A DISSERTATION ON

A STUDY OF ISCHEMIC STROKE IN YOUNG

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CERTIFICATE

This is to certify that this dissertation entitled "A study of Ischemic Stroke in Young " submitted by Dr.A.GUNASEKARAN appearing for D.M. (NEUROLOGY) Degree examination in August 2007, is a bonafide record of work done by him under my direct guidance and supervision in partial fulfillment of regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr.M.G.R. Medical University, Chennai, Tamil Nadu, India.

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DECLARATION

I, **Dr.A.GUNASEKARAN** solemnly declare that the dissertation titled "A study of Ischemic Stroke in Young **"** is done by me at Madras Medical College & Govt. General Hospital, Chennai during Jan.2005 – Dec.2006.

The dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University towards the partial fulfilment of requirements for the degree of D.M.(NEUROLOGY). I also declare that this dissertation have not formed the basis of the award of any degree or diploma of any university.

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CONTENTS

INTRODUCTION

The World Health Organisation defines the Stroke as “rapidly developing clinical signs of focal disturbance of cerebral function, with symptoms lasting for 24 hours or longer or leading to death, with no apparent cause other than of vascular origin[1"].

The National Institute of Neurological Disorders and Stroke (NINDS) applies the term “ Stroke “ to any one or all of a group of disorders including cerebral infarction, intracerebral hemorrhage or subarachnoid hemorrhage.

Age is the most powerful predictor of the stroke .The incidence of the stroke increases exponentially with the age.

It is now well known that stroke in young adults is not a rare event. Although the frequency of stroke is lower than in general population, stroke is particularly dramatic in younger patients because it involves a previously healthy adult and the burden is extremely heavy on the spouse and the family.

Stroke in young patients constitutes a challenge because of its social impact and also because of the large variety of associated diagnostic and therapeutic problems.

The causes of stroke are more heterogenous than in older population. Cardiac disease, hematological disease, nonatherosclerotic

arteriopathies, migraine and drug abuse are more important causes for stroke in young adults than in adults. The differential diagnosis includes many genetic, congenital, metabolic and systemic disorders that are rarely encountered in mature adult populations.

Brain and vascular location of lesions are somewhat different in the young .Cerebral infarcts tend to be more often limited to deep regions of cerebral hemispheres , especially striatocapsular region. Vascular occlusive lesions are more often intracranial, affecting especially supraclinoid internal carotid artery , proximal middle cerebral artery and basilar artery. Extracranial occlusive disease is much less common.

The causes of stroke differ considerably with age .For example, the differential diagnosis of stroke in a young baby is quite different from that in a 40 year old young adult, yet both are referred to as stroke in young .“ The stroke in young “ can be subdivided into three groups:

1. Perinatal and neonatal
2. Children (ages 1–15 years)
3. Adolescents and young adults (ages 16 – 40 years)

In this study, the cause of ischemic stroke occurring in young adults of ages between 16 and 40 years were analysed.

AIMS OF THE STUDY

To study

1. The clinical profile

2. The patterns of vascular involvement

3. The possible etiologies

SUBJECTS AND METHODS

The study was conducted during the period of January 2005 to December 2006 among the patients admitted to or consulted as outpatients in Government General Hospital, Chennai.

All the patients aged between 16 and 40 years with clinical features suggestive of stroke were taken. All were subjected to CT scan of brain and patients with evidence of ischemic infarct were taken up for the study.

Inclusion criteria

1. All the patients aged between 16 and 40 years with clinical features suggestive of stroke.
2. Imaging showing ischemic infarcts in the brain

Exclusion criteria

1. Imaging showing evidence of hemorrhage.
2. Imaging showing evidence of venous infarct.

Patients' details regarding age, sex, family history, risk factors like hypertension diabetes mellitus, hypercholesterolemia, valvular heart disease, atrial fibrillation , trauma, smoking, substance abuse were recorded. The onset and details of the symptoms and clinical signs were recorded.

All patients underwent a basic examination protocol that included complete blood counts , erythrocyte sedimentation rate, blood glucose, urea ,creatinine, electrolytes, lipid profile (triglycerides, total cholesterol, and fractions) CT brain, chest x-ray, electrocardiogram; transthoracic echocardiogram.

MRI brain with MRA, B-mode carotid ultrasonography, carotid and vertebral Doppler study had been done in many patients.

Other laboratory tests such as homocysteine, fibrinogen, prothrombin time , partial activated thromboplastin time, antinuclear antibodies, anticardiolipin antibody,lupus anticoagulant autoantibodies (anti-SM, anti-SSA, and anti-RNA), were done in selected patients.

Specific studies for the detection of natural anticoagulant deficiency, such as measurement of protein C, protein S, and antithrombin III, were carried out for patients with an undetermined diagnosis and when personal or family history indicated a prothrombotic disorder.

REVIEW OF LITERATURE

The brain, in contrast with other organs, localizes specific functions to particular regions. Therefore, occlusion of an artery supplying a small area of the brain has a profound and specific effect. Although regeneration or at least functional compensation by the remaining tissue is the rule with most organs, significant regeneration does not occur in the brain. Functional compensation does occur, but the margin of safety is not nearly so great as in the kidney or other organs. Therefore, vascular occlusion and focal injury is significantly more serious in the brain.

BLOOD SUPPLY OF BRAIN

The brain makes up only 2% of total body weight but uses more than 10% of the oxygen metabolized by the body, uses almost 20% of the glucose, and receives almost 20% of the cardiac output. This amounts to about 50-80cc of blood per 100 grams of brain tissue per minute in gray matter and a third to a half of this in white matter. If blood flow falls below about 15cc per 100 grams per minute, dysfunction of neurons begins, and the longer the brain is ischemic the more likely there is to be cell death and necrosis. Neurons respire only aerobically and therefore are dependent on an uninterrupted supply of metabolic substrates.

There are well-developed safety factors that help to protect the brain when its blood supply is threatened. The brain vasculature is able to adjust its arterial perfusion over wide changes of blood pressure to keep a elatively constant and adequate blood supply. This autoregulation self-adjustment or autoregulation causes cerebral vasodilatation when the mean blood pressure drops below normal levels and maintains an adequate blood supply until the mean arterial pressure reaches approximately half the normal levels (50 - 60 mm Hg); lower pressures are associated with focal and diffuse cerebral dysfunction.

The cerebral arterial system, through a direct myogenic reflex contraction, responds to increasing blood pressure by constriction, thus keeping perfusion within normal ranges and avoiding the possible hemorrhagic consequence of excessive pressures.

During systemic hypoxia, the brain is able to extract oxygen from the blood in increasing amounts and thus compensate for arterial hypoxia down to a tension of 50 mm Hg. Beyond this, some vasodilatation probably occurs, possibly on the basis of tissue hypoxia and associated local tissue acidosis, which is a strong stimulant of cerebral arteriolar and capillary dilatation. Small changes in the arterial CO2 partial pressure cause marked changes in cerebral blood flow, presumably by changing the perivascular hydrogen ion concentration. High CO2 tensions such as occur with pulmonary disease result in a

lower pH in tissue and cerebral vaso- dilatation, which is an indirect protection against the associated hypoxia to which the brain vasculature is less reactive. Low CO2 partial pressures, such as occur with hyperventilation, cause a decrease in the perivascular hydrogen ion concentration and subsequent vasoconstriction.

