

## ORIGINAL ARTICLE

# Anosmia, Dysgeusia, and Comorbidity in COVID-19 Patients with Respiratory Tract Manifestations

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## ABSTRACT

**Introduction:** Olfactory and special sensory disturbances such as anosmia and dysgeusia have been found among COVID-19 patients. These manifestations may cause post-covid sequelae, disturbing patients' quality of life who have recovered from COVID-19. This study aimed to analyze the association between anosmia and dysgeusia with the comorbidities in adult COVID-19 patients admitted to Dr. Soetomo General Hospital, Surabaya, from 1 January 2020 to 30 September 2021.

**Methods:** This was a cross-sectional retrospective analysis study based on the medical records of all patients who met the criteria (n = 158). The minimal age inclusion was 18 years old, and the patient must be positively diagnosed with COVID-19 (reverse transcription polymerase chain reaction/RT-PCR).

**Results:** Out of 158 patients, all had a fever, and approximately 93% of patients showed respiratory signs and symptoms. There were 128 patients (81%) who suffered from anosmia, and 15 patients (9.5%) had dysgeusia. Significant associations were found between anosmia with dysgeusia (p = 0.049) and between anosmia with cough (p = 0.003) and dyspnea (p = 0.000). The predominant comorbidities reported were overweight (60%), hypertension (42%), and type-2 diabetes mellitus (37%).

**Conclusion:** There were significant associations between anosmia with dysgeusia and the respiratory tract signs and symptoms instead of the comorbidities reported.

## INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) is a new global pandemic that has changed people's lives, habits, economics, education, business, and health. By early January 2021, COVID-19 made a global impact, with more than 83 million confirmed cases and more than 1.8 million deaths worldwide.<sup>1</sup> COVID-19 is a new disease. Therefore, there is no immunity in the community. This means that COVID-19 could spread widely and quickly. This virus is characterized by its

rapid human-to-human transmission through fomites (objects or materials that are likely to carry infection, such as clothes and utensils), physical/close contact with an infectious person, aerosol droplets from an infected person's cough and sneeze, touching objects and surfaces that have droplets from an infected person then touching the face and mouth, and the potential of asymptomatic cases to infect others.<sup>2</sup>

In several cases, severe neurological symptoms of COVID-19 commonly manifest as anosmia and dysgeusia.<sup>3-5</sup> Interestingly, these olfactory issues were

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reported before other symptoms occurred.<sup>6</sup> These manifestations commonly occur in COVID-19 patients with respiratory tract impairment, including coughing and dyspnea.<sup>7</sup>

However, several other studies reported that the olfactory and special taste alteration among COVID-19 patients could also be found in non-respiratory manifested cases. The underlying mechanisms are still debatable, i.e., the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) infected the olfactory cranial nerves located at the superior nasal meatus, impairing the olfaction synapse into the pyriform gyrus near the gyrus that processes particular sensory of taste, namely gustatory cortex, thus produces dysgeusia.<sup>8</sup> The sense of taste and smell typically recovers within days to weeks. This distinguishes COVID-19 symptoms from other viral illnesses due to the sudden onset and recovery period. Although these symptoms are widespread, their prevalence varies significantly by region. Research shows that COVID-19 patients in East Asian countries had a 22.4% prevalence of anosmia, while Western countries showed a higher prevalence of 48.4%. Similarly, dysgeusia had a higher prevalence in Western countries at 50.3%, compared to East Asian countries with a 16.2% prevalence. In Western COVID-19 patients, smell and taste deficits had a 54.7% prevalence, while East Asian patients had a 23.4% prevalence. However, these figures may be underestimated as they rely on patients' subjective impressions of sensory deficits, making it challenging to determine the exact prevalence statistics of these symptoms.<sup>9</sup>

COVID-19 is a newly emerging infectious disease, where much about the clinical course remains uncertain, particularly the possible long-term health consequences and the impact of the severity of the disease on them. This neuropsychiatric manifestation may cause post-COVID "disabilities"/sequelae. Hence disturbing the quality of life of the COVID-19 survivors.<sup>10</sup> It is reported that patients with pre-existing comorbidities have a higher fatality rate. These comorbidities include diabetes, respiratory disease, cardiovascular disease, hypertension, and oncological complications. Patients without comorbidities have a lower fatality rate than those with pre-existing comorbidities.<sup>2</sup>

This study aimed to analyze the association between anosmia and dysgeusia with the comorbidities found among patients admitted with COVID-19 in the Emergency Department, Dr. Soetomo General Hospital, Surabaya, from 2020-2021, and their potential associations with the respiratory tract signs and symptoms.

