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ORIGINAL ARTICLE

THE ROLE OF OLFACTORY FUNCTION AND MULTIMORBIDITY IN COGNITIVE IMPAIRMENT

Peranan Fungsi Penghidu dan Multimorbiditas Terhadap Fungsi Kognitif

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ABSTRACT

Background: As the population ages, the issue of cognitive impairment is becoming increasingly worrisome, especially with the rise in conditions like multiple chronic diseases and loss of smell among the elderly. **Purpose:** The goal of this research is to explore how multiple chronic diseases, sense of smell, and cognitive impairment are linked among the senior population. **Methods:** This study involved 128 individuals at a senior community in Jakarta with an average age of 68.34 years. The presence of multiple chronic diseases was determined by looking for highest prevalence of disease pairs, and the sense of smell was tested with an 8-smell test. Cognitive function was measured with the CERAD questionnaire, with a score below 52 indicating cognitive impairment. The analysis included Chi-square tests at a 95% confidence level. **Results:** The findings suggest a clear link between lower levels of education and cognitive impairment (p=0.018; OR=3.214), as well as between loss of smell and cognitive deterioration (p=0.049; OR=2.565). However, having more than three chronic diseases was found to significantly increase the risk of cognitive impairment (p=0.018; OR=2.678), but there was no significance to support that certain disease pairs were more likely to lead to cognitive impairment. **Conclusion:** This research underscores the significance of sense of smell and the presence

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of multiple chronic diseases, especially in greater numbers, as major risk factors for cognitive impairment in the elderly.

ABSTRAK

Latar Belakang: *Seiring dengan bertambahnya usia populasi, masalah penurunan kognitif menjadi semakin mengkhawatirkan, terutama dengan meningkatnya kondisi seperti penyakit kronis dan kehilangan fungsi penciuman di kalangan lansia.* ***Tujuan:*** *Penelitian ini bertujuan untuk mengeksplorasi hubungan antara multimorbiditas, fungsi penciuman, dan penurunan kognitif di kalangan populasi lanjut usia.* ***Metode****: Studi ini melibatkan 128 lansia dari komunitas lansia di Jakarta dengan usia rata-rata 68,34 tahun. Keberadaan multimorbiditas ditentukan berdasarkan pasangan penyakit dengan frekuensi tertinggi, dan fungsi penciuman diuji dengan tes 8 aroma. Kemampuan kognitif diukur menggunakan kuesioner CERAD, dengan skor di bawah 52 menunjukkan gangguan kognitif. Analisis dilakukan menggunakan uji chi-square pada tingkat kepercayaan 95%.* ***Hasil:*** *Temuan menunjukkan adanya hubungan yang signifikan antara tingkat pendidikan yang lebih rendah dan penurunan kognitif (p=0,018; OR=3.214), serta antara kehilangan fungsi penciuman dan penurunan kognitif (p=0,049; OR=2,565). Selain itu, keberadaan lebih dari tiga penyakit kronis secara signifikan meningkatkan risiko penurunan kognitif (p=0,018; OR=2,678), namun tidak ada hasil signifikan bahwa pasangan penyakit tertentu lebih mungkin menyebabkan penurunan kognitif.* ***Simpulan:*** *Penelitian ini menekankan pentingnya fungsi penciuman dan multimorbiditas, terutama dalam jumlah yang lebih banyak, sebagai faktor risiko utama terhadap penurunan kognitif di kalangan lansia.*

INTRODUCTION

As the average lifespan around the globe keeps getting longer, the planet is confronted with fresh obstacles tied to growing older populations. It is anticipated that, by the year 2050, the average lifespan will climb from 73.6 years in 2022 to 78.1 years, with even more significant increases seen in nations that currently have lower average lifespans (1). Reflecting this global shift, Indonesia is experiencing a growing burden of dementia: according to the 2022 STRiDE report, the estimated prevalence of dementia among older adults was 23.40%, while only 0.20% had received a formal diagnosis. Furthermore, the number of people living with dementia in Indonesia is projected to increase dramatically from approximately 1.2 million in 2015 to nearly 4 million by 2050 highlighting the urgent need for national strategies to safeguard cognitive health in aging populations (2). This enhancement in how long people live is accompanied by a change in the types of health issues people face, including cognitive function and chronic conditions like heart disease, diabetes, and many more (3).

