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Original Research Article

A HOSPITAL BASED OBSERVATIONAL STUDY TO DETERMINE THE PSYCHIATRIC MORBIDITY, SUBSTANCE USE, QUALITY OF LIFE IN PERSON WITH EARLY ONSET AND LATE ONSET DEMENTIA

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ABSTRACT

Background: Dementia is typically defined as a clinical syndrome of cognitive decline that is sufficiently severe to interfere with social or occupational functioning. Early onset dementia (EOD) patients differ from late onset dementia (LOD) patients on a number of clinical, neuropsychological, neuropathological, and neuroimaging variables. With this background, the current research was done to determine the psychiatric morbidity, substance use, quality of life in persons with early onset and late onset dementia and to compare the differences in above factors between early onset and late onset dementia.

Material and Methods: This is a hospital based prospective study done on 50 Patients attending the department of psychiatry, SMS Medical College, Jaipur, Rajasthan, India during one-year period. Study sample had been grouped into two categories as early onset and late onset dementia (25+25) based on the age of onset (< 65). DEMENTIA SEVERITY RATING SCALE will be administered to grade the severity of dementia. Psychiatric comorbidity and substance use were assessed using MINI PLUS INTERNATIONAL NEUROPSYCHIATRY INTERVIEW scale. Quality of life was measured using DEMQOL & DEMQOL proxy scale. Data was entered into excel and analyzed using SPSS v 16.0. Mean and standard deviation were calculated to summarize continuous variables such as age, DSRS scores and DEMQOL scores Number and percentage was used to present the categorical data pertaining to the following distribution of the various socio-demographic variables, types of psychiatric co-morbidities and dementia.

Results: Our study showed that the patients in late onset category were significantly older than the other group. However, majority of the patients in early onset were males (64%) and hence a little more half of the patients (52%) were accompanied by their wife. There was statistically significant higher DSRS scores ($p<0.05$) among those in early onset group on comparison with the late onset group. In line with the DSRS scores, the quality of life as measured by the DEMQOL scale was significantly higher ($p<0.05$) in late onset dementia group on comparison with early onset dementia group. All the subscales of DEMQOL construct had significantly higher scores in patients with late onset dementia.

Conclusion: We concluded that participants with both early and late onset dementia had no significant differences in psychiatric co- morbidities and substance abuse. However, those with early onset dementia had significantly higher DSRS scores and less QOL scores indicating higher functional disabilities and the need for early intervention in this subgroup for better quality of life.

Keywords: Early Onset Dementia, Late Onset Dementia, QOL, DEMQOL, DSRS, MINI Plus scale.

INTRODUCTION

Dementia is typically defined as a clinical syndrome of cognitive decline that is sufficiently severe to interfere with social or occupational functioning. It is an umbrella term for a group of cognitive disorders characterized by progressive decline in cognitive function interfering with independently carrying out activities of daily life due to brain damage or disease, but not related to delirium or depression.[1]

Dementia is a neurodegenerative syndrome characterized by multidimensional progression consisting of three core dimensions: cognitive, functional and psychiatric symptoms, with functional symptoms being defined as a decreased ability to independently perform daily life activities.[2] Its prevalence is increasing rapidly due to aging of most societies, though incidence seems to decline in people with high educational levels in high income countries.

According to the definition provided by the World Health Organization (WHO, 2017), dementia is "an umbrella term for several diseases affecting memory, other cognitive abilities and behaviour that interfere significantly with the ability to maintain daily living activities. Although age is its strongest known risk factor, dementia is not a normal part of aging". The associated brain diseases can cause a long-term, often gradual decrease in cognitive abilities, "emotional problems, language difficulties and decreased motivation". The definition provided by the U.S. National Institute of Neurological Disorders and Stroke (NINDS, 2018) is more detailed in stating that dementia is "a group of symptoms caused by disorders that affect the brain. It is not a specific disease" and "memory loss is a common symptom of dementia. However, memory loss by itself does not mean having dementia. People with dementia have serious problems with two or more brain functions, such as memory and language. Although dementia is common in very elderly people, it is not part of normal aging.[3]

