ISCHAEMIC STROKE - CLINICAL PROFILE AND EVALUATION WITH ELECTROENCEPHALOGRAPHY AND MRI BRAIN

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ABSTRACT

BACKGROUND

Acute Ischaemic Stroke (AIS) is characterised by thrombotic or embolic occlusion of a cerebral artery. Electroencephalography (EEG) is an electrophysiological monitoring method to record electrical activity of the brain measuring voltage fluctuations resulting from ionic current within the neurons of the brain. Our study evaluated stroke with EEG and MRI Brain.

MATERIALS AND METHODS

Our cross-sectional study enrolled 150 patients of ischaemic stroke from July 2012 till July 2015. A detailed study of 150 cases of ischaemic stroke with mode of presentation, Laboratory data, MRI scan and EEG features has been made.

RESULTS

Majority of patients are aged above 60 years. Regarding risk factors, 76% (114) of patients had hypertension, 66% (99) had diabetes mellitus, 62% (93) were smokers and 42% (63) had history of alcoholism; 105 patients (70%) had abnormal total cholesterol level, 114 patients (76%) had abnormal triglyceride levels and 117 patients (78%) had abnormal HDL levels. Abnormal EEG was observed in 87 patients (58%) out of a total of 150 patients, out of which 45 patients developed post stroke seizures.

CONCLUSION

Elderly individuals are at increased risk of stroke. Comorbidities and lipid abnormalities increase the risk significantly. MRI is the most useful investigation for diagnosis and management in ischaemic stroke. Abnormal EEG and generalised slowing pattern observed specifically are associated with complications and mortality after acute ischaemic stroke. Larger infarct volume is associated with higher delta power in EEG.

KEYWORDS

Ischaemic Stroke, Encephalography, MRI Brain, Periodic Lateralised Epileptiform Discharges.

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BACKGROUND

Acute Ischaemic Stroke (AIS) is characterised by the sudden loss of circulation to an area of the brain, resulting in loss of neurologic function corresponding to it. It was previously known Cerebrovascular Accident (CVA) or stroke syndrome. Stroke is a nonspecific state of neuronal dysfunction with brain injury associated with several pathophysiologic causes. Strokes are divided into 2 types: haemorrhagic and ischaemic. Acute Ischaemic Stroke (AIS) is characterised by thrombotic or embolic occlusion of a cerebral artery. Ischaemic and haemorrhagic stroke cannot be clearly differentiated only on

the basis of clinical examination findings, as there is considerable overlap of clinical features. Evaluation with Computed Tomography [CT] scanning or Magnetic Resonance Imaging [MRI] is required.

Stroke is a major cause of disability and the fifth leading cause of death in the United States.^{[1],[2]} Each year in the United States, about 795,000 people experience new (610,000) or recurrent (185,000) stroke.^[3] Epidemiologic studies indicate that 82% - 92% of strokes in the USA are ischaemic. Stroke was the second most common cause of death globally in 2011, causing 6.2 million deaths (~11% of the total).^[4] Approximately, 17 million people suffered a stroke in 2010 and 33 million people have previously had a stroke and were still alive.^[5] Between the years 1990 and 2010, the number of strokes decreased by 10% in the developed world and increased by 10% in the developing world approximately.^[5]

A total of two-thirds of strokes occurred in individuals over the age of 65 years.^[5] South Asians are at increased risk of stroke, accounting for 40% of stroke deaths worldwide.^[6] The incidence of stroke increases from 30 years of age and the aetiology varies with age.^[7] Men have 25% higher chance of

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suffering from strokes than women.^[8] However, 60% of deaths from stroke occur in women as they live longer, and are older on average at stroke onset. Important risk factors in women are pregnancy, childbirth, menopause and hormone replacement.

Acute occlusion of an intracranial vessel causes reduction in blood flow to the brain region it supplies. The magnitude of flow reduction is a function of collateral blood flow and this depends on individual vascular anatomy and the site of occlusion. A fall in cerebral blood flow to zero causes death of brain tissue within 4 - 10 mins; values < 16 - 18 mL/100 g tissue per min cause infarction within an hour; and values < 20 mL/100 g tissue per min cause ischaemia without infarction unless prolonged for several hours or days. If blood flow is restored prior to a significant amount of cell death, the patient may experience only transient symptoms, i.e. a TIA. Tissue surrounding the core region of infarction is ischaemic, but reversibly dysfunctional and is referred to as the ischaemic penumbra. The penumbra may be imaged by using perfusion-diffusion imaging with MRI.

