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Study of Clinico-Radiological Risk Factors and Laboratory Parameters in Association with Post Stroke Vascular Cognitive Impairment

Dr. Anil Sejwar[1], Dr. Gopal Krishna[2*], Dr. Arpit Dhiran[3]
[1]MD General Medicine, Assisted. Prof. Department of Medicine, GMC, Bhopal, Madhya Pradesh, India
[2]MD General medicine, Senior resident, Dept of Medicine, GMC, Bhopal, Madhya Pradesh, India
[3]MD General Medicine, GMC, Bhopal, Madhya Pradesh, India

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***Corresponding author**
Dr. Gopal Krishna

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Abstract: Cognitive impairment due to cerebrovascular disease is termed." vascular cognitive Impairment "(vici,) and forms a spectrum that includes vascular dementia and milder forms of cognitive impairment referred to as vascular mild cognitive impairment (vci)[1]. Vascular cognitive impairment (vci) has some varied and diverse aetiology. This is particularly important as apart from age. Vascular risk factors are the most important and presently the only treatable precursor to dementia. This prospective observational study was carried out in in department of medicine, Gandhi medical College and associated Hamidia Hospital bhopal. This study covered population of bhopal and neighbouring districts. A standard protocol was applied at admission and 3 months after stroke, this protocol included clinical, functional and cognitive assessments, heamogram and serum biochemistry, ecg, non-contrast CT scan, 2d echo, carotid Doppler and MMSE (mini mental state examination). Mean age of patients having mild cognitive impairment is 63±6. In these study 62% patients belongs to low socioeconomic status. The percentage of patients having low socioeconomic status and low educational status is more in patients having vascular cognitive impairment. Amongst the various risk factors hypertension, diabetes mellitus, prior stroke, dyslipidemia, ischaemic heart disease, tobacco chewing, smoking family history of dementia were more frequently seen vascular cognitive impairment group. In this study, the frequency of patients having post stroke vascular cognitive impairment (VCI) is 54%. 18% of the patients had VaD(Vascular dementia), 36% of the patients had VMCI(vascular mild cognitive impairment), 46% of the patients had NO VCI (no vascular cognitive impairment. There was significant association of risk factors like Hypertension (p=0.022) diabetes mellitus (P=0.038), dyslipidaemia (p=0.034), prior stroke (p=0.046) with development of vascular cognitive impairment. To conclude, post-stroke cognitive impairment is commonly seen and is associated with considerable morbidity and poor functional outcome. Both ischemic and haemorrhagic stroke may result in cognitive impairment. The predictors of development of Vascular cognitive impairment following stroke in this study are lower educational status, Hypertension, Diabetes mellitus, Dyslipidaemia, Prior stroke, Urinary incontinence, High systolic blood pressure, NIHSS score, LDL level, abnormal ECG, Strategic site lesion and greater severity of age related white matter changes.

Keywords: Cognitive impairment, vascular cognitive Impairment, Vascular risk.

INTRODUCTION

Cognitive impairment due to cerebrovascular disease is termed." vascular cognitive Impairment "(vci,) and forms a spectrum that includes vascular dementia and milder forms of cognitive impairment referred to as vascular mild cognitive impairment (vici)[1].

It is now clear that vci is not a single entity, but represents a complex neurological disorder that AA as a result of interaction between vascular risk factors such as hypertension, diabetes, obesity, dyslipidaemia, and brain parenchymal changes such as macro and micro infarction, haemorrhages, white matter changes and brain atrophy occurring in aging brain. Since (vci) is amenable to prevention and treatment, there is pressing need to identify factors that protect or predispose to it [2-5].

Vascular cognitive impairment (vci) has some varied and diverse aetiology, the various forms include cognitive impairment following single strategic

infarction, subcortical (vci), and multiinfarcts dementia, vci rather than vascular dementia (vad) is the more appropriate term, as the correct objective should be to identify the condition before it develops into frank dementia. This is particularly important as apart from age. Vascular risk factors are the most important and presently the only treatable precursor to dementia. Reason for a stroke patient to become demented is still insufficiently understood. All individuals with stroke do not develop dementia; therefore, it is important to determine the risk factors. Some studies have investigated the risk factors, but there has not been a consensus about them [6-10]. Demographic, clinical, stroke related and lesion related radiological factors have been reported to predict dementia in stroke patients.