During central neurogenic hyperventilation caused by midbrain or pontine dysfunction, this decrease in volume may have some protective effect against progressive rostrocaudal deterioration.

COLLATERAL CIRCULATION

Collateral circulation is the major safety factor that helps protect the brain from damage caused by occlusion of one or more of its major arterial inputs. The circle of Willis is the most important channel for collateral circulation. It is occasionally developmentally incomplete, and even when complete is often an unsuccessful collateral channel unless vessel occlusion occurs gradually as in atherosclerotic thrombotic occlusion, which gives an opportunity for increased compensatory flow through the usually small posterior and/or anterior communicating arteries.

The most frequently occluded major vessel is the internal carotid artery in the cervical region just above the bifurcation of the common carotid artery. Following occlusion and despite frequent anomalous variations in the circle of Willis, collateral flow is possible in

approximately 90% of the population from the opposite carotid system via a patent anterior communicating artery or from the vertebrobasilar system through a patent ipsilateral posterior communicating artery, or from both sources.

This rather optimistic view of the compensatory potential of the Circle of Willis is somewhat dampened by the realization that age and associated cerebral atherosclerosis can also affect these potential collateral channels. Also, if atherosclerosis predisposes to thrombus formation and subsequent embolus, and if the emboli lodge beyond the circle of Willis (such as in the middle cerebral artery or its branches), then the circle proves useless as a collateral supply. The rapidity of occlusion with embolism also tends to preclude a useful development of collateral from other sources.

There is some anastomosis between the distributions of the main cerebral arteries and the main cerebellar arteries. These anastomoses largely occur at the arteriolar level in the pia over the respective hemispheres. These channels are variable and also limited by the same factors that limit the effectiveness of the circle of Willis, i.e., anatomical variability, difficulty responding to rapid occlusion, and the condition of the vessels.

Based on this anatomy of anastomosis, there is an area of Overlapping blood supply in the regions between major blood vessels. With ischemia in the distribution of a single-vessel system (e.g., the

middle cerebral,), these areas of overlap are often able to avoid major damage. However, if blood flow is affected diffusely (such as with severe systemic hypotension/shock), these areas, somewhat inappropriately called watershed areas, become the regions of the greatest damage. This is because they are at the farthest reaches of blood supply and therefore are the first to develop decreased flow with low systemic perfusion pressure.

A third group of potential collateral circulation channels consist of connections between the external and internal carotid arteries (e.g., external maxillary–ophthalmic-internal carotid). These potential channels are rarely significant as a sole source of collateral circulation in persons with acute stroke but helpful in a very gradual and probably staggered carotid and vertebral occlusion . In such patients, arteriograms reveal large collateral channels from the external carotid system that anastomose with the intracranial arterial systems through the orbit and/or foramen magnum.Almost 50% of persons who suffer a complete ischemic stroke have stenotic or occlusive disease in the cervical vessels.

Also, approximately half of patients with completed ischemic stroke have a history of prodromal symptoms and signs referable to ischemia in the areas supplied by the involved vessels. These episodic signs and symptoms take the form of transient ischemic attacks(TIAs).

Cardio embolism

Cardio embolism is one of the three most common causes of stroke in young[2]. It has been found to be the cause in 14 % to 36 % of stroke in young adults .This variable rate could be explained by variable diagnostic criteria for thromboembolism and by potential geographic variations . Rheumatic heart disease is much more prevalent cause of stroke in India and other developing countries while MVP or PFO are common causes in Europe and North America[3].

The high rate of recurrence and possibility of avoiding this by appropriate treatment make cardioembolism the first etiology to determine.

The abrupt onset of the maximal neurological deficit, multiple infarcts and sometimes associated with losss of consciousness is suggestive of cardioembolic stroke. Biller et al diagnosed cardioembolic sources in 27.1% of 96 patients.

Although nonvolvular atrial fibrillation and ischemic heart disease are the most common causes of cardioembolic stroke in older people , the causes in young adults are more diverse. Valvulopathies with or without atrial fibrillation were the most common finding in young adults. Rheumatic mitral valvular lesions are the commonest lesion The lifetime risk of thrombo-embolism with rheumatic mitral stenosis is 20 % and it is greater if there is associated atrial fibrillation.

Atrial fibrillation may be a manifestation of rheumatic heart disease or a complication of congenital heart disease surgery or independent of any underlying structural heart disease.

Thromboembolism can complicate cardiac surgery using cardiopulmonary bypass with deep hypothermia and cardiac arrest. Stroke may follow the use of extracorporeal membrane oxygenator . Mechanical prosthetic valves are commonly associated with embolic complications than bioprosthetic valves.

The strokes are common in patients with infective endo-carditis and possible mechanisms include septic embolization, mycotic aneurysm and vasculitis.

Impaired fibrinolysis due to increased plasma levels of tPA inhibitor occurs in young survivors after a myocardial infarction and has been identified in recurrent venous thrombosis. Mettinger et al demonstrated disturbed fibrinolysis in patients 6-16 weeks after cerebral infarction and proposed defective release of tPA from the vessel wall as the mechanism.

During right- to- left shunting ,as in atrial or ventricular septal defect or patent foramen ovale , there is opportunity for passage of thrombi leading to paradoxical embolism. Masi et al[4]. demonstrated PFO in 58 % of young patients with cerebral ischemia versus 11 % of age matched controls .Mitral valve prolapse was common in the series

of Bogousslavsky and Regli[5] (12 out of 41 ,29 %) but was infrequent in other series.

Most young adults with MVP and cerebral infarction have another cause for the cerebral infarction and usually it is an incidental finding[6] . The thickening of the leaflets and concomitant aortic valve prolapse is suggestive of its contribution to the stroke.

While the cardioembolic source is often apparent , it may be occult. Transthoracic echocardiography could detect left ventricular dysfunction, mitral valve prolapse and PFO when done with a microbubble test. Transesophageal echocardiography is indicated to rule out left atrium and appendage dysfunction , interatrial septum aneurysm and aortic arch abnormalities. Other investigations such as continuous ECG monitoring and electrophysiological studies with Hiss beam are not necessary since arrythmias are relatively rare in isolation in young adults.

When the cause of ischemic stroke in a young adult is unclear after a thorough initial diagnostic evaluation , it is worthwhile to take a second look at the heart[7]

Atherosclerosis

It accounts for about 20 to 30 % of cases of stroke in young adults. The prevalence of atherosclerosis increases with age after 30 years. Premature cerebral atherosclerosis is generally the result of risk factors such as hypertension, diabetes mellitus, hyperlipidemia and cigarette smoking.

Premature atherosclerosis was assumed if there were two or more risk factors for atherosclerotic disease in the absence of other identifiable causes of cerebral infarction. These risk factors for atherosclerosis included hypertension (sustained systolic blood pressure of > 160 mm Hg and diastolic blood pressure of >90 mm Hg for at least 1 week after the stroke), diabetes mellitus (history of the disease requiring drug or dietary treatment before the stroke), transient ischemic attacks, coronary artery disease, hyperlipidemia (triglyceride concentration of >160 mg%, cholesterol concentration of >230 mg%, and/or high density lipoprotein concentration of < 35mg %), smoking, and peripheral vascular disease [8].

