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Tel. (0341) 569117 ext. 151; Fax. (62) (0341) 564755

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Research Article

- | | | |
|--|---|-------------------|
| <p><i>Tantin Ermawati
Qurratul Aini Wahyu Pratiwi
Zahara Meilawaty
Happy Harmono</i></p> | <p><i>The Potency of Polyphenols Extract of Robusta Coffee Bean (<i>Coffea robusta</i>) on COX-2 Inhibition in Neutrophil Cells</i></p> | <p>205</p> |
| <p><i>Wizni A'dila A'ziza
Christiana Cahyani Prihastuti
Mutia Rochmawati
Alya Ghina Rosyada
Myrna Evana Amanda Putri</i></p> | <p><i>Aloe vera Extract Sheet and Egg Albumin (<i>Gallus domesticus</i>) Reduce the Number of Lymphocytes on Gingival Incision Wound Fracture</i></p> | <p>211</p> |
| <p><i>Fairuz Fairuz
Khory Aurora Berty
Humaryanto Humaryanto</i></p> | <p><i>The Effect of Psychotria malayana Extract on Wound Healing in Male White Rats (<i>Rattus Novergicus</i>) Sprague Dawley Strain</i></p> | <p>217</p> |
| <p><i>Monica Anggriana Salim
Pricilia Gunawan Halim
Ari Yunanto
Pudji Andayani</i></p> | <p><i>The Relationship between APGAR Score and Delivery Mode with Neonatal Sepsis in Ulin Regional Hospital Banjarmasin</i></p> | <p>223</p> |
| <p><i>Oberson Nainggolan
Lia Sasmithae
Ratna Widayati³</i></p> | <p><i>The Effect of Antiretroviral Therapy (ART) Duration on CD4 Counts in Human Immunodeficiency Virus (HIV) Patients in dr. Doris Sylvanus Regional Hospital</i></p> | <p>228</p> |
| <p><i>Udi Heru Nefihancoro
Ricat Hinaywan Malik</i></p> | <p><i>The Profile of Osteogenesis Imperfecta in Dr. Moewardi General Hospital Year 2020-2021: A Retrospective Study</i></p> | <p>233</p> |
| <p><i>Bety Semara Lakshmi
Irena Ujianti
Fahrozi Fahrozi
Ibnu Albantani
Ananda Putri
Nofrizal Nofrizal
Agus Rahmadi
Endin Nokik Stujanna
Zahra Nurushofa
Wawang S Sukarya</i></p> | <p><i>The Correlation between Sleep Quality and Level of Stress among Students in Islamic Boarding School Bogor</i></p> | <p>240</p> |
| <p><i>Bunga Fardah Nahdiyah Achmada
Dian Mutiasari
Abi Bakring Balyas
Lia Sasmithae
Helena Jelita</i></p> | <p><i>The Effect of Personality Types on Blood Pressure in Female Patients Over 17 Years of Age</i></p> | <p>246</p> |
| <p><i>Ari Tri Wanodyo Handayani
Zahreni Hamzah
Dwi Prijatmoko
Dyah Indartin Setyowati
Hosea Roinaldo Ferdinan</i></p> | <p><i>Study of Dysgeusia and Anosmia Frequency and Risk Factors in Pre-Elderly Post-Covid-19</i></p> | <p>251</p> |

Case Report

<i>Yosi Rizal Eka Yudha Rahman</i>	<i>Emphysematous Cystitis with Bladder Mass caused by Colovesical Fistula: A Rare Case Report</i>	258
<i>Taufiq Abdullah Ali Haedar Budi Soenarto</i>	<i>Octreotide Treatment for Hypoglycemic Refractory Case Caused by Sulfonylureas with Impaired Renal Function</i>	262
<i>Muhammad Baihaqy Ibnu Hakim Taufiq Nur Budaya Besut Daryanto</i>	<i>Iatrogenic Penile Amputation Due to Circumcision Clamp in an Eight-Year-Old Boy</i>	265
<i>Prilian Akbaril Satryo Pamungkas Besut Daryanto Andri Kustono</i>	<i>Management of Iatrogenic Ureteral Trauma Post Caesarean Section</i>	269

MEDICAL JOURNAL of BRAWIJAYA

INSTRUCTIONS TO AUTHORS

Medical Journal of Brawijaya (*Jurnal Kedokteran Brawijaya, JKB*) is a six-monthly Periodic Journal (February and August) containing various articles/manuscripts in the forms of research, systematic reviews, case reports, and short communications in the field of medicine focusing on basic medicine, clinical medicine and epidemiology as well as medicine prevention (social medicine). JKB only receives full original text that has never been published in a journal or other publication forms (except for blogs and personal communication), or being sent to another journal at the same time. Had the manuscript been presented in a symposium or particular seminar and only published in abstract form, it will be written in the note. The sequence of names of the authors to the manuscript must be ensured to reflect the contribution of the authors, and all authors must have read and approved the submitted manuscript. Research manuscript sent to JKB must meet the ethical feasibility and research using humans as subjects must have written approval (signed informed consent).

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The writing systematic should meet the following conditions:

Title

Title of the article is written briefly and clearly both in Indonesian and in English, a maximum of 16 words in Indonesian and 14 words in English.

