

Clinical Profile Of Dementia And Its Association With Homocysteine

Narender Pal Jain*, Shweta Gupta**, Sanjeev Kumar Singla***, Rajinder Kumar Bansal****, Manbir Singh*****

*Associate Professor, Department of Medicine, **Associate Professor, Department of Obstetrics & Gynaecology, ***Associate Professor, Department of Surgery, ****Professor, Department of Neurology *****Department of Medicine, Dayanand Medical College & Hospital, Ludhiana 141 001, Punjab, India

Abstract : Background & Objectives : Dementia is a serious loss of cognitive ability in a previously unimpaired person, beyond what might be expected from normal ageing. This cross sectional study was undertaken to study clinical profile of dementia and its association with plasma homocysteine levels. Methods : 30 patients (indoor or outdoor) > 55 years with dementia were screened on Mini-Mental State Examination (MMSE) and Clinical Dementia Rating (CDR) Scale. A clinical dementia rating questionnaire was asked and plasma homocysteine levels measured by ELISA using Bio-rad reagents. Data was collected and statistically analyzed. Results : There was a statistically significant correlation between loss of memory ($p = 0.047$), orientation ($p = 0.038$), judgement/problem solving ($p = 0.048$), outer ($p = 0.042$), household ($p = 0.048$) and personal care activity ($p = 0.0099$) with hyperhomocysteinemia. A statistically significant correlation was found between CDR ($p = 0.0081$) and MMSE ($p = 0.0095$) score with hyperhomocysteinemia. Interpretation & Conclusion : A significant correlation was seen between memory loss, worsening of cognitive dementia, limitation of household activity, worsening of personal care, impairment of judgment and problem solving with hyperhomocysteinemia. As hyperhomocysteinemia can be effectively treated with a low cost therapy of B vitamin supplements, it is important to recognize these problems and treat them early. [Jain N et al NJIRM 2013; 4(4) : 80-84]

Key Words: Clinical dementia rating score, cognitive impairment, hyperhomocysteinemia, Mini-Mental State Examination score.

Author for correspondence: Dr. Narender Pal Jain, E-37, Tagore Nagar, Ludhiana 141001, Punjab, Fax: 0161 2302620 Mo: 09814702016, Email id: narenjain@sify.com

Introduction: Dementia is a serious loss of cognitive ability in a previously unimpaired person, beyond what might be expected from normal ageing. It may be static, the result of a unique global brain injury, or progressive, resulting in long-term decline due to damage or disease in the body.

Alzheimer disease is the most common type of dementia. Although dementia is far more common in the geriatric population, it may occur in any stage of adulthood¹. It is a complex disorder; genetic, environmental and/or lifestyle factors may be involved in the onset and progression of disease². The rapid growth of the elderly population and of the population with dementia will impose significant economic and psychosocial burdens on caregivers and societies, likely posing major problems. To reduce these societal and individual burdens; prevention, early detection and early treatment may be the most important steps to take.

Many studies designed to identify risk factors and correlates of dementia and programs for the early detection and treatment of dementia patients in the general population have been reported³. One of

such factor is homocysteine levels. Relatively small changes in homocysteine may dispose to pathological outcomes⁴. Normal levels of homocysteine are 0.54-2.3 mg/L (4-17 $\mu\text{mol/L}$). Patients with Alzheimer disease have both lower B vitamin and higher total homocysteine concentrations than do nondemented patients. Furthermore, lower concentrations of B vitamins and elevated homocysteine have been related to the severity of disease⁵. Imaging studies of brain morphology generally support associations between hippocampal atrophy and white matter hyperintensities and high homocysteine concentrations^{3,6}.

As elevated plasma homocysteine can be effectively treated with B vitamin supplements (folic acid, vitamin B-12, and vitamin B-6), a therapy that is inexpensive, it lays further stress on the need of studying this factor in bigger perspective. This is a cross sectional study undertaken to study clinical profile of dementia and the association between dementia and plasma homocysteine levels.

Material and Methods: The patients (indoor or outdoor) ≥ 55 years of age, presenting with the

complaints of recent memory or cognitive impairment in the departments of Medicine, Neurology or Psychiatry of Dayanand Medical College and Hospital Ludhiana over a period of 18 months (01.01.2011 to 30.06.2012) were enrolled in the study after obtaining approval from the ethical committee. The patients with a history of stroke, ischaemic heart disease, other co-morbid neurological disease or psychiatric disease were excluded. The patients who met the criteria of dementia (ICD 10/DSM IVTR) of any type were screened on Mini-Mental State Examination⁷ (MMSE) and Clinical Dementia Ratings (CDR) Scale⁸ was used for further evaluation after obtaining the informed consent. A clinical dementia rating questionnaire was asked and plasma homocysteine levels were measured by ELISA using Bio-rad reagents. A total number of 30 cases were studied. Statistical analysis was done using student 't' test and z test.