While the pathophysiology of atherothrombosis is similar to the pathophysiology of occlusion in many other vascular beds, the small vessels of the brain appear to be particularly susceptible to the effects of ageing, complicated by hypertension and diabetes. These vessel walls can undergo a change known as "lipohyalinosis" that can damage the wall and compromise the lumen.

There are many factors, in addition to hypertension, that contribute to atherosclerosis. Obesity, hyperlipidemia, sedentary lifestyle, and cigarette smoking, are major factors. Homocysteine, an amino acid by-product of the metabolism of Methionine has been linked to the atherosclerotic process. It may interact with the "bad" form of cholesterol (low density lipoprotein: LDL) in the pathological process. If inadequate amounts of folic acid, Vitamins B12 or B6 are present in the diet, homocysteine accumulates and may be damaging. Low-density lipoproteins (LDL) appear to be critical to the process(they are the major lipid component of the "plaque")[9]

Bansal et al found that 60 % of 25 patients less than 40 years with stroke had type II hyperlipidemia[10]

Persons with diabetes mellitus are predisposed to atherosclerosis and occlusive stroke.. It appears that the prime mechanism of damage is due to osmotic effects of glucose and its breakdown products on endothelial health so glucose control would be predicted to help.

The use of oral contraceptives is associated with a nine fold increased risk of cerebral infarction in women. The Collaborative Group[11] for the Study of Stroke in Young Women found that the risk of stroke with the use of oral contraceptives rose sharply in women with hypertension or migraine and those who were smokers.

Oral contraceptives alter platelet aggregation, enhance antithrombin III activity,decrease serum antithrombin levels, andincrease the levels of certain coagulation factors, especially factor VII.

NON ATHEROSCLEROTIC ARTERIOPATHIES

In Lausanne stroke registry [29]nonatherosclerotic arterial diseases had been found to be the second most common causes of stroke in total of 323 patients younger than 45 years. It consists of various pathological conditions.

Non –inflammatory causes

Dissection, fibromuscular dysplasia, moyamoya disease, Marfan syndrome, Sneddon syndrome, Homocystinuria, Fabry disease, reversible cerebral angiopathies

Inflammatory causes

Takayasu's arteritis, granulomatous arteritides, systemic arteritides (Wegener syndrome, systemic lupus erythematosus rheumatoid arthritis, Bechet's disease, polyarteritis nodosa) infective arteritides (tuberculosis, syphilis, AIDS, mycoses, mycoplasma pneumonia), some toxic angiopathies.

Dissection

Arterial dissections of the cervical carotid and vertebral arteries are an important cause of stroke in otherwise healthy young adults, accounting for 4% to 22 % of brain infarcts[12]. Most dissections involve the extracranial internal carotid artery. Vertebrobasilar and intracranial carotid artery dissections are less common.

Dissection occurs when blood extrudes into the arterial wall, collecting subintimally or intramedially and resulting in compression of the true lumen. Unusual neck torsion or trauma , though oftenquite minor, precedes the onset of symptoms in many patients, particularly those with vertebral artery dissections. Associated fibromuscular dysplasia , Marfan syndrome, cystic medial necrosis increase the risk.

The hallmark of cervical carotid artery dissection is prominent pain in the ipsilateral neck, face or head, coupled with brain ischemia in a relatively young person . An ipsilateral partial Horner's syndrome is present in half of patients.

Arteriographic features include the presence of string sign, pearl and string sign, double lumen sign and pseudoaneurysm formation .MRA provide valuable information and may replace conventional angiography in the future.

If a defect in a component of the arterial wall plays a role in genesis of dissections, it is possible that progressive increasing wall rigidity with ageing may preclude the development of arterial dissection.

Vasculitis

Vasculitis is defined as inflammation and fibrinoid necrosis of the blood vessel wall. Vasculitis can produce focal or multifocal cerebral ischemia by means of inflammation and necrosis of extracranial or intracranial blood vessels. Vasculitis of the central nervous system (CNS) often presents as cognitive disturbances, headache, and seizures (encephalopathy).

Because vascular damage is commonly diffuse, these nonfocal neurologic abnormalities occur more frequently with vasculitis than in focal ischemic disorders. Diagnosis is often difficult because the signs and symptoms are often nonspecific.

Angiographic appearance of a "beadlike"segmental narrowing of cerebral blood vessels, when present, is virtually diagnostic, but cerebral angiograms are often normal in histologically proven cases. The definitive diagnosis requires demonstration of characteristic inflammatory histopathology in leptomeningeal or cortical biopsy specimens.

It is to be considered in the following clinical conditions:

1. Young adults with recurrent stroke
2. Stroke associated with encephalopathic changes, seizures or headache
3. Stroke with fever ,unexplained skin lesions ,stroke with glomerulopathy or elevated ESR

Many infectious and multisystem noninfectious inflammatory diseases cause cerebral vasculitis

Primary CNS arteritis, giant cell arteritis, and vasculitis associated with certain CNS infections may present initially or solely with neurologic abnormalities. Primary CNS vasculitis, Behçet's disease, Takayasu's arteritis and temporal arteritis are notable for their infrequent involvement of the peripheral nervous system.

Primary arteritis of the CNS causes headache and other encephalopathy like symptoms in young or middle-aged individuals. The course is usually insidiously progressive but may wax and wane for periods of several months. A few of these patients present with a strokelike episode.

Takayasu's arteritis[15] also called pulseless disease, is a chronic, idiopathic inflammatory disorder, primarily of young women. It is suspected in patients with absent carotid or radial pulses, cervical bruits, asymmetrical blood pressure measurements, fever, elevated ESR.

It mainly affects the aortic arch, the large brachiocephalic arteries, and the abdominal aorta. Mononuclear infiltrates and fibrous proliferation produce progressive narrowing of the lumen of these vessels, causing reduced flow into the upper extremities and cerebral ischemia.

Systemic lupus erythematosus (SLE)

SLE is a chronic autoimmune disease that can affect almost any organ system. Its presentation and course is highly variable, ranging from indolent to fulminant. It has various neuropsychiatic manifestations.

Headache is the most common neurological symptom, often with migraine or complex migraine features. Stroke and transient ischemic attack (TIA) may be related to antiphospholipid antibody syndrome or vasculitis. Strokes in patients with SLE may result from cardiogenic embolism (Libman-Sacksendocarditis) antiphospholipid antibodies, underlying vasculitis or less often an immune mediated vasculitis.

In patients with high clinical suspicion screening tests to diagnose possible SLE should include a complete blood count, serum creatinine, urinalysis with microscopy, ANA and basic inflammatory markers.

The following are autoantibody tests used in SLE diagnosis:

- ANA - Screening test; sensitivity 95%; not diagnostic without clinical features[14.]
- ANA subtypes are Sm, SSA, SSB, and ribonucleoprotein (RNP)Anti-dsDNA - High specificity; sensitivity only 70%; level variable based on disease activity.
- Anti-Sm - Most specific antibody for SLE; only 30-40%

Sensitivity.

- Anti-SSA (Ro) or Anti-SSB (La) - Present in 15% of patients with SLE

- Anticardiolipin - IgG/IgM variants measured with ELISA among the anti phospholipid antibodies used to screen for antiphospholipid antibody syndrome.