Electroencephalography (EEG) is an electrophysiological monitoring method to record electrical activity of the brain measuring voltage fluctuations resulting from ionic current within the neurons of the brain. EEG was previously used as a first-line method of diagnosis for tumours, stroke and other focal brain disorders, but its use has decreased with the advent of Magnetic Resonance Imaging (MRI) and Computed Tomography (CT). In the present study, an endeavour is made to document the cases of Ischaemic Stroke and an effort is made to elucidate EEG findings and aetiological factors. A detailed study of 150 cases of Ischaemic Stroke with mode of presentation, laboratory data, MRI scan, EEG features has been made. Detailed analysis of results done.

MATERIALS AND METHODS

Our cross-sectional study enrolled 150 patients of ischaemic stroke from July 2012 till July 2015. Even though 183 patients were initially enrolled, 33 patients were lost for followup and did not get all the investigations, hence excluded. Complete history and examination of patients was documented. Investigations including complete haemogram, renal function tests, MRI brain, lipid profile, chest x-ray, ECG and EEG were done. All patients will be treated with supportive therapy, anti-platelet agents and results were tabulated. Results were discussed later in correlation with other studies. EEG and MRI brain results during diagnosis and followup were correlated to clinical condition. EEG was done at initial presentation of patient at emergency medicine, ICU or medical ward during discharge and followup.

Inclusion Criteria

1. Patients from age group above 18 yrs. and below 80 yrs. with clinical features suggestive of stroke.
2. Patients with sudden onset of loss of consciousness where MRI brain is suggestive of stroke.
3. Patients with hemiparesis with or without loss of consciousness and MRI brain showing ischaemic changes.
4. Patients with recent onset of other focal neurological deficits with MRI brain showing evidence of stroke.

5. Patients with clinical features of hemiparesis, neurological deficits without any evidence in initial MRI scan.

Exclusion Criteria

1. Recent head injury (less than 6 weeks).
2. Epileptic disorders.
3. Recurrent stroke.
4. Mental retardation and structural abnormalities of brain.
5. Neuro-infections (TB meningitis, Bacterial meningitis, etc.)
6. Pregnant women.
7. Strokes more than 7 days' duration.
8. Age less than 18 or more than 80 yrs.

RESULTS

Out of 150 patients enrolled in the study males constituted 72% of patients, while females constituted 28% of patients [Table 1, Figure 1]. Regarding age distribution of patients, 40% of patients were in the age group of 60 - 69 years followed by 24% of patients in the age group of 50 - 59 years, followed by 14% of patients in the age group of 40 - 49 years. The results of age distribution are represented in Table 2 and Figure 2. Regarding the mode of onset, 90% of patients had sudden onset of symptoms, while 10% had gradual onset of symptoms [Figure 3].

Regarding risk factors 76% (114) of patients had hypertension, 66% (99) had diabetes mellitus, 62% (93) were smokers and 42% (63) had history of alcoholism [Table 3, Figure 4]. Regarding abnormalities in lipid profile, 105 patients (70%) had abnormal total cholesterol level, 114 patients (76%) had abnormal triglyceride levels, 117 patients (78%) had abnormal HDL levels [Table 4, Figure 5]. Regarding pattern of weakness, 105 patients (70%) had left hemiparesis, while 45 patients (30%) had right hemiparesis [Table 5, Figure 6].

Regarding site of arterial infarction 111 patients (74%) had middle cerebral artery involvement, 54 patients (36%) had posterior cerebral artery involvement, 39 patients (26%) had anterior cerebral artery involvement and 24 patients (16%) had combined arterial involvement. Regarding family history of risk factors, 45 patients (30%) had family history of hypertension, 39 patients (26%) had family history of diabetes mellitus, 18 patients (12%) had family history of stroke and 15 patients (10%) had family history of coronary heart disease. EEG in stroke:

Abnormal EEG was observed in 87 patients (58%) out of a total of 150 patients, out of which 45 patients developed post stroke seizures. Abnormal EEG was more common in patients aged more than 50 years compared to patients aged below 50 years ($p < 0.001$). Overall, the commonest EEG abnormality was focal slowing observed in 41 out of 87 patients (47.12%) with EEG abnormalities. In the patients who had abnormal EEG and generalised slowing, the association of complications is higher compared to other groups. Larger infarct volume observed in MRI brain was associated with higher delta power in EEG bilaterally.

