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Research Article

Analysis Descriptive of Anosmia and Dysgeusia in SARS CoV-2 Patients: Overview of Epidemiology, Pathogenesis, Prognosis, and Treatment Options

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ABSTRACT

Introduction: SARS CoV-2 (COVID-19) is a respiratory infectious disease whose cause has been identified as the seventh type of the coronavirus family that attacks humans. Common symptoms among patients with COVID-19 include fever, dry cough, shortness of breath (dyspnea), muscle aches (myalgia), confusion, headache, sore throat, rhinorrhea, chest pain, diarrhea, nausea / vomiting, conjunctival congestion, nose. congestion, sputum production, fatigue (malaise), hemoptysis, and shivering. However, the spread of COVID-19 infection has shown new symptoms of the disease: patients with dysfunction of smell, taste and indigestion. Methods: Literature review by taking libraries from 34 journals and 2 textbook. The journal obtained from the Google, NCBI and Pubmed search engine, as well as processing research materials into new information related to the research objectives. Results: One hypothesis currently developing is that SARS-CoV-2 will cause olfactory changes through direct access and damage to the CNS through its penetration by the cribriform plate. Another hypothesis that is also developing suggests direct viral damage to olfactory cells and taste receptors. Glial cells, neurons, and the oral cavity present the ACE-2 receptor which appears to be a mechanism of cell invasion by viruses. Conclusion: People who have lost their smell or taste are six times more likely to become positive for COVID-19. Likewise, people who have anosmia have a 10-fold higher chance of being diagnosed with

COVID-19. Taste and smell disorders with ageusia have a 10 times higher chance of catching COVID-19.

1. Introduction

COVID-19 is a health problem for the world today and in the future. In December 2019, the first COVID-19 patient was notified by the Chinese government with a location in Wuhan Province. Over the next few months, coronavirus 2 (SARS-CoV-2) rapidly spread around the world and resulted in the COVID-19 pandemic. SARS CoV-2 (COVID-19) is a respiratory infectious disease whose cause has been identified as the seventh type of the human coronavirus family (Biadsee et all., 2020). As of 23 April 2020, there were more than 2.4 million confirmed cases worldwide in more than 213 countries, territories or territories, resulting in 169,000 deaths (Coleman et all., 2020). As of June 30, 2020, WHO reported 10,185,374 confirmed cases with 503,862 deaths worldwide.

Common symptoms among patients with COVID-19 include fever, dry cough, shortness of breath (dyspnea), muscle pain (myalgia), confusion, headache, sore throat, rhinorrhea, chest pain, diarrhea, nausea/vomiting, conjunctival congestion, nasal congestion, sputum production, fatigue (malaise), hemoptysis, and chills (Lee et al., 2020). However, the spread of COVID-19 infection in Europe has shown a new symptom of this disease: patients with olfactory, taste and digestive disorders (Lechien et all., 2020).

2. Materials and Methods

This literature review uses the literature review method by taking literature from 25 journals. Journals are obtained from search engines Google, NCBI and Pubmed, and process research materials into new information related to research objectives. In this search, researchers found 143 research articles according to the keywords that the researcher wants. Furthermore, there are 65 articles from those found are carried out in a screening process to see suitability journal/article desired by the researcher. The next stages are found as many as 25 articles were appropriate when the author read the abstract with researcher analysis.

3. Results and Discussions

One hypothesis currently developing is that SARS-CoV-2 will cause olfactory changes through direct access and damage to the CNS through its penetration by the cribriform plate. Another hypothesis that is also developing suggests direct viral damage to olfactory cells and taste receptors. Glial cells, neurons, and the oral cavity present the ACE-2 receptor which appears to be a mechanism of cell invasion by viruses.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first discovered in China in late 2019 and is now an ongoing pandemic. SARS-CoV-2 is known as a chain RNA coronavirus and its genome size is one of the largest among RNA viruses. SARS-CoV-2 have resemblance to Severe acute respiratory syndrome coronavirus (SARS-CoV) (Mahraeen et all., 2020). In Indonesia, the incidence of COVID-19 always increases every day and as of February 24, 2021, there have been 1,306,141 confirmed positive people, 35,254 confirmed deaths, and 1,112,725 confirmed recovery (Kemenkes Ri, 2020).

Currently the spread of COVID-19 from human to human is a major transmission, causing an increase every day. Transmission of COVID-19 from patients who have been confirmed positive or from people without

symptoms occurs through droplets or coughs that arise when sneezing. Several other studies have also stated that the mechanism of transmission of COVID -19 has not yet been found.

