

## Cognitive Impairment after Stroke

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### ABSTRACT

**Background :** Stroke remains an important cause of morbidity worldwide resulting not only in physical disability but also significant cognitive impairment. Most studies have focussed on physical consequences of stroke with only scarce data available on post stroke cognitive decline. Hence, the present study was undertaken to assess cognitive impairment after stroke and to evaluate other vascular risk factors contributing to it.

**Materials and methods :** This hospital based case control study of 84 cases was undertaken with the aim to assess cognitive impairment in cases of first ever ischaemic stroke. Association between cognitive impairment and physical disability, stroke territory, and conventional vascular risk factors for stroke were assessed. Cognitive impairment was assessed using MMSE scale, physical disability was calculated according to Modified Rankin Scale and stroke territory was classified according to the Oxfordshire Community Stroke Project (OCSP). All cases underwent detailed clinical evaluation as per a pre designed interviewer based questionnaire.

**Results :** Out of the 84 cases of first ever ischaemic stroke studied, 48(57.14%) had cognitive impairment at presentation and 41 (48.8%) had persistence of cognitive impairment at the end of 1 month. Cognitive impairment was significantly higher in cases with increasing severity of physical disability [ $r=-0.656$ ,  $p<0.0001$ , HS].

Cognitive impairment was most profound in cases of TACI(92.3%) and least in cases with lacunar stroke (36.84%). Hypertension, diabetes, dyslipidemia, obesity were significantly associated with cognitive impairment in cases of stroke. On multiple logistic regression analysis ischaemic stroke was independently associated with cognitive impairment.

**Conclusion :** Cognitive impairment is a prominent sequelae of stroke. Its frequency increases with increasing degree of physical disability, increased size of infarct and coexistence of conventional risk factors for stroke. However ischaemic stroke itself remains independent and significant predictor of cognitive impairment.

**Key-words :** Stroke, cognitive impairment.

### Introduction :

Cerebrovascular disease is an important cause of morbidity worldwide, resulting not only in physical disability, but also significant cognitive impairment. Most studies on stroke outcomes have focussed on physical consequences, only a handful have examined intellectual deficits<sup>1</sup>. Approximately one quarter of patients remain demented three months after a stroke. Even among those who remain cognitively intact after their index stroke, hospital and population based studies have revealed a significant risk of developing delayed dementia in them. Current global trends of ageing and decline in

stroke mortality result in an increased incidence of post stroke cognitive impairment, thus significantly increasing healthcare expenditure. There are still no adequate answers to questions such as why stroke patients are at higher risk for cognitive impairment and what mechanisms characterize the development of dementia<sup>2</sup>.

Hence the present study was carried out to evaluate cognitive impairment after ischaemic stroke, to identify vascular risk factors for post stroke cognitive impairment and clinical determinants of cognitive impairment in acute phase of stroke.

### Aims and Objectives :

The current study was undertaken in cases of first ever stroke with the aim

1. To assess cognitive impairment in patients with first ever ischaemic stroke at initial presentation and after 1 month and compare it with age and gender matched controls.

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2. To correlate cognitive impairment with physical disability at presentation.
3. To correlate cognitive impairment with territory of infarct.
4. To study the association of cognitive impairment with vascular risk factors viz - obesity, hypertension, diabetes mellitus, dyslipidemia and smoking.

#### Methodology :

After obtaining the approval from the Institutional Ethics Committee this hospital based case control study was initiated. 84 consecutive and consenting cases of CT proven acute ischaemic stroke were enrolled in the study. Patients <40 years and >65 years were excluded from the study. Subjects with previous history of stroke, stroke due to haemorrhage or head injury or non vascular causes like abscesses and neoplasms were also excluded from the study. Also, subjects with aphasia, history of psychiatric disorder and other causes of dementia viz- Alzheimer's, Parkinsonism, multiple sclerosis, hypothyroidism, vitamin deficiencies. Alcoholism, meningitis were excluded from the study.

Cognitive impairment was assessed using the Mini Mental Status Examination Score (MMSE).<sup>3</sup> Physical disability was calculated using the Modified Rankin Scale (MRS).<sup>4</sup>

Ischaemic stroke was classified into territorial subtype, using the Oxfordshire Community Stroke Project (OCSP)<sup>5</sup>.

A thorough clinical examination of all enrolled subjects was undertaken. Demographic information, behavioural risk factors like smoking and history of hypertension, diabetes mellitus, ischaemic heart disease were recorded by an interviewer administered questionnaire which was predesigned.

