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DSM-5 in Vascular Dementia-Comparison with other diagnostic criteria in a retrospective study

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Abstract

Context: The studies comparing different diagnostic guidelines for vascular dementia (VaD) demonstrated that they differ in their requirements. The more recent guideline, Diagnostic and Statistical Manual of Mental Disorders–5th Edition (DMS-5) does not have an established comparison. This study compared DSM-5 with other diagnostic guidelines for VaD and its degree of association with them.

Methods and Material: It is a retrospective analysis of the clinical case files of 91 patients who were diagnosed to have VaD between 1st April' 2013 to 31st March'2014. Based on the information about history, clinical findings, and neuroimaging findings, the cases were diagnosed according to DSM-5, National Institute of Neurological Disorders and Stroke -Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) with and without modification for sub-cortical ischemic vascular dementia (SIVD), International Classification of Diseases, 10th Revision (ICD-10), and State of California Alzheimers Disease Diagnostic and Treatment Centers (ADDTC). The association of DSM-5 with other guidelines was measured by the concordance rate, Kendell Tau B (for effect size estimate) and Spearman correlation coefficient (for degree of convergence).

Results: For only 30% (28 out of 91) cases, all diagnostic guidelines agreed to the diagnosis of same category of VaD. The total positive cases rose to 95.6% (87 out of 91) cases when it was considered even if anyone guideline gives the diagnosis of VaD. There was almost equal proportion of probable (40.6%) and possible (42.9%) The concordance rate of DSM-5 was maximum with ADDTC (67.3%) followed by with ICD-10 (53.8%), NINDS-AIREN with modification for SIVD (51%) and NINDS-AIREN without modification for SIVD (46.2%). The degree of convergence and effect size of association was of moderate level ranging from 0.29 to 0.39 and all were statistically significant. ADDTC had the highest values for all measures of its association with DSM-5.

Conclusion: DSM-5 contributes to increase in total number of positive cases of VaD by using diagnostic guidelines. The moderate degree of association of DSM-5 with other guidelines indicates the incorporation of some of their criteria by DSM-5 and simultaneous consideration of the recent valid features of VaD.

Keywords: *Vascular Dementia; Diagnostic guidelines; Concordance for diagnosis; Subcortical Ischemic Vascular Dementia; DSM-5; DSM-IV*

Abbreviations: ADDTC: State of California Alzheimer's Disease Diagnostic and Treatment Centers; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; DSM-5: Diagnostic and Statistical Manual of Mental Disorders–5th Edition; FND: Focal Neurological Deficit; HMSE: Hindi Mental State Examination; ICD-10: International Classification of Diseases, 10th Revision; SIVD: Sub-cortical Ischemic Vascular Dementia; NINDS-AIREN: National Institute of Neurological Disorders and Stroke -Association Internationale pour la Recherche et l'Enseignement en Neurosciences; VaD: Vascular dementia.

Introduction

Vascular dementia (VaD) is the second biggest leading cause of dementia after Alzheimer's Disease globally [6]. With time, different diagnostic guidelines for VaD have developed differing in their definition and evolution of cognitive syndrome and confirmation of vascular cause. Currently, commonly used ones are National Institute of Neurological Disorders and Stroke -Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) guideline [3] the State of California Alzheimer's Disease Diagnostic and Treatment Centers (ADDTC), [2] the International Classification of Diseases, 10th Revision (ICD-10), [4] and recently, the Diagnostic and Statistical Manual of Mental Disorders–5th Edition (DSM-5) [1] was launchedas the edition over DSM-IV [5]. All dementias are called as Neurocognitive Disorder in DSM-5.

Studies have looked into variability of these diagnostic guidelines. The cases fulfilling all guidelines varied from 8.5% to 29% [7,8] reflecting the poor concordance of these guidelines. The diagnosis of VaD is made more commonly with DSM-IV and ADDTC than with ICD-10 or NINDS-AIREN. Assignment to various categories of VaD also differs in these guidelines. The credibility of these diagnostic guidelines is poor, particularly for sub-cortical ischemic VaD (SIVD) [9,10].

No study has compared DSM-5 with the other existing diagnostic guidelines for VaD. Compared to DSM-IV, there are significant changes in DSM-5, including the provision to consider SIVD as probable VaD. Some of these features of DSM-5 resemble to that of NINDS-AIREN and ADDTC. This study aimed to assess the measures of association of DSM-5 with other available diagnostic guidelines for VaD and looked into possible features contributing to it.