## METHODS

This was a cross-sectional study, with retrospective analysis using secondary data from medical records. This study used a total sampling of all patients admitted to the Emergency Department, Dr. Soetomo General Hospital, Surabaya, with COVID-19 from 1 January 2020 to 30 September 2021. The inclusion criteria included all adult patients (aged over 18 years old) with the primary diagnosis of COVID-19, which had been confirmed by polymerase chain reaction (PCR) test, with complete data of anosmia and dysgeusia, as well as comorbidities and respiratory tract signs and symptoms (coughing or dyspnea) in the medical record during the research period. The signs and symptoms of anosmia, dysgeusia, coughing, and dyspnea were checked by the in-charge medical doctors in the emergency room (ER). The comorbidities, however, were stored in each patient's medical record from the anamnesis of these medical doctors.

The COVID-19 diagnosis of each patient was confirmed by the reverse transcription PCR (RT-PCR) conducted in the ER. The systolic and diastolic blood pressure to diagnose hypertension in this study was measured by the same in-charge medical doctors using the American Heart Association (AHA) classification 2020.<sup>11</sup> The overweight classification in this study was using the Asia-Pacific body mass index (BMI) adjusted by the World Health Organization (WHO) which is 23-24.9.<sup>12</sup> The collected data was processed in the data processing stages which include data coding, data entry, and cleaning by two independent observers. Then, it was grouped according to the research variables and processed using the Statistical Package for the Social Sciences (SPSS) 26.0 (USA) for further analysis using descriptive statistics to determine each variable's frequency. The association between variables was analyzed using the Chi-Square test with a significance level of  $p < 0.05$ . The ethical clearance for this study had been granted by the Ethical Committee of Dr. Soetomo General Hospital, Surabaya (No. 0683/LOE/301.4.2/XI/2021).

## RESULTS

Before the exclusion, the total number of COVID-19 patients admitted to the ER during this period was 415. This study found 158 patients who met the inclusion criteria, 81 males and 77 females. The average age of these patients was  $\pm$  44-59 years old. The numbers and frequency of patients suffering from anosmia, dysgeusia, dyspnea, coughing, and their comorbidities are detailed in Table 1 and Table 2.

**Table 1.** Frequency of respiratory manifestation

Variable (n = 158)	Frequency (%)
Anosmia	128 (81%)
Dysgeusia	15 (9.5%)
Dyspnea	148 (93.7%)
Coughing	156 (98.7%)

It can be seen from Table 1 that 128 patients suffered from anosmia (81%), 15 patients suffered from dysgeusia (9.5%), 148 (93.7%) patients suffered from dyspnea, and 156 (98.7%) patients suffered from coughing.

**Table 2.** Frequency of comorbidities

Comorbidity (n = 158)	Frequency (%)
Hypertension	67 (42%)
Type-2 diabetes mellitus	58 (37%)
Cancer	3 (2%)
Dyslipidaemia	0 (0%)
Overweight	95 (60%)
Cardiovascular disease	6 (4%)
Autoimmune	3 (2%)
Allergy	1 (1%)

The comorbidities observed among COVID-19 patients admitted to Dr. Soetomo General Hospital, Surabaya, could be categorized as overweight, with 95 patients (60%) affected, followed by hypertension with 67 patients (42%), and type-2 diabetes mellitus with 58

patients (37%). Cardiovascular disease was observed in only 6 patients (4%). Both cancer (2%) and autoimmune (2%) were found in 3 patients each. The least observed comorbidity was allergy, with only 1 patient (1%) affected.