The ongoing COVID-19 is still spreading rapidly around the world. So it is very important to pay attention to the early signs of COVID-19 and get information about its development as soon as possible. Most COVID-19 patients complain of no symptoms or mild symptoms in the early stages although cough, fever and difficulty breathing are the main symptoms. To date, the number of COVID-19 sufferers is increasing rapidly, although the onset of Anosmia (loss of sense of smell) and/or Dysgeusia (loss of sense of taste) in COVID-19 patients is reported to vary, in general, most of these 2 symptoms may precede or accompanied by other major generalized symptoms or no other symptoms (Coleman et all., 2020; Jin Y et all., 2020; Klopfenstein et all., 2020).

There are several studies that discuss the association of COVID-19 with Anosmia and Dysgeusia . In a study conducted by Abalo-Lojo et al., (2020) it was mentioned to identify excessive taste and smell dysfunction as a clinically relevant manifestation of the COVID -19 disease. 50.4 years, 42.6% male, 57.4% female), diagnosed by PCR from nasopharyngeal swab samples. more than half of the patients reported both Dysegusia and Anosmia (72/131, 55.0%), 39.7% (52/131) no taste dysfunction or anosmia, 3.8% (5/131) only anosmia, and the remaining 1.5% (2/131) reported taste dysfunction. In patients with taste disturbances and anosmia, both symptoms occur simultaneously. These symptoms appeared at the onset of the disease in 13.9% of cases (11/79), on the next 3 days in 70.9% of cases (56/79), and after the fourth day in the remaining 15.2% of cases (12/79). 79) (Abalo-lojo et all., 2020).

Whereas in a subsequent study also mentioned in a comparative setting that was analyzed for power, the study included 128 subjects for the study and was divided into 2 groups (COVID-19 positive and COVID-19 negative) of 64 subjects each. The test results are based on RT-PCR testing. Both groups underwent assessment through the anosmia reporting tool developed by AAO-HNS in March 2020. When compared with COVID-19 negative subjects , multivariate analysis showed that subjects who tested positive for COVID-19 experienced an approximately 7-fold decrease in taste and smell. higher than those who tested negative for COVID-19 . Decreased taste and smell mainly occurs in the form of hyposmia / hypogeusia. COVID-19- related odor nuisance was not initially. Immediately following this report, the AAO-HNS released an anosmia reporting tool to collect data and to clarify the findings of these observations. Of the first 237 subjects, in 26.6% of the subjects, anosmia was an early symptom of COVID-19 . The results of this study also showed that COVID-19 positive subjects experienced significantly higher odor/taste disturbances than COVID-19 negative subjects . However, most of these disorders are not in the form of anosmia/ageusia but in the form of hyposmia/hypogeusia and parosmia/dysgeusia. Although not significant between groups, at the time of the study, 45.7% of subjects in the COVID-19 positive group and 64.7% of subjects in the COVID-19 negative group , taste and smell disturbances returned to normal. Although not significant in the multivariate analysis, the presence of rhinorrhea was significantly high among COVID-19-negative subjects , and complaints described as 'other' were significantly high among COVID-19- positive subjects . This may indicate a need for more detailed symptom questions in anosmia reporting tools (Sayin et all., 2020; Wang-Huei Sheng et all., 2020; U Mohammed et all., 2020).

Furthermore, in another study conducted by Biadsee et al., (2020) it was mentioned that the URTI virus is one of the most frequently identified causes of olfactory dysfunction. Olfactory disturbances can be classified into conductive loss stemming from nasal obstruction and sensorineural causes from damage to

the olfactory neuroepithelium, which is most commonly associated with postviral olfactory loss. In this study it was also stated that anosmia was the first symptom among more than about 25% of COVID-19 patients (Biadsee et all., 2020). In this study, 38.3% reported olfactory dysfunction as the first symptom and 66% reported the presence of olfactory dysfunction during the period of illness. In an effort to find the factors driving the high prevalence of olfactory dysfunction, this study found a significant association with nasal congestion. This implies that the blocked nasal passages may have served as an important component of the olfactory disorder. However, it is worth mentioning that we found no correlation between nasal congestion and anosmia. It is possible that damage to the olfactory neuroepithelium has a significant contribution to anosmia. Actual loss of taste is very rare, and usually occurs before it is caused by an inability to perceive the smell of food due to olfactory dysfunction. In the analysis of this study, 25.8% reported impaired sense of smell with impaired sense of taste in the absence of other symptoms. So we believe that these results may indicate the need to examine and isolate patients with olfactory and taste disorders to reduce the rate of COVID-19 infection (Biadsee et all., 2020; Dos Santos et all., 2020).