Materials and Methods

This study was the review of clinical case files of 91 patients who were diagnosed to have VaD in the out-patient or in-patient setting of tertiary-care hospital, National Institute of Mental Health and Neurosciences (NIMHANS), India. The time-period chosen was from 1st April 2013 to 31st March 2014. The diagnosis was made clinically based on history, neurological examination, and cognitive functions assessment. Hindi Mental State Examination (HMSE) [11] was used to get impression about overall cognitive impairment. The presences of vascular lesions were confirmed by brain neuroimaging. The considered brain lesions were multi-infarcts, strategic infarcts, watershed infarction, sub-cortical infarcts, lacunar infarcts, and infarcts in perivascular spaces [12].

The socio-demographic profile, clinical findings and neuro-imaging findings were noted. The clinical findings included both cognitive functions as well as details of cerebro-vascular events in terms of both history and examination. Current behavioural symptoms, psychiatric comorbidity including substance use, physical co morbidity including metabolic disorders and cardio-vascular events, and family history for both dementias were noted. For metabolic risk factors, the information about obesity (BMI > 25), hypertension, diabetes, and dyslipidemia were recorded [13].

Based on this information, the diagnosis of possible, probable or unlikely to be VaD according to DSM-5, NINDS-AIREN, ICD-10, and ADDTC were made. For sub-cortical ischemic VaD, modification for SIVD was included in NINDS-AIREN guideline [14]. The chief features of these guidelines are described in brief in Box 1-3. For calculating the total number positive cases of VaD by a diagnostic guideline, all "probable" and "possible" cases were considered.

The concordance between DSM-5 and other diagnostic guidelines was calculated based on the consideration of the same category of VaD by both guidelines i.e "probable" vs "probable", "possible" vs "possible", and "unlikely" vs "unlikely". For determining concordance between DSM-5 and ICD-10, the two considered categories were "positive" and "unlikely" diagnosis of VaD. The effect size of the association and the degree of convergence were determined with Kendell Tau B and Spearman correlation coefficient respectively. This was chosen based on the nature of data being ordinal and non-parametric. Kendell Tau C was considered for the association between DSM-5 and ICD-10 as they have unequal number of categories. The significance level was fixed at 0.05.

Results

There were 70 males and 21 females and 45% cases were either illiterate or received only primary education. 62 (68%) patients had age of onset of dementia below 65 years with the mean age of onset of dementia was 61.23 years (± 22.9 years). 48 (52.7%) patients had abrupt onset; 43 (47.3%) had insidious onset. The progression of dementia was step-ladder in 31 (34.1%) patients, gradual in 46 (50.5%) patients, and rapid in 14 (15.4%) patients. Mean HMSE scores was 18.55 (SD = 3.35). Among risk factors, highest prevalence was of hypertension 82.3% patients had hypertension, which was controlled in 26% of them only; 63.6% patients were obese; 50.5 % patients had diabetes, which was controlled in 30.4% of them; 48.4% patients had dyslipidemia, which was controlled in 20.5 % of them.

87 (95.6%) out of 91 clinically diagnosed as VaD cases could be diagnosed as probable or possible VaD by at least any one diagnostic guideline. And 81 (89%) cases had the diagnosis of VaD with at least two guidelines. 28 cases (30%) received the same category of diagnosis of VaD, including 4 (4.4%) cases of unlikely VaD by all four guidelines. Figure 1 gives the distribution of VaD cases as probable, possible or unlikely by each diagnostic guideline. The prevalence of probable VaD was highest with ADDTC (58.2%) and the diagnosis of unlikely VaD was highest with ICD-10 (49.5%).

Table 1 gives the measures of association of DSM-5 with other diagnostic guidelines. The highest concordance of DSM-5 was with ADDTC (67.7%). For other guidelines, it varied from 46% to 57%. The Spearman correlation coefficient and Kendell Tau B estimating the convergence and effect size of association respectively for DSM-5 were also highest between DSM-5 and ADDTC. However, the values of measures of association for all guidelines differed mildly with each other. All of them were in the range of 0.29 to 0.39 and all were statistically significant.

