

Risk Factors for Olfactory Dysfunction in Patients with Type 2 Diabetes Mellitus

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Abstract

Introduction:

Patients with type 2 Diabetes Mellitus (DM) often experience olfactory dysfunction; however, the relationship between disease duration and comorbidities remains unclear.

Materials and Methods:

An analytical observational study was conducted at the Endocrinology and Metabolic Polyclinic of the H. Adam Malik General Hospital, Medan. The study included 66 patients with type 2 DM who met the inclusion criteria. Data were collected from medical records, questionnaires, routine ENT examinations, and the Sniffin' Sticks Test ($P < 0.05$).

Results:

No significant relationship was observed between sex and olfactory function in patients with type 2 DM. However, a significant correlation was observed between age and the olfactory function score ($P = 0.012$) as well as between the duration of type 2 DM and the olfactory function score ($P = 0.005$). There was no significant difference in olfactory function scores between patients with type 2 DM with and without comorbidities.

Conclusions:

This study revealed that increasing age and the duration of type 2 DM correlated with declining olfactory function. However, no differences were observed in olfactory function between patients with type 2 DM with and without comorbidities. These findings provide additional insights into the factors that influence olfactory function in patients with type 2 DM.

Keywords: Type 2 Diabetes Mellitus, Olfactory Function, Aging, Disease Duration, Comorbidities, Sniffin' Sticks Test.

Received date: 06 Mar 2024

Accepted date: 14 Aug 2024

*Please cite this article; Sani BM, Rambe AYM, Yudhistira A, Nursiah S, Harahap M.PH, Ashar T. Risk Factors for Olfactory Dysfunction in Type 2 Diabetes Mellitus Patients. *Iran J Otorhinolaryngol.* 2024;36(6):655-661.
Doi:10.22038/ijorl.2024.78347.3647

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Introduction

Diabetes Mellitus (DM) is a metabolic disorder characterized by persistent hyperglycemia resulting from inadequate insulin secretion, peripheral insulin resistance, or a combination of the two.

The International Diabetes Federation reported that approximately 463 million individuals had diabetes globally in 2019, which translates to approximately 9.3% of the population aged 20–79 years. China, India, and the United States have the highest number of patients with diabetes worldwide. Indonesia has a substantial number of persons with diabetes, estimated at 10.7 million in 2020 (1). The incidence of DM in Indonesia increased from 1.5% in 2013 to 2% in 2018 (1), indicating a substantial increase in the disease burden in this country. Diabetes-related complications, particularly those associated with microvascular disorders such as retinopathy, nephropathy, and neuropathy, and cardiovascular disease-related complications that increase microvascular risk, can lead to disability and mortality (2).

In addition to physical challenges, diabetes can lead to central nervous system dysfunction, cognitive decline, and depression (3). Studies have revealed that olfactory dysfunction is prevalent among individuals with diabetes, but its underlying mechanisms and contributing factors remain unclear (4).

Odors have a significant impact on various aspects of life, including safety, nutrition, social interactions, and general quality of life (5). Odor inspection has been employed as a predictive tool for conditions such as Parkinson's disease, dementia, and Alzheimer's disease (6). The prevalence of olfactory dysfunction in non-clinical populations varies greatly, ranging from 2.7% to 76.8%, which can be attributed to factors such as sinonasal disease, head trauma, and other underlying causes (7). Several studies have shown a connection between olfactory dysfunction and DM, with various mechanisms proposed, including the influence of medications, metabolic changes, central nervous system neuropathy, insulin resistance, and microvascular and macrovascular diseases. However, the reported findings are not always consistent, and the relationship between DM complications and olfactory dysfunction remains debatable (6). The Sniffin' Sticks Test is a widely used method for assessing olfactory function,

and its reliability has been demonstrated in previous studies. This test has been used in various countries, including those in Asia (8). Consequently, this study utilized the Sniffin' Sticks Test to evaluate the risk factors associated with impaired olfactory function in patients with type 2 DM.

The primary objective of this study was to analyze the risk factors for impaired olfactory function in patients with type 2 DM using the Sniffin' Sticks test.

Materials and Methods

This was an analytical observational study with a cross-sectional design conducted at the Endocrinology and Metabolic Polyclinic of H. Adam Malik Hospital in Medan. The study population comprised of patients with type 2 DM who were treated at polyclinics and met the inclusion and exclusion criteria. The inclusion criteria were age between 41 and 85 years with no history of allergic rhinitis, nose or head trauma, upper respiratory tract infection, nasal mass, or tumor. A minimum sample size of 66 was obtained using a non-probability consecutive sampling method. The study variables included type 2 DM, age, sex, duration of symptoms, comorbidities, and olfactory function. Data were collected from medical records, questionnaires, routine ENT examinations, and the Sniffin Sticks Test. The ethical approval number for this study was 443/KEPK/USU/2023. Statistical data was analyzed, including independent *t*-test, Fisher's exact test, chi-square test, and Pearson's correlation, were performed using SPSS.

