Original Article

Anosmia Marker of Cognitive Impairment in Elderly

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ABSTRACT

Background : The prevalence of olfactory impairment and cognitive impairment increase with age. Olfactory impairment has been associated with neurodegenerative diseases, such as Alzheimer's disease (AD) and Parkinson's disease. 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

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 and, 3) To find out the association of anosmia and cognitive impairment in the elderly.

Methods : Present study is a hospital based, observational, case-control study, in which 100 elderly subjects age > 65 years attending the geriatric OPD, were included as cases and 100 subjects < 65 years, as controls. Anosmia was assessed by Indian Smell Identification Test (INSIT), in which 10 essences were used & 1 point was awarded for correct & 0 for incorrect identification. A score of ≤ 4 indicates anosmia. Cognitive impairment was diagnosed by 30 point mini-mental state examination (MMSE) where scores ≤ 23 indicates cognitive impairment.

Results : 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 controis 7.36 + 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, ($p<0.001$). Univariate analysis revealed significant association of anosmia and cognitive inpairment in elderly subjects however, present study did not demonstrate independent association of anosmia with hypertension, Diabetes mellitus and dyslipidemia. There were no significant gender differences in prevalence of anosmia and cognitive impairment in elderly subjects.

Conclusions : Anosmia is prevalent in elderly. In elderly subjects, anosmia is associated with cognitive impairment.

Key Words : Anosmia, Cognitive impairement, Dementia, INSIT Score, MMSE.

Introduction :

The prevalence of olfactory impairment and cognitive impairment increase with age.[1-3] Olfactory impairment has also been associated with neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease.[4-6]

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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.[7-9] A recent study found the density of tangles present in the central olfactory system was inversely related to odor identification ability.[10]

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 and
3) To find out the association between anosmia and cognitive impairment in the elderly.

Methods :

Present study is a hospital based, cross sectional, observational study carried out on 100 elderly subjects with age > 65 years attending geriatric out patient 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 as 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. The odorants were kept in 20 ml air tight commercially available bottles. Cotton buds dipped in the essence were placed 1 cm in front of each nostril with the other nostril closed and the procedure repeated with the other nostril. The subjects were asked to sniff and identify smell from the answer card containing 4 choices ror each odorant. First response was considered as the answer and score of 1 was awarded for correct and 0 for wrong answer, 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.[11]

Cognitive impairment was assessed by Mini Mental State Examination (MMSE) Score < 23 is considered as presence of cognitive impairment. MMSE assessment was performed by the person blinded for the study. All subject underwent clinical examination. Comorbidities 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.

Results :

In the present study, 100 (M 64, F 36 ratio 1.7:1) elderly subjects (age > 65 years) were compared against 100 controls (< 65 years) 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. M 64, F 36, M:F 1.7:1 in cases, M:F 1.1:1 in Controls. Anosmia was detected in 64% of cases as compared to controls 4% ($p<0.01$) ***(Fig. 1).*** Mean INSIT score was significantly lower (4.02 + 1.88) in cases as compared to controls (7.36 + 1.35, $p<0.01$) ***(Table 1).***

Cognitive impairment was prevalent in 50% of cases as compared to controls 1%, $p<0.001$ ***(Fig. 2).*** Mean MMSE score was also significantly lower in cases (20.99 + 5.13) than controls (27.47 + 1.79, $p<0.001$) ***(Table 2).***

Present study demonstrated association of anosmia with cognitive impairment in elderly subjects. However there was no gender differences in prevalence of anosmia in cases. ***(Table 3 & 4).***

Diabetes mellitus was documented in 11% of cases as compared to controls (zero%, p<0.001) hypertension was noted in 42% of cases and 16% (p<0.001) of controls. Ischaemic heart disease was present in 20% cases and 11% of controls p<0.07, NS Dyslipidemia 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).***

Univariate analysis revealed significant association of anosmia and cognitive inpairment in elderly subjects however, present study did not demonstrate independent association of anosmia with hypertension, Diabetes mellitus and dyslipidemia ***(Table 6).***

Discussion :

Present study demonstrated anosmia to be prevalent (64%) in elderly. Doty *et al*[12] reported that decreased olfactory function is very common in elderly population, being present in > 50% in subjects between the age group of 65 to 80 years and 75% in those above 80 years. Murphy *et al*[13] found prevalence of impaired olfaction in the US to be 62.5, 5 of people aged above 80 years. Wilson *et al*[14] reported that a negative correlation exists between age and olfaction scores on UPSIT.

Our study reported cognitive impairment to be prevalent in 50% in elderly. Mary *et al*[15] reported prevalence of mild cognitive impairment in the community dwelling subjects over 65 years to be 19.4%. Higher prevalence 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*[16] 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*[17] 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*[18] 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).

Anosmia has been documented by INSIT test in the present study, which has been standardised and validated by George *et al* for use in Indian patients[19]. UPSIT (University of Pennsylvania Smell Identification Test) is used in various studies worldwide was not chosen because it is costly and many Indian patients are not familiar with the ingredients used in the test.[20] In the present study, odour identification has been assessed. However, odour threshold has not been tested. Odour threshold, discrimination and quantification assessment can give further insights into the role of olfactory function in neuro degeneration. Association with neuroimaging abnormalities has also not been analysed in the present study. Present study is a hospital based, cross sectional 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

Conflicts of interest : none reported by authors.

