



Risk Factors for Smell and Taste Disorder in Mild and Moderate Covid-19 in Semarang

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ABSTRACT

Background: COVID-19 can cause smell and taste disorders due to Angiotensin Converting Enzyme 2 (ACE2) binding to olfactory tracts and taste buds affected by gender, age, comorbid and COVID-19 severity.

Objective: To analyze age, gender, comorbidities and severity of COVID-19 as risk factors for smell and/or taste disorders in mild and moderate COVID-19 patients in Semarang.

Methods: Observational research using a cross-sectional design. The sample was COVID-19 patients aged >10 years with mild and moderate severity who were not hospitalized and registered at the Semarang City Health Center in June – July 2021. The sampling method used purposive sampling with secondary data. The relationship between variables is analyzed using the Chi-square test or Fisher's exact test and multivariate analysis with logistic regression.

Results: Research on 4337 people, 2.0% had smell disorder and 0.5% had taste disorder. The prevalence of COVID-19 is highest in women, 50.5%, and adults (20-60 years old), 82.5%. The risk factors of gender, age and severity of COVID-19 were not associated with smell and taste disorder in COVID-19 patients ($p < 0.05$). Chronic liver disease is a risk factor for only smell disorders in COVID-19 patients ($p = 0.04$, CI 3.029-786.993, RP 48.828).

Conclusion: Chronic liver disease is a comorbidity that is a risk factor for smell disorders in COVID-19 patients in Semarang. Meanwhile, age, gender and other comorbidities are not risk factors for smell and/or taste disorders.

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1. Introduction

COVID-19 cases reached 1,604,348 people in April 2021, with an average additional case of 5,000 per day and deaths in Indonesia of 43,424 people. In Semarang, the total cases in April 2021 were 34,753 people, with 1,863 deaths.¹⁻³

The COVID-19 pandemic has significantly impacted global health systems and economic stability.³ Early reported symptoms of COVID-19 include fever, cough, shortness of breath, sore throat, runny nose, and conjunctivitis. Other symptoms currently found are chemosensory disorders in the form of smell disorders 68-85% and taste disorders 71-88.8%.⁴⁻⁶ Factors that influence the incidence of smell and taste disorders are age, gender, severity of disease, geographical region and ethnicity.⁷⁻¹⁵ This is related to Angiotensin Converting Enzyme 2 (ACE2), which was identified as a cellular receptor for SARS-CoV-2, which is distributed in the membranes of the oral and nasal cavities as well as angiotensin II inhibitors. Gender, age, comorbidities and disease severity can influence.¹⁶⁻¹⁹ Expression of ACE2 receptors.²⁰⁻²⁵ This study aims to determine age, gender, comorbidities and degree of COVID-19 infection as risk factors for smell and/or taste

disorders in mild and moderate COVID-19 patients in Semarang.

2. Methods

This research is an observational analytical study with the cross-sectional method. The research subjects were mild and moderate COVID-19 patients aged >10 years in Semarang who underwent self-isolation and had complete data. Samples were taken from secondary data on COVID-19 patients recorded at the Semarang City Health Service, and then samples were taken using the purposive sampling method.

The data analyzed were complaints of smell and/or taste disturbances with risk factors assessed, including age, gender, comorbidities, and degree of COVID-19 infection. Data analysis used the Chi-Square and Fisher Exact tests, significant if $p < 0.05$, with a 95% confidence interval. The analysis continued by calculating the prevalence ratio and multivariate analysis with logistic regression.

This research has received approval from the ethics committee of Kariadi Hospital with No.983/EC/KEPK-RSDK/2021 and research permit No.9429/UN7.5.4.2.1/PP/2021 from the Semarang City Health Service.

3. Result

The COVID-19 patients in Semarang during June-July 2021 were 39,272 people, and 4,337 people met the inclusion criteria. According to Table 1, COVID-19 mainly occurred in adults (82.5%), with slightly higher prevalence among females (50.5% vs 49.5%) and mild clinical severity (85.7%).

Table 1. Characteristics of research subjects

Variable	n	%
Gender		
Men	2146	49.5
Women	2191	50.5
Age		
Teenage (11-19 y.o)	343	7.9
Adult (20-60 y.o)	3579	82.5
Elderly (>60 y.o)	415	9.6
COVID-19 degree		
Mild	3716	85.7
Moderate	621	14.3

The characteristics of COVID-19 symptoms (table 2) were smell disorders at 2% and taste disorders at 0.5%; the most common other symptoms are cough (74.4%), runny nose (42.7%) and headache (40.9%).