Many different diseases can cause dementia, including Alzheimer disease (AD), fronto-temporal dementia (FTD), Lewy body dementia (LBD), vascular dementia (VD), syphilitic dementia (SD), mixed dementia (MD), senility dementia (SD), or the combined effect of two or more dementia types, and even stroke. About 10% of individuals present with Mixed Dementia, a usual combination of AD and another type of dementia such as FTD or VD. However, not being a specific disease, the above potential contributors do not reach to the primary cause of the disease. There lies our greatest shortcoming: unable to pinpoint the root cause of the disease, we are powerless in treating it. Sure, drugs are available to treat some of the symptoms of these contributing diseases but not the diseases themselves. Likewise, drugs available for dementia can also only alleviate its symptoms; they cannot cure it or repair brain damage. They may improve symptoms or at best slow down the disease. Indeed, there is no known cure for dementia. This is a sad observation on the state of the situation. It stems from our incomplete understanding of the deep biology of the contributing diseases and associated epigenetic/ Eco genetic influences.[2,4-6]

Most common early-onset neurodegenerative dementia is EOD. Vast majority of the cases are non-familial as indicated in few Epidemiological studies, making up about 4–6% of all Dementia, with an annual incidence rate of about 6.3/100,000 and a prevalence rate of about 24.2/100,000 in the 45–64 year age group, or between 220,000 and 640,000 Americans. As patients approach age 65 these incidence and prevalence rates rise exponentially. Since EOD is often atypical it is unfortunately missed often, leading to a 1.6-year average delay in diagnosis compared to older patients. Yet, EOD accounted for a more number of premature deaths among US adults aged 40–64 with many years of potential life lost as well as losses in productivity based on a mortality report from 1999 to 2010.[7,8]

Early onset dementia (EOD) patients differ from late onset dementia (LOD) patients on a number of clinical, neuropsychological, neuropathological, and neuroimaging variables. Several studies indicate that the clinical course tends to be more aggressive in early-onset dementia patients. Compared to LOD, EOD presents less commonly with memory deficits and more frequently as focal cortical or phenotypic variants. Overall, EOD patients have better memory recognition scores and semantic memory, but they tend to have worse attention, executive functions, ideomotor praxis, and visuospatial skills compared to comparably impaired LOD patients.[9,10] On magnetic resonance imaging (MRI), greater neocortical atrophy, particularly in parietal cortex, with less atrophy in the mesial temporal lobe (MTL) is seen in EOD patients.[10]

Even though studies in various western countries have differentiated the differences between pathological and morphological changes in EOD and LOD, there are a dearth of studies in India profiling the differences in risk factors for these two subtypes. With this background, the current research was done to determine the psychiatric morbidity, substance use, quality of life in persons with early onset and late onset dementia and to compare the differences in above factors between early onset and late onset dementia.

MATERIAL AND METHODS

This is a hospital based prospective study done on 50 Patients attending the department of psychiatry, SMS Medical College, Jaipur, Rajasthan, India during one-year period.

Inclusion Criteria

- Patient diagnosed as dementia as per ICD-10 criteria.

- Patients and caregivers who give written and informed consent.
- Both males and females.

Exclusion Criteria

- No reliable informant
- Not given informed consent
- Acute confusional state
- Cognitive impairment due to primary psychiatric illness
- Past history of any major psychiatric illness except substance use

Sampling Procedure

Patients newly diagnosed with dementia as per ICD -10 were continuously enrolled for the study after obtaining informed consent. The enrolment was continuous till the adequate sample size was achieved. Necessary precautions were made to have a sample of 25 in early onset and 25 in late onset dementia types.

1. Dementia Severity Rating Scale

It is usually completed by caregiver and rates the subject in 11 categories across 12 items in a multiple-choice format to obtain information about the subject's ability to function in their home and environment. Interestingly Washington University Clinical Dementia Rating scale mirrors the first 6 items of this scale. The care giver rates the subject according to the descriptions in increasing degree of severity from zero and the total score is derived from adding the numbers chosen from each category. Therefore, a score of zero indicates normal functioning and a maximally impaired person would score 51. It is most widely used because of its high reliability and better correlation with measures of overall severity and specific cognitive functions.