Cognitive function is essential for elderly well-being, influencing memory, attention, decision-making, and daily functioning. Its preservation is crucial for maintaining independence and quality of life (4). Cognitive impairment, including conditions like dementia, poses a growing challenge as the population age, placing significant burdens on healthcare systems and caregivers (5). Effective interventions, such as regular physical activity and addressing risk factors like multimorbidity and olfactory dysfunction, have been shown to support cognitive health in older adults (6). Therefore, early detection and management are essential to promote healthy aging, especially in high-risk groups (7).

Several risk factors have been linked to cognitive impairment, such as age, gender, education, lifestyle, diet habits, chronic health conditions and sensory deficits (7–10). In particular, multimorbidity—the co-occurrence of multiple chronic diseases—and olfactory dysfunction, have been highlighted in recent

research as potential contributors to cognitive impairment (11).

Apart from the affirmation of chronic disease, problems of olfactory function may have a direct association with cognitive impairment, though they tend to be underestimated in current clinical settings. The association between olfactory dysfunction and cognitive remains controversial, as it is still unclear whether olfactory impairment independently influences cognitive abilities or is itself a manifestation of multimorbidity (12).

Like many other developing countries, Indonesia is at the beginning of a phase where a significant portion of its population are more than 60 years old, accounting for 9% for the entire population (13). As life expectancy rises and the population ages, the prevalence of chronic conditions also increases, contributing to the growing healthcare burden, including cognitive impairment (14). Recent research has highlighted the large number of chronic diseases in Indonesia, but there is a lack of information on how common multiple chronic conditions are among the population (15). This study aim to determine the role of multiple chronic diseases, olfactory function, and cognitive impairment among older adults. Also, we describe the association between aforementioned variables conditions.

METHODS

This is a cross-sectional study conducted in a community of elderly individuals residing in Jakarta between March-April 2024. The independent variables were demographic factors such as age, gender, and education level. In addition to sociodemographic data, health-related variables were also analyzed, such as obesity status, which was determined using body mass index (BMI) calculations, and smoking history.

Multimorbidity, a central focus of this study, was defined based on the participants' self-reported history of chronic diseases. Multimorbidity categories were determined by identifying the most frequently occurring combinations of diseases using Charlson Comorbidity Index (CCI). These combinations were used to create specific categories of multimorbidity for further analysis, allowing the study to investigate how these disease pairings influenced health outcomes in this elderly population.

In addition, this study assessed olfactory function as a potential indicator of cognitive and sensory decline. In terms of olfactory test, it involves eight specific aromas, such as coffee, lemon, orange, eucalyptus, lemongrass, menthol, aromatic ginger, and jasmine. The cut-off score for olfactory dysfunction was set at 3, based on normative data established in previous olfactory research of University of Pennsylvania Smell Identification Test (UPSIT) about odor identification as a rapid quantitative of olfactory function test in clinic setting (16). This cut-off helped classify individuals with potential olfactory disorders, providing further insight into their overall sensory and cognitive health. Cognitive function was evaluated using the CERAD (Consortium to Establish a Registry for Alzheimer's Disease) questionnaire, administered by trained enumerators to ensure accuracy and consistency in data collection. The cut-off score for cognitive impairment was set at 52, based on the mean CERAD scores identified in this population. This threshold allowed for the classification of cognitive dysfunction, enabling the study to explore the relationship between cognitive health, multimorbidity, and other health-related variables in the elderly community.

The dependent variable for this study is cognitive function, while all other variables are considered independent variables. Each variable in this study is categorized according to its value. Data presentation and bivariate analysis were conducted using a statistical program, with analysis performed using the Chi-square test at a 95% confidence interval. A significant association was determined by a p-value of <0.05.

