Prevalence of Cognitive Impairment and Dementia After Intracerebral Hemorrhage

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Abstract

Objective: To study the prevalence of cognitive impairment in survivors of intracerebral hemorrhage (ICH). **Methods:** Survivors of spontaneous ICH were followed up in the neurology outpatient department when they reported for follow-up after 6 months. Neuroimaging records at the onset and at follow-up visits are studied for the location of ICH, volume of ICH, intraventricular extension, and hydrocephalus. The volume of ICH is calculated by ABC/2 method on a CT scan. All patients underwent cognitive assessment with Addenbrooke's cognitive examination ACE III and were categorized as patients having cognitive impairment (or) no cognitive impairment. **Results:** A total of 120 patients were studied, out of which 77 (64%) are males and 43 (36%) are females with age groups ranging from 26 to 75 years. In the study population, the mean age was found to be 62.3 years. Specifically, the mean age for males was 56.9 years, while for females it was 63.4 years. Cognitive impairment was noted in 34 of 120 patients (28%) during 6 to 12 months of examination, of which 11 of 19 were in lobar location, 21 of 94 were in sub-cortical location, and 2 of 7 were in infratentorial location. **Conclusion:** It was found that 28% of survivors of ICH were cognitively impaired. Hence, it is essential to assess cognition in post-ICH patients during follow-up, so that suitable adjustments can be made in their employment, and also in educating family members in providing a good quality of life.

Keywords: Cognitive impairment, dementia, DSM-V, intracerebral hemorrhage (ICH)

Introduction

Spontaneous Intra cerebral Haemorrhage (ICH) is due to bleeding into the brain parenchyma because of the rupture of small vessels. ICH represents only 10 to 10% of all strokes, but it has an increased risk of morbidity and mortality when compared to ischemic stroke.[1,2] It has been established through previous studies that the underlying pathologic mechanism is different for different locations of ICH such as ICH located in lobar regions (lobar ICH), predominantly due to rupture of medium and small-sized arterial perforators in the cortex.[3] Whereas deep ICH is located in deep brain regions due to rupture of small arterioles predominantly in the putamen or thalamus.[4-6]

Progressive beta-amyloid deposition within small vessel walls and small cortical vessels accounts for most of the lobar ICH,[7-10] whereas vasculopathy affecting deep perforating vessels (lipohyalinosis, arteriosclerosis, fibrinoid necrosis) results in deep ICH.[3] In both forms of ICH, high rates of daily living dysfunction were reported.[11-15]

Despite the high prevalence of cognitive impairment of ICH (5%–44%),[16] much attention has not been focused on the same, regarding the mechanism and pathophysiology leading to it. Earlier studies suggested that cognitive impairment may be one of the predictors of mortality in patients surviving ICH.[17]

Hence, a thorough knowledge of the association between cognitive impairment and ICH would be important to guide the clinical management of survivors.

Aims and Objectives

Aim

To study the prevalence of cognitive impairment and dementia in survivors of spontaneous ICH after 6–12 months.

Objectives

1. To estimate the prevalence of cognitive impairment in a cohort of patients of spontaneous ICH after 6–12 months follow-up.
2. To study the association between the location of ICH and cognitive impairment.
3. To study the association between the volume of ICH and cognitive impairment.
4. To study the correlation between the clinical features at onset and cognitive impairment.

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Method of Data Collection

Survivors of spontaneous ICH were followed up in the neurology outpatient department when they reported for follow-up after 6 months. The demographic profile, risk factors, co-morbidities, and family history were verified at the follow-up visit. Neuroimaging records at the onset and follow-up visits are studied for the location of ICH, the volume of ICH, intraventricular extension, and hydrocephalus. The volume of ICH is calculated by the ABC/2 method on a CT scan. All patients underwent cognitive assessment with Addenbrooke's cognitive examination ACE III and were categorized as patients having a cognitive impairment (or) no cognitive impairment. A cut-off score of 82 out of 100 denotes the presence of dementia with a sensitivity of 84% and specificity of 100%, whereas a cut-off score of 88 denotes the presence of dementia with a sensitivity of 94% and specificity of 89%. The data collected based on Addenbrooke's proforma is extracted and studied according to DSM-V criteria for categorization of patients into cognitively impaired or not impaired.

