Journal of Positive School Psychology http://journalppw.com
2022, Vol. 6, No. 5, 3246-3253

Facial And Oral Manifestations Following COVID-19 Vaccination

Sangamesh N C[*] [1], Silpiranjan Mishra [2], Pushpraj Singh [3], Atul Anand Bajoria [4], Mahesh Shenoy [5], Nishath Sayed Abdul [6], GC Shivakumar [7]

[1] Professor & Head, Department of Oral Medicine & Radiology, Kalinga Institute of Dental Sciences, KIIT DU, Bhubaneswar, Odisha, India., sangamesh.chinnannavar@kids.ac.in*
[2] Reader, Department of Oral Medicine & Radiology, Kalinga Institute of Dental Sciences, KIIT DU, Bhubaneswar, Odisha, India.
[3] Senior Lecturer, Department of Dentistry, Government Medical College, Shahdol. India.
[4] Lecturer, Department of Oral Medicine and Radiology, Kalinga Institute of Dental Sciences, KIIT DU, Bhubaneswar, Odisha, India.
[5] Assistant Professor in Oral Pathology, College of Dentistry, Riyadh Elm University, Riyadh, Saudi Arabia.
[6] Assistant Professor in Oral Pathology, College of Dentistry, Riyadh Elm University, Riyadh, Saudi Arabia.
[7] Professor, Department of Oral Medicine and Radiology, People's College of Dental Sciences and Research Centre, Bhopal, Madhya Pradesh, India

Abstract

Background: In late 2019, the severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2), also referred to as the COVID-19 by the general populous, was discovered in Wuhan, China. The discovery of efficacious SARS-CoV-2 vaccines has been incredibly swift. Based on clinical trials, orofacial side effects of BNT162b2 and mRNA-1452 vaccinations are believed to be uncommon. The goal of this survey-based study was to look at the face and oral symptoms of COVID-19 vaccination.

Methods: The survey was designed using Google Forms and disseminated anonymously to 900 medical personnel.

Results: 403 individuals, mostly BNT162b2 vaccine recipients, responded to the survey. Only 3.1 percent and 5.4 percent, respectively, had oral and facial problems. The presence of general disorders and age have a substantial impact on the likelihood of developing oral complaints following the second dose. Medication adherence, gender and tobacco use all have an impact on the likelihood of taking a sick day. The duration of symptoms after the second dose is affected by gender, age, and smoking.

Conclusion: According to the findings of this exploratory study, there is no evidence of a link between COVID-19 vaccination administration and facial or oral signs.

Keywords: COVID-19, vaccines, BNT162b2, mRNA-1273, survey, orofacial manifestations

Introduction

During the first half of 2020, the world was gripped by a pandemic, with the second wave emerging in the fall. It was first identified as a new coronavirus (SARS-CoV-2, or severe acute respiratory syndrome coronavirus 2), and then renamed Coronavirus Disease-19, or

COVID-19. It began in the Chinese city of Wuhan in the Hubei province, but it quickly spread over the world, causing a human catastrophe and massive economic devastation. COVID-19 had been reported in about 63 million cases worldwide by the end of November 2020, with over 1.4 million deaths. SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) is a single-chain RNA virus that causes COVID-19, a novel coronavirus illness. Fever, headache, sore throat, dyspnoea, dry cough, stomach pain, vomiting, and diarrhoea are the most prevalent clinical signs. The SARS-CoV-2 receptor, angiotensin converting enzyme 2 (ACE 2), is located in the lung, liver, kidney, gastrointestinal tract, and even on the epithelial surfaces of sweet glands and the endothelia of dermal papillary arteries. Varicelliform lesions, pseudo-chilblain, erythema multiforme-like lesions, urticaria form, maculopapular, petechiae and purpura, and mottling have all been documented as cutaneous signs of COVID-19 disease. (1) (2)

