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RESEARCH ARTICLE

GENDER DIFFERENCES IN INDIAN SUBJECTS WITH VASCULAR DEMENTIA

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ABSTRACT

Background: Gender differences in Indian subjects with Vascular Dementia have not been studied systematically.
Materials and Methods: Subjects with Vascular Dementia presenting to a tertiary care hospital over a period of 16 months were assessed for socio demographic factors, dementia severity using Clinical Dementia Rating (CDR) Scale and for the presence of four vascular disease factors namely Hypertension, Diabetes, Dyslipidaemia and Ischemic Heart Disease. Data was analysed using SPSS version 17.
Results: The 159 subjects (M: F = 54.7: 45.3 % p = 0.27) of Vascular Dementia (Mild: Moderate: Severe Dementia = 39.7%, 38.4% and 21.9%) had a mean age of 69.35 (±7.51) years and a mean education of 11.34 (± 3.76) years with females being less educated (p=0.000). More four- fifths of subjects had multiple vascular disease risk factors. The female subjects had a similar severity level of dementia (p=0.401) and vascular disease burden (p= 0.543) despite being significantly younger (p= 0.002).
Conclusion: Female subjects of Vascular Dementia were significantly younger than male counterparts despite having a similar vascular risk profile as the male subjects though lower educational levels in females may have also contributed to the cognitive decline.

INTRODUCTION

Dementia is a leading public health issue globally. World Health Organization has estimated that the total number of people with dementia worldwide is 35.6 million in 2010 with 7.7 million new cases every year. Further, the prevalence of dementia is expected to double by 2030. Further, Dementia ranks second only to blindness as the leading cause of years of life lived with disability. Thus, Dementia is a not only a prevalent disorder in the elderly, it contributes significantly to morbidity and Disability Adjusted Life Years (WHO, 2012). All these facts make Dementia a strong public health priority globally. India, with its demographic transition and improved life expectancy, now has a vast population of older people. India has about nearly 4 million persons with dementia currently and this number is projected to double by 2030 (Shaji *et al*., 2010). India also has a huge burden of vascular factors which contribute to the development of Vascular Dementia.

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The ICMR-WHO study on Burden of Disease (ICMR, 2006) and WHO supported ICMR multi-centric study on risk factors for non-communicable diseases (Shah *et al*., 2010) showed that a high proportion of Indians had substantial vascular risk factors like Hypertension, Dyslipidaemia and Diabetes. Vascular Dementia is the second most common type of dementia in clinical practice in India and is a leading cause of preventable dementia. Gender issues have not been adequately investigated in Vascular Dementia. The present study focuses on the gender profile of subjects with Vascular Dementia reporting for treatment at a memory clinic at a tertiary care teaching hospital in New Delhi.

MATERIALS AND METHODS

Ethical Clearance: The study protocol was duly approved by Institutional Ethics Committee of PGIMER and Dr Ram Manohar Lohia Hospital in accordance with the Declaration of Helsinki. The study had a cross sectional observational design

Data Collection: The study was conducted at the memory clinic in our tertiary care hospital which is an outpatient service dedicated to dementia assessment and management.

Subjects with subjective memory loss attending memory clinic between 1/6/2013 and 31/10/2014 were screened for Vascular Dementia using National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherché et l'Ensignement en Neurosicences {NINDS-AIRENS} criteria (Roman *et al*., 1993). All subjects were evaluated using clinical examination, Montreal Cognitive Assessment (MoCA) (Nasreddine *et al*., 2005), routine investigations and MRI scans. Subjects with cognitive decline due to any other cause like Dementia due to any other aetiology, Current Delirium, Current Major Depressive Disorder, Hepatic, Renal or Thyroid dysfunction, previous significant head injury, Mental Retardation, history of psychiatric disorders associated with cognitive deficits like Schizophrenia and Bipolar Disorder, micronutrient deficiencies known to impair cognition like B12 and Folate, history of any Substance Dependence other than nicotine were excluded from the study.

