Management and Outcome of Stroke in a Sample of Children Admitted to Children Welfare Teaching Hospital/Baghdad

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ABSTRACT:

BACKGROUND:

Stroke in children is a serious disorder in which little has been published. Population-based estimates of the annual incidence of childhood stroke (ischemic and haemorrhagic) range from 2·3 to 13·0 per 100 000 children and incidence rates in neonates are closer to 1 per 5000 live births

CONCLUSION:

To determine clinical presentation, etiologies, diagnostic procedures, treatment options and outcome of children with stroke**.**

METHODS:

Descriptive study of patients with stroke admitted to Children Welfare Teaching Hospital/Baghdad from October 2011 to September 2012 was conducted. Cases were classified radiologically into ischemic stroke (IS) and hemorrhagic stroke (HS) and their management modalities were studied.

RESULTS:

Out of 21 patients; 13 (61.9%) had hemorrhagic and 8 (38.1%) had ischemic stroke. Female:male ratio was 1.3:1. Haemorrhagic stroke was more among males and infants; ischemic stroke was more among females and older children. In 16 (76%) patients, the diagnosis was established after more than 24 hours of onset. Patients with ischemic stroke spend longer time in hospital. Seizure was the commonest clinical feature in both types (17 patients (81%)) followed by altered mental status (16 patients (76.2%)). CT-scan was abnormal in 20 patients and MRI in 11 patients. Complete recovery was noticed in 7 (54%) patients with hemorrhagic type, while 7 (87.5%) patients with ischemic type recovered with sequelae.

CONCLUSION:

Stroke was more common among female and children younger than 12 months. Seizure and altered mental status were the commonest presentations. A delay in performing neuroimaging was obvious in the current study. Patients with ischemic stroke tend to spend longer time in hospital. Antibiotic were the medication most often used. The majority of children were discharged well.

KEYWORDS: ischemic stroke, hemorrhagic stroke.

INTRODUCTION:

Stroke is increasingly recognized as a cause of childhood disability and lifelong morbidity: population-based estimates of the annual incidence of childhood stroke (ischemic and haemorrhagic) range from 2·3 to 13·0 per 100 000 children and incidence rates in neonates are closer to 1 per 5000 live births. [1]

Recently the availability and widespread use of the noninvasive neuroimaging techniques in Baghdad's hospitals have led to increased recognition of stroke in children who might otherwise receive other diagnoses and have contributed to increment in the reported cases admitted to the hospitals. Guidelines for managing this condition are not well established in our hospital and mostly based on adult studies or experts opinions. The majority of paediatric stroke data was reported from developed countries [2]. Except few population studies, data from developing countries were mostly derived from case reports and series [2]. Two studies have been conducted in CWTH during the last few years. One study [3] pointed to patients who presented with hemiplegia only without listing the inclusion and/or exclusion criteria or the neuroimaging as definitive diagnostic criteria.

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The other study [4] showed that the calculated annual hospital frequency rate of stroke was 54.2/100000 children. This result is much higher than what was reported in a study performed in Saudi Arabia [5]. As a tertiary center CWTH drains a very wide area and this may partially explain this difference. The present study is focused on clinical presentation, underlying diseases, diagnostic imaging and lab-tools. It might be a step toward more essential multi-center collaborative researches into paediatric stroke. Therapeutic approaches are briefly discussed as a basis for the development of randomized controlled trials in Iraqi children with stroke.

AIMS OF THE STUDY:

The study aimed to review the demographic characteristics of children with stroke, study the presenting symptoms and time taken from occurrence of symptoms to hospital admission and diagnosis and to describe the management and outcome of stroke in children admitted to Children Welfare Teaching Hospital/neurological ward.

MATERIALS AND METHODS:

Study Design

A cross sectional study was carried out to describe the management and outcome of stroke in children admitted to Children Welfare Teaching Hospital (CWTH)/neurological ward during the period from first of October 2011 to first of September 2012. Carers have given informed consent to the research and to publication of the results. Ethical approval was obtained from the Research Ethical Committee - Human Resources Development and Training Center - Ministry of Health, Iraq.

Setting:

The patients admitted to the emergency unit at Children Welfare Teaching Hospital, where they were examined by the resident doctors and the specialist who decided to admit the patient either directly to the neurological ward if beds are available or to the waiting room if not, to be managed by one of senior pediatrician (one of the researchers).