METHODS

This prospective observational study was carried out in in department of medicine, Gandhi medical College and associated Hamidia Hospital bhopal. This study covered population of bhopal and neighbouring districts.

A standard protocol was applied at admission and 3 months after stroke, this protocol included clinical, functional and cognitive assessments, hemogram and serum biochemistry, ecg, non-contrast CT scan, 2d echo, carotid Doppler and MMSE (mini mental state examination). Demographic and clinical characteristics included are age sex educational level (low level of education defined as Defined as less than 10 years of formal education), socioeconomic status, occupation, family history of dementia, smoking habits, hypertension, diabetes mellitus, hypercholesterolemia, atrial fibrillation, ischaemic heart disease, history of alcohol intake, transient ischaemic attacks, prior stroke and any other ischaemic illness. all patients were subjected to cardiac examination included an electrocardiogram (ecg) and echocardiography of the heart.

Laboratory measurements included are blood sugar on admission, renal and liver functions and lip gram (serum total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol LDL-c, high density lipoprotein cholesterol HDL-c complete blood picture.

Neuroimaging characteristics

A noncontract CT brain examination was done for all patients. The following radiological data were collected: Presence of haemorrhages, infarct subtypes, number, and laterality of lesions and strategic site of the lesion that was defined as the lesions involving areas like thalassemia, causation, Globus pallidus, and anterior limb of internal capsule. Age related white matter changes (ARWMC) were evaluated in all the patients on CT based upon ARWMC scale. White matter changes on MRI were defined as bright lesions >_ 5mm on T2, PD, or flair images. Lesions on CT were defined as hypo dense areas of>_5mm, left and right he. Hemispheres were rated separately. The following brain areas were used for rating: frontal, parito-occipital, temporal, infratentorial /cerebellum and basal ganglia (striatum, globus pallidus, thalamus, internal/external capsule, and insula) Total ARWMC score was calculated as sum of scores in all five regions on both the sides.

Observations

Table-1:Number of patients in different groups

PATIENT GROUP	Frequency	Percent
NOVCI	46	46.0
VMCI	36	36.0
VAD	18	18.0
Total	100	100.0

Table-2: Distribution of patients in different groups according to sex

		ptgroup					
		NOVCI		VMCI		VAD	
		Count	Row N%	Count	Row N%	Count	Row N%
SEX	Female	15	40.50%	15	40.50%	7	18.90%
	Male	31	49.20%	21	33.30%	11	17.50%

						Significance	
		NOVCI		VCI(VMCI & VaD)			
		Count	Row N%	Count	Row N%	Chi square	P value
SEX	female	15	40.50%	22	59.50%	0.7	0.4
	male	31	49.20%	32	50.80%		

Table-3: Mean age in various groups

	ptgroup					
	NOVCI		VMCI		VAD	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
AGE	62	5	63	6	65	6

					Significance	
	NOVCI		VCI(VMCI & VAD)			
	Mean	Standard Deviation	Mean	Standard Deviation	T test	P value
Age	62	5	64	6	1.96	0.05

Table-4: Clinical parameters in various groups

		vci				significance	
		NOVCI		VCI			
		Count	Row N%	Count	Row N%	Chi square	P value
GAIT ABNORMALITY	absent	39	45.90%	46	54.10%	0	0.96
	present	7	46.70%	8	53.30%		
BULBARFEATURES	absent	40	44.40%	50	55.60%	0.88	0.35
	present	6	60.00%	4	40.00%		
PERIPHERAL SIGNS OF ATHEROSCLEROSIS	absent	36	50.70%	35	49.30%	2.18	0.14
	present	10	34.50%	19	65.55%		
HANDEDNESS	left	1	14.30%	6	85.70%	3.05	0.08
	right	45	48.40%	48	51.60%		
	yes	15	51.70%	14	48.30%		
ATRIAL FIBERILLATION	absent	33	47.80%	36	52.20%	0.3	0.59
	present	13	41.80%	18	58.10%		
URINARY INCONTINACE	absent	43	51.80%	40	48.20%	6.63	0.01
	present	3	17.60%	14	82.40%		
SENSORY ABNORMALITY	absent	36	43.90%	46	56.10%	0.81	0.37
	present	10	55.60%	8	44.4		

