Details regarding the patients such as age, gender, vaccination status, type of vaccine and number of doses taken, the presence of symptoms of anosmia and dysgeusia, the resolution of these symptoms, previous history of asthma or allergy or sinusitis were recorded and evaluated. We were thus able to compare the efficacy between covishield and covaxin, and the number of doses of vaccination in the resolution of anosmia/dysgeusia

TESTS FOR ANOSMIA AND DYSGEUSIA:

In order to assess for anosmia, a comprehensive examination was conducted wherein a diverse array of stimuli was introduced into an opaque container and subsequently presented to each nostril (Fig 2). The olfactory stimuli encompassed a range of distinct odorants, namely baby powder, chocolate, cinnamon, coffee, mothballs, peanut butter, and soap. Patients were evaluated on whether they were able to perceive and identify the odor. Using a spatial test, the taste function in various regions of the tongue and oral cavity was evaluated. The presence or absence of dysgeusia was determined by using cotton-tipped swabs soaked in the four fundamental tastes (sweet, salty, sour, and bitter) as an applicator (Fig 3).

Fig 2 Shows test being done for detecting anosmia

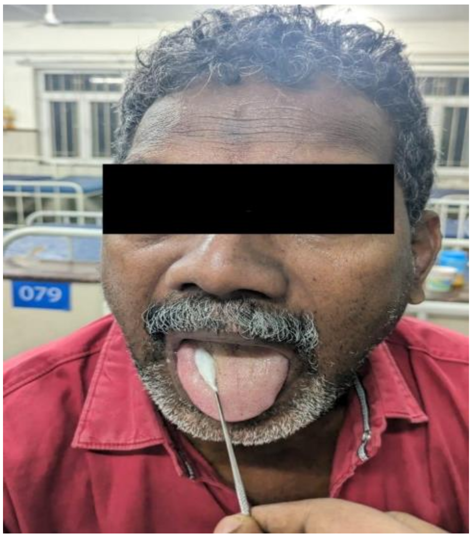

Fig 3 Shows the test being done for detecting dysgeusia

4. Results

Out of 300 patients, 203 were vaccinated (67.67%) with either 1 or 2 doses while 97 patients (32.33%) did not receive any dose of vaccine.105 patients were vaccinated with covaxin and 98 patients were with covishield. 106 patients had taken two doses while 97 patients had taken

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(6), 365-372 | ISSN:2251-6727

one dose of vaccination. 265 patients (88.83%) had symptoms of either anosmia or dysgeusia(Table 1).
Among them, 177 patients were females while 88 patients were males. Among the vaccinated population, 177 patients had symptoms of anosmia or dysgeusia while 88 patients exhibited the symptoms among the unvaccinated group. On calculating the odds ratio, it was less than 1 (0.696) thus indicating non non-vaccinated had a higher risk of developing anosmia and dysgeusia than the vaccinated population. In contrast, while applying the chi-square test there was no significant difference (p-value 0.373) among the vaccinated and non-vaccinated for developing anosmia and dysgeusia (Table 2).

In correlating the development of anosmia or dysgeusia with a previous history of asthma, allergy, or sinusitis, the odds ratio was more than 1 (2.471), thus indicating the higher risk which was also statistically significant (p-value 0.028) (Table 3). Among patients with symptoms of anosmia or dysgeusia, the duration of resolution was compared in various groups (Table 4).
On applying Mann Whitney U test there was a significant difference between vaccinated and non-vaccinated for the duration of resolution with the vaccinated having a lower mean duration compared to non-vaccinated (p-value <0.0001) thus indicating faster resolution of symptoms in the vaccinated population. On applying Mann Whitney U test, there was no significant difference between covaxin and covishield for the duration of resolution and there was no significant difference between one dose and two doses of covaxin (p-value = 0.460) and covishield for the duration of resolution (p-value = 0.391).

