Abstract

Objectives: Vascular dementia (VaD) is high in Indian population and is preventable to some extent but there is paucity of literature. Hence we decided to study the clinical and laboratory spectrum of VaD.

Methods: It was retrospective hospital based study. The patients who satisfied Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV criteria) for VaD and age of more than 40 years were identified on the basis of case file code which is uniformly used by the hospital.

Results: Of the 83 patients included, 72.3% (60) were males (mean age: 65.3 ± 8.6 years) and 27.3% (23) females (mean age: 65.7 ± 1.1 years). Mean age of the patients was 65.4 ± 9.2 years. Abrupt onset was seen in 42 (51%) patients and 41 (49%) had insidious onset. There was gradual progression in 48 (57.8%), stepwise progression in 33 (39.8%) and 2 patients had rapid progression. Naming impairment was seen in 64 (77.1%), visuospatial disorientation was present in 49 (59%), dyscalculia in 55 (66.3%), emotional lability in 26.5%. Hypertension was the single most important risk factor (71.1%) followed by smoking (46.9%) and dyslipidaemia (45.8%). Neuropsychological testing showed Executive function involvement in 18 (66.7%) followed by memory in 16 (59.3%) patients. The total white matter hyperintensity score (12.39 ± 6.73) significantly correlated with mini mental scores (r: -0.4; p: 0.02).

Conclusion: We found that in our patients with vascular dementia, gradual progression, naming impairment and small vessel disease in imaging were the most common abnormalities. Hypertension was the single most important risk factor.

Introduction

Vascular dementia (VaD) accounts for 10 to 30% of all dementias. Literature has shown that the south Asians are predisposed to higher prevalence of vascular risk factors (glucose intolerance, higher total and low density lipoprotein (LDL) cholesterol, higher triglycerides, and lower high density lipoprotein (HDL) cholesterol, and much greater abnormalities in novel risk factors including higher concentrations of fibrinogen, homocysteine, lipoprotein (a), and plasminogen activator inhibitor-1). It explains the higher rates of cardiovascular disease among South Asians compared with Europeans and Chinese. Magnetic Resonance imaging (MRI) plays a very important role in evaluation of VaD. Studies in VaD have shown the utility of estimating the white matter lesion (WML) load in a semiquantitative and quantitative way, measurement of brain volume, estimation of microbleeds and diffusion tensor imaging (DTI) in small vessel disease.

Studies from India have shown that VaD is a common form of dementia in contrast to West. In rural Kerala vascular dementia constituted 58% of total dementia cases. In studies conducted in rural and urban communities in Tamilnadu, VaD constituted 27% and 26% respectively of total dementia cases. The relative proportion of VaD ranged from 22 – 58%.

The reason for higher prevalence of VaD in India may be due to higher prevalence...
of vascular risk factors and poor control of these risk factors in the young in India. A systematic analysis of six Indian studies showed, prevalence of VaD to be 1.1% (1.2-2.9%) with marginally fewer cases in urban compared with rural areas and in Northern versus Southern studies.10,11,13

This study was done to examine risk factors, cognitive and focal deficits in vascular dementia as well as the relation of dementia with other clinical features and imaging spectrum in an Indian tertiary health care setting.

**Methods**

The present study was a retrospective hospital based study, conducted at tertiary referral hospital, which serves a large community of people in South India. Study period was 6 ½ years from 1st January 2004 to 31st July 2010. The cases were identified by the code used for classifying vascular dementia at our institute.

**Inclusion and exclusion criteria**

All patients fulfilling the diagnostic criteria of vascular dementia based on DSM IV (American Psychiatric Association 1994) criteria and aged above 40 years were included in the study. Patients with delirium, substance abuse, head injury, mixed dementia as well as patients with signs and symptoms of acute or chronic neuroinfection (fever, meningeal signs) and past history of encephalitis were excluded from the study. Patients with long standing psychiatric illness, intracranial surgery or radiation and patients with mixed dementia were also excluded from the study. Mixed dementia was considered when infarcts occurred on premorbidly declining patients.