The COVID-19 pandemic spread fast over the world, affecting tens of millions of individuals. (3) During the period of inception of the COVID-19 pandemic, it was thought that the lack of oral involvement distinguished COVID-19 exanthema from previous viral exanthemas. SARS-CoV-2 has recently been found in patient saliva, and it has been established that saliva reverse transcriptase-polymerase chain reaction (RT-PCR) is a more sensitive test than the nasopharyngeal test. Additionally, ACE2 has been discovered in oral mucosa, with higher density on the dorsum of the tongue and salivary glands than in buccal or palate mucosa. The most prevalent oral signs of COVID-19 disease include aphthous-like lesions, herpetiform lesions, candidiasis, and oral lesions of Kawasaki-like disease. The most prevalent characteristics that predict the severity of oral lesions in these patients appear to be their age and the degree of COVID-19 disease. The most important predisposing factors for the development of oral lesions in COVID-19 patients are poor oral hygiene, opportunistic infections, stress, underling diseases (diabetes mellitus, immunosuppression), trauma (secondary to intubation), vascular compromise, and hyper-inflammatory response secondary to COVID-19. The incidence of various oral signs and symptoms in COVID-19 individuals has been reported in conflicting ways in the literature. The most common of these was gustatory impairment. White and erythematous lesions, ulceration, blisters, petechiae, vascular diseases, stomatitis, and necrotizing periodontal disease are only a few of the oral conditions that have been reported. The bulk of these clinical manifestations were most likely caused by COVID-19-related immunosuppression and a proclivity for opportunistic infections like candidiasis. Some investigators, nonetheless, emphasise SARS-CoV-2 direct infection and replication in oral keratinocytes and fibroblasts in minor salivary glands, which results in mouth ulceration, necrosis, and bleeding. (2) (4)

Despite the fact that life as we know it has changed dramatically, pandemics are not uncommon. The 1918 Spanish influenza pandemic, which is considered one of the deadliest occurrences in human history, killed 50 million or more people. Other pandemics in history include the HIV/AIDS pandemic (1981), H1N1 influenza (2009), Chikungunya (2014), and Zika (2015), as well as Ebola fever pandemic-like outbreaks across huge swaths of Africa, from the year 2014 to the present date. The advent of the outbreak prompted a race to develop a vaccine that would provide herd immunity and reduce COVID-19's harmful consequences. Efforts to produce a vaccine are currently paying off. Some vaccine candidates have showed promising outcomes, and national rollouts have begun. The discovery of effective and safe SARS-CoV-2 vaccines has been lightninging rapid. (5) The creation of BNT162b2 began in early January 2020, following the Chinese Centre for Disease Control and Prevention's release of the SARS-CoV-2 genetic sequence and its global dissemination through the Global Initiative on Sharing All Influenza Data (GISAID) database. In a study with a total of 43,584 people randomised to vaccine or placebo, the safety and efficacy of BNT162b2 (Pfizer and BioNtech) was proven. (6) It is a nucleoside-modified RNA vaccine made with lipid nanoparticles that works against the S protein of the SARS-CoV-2 virus. This vaccination permits the body to produce antibodies to neutralise the virus, which requires the S protein to enter type 2 alveolar cells via the ACE2 receptor. (6) There are product monographs available that include information from the experiment. One of the research

projects compiled a list of orofacial side effects of BNT162b2 and mRNA-1273 for patients and healthcare providers. The effects listed vary by country and area, as well as between vaccines given to individuals and healthcare professionals. Swelling of the lips, face, and/or throat, as well as transitory unilateral facial drooping, are known side effects. They are very rare. (7)

Dentists, among other clinical specialists, are expected to provide treatment to the vaccinated population as vaccination campaigns are rolled out around the world, with several billion doses expected to be administered in the near future. (8) It is critical to follow Hill's criteria of causal inference and keep meticulous anamnestic records in order to provide the best care to patients. (9) In Europe, vaccination campaign policies are organised at the local and regional levels, and each member state has autonomy in deciding which population groups should be vaccinated first. In far-flung countries such as India, priority was given to medical personnel, while in Germany and the Netherlands, it was given to the elderly.

As a result, the goal of this survey-based study was to look at the face and oral symptoms of COVID-19 vaccination.

Materials and methods

The survey was created with Google Forms and distributed anonymously to 900 medical professionals.