In another study, which differed slightly from previous studies, the odds ratio (OR) for the association of anosmia or dysgeusia or both with SARS-CoV-2 positivity was 20.0 (95% confidence interval [CI] 7.3-54.6) and did not differ significantly for women (16.9, 95% CI 7.6-37.4) and men (26.9, 95% CI 8.7-82.8). Some symptoms were associated with SARS-CoV-2 infection in the bivariate analysis but were no longer significant after adjustment for confounders. Independent symptoms associated with SARS-CoV-2 infection were anosmia or dysgeusia or both (OR 62.9, 95% CI 11.0-359.7), presence of myalgia (OR 7.6, 95% CI 1.9- 29.9), blurred vision (adjusted OR 0.1, 95% CI 0.0-0.8) and chest pain (adjusted OR 0.1, 95% CI 0.0-0.6). The final multivariable regression model also included other variables that significantly increased model fit but were not significantly associated with outcomes. These variables were loss of appetite (OR 2.2, 95% CI 0.8-5.9), sneezing (OR 0.4 adjusted, 95% CI 0.1-1.1) and asthenia (OR 1.3 adjusted, 95% CI 0.5–3.3). To further investigate the association between anosmia and dysgeusia and SARS-CoV-2 infection , this study performed an evaluation of gustatory and olfactory function among SARS-CoV-2- positive patients who described anosmia and dysgeusia as strongly correlated: 67 patients had both, 2 patients only had anosmia, and 18 patients had only dysgeusia ($p < 0.001$). However, the symptoms most frequently described in this study as presenting by SARS-CoV-2- positive patients were sore throat (21 patients [15.7%]) and cough (39 [29.1%]). Anosmia and dysgeusia were not reported frequently as positive manifestations of SARS-CoV-2 (3 patients [2.2%] and 2 patients [1.5%], respectively). The most severe symptoms reported by respondents were cough (26 patients [19.4%]), asthenia (22 [16.4%]) and headache (16 [11.9%]). Anosmia (4 patients [3.0%]) and dysgeusia (5 [3.7%]) were rarely reported as the most severe symptoms. Anosmia or dysgeusia, or both, without fever or cough, was observed in nearly one third of patients (16 of 57 [28%]) but was reported as the only symptom in only 2 of 134 patients (1.5%) (Carignan et all., 2020; Syed Q et all., 2016; Liguori et all., 2020).

Research conducted by Carrillo-Larco and Altez-Fernandez, (2020) yielded 31 results, of which 14 met the inclusion criteria and were studied in detail; Finally, six (n = 2,757) reports were selected for data extraction. Of the selected reports13-18, six provided information for the first objective (frequency of anosmia and dysgeusia in COVID-19 patients), and two informed the second goal (relationship between anosmia and dysgeusia and the diagnosis of COVID-19). The present study also did not find any reports studying the association between anosmia and dysgeusia with impaired outcomes (eg, admission to intensive care) in COVID-19 patients . Frequency of anosmia and dysgeusia in patients with COVID-19 . The frequency of anosmia in patients with COVID-19 ranges from 22% to 68%. The definition of taste disturbance is more

heterogeneous, with dysgeusia present in 33% of COVID-19 patients , ageusia in 20%, and taste distortion found in 21% of patients with COVID-19 . The association of anosmia and dysgeusia with the diagnosis of COVID-19 , and we found none reported studying anosmia and dysgeusia with poor outcome in COVID-19 patients (Carrillo-Larco and Altez-Fernandez, (2020; Wu Y et all., 2020).

In a systematic review and meta-analysis conducted by Akosua Adom, (2020) , it was mentioned that approximately 41% and 38% of confirmed patients with a COVID-19 diagnosis had olfactory dysfunction or impairment, respectively. Increasing age was correlated with a lower prevalence of olfactory and gustatory dysfunctions (OGD), while the use of objective assessment methods was correlated with a higher prevalence of olfactory dysfunction. There was no significant moderation of the prevalence of OGD by sex. The exact mechanism underlying OGD among patients with COVID-19 infection remains unclear. However, impaired smell after upper respiratory tract infection is a common clinical occurrence. In particular, postviral olfactory dysfunction has been implicated in 40% of cases of anosmia in adults,39 with coronavirus accounting for 10% to 15% of cases.5 Olfactory dysfunction in COVID-19 infection may be associated with involvement of the olfactory bulb or peripheral damage to olfactory receptor cells. in the nasal neuroepithelium.40 This assertion is based on the potential neurotrophic features of SARS-CoV-2 . In particular, it has been demonstrated in transgenic mice that after intranasal administration of SARS-CoV (which has similarities to SARS-CoV-2), the virus can penetrate into the brain via the olfactory bulb, leading to rapid transneuronal spread. It is also well recognized that changes in the volume and composition of saliva can impair taste sensation. Previously, epithelial cells lining the salivary gland ducts were found to be the initial target cells for SARS coronavirus infection in the upper respiratory tract of the rhesus machine. The phylogenetic similarity between SARS-CoV and SARS-CoV-2 means that the latter may also alter gustatory sensation in affected patients (Akosua et all., 2020; Lee Y et all., 2020; Pascarella et all., 2020). While anosmia generally occurs due to a damage to the organ of the olfactory process, damage can occur in the olfactory neuroepithelium, olfactory bulb, and olfactory cortex in the brain. Damage to the olfactory neuroepithelium can result in impulses not being captured adequately or not at all, so that no incoming impulses will be interpreted. Damage to the olfactory bulb also causes impulses to not be transmitted or no could transmitted to the cerebral cortex. Damage to the olfactory cortex in the cerebral cortex, for example caused by head trauma, causes the impulses transmitted by the olfactory bulb to not be interpreted, so that the individual cannot perceive or interpret the scent stimulus. There are mechanisms that cause olfactory disturbances, such as : disruption of action potentials of cell membranes, disturbances in neurotransmitters and changes in the mucous surface. Mechanism described _ This affects the process of conducting impulses from the olfactory neuroepithelium to the cerebral cortex, so that later cause odor stimulus cannot be interpreted (Chan KW et all., 2020; Esraghi et all., 2020; Gouvea W, 2020).