A total of 45 patients (30%) had post stroke seizures. Mean age was 64.6 years; 37.7% (n=17) patients were in awake state, 28.8% (n=13) patients were drowsy, 15.6% (n = 7) were

sedated, 11.11% (n=5) were semiconscious, 4.44% (n=2) were unconscious and 2.2% (n=1) was in asleep state. The most common seizure semiology observed was generalised seizures in 64.4% (n=29), focal seizures in 24.44% (n=11) and focal with secondary generalisation in 11.11% (n=5) patients; 66.7% (n=30) patients had right hemispheric involvement and 33.3% (n=15) had left hemispheric involvement.

The commonest EEG finding observed in post-stroke seizures was generalised slow waves seen in 40% (n=18) patients. Other abnormalities observed were focal slowing in 20% (n=9), focal sharp and slow waves in 13.33% (n=6), focal spikes and slow waves in 6.67% (n=3), focal sharp waves in 6.67% (n=3) of the patients. Focal spike waves in 6.67% (n=3) and PLEDs were seen in 6.67% (n=3) patients [Figure 9].

Gender	No. of Patients	Percentage
Males	108	72%
Females	42	28%

Table 1. Gender Distribution in Study Group

Age	No. of Patients	Percentage
20 - 29 yrs.	6	4%
30 - 39 yrs.	12	8%
40 - 49 yrs.	21	14%
50 - 59 yrs.	36	24%
60 - 69 yrs.	60	40%
70 - 79 yrs.	15	10%

Table 2. Age Distribution in Study Group

Risk Factor	No. of Patients	Percentage
Diabetes Mellitus	99	66%
Hypertension	114	76%
Smoking	93	62%
Alcoholism	63	42%

Table 3. Risk Factors of Stroke in Patients

Lipid Abnormality	No. of Patients	Percentage
Total cholesterol $\geq$ 200 mg/dL	105	70%
Triglycerides $\geq$ 150 mg/dL	114	76%
HDL $<$ 40	117	78%

Table 4. Abnormal Lipid Profile in Study Population

Pattern	No. of Patients	Percentage
Right Hemiparesis	45	30%
Left Hemiparesis	105	70%

Table 5. Pattern of Weakness in Study Population

Infarct Territory	No. of Patients	Percentage
ACA	39	26%
MCA	111	74%
PCA	54	36%
ACA and MCA	24	16%
MCA and PCA	24	16%
ACA and PCA	3	2%

Table 6. Site of Arterial Infarction in Brain

Risk Factors	No. of Patients	Percentage
Hypertension	45	30%
Diabetes Mellitus	39	26%
C.H.D	15	10%
C.V.A	18	12%

Table 7. Family History of Risk Factors

Variables	Number (%)	P value
50 - 79 years	80/111 patients (72%)	< 0.0001
< 50 years	7/39 patients (18%)	
Focal slowing in EEG	41/87	0.1707
Generalised slowing in EEG	31/87	
Generalised slowing and complications	29/41	0.0206
Focal slowing and complications	7/31	

Table 8. EEG Abnormalities in Ischaemic Stroke

Grade	CBF (mL/100g/min)	EEG Changes
0	35 - 70	Normal
I	25 - 35	Loss in faster beta frequencies
II	18 - 25	Slowing of background to 5 - 7 Hz (theta)
III	12 - 18	Slowing to 1 - 4 Hz (delta)
IV	< 8 - 10	Suppression of all frequencies with neuronal death (Cortical suppression)

Table 9. EEG Abnormalities in Cerebral Ischaemia

Figure 1. Gender Distribution in Study Group

Figure 2. Age Distribution in Study Group

Figure 3. Pattern of Onset of Symptoms

Figure 4. Risk Factor Distribution in Study Population

Figure 5. Abnormal Lipid Profile in Study Population (150 Patients)

Figure 6. Pattern of Weakness

Figure 7. Site of Arterial Occlusion

Figure 8. Family History of Risk Factors

Figure 9. EEG Abnormalities in Post-Stroke Seizures

DISCUSSION

Ischaemic stroke manifests usually in the form of thrombotic stroke, embolic stroke, systemic hypoperfusion or venous thrombosis.^[9] In case of severe or prolonged haemodynamic instability, focal and diffuse cerebral changes occur due to the effect of ischaemia, which is reversible or irreversible, depending on the degree and duration of blood flow. In ischaemic stroke, paradoxical increase of Cerebral Blood Flow (CBF) can be observed at the involved site and is known as luxury perfusion.^[10]

Core ischaemic regions (blood flow < 15%), penumbral regions (blood flow < 40%) and extra-penumbral cortical regions (blood flow rate > 40%) can result in both proximal and distal to arterial occlusion. This approximate flow based definition of core and of penumbra as well as extra-penumbral region is generally agreed upon.^[11] Ischaemic penumbra generally occurs usually in the periphery of the brain when blood flow is reduced to cause hypoxia, but not very severe to cause irreversible failure of energy metabolism to cause cellular necrosis.^[12] The margins of ischaemic area are hyperaemic with minimal or no parenchyma damage.