The questionnaire was divided into four sections: Part A: geographic, demographic, and professional information (n = 5 questions); Part B: COVID-19 vaccine, number of doses, date of inoculation, premedication, and general symptoms (n = 11 questions); Part C: facial and oral manifestations (n = 4 questions); and Part D: underlying medical conditions and lifestyle factors (n = 9 questions).

Changes in sensitivity, face paresis, and facial aesthetic paresis were investigated in this study, as were burning sensations, oral aphthous-like lesions, taste alteration, xerostomia, tongue depapillation, discomfort, stomatitis/mucositis, commissural cheilitis, and oral candidiasis.

Correlation coefficients between age, gender, and symptoms-related factors were evaluated. The likelihood of experiencing oral and facial symptoms, as well as taking an absence day, was investigated using logistic regression models. Linear regression models for symptom duration were also investigated. Gender, age, the presence of autoimmune pathology, diabetes and/or general disorders, being a smoker and/or allergy, and regular medication use were all investigated as demographic and health factors. The Akaike information criterion was used to choose the best models (AIC). At p 0.1, the results were judged statistically significant.

Results

A final tally of 403 individuals responded to the survey, with 91 (22.5%) males and 312 (77.5%) females. In 358 cases, the Pfizer/BioNTech vaccine was utilised, whereas AstraZeneca was used in 23 cases and Moderna was used in 22 cases. Two hundred and seventy-six subjects received both doses, while 127 only received the first.

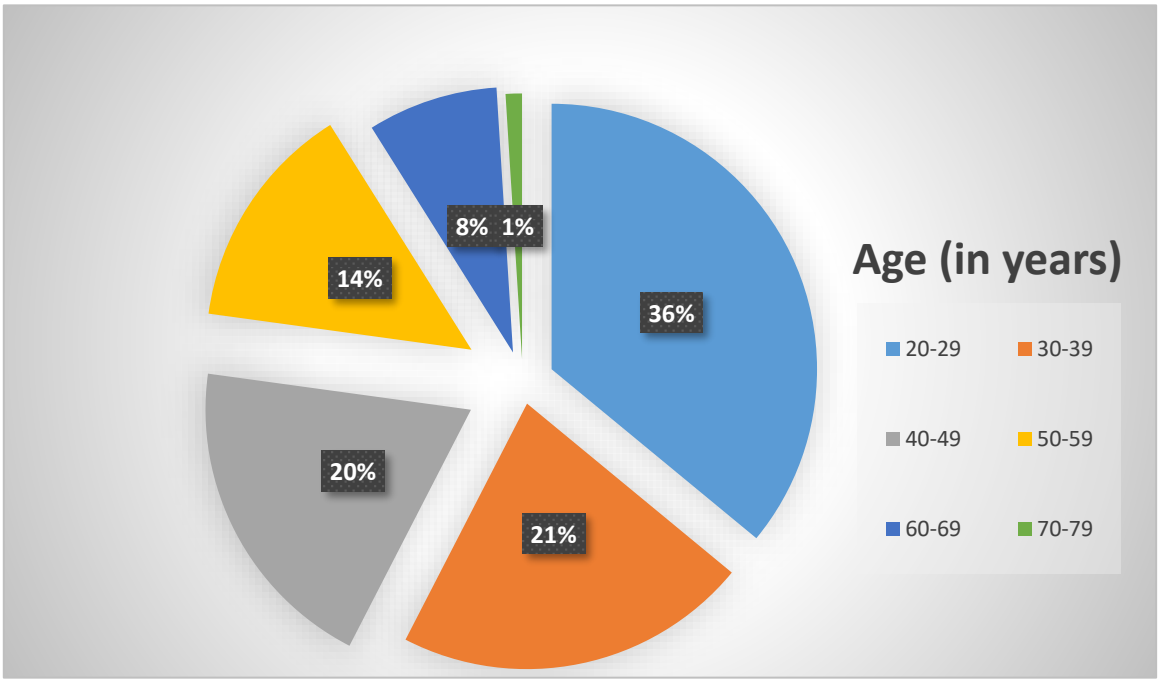

Figure 1: Subjects divided into different age groups

Subjects' ages (as shown in figure 1) were treated as a semi-continuous variable with values in the middle of the chosen interval. The period of illnesses was measured in days, with the 1-week choice on the questionnaire translating to a period of 7 days.
The binary variables that were taken into account in the study are represented in table 1.