- Lupus anticoagulant - Multiple tests (eg, Direct Russell Viper Venom test) to screen for inhibitors in the clotting cascade in antiphospholipid antibody syndrome.

Infectious causes of vasculitis include tuberculosis , meningo-vascular syphilis ,mycoplasma pneumonia,coxsackie-9 virus and larval stage cysticercosis. Herpes zoster may cause a necrotizing arteritis pathologically similar to granulomatous angitis .Mycotic infections can cause arteritis,aneurysm , thrombosis and cerebral infarction . AIDS can cause stroke by variety of mechanisms.

Recently, the concept of reversible angiopathy with transient segmental narrowing of middle sized intracerebral arteries has progressively emerged. Characteristically, the segmental narrowing seen in arteriography disappear within a few days or few months and clinical recovery is complete. These reversible vasoconstrictions may correspond to vasoconstriction response to intermittent or prolonged bursts of severe hypertension, in the absence of chronic hypertension.

Peripartum angiopathy develops during the last days of delivery In the absence of toxemia. This may be due to hypertension or administration of ergot derivatives. Cerebral angiopathy of toxemia in which hypertensive crisis is the obvious contributing factor. Toxic angiopathies can be caused by cocaine, amphetamine or phenyl propanolamine like substances.

Hematological disorders

Blood disorders have been implicated in significant proportions of ischemic stroke, with an increased frequency in younger patients. Hyperviscosity and hypercoagulable states predispose to arterial occlusive disease, and the risk is greatly amplified if arteriosclerotic vessel changes are already present.

Hyperviscosity that causes a sluggish blood flow and a predisposition to coagulation is associated with dehydration, dysproteinemias (e.g., macroglobulinemias, cold agglutinins), polycythemia, leukemia, and sickle cell disease.

Thrombocythemia, thrombotic thrombocytopenia purpura and rare cancer-associated coagulopathies are examples of excessive clotting capacity that predisposes to arterial occlusion.[16]

The maintenance of hemostasis requires a complex interplay between a large number of checks and balances in the coagulation pathways. Deficiencies of factors inhibiting coagulation (anti –thrombin

III [AT III], protein S, and protein C), increased levels of factors promoting coagulation (factors V and VII), and decreased activity in the fibrinolytic pathway (plasminogen or plasminogen activator deficiencies) have all been implicated in ischemic stroke.

The classic triad of the basis for clotting was first proposed by Virchows in 1862:

1. Damage to the blood vessel wall,
2. Blood flow stasis, and
3. Changes to the coagulability of blood.

These factors interrelate, often in complex ways, to promote pathological thrombosis.

The term “hypercoagulable state” can be defined as any prothrombotic condition caused by a specific disorder of blood coagulation. The most frequently encountered hereditary hyper-coagulable states are: activated protein C (APC) resistance due tofactor V Leiden (FVL) mutation, prothrombin 20210A mutation,protein C deficiency, protein S deficiency, and AT III deficiency. The most common acquired disorder is antiphospholipid antibody syndrome (APS).

Patients with a hypercoagulable state commonly present with a venous thrombosis. Less commonly, arterial thrombosis (ischemic

stroke, myocardial infarction [MI], or peripheral or systemic / visceral arterial thrombosis) may occur.

Abnormalities in the protein C anticoagulant pathway are a main theme in several of the clinically important hypercoagulable states . Protein C, a vitamin K-dependent anticoagulant, circulatesin blood plasma as an inactive protein. In the presence ofthrombin (a coagulation protease) and thrombomodulin (an endothelial cofactor), protein C is converted to its active form, APC.

Both protein S and APC shut off the coagulation cascade: they inactivate the essential procoagulant activated coagulation factor V (factor Va).[17]AT III inhibits coagulationby inactivating thrombin, activated coagulation factor X, and other coagulation proteases. This anticoagulant pathway is impaired in patients with inherited deficiency of protein C or protein S or AT III.

FVL mutation impairs the protein C anticoagulant pathway. FVL is a mutation in the factor Va molecule that makes it resistant to the anticoagulant effects of APC. FVL is the most common cause of APC resistance.

A reduction in the levels of protein C can be seen with hepatopathy, leukemia, and DIC.. Acquired deficiency of AT III has been reported with severe liver disease, DIC, nephrotic syndrome, and the use of oral contraceptives.

The myeloproliferative disorders such as polycythemia vera, myeloid metaplasia, and essential thrombocythemia, have been associated with increased risk of ischemic stroke Thrombosis in patients with myeloproliferative disorders may result from increased red blood cell or platelet mass, or from abnormal platelet function.

Thrombotic thrombocytopenic purpura (TTP)

TTP is a rare, intravascular platelet-clumping disorder results from a deficiency or possibly inhibition of plasma von Willebrand factor–cleaving protease activity during acute episodes, thereby causing exceptionally large multimers of von Willebrand factor to be secreted by endothelial cells. These multimers cause platelet aggregation.

Neurological features are the most frequent presenting manifestations. The more common neurological manifestations are headache, organic brain syndromes, coma, paresis, dysarthria, seizures, and cranial nerve palsies. Involvement of the visual pathways commonly results in homonymous field defects, but ocular changes of exudative retinal detachment, retinal and choroidal hemorrhages and papilledema may occur.

Antiphospholipid antibody syndrome (APLA)

Antiphospholipid syndrome, also known as "sticky blood," is an autoimmune disorder in which the body makes antibodies to its own phospholipids or plasma proteins. Antiphospholipid syndrome (APLA) may occur with systemic lupus erythematosus (SLE) or another rheumatic or autoimmune disorder. This is called secondary APLA syndrome. The disorder can also occur in individuals without any associated disease. This is called primary APLA syndrome.

Antiphospholipid antibodies (aPLs) are circulating immunoglobulins IgG, IgM, IgA isotypes that bind anionic and neutral phospholipid containing moieties. The two most clinically studied and relevant aPLs are the lupus anticoagulant and anticardiolipin antibodies (aCLs).

The American College of Rheumatology has proposed the following clinical classification criteria. At least 1 clinical criterion and 1 laboratory criterion must be present for a patient to be classified as having APLA syndrome.

Clinical features:

- One or more episodes of arterial, venous, or small vessel thrombosis in any tissue or organ including the cerebro-vascular system confirmed by findings from imaging, Doppler studies, or histopathology.

- Frequent miscarriages or premature births because of severe pre-eclampsia or eclampsia or severe placental insufficiency.

Laboratory features:

- Anticardiolipin Ig G or Ig M antibody (medium to high titre) on two occasions 6 weeks or more apart

- Presence of Lupus anticoagulant and /or anti-B2 microglobulin.

The following features are not in the classification but may suggest the diagnosis:

Non-thrombotic neurological symptoms, such as migraines, chorea, seizures, transverse myelitis, Guillain-Barré syndrome, or dementia (rare), Heart murmur or cardiac valve vegetations, Thrombocytopenia or haemolytic anemia, Renal vein thrombosis. Livedo reticularis, Avascular necrosis of bone in the absence of other risk factors, Pulmonary hypertension.

The mechanisms by which aPL could lead to stroke and other thrombotic manifestations are multiple and varied. Effects on platelets, coagulation proteins, and endothelial cells by aPL have been demonstrated.