Table 1 Characteristics of the study population

Parameters (n=300)	Yes	No	Yes %	No %
Vaccinated	203	97	67.67	32.33
Anosmia/Dysgeusia	265	35	88.33	11.67
Past History of Asthma/ Allergy/ Sinusitis	120	180	40	60

Table 2 Cross-tabulation of vaccination status and presence of anosmia or dysgeusia

		ANOSMIA/ DYSGEUSIA		Total
		YES	NO	
Vaccinated	YES	177	26	203
	NO	88	9	97
Total		265	35	300

Table 3 Cross-tabulation of previous H/O asthma/allergy/sinusitis with presence of anosmia or dysgeusia

		ANOSMIA /DYSGEUSIA		Total
		YES	NO	
PREVIOUS H/O ASTHMA/ ALLERGY/ SINUSITIS	YES	112	8	120
	NO	153	27	180
Total		265	35	300

Table 4 Comparing the mean duration of resolution with various groups

Statistics	V	NV	COV-AX	COVI	COVAX 1	COVAX 2	COVI 1	COVI 2
N	177	88	93	84	46	47	39	45
Mean	5.04	9.47	5.1	4.98	5.33	4.87	4.74	5.18
SE of Mean	0.207	0.545	0.293	0.293	0.442	0.388	0.461	0.376
Median	5	9.5	5	5	6	4	4	5
SD	2.754	5.108	2.825	2.689	2.997	2.659	2.881	2.525
Percentile 25	2.5	5	2.5	2.25	2	3	2	2.5
Percentile 50	5	9.5	5	5	6	4	4	5
Percentile 75	7	14	7	7	7.25	7	7	7

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(6), 365-372 | ISSN:2251-6727

5. Discussion

THE OLFACTORY PATHWAY:

The perception of odors is predominantly mediated by the olfactory nerves (CN I). Ciliated olfactory receptors make up olfactory neuroepithelium. Nerves enter each nasal cavity 7 cm from the nose. They surround the nasal cavity by 2 millimeters on each side from beneath the right and left cribriform plates. Olfactory area includes middle turbinate, superior nasal septum, supreme turbinate, and superior-lateral nasal wall. Primary olfactory neurons are nasal mucosa-based.(3) These neurons (filia olfactoria) send bundles of axons up the 15 to 20 cribriform plate foramina to the olfactory bulb. The olfactory pathway is organized in a multilevel, intricate fashion. Primary-order neurons with bipolar olfactory receptors detect odorants. These synaptically connect to the mitral and tuffed cells of the olfactory glomerulus, second-order neurons in the olfactory bulb. The signal then travels through the olfactory tracts to the olfactory cortex, which includes the periamygdaloid cortex, cortical nucleus of the amygdala, prepiriform cortex, lateral entorhinal cortex, and prepiriform cortex.(4) Interestingly, olfactory neuroepithelium has the ability to regenerate.(Fig 4)

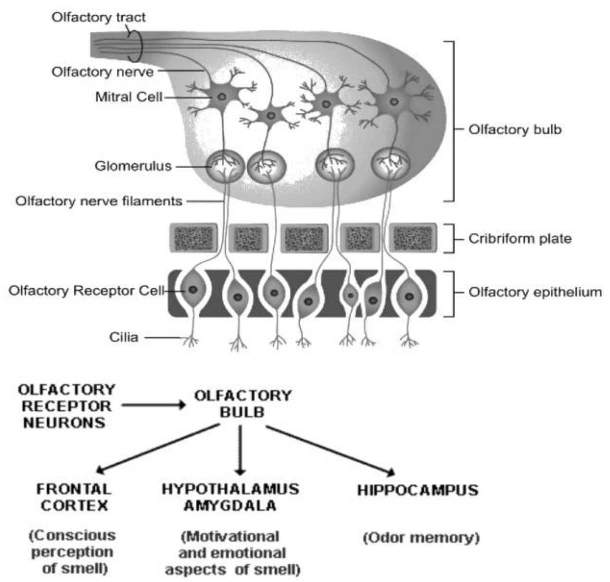

Fig 4 The olfactory pathway

PATHOPHYSIOLOGY OF ANOSMIA IN COVID 19:

The diminution of the lifespan of neurons in the olfactory epithelium is attributed to a decline in trophic support provided by the bulb to the sensory neurons. This is caused by the absence of dendrites from the glomerular layer of the surviving mitral and tufted cells, as well as the loss of mitral cells. While the exact pathophysiology of anosmia in COVID-19 is not fully understood, several mechanisms have been proposed (Fig 5)

1. DIRECT VIRAL INVASION: The SARS-CoV-2 virus primarily infects respiratory epithelial cells through the angiotensin-converting enzyme 2 (ACE2) receptor. The olfactory epithelium contains a high concentration of ACE2 receptors, making it a potential target for viral invasion. Direct viral damage to the olfactory sensory neurons and supporting cells may contribute to anosmia.(5,6)