The Scope of Research

The present study had several limitations. First, its cross-sectional design does not allow determination of causality between DM and olfactory function. Second, the study did not collect information on additional factors, including HbA1c, lipid profile, and comorbidities, such as obesity and dyslipidemia, which may affect olfactory function.

Results

This study included 66 individuals diagnosed with type 2 DM. The demographic characteristics of the participants are presented in Table 1.

Table 2 presents the results of the Sniffin' Sticks Test, which evaluates olfactory function in patients with type 2 DM. Of the 66 participants, 27.3% had normosmic olfactory function, whereas the remaining 72.7% had hyposmic olfactory function.

Table 3 presents the outcomes of the examination of the association between sex and olfactory function in patients with type 2 DM. Among the 39 men participants, 71.8% experienced hyposmia, and among the 27 women participants, 74.1% experienced hyposmia.

Table 4 shows the results of the analysis examining the relationship between age and olfactory function in patients with type 2 DM (DM) using the Sniffin' Sticks Test.

Table 5 shows the results of the analysis of the

relationship between the duration of DM and olfactory function in patients with type 2 DM based on the Sniffin' Sticks Test. A significant relationship was found between the duration of type 2 DM and olfactory function score ($p = 0.005$), with a negative correlation indicating a decrease in olfactory function as the duration of suffering increased.

Table 6 presents the results of olfactory function assessment conducted in patients with type 2 DM, both with and without accompanying comorbidities. The results of this study revealed no discernible differences in odor function scores between the two groups. Additionally, the categorization analysis of the total olfactory function score demonstrated no variation in olfactory function between patients with and without comorbidities ($p = 1.000$).

Table 1: Demographic of Characteristics

Demographic Characteristics	n = 66
Sex, %	
Men	59.1
Women	40.9
Age (year)	
Mean (SD)	58.56 (8.58)
Median (Min – Max)	58.5 (41 – 85)
Duration of Diabetes (years)	
Mean (SD)	9.8 (8.05)
Median (Min – Max)	8.5 (0.08 – 30)
Comorbidities, %	
No comorbidities	16.7
CHD	12.1
CHF	4.5
CHF and Hypertension	3
Hypertension	60.6
CHD and Hypertension	3

Discussion

That most participants (59.1 %) were men. This finding aligns with the global prevalence of type 2 DM, which is higher in men than in women (Reed et al., 2021). Other studies have reported a higher incidence of type 2 DM among men (10,11). The average age of patients with type 2 DM was 58.56 years. Research conducted in Sweden and Hungary reported average ages of approximately 61.79

and 66.14 years, respectively (11,12). Additionally, the average duration of diabetes was 9.8 years, which was shorter than the approximately 14.6-year average reported in previous studies (13). The most common comorbidity was hypertension, affecting 60.6% of participants, followed by CHD (12.1%). Other studies have also reported that hypertension (84.9 %) and CHD (22.8 %) have the highest prevalence (14).

Table 2: Results of Olfactory Function Examination Based on the Sniffin' Sticks Test in Patients with Type 2 DM

Olfactory Function	N = 66
Threshold Score	
Mean (SD)	7.97 (1.28)
Median (Min – Max)	8 (5 – 11.75)
Discrimination Score	
Mean (SD)	9.37 (2.16)
Median (Min – Max)	9.5 (4 – 15)
Identification Score	
Mean (SD)	10.55 (1.85)
Median (Min – Max)	11 (4 – 15)
Olfactory Function Score	
Mean (SD)	27.89 (3.27)
Median (Min – Max)	28 (20.25 – 36)
Olfactory Function, %	
Normosmia	27.3
Hyposmia	72.7

The results of the Sniffin' Sticks Test, which evaluates olfactory function in patients with type 2 DM. Of the 66 participants, 27.3% had normosmic olfactory function, whereas the remaining 72.7% had hyposmic olfactory

function. These results are consistent with those reported in studies on hyposmia, where 74.2% of the subjects experienced hyposmia and 22.4% had normosmia (14).

Table 3: Relationship between Sex and Olfactory Function Based on the Sniffin' Sticks Test in Patients with Type 2 DM

Characteristics Demographics	Olfactory Function		p value
	Hyposmia	Normosmia	
Sex, %			
Men	71.8	28.2	0.838
Women	74.1	25.9	

The outcomes of the examination of the association between sex and olfactory function in patients with type 2 DM. Among the 39 men participants, 71.8% experienced hyposmia, and among the 27 women participants, 74.1% experienced hyposmia. After statistical analysis using the chi-square test, no significant

association was observed between sex and olfactory function in patients with type 2 DM ($p=0.838$). These results align with those of a previous study conducted in Iran, which also failed to find a significant relationship between olfactory dysfunction and sex in patients with type 2 DM (15).