Table 2. Characteristics of symptoms in patients with mild to moderate degrees of COVID-19.

Variable	n	%	Variable	n	%
Smell disorder			Headache		
Yes	88	2.0	Yes	1776	40.9
No	4249	98.0	No	2561	59.1
Taste disorder			Weakness		
Yes	21	0.5	Yes	1173	27.0
No	4316	99.5	No	3164	73.0
Fever			Myalgia		
Yes	1350	31.1	Yes	89	2.1
No	2987	68.9	No	4248	97.9
Cough			Vomiting		
Yes	3226	74.4	Yes	1065	24.6
No	1111	25.6	No	3272	75.4
Runny nose			Abdominal pain		
Yes	1851	42.7	Yes	27	0.6
No	2486	57.3	No	4310	99.4
Sore throat			diarrhoea		
Yes	1231	28.4	Yes	471	10.9
No	3106	71.6	No	3866	89.1
Dyspnea					
Yes	634	14.6			
No	3703	85.4			

Comorbidities found in research participants were hypertension 65(1.5%), diabetes mellitus 39(0.9%), heart disease 16(0.4%), chronic lung disease 7(0.2%), chronic liver disease 2(0.0004%), malignancy 1 (0.0002%), chronic kidney failure 1 (0.0002%), and neurological disorder 1 (0.0002%). There were no pregnant patients or patients with

immunological compromise among the research participants.

The results of statistical test analysis of gender, age and degree of COVID-19 on smell disorders show no significant relationship between gender, age and degree of COVID-19 and olfactory disorders in COVID-19 patients in Semarang. The results of the statistical test analysis of comorbidity of smell disorders (table 5) show that diabetes mellitus, heart disease, hypertension, malignancy, chronic kidney failure, neurological disorders and chronic lung disease have no relationship with the incidence of smell disorders in COVID-19 patients in Semarang City. There is a relationship between chronic liver disease and smell disorders in COVID-19 patients in Semarang. Pregnancy and immunological disorders were not analyzed.

Table 4. Analysis of gender, age and degree of COVID-19 on olfactory disorders.

Variable	Smell disorder		p	95% CI	RP
	Yes	No			
Gender					
Men	44 (1.0%)	2102 (48.5%)	1.000	0.670-1.558	1.021
Women	44 (1.0%)	2147 (49.5%)			
Age					
< 60 y.o	79 (1.8%)	3481 (80.3%)	0.057	0.258-1.034	0.516
> 60 y.o	9 (0.2%)	768 (17.7%)			
COVID-19 degree					
Mild	79 (1.8%)	3637 (83.9%)	0.340	0.737-2.959	1.477
Moderate	9 (0.2%)	612 (14.1%)			

Chi-square test, significant if $p < 0.05$

Table 5. Analysis of comorbidity of olfactory disorders

Variable	Smell disorder		p	95% CI	RP
	Yes	No			
Diabetes mellitus					
Yes	1 (0.02%)	38 (0.9%)	0.552 [^]	0.170-9.380	1.274
No	87 (2.0%)	4211 (97.1%)			
Heart disease					
Yes	1 (0.02%)	16 (0.4%)	0.720 [^]	1.016-1.025	1.021
No	87 (2.0%)	4233 (97.6%)			
Hypertension					
Yes	1 (0.02%)	64 (1.5%)	0.618 [^]	0.103-5.480	0.752
No	87 (2.0%)	4185 (96.5%)			
Malignancy					
Yes	0 (0.0%)	1 (0.02%)	0.980 [^]	1.016-1.025	1.021
No	88 (2.0%)	4248 (97.9%)			
Chronic kidney failure					
Yes	0 (0.0%)	1 (0.02%)	0.980 [^]	1.016-1.025	1.021
No	88 (2.0%)	4248 (97.9%)			
Chronic liver disease					
Yes	1 (0.02%)	1 (0.02%)	0.040 [^]	3.029-786.993	48.828
No	87 (2.0%)	4248 (97.9%)			
Neurology disorder					
Yes	0 (0.0%)	1 (0.02%)	0.980 [^]	1.016-1.025	1.021
No	88 (2.0%)	4248 (97.9%)			
Chronic lung disease					
Yes	1 (0.02%)	6 (0.1%)	0.134 [^]	0.968-68.236	8.128
No	87 (2.0%)	4243 (97.8%)			

The results of the statistical test analysis of gender, age and degree of COVID-19 on taste disorders (table 6) show that there is no significant relationship between gender, age and degree of COVID-19 and taste disorders in COVID-19 patients in Semarang.

