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Pakshaghata viz a viz hemiplegia: risk factors, pathology, clinical presentation and prognostic criteria in modern perspective.

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Abstract

Cerebrovascular diseases are the third most common cause of death in developed world, which is only behind to ischeamic heart disease and cancer, and are responsible for a large proportion of physical debility becoming more frequent with increasing age. Increasing longevity, growth in population size and increasing survival with coronary heart disease and other cardiovascular disease are likely to increase the number of strokes in future. It is clear that with an aging population, cerebrovascular disease impose an increasingly heavy burden upon hospital and community services. The loss of these patients from the work force and the extended hospitalisation they required during recovery period of the disease make the significant economic impact which is one of the most devastating in the field of medicine. Cerebro Vascular Accident (CVA) or stroke is the commonest neurological disorder and is the commonest cause of death and single most important cause of disability.

KEY WORDS: Hemiplegia, *Pakshaghata*

Introduction

Hemiplegia may be defined as paralysis of one side of the body due to disease or damage to the upper motor neurons at various levels in the central nervous system[1] According to Michael[2], hemiplegia is paralysis of one side of the body involving the arm and leg, and usually also of the face (*facio-brachio-crural hemiparesis*). The word hemiplegia literally means "the paralysis of one side either entire left or right side of the body". Hemiplegia consist of two words i.e., "hemi" which means the half and "plege" which means stroke or sudden attack of loss of function[1]. Hemiplegia is some times used synonymous for *hemiparesis*.

Hemiplegia is of various types on the basis of the site of the lesion at the central nervous system, nature of onset, age of the subject and the signs and symptoms. They are; *Hemiplegia alternans hypoglosica*: that is due to a lesion in the medulla oblongata with paralysis of the tongue on one side of the body and limb paralysis on the other side. eg; crossed hemiplegia. It is also called alternate hemiplegia; *Ascending hemiplegia*: that presenting peripherally and extending upwards; *Congenital hemiplegia*: that due to cerebral damage at birth, or due to developmental causes during the foetal life; *Hemiplegia cruciata*: that cranial nerve paralysis on one side with limb paralysis on the opposite side of the body which , is also called crossed paralysis; *Flaccid hemiplegia*: that with lack of muscle tone instead of the usual spasticity; *Hysterical hemiplegia*: hemiplegia with out organic basis; *Infantile hemiplegia*: hemiplegia occurs in infancy often during a febrile illness; *Spastic hemiplegia*: hemiplegia with increased muscle tone; *Stuttering hemiplegia*: hemiplegia progressing in sudden episodes; *Superior alternate hemiplegia*: this is also called *Waber's syndrome*. Hemiplegia may result in cerebro-vascular accident that is synonymous to *stroke* as well as to *apoplexy*.

Apoplexy

On the other hand, the sudden loss of functions of the body or sudden loss of consciousness is termed as ***Apoplexy*** or ***Stroke.*** Apoplexy, a Greek word introduced by the great Hippocrates; meaning, "strike by god's hand". Apoplexy may be defined as sudden loss of consciousness the result of an acute vascular disturbance caused by the rupture of an intracerebral artery or its occlusion by thrombosis or embolism[1]. Hemiplegia may develop as a result of an apoplexy (or stroke) at the level of internal capsule of the brain[3].

Stroke:

Stroke literally means a sudden seizure or strike and the commonly used lay term for apoplexy.

There are a large number of types of strokes. By the foregoing, haemiplegia is of various aetiological as well as pathological factors. Out of all possible aetiological factors, any thing other than vascular origin is of 1% or less[4]. That means the main aetiopathological factor for hemiplegia is cerebrovascular accident or stroke. Acute focal stroke characterised by the sudden appearance of a focal deficit of brain functions most commonly hemiplegia with or with out sings of focal higher cerebral dysfunctions such as aphasia, hemi-sensory loss, visual fields defects or brain stem defects which will be discussed later.