Abstract And Keywords

Abstract is written without subtitles and should be clear and concise both in Indonesian and in English in one paragraph, so it allows readers to understand the important new aspects without having to read the entire article. Abstract of research article contains no more than 250 words, containing background, objectives, method, results, and conclusions while abstract of case report article consists of background, objectives, case summaries, and conclusion. Abstracts of article review and case reports contain no more than 150 words. Keywords are written below abstract by choosing three to six words

that can assist for indexing purposes.

Introduction

This chapter describes the background and review of previous studies, the hypothesis (if any), and the research purposes. The introduction must be able to show the gap and state of the art knowledge that describes the quality, significance, and novelty of ideas.

Method

This chapter (for research article) describes the design and research methods that are clearly and concisely written along with the reference. Method section should explain the design, the population, the selection of subjects or study sample, the data collection methods and instrument used, and the data analysis methods. Method explanations should be clear but brief that allows the reader to replicate. If the methods (including statistical analysis) used are new or have not been widely used, it must be written along with the references.

Results

In the Results section, the authors should present an interpretation on any presentation form of the results both tables and images. Narrative interpretation explains the meaning of data and not a repetition of the contents of images or tables. This chapter (for article research or case reports) may contain a maximum of 6 tables. Each table is given a number and a short title in accordance with the appearance in the text, and each column is given a brief subtitle. Title of tables and figures should be able to describe the contents.

The results of the research or case reports can also be displayed in the form of images, either photographs or graphs, a maximum of 10 pieces. Table and figure insertion must be done efficiently without duplication. One result only needs to be presented in one presentation form either table or figure, and not both.

Images must be made professionally with sharp color prints. Serial number and the title of the image must be written in accordance with the appearance in the text. When an image is obtained from a source/someone or a published illustration, then it must be stated in the description. Tables and figures explanations including meaning of non-standard abbreviations and symbols are written in the caption below the table or picture. Caption is not explaining the meaning of the image. The use of color is restricted only when color differences are necessary and cannot be replaced with black and white.

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made without displaying horizontal and vertical lines. Chart presentation should clearly include the title and the units on the vertical and horizontal axis.

Example

Table 1. Differences of subject characteristic, clinical features, and TNF- α levels

Basic Characteristics	Febrile Seizures (n = 19)	Non-Febrile Seizures (n = 19)	Test Comparison
Gender			0,271
Male	13/19	9/19	
Female	6/19	10/19	
Mean of age, x \pm SD (month)	20,68 \pm 12,69	3547 \pm 23,23	0,022
Mean of seizure rectal temperature, x \pm SD ($^{\circ}$C)	38,78 \pm 0,67	38,81 \pm 0,55	*0,896
Mean of leukocyte, x \pm SD (mg/dl)	9200 \pm 3827	8517 \pm 4257	0,606
Mean of CRP, x \pm SD (mg/dl)	0,98 \pm 1,58	0,69 \pm 0,67	*0,686
Mean of TNF-α levels	8,14 \pm 4,40	4,08 \pm 2,54	0,002

Remarks: *Mann Whitney test

Figure

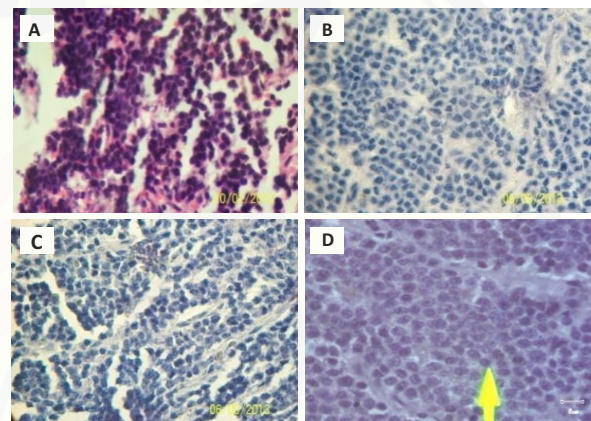


Figure 1. Histopathological biopsy results of the tumor in the left groin

Note:

- Hematoxylin Eosin staining reveals densely scattered malignant cells with uniform round shape
- CD20 immunohistochemical staining reveals negative Cd20
- LCA immunohistochemical staining reveals negative LCA
- Cytokeratin immunohistochemistry staining reveals negative cytokeratin

Discussion

This chapter discusses the results and highlights new discoveries, whether suit, reinforce, or oppose the previous discoveries, theories, and opinions. Discussion chapter also explains why the research obtains such results matching the findings, the mechanism of the results, and the reasons on the differences and similarities with previous research.

The conclusion is expressed in the last paragraph (discussion) that contains sentences stating the relationship among the variables studied (the relationship between independent variables and the dependent variable) and is narrated in a single paragraph, without bullet points, brief, concise and clear, and does not contain suggestions.

Acknowledgements

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Bibliography

The number of references for the research articles and case reports is at least 10 pieces while for article review is minimum 20 pieces. References are written based on JKB-Vancouver system where the authors are numbered in the text in order of their appearance instead of alphabetically. Cited references are maximum the last ten years. At least 80% of the references are the primary references (research results) from recent decades, except for standardized information and no new referrals. Papers that have been submitted for publication but not yet published can be used as references and stated "in press". Referral on personal communications must be avoided wherever possible except for information that is not obtainable from public sources by mentioning the name of the source and date of the communication. Non-scientific sources such as blogs are not allowed. Names of all the authors are included if the total is not more than six people by writing the surname and followed with the first letter of the given name. When the authors are more than six people, only the three first authors are listed, and followed by "et al.". The title is written in accordance with the original title. The journal's name is written completely as its official name, followed by the year, volume (number), and the page of the journal article.

