Anosmia in Elderly: Predictor of Cognitive Impairment

Gaurav Kumar Yadav[1,*], Madhuri Sunil Pandharipande[2], Rakhi W Joshi[3], Mrinalini D Motlag[4], K. Nagpure[5], PP Joshi[6]

[1]UG Student, [2]Associate Professor, [3,4,5]Assistant Professor, [6]Professor & HOD, Dept. of Medicine, IGGMC, Nagpur

***Corresponding Author:**
Email: yadavgauravmn5@gmail.com

Abstract

The prevalence of olfactory impairment and cognitive impairment increases with age. Olfactory impairment has been associated with neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease. The present study was carried out to find out the prevalence of anosmia in the elderly and cognitive impairment in the elderly along with the association of anosmia and cognitive impairment in the elderly. Present study is a hospital based, observational, case-control study, in which 100 elderly subjects (age >65 years, Males 64, Females 36, ratio 1.7:1), attending the geriatric OPD, were included as cases and 100 subjects (<65 years, Males54, females 46, ratio-1.1:1) as controls. Anosmia was assessed by Indian Smell Identification Test (INSIT), in which 10 essences were used and 1 point was awarded for correct and 0 for incorrect identification. A score of ≤ 4 indicates anosmia. All cases were subjected to thorough clinical examination and lab investigations. Cognitive impairment was diagnosed by 30 point mini-mental state examination (MMSE) where scores ≤ 23 indicates cognitive impairment. Statistical analysis was performed by using students 't' test, chi square test p value and univariate analysis. Mean age in cases was 68.4±3.7 years and in controls is 39.4±7.9 years. Anosmia was detected in 64% of cases as compared to controls 4% (p <0.01). Mean INSIT score was significantly lower (4.02±1.88) in cases as compared to controis7.36±1.35, p< 0.01. Cognitive impairment was present in 50% of the cases and 1% control, (p<0.001). Mean MMSE score was also significantly lower in cases (20.99±5.1) than controls (27.47±1.79, p <0.001. Anosmia is found to be significantly associated with cognitive impairment in cases. Anosmia, a surrogate marker of cognitive impairment, is prevalent in elderly. Cognitive impairment is also prevalent in elderly. In elderly subjects, anosmia is associated with cognitive impairment.

Keywords: Anosmia, Cognitive impairment, Geriatric age group.

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Introduction

The prevalence of olfactory impairment and cognitive impairment increases with age[(1-2)]. Olfactory impairment has also been associated with neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease[(3-4)]. Some studies have reported that olfaction impairment appears to precede clinical signs of cognitive impairment or AD and have hypothesized that it may be an early indicator of brain changes. Autopsy studies have found neurofibrillary tangles, pathology thought to be associated with AD, appear first in the entorhinal cortex and olfactory bulb areas of the brain both in people with AD and/or dementia as well younger people with no clinical signs of dementia[(5-6)]. A recent study found the density of tangles present in the central olfactory system was inversely related to odour identification ability[(7)].

Because of the suggestion that olfactory impairment may be an early indicator for cognitive impairment, there has been interest in the possibility of using olfactory testing to assist in diagnosis of AD or predict who will develop AD or cognitive impairment. However there has been limited research on the association of olfaction and cognition in a general population of older adults not at high risk for AD or cognitive impairment. The purpose of this study is to determine if odour identification ability is associated with cognitive impairment in the elderly subjects.

Aims and Objectives

1. To find out the prevalence of anosmia in the elderly
2. To find out the prevalence of cognitive impairment in the elderly
3. To find out the association between anosmia and cognitive impairment in the elderly.

Material and Methods

Present study is a hospital based, cross-sectional, observational study carried out on 100 elderly subjects with age >65 years attending geriatric outpatient clinic at a tertiary care hospital, 100 subjects with age <65 years were included as controls. Cases with history of head injury, cranial surgery, sub arachnoid haemorrhage, metabolic abnormalities (thiamine deficiency, adrenal and thyroid deficiency, cirrhosis, renal failure, Wegener's granulomatosis, compressive and infiltrative lesions viz. Craniopharyngioma, meningioma, aneurysm, meningoencephalocoele, Vit. B12 deficiency, hyperthyroidism, alcohol consumption

>80 gm /day, known psychiatric disorders schizophrenia, depression, acute medical conditions, temporal lobe epilepsy, chronic rhinitis and smokers were excluded as cases as well controls. Permission from institutional ethics committee was obtained. All cases were evaluated for anosmia by Indian smell identification test. The sensitivity of INSIT test is 79.2% and specificity is 78% at the cut off value of 4. The Indian Smell Identification Test uses the essence of 10 commonly used items as odorants (cardamom, kewra, khus, lemon, mango, orange, pineapple, rose, thinner, vanilla) which represent familiarity in day to day life. A score of ≤4 indicate anosmia. INSIT was performed by the person blinded for the study. All subjects underwent ENT examination and evaluation to rule out local causes of anosmia.

