

Clinical Features, Etiological Factors, Neurological Imaging and Outcome in Children with Ischemic Stroke

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ABSTRACT

Objective was to study etiological factors, clinical features, neuroradiological findings, Outcome in infants and children who present with ischemic stroke.

Study design: It was a descriptive study.

Setting: It was a hospital based study which was conducted in the Children Hospital, Pakistan Institute of Medical Sciences from 1st August 2002 to 30th December 2003.

Method: In this study children were included who presented with weakness, altered sensorium, seizures, or any focal deficit. CT brain was done in all these children. Those having evidence of infarct were studied for clinical features, etiological factors and out come. Those having neurological infection, trauma, brain tumor, and abscess were excluded from the study. For data analysis, SPSS 8 software was used.

Results: Total of studied thirty patients were enrolled in the study. Age range was from two month to twelve years. Male to female ratio was 3.3 to 1. Sixteen (53%) were 6-12 years of age while 12 (40%) were 2-5 years age and only 2 (6.6%) were below one year of age. Etiological factors were identified in 12 (40%) of the patients, out of which cardiac pathology was found in most of the patients i.e. is 10 (33.3%). There were 2 (6.6%) patients having deficiency of protein C and S. No predisposing factor was identified in 18 (60%) patients. Clinical presentation was studied and was found 29 (96.6%) patients presented with hemiparesis. Facial weakness was present in 15 (56%) of children. Seizures were present in 16 (53.3%) of patients, while 11 (13%) were unconscious. Thirteen (43%) were febrile on presentation. Seven (23%) were having swallowing problem, 4 (13.3%) were having headache and only 3 (10%) got visual problem. Middle cerebral artery infarct was commonest seen in that is 19 (63.3%) cases. Lenticulo striate artery infarct was found in 5 (16.3%). Anterior cerebral artery infarct was 4 (13.3%) and only 2 (6.6%) were having Posterior cerebral artery infarct. Complications were also studied in these patients. Seizures were present in 18 (60%) of patients. Nine (30%) developed mild to severe chest infection, while 10 (33.3%) later on develop urinary tract infection. Weight loss was observed in 11 (36.6%) patients. Outcome was studied with the help of Glasgow coma outcome scale. Ten (33.3%) patients showed good outcome, moderate disability was present in 14 (46.6%) of patients, and severe disability was present in 4 (13.3%) of patients, 2 (6.6%) patients died.

Conclusion: It was concluded that ischemic stroke is not rare in Pakistani children. Cardiac disease is the most important and preventable predisposing factor for ischemic stroke. Every effort should be made to diagnose and treat the congenital cardiac disease as early as possible. Middle cerebral artery infarct was the most common infarct. Computed tomography of brain was found to be very useful and sensitive investigation for diagnosis of ischemic infarct. If available neuroimaging studies should be performed in suspected stroke children. Mortality is low while morbidity was quite high among the survivors. Since this was a hospital based study and may not represent general pediatric age group, therefore large scale population based studies should be planned for the future.

Key Words: Ischemic stroke, Children, CT scan.

INTRODUCTION

Pediatric ischemic stroke is defined as, when the blood supply to any part of the brain is interrupted, resulting in tissue death and loss of brain function.¹ Childhood stroke is emerging as a serious and frequent disorder. In contrast to adult stroke, the study of childhood stroke is in a very early stage of research development with no randomized controlled trials conducted to date outside of sickle cell stroke.²

The incidence of childhood ischemic stroke exceeds 3.3 per 100,000 children per year, more than double the estimated from past decades.³ Tremendous progress has been made in the diagnosis, prevention and treatment of pediatric stroke.⁴ Etiologies seen in this age group are different from those commonly seen in adults.^{5,6} Cardiac disorders and hemoglobinopathy are the most common causes of ischemic infarction. Various congenital anomalies of blood vessel or defects in coagulation and platelet function are often found in children with intra parenchymal haemorrhage.⁶⁻⁹ The role of infection and inflammatory causes of stroke is much more significant in children than in adults.⁹

Cerebral emboli typically present acutely with a sudden loss of neurological function. Thrombi may also present in a subacute or stutterial fashion, with prodromal transient ischemic attacks. The signs and symptoms depend on the location and the size of occluded vessel, as well as patient's age. Anterior circulation strokes are much more common than posterior, and left hemisphere is affected more often than right. Two third of children with acute hemiplegia, seizures, facial palsy, visual disturbances, lethargy and coma. Infants may have no clinical manifestation or a profound motor weakness.^{5,10}

Advances in neuro-imaging and in genetic and other laboratory testing approaches have resulted in an increase identification of stroke sub types and predisposing factors.² Computed tomography (CT) scan and Magnetic Resonance Imaging (MRI) provide reliable non-invasive methods of investigating childhood stroke, aiding in both better diagnosis and management of this problem.^{1,6} Magnetic Resonance Angiography (MRA) is sensitive enough to provide an adequate initial evaluation of arterial brain disease in childhood.¹¹ Cerebral angiography is usually indicated if a definitive diagnosis is not made on MRI.¹¹ The prognosis for childhood stroke is variable and mostly depend upon underlying etiology.¹⁰ In United States mortality from stroke in children has decreased dramatically over the last 20 years. Identification of under-

lying predisposing factors for cerebrovascular disorder in children is important because many of the risk factors can be treated, reducing the risk of subsequent stroke.⁷

At present data about cerebrovascular accident in infants and children is limited. This study is planned to determine the etiological factors, clinical features, neuroimaging abnormalities and long term outcome in pediatric stroke.