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Journal

Boddie AM, Dedlow ES, Nakashi JA, Opalko FJ, and Kouwell GP. *Folate Absorption In Women With A History Of Neural Tube Defect-Affected Pregnancy*. The American Journal of Clinical Nutrition. 2000; 72: 154-158.

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Rhoades R and Pflanzer R. *Human Physiology*. 3rd edition. Orlando, Florida: Saunders College Publishing; 1996; p. 137-350.

Chapters in books

Katzung BG dan Chatterjee K. *Vasodilator dan Pengobatan Angina Pektoris*. Di dalam: B.G. Katzung (Ed). *Farmakologi Dasar dan Klinik* edisi 6. Jakarta: EGC; 1998: p. 184-201.

Proceedings

Abdurrahman. *Pendekatan Multidisiplin pada Penanganan Patologi Muskuloskeletal*. Proceeding Scientific Meeting & Workshop of Indonesian Musculoskeletal Pathology. Surabaya, March 22-23, 2003; p. 1-8.

Thesis/Thesis/Dissertation

Hoving EW. *Frontoethmoidal Encephalocele, a Study of Their Pathogenesis*. [Disertasi]. Rijk Universiteit, Groningen. 1993.

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Bina A. *Propolis: Sang Penyembuh Luar Biasa*. (Online) 2008. di <http://www.binaapiari.com/tips-penyembuhan/propolis-sang-penyembuh-luar-biasa/> [diakses tanggal 11 September 2014].

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Editorial Secretariat of Medical Journal of Brawijaya
Medical Faculty University of Brawijaya
Jl. Veteran, Malang, Tel. (0341) 569117, 567192, 580993
ext. 151; Fax. (0341) 564755
E-mail : jkb@ub.ac.id
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Research Article

Study of Dysgeusia and Anosmia Frequency and Risk Factors in Pre-Elderly Post-Covid-19

Kajian Frekuensi dan Faktor Resiko Dysgeusia serta Anosmia Pada Pralansia Post Covid-19

Ari Tri Wanodyo Handayani¹, Zahreni Hamzah², Dwi Prijatmoko³, Dyah Indartin Setyowati⁴, Hosea Roinaldo Ferdinan⁵

¹Department of Public Dental Health Faculty of Dentistry Universitas Jember Jember

²Department of Biomedical Dentistry Faculty of Dentistry Universitas Jember Jember

³Department of Orthodontic Faculty of Dentistry Universitas Jember Jember

⁴Department of Oral Medicine Faculty of Dentistry Universitas Jember Jember

⁵Faculty of Dentistry Universitas Jember Jember

ABSTRAK

Covid-19 is a respiratory obstruction caused by infection with SARS-CoV-2. The appearance of dysgeusia and anosmia can be a sign that someone has contracted this virus. This study aims to review the frequency and risk factors that cause dysgeusia and anosmia in pre-elderly post-Covid-19. This type of research is descriptive observational with a cross-sectional approach. In this study, only 5.15% of respondents experienced anosmia, 10.31% of dysgeusia alone, and 28.86% of dysgeusia accompanied by anosmia. Dysgeusia and anosmia can be found in every vaccination status. Respondents with ≥ 1 dominant comorbid were found in respondents who experienced dysgeusia accompanied by anosmia. Symptoms of fever, cough, rhinorrhea, and pneumonia are common in dysgeusia and anosmia disorders. The time of appearance of the disturbance ranges from 1-7 days, with the duration of the disruption 1-14 days. Symptoms of dysgeusia accompanied by anosmia in the pre-elderly post-Covid-19 show a higher frequency than dysgeusia alone and anosmia alone. In pre-elderly, men were found to be more at risk than women. Several risk factors, including the aging process, co-morbidities, smoking habits, and vaccination status, support the emergence of these symptoms.

Keywords: Aging, anosmia, Covid-19, dysgeusia, pre-elderly

ABSTRAK

COVID-19 adalah penyakit respiratori yang disebabkan oleh infeksi SARS-CoV-2. Kemunculan dysgeusia dan anosmia dapat dijadikan tanda seseorang terinfeksi virus ini. Penelitian ini bertujuan untuk mengkaji frekuensi dan faktor-faktor yang menyebabkan dysgeusia dan anosmia pada pralansia post Covid-19. Jenis penelitian ini adalah observasional deskriptif dengan pendekatan *cross-sectional*. Pada penelitian ini didapatkan bahwa responden yang mengalami anosmia saja sebanyak 5,15%, dysgeusia saja sebanyak 10,31%, dan dysgeusia disertai dengan anosmia sebanyak 28,86%. Dysgeusia dan anosmia dapat ditemukan pada setiap status vaksinasi. Responden yang memiliki >1 komorbid dominan ditemukan pada responden yang mengalami dysgeusia disertai anosmia. Gejala demam, batuk, rhinorea, dan pneumonia umum ditemukan pada gangguan dysgeusia dan anosmia. Waktu kemunculan gangguan berkisar antara 1-7 hari dengan durasi gangguan 1-14 hari. Gejala dysgeusia disertai anosmia pada pralansia post Covid-19 menunjukkan frekuensi yang lebih tinggi daripada dysgeusia saja dan anosmia saja. Pada pralansia laki-laki ditemukan lebih berisiko daripada perempuan. Kemunculan gejala ini didukung oleh beberapa faktor, antara lain: proses penuaan, penyakit penyerta, kebiasaan merokok, dan status vaksinasi.