COMPARISON OF VARIOUS IN VMCI vs vad GROUPS

Table-5: Significance of difference between VMCI Vs VAD

Variables	Chi square	P value
sex	0.04	0.85
Low education	0.17	0.68
Socioeconomic status	0.38	0.54
Handedness	0	1
Hypertension	0.98	0.47
Diabetes	0	1
Alcohol	0.08	1
Smoking	0.05	0.83
Tobacco	0.64	0.43
Ischemic heart disease	0.6	0.44
Dyslipidemia	1.83	0.18
Prior stroke	0.16	0.69
Family h/o dementia	0	1
Atrial fibrillation	0.38	0.54
Urinary incontinence	2.36	0.12
Sensory abnormality	0.07	1
Gait abnormality	0.07	1
Bulbar features	0.14	1
Peripheral signs of atherosclerosis	0.04	1
Ecg	0.6	0.44
Echo	0.04	0.85
Type of stroke	0.84	0.39
Hemisphere involved	0.75	0.69
Type of lesion	0	1
Strategic site lesion	0.34	0.56
Age group	0.73	0.69

Table-6: Showing laboratory parameters in different groups

	ptgroup					
	NOVCI		VMCI		VAD	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
TOTAL CHOLESTROL	135	32	135	40	155	66
LDL	156	45	164	51	190	49
HDL	44	3	43	3	44	4
TRYGLYCRIDE	179	77	154	48	163	53
BLOOD SUGARON ADMISSION	141	45	150	45	152	57

		ptgroup					
		NOVCI		VMCI		VAD	
		Count	Row N%	Count	Row N%	Count	Row N%
ECG	normal	31	55.40%	18	32.10%	7	12.50%
	abnormal	15	34.10%	18	40.90%	11	25.00%
ECHO 2D	normal	22	50.00%	15	34.10%	7	15.90%
	abnormal	24	42.90%	21	37.50%	11	19.60%

Table-7: Neuroimaging characteristics

		Pt group					
		NOVCI		VCI		VAD	
		COUNT	ROW N %	COUNT	ROW N%	count	Row N%
TYPE OF STROKE	ISCHEMIC	44	47.8	33	35.9	15	16.3
	HAEMORHAGIC	2	25.0	3	37.5	3	37.5
HEMISPHERE INVOLVED	NON DOMINANT	17	51.5	12	36.4	4	12.1
	DOMINANt	22	40.7	20	37.0	12	22.2
TYPE OF LESION	SINGLE	28	53.8	16	30.8	8	15.4
	MULTIPLE	18	37.5	20	41.7	10	20.8
STRATEGIC SITE LESION	ABSENT	39	56.5	21	30.4	9	13.0
	PRESENT	7	22.6	15	48.4	9	29.0

		vci				significance	
		NOVCI		VCI			
		COUNT	ROW N %	COUNT	ROW N%	Chi square	P value
TYPE OF STROKE	ISCHEMIC	44	47.8	33	35.9	1.54	0.214
	HAEMORHAGIC	2	25.0	3	37.5		
HEMISPHERE INVOLVED	NON DOMINANT	17	51.5	12	36.4	1.33	0.515
	DOMINANt	22	40.7	20	37.0		
TYPE OF LESION	SINGLE	28	53.8	16	30.8	2.68	0.101
	MULTIPLE	18	37.5	20	41.7		
STRATEGIC SITE LESION	ABSENT	39	56.5	21	30.4	9.92	0.002
	PRESENT	7	22.6	15	48.4		

RESULTS

This study was aimed to study the cognitive functions at 3 months post-stroke and to determine the clinical, neuro-imaging, laboratory predictors of post stroke cognitive impermanent.