Several studies have also revealed that people who lose their sense of smell and taste are six times more likely to be positive for COVID-19 . Similarly, people with anosmia have a 10-fold higher chance of being diagnosed with COVID-19 . Other work also studying taste and smell disorders reported that people with ageusia had a 10 times higher chance of catching COVID-19 . Estimates of numbers were also adjusted for covariates including age, sex and other symptoms. Most patients describe a sudden and severe loss of their sense of smell or taste, or both. This loss is reflected in their ability to recognize the smell of perfume, smoke, garbage, and coffee (Mahraeen et all., 2020; Printza and Constantinidis., 2020; Tong JY et all., 2020).

No	Author	Tittle
1.	Abalo-Lojo, J. M et all	Taste and Smell Dysfunction in COVID-19 Patients
2.	Akosua A et all	Smell and Taste Dysfunction in Patients With *COVID-19*: A Systematic Review and Meta-analysis
3.	Biadsee A et all	Olfactory and Oral Manifestations of COVID-19: Sex-Related Symptoms—A Potential Pathway to Early Diagnosis.
4.	Carignan et all	Anosmia and dysgeusia associated with SARS-CoV-2 infection: an age-matched case–control study
5.	Carrillo-Larco RM, Altez-Fernandez C	Anosmia and dysgeusia in COVID-19: A systematic review
6.	Chan KW et all	COVID-19: An Update on the Epidemiological, Clinical, Preventive and Therapeutic Evidence and Guidelines of Integrative Chinese-Western Medicine for the Management of 2019 Novel Coronavirus Disease
7.	Colemann et all	COVID-19: to be or not to be; that is the diagnostic question.
8.	DosSantos et all	Neuromechanisms of SARS-CoV-2: A Review.
9.	Eshraghi et all	Potential Mechanisms for COVID-19 Induced Anosmia and Dysgeusia
10.	Gouvea W	Natural history of COVID-19 and current knowledge on treatment therapeutic options
11.	Jin Y et all	Virology, Epidemiology, Pathogenesis, and Control of COVID-19.
12.	Kemenkes RI	Pedoman dan Pencegahan Coronavirus (COVID-19).
13.	Klopfenstein et all	Features of anosmia in COVID-19.
14.	Lee Y et all	Prevalence and Duration of Acute Loss of Smell or Taste in COVID-19 Patients
15.	Lechien et all	Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study
16.	Liguori et all	Subjective neurological symptoms frequently occur in patients with SARS-CoV2 infection.
17.	Mahraeen et all	Olfactory and gustatory dysfunctions due to the coronavirus disease (COVID-19): a review of current evidence

18.	Pascarella et all	COVID-19 diagnosis and management: a comprehensive review
19.	Printza A and Constantinidis J.	The role of self-reported smell and taste disorders in suspected COVID-19
20.	Sayin et all	Taste and Smell Impairment in COVID-19: An AAO-HNS Anosmia Reporting Tool-Based Comparative Study
21.	Syed et all	The Impact of Aging and Medical Status on Dysgeusia
22.	Tong JY et all	The Prevalence of Olfactory and Gustatory Dysfunction in COVID-19 Patients: A Systematic Review and Meta-analysis
23.	U Mohammed et all	SARS-CoV-2/COVID-19: Viral Genomics, Epidemiology, Vaccines, and Therapeutic Interventions.
24.	Wang-huei sheng et all	Dysosmia and dysgeusia in patients with COVID-19 in northern Taiwan.
25.	Wu Y et all	Nervous system involvement after infection with COVID-19 and other coronaviruses.

4. Conclusions

Most infected patient COVID-19 describe loss ability smell or tasting or both of them by suddenly. People who lost smell or taster have possibility six times higher for Becomes positive COVID-19. As well, people with anosmia have 10 times chance higher for diagnosed with COVID-19. Taste disturbances and smell with ageusia have 10 times more chance tall for caught COVID-19.

5. Acknowledgment

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