The results of the statistical test analysis of comorbidity of taste disorders (table 7) show that comorbidities of diabetes mellitus, heart disease, hypertension, malignancy, chronic kidney failure, chronic liver disorders, neurological disorders and chronic lung disorders have no association with the incidence of taste

disorders in COVID-19 patients in Semarang. Pregnancy and immunological disorders were not analyzed.

The results of the logistic regression test for smell disorders (table 8) show that chronic liver disorders strongly influence the incidence of olfactory disorders. A logistic regression test was not carried out for taste disorders because it did not meet the requirements.

Table 6. Analysis of gender, age and degree of COVID-19 on taste disorders

Variable	Taste disorder		p	95% CI	RP
	Yes	No			
Gender					
Men	10 (0.2%)	2136 (49.3%)	1.000*	0.393-2.189	0.928
Women	11 (0.3%)	2180 (50.3%)			
Age					
< 60 y.o	17 (0.4%)	3543 (81.7%)	0.781 [^]	0.362-3.214	1.078
> 60 y.o	4 (0.1%)	773 (17.8%)			
COVID-19 Degree					
Mild	16 (0.4%)	3700 (85.3%)	0.172 [^]	0.194-1.460	0.533
Moderat	5 (0.1%)	616 (14.2%)			

Table 7. Analysis of comorbidity of taste disorders

Variable	Taste disorder		<i>p</i>	95% CI	RP
	Yes	No			
Diabetes mellitus					
Yes	39 (0.9%)	0 (0.0%)	0.827 [^]	1.003-1.007	1.005
No	4277 (98.6%)	21 (0.5%)			
Heart disease					
Yes	16 (0.4%)	0 (0.0%)	0.925 [^]	1.003-1.007	1.005
No	4300 (99.1%)	21 (0.5%)			
Hypertension					
Yes	65 (1.5%)	0 (0.0%)	0.728 [^]	1.003-1.007	1.005
No	4251 (98.0%)	21 (0.5%)			
Malignancy					
Yes	1 (0.02%)	0 (0.0%)	0.995 [^]	1.003-1.007	1.005
No	4315 (99.5%)	21 (0.5%)			
Chronic kidney failure					
Yes	1 (0.02%)	0 (0.0%)	0.995 [^]	1.003-1.007	1.005
No	4315 (99.5%)	21 (0.5%)			
Chronic liver disease					
Yes	2 (0.04%)	0 (0.0%)	0.990 [^]	1.003-1.007	1.005
No	4314 (99.5%)	21 (0.5%)			
Neurology disorder					
Yes	1 (0.02%)	0 (0.0%)	0.995 [^]	1.003-1.007	1.005
No	4315 (99.5%)	21 (0.5%)			
Chronic lung disease					
Yes	7 (0.2%)	0 (0.0%)	0.967 [^]	1.003-1.007	1.005
No	4309 (99.4%)	21 (0.5%)			

Table 8. Logistic regression test for smell disorders

Variable	<i>p</i>	95% CI	RP
Age	0.341	0.770-2.133	1.281
Chronic liver disease	0.044 [^]	1.085-290.814	17.761
Chronic lung disease	0.643	0.126-28.636	1.901