Variables	Positive	Negative	Unanswered
1st dose related oral symptoms	16	372	15
2nd dose related oral symptoms	8	383	12
1st dose related oral symptoms during absence day	11	370	22
2nd dose related oral symptoms during absence day	9	375	19
History of diabetes	129	274	-
History of smoking	77	278	48
History of allergies	56	345	2-
Any other systemic/general disease	91	312	-

Table 1: Different variables in the study

None noteworthy influences on the onset of oral symptoms after the first dose were identified. The low frequency of such symptoms (16 out of 403, or 4.0 percent) could be part of the cause for this. Though, it must be mentioned that the existence of general disease and age have a substantial impact on the likelihood of developing oral symptoms. In the presence of general disease, the log of the odds ratio increased by 3.19 and dropped by 0.77 for just about every 10 years of age. The existence of general disorders has a considerable impact on the likelihood of developing facial symptoms after the first dose, increasing the log odds ratio by 1.82.
Occurrence of autoimmune diseases and age have a substantial impact on the likelihood of facial symptoms following the second dose. When autoimmune diseases are present, the log odds ratio increases by 2.08 and reduces by 1.21 for every 10 years of age.
There were no significant characteristics that influenced taking an absence day after the first dose.
Gender, smoking, and regular medication use all have an impact on the likelihood of taking a sick day. For smokers, the log odds ratio increased by 2.06, fell by 0.95 for frequent medication use, and was 1.77 smaller for males than females.
The duration of symptoms after the first dose was significantly influenced by gender and regular medication ingestion. Males had a 0.72-day shorter predicted symptom duration than females, while regular medication users had a 0.73-day shorter expected symptom duration.
The duration of symptoms after the second dose was significantly influenced by gender, age, and smoking. Males had a 0.63-day shorter anticipated duration of symptoms than females, 0.53-day longer for smokers, and 0.52-day longer for those with general disease.

Discussion

Covid-19 has a wide spectrum of clinical symptoms, and diagnosis is primarily dependent on clinical observations or suspicions given to the large number of people implicated. Coronavirus infection causes a varied inflammatory response that can lead to vascular inflammation. COVID feet are skin lesions such as erythematous rashes on the body and notably on the feet. (10) Erythematous rash has been described and may be due to an inflammatory response. After a brief period of macular erythematous lesion produced by vasculitis, the irregular ulcer on the tongue appears. (11) This lesion usually begins with a painful inflammation of the tongue papillae that is followed by an erythematous macula that lasts for 24 hours before growing into an irregular and asymptomatic ulcer. The ulcer can heal entirely without scarring within 10 days. The toe lesions arise after the oral lesion, although more research is needed to confirm this. (12) Major and minor salivary gland

infection, with subsequent particle release into saliva via salivary ducts, is another mechanism for COVID-19 to enter the oral cavity. It's important to note that SARS-CoV can infect salivary gland epithelial cells a short time after infection in rhesus macaques, implying that salivary gland cells could be a major source of the virus in saliva. (13) It is believed that transmission will occur through contact with droplets from talking, coughing, sneezing, and aerosols generated during clinical procedures. Droplets might come from the nasopharyngeal or oropharyngeal cavities, which are generally linked with saliva. (14) (15)

The prospective research study aims to evaluate face and oral symptoms following vaccination with COVID-19. The study found extremely few cases of these symptoms (16 out of 403, 4.0 percent after the first dosage; and 8 out of 403, 1.9 percent after the second dose), and the Pfizer/BioNTech vaccine was given to the vast majority of respondents (88.8%). The majority of the study participants (77.5%) were female, with 24.5 percent being male. 112 people said they had type 1 diabetes, 17 said they had type 2 diabetes, 77 said they smoked, 56 said they had allergies, and 91 said they had a general ailment. The survey was done during the first three weeks of April 2021 in order to include respondents with a median follow-up period of two months after the second dose.