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Fig. 1 : **Prevalence of anosmia in cases and controls**

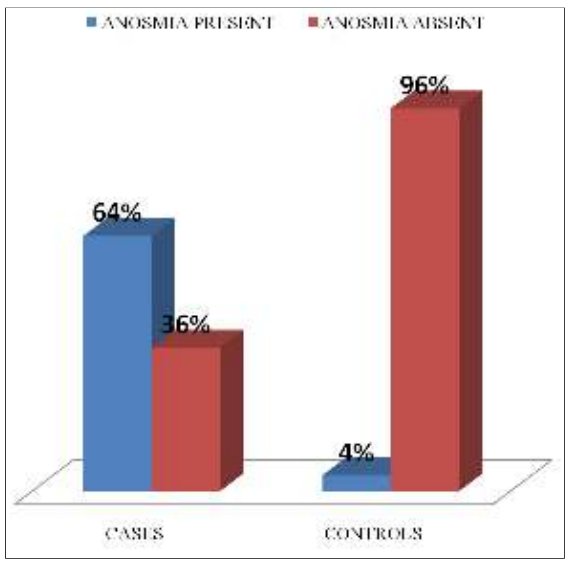

Fig. 2 : **Prevalence of cognitive impairment in cases and controls**

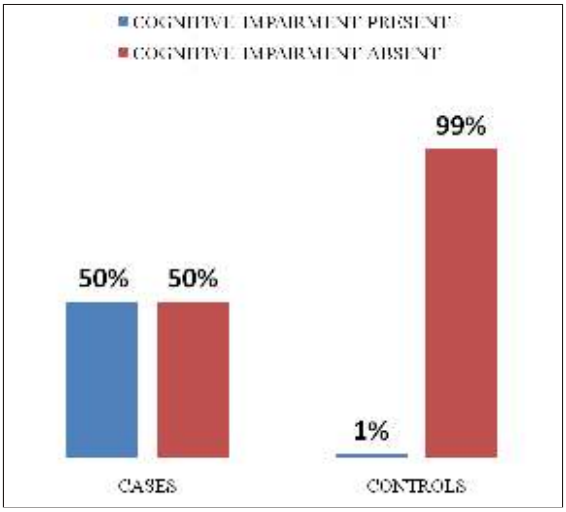

Table 1 : **INSIT Score in Cases and Controls**

Mean Insit Score	Cases N = 100	Controls N = 100	P Value
	4.02 ± 1.88	7.36 ± 1.35	<0.001

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

Table 4 : **Anosmia and Cognitive Impairment - Gender Differentiation in Cases**

	Males N = 64	Females N = 36	
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 = 0.67NS
Without Cognitive Impairment	33 (51.56%)	17 (47.22%)	

S = Statistically significant.
NS = Statistically not significant

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 x 10-14
Cases Without Cognitive Impairment N= 50	14 (21.87%)	36 (100%)	

Table 5 : **Biochemical Parameters in Cases and Controls**

Parameters	**Cases**	**Controls**	**P Value**	
FBS	96.54 ± 21.67	90 ± 6.96	0.002	S
PPBS	129.55 ± 30.23	120.94 ± 7.55	0.003	S
Cholesterol	150.68 ± 36.13	146.02 ± 25.33	0.14	NS
Triglycerides	114.67 ± 40.77	102.23 ± 31.26	0.008	S
VLDL	23.45 ± 8.24	21.1 ± 6.03	0.011	S
HDL	39.25 ± 9.17	43.05 ± 6.92	0.0005	S
LDL	89.23 ± 36.48	78.94 ± 23.90	0.009	S
T3	1.08 ± 0.23	1.036 ± 0.22	0.06	NS
T4	6.51 ± 0.60	6.61 ± 0.44	0.09	NS
TSH	1.40 ± 0.44	1.34 ± 0.30	0.12	NS
Haemoglobin	12.47 ± 0.96	12.95 ± 0.91	0.0001	S
Blood Urea	16.4 ± 3.86	15.29 ± 3.20	0.01	S
Creatinine	0.82 ± 0.22	0.778 ± 0.18	0.04	S

S = Statistically significant. NS = Statistically not significant

Table 6 : **Univariate Analysis of Cases**

		Anosmia Present (N=64)	**Anosmia Absent (N=36)**	**P Value**
Cognitive Impairment	+	50 (78.12%)	0 (0%)	Chi Sq. = 56.25
	-	14 (21.87%)	36 (100%)	P Value < 0.001
				S
Diabetes Mellitus	+	9 (14.06%)	2 (5.55%)	Chi Sq.= 1.70
	-	55 (85.94%)	34 (94.44%)	P Value = 0.19
				NS
Dyslipidemia	+	50 (78.12%)	22 (61.11%)	CHI SQ. = 3.30
	-	14 (21.87%)	14(38.88%)	P Value = 0.068
				NS
Hypertension	+	31 (48.44%)	11 (30.55%)	Chi Sq.= 3.02
	-	33 (51.56%)	25 (69.44%)	P Value = 0.08
				NS

S = Statistically significant. NS = Statistically not significant