The clinical diagnosis was subcortical ischemic VaD in 40 (44%) cases and single or multiple infarct dementia in 18 (19.8%) cases. In 23 (25.2%) cases, the diagnosis was mixed VaD. 10 (11%) cases had another differential diagnosis of Alzheimer's disease or fronto-temporal dementia. Neuroimaging was available in 86 (94.5%) cases only. In neuro-imaging, single strategic or multiple cortical infarcts were present alone in 10 (11.6%) cases. Lacunar infarcts or periventricular white matter infarcts were present without cortical infarct in 48 (55.8%) cases. The cortical and sub-cortical infarcts were found together in 28 (32.6%) cases. Thus, the neuroimaging criteria of significant cortical infarcts with or without sub-cortical infarcts for diagnosing VaD were satisfied by 38 (44.2%) cases. Besides, Figure 2 gives distribution of clinical features which are considered for diagnosing VaD. Here, focal neurological deficit (FND) was the most frequent (83.5%) clinical feature, which aided in the diagnosis, followed by impaired cognitive functions other than memory (63.5%) and abrupt onset (52.7%). Table 2 provides the distribution of various FNDs in the study population, with prevalence in the range of 30-40% for first five of them.

Discussion

This study compared DSM-5 with other available diagnostic guidelines for VaD, which has not been done till date. We also determined degree of convergence and the effect-size for the association between DSM-5 and the other guidelines.

In our study, 95.6% of clinical cases of VaD could be diagnosed as VaD by at least any one of the diagnostic guidelines. This proportion is more than that (86.4%) found in the study by Wetterling., *et al*. [7]. which had DSM-IV instead of DSM-5 for comparison. . There is a possibility that the missing of positive cases might have been due to this difference (Table 3). The absence of specific duration to establish temporal correlation between vascular event and cognitive impairment, and the approval of SIVD as a valid diagnosis by DSM-5 are the distinguished features (Box 3). These features would have widened the horizon of diagnosis by DSM-5. The other difference was that the sample population was of patients with dementia having vascular lesions in the previous study, where as it was clinically diagnosed cases of VaD in our study.

The positive VaD diagnosis individually with each diagnostic guideline varied from 50.5% to 89%. Previous studies have this variation from 20.3%-76.3% [7] to 36.4%-91.6%. [8] The variation again, could be due to the different type of sample population and the absence of DSM-5. Nevertheless, all these studies highlight the limitations of the various diagnostic guidelines as a sufficient entity for the diagnosis of VaD.

The cases in which all diagnostic guidelinesagreed to the diagnosis of same category of VaD accounted for 27 out of all 91 cases (28.6%) with VaD. This value of concordance among all diagnostic guidelines, although unsatisfactory, is better than other studies, which quoted 5 out of 59 cases (8.5%) with VaD [7] and 8 cases out of 124 patients (6.4%) with either VaD or Alzheimer's disease [15]. DSM-5 being one of the analysed diagnostic guidelines in the current study can be the possible reason. This might indicate indirectly the better concordance of DSM-5 with other guidelines. In addition, the nature of sample population would have also played the role here. The study considering only post-stroke dementia found better concordance of 29% (31 out of 107 patients) among all guidelines, even though DSM-IV was there [8]. The proportion of the cases rebutted by all 4 guidelines was similar in our study (4.4%) and the latter study (4.6%).

The most important finding of this study, the degree of association between DSM-5 and other diagnostic guidelines indicate the best concordance (67.7%) of DSM-5 with ADDTC. This was also evident in the degree of convergence and effect size estimate (Table 1); both were moderate and statistically significant. The next best concordance and other measures of association of DSM-5 were with NINDS-AIREN with modification for SIVD. Both diagnostic guidelines had also similar frequencies of cases for various diagnostic categories of VaD (Figure 1). These concordance values of DSM-5 in our study were better for NINDS-AIREN without modification for SIVD (46.2% vs 23.9% to 35.7%) and ICD-10 (53.8% vs 32%) compared to what had been noted in the studies related to DSM-IV [7,8]. In these studies, compared to other diagnostic guidelines, ADDTC had better concordance (47.8 to 87.3%) with DSM-IV [7,8]. However, in some studies ADDTC had poorest case finding rate and concordance with other diagnostic guidelines [16].

