Research Article
iMedPub Journals
http://www.imedpub.com/

Cellular & Molecular Medicine: Open access
ISSN 2573-5365

2022
Vol:8 No:3

Anosmia and Disgeusia in individuals with Covid-19 in the State of Pará

Antônio Leonardo Jatahi Cavalcanti Pimentel[1], Louise Andrade Lobo da Silva Barata[1], Enzo Crispino Calheiros Silva[1], Carlos Henrique Lopes Martins[3], Hugo Fischer Rocha[3], Isamu Komatsu Lima[1], Maria Luiza do Socorro Alves Lucas[1], Silvana Nobre de Assis Mazivieiro[1,2]

Universidade do Estado do Pará[1], Universidade Federal do Pará Pará[2], University Center of the State of Pará [3]

***Corresponding author:** Silvana Nobre de Assis Maziviero, , Universidade do Estado do Pará, Brazil, Tel: 55 (91) 991145298; E-mail: nobreorl@hotmail.com

Received date: May 14, 2022; **Accepted date:** May 20, 2022; **Published date:** May 28, 2022

Citation: Silvana Nobre de Assis Mazivieiro (2022) Anosmia and Disgeusia in individuals with COVID-19 in the State of Pará. Cellular &Molecular Medicine. Vol.8 No.3.

Abstract

Objective: Coronavirus in its variant form SARS-CoV-2 originated COVID-19, caused a pandemic scenario. the symptoms may vary on intensity, from mild conditions to ICU admission, like variable fever, cough, respiratory distress. Subsequently, nasal symptoms such as anosmia and dysgeusia were observed and reported in patients, being as important for diagnostic determination as RT-PCR (reverse-transcriptase polymerase chain reaction) and/or chest tomography. Because they are one of the first symptoms in the course of SARS-CoV-2 infection, in the present study we sought to compare the prevalence of olfactory and gustatory dysfunctions in patients with COVID-19 in the state of Pará.

Methods: Seventy patients diagnosed with COVID-19 and changes in smell and/or taste were evaluated using an online form (GOOGLE FORMS), to study this complaint in the population of the state of Pará (amazon region) in 2020, since there is a lack of regionals studies on this subject.

Results: Anosmia and/or Dysgeusia were present in 97.1% of the individuals for 2 weeks (32.9%) or ranging from 30 days to 6 months (32.9%), with a higher prevalence in the age group between 19-30 years. The clinical-epidemiological diagnosis detected 54% of the cases of COVID-19 in the population studied.

Conclusions: The findings support the possibility of using these symptoms as indications of SARS-CoV-2 infection in the Amazon region and population, where the study was performed. Such findings may help in the diagnosis of COVID-19 in remote regions in the absence of RT-PCR and/or access to chest tomography, such as in riverside and indigenous areas.

Keywords: Coronavirus infections, Anosmia, Dysgeusia, Cross-Sectional Studies.

Conflicts of Interest
Authors declared that there are no conflicts of interest.

Introduction

Coronaviruses belong to a family of viruses related to respiratory diseases, being transmitted by droplets, coughing and sneezing, suspended in the air, by contact with secretions, such as saliva and nasal mucus, or direct contact between people[1]. The new variant discovered, SARS-CoV-2, is responsible for COVID-19 (Coronavirus Disease 2019), an infectious disease originating in Wuhan, China, that promoted a pandemic and high mortality scenario. Because of this, it has become the focus of society to contain the disease[2]. In Brazil, until March 2022 there were about 31 million cases of the disease, of which 660,000 died, most of them in the Southeast3. The exact pathophysiology has not yet been discovered, but there is a relationship with inflammatory process and edema formation in pneumocytes and nasal and bronchial neuroepithelium, being aggravated in elderly patients and people with preexisting comorbidities[4,5]. There are a wide variety of symptoms, the most common being: fever, dry cough and respiratory distress, which characterizes a flu-like syndrome[6,7]. In addition, symptoms such as hyposmia/anosmia/parosmia, hypogeusia/ageusia and dysgeusia (taste distortion) were observed, which initially had not been listed by the Chinese authors as manifestations of COVID-19, became a known and frequent symptom after the arrival of the disease in Europe, in which they appeared in more than 80% of infected Europeans; this divergence of information was justified by the lack of study on the subject in its beginning[8]. Currently, they are described frequently in covid cases and considered one of the main important symptoms of the disease[9]. Such symptoms are fully or partially recovered in an average of 15 days, with few cases in which they remained unimproved[10]. Nevertheless, they are not considered severe, but are important to detect the onset of the disease with Alpha, Beta, Delta and Gamma variants, without the need for RT-PCR (reverse-transcriptase polymerase chain reaction)[11]. and favoring early isolation, since most of the infected exhibit these mild signs. Patients with the Variant Omicron are less reached by these symptoms.

On the other hand, the most severe cases of the disease represent around 10% and there is mainly the manifestation of respiratory diseases, such as pneumonia and severe respiratory syndrome, which often makes it necessary to be admitted to ICUs and the use of mechanical ventilation support[12]; asymptomatic patients, by estimation, represent less than half of the cases, as they cannot be recognized without the RT-PCR 13 test, or a posteriori with the IGG and IGM antigen test[14]. Changes in smell and taste have been reported in many parts of the world. Because it is a disease with variable manifestation of symptoms, it is important to characterize the symptoms reported for understanding, exchange of scientific information in order to relieve and treat the complaint of patients. Therefore, knowing these complaints in our reality of the Amazon population is essential, where distances and deficiencies of resources for diagnosis may not be available quickly.