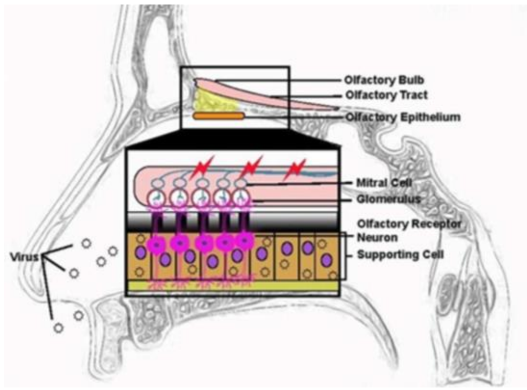

Fig 5 Shows the pathophysiology of anosmia in Covid infection

2. INFLAMMATORY RESPONSE: The immune response triggered by the viral infection may lead to inflammation in the nasal and olfactory tissues. Cytokines and inflammatory mediators released during this response might cause damage to the olfactory sensory neurons or interfere with the normal functioning of olfactory receptors.(7) In specific viral infections, the functionality of the mucociliary system, which is regulated by ciliated cells, becomes compromised. The initial proposition of this hypothesis stems from the observation that numerous viral infections affecting the respiratory system manifest symptoms of nasal airway obstruction or nasal congestion. The interplay between odorants and olfactory receptors is hindered by specific impediments, consequently leading to a compromised olfactory perception . The potential obstruction may arise from the presence of nasal discharge or inflammation within the nasal cavity (8).

3. NEURONAL TRANSMISSION DISRUPTION: The virus may disrupt the transmission of signals along the olfactory nerve pathways. This interference could occur at various points, including the olfactory receptor cells, the olfactory bulb, or the higher olfactory processing centers in the brain. (9,10).

4. BLOOD-BRAIN BARRIER DYSFUNCTION: COVID-19 has been associated with vascular complications, and

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(6), 365-372 | ISSN:2251-6727

there is evidence suggesting that the virus may affect the blood-brain barrier. Disruption of the blood-brain barrier could allow the virus or inflammatory mediators to enter the central nervous system, potentially impacting the olfactory system.

5. NEUROTROPIC PROPERTIES: Some studies suggest that SARS-CoV-2 may have neurotropic properties, meaning it has an affinity for neural tissues. The virus may travel along nerves or even directly infect neural cells, leading to dysfunction of the olfactory system(9,10). The olfactory perception is initiated upon the interaction between odorants and olfactory sensory neurons (OSNs) within the olfactory epithelium situated in the nasal cavity. Subsequently, these OSNs transmit the acquired sensory information to the olfactory bulb in the cerebral cortex via their axonal projections (11).

In accordance with this theoretical framework, it has been postulated that the affliction caused by a viral assault on the receptor neurons ultimately leads to disruptions in the olfactory function. Nevertheless, it is important to note that this supposition continues to be a subject of contention, as a number of recent investigations have documented the nonexistence of angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS), which are pivotal elements for viral cellular entry (12), within the olfactory sensory neurons (OSNs). Other mechanisms through which anosmia could occur include damage to the brain's olfactory center, impairment of olfactory supporting cells, and olfactory epithelium dysfunction due to inflammation.

THE TASTE PATHWAY:

Taste is initially perceived in the taste buds, which consist primarily of clusters of receptor cells situated on the tongue. Organized as minute red formations situated at the apex and anterior two-thirds of the tongue, the fungiform papillae are supplied with nerve VII innervation via the chorda tympani. Circumvallate papillae are elevated circular formations situated posterior to the tongue that are supplied with nerve IX of the glossopharynx. Located between pleats along the lateral margins of the tongue, foliate papillae are also supplied with nerve IX of the cranium. (13)Taste receptors are absent from the filiform papillae, which therefore have no bearing on the taste function.(Fig 6)