**Study methodology**

Medical case records of all adult patients who were diagnosed as vascular dementia from 1st January 2004 to 31 July 2010 was analysed. A total of 203 case files were available for review. Out of these 83 patients were included. This is because the data is from retrospective information and entries were incomplete in the rest of the files. However, most of the population based cohort studies available from India had included all dementias in a non-selective way. With reference to vascular dementia the maximum number studied according to our knowledge is hospital based using 42 patients.20 Details of information regarding clinical symptomatology, neurological findings, laboratory tests including imaging findings were recorded as per pre-designed form. Details of mini mental status examination (MMSE) and modified hachinski ischaemic scale (mHIS) were also recorded.14 Risk factors were defined as per TOAST (trial of org 10172 in acute stroke treatment) classification.15 Neuropsychological tests applied are as follows:

1. Story memory test (Immediate recall) in which patients are asked to listen to a short story and then immediate memory is tested in the form of how many words in that story they can recall.
2. Design construction is tested by presenting the patient with 5 different designs constructed by match sticks and ability of patients to copy and recall these designs.
3. Digit repetition forwards and backwards is tested by predesigned numbers which are arranged in the ascending order of complexity. Number of digits correctly recalled are noted.
4. Visual memory tested by spatial span both forwards and backwards.
5. Story memory test (delayed recall) tested during which patients are asked to recall the story presented to them earlier.
6. Category fluency test patients asked to generate as many names of animals as possible in one minute, similarly phonemic fluency by asking the patients to generate as many words as possible starting from letter S.
7. Design construction (delayed recall) tested by asking the patient to draw same designs presented to them earlier.
8. Attention trial – Patient has to cancel wherever lock and bulb comes from a set of designs, time taken to complete the task and numbers of omission and commission errors were noted.
9. Word list trial : 10 different words and ability to recollect these words was noted in 3 trials. Later was presented with 20 different words which were containing the 10 words presented earlier and ability to identify the correct words was noted in yes-no answers. After this the delayed recall for same 10 words presented earlier was noted.
10. Go-no-go test done by asking the patients initially to tap twice when examiner taps once and not to tap when the examiner taps twice. Total 6 trials were done. Second step is to tap once when examiner taps twice and to tap twice when the examiner taps once and total 15 trials were given. Tests were chosen from NIMHANS neuropsychological battery which are validated for persons up to sixth decade and normative data is available in NIMHANS Neuropsychological battery.(NIMHANS neuropsychology battery-2004, manual,1st ed. Shobini L. Rao, D.K. Subbakrishna and K. Gopukumar, published 2004 by National Institute of Mental Health and Neurosciences in Bangalore).

**Imaging data**

Imaging data in the form of both Computed tomography (CT) scan and Magnetic resonance
imaging (MRI) of brain was analysed as per pre designed proforma. Detailed imaging analysis was done in the MRI scans done at NIMHANS in 3 Tesla (Phillips MR scanner - Achieva, Philips Health care, Best, The Netherlands) and 1.5 Tesla (Magnetom vision-plus, superconducting system - Siemens AG, Erlangen, Germany) MR scanners. Imaging analysis of MRI was done with National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l’Enseignement en Neurosciences (NINDS-AIREN) imaging protocol and using Scheltons scale for white matter hyper intensities.

Neuropsychological evaluation was done in 27 out of 83 patients. Also tests for agnosia, apraxias, acalculia, agraphia, alexia and aphasias were performed. Correlation of imaging and neuropsychological data with clinical features and co-morbidities was done.

**Statistical Methods**

Data was managed on Excel worksheet. All the entries were checked for any keyboard errors. Analysis was done using SPSS 15. Mean and standard deviation was calculated for Hachinski score, MMSE and other white matter scores. Pearson’s correlation test was used to investigate the relationship between mini mental status examination score and white matter hyperintensity scores.

**Results**

Of the 83 patients included, 72.3% (60) were males (mean age: 65.3 ± 8.6 years) and 27.3% (23) females (mean age: 65.7 ± 1.1 years). Age group ranged from 45 to 91 years. Mean age was 65.4 ± 9.2 years. Majority of patients were in 7th decade (31 patients) followed by 6th and 8th decade (22 in each decade respectively). Most of patients had an income greater than 2500 rupees per month (50 US$; 44 patients). Forty two patients had diabetes mellitus. Dyslipidaemia was seen in 49% of patients. Twenty four patients (28.9%) had diabetes mellitus. Twenty four patients (28.9%) had diabetes mellitus. Dyslipidaemia was seen in 49% of patients. Forty seven percent of patients had history of smoking and 26.5% had history of alcohol intake. Around 20% of patients had past history of stroke. The results of neuropsychological involvement were available for 27 patients (Table 2).