Kata Kunci: Anosmia, Covid-19, dysgeusia, pralansia, penuaan

Correspondence: Ari Tri Wanodyo Handayani. Department of Public Dental Health Faculty of Dentistry Universitas Jember, Jl. Kalimantan No. 37 Tel. +62331330224 Email: aritri.fkg@unej.ac.id

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INTRODUCTION

Coronavirus Infection Diseases-2019 (Covid-19) is a respiratory disease that was first reported to have appeared in Wuhan, Hubei Province, China on December 8, 2019 (1,2). Initially, this disease was called the 2019 novel coronavirus (2019-nCoV). However, on February 11, 2020, the World Health Organization (WHO) changed the term 2019-nCoV to COVID-19. The cause of this disease is Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection. On March 12, 2020, WHO officially announced that Covid-19 had the potential to become a pandemic (3).

According to *Kamus Besar Bahasa Indonesia* (KBBI), the official dictionary of the Indonesian language, a pandemic is an epidemic that spreads simultaneously everywhere, covering a wide geographical area. Based on Covid-19 data on 26-31 October 2021, Indonesia has experienced increases and decreases in cases. It is related to the transmission process. SARS-CoV-2, as the cause of Covid-19, has a simple transmission process. This transmission can occur directly or indirectly through the binding of Angiotensin Converting Enzyme 2 (ACE-2) as the SARS-CoV-2 receptor (4). During its development, the Delta variant appeared due to a gene mutation in SARS-CoV-2. According to WHO, the Delta variant is twice as infectious as the Covid-19 virus that appeared for the first time. It is around 50% more virulent than the other variants that have been detected (5).

People infected with SARS-CoV-2 will display symptoms such as fever, dry cough, tachypnea, shortness of breath, chest pain, vomiting, nausea, sore throat, sneezing, anosmia, and dysgeusia (4). Susanto also concluded that symptoms often found in Covid-19 patients are fever, dyspnea, sore throat, runny nose, and anosmia. Anosmia and dysgeusia are symptoms experienced by most Covid-19 patients, among other symptoms (6).

Anosmia is a term used to describe a person's condition when they experience a decreased function and even lose their sense of smell. Anosmia is classified as a chemosensory dysfunction involving the sense of smell. The mechanism that causes anosmia induced by Covid-19 begins with the binding of SARS-CoV-2 to the ACE-2 receptor in the nasal mucosa. Then the virus penetrates the olfactory neuroepithelial cells and replicates so that the cells will respond to significant damage to these cells (7).

Another symptom that is often found in Covid-19 patients is dysgeusia. Dysgeusia is a term used to describe a person's condition when the sense of taste has decreased function; for example, it loses the ability to detect various sweet, salty, sour, bitter, and umami tastes. In addition, some patients complain of a persistent metallic taste (8). Dysgeusia can also be interpreted as a term to identify all types of taste sensation disturbances, both qualitative and quantitative. Quantitatively, it is a distorted taste sensation, while qualitatively, it is a decrease in the sharpness of the sense of taste. The mechanism that causes dysgeusia induced by Covid-19 is the invasion of SARS-CoV-2 to the taste buds (neurotropism) which causes neurological damage (9).

According to several studies, the onset of symptoms of dysgeusia and anosmia in Covid-19 patients is 7-14 days, with a duration of approximately eight days (10,11).

Factors that influence the onset of dysgeusia and anosmia are thought to involve age, gender, and comorbidities owned by the patient. Not all Covid-19 patients experience dysgeusia accompanied by anosmia. A study by Patel *et al.*, found that 2% of Covid-19 patients experienced anosmia alone, 6% experienced dysgeusia alone, and 55% experienced dysgeusia accompanied by anosmia (11)

Jember Regency is one of the regencies in East Java, to the east of Lumajang Regency and the west of Banyuwangi Regency. Jember Regency consists of 31 districts, one of which is Summersari District. Based on the 2020 population census, Summersari District ranks eighth with the most population of the 31 other districts, namely 107,631 people with a population density of 2,906 people/km². Based on population census data for 2010 and 2020, the number of pre-elderly residents in the Summersari District has increased. In 2010, the number of pre-elderly residents in Summersari District, Jember Regency, was 18,709 people; in 2020, it increased to 22,179 people (12). An increase in the pre-elderly population can indirectly affect the number of Covid-19 cases.

Covid-19 can occur in all age groups. However, the pre-elderly group (45-59 years) needs attention because the positive prevalence of Covid-19 in this age group is relatively high compared to the age group of the elderly, children, and toddlers. One of the reasons for the high risk in the pre-elderly age group is physiological changes along with the aging process (13). Aging factors are known to cause increased expression of ACE-2 in the nasal and oral mucosa, positively correlated with the prevalence of dysgeusia and anosmia in the elderly. In addition, risk factors in the form of co-morbidities and drugs influence the body's response to infection (14,15).