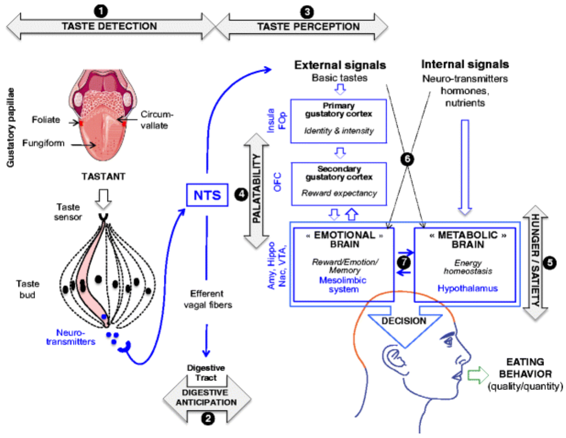

Fig 6 The taste pathway

The initiation of the flavor process occurs through the physical interaction of a chemical compound with the taste buds. Chemical signals are converted to electrical signals by the taste receptors, which are then transmitted to the nerve fibers. Cranial nerves VII, IX, and X terminate their taste fibers in the rostral nucleus solitarius located in the medulla(14). The taste pathway then proceeds ipsilaterally to the parietal lobe of the brain, where it terminates at the ventroposteromedial nucleus in the thalamus. The five gustatory attributes—saltiness, sweetness, sourness, bitterness, and umami—are perceptible in the areas housing the taste receptors.

PATHOGENESIS OF DYSGEUSIA IN COVID 19 INFECTION:

Dysgeusia, or the altered sense of taste, is another common neurological symptom associated with COVID-19. The pathophysiology of dysgeusia in COVID-19 is not fully understood, but several mechanisms have been proposed: (Fig 7 and Fig 8)

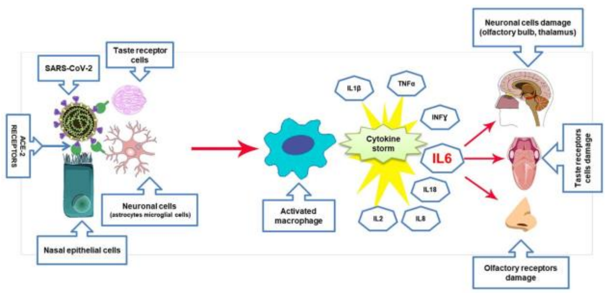

Fig 7 Shows the pathogenesis of anosmia and dysgeusia in covid infection

1. DIRECT VIRAL INVASION: Similar to anosmia, the SARS-CoV-2 virus may directly invade taste receptor cells. ACE2 receptors, which the virus uses to enter cells, are present in the oral mucosa, including on the surface of taste

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(6), 365-372 | ISSN:2251-6727

buds. The virus may disrupt the normal function of taste receptor cells, leading to altered taste perception.(15)

2. INFLAMMATORY RESPONSE: The immune response triggered by the viral infection can lead to inflammation in the oral cavity and affect taste perception. Inflammatory mediators released during the immune response may interfere with the signaling pathways involved in taste perception.(16)

3. NEURONAL TRANSMISSION DISRUPTION: The virus may disrupt the transmission of signals along the gustatory nerve pathways. This interference could occur at various points, including taste receptor cells, the gustatory nerve, or the central processing centers in the brain responsible for taste perception. COVID-19 frequently induces concurrent olfactory and gustatory dysfunctions owing to the strong association between the peripheral and central components of the olfactory and gustatory systems (17).

4.INTERFERENCE WITH NEUROTRANSMITTERS: Changes in the levels of neurotransmitters such as serotonin or dopamine in the oral mucosa or central nervous system could contribute to altered taste sensations. There are multiple reasons that elucidate the development of dysgeusia in persons affected by COVID-19.(18)

5. MUCOSAL DAMAGE: The virus may cause damage to the oral mucosa, including the taste buds, through direct infection or inflammatory processes. This damage could impair the normal function of taste receptor cells and contribute to dysgeusia. (19)

Gustatory impairment consistently manifests concomitantly with olfactory dysfunction; nonetheless, it possesses an independent mechanism and frequently lacks a direct association. One further hypothesis about the phenomenon of dysgeusia in relation to COVID-19 is the potential role of zinc deficiency [11]. It has also been suggested that SARS-CoV-2 has the potential to induce dysgeusia through its interaction with sialic acid receptors [12,13]

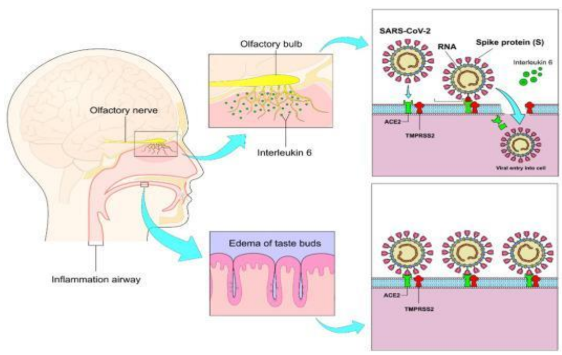

Fig 8 shows the pathogenesis of anosmia and dysgeusia in covid infection

The present study is a cross-sectional investigation that aims to elucidate the prevalence and potential risk factors associated with anosmia and ageusia in individuals diagnosed with COVID-19, as well as their impact on patient's quality of life.