For example aPL can induce a dose-dependent increase in the activation and aggregation of human platelets. This effect appears to be mediated through binding to phosphatidylserine or ß2-glycoprotein 1. The aPL can interfere with the protein C pathway by inhibiting thrombin formation, interfering with thrombomodulin expression, and inhibiting the degradation of Protein C.

Coagulation assays will detect lupus anticoagulants while enzyme-linked immunosorbent assays detect anticardiolipin antibodies.

APLA is found 10-46% of young patients with strokes and in 10% of stroke patients overall. Stroke patients with APLA tend to be younger (42 years vs 62 years). These patient also have a recurrence rate of 6-30% / year and a mortality rate of 10% / year. Certain groups of patients appear to be at even higher recurrence rates. These would include SLE patients with APLA and patients with Sneddon's syndrome

A variety of neurological disorders have been associated with APLA. The underlying cause of these symptoms appear to be thrombosis. Some patients have large vessel disease while many patient have small vessel involvement. Transient ischemic attacks or strokes are the most common neurologic manifestations . Patients with

APLA often will have multiple MRI abnormalities consistent with small white matter infarcts. Amaurosis fugax, retinal artery and vein thrombosis have been reported in multiple case reports to be a part of the APLA syndrome. APLA are found in as many as 50% of patients who get migraines. As will be discussed below, patients may have encephalopathy as part of severe APLA.

Hyperhomocystinemia

The mechanisms by which homocysteine may increase the risk of vascular disease have not yet received an indisputable explanation. However, results from in vitro studies suggests that homocysteine may exert a procoagulant effect by an alteration of the activity of tissue plasminogen activator secretion. It is recently shown that young stroke patients have low tissue plasminogen activity and high plasminogen activator inhibitor-1 (PAI-1) activity and tissue plasminogen mass concentration.

Kristeinsen in his study[33] , fasting homocysteine levels were not significantly higher in patients with cerebrovascular disease than controls.

The normal fasting tHcy concentration is not synonymous with normal homocysteine metabolism in a young stroke population and that methionine loading is required for the diagnosis of hyper-homocysteinemia. The reason for the high frequency of abnormal

postmethionine loading tHcy is unclear. Vitamin B_6 deficiency may contribute to an abnormal methionine loading test.

It is found that an exaggerated tHcy increase after methionine loading represents a cerebrovascular risk factor in premature ischemic stroke. This association was present also after adjustment for other conventional cerebrovascular risk factors, including fibrinogen. Homocysteine may thus participate as an additional "hit" in Abnormalities in coagulation and vascular cell functions in young adults with ischemic stroke.

MISCELLANEUS CAUSES

Migraine

Solomon et al[18] found a 27% incidence of migraine among young adults with stroke and attributed all of the strokes to migraine. In another study, Adams et al. found that while 14% of their patients had a history of migraine, only 3% of the ischemic events were linked to migraine attacks.

Criteria for migrainous stroke included

1. a well established history of migraine,
2. a typical migraine headache at the time of the a acute stroke, and

3. the absence of other identifiable causes for the stroke.

Cerebral infarction is a potential complication of migraine headaches. Mechanisms by which migraine may produce stroke include vasospasm and/or arteriopathy, embolism, and platelet abnormalities.

Patients with migraine have evidence of vasomotor Instability and platelet disturbances . CT and MRI will demonstrate an infarct, but often the angiogram is normal.

Rothrock et al prospectively evaluated 22 patients with acute migraine-associated stroke and demonstrated cerebral infarction or ICH by CT/MRI in 55% of cases.

Trauma

Traumatic cerebro vascular disease may result in arterial thrombosis, rupture, arterial dissection, pseudoaneurysm or arteriovenous fistila. Children may prone to carotid artery injuries by a lollipop or pencil in the region of the tonsillar fossa with resultant thrombosis or dissection.

Alcohol

Various studies suggested that alcohol was a frequent contributing factor in the development of stroke. Alcohol contributes to stroke in several ways:

1. Induction of cardiac arrhythmias and cardiac wall abnormalities (which predispose to cerebral embolism), induction of hypertension,

2. Enhancement of platelet aggregation,

3. Activation of the clotting cascade,

4. Reduction of cerebral blood flow by stimulating cerebral vascular smooth muscle contraction, and

5. Alteration of cerebral metabolism.

Although MVP, oral contraceptives, alcohol, and migraine need to be considered in patients with cerebral infarction and may be relatively frequent factors contributing to the development of a stroke, they are infrequent sole causes of stroke in the young.

OBSERVATION AND RESULTS

A total of 63 young patients aged between 16 and 40 years who were admitted to or consulted as outpatients in Govt. General Hospital Chennai, between January 2005 and December 2006 with clinical features and imaging suggestive of ischemic stroke were included in the study.

Age distribution

Among 63 patients, the maximum number of patients were in the age group between 31 and 40 years.

Table 1: AGE DISTRIBUTION IN STUDY GROUP

Age group in years	No. of patients	% of patients
16 – 20 years	7	11.11%
21 – 30 years	20	31.74%
31 - 40 years	36	57.14%

Sex distribution

Among 63 patients, there were 41 (65.08%) males and 22 (34.92 %) females.

Table 2: SEX DISTRIBUTION IN STUDY GROUP

Sex	No. of patients	% of patients
Male	41	65.08%
Female	22	34.92%
Total	63	100%

Clinical features

The clinical features of all the patients were studied. The commonest presentation was the weakness of the extremities with or without speech disturbances and sensory complaints. The other symptoms associated with weakness were convulsions, headache, giddiness, fever, altered sensorium and visual disturbances.

Table 3: CLINICAL FEATURES

S No:	Clinical Features	No.of Patients	% of Patients
1	Weakness	59	93.65%
2	Sensory disturbances	27	42 .85%
3	Speech disturbances	38	60.32%
4	Altered sensorium	9	14 .29%
5	Convulsions	8	12.70%
6	Headache	12	19.05%
7	Visual disturbances	6	9 .52%
8	Giddiness	11	17 .46%
9	Cerebellar symptoms	7	11 .11%

Few patients mainly presented with headache or seizures and subsequently found to have infarcts on imaging.

Imaging

CT scan brain was done in all patients. In many of the patients MRI with MRA was done. The carotid territory was involved in about 80%, the vertebrobasilar territory was affected in 15 %, and multiple territories were involved in about 5 % of the patients.

Table 4: LOCATION OF INFARCTIONS

Location of Infarctions	No.of patients	% of patients
MCAterritory	47	74.6%
PCA territory	6	9.52%
Basilar artery	1	1.59%
PICA territory	3	4.76%
SCA territory	1	1.59%
ACA territory	2	3.17%
Multiple territories	3	4.76%

Etiology

The possible etiology for the ischemic stroke were summarized in table 5.

Table 5: ETIOLOGY GROUPS FOR THE STROKE

Etiology Group	No. of Patients	% of Patients
Cardioembolism	18	28.57%
Atherosclerosis	9	14 .29%
Nonatherosclerotic Arteriopathies	11	17.46%
Hematological	7	11.11%
Miscellaneous	4	6.35%
Unknown Cause	14	22.22%

In 14 patients (22.22%), no cause was identified even after adequate investigations.

Cardioembolism

Of the identifiable causes, Cardioembolism was the single most common etiology. Rheumatic mitral valvular disease was the most important cause followed by the prosthetic valve or cardiac surgery. Transthoracic echocardiography was done in almost all patients.