According to DSM-V, cognitive impairment is defined as

A. Evidence of significant cognitive decline from the previous level of performance in one or more cognitive domains.
   - I. Learning and memory
   - II. Language
   - III. Executive function
   - IV. Complex attention
   - V. Perceptual motor
   - VI. Social cognition

B. The cognitive deficits interfere with the independence of everyday activity. At a minimum, assistance should be required for complex instrumental activities of daily living.

C. The cognitive deficits do not occur exclusively in the context of delirium.

D. The cognitive deficits are not better explained by another mental disorder.

Based on the above criteria, patients were categorized into whether they were cognitively impaired or not.

Inclusion and exclusion criteria

Inclusion criteria

1. Survivors of ICH in the age group of more than 18 years.
2. Only cases of spontaneous ICH included.

Exclusion criteria

1. ICH secondary to infection.
2. ICH secondary to vascular malformations and head trauma.
3. ICH secondary to CVT, tumor, hemorrhagic, and transformation of the infarct.

Results

A total of 120 patients were studied, out of which 77 (64%) were male and 43 (36%) were female within the age group ranging from 26 to 75 years. The mean age in the study population was 62.3 years; 56.9 years for males and 63.4 years for females correspondingly. Preexisting illness in the form of hypertension was noted in 70 people (M = 37, F = 33), diabetes mellitus was seen in 25 (M = 14, F = 11), Coronary Artery Disease (CAD) in 6 (M = 3, F = 3), and cerebrovascular accident (CVA) in 9 subjects (M = 6, F = 3).

Table 1 demonstrates the demographic profile. All the patients were examined between 6 and 12 months following ictus/hemorrhage.

Imaging characteristics

Based on CT brain findings [Figure 1], of the 120 subjects, 94 (78%) had a bleed involving subcortical locations, including the basal ganglia (62%) and thalamus (16%). Lobar bleed was seen in 19 (16%) patients, and infratentorial bleed was observed in 7 patients (6%). Of all the subjects, 66 had a bleed volume of fewer than 10 ml (55%), 26 had a bleed volume of 1020 ml (22%), 13 patients had a bleed volume of 2030 ml (11%), 7 patients had a bleed volume of 3040 ml (6%), and 8 were noted to have a bleed volume of more than 40 ml (6%).

Table 1: Demographic profile

Characteristics	Distribution
Age	62.3 (± 11.24)
Mean±SD	56.9 (± 11.74) (m), 63.4 (± 10.74) (f)
Gender *n* (%)	
Male	77 (64)
Female	43 (36)
Premorbidities *n* (%)	
Hypertension	70 (58)
Diabetes mellitus	25 (20)
Cerebrovascular accident	06 (05)
Coronary artery disease	09 (08)
Others	03 (03)
Nil	07 (06)
Risk factors *n* (%)	
Smoking	52 (43)
Alcohol	21 (18)
Others	06 (05)

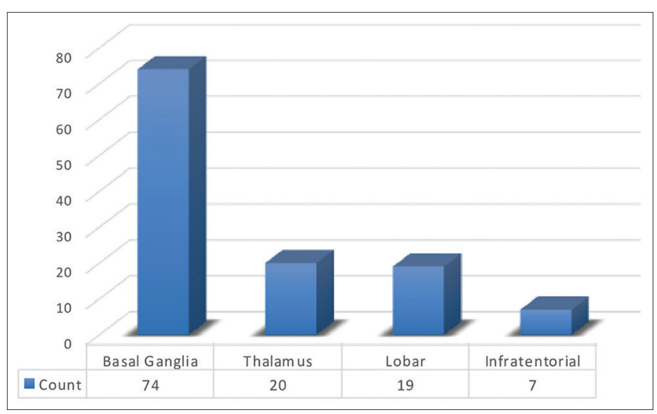

Figure 1: Location of bleed. X-axis: location of bleed, Y axis: number of cases

Clinical presentation [Table 2]

Hemiparesis was the presenting symptom in 56 patients (47%) whereas 39 patients presented with altered sensorium (33%), 4 patients (3%) presented with seizures, and the remaining 27 patients (22%) presented with other symptoms such as headache, loss of consciousness, etc.