MATERIAL AND METHODS

This study was hospital based and conducted at Children Hospital Pakistan Institute of Medical Sciences Islamabad. It is a tertiary level hospital having intensive care and surgical facilities, this study was conducted from 1st August 2002 to December 2003.

This study was conducted on 30 patients aged more than 4 months and less than 12 years, including both sexes. These patients were selected on the basis of history, clinical features and CT scan findings, showing the evidence of infarct. Those having trauma or evidence of infection were excluded from the study.

The patients were studied on the basis of proforma that included complete biodata of the child such as name, age, sex, and duration of stay in hospital. The symptoms like headache, fever, weakness, altered sensorium, seizures, visual problems, speech or swallowing problem were inquired. Glasgow coma scoring of patient was done to assess the conscious level. Complete neurological examination such as motor weakness, reflexes, planters and cranial nerve palsies were noted. Fundoscopy was done to look for papilloedema. Examination of rest of system was also documented. Investigations including findings of CT scan brain were noted for the site of infarct. For the determination of etiological factors number of investigations were done like complete blood count with red cell morphology, echocardiography for underlying structural cardiac problem, protein C and S level, anti nuclear antibody, rheumatoid factor, ASO titer for autoimmune problem. Therapy given to these patients was noted. Follow up of these patients varied from three to six months and outcome was assessed with Glasgow coma outcome score.

GLASGOW COMA OUTCOME SCALE

GRADE V: Good recovery, resumption of normal life.

GRADE IV: Moderate disability, disable but independent.

GRADE III: Severe disability, dependent for daily support.

GRADE II: Vegetative state, unresponsive and speechless.

GRADE I: Death.

GLASGOW COMA SCORE

Score	Best Eye	Best Verbal	Best Motor
6	-	-	obeys
5	-	oriented	localizes pain
4	spontaneous	confused	withdraws to pain
3	to speech	inappropriate	flexor (decorticate)
2	to pain	incomprehensible	extensor (decerebrate)
1	none	none	none

The different variables were age, sex, etiological factors, and neurological status at the time of presentation, C.T. scan findings, and Glasgow outcome scale. It was a descriptive study. Disease to be studied was ischemic stroke in children, which is defined as, when the blood supply to any part of the brain is interrupted, resulting in tissue death and loss of brain function.¹ Data was entered in version of SPSS 10 and descriptive statistics were used to calculate the frequencies of clinical features, etiological factors, neuroimaging, and outcome. All children were included who fulfill one or more of following criteria.

- More than four weeks and less than twelve years.
- Weakness of one or more limbs.
- Cranial nerve palsies.
- Altered sensorium.
- Fits.
- Any focal sign.
- CT/MRI consistent with infarction.

Children were excluded whose C T scan consistent with tumor, tuberculoma or brain abscess, tuberculous meningitis, head injury and.CNS infection.

RESULTS

Forty patients presented with symptoms and signs consistent with stroke. CT scan brain was done in all the patients. Out of these 30 patients were included in the study. Ten patients were excluded from the study because of either having haemorrhagic stroke or having evidence of central nervous system infection. Among them twenty three were male and seven were female. Male to female ratio was 3.3 to 1. Age range was from two month to twelve years. Mean age was seven years. Most of them i.e. is 16 (53%) were from 6-12 years of age while 12 (40%) were in between 2-5 years age group and only 2 (6.6%) were below one year of age.

Underlying etiological factors were identified in 12 (40%) patients, out of which cardiac pathology was

identified in most of the patients i.e. is 10 (33%) Among them 6 (20%) were having congenital cyanotic heart disease and 4 (13%) were having acyanotic heart disease either congenital or acquired like rheumatic heart disease. There were 2 (6.6%) patients having deficiency of protein C and S. None of the child was found to have Sickle cell disease or any autoimmune disease. No predisposing factor was identified in 18 (60%) patients, although patients were not screened for some unusual disorder e.g. MELAS syndrome, Moyamoya disease, Homocystine urea, and post Vari-cella syndrome (Table A).