2. MINI PLUS SCALE- For diagnosing psychiatric comorbidity as per ICD-10 criteria & to asses substance use

For DSM-IV and ICD 10 psychiatric disorders psychiatrist and clinicians in the United States and Europe jointly developed a short structured diagnostic interview scale called M.I.N.I plus (Mini international Neuropsychiatric Interview) scale which can bead ministered within 15 minutes. It can be used as a first step in outcome tracking in non-research setting and in epidemiology studies and multicenter clinical trials as it is designed to meet the need for an accurate but short structured psychiatric interview required in those settings. Because of its good psychometric properties, it is more widely used in psychiatry to support the diagnostics of more common psychiatric disorders according to ICD 10 and axis I DSM IV TR.

3. DEM-QOL (Quality of life)–patient version and proxy version

Health related quality of life is assessed at all stages of dementia severity by means of DEM-QOL and DEM-QOL proxy on a 4-point Likert- type response scale. DEM-QOL consists of 28 questions and DEM-QOL- Proxy consists of 31 questions derived from five conceptual domain namely health and wellbeing, cognitive functioning, daily activities, social relationships and self-concept. It is administered by interviewer. Apart from this there are also additional overall quality of life questions which is also answered on a 4-point likert scale which includes very good, good, fair, poor.

After completing all the questions according to standard algorithm the items are scored to produce overall score in which better health related quality of life is represented by higher scores. This scale is also designed to work across various dementia subtypes thereby establishing disease specific instrument. This scale is also validated in a UK population and shows psychometric properties comparable with the best available instruments therefore most often used in research studies like QoL-AD.

Statistical analysis:

Mean and standard deviation were calculated to summarize continuous variables such as age, DSRS scores and DEMQOL scores Number and percentage was used to present the categorical data pertaining to the following distribution of the various socio-demographic variables, types of psychiatric co-morbidities and dementia. The distribution of continuous variables with normal distribution among the two patient groups was analyzed using Independent t test. For those variables with continuous skewed distribution, association between two patient groups was studied using Mann- Whitney U test. Statistical significance was set at p value of less than or equal to 0.05.

RESULTS

Our study showed that the patients in the late onset category were significantly older than the other group. However, majority of the patients in early onset were males (64%) and hence a little more half of the patients (52%) were accompanied by their wife. [Table 1] Both the groups had a median duration of illness of around 2 years. However, patients in late onset dementia had a wider range of duration of illness starting from few months to 8 years.

The present study shows that the distribution of the Psychiatric Co-morbidity among the two-patient group based on ICD 10 codes in Mini plus scale. Among those with early onset dementia, the leading psychiatric co-morbidities were F06.2-Psychotic disorder due to general medical condition (8%), F41.1-Generalized Anxiety disorder (8%) and F10.2-Mental and behavioural disorders due to use of alcohol – Dependence syndrome (8%). In late onset dementia patients, the top psychiatric co-morbidities were F41.1-Generalized Anxiety disorder (12%) and F32.x-Major depressive episode- current (12%). The distribution of these psychiatric co-morbidities wasn't statistically significant. [Table 2]

Table 3 shows the distribution of psychiatric comorbidity as per the MINI plus module among the two-patient group. Among those with early onset dementia, the leading psychiatric co-morbidities (MINI plus module) were A -Major Depressive Episode (16%), P-Generalized Anxiety Disorder (12%) and K-Alcoholic Dependence (12%). In late onset dementia patients, the top MINI plus module psychiatric comorbidities were A -Major Depressive Episode (16%) and P-Generalized Anxiety Disorder (16%). The distribution of these MINI plus codes wasn't statistically significant.

Among patients with early onset dementia, an equal proportion (16%) of patients consumed alcohol, tobacco and both. In patients with late onset dementia, about 16% consumed alcohol, 8% tobacco and 12% both alcohol and tobacco (table 4).