Results : The mean age of the subjects in this study was 72 years; 17 (56.67%) of age ≤ 72 and 13

(43.33%) of > 72 years (p = 0.15976). Majority (40%) of the subjects were in 55 – 65 years and 13 % were between 86 -95 years.

There was a statistically significant association (p = 0.047) of gender with dementia as 19 (63.33%) of the subjects were male indicating towards male sex predilection. 17 (90%) of the subjects were literate with majority i.e. 11 (36.67%) subjects educated up to high school age and graduation each. 3 (10%) subjects were illiterate and 3 (10%) were postgraduate. 100 % of the subjects analyzed in this study were married.

29 (96.67%) of the subjects were not working at the time of study. Most (36.67%) of them had been employed in various services. The second most common profession had been business (26%). Of these 5 (16.67%) women had been housewives. 100% of the subjects were vegetarian. There was a statistically significant loss of memory, orientation, judgement/problem solving, outer and personal care activity in patients with dementia (Table 1)

Table 1: Distribution of subjects according to various symptoms

	Memory loss No. (%)	Orientation loss No. (%)	Judgement/ problem solving No. (%)	Outer activity No. (%)	Household activity No. (%)	Personal care activity No. (%)
Nil	0	0	0	3 (10.00)	1 (3.33)	11 (36.67)
Slight	7 (23.33)	4 (13.33)	9 (30.00)	7 (23.33)	11 (36.67)	0
Mild	11 (36.67)	13 (43.33)	9 (30.00)	9 (30.00)	7 (23.33)	10 (33.33)
Moderate	9 (30.00)	11 (36.67)	11 (36.67)	6 (20.00)	9 (30.00)	6 (20.00)
Severe	3 (10.00)	2 (6.67)	1 (3.33)	5 (16.67)	2 (6.67)	3 (10.00)
Mean	1.38	1.43	1.28	1.32	1.22	1.03
SD	0.80	0.70	0.72	0.98	0.82	1.00
≤1	7 (23.33)	4 (13.33)	9 (30.00)	10 (33.33)	12 (40.00)	11 (36.67)
>1	23 (76.67)	26 (86.67)	21 (70.00)	20 (66.67)	18 (60.00)	19 (63.33)
p-value	0.00625	0.00454	0.00838	0.00999	0.10651	0.04744

A statistically significant correlation was observed between loss of memory, orientation, judgement/ problem solving, outer, household and personal care activity with hyperhomocysteinemia (Table 2). 60 %

of the subjects had CDR score more than 5. 83% of the subjects had MMSE score up to 23 (Table 3)

Table: 2 Relationship between various symptoms and plasma homocysteine levels

	Abnormal Homocysteine Mean	Abnormal Homocysteine SD	Normal Homocysteine Mean	Normal Homocysteine SD	p-value
Memory loss	1.67	0.88	1.10	0.60	0.04728
Orientation loss	1.73	0.78	1.13	0.48	0.03862
Judgment/ problem solving	1.53	0.72	1.03	0.64	0.04875
Outer activity	1.70	0.98	0.93	0.84	0.04242
Household activity	1.50	0.85	0.93	0.70	0.04888
Personal care	1.47	1.13	0.60	0.63	0.00991

Table 3: Distribution of subjects according to CDR and MMSE score

CDR score	No.	%	MMSE Score	No.	%
Up to 5	12	40.00	Up to 23	25	83.33
5-10	12	40.00	> 23	5	16.67
>10	6	20.00	Mean	17.56	
Mean	7.12		SD	5.15	
SD	3.74		p-value	0.00500	
p-value	0.04744				
Up to 5 vs. 5-10	NA				
Up to 5 vs. >10	0.09762				
5-10 vs. >10	0.09762				

Table 4: Distribution of subjects according to plasma homocysteine levels

Homocysteine ($\mu\text{mol/L}$)	No.	%age
Up to 10	8	26.67
10-20	11	36.67
20-30	7	23.33
>30	4	13.33
Mean	17.77	
SD	10.30	
Up to 18	18	60.00
>18	12	40.00
p-value	0.10651	