Time taken before admitting the children with stroke was studied and 6 hours was used as a cutoff point. Time factor is very important for both the management and prognosis of stroke, and previous evidences from adult studies showed that lytic therapy needs to be given within the first 6 hours of symptoms yet children often present significantly later [6].

The initial and most available neuroimaging used to confirm the diagnosis of both types was Computerized Tomography Scan (CT-brain) to be followed (if available) by Magnetic Resonance Imaging (MRI) sequences, and according to availability, Magnetic Resonance Angiography (MRA) was used in cases of arterial ischemic stroke or haemorrhagic type while Magnetic Resonance Venography (MRV) was used in cases of cerebral venous thrombosis. Time of diagnosis of stroke is the time when CT scan or MRI confirmed the diagnosis, and according to that, patients were grouped into those for whom neuroimaging was done within 24 hours of onset of illness and those whose neuroimaging studies were done after 24 hours.

Patients were followed up daily during their stay in the ward by the residents and specialist.

Inclusion Criteria:

Cases were classified into ischemic and hemorrhagic stroke as follow [7]:

1. Ischemic stroke; Acute ischemic stroke was defined as acute neurologic deficits lasting more than 24 hours and caused by cerebral ischemia, with neuroimaging showing parenchymal infarction.
2. Hemorrhagic stroke; Hemorrhagic stroke was defined as an acute neurologic deficit lasting more than 24 hours, with neuroimaging showing intracranial hemorrhage.

Exclusion Criteria: all

1. Cases with traumatic intracranial hemorrhage.
2. Cases with hemiplegia but normal neuroimaging [as the patients' eligibility required a radiological diagnosis of ischemic stroke or lesion consistent with it].

Aspecial data collection form was prepared to register the demographic characteristics of the patients, history, presenting complaints, signs and symptoms, duration from onset of illness to admission and to confirmation of diagnosis of stroke, investigations, treatment modalities, and results of neurological examination at the time of discharge, recording any neurological sequelae or deficits. The first interview is the most important one for baseline data performed at admission to the neurological ward with the parents and/or caregiver, and updated information is usually added during daily follow up to complete the requested data.

Statistical Analysis

Microsoft Office Word and Excel 2007 were used for data input and analysis. Chi square test for independence and Fisher's exact test were used to test the significance of association between discrete variables. Student's t test was used to test the significance in observed difference in mean of continuous variables.

Findings with P value less than 0.05 were considered significant.

RESULTS:

During the study period, 21 children with stroke were studied; more than two thirds of them (15 patients (71.4%)) were aged one year or less, patients with haemorrhagic stroke (HS) tend to present at earlier ages (range 1.1-36 months, mean 5± 9.4 months) than ischemic stroke (IS) (range 3-144 months, mean 43.3 ± 51.01 months), girls were more than boys with Girls: Boys ratio of 1.3:1. Haemorrhagic stroke was diagnosed in 13 (61.9%) and the rest were diagnosed as ischemic stroke (8(38.1%), two of them due to venous thrombosis). Haemorrhagic stroke was more among boys (7 patients (53.8%)) and during the first year of life (12 patients (92.3%)), ischemic stroke was more among girls (6 patients (75%)) and older than one year (5 patients (62.5%)) (Significant association was found regarding age of onset and type of stroke only). Three of the patients developed recurrent strokes; two with hemorrhagic stroke (One patient had five strokes, one had two strokes) and one with ischemic stroke (had three strokes) as shown in Table (1).

Table 1: Distribution of patients by age of onset, sex and type of stroke.

Demographic Characteristics	HS (13)	IS (8)	Total	P value
	No. (%)	No. (%)	No. (%)	
Age of presentation (in months) Range Mean ± SD Median	 1.1 -36 5 ± 9.4 2.2	 3-144 43.3± 51.01 20.5	 1.1-144 19.6 ± 36.4 3	
Age of Onset ≤ 1 year >1 years	 12 (92.3) 1 (7.7)	 3 (37.5) 5 (62.5)	 15 (71.4) 6 (28.6)	0.01*
Sex Boys Girls	 7 (53.8) 6 (46.2)	 2 (25.0) 6 (75.0)	 9 (42.9) 12 (57.1)	0.36*
Patients with recurrent stroke	2 (15.4)	1 (12.5)	3 (14.3)	

* The significance of association was tested using Fisher's Exact test

Table (2) showed that only 5 patients (23.8%) patients were admitted to the hospital within less than 6 hours from the onset of symptoms, the majority (16 patients (76.2%)) were late in seeking medical advice, and this was more obvious among those with hemorrhagic stroke (11 patients (84.6%)) compared to those with ischemic stroke (5 patients (62.5%))Patients with ischemic stroke tend to spend longer time in hospital (mean of 18.4 ± 10.5 days) compared to those with hemorrhagic type (mean of 12 ± 5.6 days).