MATERIAL AND METHODS

This cross-sectional and observational study collected data from 70 individuals who had COVID-19 in 2020. Participants were grouped according to their gender and age group: up to 12 years, 13-18 years, 19-30 years, 31-40 years, 41-50 years, 51-60 years, more than 60 years. The questionnaire was created on the online platform Google Forms, being disclosed its link on social networks, where the target audience could contact the search and participate. Questions about anosmia and dysgeusia related to patients who had COVID-19 in 2020 were postulated. In total, nine questions were asked: two about the characteristics of the patients, one about the covid-19 diagnostic method, and six about anosmia and dysgeusia.

The duration of symptoms of anosmia and dysgeusia was recorded in days of the research participants, and the presence of symptoms was recorded on a scale of zero up to one hundred and eighty days. In addition, the characterization of anosmia and dysgeusia was requested at the time of filling out the form. Nevertheless, the relationship between the duration of symptoms and the age group of the individuals in the study was evaluated.

The statistical analysis was made with the data compiled in Microsoft Excel and Word 2019, applying the chi-square test in the Biostat 5.4 software to evaluate the collected results and the relationship with the expected phenomenon. The study was exempted from analysis by the Ethics and Research Committee because it was an online survey, as well as the signing of the Free and Informed Consent Form (Informed Consent) in the pandemic scenario was also not necessary. The study did not involve the collection of biological material.

RESULTS

There is a slight prevalence of women in the number of patients with COVID-19 who presented anosmia and dysgeusia in our study, it is worth noting that the female sex makes up the majority of patients in the office.

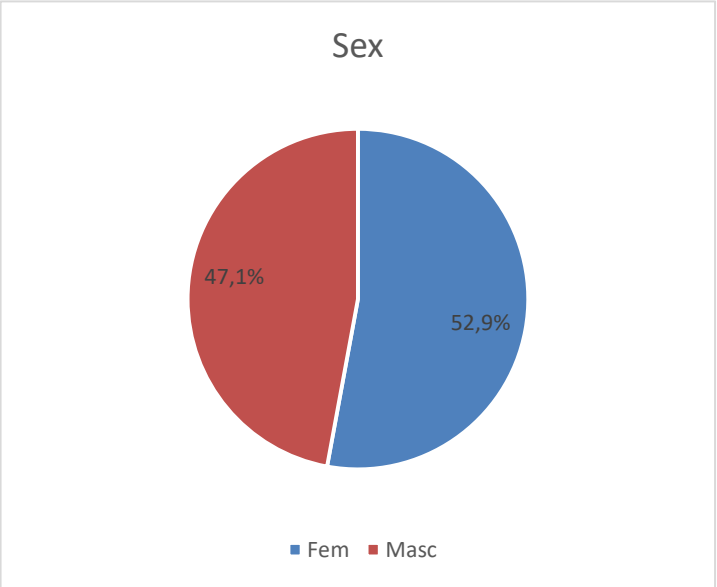

Figure 1: Sex of individuals

75.7% of the sample is in the age group of 20-40 years, a sample expected probably due to younger patients presenting more familiarity with digital media.

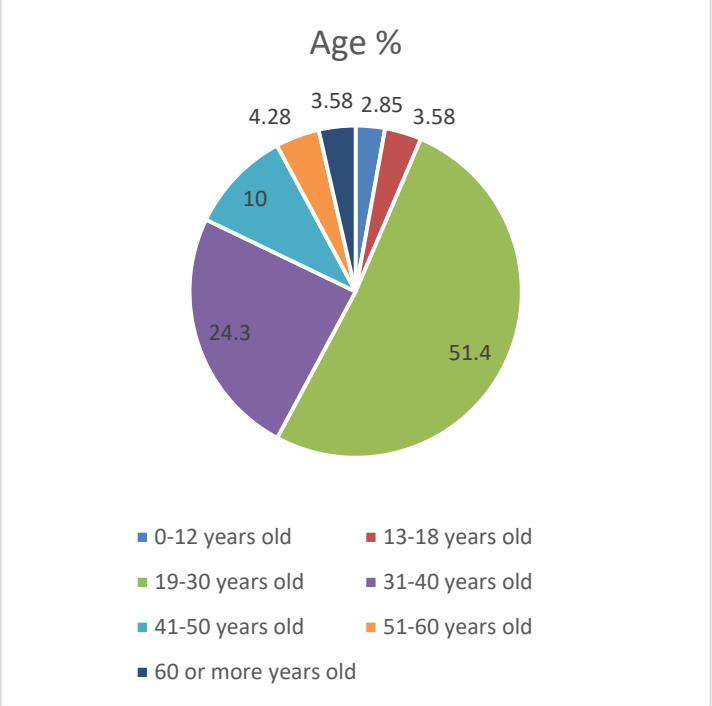

Figure 2: Age of individuals

Half received a clinical and epidemiological diagnosis, one quarter received a diagnosis via RT-PCR, the others underwent other laboratory or imaging tests.