Differential Diagnosis of Hemiplegia

Apart from cerebrovascular disease, focal or global neurological deficit including hemiplegia may result from some other brain pathologies. They have been rule out below;

- Primary cerebral tumors.
- Metastatic cerebral tumors.
- Subdural haematoma.
- Cerebral abscess.
- Todd's paresis (after epileptic seizures).
- Demyelination.
- Hypoglyceamia.
- Encephalitis.
- Hysterical conversion.

Out of all such possible causative factors, cerebrovascular diseases (CVD) are the most common cause for hemiplegia and other types of motor deficits.

Cerebrovascular Accident (CVA) or Stroke

Hippocrates (460-350B.C.) described cerebrovacular accident as "spasms of brain, convulsions of entire body, derangement of intelligence, choking, and cessation of speech"[5]. Gallan (129-260 A.D.) described cerebrovascular accidents as "sudden loss of feelings and movements of entire body with the exception of respiration". But the major work was done on CVA in mid 20th century about pathology haemorrhage and infarction of brain. The term cerebrovascular disease refers to all disorders in which there is an area of brain transiently or permanently affected by ischemia or haemorrhage and/or in which one or more blood vessels of the brain are permanently impaired by pathological process. CVD including CVAs can cause death or disability from occlusion of the blood vessels producing cerebral ischemia and infarction or haemorrhage through their rupture.

WHO Definition of Stroke

WHO Monica project in 1988 defined stroke as "Rapidly developing clinical signs of focal or global disturbance of cerebral functions with symptoms lasting more than 24 hours or leading to death with no apparent cause other than of vascular origin[6]. It includes subarachnoid haemorrhage but excludes subdural haematoma and haemorrhage or infarction caused by infection or tumor.

Incident

The annual incident rate of acute cerebrovascular disease in over 45 years age group in the UK is about 350 per 100,000 people[4,5], where as it is about 250 per 100,000 people in USA per annum[7]. The annual incident rate of cerebrovascular disease including all forms was 194 per 100,000 in early 1970's[8]. That means the rate of incident of cerebrovascular events is rapidly increasing with time passed. According to Kumar and Clark, CVAs are the second most common neurological disorder which is only leaded by headache[7].

Clinical Presentation of Stroke

Transient Strokes (TIA)

TIA is a transient loss of focal neurologic function due to an ischaemic cause i.e., transient strokes are almost always ischaemic and which lasts only for few minutes, some TIAs last less than 5 minutes[9]. The symptoms include dizziness; numbness or paralysis in a limb or in one side of the body, drooping of one side of the face, headache, slurred speech, partial loss of vision or doubled vision and some times nausea and vomiting also may occur[10]. TIAs are recovered completely with out any neurological deficit with in 24 hours. David L G also confirmed that TIA is in essence an ischaemic stroke with out permanent sequale. By definition TIA lasts less than 24 hours, but this duration is arbitrary and out dated because we can now identify evidence of stroke on cerebral MRI in patients whose ischaemic symptoms lasts just a few hours.[11]. In most cases of TIA symptoms lasts 2-20 minutes. Many patients who had TIA, 25% have a stroke with in the next 3 months and over 5% have a stroke with in the next 2 days[12]. The frequency of TIA is variable, but majority have 2-10 attacks and some times up to 30 episodes or more can occur in a single day ("Crescendo TIA"). With in five years, 25%-40% of TIA subjects not receiving prophylactic therapy develop a stroke, the risk being highest in the first year[11].

Complete stroke

When signs and symptoms are fully developed and stable for hours or days, subsequently tending to decrease is called completed stroke. Of presenting complete stroke 85% is cerebral infarction while 15% is intracerebral haemorrhage. Headache may accompany the onset of both infarction and haemorrhage. But headache and vomiting together at the onset of stroke is a strong indicator of haemorrhagic stroke. Persisting hypertension is common in both haemorrhagic as well as in infarction stroke. In shortly speaking, a stroke may leave the patient with a permanent fixed deficit is called Complete stroke.