Cognitive impairment was assessed by Mini Mental State Examination (MMSE) Score ≤23 was considered as presence of cognitive impairment. MMSE assessment was performed by the person blinded for the study. All subjects underwent clinical examination. Co-morbidities viz. Diabetes mellitus, hypertension, Coronary artery disease, dyslipidemia were noted. Complete blood counts and biochemical tests viz fasting and post prandial blood sugar, serum lipids, urea, creatinine were performed and thyroid functions, ECG and other investigations were performed in relevant cases.

Statistical analysis

Statistical analysis was done by statistical software 'Open Epi Info Version 2.6'. Percentages, mean, standard deviation, χ^2 (chi square) test were calculated. Student 't' test, Fisher's Exact test, and univariate analysis were done. 'P' values less than 0.05 were considered as statistically significant. As Univariate analysis revealed significant association of anosmia with only cognitive impairment, multivariate analysis was not required.

Results

In the present study, 100 (M =64 , F = 36, ratio 1.7:1) elderly subjects (age >65 years) were compared against 100 (M = 64, F = 36, ratio1.7:1), controls(< 65 years 54 M, 46 F, ratio 1.1:1) to find out prevalence of anosmia and cognitive impairment. Mean age in cases was 68.4±3.7 years and in controls was 39.4±7.9 years. Anosmia was detected in 64% of cases as compared to controls 4% (p <0.01) (Fig. 1).

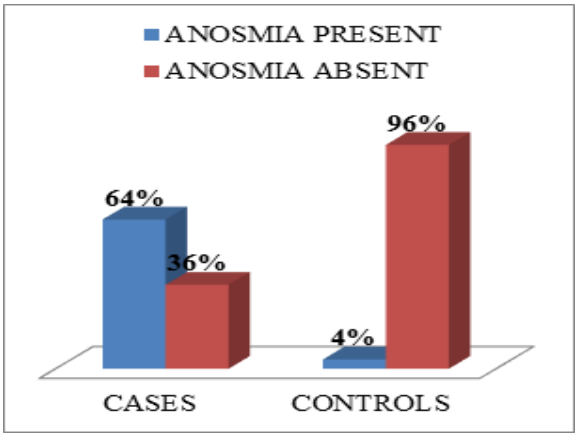

Fig. 1: Prevalence of anosmia in cases and controls

Mean INSIT score was significantly lower (4.02±1.88) in cases as compared to controis7.36±1.35, p<0.01) (Table 1).

Table 1: INSIT score in cases and controls

Mean INSIT score	Cases n = 100	Controls n = 100	p value
	4.02±1.88	7.36±1.35	<0.001

Present study demonstrated cognitive impairment to be prevalent in 50% of cases as compared to controls 1%, p <0.001 (Fig. 2).

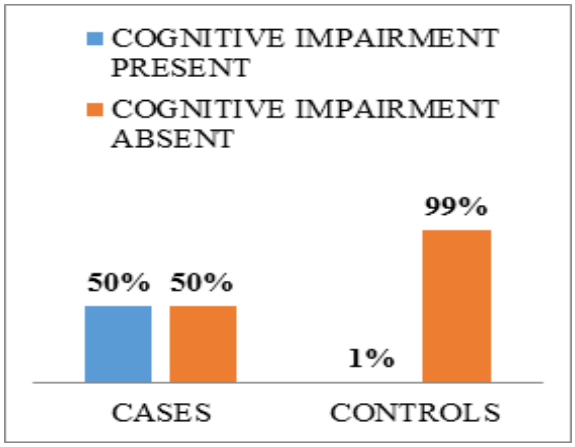

Fig. 2: Prevalence of cognitive impairment in cases and controls

Mean MMSE score was also significantly lower in cases (20.99±5.13) than controls (27.47±1.79, p<0.001) (Table 2).