Lichen planus is a chronic inflammatory T cell-mediated illness with no recognised cause. Clinically, it manifests as purplish, shiny, polygonal, pruritic, flat-topped papules on the skin, mucocutaneous membranes, nails, and scalp, with the skin, mucocutaneous membranes, nails, and scalp being the most affected. It mostly affects the stratified squamous epithelium in the oral cavity, although it also affects the oral and vaginal mucosa. Vaccinations, medicines, stress, anxiety, infection, diabetes, hypertension, dental materials, genetic predisposition, and neoplasms are all predisposing factors. (16) Moreover, oral side effects from other vaccines (such as polio or diphtheria) have been documented to be quite infrequent. Oral symptoms of all forms of vaccines are the subject of only a small percentage of total vaccine research, which is largely in the form of case reports. Oral mucosal complaints that occur in conjunction with other dermatological signs have been well discussed. Oral complaints following HBV immunisation, (7) for example, have been linked to lichen planus (LP). The association of LP with HBV vaccination is a rare occurrence that can occur regardless of the type of vaccine given to the patient, and symptoms can appear anywhere from days to three months following any of the three doses of the prescribed HBV vaccine. (17-19)

The COVID-19 immunisation method may be one of the first in the twenty-first century to expand globally in a short period of time, affecting practically every ethnic, geographical, and age category. In this setting, there's a better chance of noticing the occurrence of oral signs, which might have gone unnoticed or been mistaken for coincidence with regular seasonal immunizations. (20)

The most common side effects (unsolicited, severe, and serious) were generally similar across participants in the placebo and control groups, according to the Phase 3 clinical controlled trial of the mRNA-based vaccination for COVID-19. (21) This supports the concept of symptom self-limitation. (18)

Almost every participant in the current poll (88.8%) received the Pfizer-BioNtech vaccination. BNT162b2 is a perfusion stabilised, membrane-anchored SARS-CoV-2 full-length spike protein encoded by a lipid nanoparticle-formulated, nucleoside-modified RNA vaccine. In a population older than 16 years, a two-dose regimen of BNT162b2 provided 95 percent protection against COVID-19, according to the ongoing effectiveness trial. Temporary unilateral facial drooping and abrupt peripheral facial paralysis are among the orofacial adverse effects (OAEs) described in the patient and healthcare professional information. These orofacial effects are rare (up to 1 in 1000 people), and none of the participants in this study mentioned them, which could be due to the small sample size.

Changes in sensitivity, face paresis, facial aesthetics, and paralysis were explored in the survey questions about facial symptoms. Burning sensations, oral aphthous-like lesions, taste alteration, tongue depapillation, stomatitis/mucositis, pain, commissural cheilitis, and oral candidiasis were among the symptoms studied. After the first and second doses, 2.7 percent and 4.0 percent of the sample reported changes in sensitivity, respectively. After the first and second doses, 4.0 percent and 5.4 percent of the responders, respectively, reported oral problems. Burning sensation was

the most common oral manifestation after both the first and second dosages, with 2.7 percent and 3.4 percent, respectively. After the first and second doses, 1.6 percent and 2.7 percent of participants had oral aphthous-like lesions, respectively. Taste changes were more common (3.4 percent) after the second dose than after the first (1.1 percent).

The present study assessed the duration of symptoms in general rather than oral and face symptoms individually; nonetheless, the low prevalence of such symptoms supported the survey technique. Furthermore, the current study found that general disorders, as well as age progression, had a substantial impact on the likelihood of developing oral symptoms, which is consistent with earlier research. (22)

Furthermore, the survey looked into possible taste changes following COVID-19 vaccination, which has previously been mentioned in relation to influenza vaccine. Only three out of 403 patients reported a change in taste. (22)

However, chemosensory testing was not used to determine if these characteristics were directly related to vaccination, general disease, drug intake, allergies, diabetes type 1 and autoimmune diseases, or other factors including the intensity of general unpleasant reactions following immunisation.