Table A: *Etiological Factors of Schemic Stroke in Children.*

No.	Etiological Factors	No of Patients
1.	Idiopathic	18 (60%)
2.	Congenital Heart Disease	10 (33.3%)
3.	Protein C&S Deficiency	2 (6.6%)

Table B: *Clinical Presentation of the Patients with Ishemic Stroke.*

Clinical Presentation	No of Patients
Hemiparesis	29 (96.6%)
Seizures	16 (53.3%)
Cranial nerve palsies	15 (50%)
Fever	13 (43.3%)
Unconsciousness	11 (36.6%)
Dysphasia	7 (23.3%)
Headache	4 (13.3%)
Visual Disturbances	3 (10%)

Children presented with various clinical features, it was found that 29 (96.6%) patients were presented with hemiparesis. Facial weakness was present in 15 (56%) of children. Seizures were present in 16 (53.3%) of patients, while 11 (13%) were unconscious when came to hospital. Thirteen (43%) were febrile on presentation. Seven (23%) were having swallowing problem, 4 (13.3%) were having headache and only 3 (10%) got visual problem (Table B and Figure B).

C T scan brain was done in all the patients to find the site of infarct. Middle cerebral artery infarct was commonest among all that is 19 (63.3%), out of which 8 (26.6%) had left middle cerebral artery infarct, 7 (23.3%) had right middle cerebral artery infarct, and 4 (13.3%) had bilateral middle cerebral artery infarct. Lenticulo striat artery (lacunar) infarct was found in 5 (16.3%). Anterior cerebral artery infarct was 4 (13.3%) and only 2 (6.6%) had Posterior cerebral artery infarct (Table C).

Table C: C.T. Scan Findings.

Artery Involved in Infarction	Number of Patients
Middle Cerebral Artery	19 (63.3%)
Lenticulo Striate Artery	5 (16.3%)
Anterior Cerebral Artery	4 (13.3%)
Posterior Cerebral Artery	2 (6.6%)

Complications were also studied in these patients. Seizures were present in 18 (60%) of patients. Nine (30%) developed mild to severe chest infection, while 10 (33.3%) later on develop urinary tract infection. Weight loss was observed in 11 (36.6%) of patients.

Patients were followed up for three to six months on outdoor basis and their outcome was assessed. On follow up 10 (33.3%) patients showed good outcome (Grade V on Glasgow outcome score). Moderate disability was present in 14 (46.6%) of patients (Grade IV on Glasgow outcome score). Severe disability was present in 4 (13.3%) of patients (Grade III on Glasgow outcome scores). None of the patient was in vegetative state (Grade II in Glasgow outcome score). Two (6.6%) patients died (Grade I on Glasgow outcome score). (Table D).

Table D: Outcome of Ischemic Stroke in Children.

Neurological Grade	No of Patients
5. Good	10 (33.3%)
4. Moderate Disability	14 (46.6%)
3. Severe Disability	4 (13.3%)
2. Vegetative	0
1. Death	2 (6.6%)

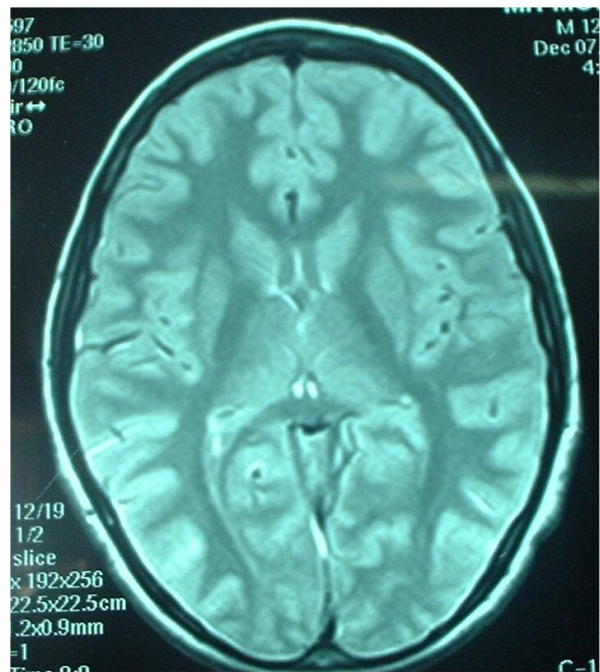
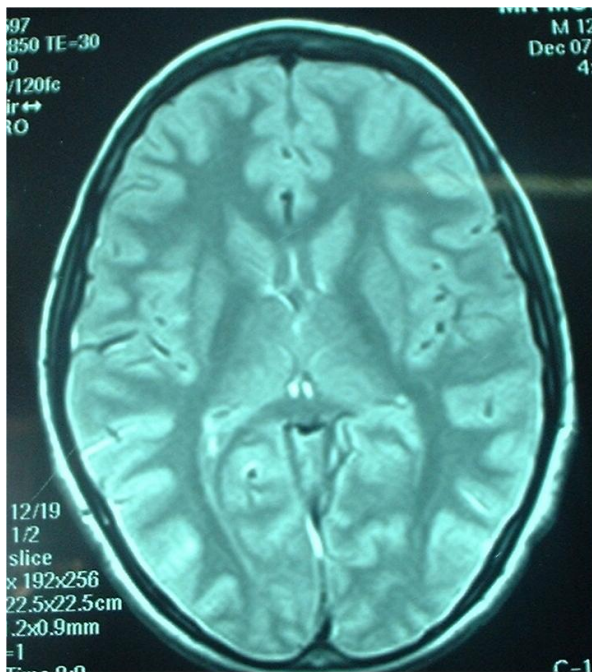


Fig. 1: T2 weighted MRI Image : Normal Anatomy of Brain.