The subjects were enrolled in the study after obtaining written informed consent from the subjects and their familial caregivers. After recording the socio demo graphic profile, the subjects were assessed for dementia severity using Clinical Dementia Rating (CDR) Scale (Morris, 1997). This scale has high inter-rater reliability and validity and evaluates cognitive and social functioning. The subjects were also assessed for the presence of four vascular disease factors namely Hypertension, Diabetes, Dyslipidaemia and Ischemic Heart Disease based on history, clinical examination, old treatment records and investigations using the following standardised definitions (Chandra *et al*., 2015a).

1. Hypertension: Systolic blood pressure of more than 140mm Hg or diastolic blood pressure more than 90 mm Hg as per Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure VII criteria (JNC VII), history of hypertension in previous treatment records, or current use of any anti hypertensive agents for treatment of hypertension as per medical records (Chobanian *et al*., 2003).

2. Diabetes mellitus: Fasting blood sugar level of ≥126 mg/dl (7.0 mmol/l) (Fasting is defined as no caloric intake for at least 8 h) or 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an Oral Glucose Tolerance Test using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water or in a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l) or A1c levels of 6.5% or above as per American Diabetes Association (ADA) guidelines, history of diabetes in previous treatment records, or current use of any oral hypoglycaemic agents or insulin (American Diabetes Association, 2013).

3. Dyslipidaemia was defined as per US National Cholesterol Education Program Adult Treatment Panel III Guidelines, history of dyslipidaemia in previous treatment records, or current use of any lipid lowering agent like statins or fenofibrate (Expert Panel on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2003).

4. Ischemic Cardiovascular disease: history of myocardial infarction, angina with ischaemic changes on graded exercise tests or positive imaging, previous coronary revascularisation procedures in previous treatment records, or current use of any anti angina agents. (Fihn *et al*, 2012)

Statistical Methodology

The data collected was analysed statistically using SPSS Version 17 using descriptive statistics to describe the study sample and analytic techniques like ANOVA for continuous variables and Chi square tests for categorical variables. The results were analysed keeping a significance level of 0.05.

RESULTS

The socio demographic profile of 159 study subjects is given in Table 1. There was no significant difference in the sex ratio (M: F= 87:72 i.e. 54.7: 45.3%)) (p=0.27). The study subjects had a mean age of 69.35 ±7.51 years.

Table 1. Socio demographic profile of subjects with vascular dementia

Domain	Total N=159	Males N= 87 (54.7%)	Females N= 72 (45.3%)	Sig (p=0.05)
AGE IN YEARS [Mean (± s.d.)]				
Total Sample	69.35 (±7.51)	71.00 (± 7.68)	67.35 (± 6.83)	0.002*
Mild Dementia n= 64; M:F= 34:30	67.08 (± 7.07)	68.91 (± 7.08)	65.00 (± 6.58)	0.026*
Moderate Dementia n= 59; M:F= 36:23	69.93 (± 7.09)	71.42 (± 7.40)	67.61 (± 6.01)	0.043*
Severe Dementia n= 36; M:F= 17:19	72.42 (± 7.84)	74.29 (± 8.50)	70.74 (± 6.99)	0.177
MARITAL STATUS				
Married	113 (71.07%)	60 (68.97%)	53 (73.61%)	0.572
Divorced	1 (0.63%)	1 (1.15%)	0 (0%)	
Widowed	45 (28.30%)	26 (29.88%)	19 (26.39%)	
EDUCATIONAL ATTAINMENT				
Education in years [Mean ± s.d.]	11.34 ± 3.76	13.05 ± 3.00	9.28± 3.58	0.000*
Illiterate N (%)	0 (0%)	0 (0%)	0 (0%)	0.000*
Primary School* N (%)	24 (15.1%)	2 (2.30%)	22 (30.56%)	
Secondary School** N (%)	86 (54.1%)	46 (52.87%)	40 (55.56%)	
Technical Diploma N (%)	1 (0.6%)	0(0%)	1 (1.39%)	
Graduation N (%)	34 (21.4%)	28 (32.18%)	6 (8.33%)	
Post Graduation N (%)	14 (8.8%)	11 (12.64%)	3 (4.17%)	

*Primary School- Less than 5 years of education
**Secondary School- 6 to 12 years of education