Hossmann summarised the threshold concept of pathophysiological changes in cerebral ischaemia. The

inhibition in protein synthesis starts to deteriorate with the CBF less than 55 mL/100 g/min. When CBF reduces to less than 35 mL/100 g/min, increased glucose utilisation and lactate accumulation occurs. As CBF falls below 26 mL/100 g/min, the acidosis causes decline in phosphocreatine and adenosine triphosphate levels. At CBF around 23 mL/100 g/min, neurological dysfunction and suppression of electrical activity in the brain and evoked potentials occur. When CBF reaches to 5 – 18 mL/100 g/min, irreversible hemiparesis and infarction occurs with terminal depolarisation, potassium efflux and calcium influx.^[13]

The EEG is the recording of cerebral electrical activity measured over scalp due to the firing of neurons in the cerebral cortex. EEG records cumulated excitatory and inhibitory postsynaptic potentials in neuronal dendrites, usually in the superficial cerebral cortex. Deeper structures like the thalamus and brainstem produce potentials of low amplitude reflecting the functional status. Electrographic activity consists of spectrum of frequencies, i.e. physiological and pathological changes in cerebral function with delta (14 Hz). Cerebral function on EEG show slower frequencies (delta and theta), produced by the thalamus and by cells in layers II-VI of cortex, while faster frequencies (alpha) from cells in layers III and V of cortex.^[14]

In stroke, EEG represents changes of CBF fall.^[15] EEG changes in cerebral ischaemia can be divided into four types based on cerebral blood flow. At CBF, 25 - 35 mL/100 g/min, EEG shows reduction in amplitude of faster frequencies. As CBF reduces to 18 - 25 mL/100 g/min, slowing of theta frequencies occurs. Further decrease of CBF to 12 - 18 mL/100 g/min causes marked suppression of frequencies. Suppression of all frequencies occurs with the reduction of CBF < 8 - 10 mL/100 g/min (Table 9).^{[16],[17]} Murri et al showed that EEG is a highly sensitive tool for temporal, fronto-central and parieto-occipital cortical-subcortical infarctions than for basal ganglia and internal capsule lesions.^[18] EEG may supplement with imaging modalities for the diagnosis and prognosis in cerebral ischaemia.^[19]

Animal models showed that EEG changes occur within 5 minutes of acute cerebral ischaemia, comparatively better than imaging techniques and clinical examination in a patient who is in altered level of consciousness or sedated. Periodic Lateralised Epileptiform Discharges (PLEDs) in EEG represent acute brain dysfunction or unilateral brain lesion, recorded in the area adjacent to cerebral infarction.^[20] PLEDs were found to be associated with cerebral infarctions.^[21] PLEDs in obtunded patients associated with focal seizures and focal neurological signs are usually transient and resolve spontaneously in 2 - 3 weeks. These discharges decrease in amplitude, repetition rate and then cease.^[20]

Our study correlated with other studies of ischaemic stroke regarding age of onset, male predominance, risk factors, dyslipidaemia and family history of risk factors.^{[22],[23],[24]} Our study showed that magnetic resonance imaging is a very sensitive and specific modality for detection of ischaemic stroke.^[25] Acutely ischaemic lesions demonstrate high signal of DWI (Diffusion Weighted Imaging) and low signal on ADC (Apparent Diffusion Coefficient) maps within minutes.^[26] FLAIR images demonstrate abnormal signal sooner than T2WI and have been shown to detect infarcts within 3 hours after onset of acute stroke.^[27]

CONCLUSION

We put forward the following observations based on our study. Our study has limitations in accurate calculation of incidence due to sample size. Male predominance is observed. Elderly individuals are at increased risk of stroke. Comorbidities and lipid abnormalities increase the risk significantly. MRI is the most useful investigation for diagnosis and management in ischaemic stroke. Abnormal EEG and generalised slowing pattern observed specifically are associated with complications and mortality after acute ischaemic stroke. Larger infarct volume is associated with higher delta power in EEG. Generalised seizures and generalised slowing on EEG were common in patients who developed seizures after stroke. EEG gives significant information about acute stroke injury that can add to the information of structural brain imaging.

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