The research findings indicate that 265 patients of the examined subjects manifested one or both of the symptoms of anosmia and/or dysgeusia. The present study reports a comparative analysis of the prevalence of 88.33 % of anosmia or dysgeusia in this specific population, in contrast to the global pooled prevalence rates of 38.2% and 36.6%, respectively (20). The observed disparity in the documented incidence is primarily ascribed to the presence of measurement bias, wherein diverse instruments with varying degrees of sensitivity were employed in numerous investigations. The potential underestimation of olfactory and taste dysfunction incidence post-COVID-19 is likely due to the subjective nature of symptom assessment.

IMPACT OF VACCINATION IN COVID-19:

COVID-19 vaccination has primarily been designed to prevent severe illness, hospitalization, and death associated with the SARS-CoV-2 virus. This study presents evidence indicating that COVID-19 vaccination has a crucial impact on reducing the occurrence of anosmia and dysgeusia in individuals who contract the virus. Furthermore, vaccination significantly contributes to the faster resolution of these distressing sensory symptoms(21)

1. REDUCTION IN SEVERE SYMPTOMS: COVID-19 vaccines have been successful in significantly reducing the risk of severe illness and related complications. The probable mechanisms by which this could occur are reduction in viral load, anti-inflammatory effect of the vaccine, preservation of gustatory and olfactory receptors, prevention of severe disease, and psychological impact of vaccination.

2. PREVENTION OF VIRAL TRANSMISSION: Vaccination helps prevent the spread of the virus, reducing the overall incidence of COVID-19. As these symptoms can occur in both symptomatic and asymptomatic cases, reducing the spread of the virus through vaccination may contribute to a decline in the occurrence of anosmia and dysgeusia.(22)

3. POTENTIAL IMPACT ON COVID Research is ongoing to fully understand the relationship between vaccination and long-term symptoms.

4. BOOSTERS AND PROLONGED IMMUNITY

Booster doses have been recommended in some regions to enhance and prolong immunity, especially in the face of emerging variants. By maintaining high levels of immunity in the population, including against new variants, vaccines may contribute to the ongoing control of COVID-19 symptoms, including those affecting the senses.(21,22)

While these mechanisms are plausible, further research is needed to fully elucidate the precise ways in which vaccination influences the occurrence and resolution of anosmia and dysgeusia in COVID-19 cases.

STRENGTH & LIMITATIONS OF THE STUDY:

The study's strengths encompassed the detailed evaluation of patients with COVID-19 infection and elucidating the characteristics of anosmia or dysgeusia when present. The findings of our study shed light on the potential of vaccination as an effective strategy for reducing sensory disturbances. This scores the significance of global immunization initiatives in controlling the transmission of the virus and reducing the impact it has on individuals and healthcare systems .

The study was limited by a small sample size and dependence on subjective olfactory or gustatory assessment by patients .

NOVELTY OF THE STUDY:

1. The novelty in our study lies in comparing the prevalence and characteristics of anosmia and dysgeusia between vaccinated and non-vaccinated COVID-positive patients.

2. A temporal analysis, examining the onset, duration, and resolution of anosmia and dysgeusia in both vaccinated and non-vaccinated groups was done. Understanding the interconnection of symptoms provided a more holistic view of the disease.

3.A longitudinal follow-up on a subset of patients to explore the persistence or resolution of anosmia and dysgeusia over time was conducted. This provided valuable information on the post-acute sequelae of SARS-CoV-2 infection (PASC) and potential differences in the vaccinated and non-vaccinated groups.

6. Conclusion

The COVID-19 disease is commonly associated with the presence of anosmia and dysgeusia. The results of our study emphasize that immunization not only decreases the occurrence of these symptoms upon contracting COVID-19 but also facilitates their prompt remission. These observations highlight the various advantages of vaccination that extend beyond its primary goal of preventing severe illness and hospitalization. However, additional research is necessary to clarify the underlying mechanisms involved and to continuously enhance our comprehension of the complex connection between immunization and sensory symptoms in COVID-19. These insights offer an additional persuasive justification for the ongoing advocacy and availability of the COVID-19 vaccine worldwide.