The mean score in the early onset group was 31.94 (±9.62) while in late onset group was 26.26 (±8.54). There were statistically significantly higher DSRS scores (p=0.026) among those in early onset group on comparison with the late onset group. [Table 5]

Our study showed that the comparison of DEMQOL scale and subscale scores among the two-patient groups. For the feeling subscores, the mean score in early onset group was 22.96 (±3.82) while in late onset group was 25.89 (±3.76). For the memory subscores, the mean score in early onset group was 13.75 (±2.31) while in late onset group was 15.38 (±3.16). Similarly, for Everyday life scores subscores, the mean score in early onset group was 18.36 (±2.33) while in late onset group was 20.45 (±3.63). For the overall subscores, the mean score in early onset group was 1.94 (±0.752) while in late onset group was 1.94 (±0.79). There were statistically significant higher DEMQOL scale and subscale scores (p<0.05) among those in late onset group on comparison with the early onset group. [Table 6]

Table 1: Distribution of the socio-demographic variables among the two patient groups

Socio-demographic variables		Late onset dementia (n=25)	Early onset Dementia (n=25)	P value
Age of the patients, mean(±SD)		73.58±6.24	62.78±4.69	<0.001*
Gender, n (%)	Male	12 (48%)	16 (64%)	>0.05
	Female	13 (52%)	9 (36%)	
Caretaker, n (%)	Daughter	9 (36%)	6 (20%)	>0.05
	Wife	6 (24%)	13 (52%)	
	Daughter in-law	2 (8%)	2 (8%)	
	Husband	1(4%)	4 (16%)	
	Son	4 (16%)	0	
	Sister	2 (8%)	0	
	Warden	1 (4%)	0	

Table 2: Distribution of Psychiatric Co-morbidity among the two patient groups

Variable		Early onset dementia (n=25)	Late onset Dementia (n=25)	P value
Psychiatric Co-morbidity, n(%)	F06.2	2 (8%)	0	>0.05
	F06.2/F19.2	1 (4%)	0	
	F06.30	0	1 (4%)	
	F06.32	2 (8%)	0	
	F10.2	2 (8%)	2 (8%)	
	F29.0	0	2 (8%)	
	F32.x	1 (4%)	3 (12%)	
	F33.x3	1 (4%)	0	
	F41.1	2 (8%)	3 (12%)	
	F41.2	1 (4%)	1 (4%)	
	Nil	13 (52%)	13 (52%)	

Table 3: Distribution of the MINIplus modules among the two patient groups

Variable		Early onset dementia (n=25)	Late onset Dementia (n=25)	P value
MINI plus module, n (%)	A	4 (16%)	4 (16%)	>0.05
	A/K/L	1 (4%)	0	
	D	0	1 (4%)	
	K	3 (12%)	2 (8%)	
	M	2 (8%)	2 (8%)	
	P	3 (12%)	4 (16%)	
	Z	1 (4%)	1 (4%)	
	Nil	11 (44%)	11 (44%)	

Table 4: Distribution of the substance abuse among the two patient groups

Variable		Early onset dementia (n=25)	Late onset Dementia (n=25)	P value
	Alcohol only	4 (16%)	4 (16%)	
	Tobacco Only	4 (16%)	2 (8%)	

Substance abuse, n(%)	**Alcohol &Tobacco**	4 (16%)	3 (12%)	>0.05
	Alcohol, Tobacco & Cannabis	1 (4%)	0	
	Nil	12 (48%)	16 (64%)	

Table 5: Comparison of DSRS scores among the two patient groups

DSRS scores, mean	Onset of Dementia		P value*
(±SD)	Early onset dementia (n=25)	Late onset Dementia (n=25)	
Scores	31.94 (±9.62)	26.26 (±8.54)	0.026