**Neuromaging**

CT imaging was available in 56 patients and 33 patients had MRI. Many of the patients had both imaging studies. All 56 patients CT image revealed hypoattenuation small vessel disease and 15 patients large vessel disease. Among patients with small vessel disease, 5 patients (8.9%) had white matter lesions (WML) only and 51 patients (91.1%) had both WML and lacunar infarcts. None of the patients had pure lacunar infarcts.

Among the 15 patients with large vessel disease majority had parietal lobe involvement (21.4%) followed by frontal (12.5%), temporal (10.7%) and occipital in (7.1%).

**MR imaging**

Detailed MR imaging analysis was done in 33 patients. The mean total white matter hyperintensity score of patients was 12.39 ± 6.7. The mean D-WMH score was 8.61 ± 4.99 and mean PVH score was 3.79 ± 2.2. The mean basal ganglia score was 8.63 ± 7. Mean infratentorial score was 25.27 ± 15.

With regard to large vessel disease, based on MRI posterior cerebral artery – inferio medial temporal (PCA-IMT), angular gyrus and parietal watershed territory was involved in 4 patients each. There was involvement of association areas of parieto-temporal and temporo-occipital territory in 3 patients each. Two patients had involvement of posterior cerebral artery – parietal temporal infarct (PCA-PTI) territory. Only one patient had involvement of anterior cerebral artery (ACA) territory.

Patients with hemiparesis had mean total white matter hyperintensity score (T-WMH) score of 11. Patients with spasticity and brisk reflexes had mean T-WMH score of 12.35. Patient with rigidity had score of 12.55 and bradykinesia had score of 15.55. Patients with abnormal gait had mean T-WMH score of 12.06.

There was statistically significant negative correlation between MMSE Score and T-WMH score (P = 0.022). There was a trend noted in correlation of MMSE score with deep matter hyperintensity score (D-WMH) score and infratentorial score, but it was not statistically significant.
**Discussion**

This study has tried to explore the different aspects of VaD in Indian scenario. The rapid change in lifestyle and increase in prevalence of vascular risk factors like diabetes and hypertension might increase the burden of VaD in India in the coming future. The mean age of the patients in our study was similar to the other studies which showed steep rise in prevalence of VaD with age from 0.3% at 60-63 years of age to 5.2 to 6.7% at 85 to 90 yrs or older.18,20,21,22

**Clinical Features**

Most of the patients had gradual progression of VaD (60%) and stepwise progression (40%). In contrast stepwise progression predominated in a previous Indian study (52.4%).20

Naming impairment was the commonest abnormality which was similar to previous studies which have demonstrated it, as the characteristic deficit in patients with VaD.25,26 Visuospatial abnormalities were present in around 60% of our patients. Paul and colleagues have shown that patients with VaD have impaired visuospatial integration, independent of naming deficits.25 A study by O’Brien has shown that emotional lability is more common in vascular dementia compared to Alzheimer’s disease which was also noted in our study (1/3rd).24 Memory disturbances were common in our patient group with almost all patients having recent memory deficits.

Presence of gait abnormality is considered as the predictor of non–Alzheimer dementia. A study by Staekenberg et al revealed hemiplegic gait abnormalities in 25% and parkinsonian gait abnormality in 28%.26 Another study from India revealed gait abnormalities in nearly 40% of patients.20 In a study by Staekenberg et al, hemiparesis was seen in 44% of patients with VaD which is comparable to our findings.25 With regard to extrapyramidal manifestations, rigidity was seen in 23% and bradykinesia in about 15% of patients. Study by Staekenberg et al revealed rigidity in 20% and bradykinesia in 33% of patients.25

The mean MMSE score was 16 (±5), with approximately 60% of patients having scores between 11 and 20. A study by Staekenberg et al revealed MMSE score of 19 (±5).25 Another study by Garrett et al, looking at neuropsychological profile of vascular dementia found, higher mean MMSE score 22.2 (±1.4).26