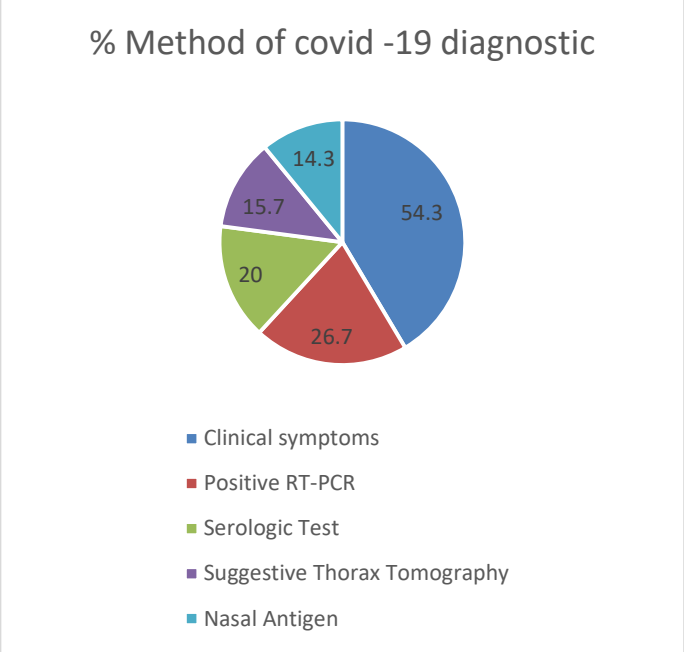

Figure 3: Diagnostic Method

The symptom of anosmia lasted on average 76.42 days, with a median of 30 days, and the fashion was between 2 extremes: 15 days and 6 months.

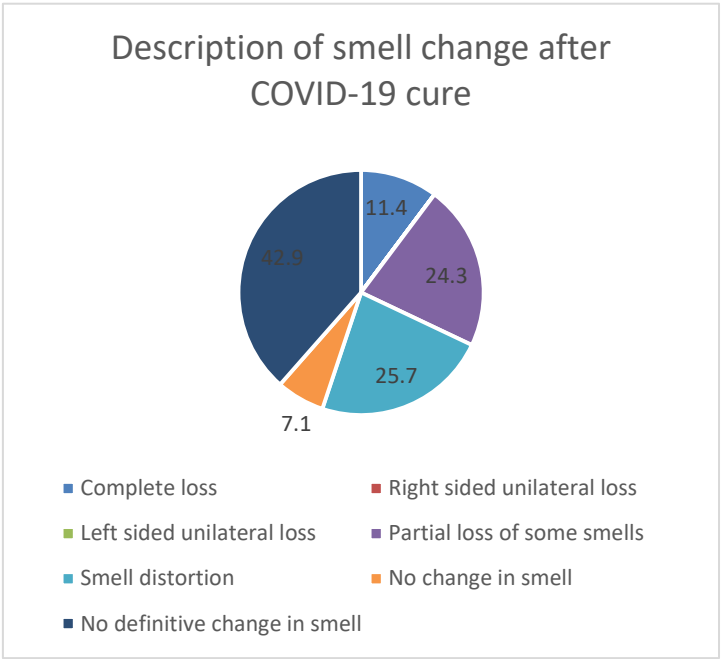

Figure 5: Characterization of loss of smell

The symptom of dysgeusia lasted on average 71.25 days, being the median 30 days, and, the fashion, is also between 15 days and 6 months.

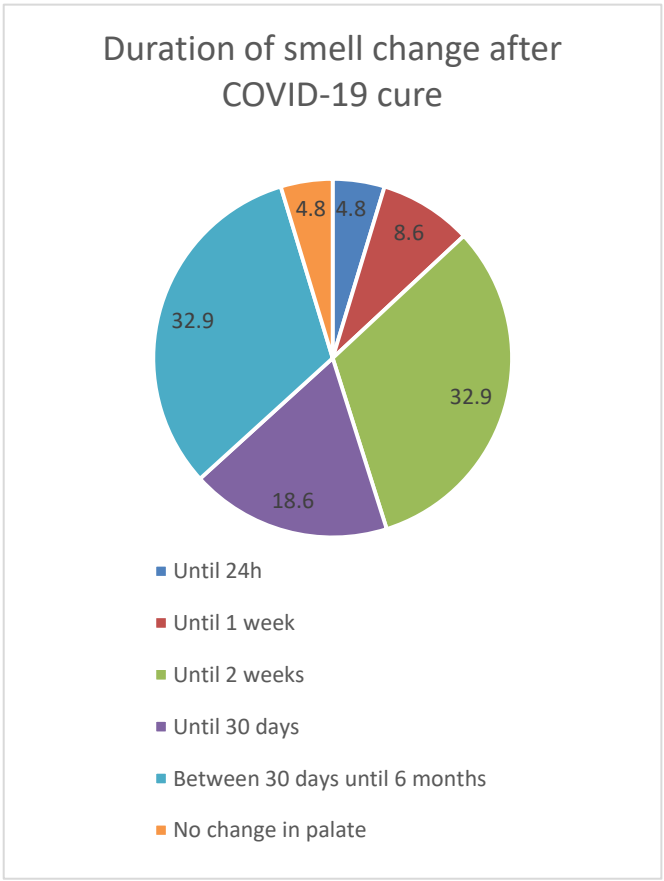

Figure 4: % of duration of loss of smell

Of the symptoms presented, it is noteworthy that no individual presented unilateral loss of smell. 42.9% had complete recovery of smell.