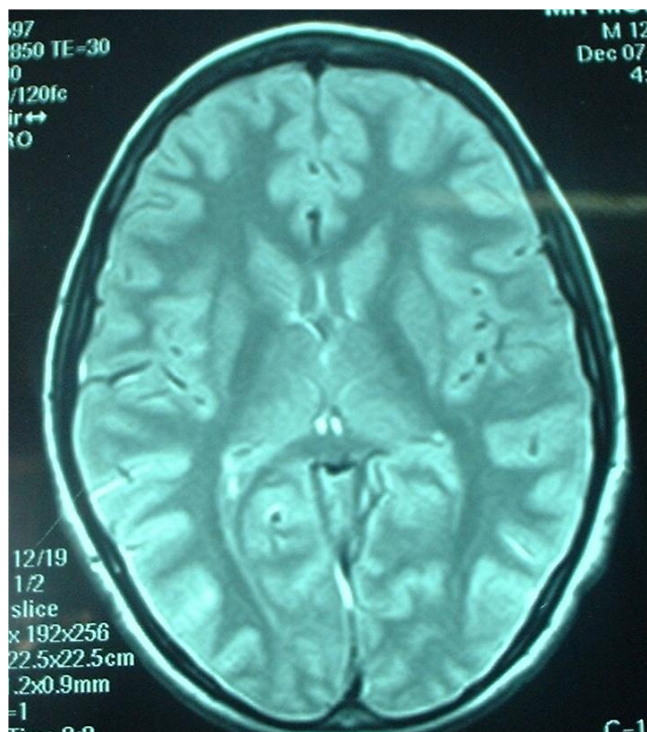


Fig. 2: MRI brain showing normal anatomy of intracranial structures.

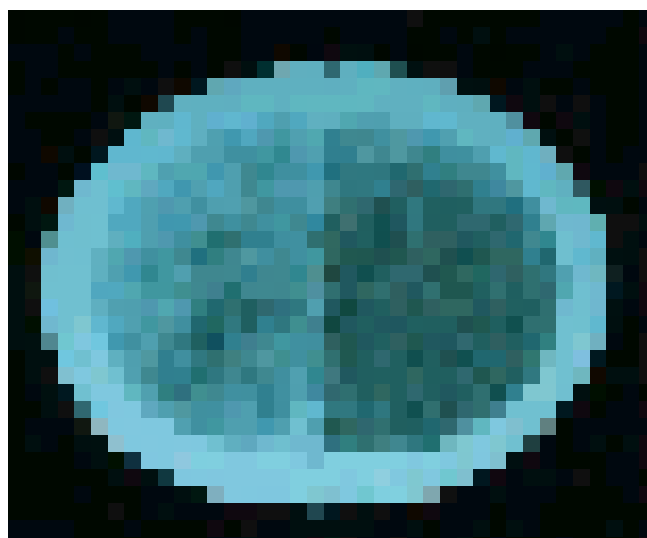


Fig. 3: Unenhanced CT brain showing large hypodense area in left cerebral hemisphere supplied by left middle cerebral artery.

DISCUSSION

Stroke in children is not a rare pathology, although there is limited published literature in Pakistani children.¹⁰