Regarding their fate; none of those with ischemic stroke recovered completely, most of them (7 patients (87.5%)) improved yet with neurological sequelae and one of them died in hospital, whereas more than half of those with hemorrhagic stroke recovered completely (7 patients (53.8%)), (3 patients (23.1%)) improved but with neurological sequelae, two patients died and one referred to the Respiratory Care Unit (RCU) as shown in Table (2).

Table 2: Distribution of patients by duration from time of onset to admission, length of hospitalization, status at discharge and type of stroke

Characteristics	HS	IS	Total	P value
	No. (%)	No. (%)	No. (%)	
Time from onset to admission* ‹ 6 hours ≥ 6 hours	 2 (15.4) 11 (84.6)	 3 (37.5) 5 (62.5)	 5 (23.8) 16 (76.2)	0.325*
Length of hospitalization (days) Range Mean ± SD Median	 1-19 12.4 ± 5.6 13.5	 2-36 18.4 ± 10.5 18.5	 1-36 14.55 ± 8.3 14.5	0.17**
Status at Discharge Recovery Sequelae Referred to RCU Died	 7 (53.8) 3 (23.1) 1 (7.7) 2 (15.4)	 0 (0.0) 7 (87.5) 0 (0.0) 1 (12.5)	 7 (33.3) 10 (47.6) 1 (4.8) 3 (14.3)	

*The significance of association was tested using $\chi 2$ Test
** The significance of difference was tested using Student's t Test

Nearly two thirds of the affected children (13 patients (60.7%)) were previously healthy, five patients (27.8%) with hemorrhagic stroke gave a family history of stroke, and two patients (one with hemorrhagic and other one with ischemic strokes) gave history of cardiac diseases. Bleeding tendency was evident in 11 (61.1%) of those with hemorrhagic stroke.

The onset of stroke was sudden in 14 patients (66.7%) of both types of strokes, Seizure was the commonest presenting feature among both types (17 patients (80.9%)), seizure and altered mental status were the commonest presentation in children with hemorrhagic stroke (11 patients (84.6%)) for both, followed by fever (8 patients (61.5%)) and vomiting (6 patients (46.2%)), whereas among those with ischemic strokes the commonest presentation was also seizure but with fever and limb weakness (6 patients (75%)) for each, followed by facial weakness, altered mental status and vomiting (5 patients (62.5%)) for each. Although slight differences in the presentation of children with different types of strokes, yet no statistically significant association were evident.

Table (3) showed that CT examination was performed within less than 24 hours from onset of illness in only 5 patients (23.8%); four of them were with hemorrhagic stroke, and in 8 patients (38.1%) the examination was performed within 24 hours of admission to EU, all the MRI examination were done after more than 24 hours from admission.

CT scan was performed for all patients; the results were abnormal in 20 patients and normal in only one patient in whom the MRI revealed abnormal findings. Among those with abnormal CT scan; MRI was performed for 13patients and was abnormal in all and was not done in 8 patients.

Table 3: Time table for performing neuroimaging.

CT examination	HS		IS		Total	
	No.	%	No.	%	No.	%
CT brain done; Within 24 hours of onset of illness More than 24 hours	 4 9	 30.8 69.2	 1 7	 12.5 87.5	 5 16	 23.8 76.2
CT brain done; Within 24 hours of admission More than 24 hours Time Not recorded	 7 6 0	 53.8 46.2 0.0	 1 5 2	 12.5 62.5 25.0	 8 11 2	 38.1 52.4 9.5
MRI brain done; Within 24 hours of admission to ER More than 24 hours Not done	 0 4 9	 0.0 30.8 69.2	 0 4 4	 0.0 50.0 50.0	 0 8 13	 0.0 38.1 61.9

Regarding other investigations, PT/PTT was performed for all patients with hemorrhagic stroke and half of those with ischemic stroke, factor assay for (5 patients (38.5%)) of patients with hemorrhagic stroke, complete blood count was performed for nearly all patients (12 patients (92.3%)) with hemorrhagic stroke and two thirds (5 patients (62.5%)) of those with ischemic stroke, biochemical profile was performed in (11 patients (84.6%)) of patients with hemorrhagic stroke compared to only half of those with ischemic one, septic screen was performed for nearly two third (5 patients (62.5%)) of patients with ischemic stroke and lumber puncture with cultures was performed for half the patients with ischemic stroke.