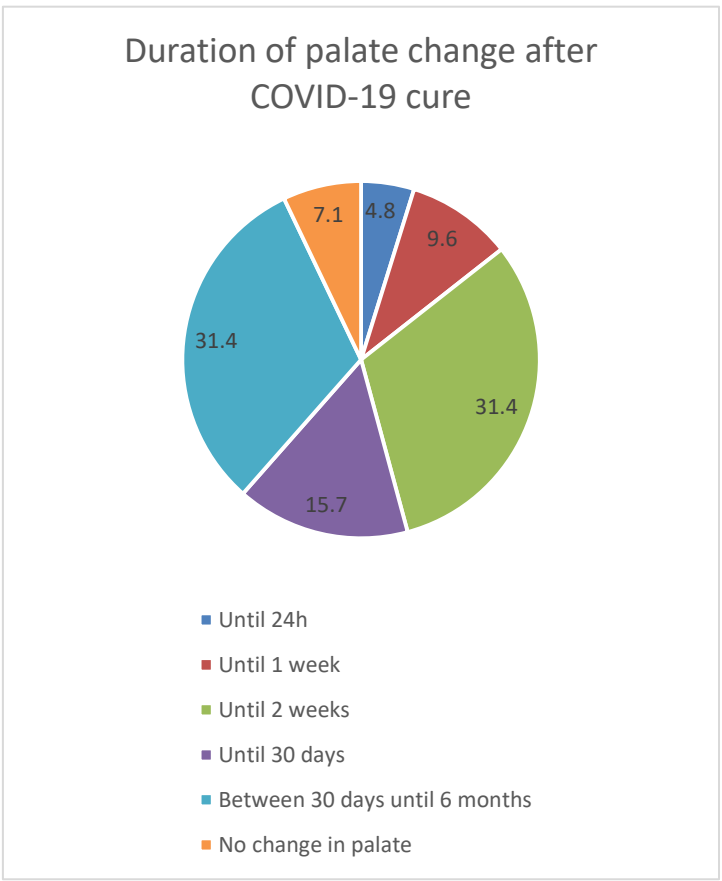

Figure 6: Duration of taste loss

Percentages similar to smell, in the questions of distortion and loss of smell were found on the functioning of the taste in the research sample. There is a slightly higher percentage of taste

recovery in relation to smell.

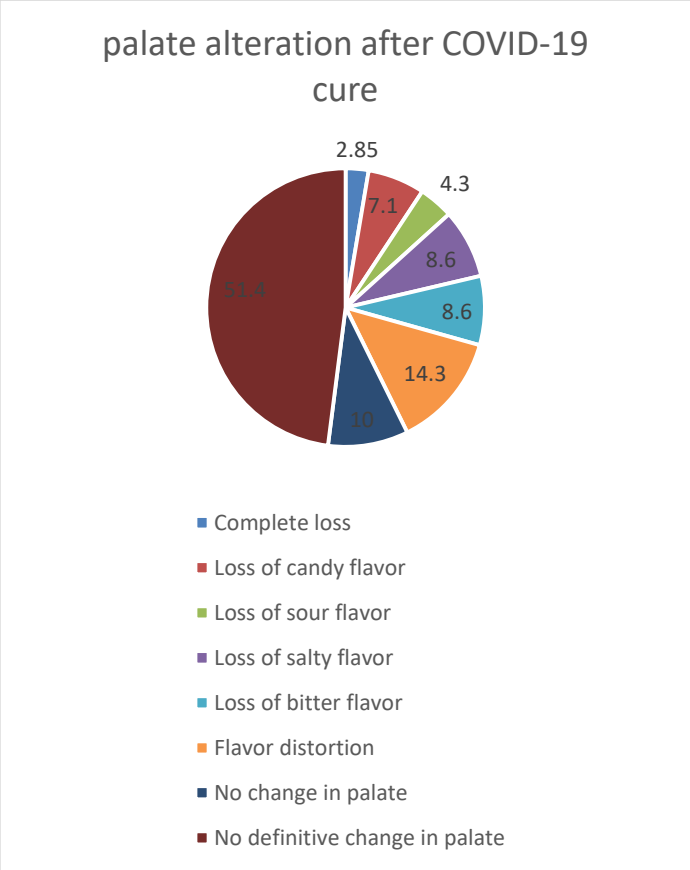

Figure 7: Characterization of palate alteration

Individual analysis of form responses showed that individuals aged 13-18 years recovered within 1 week of the onset of reported symptoms. There was no relationship between the sex of the individuals and the presence and/or duration of symptoms. Only 2 individuals with positive RT-CTR showed no symptoms.