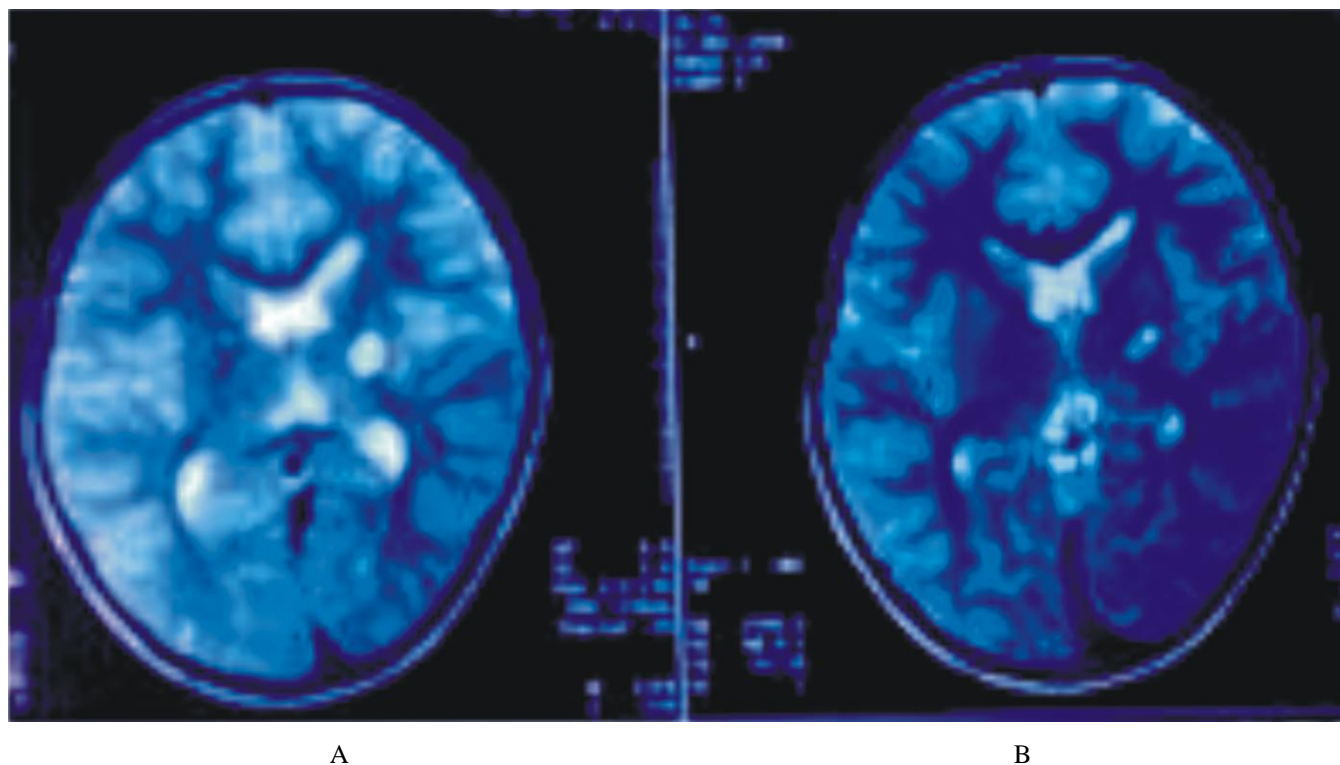


Fig. 4: MRI brain with (two sections A and B) hyperdense lesion indicating lacunar infarct in left internal capsule.

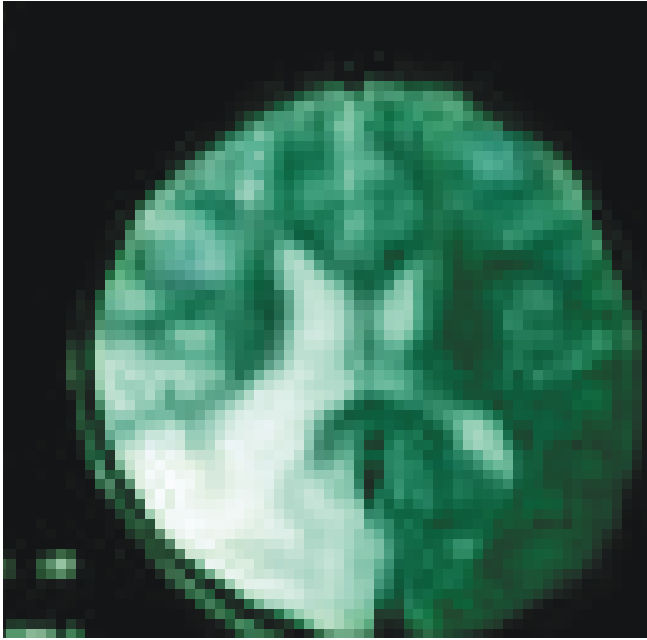


Fig. 5: MRI brain with hyperdense lesion showing infarction in right occipital lobe supplied by posterior cerebral artery.

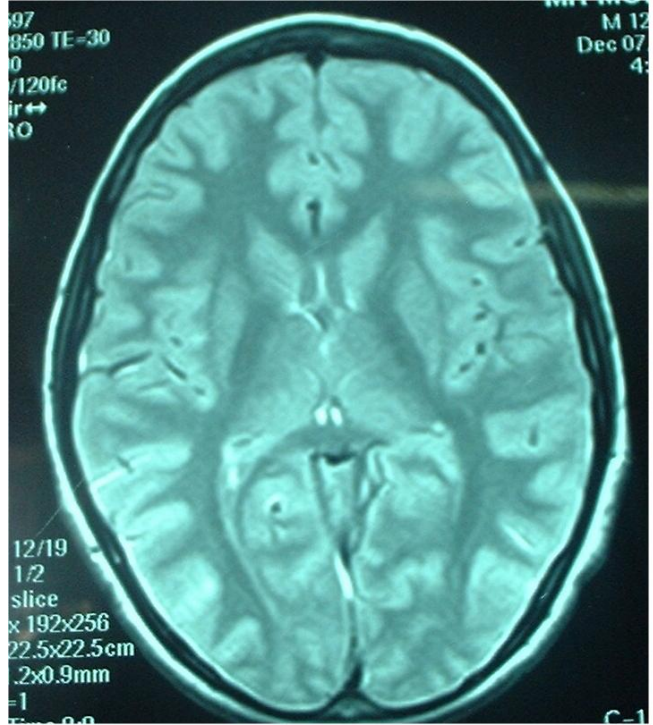


Fig. 7: MRI brain showing normal anatomy of intracranial structures.