Apart from the aging factor, the pre-elderly is an age group with better cognitive abilities than the older age group. With age, a person will experience a decrease in memory. The pre-elderly group generally experienced mild memory loss compared to the elderly group. Research reveals that the prevalence of memory loss in the pre-elderly group is 41%. This figure is still lower than the older age group, which is 52% (16). Thus, this research was conducted in the pre-elderly group in the hope that they would still be able to remember events when they were confirmed to have Covid-19. Therefore, based on the description above, it is necessary to study the frequency and risk factors of dysgeusia and anosmia in the post-Covid-19 elderly in Summersari District, Jember Regency.

METHOD

Type of Research

This type of research is descriptive observational with a cross-sectional approach. This research was conducted to observe the characteristics of dysgeusia and anosmia and to study the relationship between the risk factors that influenced them in pre-elderly post-Covid-19 in Summersari District, Jember Regency. The instrument used was a questionnaire.

Population

The population in this study was people aged 45-59 years who had been confirmed positive for Covid-19 from July to December 2021. The population was chosen from Summersari District, Jember Regency.

Research Subject

The subject-taking technique in this study used proportional cluster sampling. The cluster sampling technique was used for large and extensive populations. This study used cluster sampling based on the sub-districts with the highest number of Covid-19 patients in July-December 2021 in the Jember Regency.

Number of Research Subjects

The subject size required for this study used the proportion estimation formula from Lameshow (1997). With a 95% confidence level with a 10% degree of deviation, the required research subjects were 97 people. The selection of research subjects in the Sumbersari sub-district was carried out by determining the three selected sub-districts through proportional cluster sampling. The following is the calculation of determining the number of research subjects.

1. The data provided by the Sumbersari and Gladak Pakem Health Centers are 332 elderly, consisting of 7 sub-districts, with the following details.

Sub-districts	Number of Cases
Antirogo	13
Karangrejo	48
Sumbersari	140
Tegalgede	10
Wirolegi	9
Kebonsari	90
Kranjingan	22
Total	332

2. The three sub-districts with the highest number of cases, Karangrejo Sub-District, Sumbersari Sub-District, and Kebonsari Sub-District, were selected with the following details.

Sub-district	Number of Cases
Karangrejo	48
Sumbersari	140
Kebonsari	90

3. Based on the Lemeshow formula (1997), the number of respondents needed is 97 respondents. The proportional distribution in the three selected villages obtained the following calculations:

$$\begin{aligned} \text{Karangrejo Sub-district} &: \frac{48}{48+140+90} \times 97 \approx 17 \text{ respondents.} \\ \text{Sumbersari Sub-district} &: \frac{140}{48+140+90} \times 97 \approx 48 \text{ respondents.} \\ \text{Kebonsari Sub-district} &: \frac{90}{48+140+90} \times 97 \approx 32 \text{ respondents.} \end{aligned}$$

RESULTS

This research was completed on October 28, 2022, with 97 pre-elderly respondents (45-59 years) post-Covid-19 in Sumbersari District. The research locations were divided into three sub-districts, namely Kebonsari Sub-district, with 32 respondents; Sumbersari Sub-district, with 48 respondents; and Karangrejo Sub-district, with 17 respondents. Male respondents were 20 in Kebonsari Sub-district, 27 in Sumbesari Sub-district, and 9 in Karangrejo Sub-district. Meanwhile, the number of female respondents in the Kebonsari Sub-district was 12, in Sumbersari Sub-district 21, and Karangrejo Sub-district 8. Thus, the total number of male respondents was 56 and female respondents 41.

Table 1. shows that dysgeusia accompanied by anosmia has a higher prevalence than dysgeusia alone and anosmia alone. Based on gender, women experience relatively less anosmia and dysgeusia than men. It can be concluded that male respondents who experience dysgeusia accompanied by anosmia are more common than female respondents. This situation may be influenced by comorbidities and risk factors (smoking).

Table 1. Distribution of dysgeusia and anosmia in post-Covid-19 elderly in Sumbersari district, Jember Regency

Type of Symptoms	Gender				Total	
	M	%	F	%	n	%
Anosmia without dysgeusia	3	3.09	2	2.06	5	5.15
Dysgeusia without anosmia	5	5.15	5	5.15	10	10.31
Dysgeusia accompanied by anosmia	18	18.55	10	10.31	28	28.86
Other conditions*	30	30.93	24	24.74	54	55.67
Total	56	57.73	41	42.26	97	100

Note: (*) asymptomatic, hyposmia, and ageusia

Table 2. Distribution of dysgeusia and anosmia disorders along with disorder characteristics

Characteristic	Type of Symptoms											
	Anosmia without Dysgeusia				Dysgeusia without Anosmia				Dysgeusia accompanied by anosmia			
	Gender		Total	%*	Gender		Total	%*	Gender		Total	%*
	M	F	n	%*	M	F	n	%*	M	F	n	%*
Vaccination Status												
Not yet Vaccine	0	0	0	0	0	0	0	0	1	0	1	1.0
1 st dose of vaccine	2	1	3	3.09	1	2	3	3.09	11	7	18	18.6
2 nd dose of vaccine	1	1	2	2.06	4	3	7	7.22	6	3	9	9.3
Risk Factor for Exposure to COVID-19												
Don't know	1	0	1	1.03	3	2	5	5.15	13	5	18	18.6
Have had contact with a positive case of COVID-19	1	1	2	2.06	2	2	4	4.12	2	2	4	4.1
Workplace	1	1	2	2.06	0	0	0	0	0	2	2	2.1

Table 2. Distribution of dysgeusia and anosmia disorders along with disorder characteristics (Cont.)