***p value by independent "t" te**

Table 6: Comparison of DEM-QOL scores among the two patient groups

DEM-QOL, mean (±SD)	Onset of Dementia		P value*
	Early onset dementia (n=25)	Late onset Dementia (n=25)	
Feelings scores	22.96 (±3.82)	25.89 (±3.76)	0.002
Memory scores	13.75 (±2.31)	15.38 (±3.16)	0.034
Everyday life scores	18.36 (±2.33)	20.45 (±3.63)	0.026
Overall scores	1.94 (±0.752)	1.94 (±0.79)	0.021

DISCUSSION

Currently it is impossible to provide patients and their families with a reliable prediction of the course of their disease, as there is substantial variability in rates of decline among individuals with LOD. Knowing which factors are associated with decline would be useful for understanding and slowing disease progression, as well as for individual prognosis. Potentially influential factors are comorbidities. The detection of symptoms of a possible disease/medical condition is challenging, especially in individuals with dementia, as they might be less able to sufficiently express symptoms and the associated discomfort.

McMurtray et al in their study demonstrated that Early Onset of Dementia (EOD) is a significantly under recognized subgroup of patients with dementia. This 4-year investigation of all patients presenting to a memory disorders program found that nearly 30% of patients with dementia had an age of onset of less than 65 years. When compared with similar patients with late-onset disease, these EOD patients had more treatable or preventable conditions and less AD.[11]

The mean age of presentation of dementia in the present study is 68.92; the mean age for late onset dementia being 73.58 years and for early onset dementia mean age is 63 years. The patients in late onset category were significantly older than the other group. However, majority of the patients in early onset were males (63.3%) and hence a little more half of the patients (53.3%) were accompanied by their wife. Whereas a study done by Sumana et al shows advanced age of presentation (81years).[12]

There were no statistically significant variations in gender prevalence of early and late onset dementia in our study. Sumana M. et al in their study of prevalence of dementia and other psychiatric comorbidities in geriatric population showed similar prevalence rates (65%among females and 35% males).[12] In contrary to these findings, a study by McMurtray et al shows a significantly high male preponderance (98%).[11]

Our finding is supported by a study done by Chauhan P et al,[13] among geriatric population of South India where the prevalence of depression is 9.3 %. This is significantly different from the findings of Sumana et al, where the prevalence of depression among dementia patients were 60 %.[12] Nandi et al. (1997) in a rural community of Gambhirgachi and Paharpur villages, West Bengal found prevalence of depression as 52.2 %.[14] There are no clear or consistent associations between socio- demographic variables. However there are some suggestions that, for a given impairment, HRQL may be worse for people who develop the illness at a relatively younger age.[15] There are intriguing possibilities of a gender difference in HRQL treatment response with women benefiting most from treatment and men doing worse than women without treatment.[16] The suggestion from one study that Latinos may have worse HRQL for a given level of dementia than the white majority is of concern even if this may be mediated by education and depression.[17]

A recent study using similar Geriatric Depression Scale reported a prevalence of 45.9%.64 Similar rates were reported from Andhra Pradesh2 and Uttar Pradesh.[18] Some of the studies have reported lower prevalence of Geriatric Depression also.[13,19] This variation can be explained because of different study settings.

There is no significant association between alcohol, smoking and Dementia in our study but some studies revealed the association of smoking and alcohol drinking status with incidence of dementia.[20,21]

Park et al,[22] evaluated cognitive function impairment, smoking and drinking status in 3,174 inhabitants aged 60–64 years in Korea, with a follow-up assessment of cognitive function 7 years later. Present smokers showed a higher risk for developing cognitive function impairment than did never smokers. García et al,[23] performed a case-control study. Risk of AD was unaffected by tobacco smoking, alcohol drinkers also showed a lower risk of AD than never consumers. Nevertheless, for AD, the results examined the

association between smoking, alcohol drinking and AD, and suggested that heavy drinking and smoking and ApoE can lower the age of onset for AD in an additive fashion.[24]

Smoking was associated with an increased rate of progression of vascular brain injury and decline in executive function a decade later.25 Panza et al.26 reported that light to moderate alcohol drinking might be associated with a reduced risk of unspecified incident dementia and AD. It has been argued that joint effects of tobacco use and alcohol on ADs.[27] There is substantial evidence from observational studies that conventional risk factors such as smoking, hypertension, diabetes and dyslipidemia play a role in the development of vascular cognitive impairment.[28] In recent study, interaction between tobacco and alcohol consumption with AD was investigated.