DISCUSSION

In the present study, a similar prevalence was evidenced between the sexes in patients who tested positive for COVID-19. However, literature shows that males had the highest rates of complications and evolutions for death, regardless of age. Thus, in addition to other risk factors, obese and old men are the patients at higher risk of developing complications[15,16]. Anosmia and dysgeusia are important symptoms of screening, especially in young and female patients[17]. A study conducted in different world populations analyzed the different rates of patients with such dysfunctions, and concluded that the prevalence is higher in European and American populations, when compared to Asian populations – emphasizing that anosmia and dysgeusia are factors related to good prognosis[18], reaching about 50% of patients[19] In other pandemics, such as H1N1, morbidity is higher for young individuals, because they are the most affected population [20], however, COVID-19 is more well distributed among age, while H1N1 is more common between 10 to 18 years old and less frequent on adults over 51 years old, suggesting partial resistance to virus. There is another difference among incubation period, which is direct related to diagnostic methods.

Influenza virus has shorter incubation period, less than 3 days in general, while covid-19 virus can extend to 14 days. The present study, the majority of cases where among young population, less than 30 years old, maybe because these population is more familiar with digital insert, where the research was conducted. For both pandemic virus (H1N1 and Sars Cov -2) RT-PCR is the golden standard lab test to virus detection, but, for Sars Cov -2 CT scan was added as possible screen test, especially when clinical symptoms present, which improves its specificity[21,22].

In most countries, the diagnosis of infection in children is less frequent[23]. However, in some localities, such as Kazakhstan, the average infected infant population is almost three times higher compared to other countries studied. Thus, children should not be overlooked, especially for their role in the spread of the disease, since most children are asymptomatic and play an important role in the transmission of the virus[24]. This fact makes it compressible that, in the present study, no child under 12 years of age has been found, due to epidemiological uncertainty and absent or uncertain symptomatic manifestation.

We observed that the clinical and epidemiological aspects were sufficient to diagnose in most cases. Secondly, there is rt-pcr – a test that allows the identification of the virus in collected material. After that, serologic tests gained prominence in order to understand the response of the host – via Antibodies – to the pathogen. Suggestive Computed Tomography has also been reported, but it is often found along with one of the criteria mentioned above. It is noteworthy that, during the explosion of cases in the emergence of the Pandemic, it became unfeasible and, perhaps, impossible to apply tests to all suspicious patients, within the reality in question. Thus, with the combination of the clinic manifestations and epidemiological context, it was already possible to initiate individual isolation and reduce the chain of transmission of the virus. It is remarkable the high prevalence of olfactory and gustatory dysfunctions in patients who presented SARS-CoV-2, which may represent one of the first symptoms in the course of infection[25]. This fact was observed when comparing the presence of anosmia and dysgeusia among participants who did not present COVID-19 and those who were positive for the virus[26]. This fact was also presented in a multicenter study[27], in which 85.6% and 88.0% of the total of 417 participants positive for COVID-19 submitted to olfactory and gustatory symptom assessment questionnaires reported olfactory and gustatory dysfunction, respectively. The study was the first to present ENT symptoms, such as olfactory and gustatory dysfunctions, as indicators of SARS-CoV-2 infection, similar to the 97% prevalence of anosmia and dysgeusia symptoms in our study. The pathological mechanism of SARS-CoV-2 infection has not yet been definitively clarified, but the virus is believed to specifically target nasosinusal tract cells, including the olfactory epithelium. In them, the virus replicates, when entering the airways, with the association of its spike proteins with the angiotensin-converter enzyme 2 (ECA2)[28]. Thus, it is assumed that the symptoms caused by SARS-CoV-2 are related to the high levels of expression of this ECA2 receptor in the caliciformes and ciliated cells in the nasal epithelium, as well as in the lungs and along the epithelial cells of the respiratory tract[29]. In this context, although ACE2 is not

expressed in the olfactory receptor neuron, sustentacular cells (SUS) have high levels of these receptors, so studies suggest that these cells are the main target of SARS-CoV-2 in the olfactory epithelium[30].

Therefore, damage to SUS can cause an olfactory disorder, since they are functionally and anatomically linked to the olfactory epithelium. Added to this, another mechanism may be related to pathogenesis, since the SARS-CoV-2 induces an inflammatory immune response that can potentially damage olfactory receptor neurons: vascular phenomena. The vascular pericytes presents in the olfactory bulb has high levels of ACS2, being determinant for the maintenance of the blood brain barrier, regulation of neuroimmune response and local blood pressure. When those cells are infected, the perfusion can be altered, causing effects on the functioning of brain circuits, thus indirectly changing the perception of odor[31].

In addition to pulmonary manifestations, SARS-CoV-2 also potentially presents neurotropism, causing distinct disorders such as acute toxic encephalopathy and ischemic stroke. There are several mechanisms presented to justify neurological damage, which are due to direct brain invasion or indirect effects. Direct brain invasion can occur by viral dissipation through the cribriform plaque in the ethmoide bone, reaching the brain; through the olfactory bulb, related to the symptoms of gustatory and olfactory alterations[32]. However, it is not clear how the damage occurs through direct invasion by COVID-19 in the olfactory nerve, since no ECA2 receptors were found in the olfactory bulb.