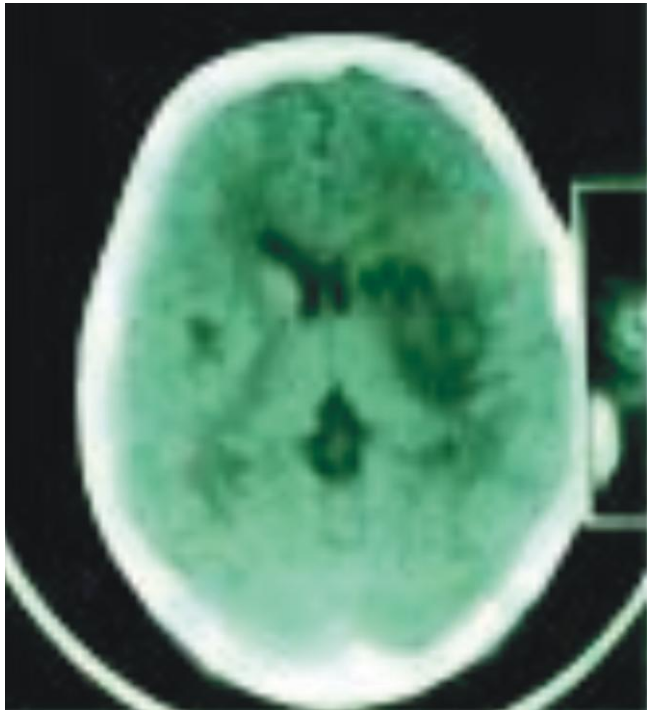


Fig. 6: Computed brain scan (unenhanced) showing infarction in left basal ganglia and internal capsule as hypodense area.

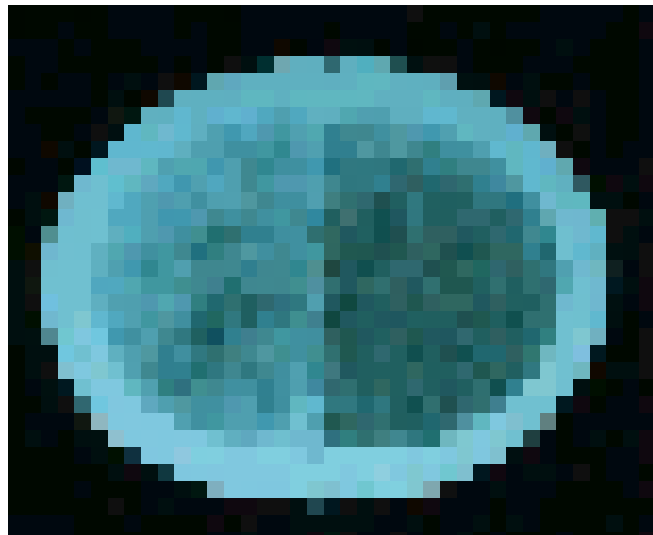


Fig. 8: Unhenced CT brain showing large hypodense area in left cerebral hemisphere supplied by left middle cerebral artery.

This study was conducted to know about pre-

entation, etiology and outcome of pediatric ischemic stroke .In our study it was found that ischemic stroke is common in older age that is 6-12 years of age as compared to younger age. This data is comparable