Table 6: SPECIFIC DISEASES CAUSING CARDIOEMBOLISM

Specific disease	No. of Patients	% of Patients
Rheumatic heart disease	9	14.29 %
Prosthetic valve	4	6.35%
Dilated cardio myopathy	1	1.59 %
Acute Myocardial infarction	1	1.59 %
Infective endocarditis	1	1.59 %
Atrial septal defect	2	3.17 %
TOTAL	**18**	**28.57%**

Atherosclerosis

Atherosclerotic vasculopathy was diagnosed as the cause of cerebral infarction in 9 patients (14.29%). Atherogenic risk factors were present in all of these patients except one. Some patients with a possible diagnosis of atherosclerotic vasculopathy were demonstrated by plaque formation in the carotid arteries and some by the presence of risk factors.

Table 7: RISK FACTORS FOR ATHEROSCLEROSIS

Risk factors	No. of Patients	% of Patients
Diabetes	5	7.94 %
Hypertension	7	11.11%
Hyperlipidemia	10	15.87%
Smoking / alcoholism	14	22.22 %
Carotid plaques	3	4.76 %

In some patients, more than one risk factors were present.

Nonatherosclerotic Arteriopathies

The main cause for nonatherosclerotic arteriopathy was vasculitis due to infective cause like tuberculosis or AIDS. In this study, 3 known SLE patients presented with features of stroke, one patient with posterior cerebral artery territory infarct and others in the middle cerebral artery territory.

Table 8: NONATHEROSCLEROTIC ARTERIOPATHIES

Specific disease	No. of Patients	% of Patients
Dissection	1	1.59 %
Takayasu arteritis	1	1.59 %
Infective arteritis	4	6.35 %
Systemic Lupus Erythematosus	3	4.76 %
Bechet's disease	2	3.17 %
TOTAL	**11**	**17.46 %**

One young female presented with features of stroke and was detected to have absent radial pulses and imaging showed features of Takayasu's arteritis. Two young male patients had oral and mucocutaneous ulcers, keratitis and stroke and subsequently diagnosed to have neurobechet's disease. Another patient presented with left hemiplegia and severe neck pain and MRA and carotid Doppler showed the double lumen and carotid artery dissection was diagnosed.

Hematological Diseases

Hemostatic tests were performed on 18 (28.58%) of the 63 patients in whom the cause of the neurologic episode was unexplained; Hematological causes had been found in 7 (11.11%) patients. It includes hyperviscosity syndromes like myelo- proliferative disease in 1 patient. He presented with stroke and severe anemia and thrombocytopenia and bonemarrow study revealed the diagnosis.

Table 9: HEMATOLOGICAL DISEASES

Specific disease	No. of Patients	% of Patients
Myeloproliferative Disorder	1	1.59 %
Antiphospholipid antibody syndrome	3	4.76 %
Protein C ,S defiency	1	1.59%
Hyperhomocystinemia	1	1.59%
Snake bite	1	1.59 %
TOTAL	**7**	**11.11%**

Three patients found to have anticardiolipin antibodies Ig M and IgG along with lupus anticoagulant and diagnosed to have antiphospholipid antibody syndrome (APLA syndrome.Among this 1 had SLE and so secondary APLA. And others were primary. One patient had defiency of protein C and S and one patient had hyperhomocysteinemia.

Miscellaneus Causes

A history of heavy alcohol ingestion within the preceding 24 hours was elicited in 4 patients. Ischemic stroke occurred in the postpartum state in 2 patients. Oral contraceptive use was the likely cause of stroke in 3 female patients with additional risk factors (2 patients had hypertension and one had migraine).

There were 2 arterial ischemic stroke in postpartum period . One female had postpartum cardiomyopathy and other was found to have hypercoagulable state.

Among 63 patients, 4 presented with massive stroke ie. MCA stem occlusion with significant mass effect .2 patients survived after surgical decompression and another 2 patients succumbed to death .1 patient had a large cerebellar infarct with edema causing brainstem compression.

Totally, 4 out of 63 patients died within a month, resulting in a case-fatality rate of 6.34%. Deaths resulted from massive cerebral edema and herniation in 2 patients and from the effects of large cerebellar infarction in 1 patient. One patient died as a result of a myocardial infarction and subsequent congestive heart failure.

Follow-up information was available on 51 of the 63 patients (80.95%). Apart from 4 deaths, 2 patients had recurrent stroke in another territory, 2 patients had had further TIAs. Other patients did fairly well.

DISCUSSION

It is well recognized that cerebral infarctions are not rare among young individuals. Bogousslavsky and Pierre[20], in a study of 1638 cases of stroke, identified 202 patients (12.3%) with first-ever ischemic stroke in patients younger than 45 years. Regardless of the percentage of cases occurring among young individuals, most authors today agree that among victims of stroke, young people are not rare.

Another common conclusion is the existence of a much broader spectrum of pathologies involved in stroke etiology among young patients compared with patients older than 50 years. However, available studies do not agree about the upper age limit to consider a patient "young," which varies between 30 and 50 years[21]. This lack of definition of an age range, as well as the absence of standardization of criteria for the classification of different stroke subtypes, impairs the comparison of results obtained in different studies.

Most of our cases were in the 30 to 40 year age range, coinciding with the observation that the incidence of ischemic stroke increases with age.

The etiologic spectrum is quite broad. Hart and Miller[22] suggested that an "aggressive" investigation permits diagnostic clarification in as many as 90% of cases.

Advances in technology, including magnetic resonance angiography, duplex ultrasonography, transesophageal echocardiography (TEE), contrast echocardiography, and new biochemical assays, have led to identification of a higher proportion of causes that remained obscure in the past. The causes and the proportion with ‘no obvious cause’ depend on these factors, and all these can change as the years go by and as more causes are discovered.

Cardioembolism

A cardiogenic cerebral embolus is one of the most common causes of stroke in the young, accounting for up to one third of the cases. In this study, 28.57 % of the cases of cerebral infarction were of cardiac origin.

In this study, rheumatic heart disease was the leading cardiac cause of ischemic stroke. However, in studies from developed countries paradoxical embolism occurring in patients with ASD or PFO is now diagnosed as the leading cardiac cause of ischemic stroke in young adults.

In the group of cardioembolic infarctions, the subgroup with synthetic valve prostheses represented one fifth of the total cases and was the most numerous. In the series of Adams et[23] al this subgroup was also the most numerous, together with the group with rheumatic heart disease. In contrast, among the cases of Bogousslavsky and

Pierre[21], synthetic valve prostheses were less important than mitral valve prolapse and patent foramen ovale.

Considering cerebral embolisms as a whole for all ages, nonrheumatic atrial fibrillation is the most frequent cause, a fact that is not observed in young patients. In young patients with stroke, there is a predominance of rheumatic heart disease with or without atrial fibrillation. It should be pointed out that rheumatic heart disease was the most important cause, since all patients with a synthetic valve prosthesis had rheumatic lesions.

Atrial fibrillation was present in 3 cases of RHD with mitral stenosis. In 3 cases (two with prosthetic valve and one with MS and atrial fibrillation) stroke occurred a few days after the cessation or decrease in dose of anticoagulant therapy with warfarin.