Similar to that in ADDTC, the convergence and effect size estimate of the association of DSM-5 with NINDS-AIREN with modification for SIVD and other guidelines were also moderate; lowest being with NINDS-AIREN without modification for SIVD (Table 1). And all of these results of our study were statistically significant. Although this moderate level of association is not completely satisfactorily, it still gives confidence that newer guidelines try to incorporate the features of the existing ones. Table 3 demonstrates these useful incorporations by DSM-5, showing the similarities and dissimilarities of each diagnostic guideline with respect to DSM-5. Some of them being the clinical validity of SIVD, prominence of executive function deficits, and no specific time period for establishing temporal correlation between vascular event and dementia [10].

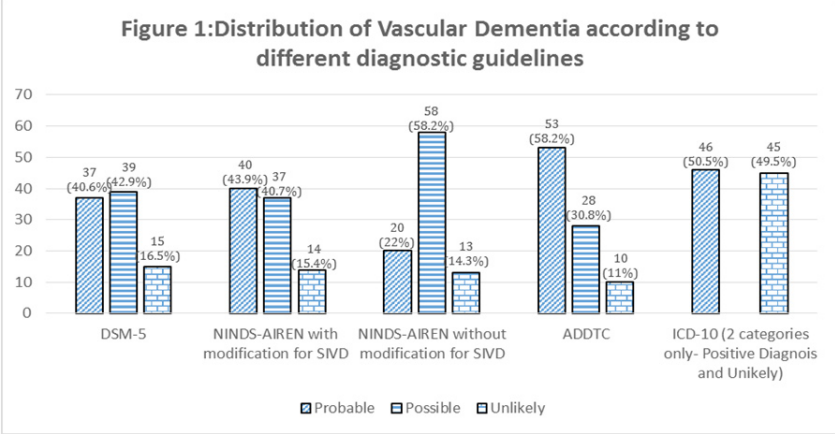
The cortical infarcts alone or with sub-cortical infarcts in neuro-imaging was only evident in 45.1% cases (41 out of 91). On the other hand, the lacunar and/or peri-ventricular infarcts were present without the cortical infarcts in 54.9% cases and additionally in 33% cases with cortical infarcts. This distribution supports the clinical importance of sub-cortical infarcts and validity of SIVD [12]. Besides, Figure 2 describes the prevalence of other essential features; it includes focal neurological deficits (83.5% cases i.e. 76 out of 91) and cognitive functions other than memory (63.7% cases i.e. 58 out of 91). It is evident that the presence of all essential features of various diagnostic guidelines was not mandatory here for the clinical diagnosis of VaD. This might be an important reason for the incomplete coverage of clinical VaD by these guidelines [16,17], as reflected in our study.

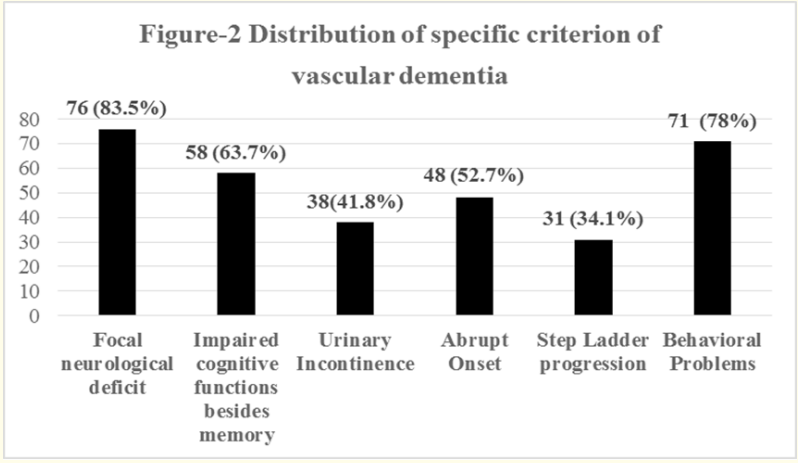
The distribution of metabolic risk factors including the improperly control of them in this study sample supports their association with vascular dementia [18]. The prevalence of various focal neurological deficits underlines their significance in the diagnosis of VaD. Many of them such as dysarthria, dysphagia, gait, rigidity, and other extra-pyramidal symptoms are particularly important in SIVD.