#### Results :

A total of 84 cases of first ever ischaemic stroke were enrolled in the study and compared with age and gender matched controls. 48 (57.14%) out of 84 cases had cognitive impairment at presentation.

The mean MMSE score in cases was 23.84 (+/- 5.89) as opposed to 28.37 (+/- 3.44) in controls demonstrating a significant cognitive impairment in cases as compared to healthy controls [p <0.001, HS]. (**Table 1&2**) At presentation 48 cases (57.14%) had cognitive impairment and at the end of 1 month 41 (48.8%) cases still had cognitive impairment [p=0.279] suggesting that there was persistence of significant cognitive decline even after 1 month of index stroke. (**Table 3**) On correlating cognitive impairment with physical disability it was found that MRS score was negatively correlated with MMSE score. Cognitive impairment was significantly higher in stroke cases with more physical disability [r= - 0.6566, p<0.0001, HS]. A TACI (Total Anterior Circulation Infarction) was associated with significant cognitive impairment (92.3%), whereas cognitive impairment was least in a stroke with lacunar infarction (36.84%). (**Table 4**)

**Table 1 : Cognitive Impairment as measured by MMSE Scale in Cases and Controls**

Cognitive Impairment	Cases (n=84)	Controls (n=84)	Chi 2	OR	95% CI	p-value
MMSE Score < 25	48 (57.14%)	15 (17.85%)	27.66	6.13	2.88 - 13.33	<0.001, HS
MMSE Score ≥ 25	36 (42.85%)	69 (84.52%)				
MMSE Score (Mean ± SD)	23.84 ± 5.89	28.37 ± 3.44	p-value 0.0001, HS			

**Table 2 : Comparison of Cognitive impairment in Ischemic Stroke Cases at Presentation and after 1 month**

Cognitive impairment	At presentation n=84	At 1 month n=84	p-value
Present (MMSE SCORE < 25) n (%)	48 (57.14%)	41 (48.80%)	0.279, NS
Absent (MMSE SCORE > 25) n (%)	36 (42.85%)	43 (51.19%)	

**Table 3 : Correlation of cognitive impairment (by MMSE) with physical disability (by mRS Score) at presentation**

mRS Score	No. of Cases (n=84)	Mean MMSE Score (mean ± SD)	r-value	p-value
0	4 (4.76%)	28.75 ± 2.5	-0.6566	0.0001, HS
1	14 (16.67%)	28.57 ± 2.31		
2	19 (22.61%)	25.15 ± 3.02		
3	31 (36.9%)	24.19 ± 4.26		
4	12 (14.28%)	17.91 ± 7.27		
5	4 (4.76%)	11.25 ± 1.5		
6	-	-		

mRS Score - modified Rankin Scale Score, MMSE - Mini Mental State Examination Score

**Table 4 : Correlation of territory of infarct with cognitive impairment**

Territory of Infarct	Cognitive impairment (n=84)	No cognitive impairment (n=36)	p-value
TACI (n=26)	24 (92.30%)	2 (7.69%)	0.0001, HS
PACI (n=10)	4 (40%)	6 (60%)	1.000, NS
LI (n=38)	14 (36.84%)	24 (63.15%)	0.0001, HS
POCI (n=10)	6 (60%)	4 (40%)	1.000, HS

Association between vascular risk factors and cognitive impairment in cases of ischaemic stroke was studied. It was found that generalised obesity, hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease but not smoking were significantly associated with cognitive impairment in cases of stroke. (**Table 5**)

Multiple logistic regression analysis was done with cognitive impairment as dependent outcome variable and other vascular risk factors as independent variables in acute ischaemic stroke. It was found that ischaemic stroke was independently and significantly associated with cognitive impairment after controlling for other risk factors of cognitive impairment.

#### Discussion :

Stroke is an important cause of morbidity, resulting not only in physical disability but also significant cognitive impairment<sup>1</sup>. Post stroke cognitive impairment is defined as cognitive deficit which develops upto 3 months after index stroke which is not associated with any other underlying disease viz metabolic, vasculitis etc<sup>2</sup>. The term post stroke dementia includes all types of dementia following an index stroke, whether vascular, degenerative (eg-Alzheimer's) or mixed<sup>6,7,8</sup>. American Stroke Association (ASA) uses a more adequate term, Vascular Cognitive Impairment (VCI), defined as any type of cognitive deficit associated with clinical stroke or subclinical vascular brain injury<sup>9,10,11</sup>.