Studies indicate that anosmia is the most prevalent olfactory dysfunction and may arise even before other clinical presentations of COVID-19, and may remain even after cure[33]. Thus, in Figure 4, we can observe that predominantly there was resolution of olfactory symptoms in 2 weeks and, equivalently, in the interval of 30 days to 6 months, with 32.9% of 70 participants in each of these periods. Regarding the resolution of olfactory disorder, in the first two weeks there is a higher rate of clinical improvement of these symptoms, which could be found in our study. In this context, the olfactory neuroepithelium has regenerative capacity, thus there may be improvement of olfactory symptoms. One of the factors related to this regeneration is time: there is a greater recovery soon after the damage, and there may be no subsequent improvement or at a slower rate[34]. This fact may explain the greater recovery of olfactory disorders in the first few weeks. In addition to a possible memory bias, because it involves a research based on a self-report questionnaire, a second hypothesis that may explain the resulting discrepant found regarding the duration of symptoms is that there is a wide clinical variability in COVID-19, based on the interaction of different biological, viral, cellular and molecular characteristics, which may vary according to ethnicity. In this sense, there are adaptations that the S-protein and the ECA2 receptor can present, thus influencing the interaction between SARS-CoV and human tissues[35]. Therefore, the level of expression and the pattern of ACS2 expression in different tissues may be determinant for the clinical and severity of the disease induced by SARS-CoV-2[36].

However, although there are studies involving European and Asian populations, there is a scarcity of information about this correlation between ethnicities and clinical presentation, even more remarkable regarding the Brazilian reality, including the Amazonian reality.

Figure 5 shows an important absence of prolonged olfactory alteration (42% of participants), which can be explained by the regeneration capacity of the olfactory neuroepithelium; in addition to a remarkable persistence of parosmia, a distortion of smell, and no reports of unilateral smell alteration. In the study conducted[27], 417 patients with COVID-19, [3,5,7] with olfactory alterations resulting from viral infection, the report of parosmia covered 32.4% of the participants. However, although present in the clinic secondary to SARS-CoV-2 infection, there are no considerable studies evaluating the prevalence and mechanism of this specific alteration. Dysgeusia is a marked alteration of COVID-19 infection. About 71% to 88.8% of the infected presented some taste alteration, whether ageusia, hypogeusia or dysgeusia[37, 38, 27]. For practical purposes, any change will be treated as dysgeusia, since there are no studies carried out to date that distinguish between the types of dysgeusia. These numbers are consistent with the present study, where 92.9% presented some degree of dysgeusia.

Chemosensory dysfunctions are common[39, 40,41]. Dysgeusia is associated with several pathologies, including Alzheimer's, diabetes mellitus, asthma, kidney disease, hepatitis C, Parkinson's, depression, candidiasis and cardiovascular diseases and various medications can cause taste changes. Data were collected regarding the duration of the taste alterations, shown in Figure 6, distributed in alterations that lasted 24 hours, 1 week, 2 weeks, up to 30 days, above 30 days and those that had no alteration. It is evident that 61.5% reported having recovered taste within 30 days and that a significant portion, 31.4%, had prolonged and possibly permanent taste changes. According to Figure 7, among those who presented prolonged alterations, and the main alteration still present, the main ones reported were complete loss, with 15.7% and taste distortion (dysgeusia) with 14.3%. In less quantity, changes to sweet were reported in 7.1%, sour in 4.3% in addition to salty and bitter both with 8.6%. The probable mechanism of the pathogenesis of COVID-19 in relation to dysgeusia is still unknown, but it is possibly related to the presence of angiotensin II-converter enzyme (ECA2) in the epithelium of the taste buds and human salivary glands. The oral mucosa presents receptors for ACE2, allowing the entry of the virus and thus triggering an inflammatory response that alters the cells of the epithelium to the point of causing alteration of function, similar to what seems to happen in the lung[37,42]. It has been demonstrated in Rhesus monkeys that salivary glands are a target of SARS-CoV-2 24 and it is possible to detect RNA from it before the appearance of lung injury, making plausible the

hypothesis of human salivary glands being affected, generating problems in saliva production, both qualitatively and quantitatively, thus resulting in dysgeusia, even in asymptomatic patients.

Other studies propose a neurological explanation for dysgeusia, since taste and smell are closely linked43, 44, damage to the olfactory system may result in dysgeusia.

There is also the possibility 45 in addition to the damage to the taste buds, of some damage to any of the nerves responsible for the taste (NC VII, IX and X) and among them the most likely is the tympanum string, branch of NC VII. CNS impairments are poorly plausible, since symptoms such as meningitis and encephalitis are much less frequent than dysgeusia.

CONCLUSION

Smell and taste complain was observed in almost all patients. None of them had unilateral anosmia or hyposmia. Parosmia and distortion on taste was more frequent. Most of patients had symptoms resolved from 15 days to 6 months. There is an important role of those symptoms on clinical diagnostic of covid-19. But further studies with new variants and others population should be conducted.