**Risk factors**

Hypertension was the most common risk factor (71%) in our study. Our finding was similar to various studies which have shown that 80% of VaD patients have hypertension (elevation of both systolic and diastolic blood pressure) as the risk factor.27,28 After age, hypertension is considered as the strongest risk factor for VaD.18,20,21 Population-based studies such as Honolulu Aging Study and the Framingham Study have also demonstrated that high blood pressure precedes cognitive impairment in individuals without symptoms or signs of cerebrovascular disease.29,30 The presence of hypertension triples the risk of vascular dementia.31 Diabetes mellitus another major risk factor was present in approximately 30% of patients in our study. Various studies have shown that, diabetes is present in up to 20% of patients with VaD.18,27 Study by Posner et al have shown that presence of both diabetes mellitus and hypertension increases the risk of developing vascular dementia by six fold.31

Prior history of stroke is considered one of the most important risk factors for vascular dementia but our study showed that only 22% had previous history of stroke. This could be due to recall bias or the inability of patient or caregivers to recall minor strokes.20 Dyslipidaemia was present in nearly 46% of our patients. Hyperlipidaemia with increased low-density lipoproteins is a strong risk factor for large vessel atherosclerosis.18,27,28 The Hisayama study found a significant association between elevated low-density lipoprotein (LDL) cholesterol levels and the incidence of atherothrombotic stroke.32 Smoking was present in 47% of patients and excessive alcohol intake history was seen in 26.5%. It has been shown smoking and high, alcohol consumption promote vascular dementia.27 Another study from India revealed history of smoking in 21% and history of excessive alcohol consumption in 24% of patients.20

In terms of Neuropsychological assessment our study was similar to a study by Wolf et al, who found neuropsychological pattern suggestive of frontal lobe involvement/Executive dysfunction.33 Another study by Kertesz et al revealed greater difficulty on tasks related to frontal lobe functions including dysgraphia, motor performance, and sequential reasoning and analysis, in patients with vascular dementia.34

**Neuro-Imaging**

Many studies have shown, cerebral white matter changes observed on CT and MRI scans of elderly individuals, serve as a surrogate marker of cognitive and motor impairment particularly in patients with vascular risk factors, cerebrovascular diseases, and cognitive and motor impairment.35,36 A case control study of CT scan in patients with multi-infarct dementia revealed WML areas in 53% and lacunae in 56% of patients.37 Other studies have demonstrated WML on CT scan ranging from 35% in dementia patients as a whole to 72% in VaD.38,39 The brain lesions that best account for these deficits are noninfarct subcortical white matter and gray matter changes due to ischaemia.40

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With regard to white matter abnormalities on MRI in our study, the mean T-WMH score in our study was similar to as reported in other studies.\(^\text{41-43}\) These studies showed correlation of mean WMH score with age, MMSE score and total UPDRS score (unified parkinson’s disease research score).\(^\text{43}\) This was in accordance with our study which showed significant correlation of mean total white matter hyperintensity score with MMSE score. In a study by Cohen et al, significant relationship was observed between the MRI indices (subcortical hyperintensities and whole brain volume) and MMSE score.\(^\text{44}\) Roman et al have suggested that at least 25% of white matter is needed to be involved before white matter alterations influence the clinical signs associated with dementia, which has been incorporated in NINDS AIREN criteria for VaD.\(^\text{16}\) The results of D-WMH score in our study are comparable to other studies with similar deep and periventricular white matter scores.\(^\text{42,43}\) A longitudinal study by Degroot et al showed that there is significant correlation between periventricular WMLs and rate of cognitive decline (documented by serial MMSE scores).\(^\text{45}\) There has been widespread debate on the impact of vascular risk factor on the pathophysiological basis of two categories of white matter hyperintensities. Results from various studies have shown age and vascular risk factors as the strongest correlate of PVH, whereas associations between vascular risk factors and DWH are much weaker.\(^\text{46,47}\) But pathological studies have found that both subtypes have common ischaemic aetiology (vascular fibrosis and lipohyalinosis).\(^\text{47,48}\)

**Limitations**

The main limitation of the study is the retrospective nature and lack of MRI and neuropsychological testing in all the patients. There is a need for a multicentric prospective study in view of the public health importance of vascular dementia.

**Conclusion**

Hypertension is the most common risk factor for vascular dementia and the total white matter score in MR imaging is an important biomarker for the severity of cognitive decline in VaD. We acknowledge that our finding are similar to those in previous studies and emphasises the need to control hypertension in community and adequate brain imaging to identify and manage this potentially treatable cause of dementia.

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**References**