Aspects	Type of Symptoms											
	Anosmia without Dysgeusia				Dysgeusia without Anosmia				Dysgeusia accompanied by anosmia			
	Gender		Total		Gender		Total		Gender		Total	
	M	F	n	%*	M	F	n	%*	M	F	n	%*
Risk Factor for Exposure to COVID-19												
Living together	0	0	0	0	0	1	1	1.03	0	0	0	0
Traveling to areas prone to COVID-19	0	0	0	0	0	0	0	0	3	1	4	4.1
Number of Concomitant Diseases and Smoking												
0 disease + no smoking	1	1	2	2.06	0	1	1	1.03	0	0	0	0
0 disease + smoking	0	0	0	0	0	0	0	0	12	5	17	17.5
1 disease + no smoking	0	0	0	0	0	0	0	0	0	0	0	0
1 disease + smoking	2	0	2	2.06	4	2	6	6.19	5	3	8	8.2
2 diseases + no smoking	0	1	1	1.03	1	2	3	3.09	0	0	0	0
2 diseases + smoking	0	0	0	0	0	0	0	0	1	2	3	3.1
Symptoms												
No symptoms	0	0	0	0	1	0	1	1.03	2	0	2	2.1
Fever	2	2	4	4.12	3	4	7	7.22	15	10	25	25.8
Cough	2	2	4	4.12	3	1	4	4.12	10	8	18	18.6
Rhinorrhea	2	1	3	3.09	2	1	3	3.09	14	5	19	19.6
Bad taste	2	0	2	2.06	1	1	2	2.06	12	7	19	19.6
Chills	1	1	2	2.06	1	3	4	4.12	8	5	13	13.4
Nasal congestion	1	1	2	2.06	0	0	0	0	7	6	13	13.4
Headache	1	0	1	1.03	0	1	1	1.03	11	7	18	18.6
Pneumonia	0	0	0	0	3	3	6	6.19	1	2	3	3.1
Out of breath	0	0	0	0	0	0	0	0	1	1	2	2.1
Digestive problems	0	0	0	0	0	0	0	0	0	1	1	1.0
Time of Appearance												
1-7 day(s)	3	2	5	5.15	5	5	10	10.31	18	9	27	27.8
8-14 days	0	0	0	0	0	0	0	0	0	1	1	1.0
14 days	0	0	0	0	0	0	0	0	0	0	0	0
Duration of Disorder												
1-7 day(s)	3	1	4	4.12	5	3	8	8.25	11	7	18	18.6
8-14 days	0	1	1	1.03	0	2	2	2.06	7	3	10	10.3
14 days	0	0	0	0	0	0	0	0	0	0	0	0
Method of Recovery												
Disappears by itself	2	0	2	2.06	5	5	10	10.31	15	6	21	21.6
Along with confirmed negative	0	2	2	2.06	0	0	0	0	2	3	5	5.2
Taste/aromatherapy	1	0	1	1.03	0	0	0	0	0	1	1	1.0
Medication	0	0	0	0	0	0	0	0	1	0	1	1.0
Health Condition when Experiencing Disorder												
Getting better	2	1	3	3.09	1	4	5	5.15	17	7	24	24.7
Worsened	1	1	2	2.06	4	1	5	5.15	1	3	4	4.1
Condition of Indra Post Confirmed Negative.												
Back to normal	2	3	5	5.15	5	5	10	10.31	18	10	28	28.9
Not back as before	0	0	0	0	0	0	0	0	0	0	0	0

Note: (*) percentage of 97 respondents

Table 2 shows that in the first and second doses of vaccination status, dysgeusia accompanied by anosmia is the most common disorder. In this type of disorder, the number of respondents who had administered the first dose of the vaccine was twice that of the second. In the first dose of vaccination status, dysgeusia alone and anosmia alone have the same amount. It can be concluded that at each respondent's vaccination status, one can find dysgeusia and anosmia.

In the section on risk factors for exposure to Covid-19, anosmia without dysgeusia occurs mainly in respondents who have had positive confirmed cases of Covid-19 and at work. Whereas in dysgeusia disorder without anosmia, respondents said they did not know. In dysgeusia disorder accompanied by anosmia, respondents stated that they did not know and partly because they had been in contact with positive cases of Covid-19. It can be concluded that

dysgeusia disorder commonly occurs due to not knowing the risk factors for exposure to Covid-19. At the same time, anosmia is expected due to having been in contact with a positive case of Covid-19.

In this study, it was also found that more experienced respondents experienced only anosmia and only dysgeusia with one comorbidity accompanied by smoking risk factors. Respondents who experienced dysgeusia accompanied by dominant anosmia were experienced respondents who did not have comorbidities but had smoking habits. Respondents with comorbidities of at least one disease are generally found in respondents who experience dysgeusia accompanied by anosmia. Based on gender, male respondents tend to be at risk of experiencing dysgeusia and anosmia compared to women. It is because men with comorbidities accompanied by smoking are more common than female respondents. Respondents

who are infected with this virus will certainly display several symptoms.