REFERENCES

1. Asadi S, Bouvier N, Wexler A, Ristenpart W. The coronavirus pandemic and aerosols: Does COVID-19 infects through respiratory particles? Aerosol Science and Technology. 2020; 54(6): 635-638.
2. Souza D. A pandemia de COVID-19 para além das Ciências da Saúde: reflexões sobre sua determinação social. Ciênc. saúde coletiva, 2020; 25(1): 2469-2477.
3. Ministério da Saúde. Painel Coronavírus [internet]. 2020 [Citado em 06 de dezembro]. Disponível em: https://covid.saude.gov.br/
4. Kaye R, Chang CWD, Kazahaya K, Brereton J, Denneny JC. COVID-19 Anosmia Reporting Tool: descobertas iniciais. Otorrinolaringologia - Cirurgia de Cabeça e Pescoço. 2020; 163 (1): 132-134.
5. Ten-caten F. A análise aprofundada dos parâmetros laboratoriais revela a interação entre sexo, idade e inflamação sistêmica em indivíduos com COVID-19. medRxiv , 2020
6. Lima C. Informações sobre o novo coronavírus (COVID-19). Radiol Bras , 2020; Abr 23, 53(2), V-VI. Disponível em: https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-39842020000200001&lng=en&nrm=iso> https://doi.org/10.1590/0100-3984.2020.53.2e1
7. Iser B et al. Definição de caso suspeito da COVID-19: uma revisão narrativa dos sinais e sintomas mais frequentes entre os casos confirmados. Epidemiologia e Serviços de Saúde. 2020; 29(3). Disponível em: https://doi.org/10.5123/S1679-49742020000300018
8. Cardoso M et al. Anosmia e disgeusia no paciente com coronavírus: revisão narrativa. Revista Eletrônica Acervo Saúde, 2020; 46: 4226.
9. Vaira LA , Salzano G , Fois AG , Piombino P , De Riu G. Patogênese potencial da ageusia e anosmia em pacientes com COVID - 19 . Int Forum Allergy Rhinol. 2020; 10: 1103 - 1104
10. Kosugi, E et al . Recuperação incompleta e tardia da perda súbita do olfato na COVID-19. Braz. J. Otorhinolaryngol, 2020 Aug, 86(4): 490-496. Disponível em http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1808869420200004004 90&lng=en&nrm=iso https://doi.org/10.1016/j.bjorl.2020.05.001
11. Pimentel BN. Disfunções olfativas e gustativas como apresentação clínica da COVID-19. Pesquisa, Sociedade e Desenvolvimento, 9(8): 649. Disponível em: https://rsdjournal.org/index.php/rsd/article/view/5072 https://doi.org/10.33448 rsd-v9i8.5072
12. Lauer SA, Grantz KH, Bi Qal. O período de incubação da doença do coronavírus 2019 (COVID-19) de casos confirmados relatados publicamente: estimativa e aplicação. Ann Intern Med, 2020; 172 (9): 577-582. https://doi.org/10.7326/M20-0504
13. Nishiura H, Kobayashi T., Miyama T., et al. Estimativa da proporção assintomática de novas infecções por coronavírus (COVID-19). 2020, Int J Infect Dis; 94: 154-155. https://doi.org/10.1016/j.ijid.2020.03.02
14. Vallinoto ACR, da Silva Torres MK, Vallinoto MC, Cayres Vallinoto IMV. The challenges of COVID-19 in the Brazilian Amazonian communities and the importance of seroepidemiological surveillance studies. Int J Equity Health. 2020 Aug 15;19(1):140. doi: 10.1186/s12939-020-01256-7 PMID: 32799872; PMCID: PMC7429088.
15. Nikpouraghdam M, Farahani J, Alishiri G, Heydari S, Ebrahimnia M, Samadinia H, Dorostkar R. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in Iran: a single center study. Journal of clinical virology. 2020 Jun; 127: 104378. https://doi.org/10.1016/j.jcv.2020.104378
16. Jin J-M, Bai P, He W, Wu F, Liu X-F, Han D-M, Liu S and Yang J-K. Gender differences in patients with COVID-19: focus on severity and mortality. 2020, Front. Public health 8:152. https://doi.org/10.3389/fpubh.2020.00152
17. Zahra, S, Iddawela, S, Pillai, K, Choudhury, R, Harky, A. Can symptoms of anosmia and dysgeusia be diagnostic for covid-19? 2020, Brain and Behavior, 10(11): 1-18
18. Pathak V, Saxena R, Pradeepti N et al. Prevalence of anosmia and dysgeusia in patients of COVID–19 in a dedicated covid hospital. 02 Set 2020, PREPRINT(1). Disponível em: https://doi.org/10.21203/rs.3.rs-65011/v1
19. Klopfensteina T, Zahrab H, Kadiane-Oussousa N, Lepillerc Q, Royera, P, Tokoa, L et al. New loss of smell and taste: uncommon symptoms in COVID-19 patients in nord franche-comte cluster, france. 2020, International

Journal Of Infectious Diseases. 100: 117-122.