Regarding treatment modalities; Antibiotics were given parentrally to all patients with hemorrhagic stroke, antiepileptic for (12 patients (92.3%)), Vitamin K was given for 10 (76.9%) patients, plasma for 9 (69.2%) patients , factor 7 was given for only one patient and steroids was given for 5 (38.5%) patients with hemorrhagic stroke. As for the 8 patients with ischemic stroke; only three patients (37.5%) were given anticoagulants and aspirin, antiepileptic drugs were given to 6 patients (75%), antibiotics were given to 5 patients (62.5%), steroids to 4 patients (50%) and vitamin K and plasma was given to only one patient.

Coagulation disorders were confirmed in 3 patients (23.1%) with hemorrhagic stroke (2 patients with coagulation factor 7 deficiency (15.4%) and one patient with coagulation factor 5 deficiency (7.7%)), one patient (7.7%) with hereditary vitamin K deficiency, two patients (15.4%) with sepsis ±DIC, and in more than half of those with hemorrhagic stroke (7 patients (53.8%)) the etiology remained unknown. Whereas central nervous system infections was the commonest etiology among children with ischemic stroke (3 patients (37.5%)), Moyamoya was evident in one patient, nephritic syndrome in another patient, Cyanotic congenital heart disease was evident in one patient with ischemic stroke and in two patients (25%) the etiology was unknown as shown in Table (4).

Table 4: Etiology of stroke.

Most probable or confirmed etiologies	HS		IS		Total	
	No.	%	No.	%	No.	%
Nephrotic Syndrome	0	0.0	1	12.5	1	4.8
Coagulation factor 7 deficiency	2	15.4	0	0.0	2	9.5
Coagulation factor 5 deficiency	1	7.7	0	0.0	1	4.8
Sepsis (±DIC)	2	15.4	0	0.0	2	9.5
Cyanotic congenital heart disease	0	0.0	1	12.5	1	4.8
Hereditary vitamin K deficiency	1	7.7	0	0.0	1	4.8
Moyamoya	0	0.0	1	12.5	1	4.8
CNS infection	0	0.0	3	37.5	3	14.3
Unknown	7	53.8	2	25.0	9	42.8

DISCUSSION:

The current study revealed that stroke, especially ischemic type, were more among females which is contrary to the great majority of the previous studies, [1,7,8,9,10,11,12],including a previous study [4]that was performed in the same department in CWTH, in which male predominated. In many studies, stroke due to trauma were involved which may explain the predominance of male [7,8,9,10,11,12,13], yet Californian study of stroke in children, found a predominance of boys that remained when trauma were excluded[13].Whereas female predominance were noticed in studies done in Brazil [14], Turkey [15] and India[16].

Hemorrhagic stroke was higher than ischemic in the current study which is consistent with the study that has been performed in Northeastern Thai [17]whereas the majority of studies [4,5,7, 12,18] have found predominance of Ischemic type.

More than 2/3 of the cases were younger than 12 months. Similar result was obtained from a previous study in CWTH [4] where about 55% of total cases occurred among children during their first year of life.

In the current study, children with stroke, presented at earlier age groups which was similar to the previous study [4] where the median age was found to be 3 months (hemorrhagic) and 21 months (ischemic) and also to studies in Saudi Arabia [5]and in Brazil [14].Other researches [6,7,11,12]showed mean and /or median ages of presentation larger than the current study. This

may be attributed to the fact that many of the previous studies involved wider range of ages [up to 19 years] , or may be explained by the fact that as time goes on, this pathology is being diagnosed earlier.

All cases with recurrent attacks in the current study had 1st subsequent recurrence within first 6 months after initial stroke. This reflects the need for further studies with larger number of incident strokes to be followed for studying the association of recurrence and type of stroke regarding both the etiologies and pathophysiologies.