Symptoms of fever, cough, runny nose, and chills were commonly experienced by both male and female respondents. Nasal congestion and rhinorrhea are common symptoms in respondents who experience anosmia, while respondents who experience pneumonia generally experience dysgeusia. Based on the number of symptoms experienced, respondents who experienced dysgeusia accompanied by anosmia had the most symptoms compared to those who experienced anosmia alone or dysgeusia alone. It can be concluded that fever, cough, rhinorrhea, and pneumonia are other symptoms in people with dysgeusia and anosmia.

Based on Table 2, the time when dysgeusia and anosmia appear is mostly 1-7 days, and only a tiny proportion of dysgeusia disorders accompanied by anosmia appear 8-14 days after testing positive for Covid-19. The time when dysgeusia and anosmia due to SARS-CoV-2 appear generally occurs 1-7 days after testing positive for Covid-19. The duration of dysgeusia and anosmia is mostly 1-7 days. However, some respondents who experienced dysgeusia disorder accompanied by anosmia occurred for 8-14 days. Based on gender, male respondents who experience dysgeusia accompanied by anosmia tend to last longer than women. It can be concluded that the duration of dysgeusia accompanied by anosmia has a longer risk than anosmia alone or dysgeusia alone, especially for male respondents.

Most of the disturbances to the sense of smell and taste experienced by respondents can disappear by themselves. It was also found that the health condition of the respondents at the time of experiencing the disorder was mainly improving. When the pre-elderly was confirmed negative, the sense of smell and taste condition returned to normal.

DISCUSSION

Dysgeusia and anosmia are commonly found in people infected with SARS-CoV-2, including the elderly. This study found that dysgeusia accompanied by anosmia had the highest prevalence when compared with anosmia alone and dysgeusia alone. It is in line with research conducted by Patel *et al.*, which concluded that dysgeusia accompanied by anosmia is higher than people who experience anosmia alone or dysgeusia alone (11). This is because in pre-elderly, there is an increase in ACE-2 expression on the oral and nasal mucosa, so the elderly will be at higher risk of experiencing dysgeusia accompanied by anosmia. Research on ACE-2 expression levels and age has been conducted by Syed *et al.*, and Verity *et al.*, who stated that the expression level of ACE-2 in oral and nasal epithelial cells is known to increase with age (13,17)

In the second place, the most common prevalence is dysgeusia alone. This is presumably because the increased expression of ACE-2 in the oral mucosa is higher than that in the nasal mucosa. ACE-2 expression is known to increase on the tongue due to aging factors, so pre-elderly people are at a higher risk of experiencing dysgeusia (15). In addition, inflammation causes a decrease in the ability of inflammatory cells to destroy microbes and their products, resulting in low-grade chronic inflammation. Furthermore, it causes the oral mucosa to become thinner

lose elasticity, and stipple and decreases keratin and laminin so that the mucosa increases its sensitivity to various pathological conditions. This condition causes the virus to enter the body quickly (18)

The binding of SARS-CoV-2 to the increased ACE-2 receptor in the oral cavity can induce significant damage to the taste buds and interference with sialic acid. Taste bud damage occurs due to the high production of pro-inflammatory cytokines such as TNF- α , IFN- γ , and IL-6, which can inhibit basal cell proliferation in regenerating taste buds. Sialic acid is a component in normal saliva that plays a role in taste processing (19,20). SARS-CoV-2 binds to sialic acid receptors and can reduce taste stimulation and perception (21). In addition, the salivary glands also experience disturbances due to inflammation and invasion of SARS-CoV-2. As a result, the salivary glands experience atrophy of the acinar tissue, impaired proliferation of the duct elements of the gland, and degenerative changes in the minor and major salivary glands. This disorder is thought to cause an imbalance in the composition of saliva and reduced salivary flow, which results in dysgeusia (18,22).

The prevalence of anosmia alone is the smallest when compared to that of the others. The small prevalence of anosmia alone illustrates that an increase in ACE-2 in the nasal mucosa alone is rare in pre-elderly post-Covid-19 at that time. Based on several studies, anosmia in the elderly can occur due to increased expression of ACE-2 in SuC cells due to increasing age (13,23). This condition is also supported by Demanelis *et al.*, who state that in the aging process, telomere shortening occurs, which accumulates from various damage to body tissues, resulting in increased ACE-2 expression in the nasal mucosa (24). Increased ACE-2 expression in the nasal mucosa alone might explain why older individuals are more susceptible to SARS-CoV-2 infection, so they are at risk of experiencing anosmia alone (14).

Telomere shortening is examined due to the presence of Reactive Oxygen Species (ROS) in the body, which is not in balance with the antioxidant capacity of tissues to form oxidative stress or free radicals. Free radicals are chemical species that do not have a partner in their outer orbital, resulting in an unstable configuration and energy being released through reactions with the surrounding molecules. Free radicals are responsible for age-related cell and tissue damage that triggers DNA damage in mitochondria, dysfunction, and increases cell apoptosis. An increase in telomere losses due to an imbalance in ROS production is one of the factors in the aging process (25)

Based on gender, males pre-elderly relatively more experience anosmia and dysgeusia than women. This is presumably because men are at greater risk of exposure to SARS-CoV-2 due to activities that involve many people than women. In line with epidemiological research by Schubert *et al.* (2012), men have a higher risk than women experiencing smell disorders (26). In this study, the risk factors for exposure to SARS-CoV-2 were the most unknown with certainty so that respondents can be exposed to SARS-CoV-2 indirectly through infectious objects. According to Lotfi *et al.*, indirect transmission can occur through objects contaminated with SARS-CoV-2. These objects are touched by hands and come into direct contact with the oral and nasal mucosa, thus providing a pathway for the virus to penetrate the body (4)

In each pre-elderly vaccination status, symptoms of dysgeusia and anosmia can be found. This is because

vaccination does not make a person free from COVID-19. Hence, the symptoms of anosmia and dysgeusia still have a chance to occur in the elderly even though the pre-elderly has received the vaccine. This happened because the Covid-19 variant at that time was considered to be more infectious (5). Therefore, people were encouraged to receive the first dose of the vaccine immediately but could continue with the second dose after some time.