**Table 3.** Association between anosmia with respiratory manifestation and each comorbidity

		Anosmia		p-value
		Positive N (%)	Negative N (%)	
Dysgeusia	Positive	15 (9.5%)	0 (0%)	<b>0.049*</b>
	Negative	113 (71.5%)	30 (19%)	
Cough	Positive	128 (81%)	0 (0%)	<b>0.003*</b>
	Negative	28 (17.7%)	2 (1.3%)	
Dyspnea	Positive	125 (79.1%)	3 (1.9%)	<b>0.000*</b>
	Negative	23 (14.6%)	7 (4.4%)	
Comorbidities:	Hypertension	Positive	13 (8.2%)	0.909
	Negative	74 (46.8%)	17 (10.8%)	
Type-2 diabetes mellitus	Positive	46 (29.1%)	12 (7.6%)	0.678
	Negative	82 (51.9%)	18 (11.4%)	
Cancer	Positive	3 (1.9%)	0 (0.0%)	0.397
	Negative	125 (79.1%)	30 (19.0%)	
Overweight	Positive	80 (50.6%)	15 (9.5%)	0.208
	Negative	48 (30.4%)	15 (9.5%)	
Cardiovascular disease	Positive	6 (3.8%)	0 (0.0%)	0.227
	Negative	122 (77.2%)	30 (19.0%)	
Autoimmune	Positive	2 (1.3%)	1 (0.6%)	0.522
	Negative	126 (79.7%)	29 (18.4%)	
Allergy	Positive	1 (0.6%)	0 (0.0%)	0.627
	Negative	127 (80.4%)	30 (19.0%)	

\*Significant (Chi-Square test)

Table 3 shows the association of each comorbidity with anosmia. There were significant associations between anosmia with dysgeusia ( $p = 0.049$ ), cough ( $p = 0.003$ ), and dyspnea ( $p = 0.000$ ).

**Table 4.** Association between dysgeusia with respiratory manifestation and each comorbidity

		Dysgeusia		p-value
		Positive N (%)	Negative N (%)	
Anosmia	Positive	15 (9.5%)	113 (71.5%)	<b>0.049*</b>
	Negative	0 (0.0%)	30 (19%)	
Cough	Positive	15 (9.5%)	141 (89.2%)	0.645
	Negative	0 (0%)	2 (1.3%)	
Dyspnea	Positive	15 (9.5%)	133 (84.2%)	0.290
	Negative	0 (0%)	10 (6.3%)	
Comorbidities:				
Hypertension	Positive	5 (3.2%)	62 (39.2%)	0.455
	Negative	10 (6.3%)	81 (51.3%)	
Type-2 diabetes mellitus	Positive	6 (3.8%)	52 (32.9%)	0.781
	Negative	9 (5.7%)	91 (57.6%)	
Cancer	Positive	0 (0.0%)	3 (1.9%)	0.571
	Negative	15 (9.5%)	140 (88.6%)	
Overweight	Positive	10 (6.3%)	85 (53.8%)	0.587
	Negative	5 (3.2%)	58 (36.7%)	
Cardiovascular disease	Positive	0 (0.0%)	6 (3.8%)	0.419
	Negative	15 (9.5%)	137 (86.7%)	
Autoimmune	Positive	0 (0.0%)	3 (1.9%)	0.571
	Negative	15 (9.5%)	140 (88.6%)	
Allergy	Positive	0 (0.0%)	1 (0.6%)	0.745
	Negative	15 (9.5%)	142 (89.9%)	

\*Significant (Chi-Square test)

## DISCUSSION

Anosmia, the loss of sense of smell, is a common symptom in COVID-19 patients. Meng, *et al.* (2020) showed that COVID-19 patients are more likely to experience olfactory symptoms than other respiratory illnesses.<sup>7</sup> They found that anosmia and dysgeusia often occur together in COVID-19 patients.<sup>7</sup> Dysgeusia, the loss of sense of taste, is also common in COVID-19 patients. Angiotensin-converting-enzyme-2 (ACE2) receptors are found in the epithelium of taste buds and salivary glands. It is hypothesized that human salivary glands may be affected early on by COVID-19 infection, leading to salivary gland dysfunction and dysgeusia as an early symptom in patients with COVID-19.<sup>13</sup> In this study, there were 15 patients (9.5%) who suffered from dysgeusia.