This was a prospective observation study conducted in department of Medicine, Gandhi medical college and Hamidia hospital Bhopal for duration of 1year and following observations were made:

- In this study, the frequency of patients having post stroke vascular cognitive impairment (VCI) is 54%. 18% of the patients had VaD(Vascular dementia), 36% of the patients had VMCI(vascular mild cognitive impairment), 46% of the patients had NO VCI (no vascular cognitive impairment).
- There was no gender preponderance in both the group.
- In our study mean age of patients having no vascular cognitive impairment is 62 ± 5years. Mean age of patients having mild vascular cognitive impairment is 63±6 years and Mean age of patient having vascular dementia (VaD) is 65±6 years.
- In this study 62% of the patients belong to low socioeconomic status and 38% of patients belong to middle socioeconomic status.
- In our study, patients with vascular cognitive impairment 9VCI) had significantly lower educational status (p=0.036), as compared to those who did not develop vascular cognitive impairment (VCI).
- There was significant association of risk factors like Hypertension (p=0.022) diabetes mellitus (P=0.038), dyslipidemia (p=0.034) , prior stroke(p=0.046) with development of vascular cognitive impairment.
- In this study, through risk factors like ischemic heart disease, tobacco chewing, smoking and family history of dementia were more frequently seen in VCI (vascular cognitive impairment) group than NO-VCI group the difference is note significant.
- In this study, the clinical parameters which significantly associated with development of vascular cognitive impairment are urinary incontinence (P=0.01), systolic blood (p=0.049), and baseline stroke severity score (p=<0.001).
- The clinical parameters like gait abnormality, peripheral signs of atherosclerosis and atrial fibrillation are more frequently found in VCI group but the difference was not stastically significant.
- The laboratory parameters which is significantly associated with vascular cognitive impairment is high LDL level (p=0.041).
- The parameters like high blood sugar on admission, high triglycerides level, and high cholesterol level were frequently found in vascular cognitive impairment group, but are not statistically significant.

- The abnormal ECG (p=0.034) is significantly associated with vascular cognitive impairment.
- In our study the neuroimaging features like strategic site lesion (p=0.002) and higher ARWMC score (p=0.001) were significantly associated with VCI.
- There is no significant association of type of stroke (ischemic vs hemorrhagic), dominant hemisphere involvement and number of lesions with vascular cognitive impairment in our study.
- Out of various demographic parameters, clinical parameters, laboratory parameters, risk factor profile and neuroimaging features, none of them was significantly differ in VMCI (vascular mild cognitive impairment and VaD (vascular dementia) group.

DISCUSSION

Cognitive impairment significantly adds to post-stroke morbidity besides physical disabilities caused by stroke it, ultimately resulting in poor functional outcome over a period of time. With time, there have been numerous modifications and changes in the terminologies related to the concept of pst-stroke cognitive dysfunction. With the introduction of the concept of vcl which represents even broader spectrum of post stroke cognitive impairment, these studies need fresh consideration.

In the present study, the frequency of vaD was 18% whereas that of VMCI was 36% Most of the studies done previously had focused on VaD [11-13] with ittle emphasis on VMCI (mild cognitive impairment) [14,15] which may be considered as a prodromal phase of vaD. higher rates were reported by pohjasvaara *et al*. [16] (31.8%) and Barba *et al*.[17] (30%). Few authors such as Madureira *et al*. [18] (6%) and Rasquin *et al*. [19] (7.7%) however, had reported considerably lesser rates of PSD. Allan *et at*. The wide range of variations in rates of PSD in these studies might be the result of different criteria which are used for diagnosing VaD as the sensitivity defers with each criterion. Thus, definition which is being used for diagnosing vaD must be given due consideration while interpreting the rates of PSD. Apart from VaD, 36% patients in this study had VMCL. Sachdev *et al*. reported that 36.7% patients developed VMCl in their study. Rasquin *et al*. reported a very high prevalence rate (61.3%) of post-stroke MCI at 6 months.