Of the 63 patients examined, 18 (28.57 %) presented potential sources of cardioembolism , results similar to those reported by Biller et al[24], who diagnosed cardioembolic sources in 27.1% of 96 patients. Radhakrishnan et al[25] found 21 % of cases of stroke in young were due to cardioembolic etiology. It should be pointed out that this expressive proportion was obtained without the aid of special techniques such as contrast echocardiography or transesophageal study, which are known to greatly increase the chance of identifying sources often inaccessible by conventional study (patent foramen ovale, atrial septum aneurysm, etc).

Mitral valve prolapse was common in the series of Bogousslavsky and Regli[5] (12 out of 41 ,29 %) but was infrequent in other series (3 out of 144) In this study ,2 patients were detected to have MVP , but along with other pathology.

Masi et al[8]. demonstrated PFO in 58 % of young patients with cerebral ischemia versus 11 % of age matched controls, but in this study 1 patient (1.59 %) had PFO.

Atherosclerosis

We found that 14.29 % of the young patients with cerebral infarction had an atherosclerotic cause; the majority of these were more than 35 years of age. Our experience is similar to that in other surveys.

Different criteria for diagnosis of atherosclerosis have been used. In some studies diagnosis is based upon the existence of risk factors, while in others evidence of atherosclerotic disease with imaging techniques is required for diagnosis. This may be one of the reasons why there is such a wide range of atherosclerosis being reported as the cause of ischemic stroke in young adults, with as less as 5 percent to as much as 50 percent of cases being attributed to atherosclerosis in different series. The percent of atherosclerosis in this study was 14.29. % based on the existence of risk factors or detection of plaque in carotid or vertebrobasilar arteries.

According to most investigators, the number of atherothrombotic

infarctions is small among young patients. The high incidence among older patients is in contrast to patients younger than 30 years. Chopra et al[26] found 60 % of patients and Bansal et al. found 29% of patients below 40 years had atherosclerosis. In this study, we detected 14 % of patients with atherothrombotic infarction.

Adams et al[28] detected a 25% rate among 144 patients aged 15 to 45 years, and Bevan et al detected a 31% rate among patients aged 25 to 40 years, results that are significantly different from ours.

In this study, lacunar infarctions were significantly more numerous in the 30- to 40-year age range compared with the 15- to 29-year age range. The significant increase in the proportion of lacunar infarctions observed here from 30 to 40 years may suggest that degenerative arteriolar alterations occur earlier than expected in patients with severe systemic arterial hypertension.

Bansal et al[27] found that 60 % of 25 patients less than 40 years with stroke had type II hyperlipidemia .We found 15.87 % patients had hyperlipidemia .Systemic hypertension , diabetes , alcoholism and smoking were found in significant proportion of patients to contribute atherosclerotic process.

Non-atherosclerotic arteriopathy

This is another major group of the causes of ischemic stroke. Nonatherosclerotic arteriopathies may be due to noninflammatory diseases like dissection, fibromuscular dysplasia,homocystinuria, Marfan syndrome or inflammatory diseases like vasculitis due to infections or systemic connective tissue disorders like SLE, or other conditions such as Takayasu's disease or Bechet's disease. Numerous rare etiologies including reversible cerebral angiopathies fall into this category.

In this study , we had patients with stroke due to vasculits associated with infections in 4 out of 63 cases (6.35%) .Two cases were due to CNS tuberculosis , 2 cases with HIV disease.

Three known SLE patients presented with stroke and imaging showed the features of vasculitis. Also we had one case of Takayasu's disease and 2 cases with Bechet's disease.

In a study conducted by Serge Blecic and Julien Bogousslavsky arterial dissection, including vertebrobasilar dissection, is the most common etiology among non-atherosclerotic arteriopathies. In some recent studies arterial dissection is diagnosed as the cause of ischemic stroke of the young adults in up to 20% of cases . In the present study, there was 1 case (1.59 %) of right external carotid arterial dissection , but remaining much behind the 20.8% rate reported by Bogousslavsky and Pierre.

Recent interest and enthusiasm have led to erroneous overdiagnosis of cervical carotid artery dissection, based on nonspecific arteriographic abnormalities. The arteriographic features of carotid dissection have been recently reviewed. As emphasized by Fisher[30] and co-workers in 1978, a tapered occlusion of the cervical carotid artery is the least specific arterio graphic abnormality and does not strongly suggest dissection unless reflux into the ipsilateral carotid siphon can be shown via collateral filling. Any cause of distal carotid occlusion can produce this arteriographic abnormality. Casual diagnosis of nonspecific arterial lesions as dissection has led to frequent errors in management.

Hematological diseases

Blood disorders have been implicated in 5% to 10% of ischemic stroke, with an increased frequency in younger patients. Most disorders are associated with an increased thrombotic tendency and therefore, an increased risk of ischemic stroke.

Typically, patients to be screened for coagulation defects will have a prior history of one or more unexplained thromboembolic events. The yield for diagnosing a hypercoagulable state is typically greatest for young stroke patients or those with a family history of thrombosis and who have no other explanations for their stroke (cryptogenic stroke).

Hematological disorders have been considered to be the cause of ischemic stroke in 2-16% of cases, most often 5 – 9 % .However, this

was 11.11 % in this study.

According to Hart and Kanter[16], this proportion of hematologic abnormalities may be higher than 4% for all strokes in the young , and this observation was supported by our results (11.11 %).

Protein C, protein S, AT III, and fibrinogen levels may be altered in the setting of acute thrombosis Therefore, laboratory testing for these conditions should be deferred until several weeks after an acute thrombotic episode. If they were tested in the acute phase, then they should be repeated. However,because protein C and protein S are vitamin K-dependent proteins, these assays are not reliable in patients treated with oral anti- coagulants. Similarly, AT III measurements are unreliable in patients receiving with heparin.

Investigation for APLA syndrome is warranted if a history of deep vein thrombosis, pulmonary embolism, acute ischaemia, myocardial infarction, or stroke (especially when recurrent) exists in a younger individual or in the absence of other risk factors.

Miscellaneus causes

Solomon et al[18] found a 27% incidence of migraine among young adults with stroke and attributed all of the strokes to migraine. In another study, Adams et al found that while 14% of their patients had a history of migraine, only 3% of the ischemic events were linked to migraine attacks.

The definition of migraine-induced stroke applied in studies conducted thus far has been inconsistent and probably explains why cerebral infarctions in the young attributed to "migrainous infarction" have varied between 1.2% and 25%. In this study only 1.59% of the patients), based on the criteria of the International Headache Society, fulfilled the criteria for migrainous infarction.

OCP has been considered to be the cause of ischemic stroke in 2-5% of cases of young adults. However, it is considered a lower priority diagnosis, and a thorough work-up rule out of higher priority diagnosis, i.e. cardiac, atherosclerotic, nonatherosclerotic vasculopathy, and hematological causes is required before OCP can be diagnosed as the cause of stroke.

A Finnish study suggested that alcohol was a frequent contributing factor in the development of stroke; in a survey of patients with cerebral infarction, 40% had been intoxicated during the previous 24 hours. In our series, 7(11.11%) of the patients were moderate to heavy drinkers of alcohol.

COMPARISION OF THIS STUDY WITH OTHER SIMILAR STUDIES

The present study was compared with other similar studies conducted by Hart & Miller et al. and Jose Ibiapina et al. and shown in the table below .