It has been reported that COVID-19 has a high affinity for the sustentacular cells of the olfactory epithelium that express ACE2 and possess substantial capacity for repair and regeneration after damage.<sup>14</sup> It is hypothesized that anosmia is caused by viral entry, infection, and death of sustentacular cells in the olfactory epithelium.<sup>15</sup>

This study found significant associations between anosmia and dysgeusia ( $p = 0.049$ ). A previous study hypothesized that people with anosmia and dysgeusia were more likely to experience other symptoms and higher odds of COVID-19 diagnosis.<sup>16</sup> This study also found significant associations between anosmia and other respiratory tract signs and symptoms, specifically cough ( $p = 0.003$ ) and dyspnea ( $p = 0.000$ ). These were similar to other previous studies that also reported that it was commonly found in COVID-19 patients with

respiratory tract signs and symptoms, although not always accompanied by dysgeusia.<sup>17</sup>

Generally, comorbidity is associated with more complex clinical management, worse health outcomes, and higher healthcare costs.<sup>18</sup> Patients who are susceptible and have underlying health conditions or comorbidities have an increasingly rapid and severe progression, which often leads to death. It has been reported that comorbidities such as obesity, hypertension, and diabetes mellitus are common among patients with COVID-19.<sup>19</sup> Comorbidities were also considered significant predictors of mortality in a previous study, including obesity and heart disease as variables.<sup>20</sup> This study also found that these comorbidities were predominantly found among the patients in the ER, while other comorbidities, including various types of neoplasm, cardiovascular disease, autoimmune disorders, and allergic history, were also recorded.

This study found no associations between either anosmia or dysgeusia with any of each comorbidity. In previous studies, obese patients were found to be at a higher risk for SARS-CoV-2 infection due to their low oro-naso-sensory capacity to taste different modalities. This may mask SARS-CoV-2-induced taste and smell sensory impairment, making them more vulnerable and prone to severe pathological consequences related to respiratory tract infections, and could lead to higher mortality.<sup>21</sup> Another study reported an association between high BMI (overweight/obese) and the loss of olfactory senses in COVID-19 patients. Instead of in obese patients, they proposed that larger adipose tissue with ACE-2 receptors is expressed more than those with lower BMI, resulting in higher susceptibility to the

infection of COVID-19. This association was commonly found in the acute phase, while it was more common among females during the post-acute phase.<sup>22</sup> COVID-19 can attack the epithelial cells in the nasal cavity as the entrance via the ACE-2 receptor of the olfactory bulb-cells. Arguably, the infection can be either forward or backward from the intracranial.<sup>15</sup>

The data of this study were considered subjective to the patients' medical records during their admission to the hospital. Thus, the accuracy of the data may be affected by the self-reports of the patients and the accuracy of the ER medical doctors who took the anamnesis from the patients and/or their families. However, this study is among the first to report on the associations between anosmia and dysgeusia with respiratory signs and symptoms and the comorbidities, although no significant relations were observed with the latter. Additionally, there are few studies discussing the association between anosmia and dysgeusia with any of the comorbidities to understand the pathophysiological mechanisms. Further studies using a prospective design might capture a clearer pattern and association between more variables. They could complete the picture of various signs and symptoms of COVID-19 and how they correlate with each other, which might determine the morbidity and mortality rate.

## CONCLUSION

This study found significant associations between anosmia and dysgeusia with the respiratory tract signs and symptoms but not with recorded comorbidities in COVID-19 patients admitted to the ER. Further analysis should be performed to elucidate the underlying mechanism. Thus, an appropriate treatment plan can be delivered for a better prognosis.

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## Conflict of Interest

The authors declared there is no conflict of interest.

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## Authors' Contributions

Data collection, data analysis, and manuscript writing: JLJS. Conception of idea, data interpretation, manuscript writing, and supervisory of the study: VPK. Data interpretation and supervisory of the study: SS. All

authors contributed and approved the final version of the manuscript.

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