This study was approved by the Ethical Committee of the School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, with referral number 07/05/KEP-FKIKUAJ/2023.

RESULTS

This study examined the traits of a total of 128 individuals, covering aspects like age, gender, history of smoking, level of education, presence of multiple chronic conditions, and sense of smell. The majority of the participants were over the age of 65 (65.63%), with 64.06% being female. There were no notable links found between age, gender, history of smoking, or the presence of multiple chronic conditions with cognitive impairment. Nonetheless, a significant link was observed between having less than nine years of education and experiencing multimorbidity with over three conditions ($p=0.018$) or with over four conditions ($p=0.031$), as well as between having issues with olfactory

function (p=0.049). The comprehensive findings of the study are outlined in Table 1.

Associations between various combinations of chronic diseases and cognitive impairment were examined as seen in Table 2. The most frequent comorbidities include hypertension and rheumatic disease, hypertension and diabetes mellitus, and rheumatic and diabetes mellitus, among others. Although none of the combinations showed statistically significant associations with cognitive impairment (p>0.05), the odds ratios (OR) suggest varying degrees of risk. For instance, the highest odds ratio was observed for the combination of diabetes mellitus and cardiovascular disease (OR=2.486, 95%CI=0.478–12.913), indicating a potential but non-significant increased risk of cognitive impairment in these patients.

Table 1
Characteristics and Bivariate Analysis of Factors Associated with Cognitive Function

Variables	All, n = 128	Cognitive Impairment		p-value	OR (95% CI)
		No	Yes		
		n (%)	n (%)		
Age, mean ± SD	68.34 ± 5.35				
60-65 years		30 (71.4)	12 (28.6)	0.847	1.083 (0.481 – 2.441)
>65 years		60 (69.8)	26 (30.2)		
Sex, n (%)					
Female	82 (64.06)	31 (67.4)	15 (32.6)	0.588	0.806 (.368 – 1.762)
Male	46 (35.94)	59 (72)	23 (28)		
History of Smoking, n (%)					
No	119 (92.97)	86 (72.3)	33 (27.7)	0.078	3.258 (0.824 - 12.880)
Yes	9 (7.03)	4 (44.4)	5 (55.6)		
Educational Level, n (%)					
≥9 years	109 (85.16)	81 (74.3)	28 (25.7)	0.018	3.214 (1.185 – 8.718)
<9 years	19 (14.84)	9 (47.7)	10 (52.6)		
Obesity, n (%)					
No	58 (45.31)	40 (69)	18 (31)	0.761	0.889 (0.415 – 1.902)
Yes	70 (54.69)	50 (71.4)	20 (28.6)		
Cluster of Chronic Conditions, n (%)					
≥2 (Multimorbidity)	93 (72.66)	63 (67.7)	30 (32.3)	0.299	1.607 (0.653 – 3.956)
≥3	74 (57.81)	46 (62.2)	28 (37.8)	0.018	2.678 (1.166 – 6.154)
≥4	46 (35.94)	27 (58.7)	19 (41.3)	0.031	2.333 (1.070 – 5.088)
Olfactory Dysfunction, n (%)					
No	107 (83.59)	79 (73.8)	28 (26.2)	0.049	2.565 (0.983 – 6.690)
Yes	21 (16.41)	11 (52.4)	10 (47.6)		

SD: Standard Deviation; OR: Odds Ratio

Table 2
Association Between Common Combinations of Chronic Diseases and Cognitive Impairment