The Quality of life is higher in the late onset group in comparison to the early onset group which is found to be significant in present study. Similar results were found in the study done by Banerjee et al,[29] where data suggest that behavioural and psychological disturbance and patient age are more strongly associated with quality of life than cognition or functional limitation. This is an important finding, as it suggests that cognitive improvement may be a poor proxy for quality of life improvement in dementia.

The observed association of quality of life with behavioural and psychological symptoms in dementia is intuitively understandable, and the negative effects of such symptoms on people with dementia and their careers are well understood. The association with patient age is of interest. Older patients and their care givers may find it easier to adapt to dementia because they have had more experience of dementia in their peers, because they are free of the expectations of the early retirement period, or perhaps because their peers are more accepting of dementia. The difference in the quality of life with on set age may be due to, accommodation to dementia over the length of the illness is less likely, given that dementia severity is controlled for in these tests. This has similarities with findings that caregivers burden in dementia is higher in younger caregivers. Patient age in this study may be a proxy for a complex web of social determinates of quality of life in dementia.[15]

CONCLUSION

In the current study, Generalized Anxiety disorder, Mental and behavioural disorders due to use of alcohol - dependence syndrome and Major depressive episodes were the common psychiatric co-morbidities among both early and late onset dementia.

REFERENCES

1. Chertkow H, Feldman HH, Jacova C, Massoud F. Definitions of dementia and predementia states in Alzheimer's disease and vascular cognitive impairment: consensus from the Canadian conference on diagnosis of dementia. Alzheimer's research & therapy. 2013 Jul;5(1): S2.
2. Diagnostic DS. Diagnostic and statistical manual of mental disorders. American Psychiatric Association pp;591-603.
3. Bathgate DF, Scotland SL. Sight, perception and hallucinations in dementia. Alzheimer's Society 2015.
4. American Speech Language Hearing Association. Dementia-Signs and Symptoms 2013.
5. Bains J, Birks J, Dening T. Antidepressants for treating depression in dementia. The Cochrane Database of Systematic Reviews 2002; (4):CD003944.
6. Barclay TR, Brasure M, Nelson VA, et al. Pharmacologic Interventions to Prevent Cognitive Decline, Mild Cognitive Impairment, and Clinical Alzheimer-Type Dementia: A Systematic Review. Annals of Internal Medicine 2018;168(1):39-51.
7. Lambert MA, Bickel H, Prince M, et al. Estimating the burden of early onset dementia; systematic review of disease prevalence. Eur J Neurol. 2014;21(4):563–569.
8. van Vliet D, de Vugt ME, Bakker C, et al. Time to diagnosis in young-onset dementia as compared with late-onset dementia. Psychol Med. 2013;43(2):423–432.
9. Stanley K, Walker Z. Do patients with young onset Alzheimer's disease deteriorate faster than those with late onset Alzheimer's disease? A review of the literature. International psychogeriatrics / IPA. 2014;26(12):1945–1953.
10. Palasi A, Gutierrez-Iglesia sB, Alegret M, et al. Differentiated clinical presentation of early and late-onset Alzheimer's disease: is 65 years of age providing a reliable threshold? J Neurol. 2015;262(5):1238–46.
11. McMurtray A, Clark DG, Christine D, Mendez MF. Early-onset dementia: frequency and causes compared to late-onset dementia. Dement Geriatr Cogn Disord. 2006;21(2):59-64.
12. Sumana M, Sreelatha CY, Sreeranga A, Arpitha B, Akshatha SP, Anand HD. Prevalence of dementia and other psychiatric morbidities among geriatric population of Salagame primary health centre in Hassan district, Karnataka, India. Int J Community Med Public Health 2016;3: 1315-7.
13. Chauhan P, Kokiwar PR, Shridevi K, Katkuri S. A study on prevalence and correlates of Depression among elderly population of rural South India. Int J Community Med Public Health. 2016; 3:236-9.
14. Nandi PS, Banerjee G, Mukherjee SP, Nandi S, Nandi DN. A study of psychiatric morbidity of the elderly population of a rural community in west Bengal. Indian J Psychiatry. 1997; 39:122-9.
15. Banerjee S, Smith SC, Lamping DL, Harwood RH, Foley B, Smith P, Murray J, Prince M, Levin E, Mann A, Knapp M. Quality of life in dementia: more than just cognition. An analysis of associations with quality of life in dementia. Journal of Neurology, Neurosurgery & Psychiatry. 2006 Feb 1;77(2):146-8.
16. Woods B, Thorgrimsen L, Spector A, et al. Improved quality of life and cognitive stimulation therapy in dementia. Aging Mental Health.2006; 10(3): 219–226.
17. James BD, Xie SX, Karlawish JH. How do patients with Alzheimer disease rate their overall quality of life? Am J Geriatr Psychiatry.2005; 3: 484–90.
18. Tiwari SC, Srivastava S. Geropsychiatric morbidity in rural Uttar Pradesh. Indian J Psychiatry. 1998; 40:266-73.
19. Rao AV, Virudhagirinathan BS, Malathi R. Mental illness in patients aged fifty and over. Indian J Psychiatry. 1972; 14:319-32.
20. Kalapatapu RK, Delucchi KL. APOE e4 genotype and cigarette smoking in adults with normal cognition and mild cognitive impairment: a retrospective baseline analysis of a national dataset. The American journal of drug and alcohol abuse. 2013 Jul 1;39(4):219-26.