In most nations, getting the COVID-19 immunisation is a major challenge. As a result, the World Health Organization and other key partners supporting the Coalition for Epidemic Preparedness Innovations (COVAX) are working to give immunisation to low- and middle-income nations by December 2021. (23) Furthermore, vaccination policies differ each country, depending on government decisions and population needs. (24)

Limitations

The limited sample size, short follow-up duration, and responder groups not being matched for gender (50:50) and age are the study's key shortcomings. However, research is continuing to overcome these limitations and present a complete epidemiological picture, including groups defined by sex and age, as well as specific illnesses. The final and comprehensive report with the necessary number of patients is scheduled to be issued by the beginning of 2022, according to the estimates.

Also, it must be noted that efficacy of vaccines was based on short-term data, while other vaccinations have shown efficacy declining with time. Furthermore, current trials have revealed no long-term issues. (25)

Suffering from COVID-19 during the period of pregnancy is linked to an increased risk of morbidity and mortality. (26) The vaccinations' safety and efficacy during pregnancy were not examined in the trials described. From another study looking into the safety of the Moderna vaccine during pregnancy, it was found that the proportion of those who had unfavourable pregnancy and neonatal outcomes were identical to those who had not been vaccinated against COVID-19. (27) However, after assessing the benefits and dangers of vaccination, pregnant women should talk with their healthcare professional to make an informed and autonomous decision.

New SARS-CoV-2 mutations also have demonstrated the potential to make existing vaccinations less effective. In the United Kingdom, ChAdOx1 showed 75 percent protection against B.1.1.7 (including asymptomatic infection). However, in a youthful population in South Africa with a median age of 30, the AstraZeneca vaccination provided just 10% protection against the B.1.351 strain, and hence the AstraZeneca roll-out was halted. (28-32)

Conclusion

According to the findings of this exploratory study, there is fair evidence of a link between COVID-19 vaccination administration and facial or oral signs, but more comprehensive and detailed studies are needed in this regard to ascertain the depth and intensity of the OAEs that were seen in individuals during this study.

References

1. Seirafianpour F, Sodagar S, Pour Mohammad A, et al. Cutaneous manifestations and considerations in COVID-19 pandemic: a systematic review. Dermatol Ther. 2020 and e13986.

2. Amorim dos Santos J, Normando AG, Carvalho da Silva RL, et al. Oral manifestations in patients with COVID-19: a living systematic review. J Dent Res. 2020 and 0022034520957289.