CONSENT

As per international standards or university standards, Participants' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

References

1. Astuti I. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): An overview of viral structure and host response. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020 Jul 1;14(4):407-12.
2. Ahmadpour D, Ahmadpoor P. How the COVID-19 overcomes the battle? An approach to virus structure. Iranian journal of kidney diseases. 2020 May 1;14(3):167.
3. Han AY, Mukdad L, Long JL, Lopez IA. Anosmia in COVID-19: mechanisms and significance. Chemical senses. 2020 Jul;45(6):423-8.
4. Hornuss D, Lange B, Schroeter N, Rieg S, Kern WV, Wagner D. Anosmia in COVID-19 patients. Clinical Microbiology and Infection. 2020 Oct 1;26(10):1426-7.
5. Mutiawati E, Fahriani M, Mamada SS, et al. Anosmia and dysgeusia in SARS-CoV-2 infection: incidence and effects on COVID-19 severity and mortality, and the possible pathobiology mechanisms - a systematic review and meta-analysis. F1000Res. 2021;10:40.
6. Babaei A, Iravani K, Malekpour B, et al. Factors associated with anosmia recovery rate in COVID-19 patients. Laryngoscope Investig Otolaryngol. 2021;6(6):1248–1255.
7. Butowt R, von Bartheld CS: Anosmia in COVID-19: Underlying Mechanisms and Assessment of an Olfactory Route to Brain Infection. Neuroscientist 2020 Sep 11:1073858420956905.
8. Altin F, Cingi C, Uzun T, et al.: Olfactory and gustatory abnormalities in COVID-19 cases. Eur. Arch. Otorhinolaryngol. 2020;277(10):2775–81.
9. Tong JY, Wong A, Zhu D, et al.: The Prevalence of Olfactory and Gustatory Dysfunction in COVID-19 Patients: A Systematic Review and Meta-analysis. Otolaryngol. Head Neck Surg. 2020 Jul;163(1):3–11.

10. Govindarajalu P, Shah R, Parsana M: Otorhinolaryngological manifestations of COVID-19-A systematic review. Res Sq 2020.
11. Brann JH, Firestein SJ: A lifetime of neurogenesis in the olfactory system. Front Neurosci 2014;8:182.
12. Hoffmann M, Kleine-Weber H, Schroeder S, et al.: SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell 2020;181(2):271–80.
13. Altin F, Cingi C, Uzun T, et al.: Olfactory and gustatory abnormalities in COVID-19 cases. Eur. Arch. Otorhinolaryngol. 2020;277(10):2775–81
14. Small DM, Prescott J: Odor/taste integration and the perception of flavor. Exp Brain Res 2005 Oct;166(3–4):345–57.
15. Lozada-Nur F, Chainani-Wu N, Fortuna G, et al.: Dysgeusia in COVID-19: Possible Mechanisms and Implications. Oral Surg Oral Med Oral Pathol Oral Radiol 2020;130(3):344–6.
16. Cazzolla AP, Lovero R, Lo Muzio L, et al.: Taste and Smell Disorders in COVID-19 Patients: Role of Interleukin-6. ACS Chem Neurosci 2020;11(17):2774–81
17. Vaira LA, Salzano G, Fois AG, et al.: Potential pathogenesis of ageusia and anosmia in COVID-19 patients. Int Forum Allergy Rhinol 2020 Sep;10(9):1103–4
18. Lozada-Nur F, Chainani-Wu N, Fortuna G, et al.: Dysgeusia in COVID-19: Possible Mechanisms and Implications. Oral Surg Oral Med Oral Pathol Oral Radiol 2020;130(3):344–6.
19. Besnard P. Lipids and obesity: Also a matter of taste?. Reviews in Endocrine and Metabolic Disorders. 2016 Jun;17(2):159-70.
20. Glezer I, Bruni-Cardoso A, Schechtman D, Malnic B. Viral infection and smell loss: The case of COVID-19. Journal of neurochemistry. 2021 May;157(4):930-43.
21. Moghadas SM, Vilches TN, Zhang K, Wells CR, Shoukat A, Singer BH, Meyers LA, Neuzil KM, Langley JM, Fitzpatrick MC, Galvani AP. The impact of vaccination on coronavirus disease 2019 (COVID-19) outbreaks in the United States. Clinical Infectious Diseases. 2021 Dec 15;73(12):2257-64.
22. Mathieu E, Ritchie H, Ortiz-Ospina E, Roser M, Hasell J, Appel C, Giattino C, Rodés-Guirao L. A global database of COVID-19 vaccinations. Nature human behaviour. 2021 Jul;5(7):947-53.