In the current study, it was found that more than 3/4 of patients reached the EU beyond 6 hours. Similar findings were found in a study done in Melbourne during 2011[7] where about 2/3 of children presented to the EU beyond 6 hours, but the larger percentage was among those with ischemic stroke. This delay in reaching the EU may be attributed to many factors like underestimation of the illness by the parents or the health care provider or partially due to the time needed to transfer the child to the tertiary care hospital especially those patients not from Baghdad city.

Pediatric AIS is similar to those in young adults in severity and long-term outcomes. After arterial ischemic stroke (AIS) an early diagnosis helps preserve treatment options that are no longer available later. Paediatric AIS is difficult to diagnose and often the time to diagnosis exceeds the time window of 6 hours defined for thrombolytic therapy in adults [11].

The mean length of hospitalization was found to be 14.55 ± 8.3 days and those patients with IS tend to spend longer time in hospital [inpatient] than those with haemorrhagic stroke. Regarding IS, this duration was found to be longer than what was found in a study done by Nazli Janjua and colleagues [19]during 2007, in USA who found mean duration of hospitalization (15.3±12.4 days) for those who have received thrombolysis agent and half the time in cases haven't received thrombolysis on one hand, on the other hand hospital stay in the current study was shorter than what was found in Netherland study [20]about the length of hospital stay in adult stroke, where average length of stay was 28 days. The reason beyond longer hospital stay in those with IS could be the time needed to complete diagnostic investigations and also to provide the medical treatment used to prevent further stroke attack. Our results are much higher than that found in a statistical brief done in 2005 in USA, which found average stay to be 5 days with the admission for haemorrhagic stroke to be longest and most costly (averaging 8.4 days) while the average stay of ischemic stroke was about 5.6 days [21].

In about 3/4 of the patients the diagnosis was confirmed after 24hours of onset of illness, in those who did CT-brain within 24 hours (5 patients), usually the neuroimaging was performed within 10-15 hours in 3 patients and 5hours in 2patients, one of them reached the EU after 7 hours the other after 18hours. So all patients had time to diagnosis exceeded the time window of 6 hours needed for thrombolytic therapy and in the rest wasn't short enough to allow prompt diagnosis and helps therapeutic options and improve outcome for both types.

All patients have done CT before MRI, CT showed the abnormalities in 20 patients and was normal in one patient. CT identified all cases of hemorrhagic stroke and only 7 cases (87%) of ischemic stroke, which was higher than what was found in previous studies done in Melbourne [7] Switzerland [11] & Canada [22]and they suggested that urgent MRI is the best imaging modality for detection of IS but unfortunately the need for sedation or GA in children younger than 5 years for performing MRI is a major time-limiting step.

The etiology of stroke was not identified in 53% of HS and 25% of IS. The latter results were comparable to that found in other studies [7,6,12].

Antibiotic were the medication most often used and this was followed by antiepileptic drugs (AED) as seizure was very frequent feature in our patients. Plasma and vitamin K were used frequently in those with hemorrhagic stroke; again this is a policy in CWTH to use them if neuroimaging show evidence of hemorrhagic stroke with or without other evidences of bleeding tendency. Anticoagulants and Aspirin were used for some of the patients. These variable treatment modalities reflect the fact that recommendation on acute intervention and secondary prevention are only at an expert consensus level and not based on guidelines.

On leaving the hospital the current study found that the majority of the children involved were discharged well yet complete recovery were found only in cases with haemorrhagic stroke while children with ischemic stroke tend to recover with sequelae. Similar finding was found in a study done on Northeastern Thai children which found that 1/3 of them had complete recovery with more cases of haemorrhagic stroke tend to recover completely and more case of ischemic stroke tend to recover partially [17].

Knowing the outcome is very important to improve the management pathway.

Being the largest tertiary center for pediatrics problem in Iraq; mostly complicated cases usually referred to CWTH, this will limit the results of the current study as many simple cases may not be referred for further analysis.

CONCLUSION:

Stroke was more common among female and children younger than 12 months. A delay in performing neuroimaging was obvious in the current study. Seizure and altered mental status were the commonest presentations. Patients with ischemic stroke tend to spend longer time in hospital. Antibiotic were the medication most often used. The majority of children were discharged well.

Recommendations

A delay in performing neuroimaging was obvious in the current study. It is important to increase awareness of childhood stroke among both health professionals and parents to ensure timely diagnosis and treatment.

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