3. Haynes B.F., Corey L., Fernandes P., Gilbert P.B., Hotez P.J., Rao S., Santos M.R.,

Schuitemaker H., Watson M., Arvin A. Prospects for a safe COVID-19 vaccine. Sci. Transl. Med. 2020 and 12:eabe0948.
4. Maciel P.P., Júnior H.M., Martelli D.R.B., Machado R.A., De Andrade P.V., Perez D.E.D.C., Bonan P.R.F. Covid-19 pandemic: Oral repercussions and its possible impact on oral health. Pesqui. Bras. Odontopediatria Clin. Integr. 2020 and S1), 20(Suppl.
5. Kaur S.P., Gupta V. COVID-19 Vaccine: A comprehensive status report. Virus Res. 2020 and 288:198114.
6. Polack FP, Thomas SJ , Kitchin N , et al . Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020 and pmid:http://www.ncbi.nlm.nih.gov/pubmed/33301246, 383:2603–15.doi:10.1056/NEJMoa2034577.
7. Cirillo N. Reported orofacial adverse effects of COVID-19 vaccines: The knowns and the unknowns [published online ahead of print, 2021 Feb 1] J. Oral Pathol. Med. 2021.
8. So A.D., Woo J. Reserving coronavirus disease 2019 vaccines for global access: Cross sectional analysis. BMJ. 2020 and 371:m4750.
9. 2021, Riad A. Oral side effects of COVID-19 vaccine. Br. Dent. J. and 230:59.
10. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of Coronaviruses on the cardiovascular system: a review. JAMA Cardiol 2020 Mar 27.
11. 26, Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. J Eur Acad Dermatol Venereol 2020 Mar.
12. Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version).
13. Lu B, Huang Y, Huang L, Li B, Zheng Z, Chen Z, Chen J, Hu Q, Wang H. Effect of mucosal and systemic immunization with virus-like particles of severe acute respiratory syndrome coronavirus in mice. Immunology. 2010 and 130(2):254–261.
14. Control, ECDC - European Centre for Disease Prevention and and (COVID-19), European surveillance for human infection with novel coronavirus.
15. Xie X, Li Y, Sun H, Liu L Exhaled droplets due to talking and coughing. J R Soc Interface 6 2009.
16. Lehman J, Tollefson M, Gibson L. Lichen planus. Int J Dermatol 2009 and 682–694, 48:.
17. Diaz-Guimaraens B, Dominguez-Santas M, Suarez-Valle A, Fernandez-Nieto D, Jimenez-Cauhe J, Ballester A. Annular lichen planus associated with coronavirus SARS-CoV-2 disease (COVID-19). Int J Dermatol 2021 and 246–247., 60:.
18. Tarakji B., Ashok N., Alakeel R., Azzeghaibi S., Umair A., Darwish S., Mahmoud R., ElKhatat E. Hepatitis B vaccination and associated oral manifestations: A non-systematic review of literature and case reports. Ann. Med. Health Sci. Res. 2014 and d, 4:829–836.
19. Rebora A., Rongioletti F., Drago F., Parodi A. Lichen planus as a side effect of HBV vaccination [published correction appears in Dermatology 1999, 1999, 198(2):222] Dermatology. and 10.1159/000018054., 198:1–2. doi:.
20. Muellenhoff M., Cukrowski T., Morgan M., Dorton D. Oral pemphigus vulgaris after anthrax vaccine administration: Association or coincidence? J. Am. Acad. Dermatol. 2004 and 10.1016/S0190-9622(03)00407-9, 50:136–139. doi:.
21. Baden L.R., El Sahly H.M., Essink B., Kotloff K., Frey S., Novak R., Diemert D., Spector S.A., Rouphael N., Creech C.B., et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N. Engl. J. Med. 2021 and 10.1056/NEJMoa2035389, 384:403–416. doi:.
22. Doty R.L., Berman A.H., Izhar M., Hamilton H.B., Villano D., Vazquez B.E., Warrum M.N., Mahbob M. Influenza vaccinations and chemosensory function. Am. J. Rhinol. Allergy. 2014 and 28:50–53.
23. Nhamo G., Chikodzi D., Kunene H.P., Mashula N. COVID-19 vaccines and treatments nationalism: Challenges for low-income countries and the attainment of the SDGs. Glob. Public Health. 2021 and 16:319–339.
24. Coronavirus (COVID-19) Vaccinations—Statistics and Research—Our World in Data, Ourworldindata. [(accessed on 15 February 2021)].
25. Doria-Rose N, Suthar MS , Makowski M , et al . Antibody persistence through 6 months after the second dose of mRNA-1273 vaccine for Covid-19. N Engl J Med 2021 and 384:2259–61.
26. Craig AM, Hughes BL , Swamy GK . Coronavirus disease 2019 vaccines in pregnancy. Am J Obstet Gynecol MFM 2021 and 3:100295.
27. Shimabukuro TT, Kim SY , Myers TR , et al . Preliminary findings of mRNA Covid-19

vaccine safety in pregnant persons. N Engl J Med 2021 and 384:2273–82.
28. Madhi SA, Baillie V , Cutland CL , et al . Efficacy of the ChAdOx1 nCoV-19 Covid-19 vaccine against the B.1.351 variant. N Engl J Med Overseas Ed 2021 and 384:1885–98.
29. 2021, Gupta RK . Will SARS-CoV-2 variants of concern affect the promise of vaccines? Nat Rev Immunol and 21:340–1.
30. Kumar VM, Pandi-Perumal SR , Trakht I , et al . Strategy for COVID-19 vaccination in India: the country with the second highest population and number of cases. NPJ Vaccines 2021 and 6:60.doi:10.1038/s41541-021-00327-2.
31. De Simone C., Caldarola G., D'agostino M., Zampetti A., Amerio P., Feliciani C. Exacerbation of pemphigus after influenza vaccination. Clin. Exp. Dermatol. 2008 and 10.1111/j.1365-2230.2008.02835.x., 33:718–720. doi:.
32. Kaur S.P., Gupta V. COVID-19 Vaccine: A comprehensive status report. Virus Res. 2020 and 288:198114.