Biads*	n (%)**	Cognitive Impairment		p-value	OR (95% CI)
		Yes	No		
		n (%)	n (%)		
Hypertension and Rheumatic	11 (8.69)	4 (36.4)	7 (63.6)	0.612	1.395 (0.383 – 5.076)
Hypertension and Diabetes Mellitus	7 (5.47)	3 (42.9)	4 (57.1)	0.433	1.843 (0.392 – 8.662)
Hypertension and Cardiovascular Disease	5 (4.69)	2 (33.3)	4 (66.7)	0.841	1.194 (0.209 – 6.815)
Rheumatic and Diabetes Mellitus	12 (9.38)	5 (41.7)	7 (58.3)	0.340	1.797 (0.532 – 6.064)
Rheumatic and Cardiovascular Disease	7 (5.47)	2 (28.6)	5 (71.4)	0.947	0.944 (0.175 – 5.095)
Diabetes Mellitus and Cardiovascular Disease	6 (4.69)	3 (50)	3 (50)	0.265	2.486 (0.478 – 12.913)

*Most-frequent combinations of chronic disease found in individuals with two or more conditions in the study.
**Percentages have been adjusted and calculated based on the total sample size of 128 individuals

DISCUSSION

The discussion in this study primarily focuses on investigating olfactory function and multimorbidity as significant risk factors affecting cognitive abilities among older adults. Specifically, we examine multimorbidity by categorizing it into distinct clusters of diseases to identify the most prevalent conditions associated with cognitive impairment. Additionally, this study considers various demographic factors, including age, sex, educational attainment, smoking history, and obesity, as contributors to cognitive function. These demographic variables were included to provide a comprehensive analysis of the influence of both health-related and sociodemographic factors on cognitive outcomes. This structured approach facilitates a more nuanced understanding of how olfactory impairment and multimorbidity, alongside demographic characteristics, contribute to cognitive impairment within the aging population.

In this research, 128 individuals were involved, with an average age of 68.34 years, divided into two age brackets: 60–65 years and older than 65 years. There was no meaningful link found between age and cognitive impairment. These findings differ in many studies that have found a significant association between age and cognitive function (12,17). With aging, structural changes occur in the brain, including potential atrophy of the prefrontal cortex and medial temporal lobe—regions essential for executive function and naming skills—as well as alterations in white matter linked to memory function. Conversely, a study by Han et al (7) has identified age as a protective factor against cognitive impairment. The discrepancies between this study's findings and those of previous research may be attributed to a relatively small sample size and the comparatively younger average age of elderly participants (mean of 68.34 years old) while a study mentioned that MCI may significantly develop above 85 years and older (17,18).

Most of the participants were women, but gender did not show a significant link to cognitive impairment. Regarding the findings on gender, similar results were reported by Hutasuhut et al. who also found no significant association between gender and cognitive function (18). In contrast to a study by Manly et al., women were more likely to experience a significant decline in cognitive function (19).

Previous research has mentioned that gender is not an independent factor related to cognitive function (20). Women are more likely to experience cognitive impairment due to involvement of educational level (21). Similarly, this study also finds that there was a clear link between educational attainment and cognitive impairment, with individuals with less than nine years of education being at a higher risk of cognitive impairment. The significance of education level has also been highlighted in several other studies as an independent factor, without any association with other variables, such as gender, as previously mentioned (6,7,11).

This study also investigated smoking history and found that some of the participants were active smokers. However, there was no meaningful statistical connection between smoking and cognitive impairment, although the risk was slightly higher among smokers. This finding contrasts with

several other studies that report an association between smoking and cognitive function (9). The differences in study results may be attributed to a substantial variation in sample sizes. Additionally, a study by Roberts et al. indicated that the lack of a significant association between smoking and cognitive impairment may be due to the more pronounced impact of cumulative chronic conditions (18). Similarly, Rasmussen et al. found an increased risk associated with the combined effect of smoking and obesity on cognitive function (22). However, a notable difference is that, in their study, obesity was linked to cognitive function, a relationship that was not observed in our research. Although the association was not significant, the OR suggests that obesity may serve as a protective factor for cognitive function. Referring to a study by Cecot et al (23), obesity has been found to act as a protective factor in middle-aged individuals. A similar effect might be present in our study, potentially due to the lower average age of the study population.