Evolving stroke or stroke in evolution

When the neurological deficit is actively worsening during the period of observation, which may take place in steps or may be, smooth progressive worsening condition is known as stroke in evolution. Large number of strokes are completed their course with in minutes to few hours. But in case of evolving stroke, it evolves in a stuttering manner over days. In this case mass lesion is suspected and evolving stroke is often due to progressive occlusion of a cerebral artery.

Reversible ischemic neurologic deficit or RIND

A true stroke that may be cleared completely with in 7 days is called RIND. RIND may persist for more than 24 hours with nearly complete recovery with in a week[1].

Subclinical ischaemia and infarction

Some infarcts may be subclinical producing no immediate symptoms even though producing sufficient necrosis and/or oedema to be visible on a CT scan. Numerous small sub clinical infarcts feel to be related to decrease in mental function.

Risk Factors of Strok

The term risk factor used in various ways. The following distinction among risk factors of stroke is worth making; 1.Inherent biological traits suchas age, sex that cannot be altered by themselves;2.Physiological characteristics that predict future occurrence of stroke (blood pressure, serum cholesterol, fibrinogen, weight/ height, blood sugar); 3.Behavior (diet, smoking, alcohol consumption, oral contraceptive pill use); 4.Social characteristics such as social or ethnicgroup; 5.Environmental features that may be physical (temperature), psychosocial or biological.

Occupation

Sedentary habits and lack of physical activity may predispose to CVD. Persons engaged in job involving a life long high level of habitual physical activity have a general lower blood pressure than sedentary city dwellers.

Herido-familial

On prospective study reported an association of family history with stroke. Whisnant concluded that hypertension, heart disease and diabetes are inherited, which increases the risk for cerebrovascular accidents. That means predisposition appears to be genetic but in some families this genetic susceptibility is due to factors that are treatable such as hypertension and heart disease.

Season

Cold might be a risk factor for cerebrovscular accidents. The mortality is reported higher in winter and spring and lowest in late summer, in patients of cerebrovascular accidents.

Smoking

Smoking is described as an important risk factor in cases of stroke. Two large prospective studies have been performed in both men and women. One of them, the Honolulu heart programme study in man show a relative risk of 2.5 for thromboembolic stroke and 2.8 for haemorrhagic stroke in smokers compared with non smokers.

Alcohol

The relationship between long-term alcohol consumption and stroke is unclear. With recent reports it seems that in middle aged persons and elderly persons who are at risk for IHD, modest consumption can be protective. But, Marc Malkoff et al proved that moderate drinking increase the risk of both intracerebral and subarachnoid haemorrhage in diverse population.

Age

Age is the strongest risk factor for cerebro-vascular accidents. Incidence of stroke is strikingly related to age with more than doubling of incidence rate in successive decades. Dalal 1968 reported that cerebral thrombosis is more common in older age group. Most cases of cerebral haemorrhage occur

in middle or late life. The incidence of CVD increases with advancing years. It is commonest between 5th to 8th decades.

Sex

There is small male excess of strokes, most prominent in middle age. Females are protected upto the age of menopause, although the risk increases thereafter. The lifetime risk of having an acute stroke is higher in man than in women. This difference is attributable to the higher mean age at stroke onset with women and to their greater life expectancy. Prognosis of stroke is slightly better in females. But the WHO statistic annual in1989 mentioned that the incidence of dying from an acute stroke is higher in females than in males.

Oral contraceptives

Use of oral contraceptives increases the relative risk of stroke in young women. Oral pill use is related to ischaemic and haemorrhagic stroke.

Previous strokes

Garraway, Whisnant et al 1979 in their study reported that the recurrence rate for stroke was 10% in first year and 20% by the fifth year. In the Framingham study by Kannel et al 1971, men had a 42% 5 years cumulative recurrence rate for ischaemic brain infarction, women had a 24% rate.

Side of hemiplegia

Airing and Meritt 1935 have reported a greater incidence of left sided hemiplegia.

Obesity

Obesity is a major risk factor for hypertension, diabetes and additional traits that may accelerate atherogenesis, including hyperlipidemia. The white hall study showed that the body mass index (BMI) is predictive of stroke in both smokers and non-smokers. It was established that over weight persons having the BMI above the bottom quintile (greater than 24kg/m2) and smoking accounts for 60% of strokes in men up to 65 years of age.