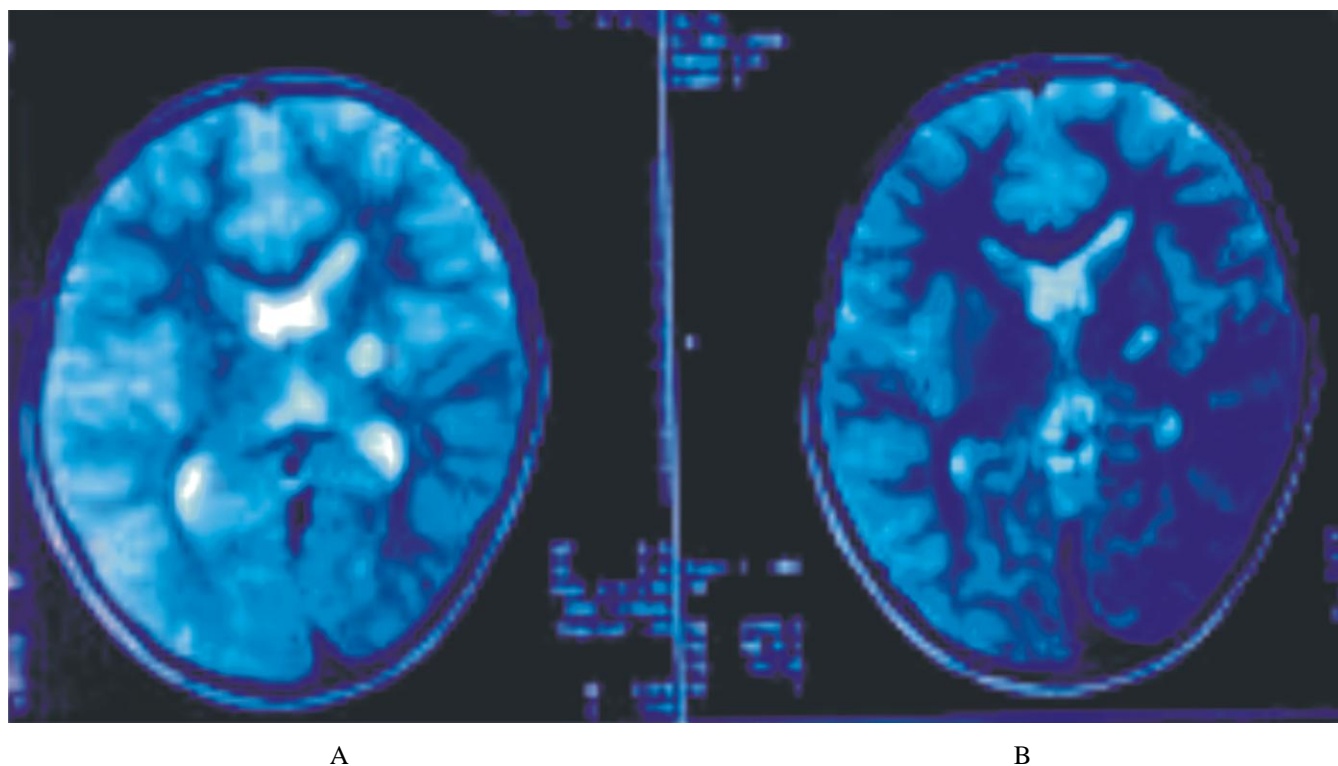


Fig. 9: MRI brain with (two sections A and B) hyperdense lesion indicating lacunar infarct in left internal capsule.

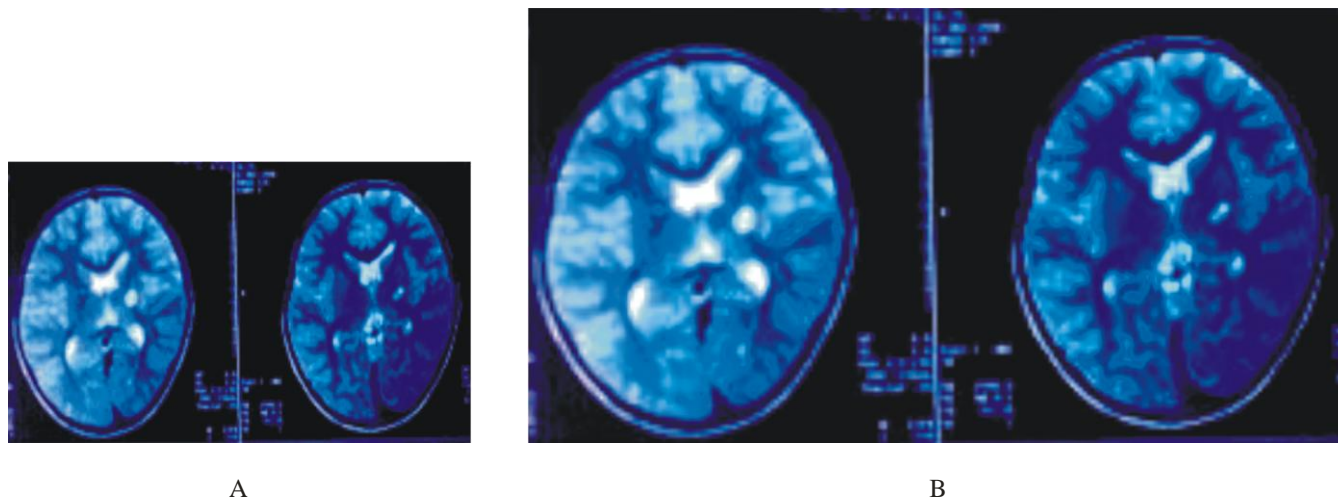


Fig. 10: MRI brain with section A, B showing hyperintense lesion indicating lacunar infarct in the left internal capsule.

with other studies.^{12,13}

Etiology seems to be multifactorial in ischemic stroke. With the availability of more sophisticated laboratory investigations, more and more children would be found to have underlying pathologies.¹⁰ These investigations may not be possible to perform in every patient because of lack of facility or limited financial resources of the patients. In our study we

were able to find out causes in about half of the patients, while a study done by De Veber G et al etiology was determined in about two third of the patients that is 60-70% of the patients.³ A study from middle east showed 65% of the children with ischemic stroke were having some predisposing cause.¹⁴

Cardiac pathology was found to be the commonest cause of ischemic stroke. In our study about one third