Hebert *et al*. found that diabetes hypertension in females, and presence of Apo lipoprotein E were found to associated with vascular dementia as compared to controls. Pohjasvaara *et al*. found that total cholesterol, associated with post stroke dementia, in another study; hypertension, atrial fibrillation, ischemic heart disease, and family history of dementia were significantly found to be associated with post stroke dementia.

They also found that patients with VaD more frequently had higher LDL and lower HDL levels, although the difference was not significant. The risk factors predispose the individuals to develop VCI by increasing the risk of stroke itself and recurrent strokes leads to cumulative cognitive dysfunction ultimately leading to VaD. So the more the risk factors, the more is the risk of developing recurrent strokes and hence the chances of developing VCI. Hyperglycemia during the acute phase of stroke may be stress related or may be due to preexisting diabetes. It may exacerbate the cellular damage in metabolically challenged tissue i.e. penumbra. It does so by inducing lactic acidosis as a result of anaerobic metabolism and by producing free radicals. Lipid peroxidation further adds to the cellular damage. Besides, insulin resistance also contributes to the risk of stroke [20]. Elevated LDL level is a well-known risk factor for atherosclerosis which also affects intracranial vasculature as a result of endothelial dysfunction thus increasing the propensity to recurrent clinical and subclinical ischemic events and predisposing the individuals to cognitive impairment.

Amongst the neuroimaging features, presence of strategic site lesion and higher ARWMC scores were significantly associated with development of VCI, but there was no correlation with type of stroke (ischemic) and laterality of stroke with VCI. Sachdev *et al*. [15] found no significant association between laterality of stroke and VCI. However, they reported that patients with post stroke cognitive impairment had significantly higher load of total as well as periventricular white mater hyper intensities (WMH) in terms of absolute volume. Sudo *et al*. [21] Found that VaMCI was significantly associated with severity of the white matter hyper intensities as graded by Fazekas scale, the higher grades being more frequently associated with development of cognitive impairment than the lower grades. Few other studies support the fact that dementia occurred more frequently in strokes involving dominant hemisphere [11, 16] other studies have mentioned smoking and myocardial infarction as the predictors of PSD.

On statistical analysis, the parameters which were significantly associated with VCI are low level of education ($\leq$ 10 years of formal education),hypertension, diabetes mellitus, dyslipidemia, prior stroke, urinary incontinence, abnormal ecg, higher LDL level, higher systolic blood pressure, strategic site lesion ,higher ARWMC score and baseline stroke severity (NIHSS) score. In addition, we compared VMCI with VaD .However the difference between two groups in various parameters was not statistically significant. Very few studies have compared these two subtypes of post-stroke cognitive.

This study had several limitations. First, we excluded a fair number of patients for various reasons.

This could have led to underestimation of the prevalence of post stroke cognitive dysfunction. Secondly, follow-up duration in this study was limited to 3 months. Studies have revealed that cognitive impairment may improve over a period of time; hence, longer follow-up with larger homogenous study population is required to study the evolution of post-stroke cognitive impairment. Thirdly we used CT scan for neuroimaging whereas MRI is more sensitive than CT.

CONCLUSION

To conclude, post-stroke cognitive impairment is commonly seen and is associated with considerable morbidity and poor functional outcome. Both ischemic and hemorrhagic stroke may result in cognitive impairment. The predictors of development of Vascular cognitive impairment following stroke in this study are lower educational status, Hypertension, Diabetes mellitus, Dyslipidemia, Prior stroke, Urinary incontinence, High systolic blood pressure, NIHSS score, LDL level, abnormal ECG, Strategic site lesion and greater severity of age related white matter changes. Better insight into the risk factors for post stroke cognitive impairment may provide preventive and therapeutic opportunities for vascular cognitive impairment.

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