Table 2. Clinical profile of subjects with vascular dementia

Domain	Total N=159	Males N= 87 (54.7%)	Females N= 72 (45.3%)	Sig (p=0.05)
No of Vascular Risk Factor Diseases (Hypertension, Diabetes Mellitus, Dyslipidaemia and Ischaemic Heart Disease)				
0	7 (4.40%)	5 (5.74%)	2 (2.78%)	0.543
1	23 (14.47%)	13 (14.94%)	10 (13.89%)	
2	51 (32.07%)	25 (28.74%)	26 (36.11%)	
3	42 (26.42%)	21 (24.14%)	21 (29.17%)	
4	36 (22.64%)	23 (26.44%)	13 (18.05%)	
Severity of Dementia				
Mild Dementia N (%)	64 (39.7%)	34 (39.08%)	30 (41.67%)	0.401
Moderate Dementia N (%)	59 (38.4%)	36 (41.38%)	23 (31.94%)	
Severe Dementia N (%)	36 (21.9%)	17 (19.54%)	19 (26.39%)	

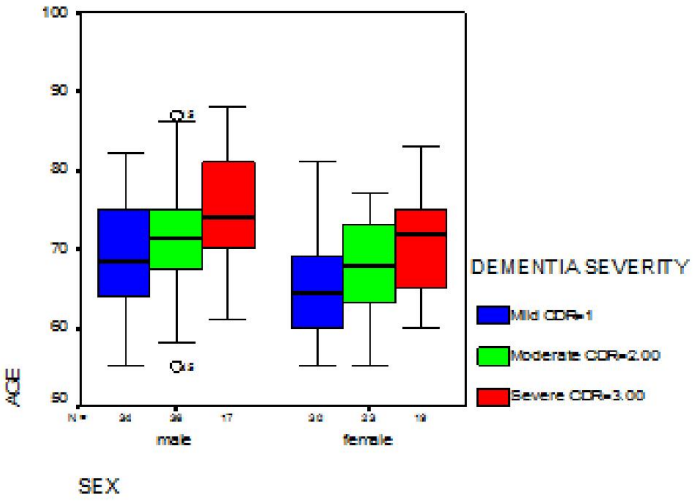

Figure 1. Age (in years) and gender wise profile of dementia severity in subjects with Vascular Dementia

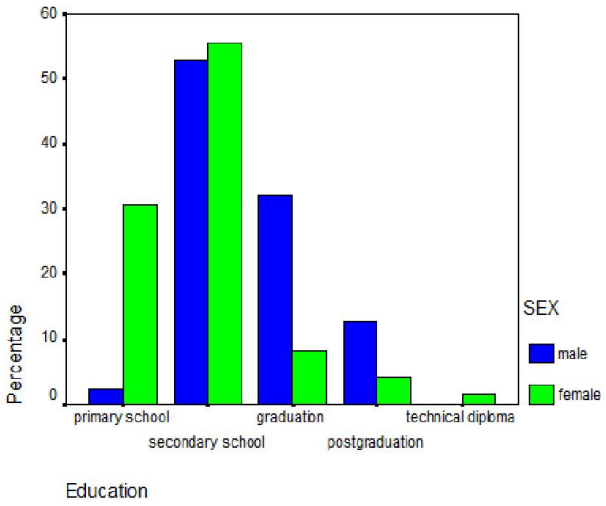

Figure 2. Gender wise profile of educational attainment of subjects with vascular dementia

Gender wise analysis revealed that there was significant difference in age (p= 0.002) with female subjects being nearly four years younger than their male counterparts. However, the difference was statistically significant in mild dementia (p= 0.026) and moderate dementia (p=0.043) but not in severe dementia group (p=0.177) (Fig 1). Most subjects were married with less than one third being widowed or divorced. None of the subjects were illiterate and the subjects had a mean educational attainment of 11.34 ± 3.76 years with females being significantly less educated (p=0.000) (Fig 2). Table 2 gives the clinical profile of the study subjects. Nearly 40% of subjects had mild and moderate dementia each while a little more than 20% of subjects had severe dementia with no gender difference (p=0.401). More than 80% of subjects had two or more vascular disease risk factors which included Hypertension, Diabetes Mellitus, Dyslipidaemia and Ischaemic Heart Disease. There was no gender difference in number of vascular risk factors (p=0. 543).