The mean CDR score in patients with normal homocysteine levels was 5.23 (SD = 2.01) and in patients with abnormal homocysteine levels was 9.0 (SD = 4.17); the difference was statistically significant ($p = 0.008$). The mean MMSE score in patients with normal homocysteine levels was 15.73 (SD = 4.32) and in patients with abnormal

homocysteine levels was 19.87 (SD = 5.00); the difference was statistically significant ($p = 0.009$). Hyperhomocysteinemia showed a significant inverse relation with MMSE scoring done in people with cognitive disorder. Table 4 shows the distribution of the subjects according to plasma homocysteine levels. 60% of the subjects had homocysteine levels up to 18, while 40% had levels more than 18; the difference was statistically non significant ($p = 0.10651$)

Discussion: The findings of our study show male predominance (63%). Similar observation has been made by other authors too⁹. Whereas Kim et al¹⁰ concluded that dementia is more prevalent in females due to cumulative social disadvantages like lack of educational opportunities which hinders access to employment and personal development¹¹. The reason for male predominance in our study may be because the consent for participation in the study was given mostly by the males.

The mean age of the subjects in this study was 72 years. High prevalence of dementia has been observed in people with mean age of 76 and 81 years by other authors^{3,11}. Majority of the subjects in our study were earlier employed and had been working in various sectors. The awareness, professional requirements, more involvement of cognitive functions in these groups may be a reason of earlier detection of the signs and symptoms of the disease.

Our study was suggestive of higher prevalence of dementia among low education and illiterate subjects which is comparable to studies done by many authors^{9,11}. It is more meaningful in Indian population as large percentage of people live in villages in India where access to formal education is less. A continuous pattern of decrease in the prevalence of dementia has been observed with an increase in the educational level⁹. The study shows significant relation between memory loss and hyperhomocysteinemia. This is supported by most of the studies done in western society¹².

In our study it was found that hyperhomocysteinemia has an impact on global cognitive function causing decline in all five functions of cognition evaluated in clinical dementia scoring. It is supported by many authors^{3, 13} who concluded that hyperhomocysteinemia might be associated with rapid cognitive decline in Alzheimer's disease and plasma homocysteine level is a strong, independent risk factor for the development of dementia.

Quadri P et al¹⁴ studied 314 consecutive subjects. Disease stage was rated by means of the CDR scale and the Mini-Mental State Examination (MMSE) - a brief cognitive test widely used in clinical practice and epidemiologic studies—was administered to grade the subjects' global cognitive impairment as similar to our study¹³. The study suggests a strong association between prevalence of mild dementia with both high plasma total homocysteine concentrations and relatively low serum folate concentrations. In our study also we found that hyperhomocysteinemia is associated with worsening of MMSE score and CDR score.

In our study we found 80 % of subjects have CDR score more than 5 and 20 % of subjects have CDR score more than 10. Relationship between CDR score and hyperhomocysteinemia was found to be statistically significant ($p = 0.0081$). 83% of subjects have MMSE score up to 20. Relationship between MMSE score & hyperhomocysteinemia was found to be statistically significant (with p value =0.005).

Kim MD et al¹⁰ studied the prevalence of dementia and its correlation with socioeconomic status; role of social support system and poor performance on MMSE score and had many results comparable to our study. They concluded that the prevalence of dementia was very high in persons with low score in Korean version of MMSE score. In this study, multivariate analysis revealed that advanced age, no education, living in a nursing home, and depression were correlated with dementia. Marital status, economic status, and urban/rural residence were not associated with dementia after controlling for age, sex, education level, and other factors like depression, traumatic brain injury, and number of medical illnesses. This study as mentioned earlier also established age and gender (female) as risk factor for dementia.

Tucker et al concluded that a high homocysteine concentration was associated with a decline in recall memory¹⁵.

Conclusion: Dementia has now become a well recognized geriatric disease which has both social and medical perspective. Our study showed an increase in the prevalence of dementia with increase in the age, a sex predilection for males and a significant association with lower education status. The study showed a significant relation between memory loss, worsening of cognitive dementia, limitation of household activity, worsening of personal care, impairment of judgment and problem solving with hyperhomocysteinemia. A significant inverse relation was observed between MMSE scoring and hyperhomocysteinemia in people with cognitive disorder. Hyperhomocysteinemia had significant relationship with worsening of cognitive dementia rating causing global worsening of cognitive function.

With progressively increasing geriatric population, the problem of dementia and cognition dysfunction is also rising. It has to be dealt with on daily basis practice as the latter seriously compromises the quality of life. The fact that the elevated plasma homocysteine can be effectively treated with B vitamin supplements (folic acid, vitamin B-12, and vitamin B-6), a therapy that is rather inexpensive, it lays further stress on the need of recognizing these problems and treating them early and effectively.

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