21. Piazza-Gardner AK, Gaffud TJ, Barry AE. The impact of alcohol on Alzheimer's disease: a systematic review. Aging & mental health. 2013 Mar 1;17(2):133-46.
22. Park B, Park J, Jun JK, Choi KS, Suh M. Gender differences in the association of smoking and drinking with the development of cognitive impairment. PloS one. 2013 Oct 4;8(10): e75095.
23. García AM, Ramón-Bou N, Porta M. Isolated and joint effects of tobacco and alcohol consumption on risk of Alzheimer's disease. Journal of Alzheimer's Disease. 2010 Apr 1;20(2):577-86.
24. Harwood DG, Kalechstein A, Barker WW, Strauman S, St. George-Hyslop P, Iglesias C, Loewenstein D, Duara R. The effect of alcohol and tobacco consumption, and apolipoprotein E genotype, on the age of onset in Alzheimer's disease. International Journal of Geriatric Psychiatry: A journal of the psychiatry of late life and allied sciences. 2010 May;25(5):511-8.
25. Debette S, Seshadri S, Beiser A, Au R, Himali JJ, Palumbo C, Wolf PA, DeCarli C. Midlife vascular risk factor exposure accelerates structural brain aging and cognitive decline. Neurology. 2011 Aug 2;77(5):461-8.
26. Panza F, Capurso C, D'Introno A, Colacicco AM, FrisardiV, Lorusso M, Santamato A, Seripa D, Pilotto A, Scafato E, Vendemiale G. Alcohol drinking, cognitive functions in older age, predementia, and dementia syndromes. Journal of Alzheimer's disease. 2009 Jan 1;17(1):7-31.
27. Tyas SL. Alcohol use and the risk of developing Alzheimer's disease. Alcohol Research & Health. 2001;25(4):299-306.
28. Rincon F, Wright CB. Vascular cognitive impairment. Current opinion in neurology.2013Feb1;26(1):29-36.
29. Banerjee, S., Samsi, K., Petrie, C.D., Alvir, J., Treglia, M., Schwam, E.M. and del Valle, M. What do we know about quality of life in dementia? A review of the emerging evidence on the predictive and explanatory value of disease specific measures of health related quality of life in people with dementia. International Journal of Geriatric Psychiatry: A journal of the psychiatry of late life and allied sciences.2009;24(1):15-24.