DISCUSSION

A similar study was done at a tertiary care university outpatient cognitive clinic in Brazil on 253 subjects with Vascular Dementia and Vascular Cognitive Impairment. The mean age of our study subjects (69.35 ±7.51 years) was similar to the Brazilian study (67.77±10.35 years). Our finding of no gender difference in rates of Vascular Dementia is in consonance with the EURODEM Study which pooled data from four population-based prospective cohort studies (Andersen *et al*, 1999). However the Rotterdam Study and the Brazilian study did show higher rates of incidence of Vascular Dementia in males but these studies did not factor in age as a variable (Ruitenberg *et al*., 2001; Siqueira-Neto *et al*., 2013). Most subjects were married with less than one third being widowed or divorced reflecting prevalent socio- cultural norms. None of the subjects were illiterate reflecting the high levels of literacy in the National Capital Region even 75 years back.

Our subjects were also more educated with a mean educational attainment of nearly 12 years as compared to Brazilian study subjects who had a mean educational attainment of less than 3 years. The lesser educational levels in female subjects in our study may be due to prevalent socio cultural practices. Greater decline in cognition in subjects with lower educational levels is well known and this may have also contributed to cognitive decline at younger age in females in our study sample. Our study shows that female subjects of Vascular Dementia are at a greater risk for mild and moderate dementia at a younger age. The lack of gender difference with respect to age in severe dementia group can be attributed to survival bias as this group was significantly older than mild and moderate dementia groups (p=0.002) Subjects with Vascular Dementia may succumb to mortality related to vascular risk factors like Hypertension, Diabetes Mellitus and Ischaemic Heart Disease

before developing severe dementia. Hence the mean age in severe dementia group may reflect survival bias.

The clustering of vascular disease factors is similar to the findings seen in other studies in Canada, USA Sweden, Singapore and certain developing countries. (Lindsay *et al*., 1997; Kalmijn *et al*., 2000; Meyer *et al*., 2000; Duron *et al*., 2008; Kalaria *et al*., 2008; Kivipelto *et al*., 2005; Takahashi *et al*., 2012). However, the similar vascular risk burden due to clustering of vascular disease factors at a younger age in females may reflect on an inherently greater vascular risk for females at a younger age.

The subjects lacking any of the investigated vascular disease factor were found to be Nicotine Dependent (Chandra *et al*., 2015b).

The lack of gender difference in vascular disease factors (p=0.543) and severity of dementia (p=0.401) indicates towards a similarity of biological risk and dementia severity state between genders despite female subjects being significantly younger by nearly four years.

The strength of the study lies in its adequate sample size with adequate number of subjects even in difficult- to- get severe dementia subgroup. Due attention was paid in the study protocol to ensure methodological robustness in assessment through use of standardised definitions, reliable rating scales and in performing appropriate data analysis. To address issues of consent by cognitively impaired subjects, written informed consent was taken from both subjects and their familial caregivers.

The major limitation of the study is that being a hospital based and not a community based epidemiological study, the findings cannot be generalised at the community level. Further, the study was not exclusively powered to investigate gender differences and their correlates in Vascular Dementia.

There are contradictory studies regarding the cognitive decline in postmenopausal females with some authors attributing the cognitive decline to lack of neuroprotective effect of Oestrogen (Fillenbaum *et al*., 2001; Ott *et al*., 2002; Sherwin, 2003; Shumaker *et al*., 2004; Henderson, 2008; Luine *et al*., 2014). However, the clustering of vascular disease risk factors at an earlier age in females as demonstrated by our study may contribute to the development of Vascular Dementia and its severity progression at a younger age in females. Such findings may be consequent to unknown but complex gender related etiopathological mechanisms.

Systematic research studies should be planned to investigate the extent of gender differences in vascular contributory factors in Vascular Dementia, the course and outcome of Vascular Dementia per se as well as biological underpinnings.

Conclusion

The study of subjects with Vascular Dementia seeking treatment at Memory Clinic at our tertiary care hospital shows that female subjects of Vascular Dementia develop dementia at a younger age despite having a similar vascular disease burden as males. Lower educational levels may have also contributed to cognitive decline at younger age in females.

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Declarations

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Conflict of interest: None

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