Respondents who have many comorbidities are known to be at greater risk of experiencing disturbances in their sense of taste and smell. The number of comorbidities suffered by pre-elderly people is, of course, related to the number of drugs used to treat the disease. This study's results align with research conducted by Guan *et al.*, and Syed *et al.*, which stated that several drugs cause pre-elderly people to be at risk of experiencing anosmia and dysgeusia. Several drugs can cause dysgeusia and anosmia, such as the antihistamine group in older people with allergies and ACE inhibitors and metoprolol in older people with hypertension (17,27)

In addition to comorbidities, smoking is a risk factor commonly found in males pre-elderly. This finding is in line with the 2018 Riskesdas, which stated that the prevalence of male smokers is higher than that of women (28). This shows that male respondents tend to be at higher risk of interference when compared to women. Smoking habits are known to induce degeneration of the neuroepithelium of the sense of smell and taste buds due to increased expression of ACE-2 (29–32). Thus, damage Nasal neuroepithelium has the potential to cause anosmia, while damage to the taste buds has the potential to cause dysgeusia.

Most of the responders infected with SARS-CoV-2 will develop symptoms. Nasal congestion and rhinorrhea are generally experienced by respondents who experience anosmia (33). This occurs because the nasal obstruction induced by SARS-CoV-2 can interfere with airflow that carries odorous stimuli to the olfactory neuroepithelium so that it manifests as anosmia. Pneumonia was generally found in respondents who experienced dysgeusia. This is presumably due to the use of various drugs to relieve pneumonia due to SARS-CoV-2 infection, such as

remdesivir and ritonavir (34). Thus, this condition causes a decrease in the perception of taste in food and drinks due to a decrease in the threshold of taste buds which can manifest as dysgeusia (22). Respondents who experience dysgeusia accompanied by anosmia are known to experience a combination of the two symptoms above.

Most of the time for dysgeusia and anosmia to appear is 1-7 days, and only a tiny proportion of dysgeusia disorders accompanied by anosmia appear 8-14 days after testing positive for Covid-19. In line with studies by Levinson *et al.*, and Patel *et al.*, the onset of symptoms of anosmia and dysgeusia in Covid-19 patients is 7-14 days (10,11). This time describes the time the olfactory and taste bud neuroepithelial cells must be entirely damaged by the massive SARS-CoV-2 infection, which manifests as dysgeusia and anosmia.

Dysgeusia and anosmia due to SARS-CoV-2 infection can last several days until they can eventually recover. The duration of dysgeusia accompanied by anosmia is known to be longer when compared to anosmia alone or dysgeusia alone. Research states that the severity of the invasion of the SARS-CoV-2 virus in several organs can affect the recovery time for the function of these organs. This occurs due to more extensive inflammation (9). Male respondents who experience dysgeusia accompanied by anosmia tend to last longer than women. This is likely due to smoking risk factors, and co-morbidities found more in male respondents than in female respondents.

In this study, it can be concluded that the symptoms of dysgeusia accompanied by anosmia in pre-elderly post-Covid-19 in Sumpalsari District, Jember Regency, show a higher frequency than dysgeusia alone and anosmia alone. Male pre-elderly is known to be more at risk than female pre-elderly. Several risk factors, including the aging process, co-morbidities, smoking habits, and vaccination status, support the emergence of these symptoms.

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Author's name:

Dr. drg. Ari Tri Wanodyo Handayani, M. Kes., FISDPH.FISPD
Dr. drg. Zahreni Hamzah, MS
Prof. drg. Dwi Prijatmoko, S.H., Ph.D
Drg. Dyah Indartin Setyowati, M. Kes
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4. Our manuscript does not contain statements that are unlawful, defamatory or otherwise, and do not contain material that violates the personal rights or property rights of any other person or entity.

I made this statement honestly and responsibly.

Jember, February , 2023

Applicant



(Dr. drg. Ari Tri Wanodyo Handayani, M.Kes., FISDPH.FISPD)

NIP: 197308182001122001

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Lampiran 1. *Informed Consent*

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Menyatakan bersedia menjadi subjek penelitian dari:

Nama : Ari Tri Wanodyo Handayani
NIP : 197308182001122001
Fakultas : Kedokteran Gigi Universitas Jember
Alamat : Jalan Tidar Perumahan Greenland GL-15 Jember


Dengan judul penelitian “Kajian Frekuensi Anosmia dan Dysgeusia Pada Pralansia Post COVID-19 di Kecamatan Sumbersari, Kabupaten Jember” dengan sebenar- benarnya tanpa ada suatu paksaan dari pihak manapun.

Jember, 2022

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