Cognitive impairment [Table 3]

Cognitive impairment was noted in 34 of 120 patients (28%) during 6–12 months of examination of which 11 of 19 were in the lobar location, 21 of 94 in the subcortical location, and 2 of 7 in the infratentorial location [Figure 2]. When a patient presents with either hemiparesis or altered sensorium, they were noted to have cognitive impairment with a significant *P* value of 0.017 and 0.001, respectively. However, when they present with either seizures or other symptoms such as headache, loss of consciousness does not find to have any strong association. Apart from presenting symptoms, the location of the bleed also has effects on cognition such as when the bleed location was in the basal ganglia, thalamus, and infratentorial region, it was noted to have a significant correlation with a *P* value of 0.000, 0.005, and 0.008, respectively. It was also not found to have any significant association with the lobar location of the bleed.

This study did not find any significant correlation between cognitive impairment and the side of the brain affected whatever may be the location.

The data between Addenbrooke's criteria and DSM-V were compared and were found that DSM-V criteria might be more accurate in detecting subjects with cognitive impairment.

Discussion

A total of 120 patients were included in the study.

The mean age group in the present study was 62.3 ± 15 years, which is similar to Garcia *et al*. (61.7 ± 14)[18] and Moulin *et al*. (67.5 ± 9).[19] Gender distribution in our study showed male predominance (1.7:1), similar to the earlier studies. Most of the patients in our study had hypertension (HTN) followed by diabetes mellitus as the premorbidities. Among 9 patients who had CVA earlier, 6 patients had cognitive impairment suggesting that there is more than one pathophysiologic mechanism underlying it. A total of 12 patients did not have any premorbidities before hospital admission and were in the age group of 49–58 years, among which 75% of patients were found to have HTN during the preceding hospital stay, and hence were started on anti-HTN medications. One patient among the above-mentioned 12 patients had a snake bite 2 weeks before presentation, and the location of ICH was the

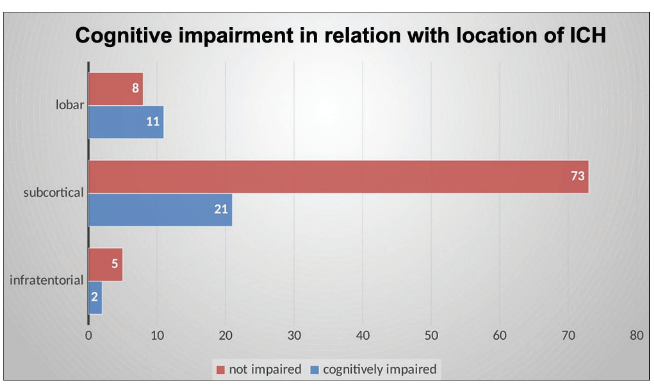

Figure 2: Cognitive impairment in relation with location of ICH. x axis: No of subjects, Y axis: Location of bleed

Table 2: Clinical characteristics

Characteristics	Distribution
Initial symptoms of stroke *n* (%)	
Hemiparesis	56 (47)
Altered sensorium	39 (33)
Seizures	04 (3)
Others	27 (17)
Location of bleed *n* (%)	
Cortical	19 (16)
Sub-Cortical	
Basal ganglia	74 (62)
Thalamus	20 (16)
Infratentorial	07 (06)
Volume of bleed *n* (%)	
0–10 ml	66 (55)
10–20 ml	26 (22)
20–30 ml	13 (11)
30–40 ml	07 (06)
>40 ml	08 (06)
Intra-ventricular extension *n* (%)	
Present	37 (69)
Absent	83 (31)
Hydrocephalus *n* (%)	
Present	24 (20)
Absent	96 (80)
Side of the brain affected *n* (%)	
Left	51 (43)
Right	69 (58)

Table 3: Studied variables and cognitive impairment

Variables	*P*	S/NS
A. Symptoms on presentation		
1. Hemiparesis	0.017	S
2. Altered sensorium	0.001	S
3. Seizures	0.328	NS
4. Others	0.865	NS
B. Location of bleed	0.008	S
C. Volume of bleed		
1. Basal ganglia	0.000	S
2. Thalamus	0.005	S
3. Infratentorial	0.008	S
4. Lobar	0.389	NS
D. Side affected (Left/Right)		
1. Basal ganglia	0.186	NS
2. Thalamus	0.178	NS
3. Infratentorial	0.179	NS
4. Lobar	0.149	NS

Significant (S), Not significant (NS)

lobar location which later presented with executive function deficits during the examination.