The study had some limitations too. It was a retrospective study and hence, the information collected might be incomplete and of limited accuracy. Besides, this study relied on HMSE and clinical cognitive assessments for the neuropsychology profile. We know that HMSE tests only orientation, registration and recall for verbal memory, attention, and language. It doesn't test visual memory, logical memory, and various executive functions [11,19]. This brings down the reliability of assessing cognitive impairment criteria of various diagnostic sets. The comparison of the specificity of various diagnostic criteria could not be done here as there was no group with other dementia. There were some cases, where the possibility of different dementia was considered. However, no case with the combined diagnosis of VaD and any other dementia were included in the study. At the same time, this diagnosis was concluded clinically and there is a fair chance that we would have included the cases with other or mixed dementia, considering them as VaD. Nonetheless, this is the

first study looking into the relationship of DSM-5 with other diagnostic criteria and had considered the cases of only vascular dementia but with all its categories.

To conclude, changes made in DSM-5 compared to DSM-IV have increased the coverage for the clinical diagnosis of VaD by including SIVD, and removing the specified duration criteria for temporal correlation between vascular event and dementia. Concurrently, DSM-5 is more stringent as it requires the structured neuropsychological testing and prominent executive functions deficits. This study showed the moderate degree of association of DSM-5 with other diagnostic criteria, highest with ADDTC. The results were statistically significant. The prospective cross-sectional and observational studies would help in establishing this inferences and utility of DSM-5.





State of California Alzheimer's Disease Diagnostic and Treatment Centers (ADDTC), [2]

Probable Ischemic Vascular Dementia

A. All of the following
    a. Dementia
    b. 2 or more ischemic strokes OR Single stroke with temporal correlation with dementia
    c. 1 infarct outside cerebellum in CT/ T1-weighted MRI
B. Confirmed supporting features
    a. Multiple infarcts in brain known to affect cognition
    b. Multiple transient ischemic attacks
    c. Vascular risk factors
    d. Elevated Hachinski Ischemic Scale
C. Supporting features awaiting further research
    a. Relatively early gait disturbance and urinary incontinence
    b. Extensive PV and deep WM lesions
    c. Focal changes in electrophysiologic or physiologic neuroimaging studies

Possible Ischemic Vascular Dementia: Either single stroke without temporal correlation with dementia or Binswanger syndrome

International Classification of Diseases, 10th Revision (ICD-10), [4]

A. General criteria for dementia must be met.
B. Unequal distribution of deficits in higher cognitive functions, with some affected and others relatively spared
C. Focal brain damage as at least one of the following:
    a. Unilateral spastic weakness of the limbs;
    b. Unilaterally increased tendon reflexes;
    c. Extensor plantar response;
    d. Pseudobulbar palsy.
D. Evidence from the history, examination, or tests, of a significant CVD, that are judged to be etiologically related to dementia

Vascular Dementia of acute onset: Develops usually within 1 month, but within no longer than 3 months) after a succession of strokes, rarely after single large stroke

Multi-infarct Dementia: Onset of the dementia is gradual (i.e. within three to six months), following a number of minor ischaemic episodes.

Subcortical Vascular Dementia: History of hypertension, and clinical examination along with investigations showing vascular disease to be located in the deep white matter of the cerebral hemispheres, with preservation of the cerebral cortex.

Box 1: *Chief features to diagnose vascular dementia under various criteria- part A.*

**PV, Periventricular; WM, White matter; CVD, Cerebrovascular disease; FND, Focal Neurological Deficits.*

National Institute of Neurological Disorders and Stroke -Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) criteria, [3]

For Probable Vascular Dementia, all should be present

A. Dementia as impairment of memory and any other 2 or more cognitive domains, preferable established by clinical examination and documented by neuropsychological
B. CVD as the presence of FND and evidence of the same in brain imaging
C. Relationship between dementia and CVD, as one or both
    a. onset of dementia within 3 months following a recognized stroke
    b. abrupt deterioration in cognitive functions; or fluctuating, stepwise progression of cognitive deficits

For Subcortical Ischemic Vascular Dementia (SIVD), the brain imaging would show either Binswanger-type white matter lesions or lacunar infarcts with the absence of cortical non-lacunar territorial infarcts and watershed infarcts, and other causes of white matter lesions. The temporal relationship may also be absent.

Diagnostic and Statistical Manual of Mental Disorders–4th Edition (DSM-IV) [5]

A. Development of multiple cognitive deficits manifested by both:
    a. Memory impairment
    b. One or more of the following cognitive disturbances: Aphasia, Apraxia, Agnosia, Disturbance in executive functioning
B. Cognitive deficits each cause significant decline from a previous level of functioning.
C. FND or neuroimaging evidence indicative of CVD that are judged to be etiologically related to dementia.