Table 2: MMSE scores in cases and controls

Mean MMSE score	Cases n= 100	Controls n = 100	p value
	20.99±5.13	27.47±1.79	< 0.001

Present study demonstrated association of anosmia with cognitive impairment in elderly subjects (Table 3).

Table 3: Association of cognitive impairment with anosmia in cases

	Cases with anosmia n = 64	Cases without anosmia n= 36	p value
Cases with cognitive impairment (n = 50)	50 (78.12%)	0 (0%)	Chi sq.=56.25 P value= 6.38×10^{14}
Cases without cognitive impairment n= 50	14 (21.87%)	36 (100%)	

Cognitive impairment was prevalent in cases of anosmia than those without anosmia. However, there were no gender differences in prevalence of anosmia in cases (Table 4).

Table 4: Anosmia and cognitive impairment- gender differentiation in cases

	Males n = 64	Females n =36	p value
With anosmia	44 (68.75%)	20 (55.55%)	(chi sq.= 0.17, P value= 0.67 NS
Without anosmia	20 (31.25%)	16 (44.44%)	
With cognitive impairment	31 (48.43%)	19 (52.77%)	chi sq.= 0.17, P value= 0.67
Without cognitive impairment	33 (51.56%)	17 (47.22%)	

Diabetes mellitus was documented in 11% of cases as compared to controls (0%, p <0.001), hypertension was noted in 42% of cases and 16% (p<0.001) of controls. Ischaemic heart disease was present in20% cases and 11% of controls p <0.07, NS. Dyslipidaemia was reported in 72% of cases as compared to controls (33% p <0.001). Fasting and post prandial blood sugar, triglycerides, and LDL, systolic and diastolic blood pressure and were significantly higher in cases as compared to controls (Table 5).

Table 5: Biochemical parameters in cases and controls

Parameters	Cases	Controls	p value
FBS	96.54±21.67	90±6.96	0.002 (significant)
PPBS	129.55±30.23	120.94±7.55	0.003 (significant)
Cholesterol	150.68±36.13	146.02±25.33	0.14 (not significant)
Triglycerides	114.67±40.77	102.23±31.26	0.008 (significant)
VLDL	23.45±8.24	21.1±6.03	0.011(significant)
HDL	39.25±9.17	43.05±6.92	0.0005(significant)
LDL	89.23±36.48	78.94±23.90	0.009 (significant)
T3	1.08±0.23	1.036±0.22	0.06 (not significant)
T4	6.51±0.60	6.61±0.44	0.09 (not significant)
TSH	1.40±0.44	1.34±0.30	0.12(not significant)
Haemoglobin	12.47±0.96	12.95±0.91	0.0001 (significant)
Blood urea	16.4±3.86	15.29±3.20	0.01(significant)
Creatinine	0.82±0.22	0.778±0.18	0.04 (significant)

Table 6: Univariate analysis of cases

	Anosmia Present (n=64)	Anosmia Absent (n=36)	P Value
Cognitive Impairment Present	50 (78.12%)	0 (0%)	CHI SQ.= 56.25 P Value <0.0001
Cognitive Impairment Absent	14 (21.87%)	36 (100%)	Significant
Diabetes Mellitus Present	9 (14.06%)	2 (5.55%)	CHI SQ.= 1.70 P Value=0.19
Diabetes Mellitus Absent	55 (85.94%)	34 (94.44%)	Not Significant
Dyslipidemia Present	50 (78.12%)	22 (61.11%)	CHI SQ.= 3.30 P Value=0.068
Dyslipidemia Absent	14 (21.87%)	14(38.88%)	Not Significant
Hypertension Present	31 (48.44%)	11 (30.55%)	CHI SQ.= 3.02 P Value=0.08
Hypertension Absent	33 (51.56%)	25 (69.44%)	Not Significant

Univariate analysis revealed significant association of anosmia and cognitive impairment in elderly subjects however, present study did not demonstrate independent association of anosmia with co-morbidities viz. hypertension, Diabetes mellitus and dyslipidemia.

Discussion

Observational and clinical studies have found a significant association between olfactory impairment and subsequent cognitive decline. A large-scale study (n=1920) by Carla R et al[4] on the relationship between olfactory identification ability and general cognitive functioning as measured by Mini Mental State Examination (MMSE) indicated that olfactory dysfunction at baseline was significantly predictive of future cognitive impairment after 5 years (odds ratio (OR)=6.62; confidence interval (CI)=4.36–10.04, also reported low sensitivity of 55.1% but high specificity (84.4%) for olfactory assessment in predicting cognitive decline.