Hemiparesis and altered sensorium as the presenting symptoms during the initial period of illness were found to be strongly associated with cognitive impairment. This set of symptoms with a correlation to cognitive impairment has not been studied earlier. The probable reason for cognitive impairment can be stroke as it is associated with varying degrees of altered sensorium ranging from the defective level of arousal to frank delirium. This appears to be multifactorial such as acute illness, and prolonged insult to brain parenchyma because of the death of neurons which may lead to poor cognitive outcomes following recovery.[20]

Similarly, the association between hemiparesis as a presenting symptom in ICH, and cognitive impairment is not studied but may be attributed to a similar pathogenic mechanism as encountered in patients with ischemic stroke.

In the present study, a few patients did not present with either hemiparesis or altered sensorium or seizures, but they presented with other symptoms such as headache, vomiting, giddiness, and loss of consciousness (n = 21). The cognitive impairment in that group does not have statistical significance ($P > 0.005$). From our study, it is evident that when a patient presents with either altered sensorium ($P = 0.001$) or hemiparesis ($P = 0.017$), they have higher chances of cognitive impairment than the patients who present with either seizures or other symptoms (giddiness, headache, loss of consciousness).

The location of ICH has a significant correlation with cognitive impairment ($P = 0.008$) that is because in lobar ICH, there is direct damage of brain areas that sub-serve cognitive functions whereas, in other locations such as subcortical or infratentorial region, the loops sub-serving the cognition are affected. In the present study, 34 patients had cognitive impairment of which 11 of 19 (57.8%) were lobar, 21 of 94 (22.3%) were subcortical, and 2 of 7 (28.5%) were infratentorial indicating that patients with nonlobar ICH have more cognitive impairment [Figure 2].

This finding was earlier mentioned by Tveiten *et al*.[21] such as the lobar location of ICH and increased age are independently associated with cognitive impairment. These findings were also mentioned by Moulin *et al*.[19] as the incidence of new-onset dementia was more than two times higher in patients with lobar ICH (incidence at 1 year 23.4%, 14.6–33.3) than for patients with non-lobar ICH (incidence at 1 year 9.2%, 5.1–14.7).

The volume of ICH has a significant correlation with cognitive impairment at the subcortical (basal ganglia $P = 0.000$, thalamus $P = 0.005$) and infratentorial region ($P = 0.008$), whereas there is no statistical significance with lobar ICH ($P = 0.389$). This might be explained by the fact that even a small hematoma involving important functional areas of the brain might have affected cognitive function.

In subcortical and infratentorial ICH, there is a strong correlation between volume and cognitive impairment. That is as the volume of the bleed increases the risk, of cognitive impairment also increases proportionally. This is because a larger volume of ICH is required to disrupt the loops as in subcortical or infratentorial regions. The relation between the volume of bleed and cognitive impairment has been mentioned by Garcia *et al*.[18] In his study, larger hemorrhage volume and ranking score >1 were found as long-term dementia predictors.

In the general population, one may expect an increase in cognitive impairment in patients with left-sided ICH. This is based on the fact that in most individuals speech areas and other areas that sub-serve cognitive functions are located left side. However, our study did not show any significant correlation between the side of ICH with cognitive impairment which was similar to the study performed by Garcia *et al*.[18] In his study 13 out of 41 on leftsided ICH and 4 out of 34 on rightsided ICH had cognitive impairment with a P value of 0.04.

The presence of hydrocephalus and intraventricular extension, which indicate that the ICH was large was not found to have any correlation to cognitive impairment.

In only 6 patients (5%), an MRI brain was performed and among them, only one had preexisting cerebral cortical microbleeds, and he was found to have the lobar location of ICH. So, in this patient, we could not conclude whether there was an underlying cognitive impairment before the onset of ICH.

In the present study, most of the patients had cognitive impairment affecting more than one domain. Among all, executive functions was the most commonly encountered abnormality followed by working memory impairment. This finding from our study is supported by a study from Garcia *et al*.[18] The reason for this is that executive function is predominantly localized to the prefrontal cortex. However, there are a few well-documented cortical-subcortical and cortical-cerebellar loops that have also been found to be implicated in executive function. Hence, damage to any of these loops may lead to executive function deficits, as observed in our study.