Diet

Diet may influence stroke by affecting blood pressure or may have other effects e.g., influencing the development of atherosclerosis. Another suggestion is that consumption of fruits and vegetables may protect against stroke and in intact of potassium may have protective effect independent of its action on blood pressure. Robert has mentioned that the main nutritional problem in developed countries are excess consumption of sugary and fatty food which cause obesity, tooth decay, and promote deposition of fat in side the blood vessels (atherosclerosis) leading to coronary heart disease and stroke[15]

Hypertension

A mean arterial pressure greater than 110 mm Hg (normal value is about 90 mm Hg) is considered to be hypertensive. This level of mean arterial pressure occurs when the diastolic pressure is greater than 90 mm Hg and the systolic pressure is greater than 135 mm Hg.Hypertension was the main causative factor for intracerebral haemorrhage, although chronic hypertension still appears to be the most important risk factor for ICH. The lethal effects of hypertension are caused mainly on three organs, i.e., Brain, heart and kidney[15]. Excess workload on the heart leads to early heart failure and coronary heart disease, often causing death as a result of a heart attack. *The high pressure frequently ruptures a major blood vessel in the brain, followed by death of major portion of the brain; this is the cerebral infarct that is clinically called stroke.* Categorily speaking, hypertensive people develop about seven times as many stroke as do normotensive.

Diabetes mellitus and impaired glucose tolerance

Diabetes is an important risk factor for ischaemic stroke and is behind only to hypertension. In diabetics, risk of stroke doubles compared to non-diabetics. In an autopsy study, a strong association was found between diabetes and intracranial atherosclerosis.

Fibrinogen:

Higher plasma fibrinogen concentration is a risk factor for stroke.

Cardiac abnormalities:

There is a significant association between the existence of cardiac disease and stroke, particularly cerebral infarction.

Myocardial infarction:

Thompson et al 1978 reported that stroke rate of 1.7% in a patient with acute myocardial infarction and stroke rate increases with the size of myocardial infarction. Similarly Komrad and Coffey et al 1984, reported incidence of stroke in myocardial infarction patients was 2.4%.

Coronary artery disease:
In cardiac patients, in addition to form thrombi in diseased coronary artery, a damaged endocardium may break up and produce systemic remobilisation. Coronary artery disease contributes independently to almost 3-fold increase in risk of stroke.

Cardiac arrhythmia:
In 24 years of observation of the Framingham cohort study, ECG abnormalities were associated with increased risk of cerebral infarction. Left ventricular hypertrophy in ECG carries 10 times increased risk of stroke in comparison to persons of same age and sex without these abnormalities.

Rheumatic heart disease:
A common complication of rheumatic heart disease is systemic embolism, 60-75% of which are resulting stroke. Most of these emboli are associated with mitral stenosis.

Atrial fibrilation:
Most frequent potential source of embolism to the brain is atrial fibrillation (AF), usually non-rheumatic in origin. The risk of cerebral embolism is increased when the valve diseases is complicated by atrial fibrillation.

Congestive heart failure:
In the Framingham study, patients with CHF had 9.0 times the risk for ischaemic cerebral infarction as that for persons of same age and sex without CH.

Serum lipid/serum cholesterol:
Wolf et al 1983, in Framingham cohort study reported a statistically significant relationship between hyperlipidemia and cerebral infarction less than 60 years of age. Cumings et al 1967 also reported no significant difference with patients and controls, however there was a suggestion of correlation in younger patients.

High haemoglobin/Haematocrit/Polycythaemia:
Marked erythrocytosis with high Hb values as in polycythaemia vera is definitely associated with a high risk of stroke. Clinical deterioration was associated with haemorrhagic transformation of infarcts in some patients.