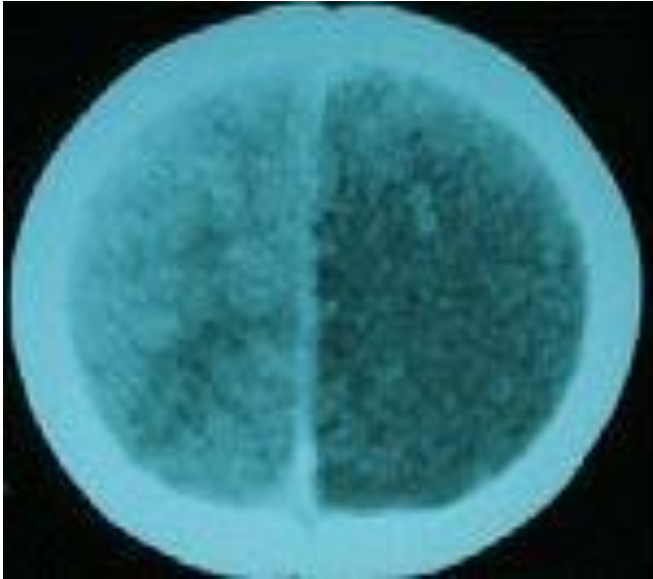


Fig. 11: Unenhanced CT brain showing large hypodense area in the left cerebral hemisphere supplied by left middle cerebral artery.

of the children had cardiac disease either congenital or acquired. Thrombosis and embolism is the cause of the cause of arterial occlusion and cell death. In a study conducted by Solman GC in 1978 about half of the children with stroke had cardiac disease.¹⁵ Latest studies showed cardiac disease in about 20% of the patients.^{5,7,22,23} In western countries management of congenital cardiac anomalies improved a lot leading to decrease incidence of ischemic stroke in cardiac patients.^{5,7} In Pakistan, asymptomatic congenital heart diseases may remain undiagnosed for few years of age. Even if they are diagnosed early are not treated promptly due to financial constrains and non availability of health facilities to all.

Other important cause in our study was hypercoagulable states due to deficiency of protein C and S, that are naturally occurring anticoagulants. Deficiency of protein C and S are rare deficiencies.¹⁸ In most of the studies those analyzed their effect on ischemic stroke were not powerful enough to detect it as a cause.¹⁸ At present therefore the role of these thrombophilia factors in ischemic pediatric stroke remain debatable, and is still an area of active research.^{19,20,22}

Children with sickle cell anemia are particularly vulnerable, carrying a 200 fold increased risk of cerebral infarction.^{13,14} Up to 1/3 of these children with the sickle cell disease show evidence of cerebral infarction at 8 years of age. Of these 12% manifest clinically as an overt stroke. It is associated with more than

20% of the stroke patients, that is equal to cardiac pathology.^{8,3,21} In our study, none of the patient was having sickle cell disease, as it is very rare in Asian population. However stroke has been reported in thalassemic children in Islamabad.¹⁰

Presentation of ischemic stroke was varied depending on site of occlusion. Hemiplegia was the commonest presenting feature in about all of the patients except one in which their was posterior cerebral artery infarct. Most of the infarcts were in middle cerebral artery territory that's why facial nerve weakness was present in concordance with hemiplegia. This feature is comparable with other studies.^{3,10} Rest of the presenting features were either non specific or due to focal neurological damage like visual problem or swallowing problem. Others have reported similar findings.^{10,15}

In our study middle cerebral artery infarct was the commonest and is far most common in first stroke. As middle cerebral artery is direct terminal branch of internal carotid artery that's why it is the commonest site of occlusion. This territory involved almost entire the lateral surface of the cerebral hemisphere that is motor area, that's why most of the patients presented with hemiplegia and facial weakness. In a study by Koga M et al occlusion of middle cerebral artery and its branches is the most common type of infarct.²² Isolated posterior cerebral artery infarct is very rare entity presented with blindness as it has a short course. Libman et al also reported anterior and posterior cerebral artery as uncommon site of occlusion.²³

Complications were noted which were either primarily due to disease or secondarily because of immobilization or hospital stay. Seizures, although was presenting feature in some of the patients but develop in other later on due to infarct. Other complications include chest infection, urinary tract infection and weight loss due to improper nursing care.

Long term out come varied from full recovery to severe disability. One third of the patients recovered having no disability, while about half of the patients had moderate disability and only few of the patients had severe disability. Mortality was less than 1%. No significant correlation was found between prognosis of childhood stroke and etiology, age at presentation or gender. Adverse out come was noted having death in 10%, recurrence in 20% and neurological deficit in 2/3 of the survivors in study from Canada.³ Bjornstad A et al reported that none of the patient died as a result of ischemic stroke; 27% recovered completely, 41% had light sequel, 18% moderate sequel, and 18% had

recurrence,⁵ while Carvalho KS et al report good prognosis comparable with our study.²⁴

CONCLUSION

It was concluded that ischemic stroke is not rare in Pakistani children. Cardiac disease is the most important and preventable predisposing factor for ischemic stroke. Every effort should be made to diagnose and treat the congenital cardiac disease as early as possible.

Middle cerebral artery infarct was the most common infarct. Computed tomography of brain was found to be very useful and sensitive investigation for diagnosis of ischemic infarct. If available neuroimaging studies should be performed in suspected stroke children.

Mortality is low while morbidity was quite high among the survivors. Since this was a hospital based study and may not represent general pediatric age group, therefore large scale population based studies should be planned for the future.

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