Etiology group	Specific disease	This study	Hart & Miller et al [31]	Jose Ibiapina et al [32]
Cardioembolism		**28.57 %**	**31.46 %**	**27.18 %**
	Rheumatic valvulopathy	14.29%		9.6%
	Prosthetic valves	6.35 %		
Atherosclerosis		**14.29 %**	**18.32 %**	**9.27%**
Non-atherosclerotic arteriopathy		**17.46 %**	**10.52 %**	**19.12%**
	Dissection	1.59 %		3.81%
	vasculitis	6.35 %		
Hematological disease		**11.11 %**	**9.28%**	**14.7 %**
	APLA syndrome	4.76 %		
Migraine		1.59 %		
Trauma		1.5 9%		
Postpartum		3.17 %	5.13 %	
Unknown cause		**22.22 %**	**27.04 %**	**16.31 %**

The proportion of young adults with ischemic stroke of unknown etiology in this study (22.22%) were slightly lower than that of Hart and Miller's study and at the same time they are slightly higher than those published in the series recently reported by Adams et al, who found 16.6% undetermined ischemic strokes among 329 patients aged 40 years and younger.

A case-fatality rate of 6.35 % in the present study was considerably lower, as expected, in comparison with elderly stroke patients but corresponds to case-fatality rates reported for similar age groups in epidemiological studies and case series.

The topography of cerebral infarctions in young adults with ischemic stroke has rarely been detailed in previous studies. In this study, MCA was involved in 75 % of cases, ACA in 3 % , PCA in 9 % and PICA in 4.5 % of cases.

The proportion of patients with involvement of the vertebrobasilar territory has varied from 15% to 34%.The relatively high proportion of involvement of the vertebrobasilar territory(41%) in study done by Hindfelt and Nilsson may at least partially be due to the extensive use of MRI investigations.

In this study,17.63 % of patients were found to have infarct in the vertebrobasilar territory .Thus, quite a few cases with ischemic lesions in this territory, including cerebellar strokes, might have gone undetected in studies mainly relying on CT scanning. Although 8 of our patients had had more than one infarction at the time of presentation, further recurrences were rare.

The etiological diagnosis of stroke in young adults has changed over time as a result of improvements in diagnostic workup. While cryptogenic stroke was the most frequent diagnosis in the past, today specific causes (non-atherosclerotic vasculopathy, large-artery atherosclerosis, cardioembolism and hematological disorder) are identified in the majority of patients.

SUMMARY

In this study, the salient features were:

- Males (65.08%) were more affected than the females.
- The age group commonly affected was between 31 and 40 years (57.14%).
- Along with weakness, headache, convulsions, altered sensorium, visual disturbances were present in a significant number of patients.
- Cardioembolism was the commonest etiology (28.57%). Among these, rheumatic mitral valvulopathy was the single most common cause.
- Atherosclerosis, infectious vasculitis, APLA syndrome were the other frequently encountered causes.
- Despite extensive investigation, no etiology was found in 14 (22.22%) patients.
- The commonest territory involved was MCA territory (74.6%).

CONCLUSION

- The ischemic strokes among young patients were caused by a broad spectrum of diseases.
- All young patients with stroke deserve detailed evaluation to determine the etiology.
- Aggressive evaluation leads to etiological diagnosis and so proper acute management as well as long term care.
- When the cause of ischemic stroke in a young adult is unclear after a thorough initial diagnostic evaluation, it is worthwhile to take a second look at the heart.
- Investigations should be tailored to suit the need of the particular case rather than a complete list of tests for all patients.

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A STUDY OF

ISCHEMIC STROKE IN YOUNG

PROFORMA

Name	:	DOA	:
Age, Sex	:	DOD	:
Address	:	MIN no	:
		IP No :	

HISTORY:

1) a) Time of onset of stroke :
   b) Time interval between onset of stroke and hospitalization
   c) Time interval between onset of stroke And CT scanning :

2) When the stroke occurred ?
   During sleep routine activity strenuous activity

3) How was the progression of the stroke ?
   Peaks immediately and improving
   Peaks immediately and static
   Progressive
   Stuttering and progressive

4) Sensorium at the onset

5) Speech disturbances
   Aphasia - expressive sensory global
   Dysarthria Mutism

6) Visual disturbances
   Facial paresis
   Swallowing disturbances

7) Headache
   Vomiting
   Convulsions
   Unsteadiness
   Sensory disturbances

Others

8) Chest pain Palpitations Diff. in breathing
Joint pain Rash Hairloss

9a) History of previous TIA s?
Visual hemi/ monoparesis sensory speech
Ataxia diplopia dysphagia vertigo

b) History of previous Strokes?
Territory
Possible etiology
Recovery

10a) Known DM duration : On R :
SHT duration : On R :
Heart d' duration : On R :
Hyperlipidemia duration : On R :

b) Other co-morbid medical conditions :

11)a) Nature of the job ?
Sedantary Moderate exertion Labourer
b) Smoking
Alcohol
Substance abuse
c) Veg / Non - veg

12) Family history
Stroke in elderly
Stroke in young
M.I.

CLINICAL EXAMINATION :

1) Obesity Pallor Jaundice Cyanosis Lymphnodes
Skinrash Purpura Xanthelasma
Pulses : carotid
vertebral
radial dorsalis pedis
Blood pressure :

2) HMF : conscious drowsy comatose
MMSE :
Lobar functions :

Speech :

Visual acuity visual field
pupils fundus
EOM

Facial palsy

Other cranial nerves :

Spasticity
Power : UL :
LL :
Abdominal reflex : cremastric :
Plantar :
BJ KJ
SJ AJ
TJ Clonus
Sensory :

Cerebellar :

EPS :

Bladder &bowel:

CVS :
RS :

INVESTIGATIONS :

1) Blood :
   a) Hb : TC : DC : ESR :
   Sugar
   Urea Creatinine
   Total cholesterol Triglyceride
   LDL VLDL HDL

   b) BT CT PT PTT
   Platelet count FDP
   Peripheral smear

   c) CRP Homocysteine
   ANA aCL LAC
   p-ANCA c-ANCA
   AT-III protein C / S

2) CXR –PA :

3) ECG :

4) ECHO :

5) Doppler studies :
   Carotid & Vertebral

6) Angiography

7) CT scan :

8) MRI :

MRA :

DIAGNOSIS :

Type of Stroke :

Territory of vessel :

Possible etiology :

OUTCOME :

Recovery : Significant
Partial
No

Disability : No
Mild
Moderate
Severe

ABBREVIATIONS AND ACRONYMS

MCA	-	Middle cerebral artery
ACA	-	Anterior cerebral artery
PCA	-	Posterior cerebral artery
PICA	-	Posterior inferior cerebellar artery
ICA	-	Internal carotid artery
CT	-	Computerised tomography
MRI	-	Magnetic resonance imaging
MRA	-	Magnetic resonance angiography
ECG	-	Electrocardiogram
ECHO	-	Echocardiogram
IMT	-	Intimal medial thickening
PSV	-	Peak systolic velocity
Hcy	-	Homocysteine
CRP	-	C-Reactive Protein
ANA	-	Antinuclear antibody
dsDNA	-	double stranded DNA
LAC	-	Lupus anticoagulant
aCL	-	anticardiolipin antibody