Regarding the presence of multiple chronic diseases, most of the participants had two or more diseases. Yet, this condition was not significantly linked to cognitive impairment. However, those with three or more chronic conditions did exhibit a slightly increase statistically significant. The finding of this study corresponds with those of Vassilaki et al (24), who found that multimorbidity, with two or more chronic conditions, was not statistically significant, becoming significant only when four or more chronic conditions were present. However, both of these findings differ from Zhang et al (11), who reported a significant association between two or more chronic conditions and cognitive function. Hu et al. also reported similar findings, showing that multimorbidity has a significant impact on mild cognitive impairment (MCI) (25). These differences in results may be influenced by factors such as sample size and the type of questionnaire used for cognitive function assessment. The differences observed between these studies may also be attributed to other factors, such as mean age and sex.

The study also found that a significant link existed between problems with olfactory function and cognitive impairment. This study aligns with the findings of Dintica et al (26), who conducted a community-based study demonstrating an association between olfactory function and cognitive performance. Impaired olfactory function has been linked to reduced volume in key brain regions, such as the fusiform gyrus, middle temporal cortex, hippocampus, and entorhinal cortex. Another mechanism underlying olfactory impairment, particularly in elderly, is increased activation of the brain's olfactory system during odor identification, which leads to degenerative alterations (27). These changes suggest that olfactory deficits may serve as predictors of cognitive impairment and early indicators of neurodegeneration.

Surprisingly, Table 2 shows that none of the common combinations of chronic diseases, including hypertension, rheumatic diseases, diabetes mellitus, and cardiovascular disease, had a statistically significant association with cognitive impairment. However, the highest odds ratios were observed in individuals with both diabetes mellitus and cardiovascular disease and those with hypertension and diabetes mellitus, suggesting a potential trend toward increased cognitive impairment risk in these groups, although not statistically significant. These findings are consistent with previous studies that report a significant association between multimorbidity, particularly combinations such as diabetes with cardiovascular disease and hypertension with diabetes, and cognitive function (28). In line with these studies, it has also been observed that analyzing the impact of a single disease on cognitive function often yields no significant effects, highlighting the importance of considering multiple coexisting conditions when assessing cognitive outcomes (29).

Research Limitations

The limitations of this cross-sectional study are that it prevents the establishment of a chronological link between issues with olfactory function, multimorbidity of chronic conditions, and cognitive impairment. Consequently, it is uncertain whether issues with olfactory come before or follow multimorbidity, both of which might lead to cognitive impairment. This restricts the ability to make clear-cut statements about cause and effect. To gain a deeper insight into how olfactory dysfunction, having several chronic conditions, and cognitive problems are related, future studies should explore a longitudinal design. Moreover, expanding the number of participants could boost the research's ability to find more significant connections, offering a fuller picture of how these elements interact over time.

Another limitation in this study is that we did not analyze the triad of multimorbidity because the chronic conditions in the Charlson Comorbidity Index (CCI) are too numerous and individually too small for effective grouping in this population.

CONCLUSION

This research has revealed a notable association between educational attainment, the presence of multimorbidity, which encompasses conditions exceeding three and four, and olfactory function with cognitive performance. These results indicate that an elevated prevalence of chronic conditions is progressively contributing to cognitive impairment. Nonetheless, additional investigation is required to pinpoint distinct clusters of chronic conditions that affect cognitive function, particularly to ascertain which patterns of multimorbidity should be of concern within the Indonesian population. Moreover, olfactory function appears to be a promising indicator for the detection of cognitive impairment among the elderly.

CONFLICT OF INTEREST

There is no conflict of interest in this paper.

AUTHOR CONTRIBUTIONS

KK: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – Original Draft, Writing – Review & Editing, Visualization, Project administration, Funding acquisition. GV: Software, Formal analysis, Data curation, Writing – Original Draft, Writing – Review & Editing. NH: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – Original Draft, Visualization. YT: Conceptualization, Methodology, Validation, Writing – Review & Editing, Supervision. YSH: Conceptualization, Methodology, Validation, Writing – Review & Editing, Supervision.

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