Box 2: *Chief features to diagnose vascular dementia under various criteria- part B.*

**PV, eriventricular; WM, White matter; CVD, Cerebrovascular disease; FND, Focal Neurological Deficits.*

Diagnostic and Statistical Manual of Mental Disorders–5th Edition (DSM-5), [1]

Vascular Neurocognitive Disorder

A. Criteria met for major or mild neurocognitive disorder.
B. Clinical features are consistent with a vascular aetiology, as either of the following
    a. Onset of the cognitive deficits is temporally related to one or more cerebrovascular events.
    b. Evidence for decline is prominent in complex attention (including processing speed) and frontal-executive function.
C. Evidence of the presence of cerebrovascular disease from history, physical examination, and/or neuroimaging considered sufficient to account for the neurocognitive deficits.

For Probable vascular neurocognitive disorder is diagnosed if one of the following is present; otherwise possible vascular neurocognitive disorder should be diagnosed:

D. Clinical criteria supported by neuroimaging evidence of significant parenchymal injury attributed to cerebrovascular disease.
E. Neurocognitive syndrome is temporally related to one or more documented cerebrovascular events
F. Both clinical and genetic (e.g., cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) evidence of cerebrovascular disease is present.

Box 3: *Chief features to diagnose vascular dementia under various criteria- part C.*

**PV, eriventricular; WM, White matter; CVD, Cerebrovascular disease; FND, Focal Neurological Deficits.*

Diagnosis of VaD	DSM-5 No. of cases (%)	NINDS-AIREN with modification for SIVD No. of cases (%)	NINDS-AIREN without modification for SIVD No. of cases (%)	ICD-10 No. of cases (%)	ADDTC No. of cases (%)
Probable	37 (40.6%)	40 (43.9%)	20 (22%)	46 (50.5%)	53 (58.2%)
Possible	39 (42.9%)	37 (40.7%)	58 (63.7%)		28 (30.8%)
Unlikely	15 (16.5%)	14 (15.4%)	13 (14.3%)	45 (49.5%)	10 (11%)

Table 1: *Distribution of Vascular Dementia cases among various criteria.*

Focal Neurological Deficit	Present N (%)	Absent N (%)
Paresis/Plegia	35 (38.5%)	56 (61.5%)
Gait Disturbances	38 (41.8%)	53 (58.2%)
Dysarthria	27 (29.7)	64 (70.3%)
Asymmetry reflexes	31 (34.1%)	60 (65.9)
Rigidity + Tremors	34 (37.4%)	57 (62.6%)
Primitive reflexes	10 (11.0%)	81 (89%)
Others*	17 (18.7%)	74 (81.3%)

Table 2: *Distribution of various focal neurological deficits.*

** Cerebellar signs, sensory dysfunction, hemineglect, upward gaze palsy.*

Criteria for VaD	Features similar to DSM-5	Features Different from DSM-5
NINDS-AIREN with/ without modification for SIVD*	• VaD can be diagnosed as probable, possible or unlikely • Significance to cognitive functions other than memory • Varied focal neurological signs consistent with stroke and related neuroimaging findings • Provision of diagnosis of SIVD as probable VaD	• Fronto-executive functions are not given significance over language, visuospatial function, praxis and motor control • Onset should be either abrupt, fluctuating or step-ladder • Need of onset of post-stroke dementia within 3months of stroke event
ICD-10	• Provision of diagnosing SIVD • Unequal distribution of impairment in higher cognitive functions	• At least one of the following four neurological signs-unilateral spastic weakness of limbs, unilateral increased tendon reflexes, extensor plantar response, pseudobulbar palsy • Need of development of dementia within specific time period after stroke event (Acute VaD- within 3months, Multi-infarct dementia- within 3 to 6 months) • No provision of probable or possible VaD separately
ADDTC	• VaD can be diagnosed as probable, possible or unlikely • Depends on overall impression of stroke as possible causative factor for dementia • No specificity about type of onset	• Fronto-executive functions are not given significance over memory • SIVD can be diagnosed

Table 3: *Features of different Diagnostic Criteria for Vascular Dementia in comparison to DSM-5.*

**In NINDS-AIREN with modification for SIVD, the features different from and similar to DSM-5 are same as that of NINDS-AIREN without modification for SIVD, except that provision of diagnosis of SIVD is there, as in DSM-5.*

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