Sleep Apnea:
Obstructive sleep apnea is the cessation of airflow for 10 seconds or more. There is unusually an effort to get air during this period, but this effort is unsuccessful due to obstruction in the airway, and as a result, no air get to the lungs. Adults do not generally die from sleep apnea because, once an apnea is detected, the body responds with an arousal that triggers sympathetic activity associated with hypertension. Snoring is often a sign of obstructive sleep apnea and the condition is most common in overweight or morbidly obese people with short necks and protuberant abdomen.

Race:
The risk of ICH (intracerebral haemorrhage) in blacks is 1.4 times as the risk of whites. The most common risk factors in black patients with ICH were preexisting hypertension (77%), alcohol use (40%) and smoking (30%)[13].

Pathophysiology of Acute Ischaemic Stroke:
The pathogenisis of brain damage from cerebrovascular occlusion may be separated into two sequential processes, **(a). Vascular and haematological events**: that cause the initial reduction and subsequent alteration of local cerebral blood flow; and **(b). Ischaemia-inducedabnormalities of cellular chemistry**: that produce necrosis of neurons, glia, and other supportive brain cells. The molecular consequences of brain ischaemia include changes in *cell signaling* (neurotransmitters, neuromoldulators); in *signal transduction* (receptors, ion channels, second messengers, phosphorylation reactions); in *metabolism* (carbohydrate, protein, fatty acid, free radicals); and in *gene regulation expression*.

Ischaemic cell damage:
In severely ischaemic brain or in moderate ischaemia of prolonged duration persistent shortage of high-energy phosphates is an overwhelmingdeterminant of injury; unless cerebral blood flow and the tissue's medium for energy exchange (ATP) are restored, necrosis is inevitable. Nevertheless, energy failure is not the immediate cause of cell death since; (a). All brain cells tolerate loss of ATP for several minutes and the great majority of neurons and glia recover fully when blood flow is restored even after an hour of complete ischaemia; (b). One or more of the branching pathways may independently kill brain cells; and (c). Once initiated, such mechanisms may no longer require the triggering event. Within minutes of the onset of ischaemia,energy demands exceed the brain's capacity to synthesise

ATP anaerobically from its major stores of glucose and glycogen, and high- energy phosphates and fuels for their synthesis are depleted. Lactate and unbuffered hydrogen ions (H^+) accumulate in tissue in proportion to the carbohydrate stores present at the onset of ischaemia. Toxicity of hydrogen ions especially their ability to facilitate ferrous iron (Fe^{2+}) mediated free radical mechanisms may be important in astroglial injury. Cerebral infarction is a process which takes some hours to complete, even though the patient's definite maximal close to the onset of the causative vascular occlusion. After the occlusion of the cerebral artery, the opening of the anastemotic channels from other arterial territories may restore perfusion of its territory. Further more, a reduction in perfusion pressure leads to other homeostatic changes to maintain oxygenation to the brain. These compensatory mechanisms can prevent even occlusion of a carotid artery from having any clinically apparent effect. When these homeostatic mechanisms fail, the process of ischaemia starts; this ultimately leads to infarction.

Intracerebral haemorrhage:

Of 15% of acute cerebrovascular diseases that are caused by haemorrhage, about half occurs, though the rupture of a blood vessel with in the brain parenchyma resulting in an (i.e., 7.5% of haemorrhagic stroke due to primary intracerebral haemorrhage) acute focal stroke. In addition, a patient with a subarachnoid haemorrhage (SAH) may present with an acute focal stroke if the artery ruptures in to the brain substance as well as in to the sub arachnoid space. Haemorrhage frequently occurs in to an area of brain infarction, and such haemorrhagic infarcts may be difficult to distinguish from primary intracerebral haemorrhage. The explosive entry of blood in to the brain parenchyma during a primary intracerebral haemorrhage causes immediate cessation of function in that area as neurons are structurally disrupted and white matter fibre tracts are split apart. A rim of *cerebral oedema* forms around the resulting blood clot, which with the haematoma acts like a mass lesion. If big enough, this can cause *transtentorial coning* and some times rapid death.