20. Cortis D. On determining the age distribution of COVID-19 pandemic. 2020, Front. Public health 8:202. Disponível em: https://doi.org/10.3389/fpubh
21. Da Costa V, Saivish M, Santos D, Silva R, Moreli M. Comparative epidemiology between the 2009 H1N1 influenza and COVID-19 pandemics, 2020, Journal Of Infection And Public Health; 13(2): 1797-1804. Disponível em: https://doi.org/10.1016/j.jiph.2020.09.023
22. Bellei, N; Melchior, T. H1N1: Pandemia e Perspectiva Atual. J. Bras. Patol. Med. Lab. 2011; 47(6): 611-617.
23. Kemelbekov K, Ospanova E, Baimakhanova B, Zhumabekov Z, Zholdas K, Yessentayeva Z, Zaidulla A. Epidemiological characteristics of new coronavirus diseases (COVID-19): features of risk factors and clinical features of the child population. Electron j gen med. 2020;17(6):252. Disponível em: https://doi.org/10.29333/ejgm/8268
24. Liu L, Wei Q, Alvarez X. Epithelial cells lining salivary gland ducts are early target cells of severe acute respiratory syndrome. 2011, J Virol; 85:4025–4030.
25. 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. 2020, Otolaryngol Head Neck Surg.;163(1):3-11.
26. Lee D, Lockwood J, Das P, et al. Self-reported anosmia and dysgeusia as key symptoms of Coronavirus Disease 2019. 2020, CJEM; 22(5):595-602.
27. Lechien J, Chiesa-Estomba C, De Siati D, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the Coronavirus Disease (COVID-19): A Multicenter European Study. 2020, Eur Arch Otorhinolaryngol; 6: 1-11.
28. Zhao Y, Zhao Z, Wang Y, et al. Single-cell RNA expression profiling of ACE2, the receptor of SARS-COV-2. 2020, Am J Respiratory Critcare Med; 202(5):756-759.
29. Brann D, Tsukahara T, Weinreb C, et al. Non-neuronal expression of sars-cov-2 entry genes in the olfactory system suggests mechanisms underlying COVID-19-associated anosmia. 2020, Sci adv;6(31):eabc5801.
30. Bilinska, K.; Butowt, R. Anosmia in COVID-19: a bumpy road to establishing a cellular mechanism. Acs chem neurosci. 2020; 11(15):2152-2155.
31. Cooper, K.W.; Brann, D.H, Farruggia, M.C. Et Al. COVID-19 andthechemicalsenses: supporting players take center stage. Neuron. 2020;107(2):219-233. Disponível em: https://doi.org /10.1016/j.neuron.2020.06.032
32. Abboud, H.; Abboud, F.Z.; Kharbouch, H.; Arkha, Y.; El Abbadi, N.; El Ouahabi, A. COVID-19 and sars-cov-2 infection: pathophysiology and clinical effects on the nervous system. World neurosurg. 2020; 140:49-53.
33. Costa, K.V.T.D.; Carnaúba, A.T.L.; Rocha, K.W. Et Al. Olfactory and taste disorders in COVID-19: a systematic review [published online ahead of print, 2020 jun 9]. Braz j otorhinolaryngol. 2020; s1808-8694(20)30066-5.
34. London, B.; Nabet, B.; Fisher, A.R. Et Al. Predictors of prognosis in patients with olfactory disturbance. Ann neurol. 2008 feb; 63(2):159-66.
35. Li, W.; Zhang, C.; Sui, J. Et Al. Receptor and viral determinants of sars-coronavirus adaptation to human ace2. Embo j. 2005 apr 20; 24(8):1634-43.
36. Cao, Y.; Li, L.; Feng, Z. Et Al. Comparative genetic analysis of the novel coronavirus (2019-ncov/sars-cov-2) receptor ace2 in different populations. Cell discov. 2020; 6:11. Published 2020 feb 24.
37. Lozada-Nur F, Chainani-Wu N, Fortuna G, Sroussi H. Dysgeusia in COVID-19: Possible Mechanisms and Implications. Oral Surg Oral Med Oral Pathol Oral Radiol. 2020;130(3):344-346. Disponível em: https://doi.org/10.1016/j.oooo.2020.06.016
38. Yan C, Faraji F, Prajapati D, et al. Association of chemosensory dysfunction and COVID-19 in patients presenting with Influenza-like symptoms [e-pub ahead of print]. 2020, Int Forum Allergy Rhinol. Disponível em: https://doi.org/10.1002/alr.22579.12
39. Quratulain S, Hendler K, Koncilja K. The impact of aging and medical status on dysgeusia. 2016, Am J Med;129(753):1-6.
40. Ackerman B, Kasbekar N. Disturbances of taste and smell induced by drugs. Pharmacotherapy. 1997; 17:482–496.
41. Wang W, Chen S, Liu I. Detection of SARS-associated coronavirus in throat wash and saliva in early diagnosis. Emerg Infect Dis. 2004; 10:1213–1219.
42. Xu H, Zhong L, Deng J. High expression of ACE2 receptor of 2019-nCov on the epithelial cells of oral mucosa. Int J Oral Sci. 2019; 12:8.
43. Lahiri D, Ardila A. COVID-19 Pandemic. A neurologic perspective. Cureus. 2020;12:E7889.
44. Obiefuna S, Donohoe C. StatPearls. StatPearls Publishing; Treasure Island, FL: 2020. Neuroanatomy, nucleus gustatory.
45. Finsterer J, Stollberger C. Causes of hypogeusia/hyposmia in SARS-CoV2 infected patients [e-pub ahead of print]. 2020, J Med Virol. Disponível em: https://doi.org/10.1002/jmv.25903