Present study demonstrated high (64%) prevalence of anosmia in elderly. Doty et al[5-7] reported that decreased olfactory function is very common in elderly population and is observed in more than 50% in subjects between the age group of 65 to 80 years and 75% in those above 80 years. Murphy et al[8-10] has found prevalence of impaired olfaction in the US to be 62.5% in people aged above 80 years. Wilson et al[11] reported that a negative correlation exists between age and olfaction scores on UPSIT.

Our study demonstrated high (50%) prevalence of cognitive impairment in elderly. Mary et al[10] has reported prevalence of mild cognitive impairment in the community dwelling subjects over 65 years to be 19.4%. Higher prevalence of cognitive impairment in our study could be because present study is a hospital based study and has a relatively small sample size.

Present study demonstrated significant association of anosmia and cognitive impairment in elderly. Peters et al[12] studied olfactory function in mild cognitive impairment and Alzheimer's disease and found anosmia in 12 out of 14 (85.7%) subjects of Alzheimer's disease and 7 out of 8 cases (87.5%) cases of mild cognitive impairment. Wilson et al[11] in his prospective study on olfactory function assessment and cognitive impairment reported that risk of developing mild cognitive impairment increased by 50% in subjects with below average scores on UPSIT. Mary et al[10] also reported the association of anosmia and cognitive impairment and mentioned that UPSIT scores were significantly related to ACE (for cognitive impairment) total scores (r=0.37, p 0.005).

Present study did not reveal association of anosmia in elderly with co-morbidities viz. Hypertension, IHD Diabetes mellitus, could be because of small sample size. However, further large sample size and prospective studies are essential to find out association of anosmia in elderly with co-morbidities.

A number of standardized olfactory tests are commercially available. Most of them evaluate the ability of patients to detect and identify odours or tastes. For example, the most widely used of these tests, the 40-item University of Pennsylvania Smell Identification Test (UPSIT). However, The Indian Smell Identification Test (INSIT) has an advantage that it represents familiarity in day to day life.

Olfactory abilities are primarily assessed by measuring threshold (lowest detectable concentration of odours), discrimination (ability to differentiate between odours) and identification (ability to identify odours). Sohrabi HR et al[13] studied association of cognitive decline and olfactory dysfunction in community dwelling subjects. The major novel finding of the study was that olfactory discrimination rather than odour identification (as measured by Sniffin' Sticks D) was a significant predictor of future cognitive decline over a 3-year period. The Author however, concluded that, the predictive value of olfactory assessment in screening those at a higher risk for AD and needs further research to improve its sensitivity and specificity.

Anosmia has been documented by INSIT test in the present study. INSIT test for detection of anosmia has been standardised and validated by George et al[14] for use in Indian patients. UPSIT (University Of Pennsylvania Smell Identification Test) has been used in various studies worldwide. In the present study, UPSIT test could not be used for detection of anosmia because it is costly and many Indian patients are not familiar with the ingredients used in the test. Present study has some limitations. Among the three components of olfactory testing, i.e. odour identification, odour threshold and odour discrimination, present study assessed odour identification. Association of anosmia with neuroimaging abnormalities has also not been analysed in the present study.

INSIT test is a simple, bedside clinical screening tool, easy to perform and is non expensive hence can be routinely performed for detection of anosmia in elderly subjects. As it is associated with cognitive impairment, it can be predicted as a marker of cognitive impairment and subjects with anosmia can be further examined and investigated for assessment of neurodegenerative diseases. Even though these diseases cannot be completely cured, interventions to prevent progression of diseases and controlling symptoms and optimising can be helpful to improve quality of life in these cases. However, large sample sized, community based, prospective and standardised studies are essential.

Conclusions

Mild cognitive impairment, an early manifestation of Alzheimher's disease is prevalent in elderly.

Anosmia, a surrogate marker of cognitive impairment and a manifestation of neurodegeneration is also prevalent in elderly and can be detected by simple bedside method i.e. 'INSIT test. In elderly subjects, anosmia is associated with cognitive impairment and can be a marker of cognitive impairment in elderly. However, multi-centric, large sample sized, better standardised prospective studies are essential to assess the exact role of anosmia in predicting neurodegeneration, morbidity and quality of life.

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