Table 4: Relationship between Age and Olfactory Function Based on the Sniffin' Stick Test Characteristics

Olfactory Function Score	Age	
	p value	r
	0.012	-0.307

The results of the analysis examining the relationship between age and olfactory function in patients with type 2 DM (DM) using the Sniffin' Sticks Test. The Spearman correlation test revealed a significant association between age and olfactory function score ($p=0.012$), with a correlation value (r) of -0.307 . This negative correlation indicated a weak

relationship between increasing age and decreasing olfactory function scores in patients with type 2 DM (Figure 1). Similarly Gouveri et al. (2014), in their Greek study, demonstrated a decrease in the odor threshold score, odor identification score, and TDI among older patients compared to younger patients (16).

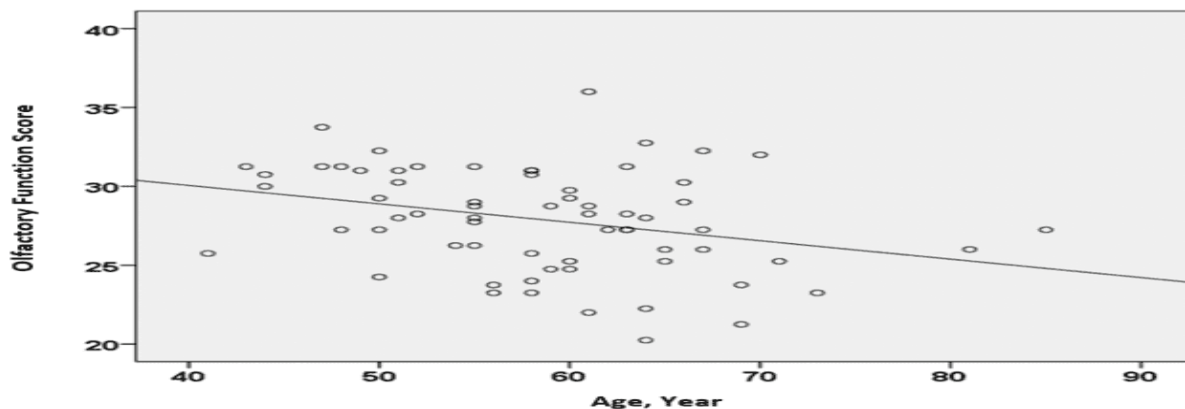


Fig 1: Scatterplot of Relationship between Age and Olfactory Function Score in Patients with Type 2 DM

The results of the analysis of the relationship between the duration of DM and olfactory

function in patients with type 2 DM based on the Sniffin' Sticks Test.

Table 5: Relationship between DM Sufferers and the Duration of Olfactory Function Based on the Sniffin' Sticks Test

Characteristics	Suffering from DM for a long time	
	p value	r
Olfactory Function Score	0.005	-0.344

A significant relationship was found between the duration of type 2 DM and olfactory function score ($p = 0.005$), with a negative correlation indicating a decrease in olfactory function as the duration of suffering increased. This finding is in line with that of Gouveri et al. (2014), who did not find a correlation between the duration of suffering from type 2 DM and general smell scores but found a negative correlation between the duration of suffering from DM and odor identification scores in patients who had suffered from it for a longer time. In contrast, other studies have shown a strong negative correlation

between the duration of type 2 DM and the TDI scores (17).

Numerous studies have demonstrated that long-standing diabetes leads to the formation of atherosclerotic lesions characterized by intimal thickening and a thin fibroatheroma layer, which have deleterious effects on both small and large blood vessels, ultimately resulting in cardiovascular disease and mortality (18). Furthermore, the negative correlation observed between increased duration of diabetes and decreased olfactory function scores in patients with type 2 DM (Figure 2) suggest a weak association between these two factors.