Surgical treatment was considered in 17 out of 120 patients in our study, when compared to previous studies, 9 of 78 patients. Out of 17 patients, 13 were in the cognitive impairment group indicating that the larger the bleed volume, the higher the need for surgical intervention and the higher the chances of cognitive impairment.

Figure 3 Depicting defective executive functions in two patients with cognitive impairment.

In our study, the prevalence of cognitive impairment was found to be 28% when patients were examined between 6 and 12 months following the intracerebral hemorrhage (ICH). This rate was reported as 23% three years after spontaneous ICH according to Garcia et al. and as 14% at the end of one year and 28% at the end of four years according to Moulin *et al*. [19] it was 14% at the end of one year, and 28% at the end of 4 years. The high prevalence of cognitive impairment in our study could be because of two reasons. Firstly, earlier studies used Mini-Mental Status Examination (MMSE). as a screening

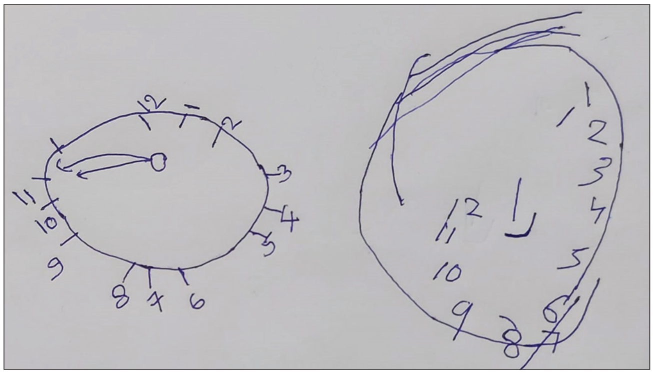

Figure 3: Depicting defective executive functions in two patients by clock drawing test

tool for cognitive examination and a validated scoring system for the examination of cognition was used by only Moulin *et al*.[19] (only a set of people whose MMSE was <27). Secondly, the educational status of our patients includes a large group of uneducated subjects.

In the secondary analysis of INTERACT 1 study conducted by Shoujiang You *et al*. found that over one-third of ICH survivors had significant cognitive impairment with MMSE less than 24 at 90 days of follow-up and the reported rate of long-term cognitive impairment up to 4 years after ICH ranging widely from 23%–61% percentage. In the present study, we found that symptoms such as hemiparesis, altered sensorium, location of bleed, and volume of bleed at subcortical location as predictors of the development of cognitive impairment.[22]

In our study, cognitive impairment was identified in 21% (26 out of 120 patients) when using the Addenbrooke's cognitive examination after 6-12 months in survivors of ICH. When DSM-V criteria were applied, cognitive impairment was identified in 28% (34 out of 120 patients). DSM-V detected a greater number of subjects with cognitive impairment (21% vs. 28%). This could be because the domains tested in Addenbrooke's scale have various subgroups; hence, if a patient has a deficit only in such sub-group, they might not have altered the total score but that deficit might have caused a significant functional deficit.

Limitations of the study

1. Education status of the study population. Our center is a referral center in south coastal Karnataka, which serves the patients of all socioeconomic groups, but most of the patients belong to a low socioeconomic group and in these populations, education standards are below than expected. Hence, there is a possibility of overestimation of cognitive impairment.
2. Because some of the patients who deceased immediately after the acute stage were likely to have suffered from cognitive disorders, it is probable that the present cross-sectional study underestimated the prevalence of dementia.
3. A lack of premorbid cognitive testing is a major concern in this type of study; without premorbid cognitive testing, it might be difficult to rule out preexisting dementia.
4. As most of our patients underwent only CT- brain, which is not an ideal imaging for the study of cerebral microbleeds. Cerebral amyloid angiopathy is a condition, which may predispose to cognitive impairment, is not estimated from the current study as MR imaging is not available for most of the patients.

Conclusion

Till date, this is the largest study from India in evaluating cognitive impairment in survivors of ICH. The cognitive domains were tested using Addenbrooke's scale, and it showed that executive functions are most commonly affected in survivors of ICH. The DSM-V has detected more subjects with cognitive impairment than Addenbrooke's scale. Hence, it is essential to assess cognition in post-ICH patients during follow-up, so that suitable adjustment can be done in their employment, and also in educating family members in providing a good quality of life.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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