4. Discussion

The general characteristics of the research were obtained from secondary data from screening results from the Semarang City Health Service. This research found that the proportion of COVID-19 in Semarang was higher in women, with 50.5%. Research conducted by Iriani et al. found that the number of female patients was greater than that of male patients.²⁷ Other research conducted by Meini et al. and Sharma et al. stated that the incidence of COVID-19 in men is four times higher than in women related to chromosome X, hormones and high-risk behaviours such as smoking and occupational exposure.^{2,12} Women in Semarang are vulnerable to COVID-19 because they are easily anxious and stressed; women are more aware of checking their symptoms, so the data for women is higher than for men.^{2,12,26,27} Chen et al. mention that COVID-19 infects older adults, especially those with comorbidities.²⁸ This research recorded that most patients were adults (20-60 years), 82.5% because this age is a productive age with higher risk behaviour. This study recorded ten comorbidities with the highest prevalence, namely hypertension at 1.5%, diabetes mellitus at 0.9%, and heart disease at 0.4%. Chen et al. 's research stated that the most common comorbidities are cardiovascular, cerebrovascular, and diabetes mellitus. Another study conducted by Sanyaolu et al. stated hypertension, COPD, diabetes mellitus and cardiovascular as significant risk factors for COVID-19.^{2,28,29}

This study found 11 symptoms other than smell and taste disorders, with the highest prevalence being cough 74.4%, runny nose 42.7% and headache 40.9% as the most common symptoms Huang et al. with the most common symptoms being fever, cough and myalgia. In another study by Chen et al., the most common symptoms were fever, cough, and shortness of breath. The degree of COVID-19 in this study was assessed as mild, namely with symptoms other than pneumonia and moderate with clinical signs of pneumonia such as fever, cough, shortness of breath, and rapid breathing who were not treated in hospital. In most studies, the degree was mild (85.7%) because the data was on COVID-19 patients who were self-isolating or not being treated in the hospital.^{28,30}

The results of this study indicate that age is not a risk factor for smell and/or taste disorders in COVID-19 in Semarang by research by Printza et al., which states that there is no relationship between age and olfactory and/or taste disorders in COVID-19 patients.³¹ This differs from other studies, which state that young age is associated with an increased risk of anosmia and ageusia.^{21,25,31}

The results of this study indicate that gender is not a risk factor for smell and/or taste disorders in COVID-19 in Semarang City. This is to previous studies by Ninchritz-Beccera et al. and Printza et al., which stated that gender did not have a significant relationship with impaired smell and taste in COVID-19.^{3,31}

The results of this study indicate that only chronic liver disorders are a risk factor for smell disorders but not for taste disorders. This is by research by Awwad et al., which shows a higher prevalence of chronic liver disease associated with anosmia due to a lack of calories, protein and micronutrients, which results in neurotransmitter disorder.³² Research by Abdelmaksoud et al. reports that zinc deficiency, which is one of the micronutrients in the body, can cause a decrease in the alkaline phosphatase activity of olfactory cells, causing neurological dysfunction.³³ In Derin et al. research, deficiencies in other micronutrients, such as B12, can also disrupt the peripheral nervous system, such as peripheral neuropathy, which results in olfactory disorders. In this study, due to the use of secondary data, the status of olfactory impairment before and after COVID-19 infection is unknown.³⁴ The role of chronic liver impairment and its association with olfactory impairment in COVID-19 patients requires further discussion in future research.³²⁻³⁴

Other comorbidities such as pregnancy, diabetes mellitus, heart disease, hypertension, malignancy, chronic kidney failure, chronic lung disorders and neurological disorders have no significant association with smell and taste disorders in COVID-19 patients in Semarang. Previous research conducted by Ninchritz-Beccera et al. stated that there was no relationship between smell and taste disorders and the presence of comorbidities.³

The results of this study indicate that the degree of COVID-19 is not a risk factor for smell and/or taste disorders. In another study conducted by Izquierdo-Dominguez, he reported mild degrees of smell and taste disorders in COVID-19 patients.²¹

The limitation of this study is the independent completion of the questionnaire by COVID-19 patients who were not hospitalized. There is a possibility of bias in understanding how to fill out the form, especially since the clinical information column does not include smell and taste disorders, so not all patients write down these symptoms. Comorbid diseases are recorded based on subjective patient data and secondary data collected by the Semarang City Health Service so that bias can occur, influencing the analysis results.

5. Conclusion

Surgery optimization depends on the type of non-epithelial ovarian cancer cells, age, and the stage when the diagnosis was first established to be a factor in the incidence of recurrence.

Ethical Approval

The study protocol was approved by the Ethics Committee Faculty of Medicine Diponegoro National Hospital Semarang No. 98/EC/KEPK/FK-RSDK/ 2021

Conflicts of Interest

There is no conflict of interest in this research.

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Author Contributions

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