**Table 5 : Association of vascular risk factors for stroke with cognitive impairment in cases**

Risk factor n (%)	Cognitive impairment (n=84)	No cognitive impairment (n=84)	OR	95% CI	p-value
Generalized Obesity	15 (31.25%)	3 (8.33%)	5.0	1.22 - 28.94	0.011, S
Hypertension	39 (81.25%)	20 (55.56%)	3.46	1.17 - 10.48	0.0108, S
Diabetes Mellitus	17 (35.41%)	5 (13.89%)	3.4	1.02 - 13.10	0.026, S
Dyslipidemia	38 (79.16%)	8 (22.23%)	13.3	4.18 - 43.76	<0.0001, HS
Smoking	9 (18.75%)	4 (11.12%)	1.84	0.46 - 8.92	0.338, NS
Ischemic Heart Disease	21 (43.75%)	7 (19.45%)	3.22	1.08 - 10.33	0.019, S

**Table 6 : Multiple logistic regression analysis for independent risk factors of cognitive impairment in study subjects**

Risk Factor	Adj OR	95% C.I.	p-value
Ischemic Stroke	3.24	1.43 - 7.32	0.005
Diabetes Mellitus	3.05	1.25 - 7.40	0.014
Dyslipidemia	5.10	2.27 - 11.44	< 0.001
Ischemic heart disease	5.57	2.04 - 15.25	0.001
Obesity	1.01	0.382 - 2.69	0.382
Hypertension	1.67	0.715 - 3.90	0.236

About 25 to 50% stroke survivors develop post stroke dementia<sup>12</sup>.

In the present study 48 out of 84 (57.14%) stroke cases had cognitive impairment. Rist PM et al in their cross-sectional study carried across ten countries, found a 30% prevalence of cognitive impairment in stroke survivors<sup>13</sup>. In the current study, cases were evaluated for cognitive impairment at the end of 1 month after their index stroke. At presentation 48 (57.14%) out of 84 stroke cases had cognitive impairment. At the end of one month 41 (48.8%) had cognitive impairment.

Uma Sunder<sup>14</sup> found 51 (31.7%) out of 764 cases to be suffering from cognitive impairment at the end of 3 months after stroke. Rasquin SM et al<sup>15</sup> found 51 (31.7%) in the Maastricht-CODAS study found that 70% of stroke cases had persistent cognitive impairment at the end of 6 months. Jacquin A et al<sup>16</sup> also demonstrated a high prevalence (47.3%) of cognitive impairment, 3 months after stroke. The current study revealed that cognitive impairment was significantly high in stroke cases with increasing physical disability [ $r=-0.656$ ,  $p<0.0001$ ]. Mukhopadhyay A et al<sup>17</sup> found a similar relationship between cognitive impairment and physical disability in cases of stroke. However, Brendan Kelly et al<sup>18</sup> found no such relationship, implying that cognitive functions have to be assessed independently.

In the present study TACI (Total Anterior Circulation Infarction) was associated with more profound cognitive impairment as compared to other stroke types, including lacunar infarcts.

Iso H et al<sup>19</sup> found large infarcts, lacunar infarcts, and dominant hemispheric lesions were more frequently associated with cognitive impairment. Nys and

colleagues<sup>20</sup> reported that fewer than 50% cases of subcortical or infratentorial strokes had cognitive impairment as compared to 74% of cortical infarcts.

In the present study, vascular risk factors like obesity, hypertension, diabetes mellitus, dyslipidemia were also associated with cognitive decline in cases of stroke. No such association was found with smoking.

Graban et al<sup>21</sup> studied vascular and biochemical risk factors in both lacunar and multiinfarct strokes. They found that coronary artery disease, atrial fibrillation, hypertension, hyperhomocysteinemia and low HDL cholesterol were significantly associated with cognitive impairment. In the current study multiple logistical regression analysis showed that ischaemic stroke was independently and significantly associated with cognitive impairment. The mechanisms explaining post stroke cognitive impairment are multifactorial including coexisting vascular risk factors and also accompanying degenerative changes. Therefore, a working algorithm for early assessment of potential modifiable and non modifiable risk factors of post stroke cognitive impairment is highly warranted for successful prevention and treatment of post stroke cognitive impairment.

#### **Conclusion :**

Sizeable number of cases of first ever ischaemic stroke have cognitive impairment at presentation and also at the end of 1 month follow up. Severe physical disability in stroke is associated with more profound cognitive impairment. Large territory strokes show more cognitive decline. Conventional vascular risk factors are more prevalent in cases of ischaemic stroke as compared to controls and are also significantly associated with cognitive

impairment. Ischaemic stroke is independently and significantly associated with cognitive impairment.

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