Course and Prognosis:

In subjects who survive an ictus, some degree of recovery is the rule. Chances of significant recovery are remote when no improvement is noted within the first 6 to 8 weeks. About 20 to 25% of the subjects with massive cerebral infarction and brain swelling die during acute phase. Here, old age, presence of severe neurological deficit with coma and pyrexia, intercurrent infections, and basilar artery thrombosis are of grave prognostic significance. Recurrent episodes are frequent, but there is no way to predict the same in a given subject. However, control of 'risk factors' is beneficial.

Differential Diagnosis:

Prodromal warning symptoms, abrupt onset of a focal neurological deficit, stuttering or intermittent progression, a constellation of symptoms and signs diagnostic of a well defined neurovascular syndrome, relative preservation of consciousness, clear CSF, some degree of recovery and evidence of vascular disease elsewhere in the body (absent carotid pulsation or bruits over the major vessels, history of angina pectoris, myocardial ischaemia or a previous stroke, arrhythmia, intermittent claudication in the legs with feeble peripheral pulsations etc.) are the principal hallmarks of cerebral infarction from thromboembolism11.

Prognosis of ICH:

ICH has a poor out come in general. Pontine haemorrhage and large dissecting haematomas any where in the nervous system lethal.

Irreversible risk factors	Modifiable risk factors
Age	Hypertension
Gender (male>female except in very young and very old)	Heart disease (heart failure,atrial fibrillation, endocarditis)
Race (Afro-Caribbian> Asian> European)	Diabetes
Heraditory	Hyperlipidaemia
Previous vascular events eg: MI Stroke, Peripheral embolism	Smoking
-	Excess alcohol consumption
-	Polycythemia
-	Oral contraceptives

Stage of cascade	Bio chemical problems	Approaches
Induction	Excess release of glutamate	Inhibit synthesis of glutamate by methionine sulfoximine Lower the temperature if patient is feverish; this lowers brain metabolism and may inhibit release of glutamate;
	Activation of NMDA receptors	NDMA receptor antagonists such as dextrorphan, CGS 19755 and MK 801
Amplification	Influx of Ca^{2+} via valtage gated Ca^{2+} channels	Dihydropyridine derivatives (eg:nipidipine) to block the channels
Expression	Production of free radicals	Free radical inhibitors (eg, 21- aminosteroids).

Good prognostic criteria.	Bad prognostic criteria.
Young age	Age older than 80 years
GCS score higher than 8	GCS score 6 or less at the time of admission.
Haemorrhage volume > 20ml	Haemorrhage volume greater than 30ml
Not midline shift or less than 3mm	A midline shift in CT scan of more than 3mm.
Absence of intra ventricular haemorrhage	Presence of intra ventricular blood
Absence of hydrocephalus	Presence of hydrocephalus.

Survival from small occult haematoma and slit haemorrhages is frequent (20%), but the neurological deficit remains severe and un changed ICH associated with fever, intercurrent infections, severe hypertension, advanced age, uncontrolled diabetes mellitus, liver diseases and bleeding tendencies carry grave prognosis[11]. In one 6-month study, 34% of patients died, 36% were dependent on out side help for daily living, and 30% were capable of independent existence. The following table indicates the prognostic criteria in haemorrhagic strokes which have adverse impact on out come as well as which have associated with a relatively favorable out come[13].

In distinguishing cerebral haemorrhage from cerebral infarction, the following collective criteria, though not always diagnostic, may prove helpful in suspecting an intracerebral bleed. These are; (i). Moderate to severe intense headache (throbbing, pulsating or pounding in a known hypertensive subject) accompanied by nausea and vomiting; (ii). Altered state of consciousness (drowsiness progressing to deepening coma) with irregular respirations; (iii). Neck stiffness accompanied by dissociated eye movements, or forced gaze deviation; (iv). Blurred disc margins or pre- retinal haemorrhage, with changes suggestive of hypertensive retinopathy; (v). Hemiparesis/hemiplegia on one side with shivering movement or even frank convulsions on the non paralysed side, or quadriparesis with an extensor plantar response on both sides, etc. The blood in CSF will help to settle the diagnosis.

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