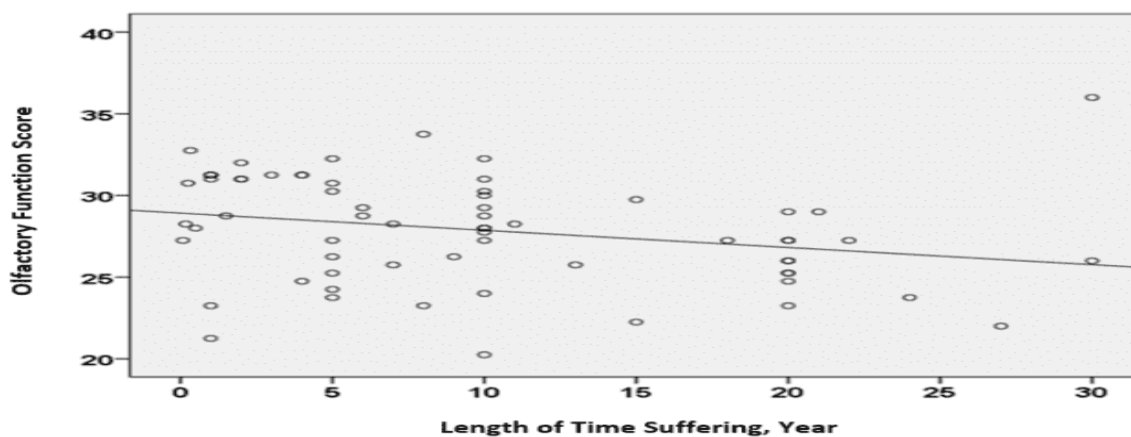


Fig 2: Scatterplot of Relationship between Length of Time Suffering from DM and Olfactory Function Scores in Patients with Type 2 DM

The results of olfactory function assessment conducted in patients with type 2 DM, both

with and without accompanying comorbidities.

Table 5: Olfactory Function Based on the Presence of Comorbidities Diseases in Patients with Type 2 DM

Olfactory Function	Comorbidities		p value
	With (n = 55)	Without (n = 11)	
Olfactory Function Score			
Mean (SD)	27.77 (3.4)	28.5 (2.49)	0.413
Median (Min – Max)	27.75 (20.25 – 36)	28.75 (23.75 – 31.25)	
Olfactory Function, %			
Hyposmia	72.7	72.7	1.000
Normosmia	27.3	27.3	

The results of this study revealed no discernible differences in odor function scores between the two groups. Additionally, the categorization analysis of the total olfactory function score demonstrated no variation in olfactory function between patients with and without comorbidities ($p = 1.000$). However, a previous study conducted by Gouveri et al. (2014) showed that hypertension was associated with lower olfactory scores, including threshold scores, odor identification, and Total Nasal Score (TDI), in patients with type 2 DM and in control patients without type 2 DM.

According to an American study, olfactory dysfunction is correlated with cardiovascular risk factors that are influenced by age, anthropometry, and cardiometabolic profile (19). Furthermore, a Korean study revealed that men with a history of stroke or coronary heart disease were more likely to experience olfactory dysfunction, whereas women with conditions such as DM, large waist circumference, hypertriglyceridemia, low serum HDL levels, and CHD were also at higher risk. The association between CHD and cardiac dysfunction was stronger in men than in women, whereas the association with abdominal obesity was more significant in women. Additionally, hormonal changes that occur with age, particularly a decrease in estrogen levels in postmenopausal women, can lead to olfactory dysfunction and cardiovascular risk (20).

Patients with type 2 DM commonly experience impaired olfactory function, which can manifest as an increase in the olfactory detection threshold, decreased ability to identify odors, and increased risk of anosmia. Despite the numerous studies using animal models of obesity and prediabetes, the underlying mechanisms remain unclear. Studies have

demonstrated that obese and insulin-resistant mice exhibit reduced tyrosine phosphorylation in brain regions crucial for olfaction. Neuroplasticity, the ability of the brain to adapt to environmental changes and detect and decode new odors, is a critical factor in this process, and GABAergic interneurons play a vital role in this adaptive capacity (21,22).

Neuroplasticity is primarily regulated by adult neurogenesis in the main olfactory bulb (MOB), a process that occurs in the subventricular zone, and relies on neural stem cells to produce doublecortin (DCX)-positive differentiated neuroblasts. Subsequently, these neuroblasts develop into interneurons and play a crucial role in MOB neuroplasticity (22).

A Swedish study examined odor disturbance detection in mice with type 2 DM, and revealed that these mice spent less time sniffing new odors and more time searching for fragrant objects. These results were associated with a decline in the detection of smells and memory, which correlated with reduced calbindin (CB) expression in the MOB, decreased parvalbumin expression, and disrupted differentiation of DCX+ neurons in the piriform cortex. This study highlighted the significance of these factors in the development of type 2 DM in mice (22).

Conclusion

This study demonstrated a significant correlation between age, duration of type 2 DM, and olfactory function. Most participants were men (59.1%), with an average age of 58.56 years and had been diagnosed with type 2 DM for 9.8 years, and 60.6% had hypertension as comorbidity. The prevalence of hyposmia among participants was 72.7%; however, there was no significant association between sex and olfaction in patient with type 2 DM.

Nonetheless, a significant relationship was observed between age, type 2 diabetes duration, and olfactory status. Furthermore, there was no significant association between olfactory function and type 2 diabetes, regardless of the presence or absence of comorbidities.

Acknowledgements

The authors would like to thank all the participants.

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