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RESEARCH ARTICLE

ACUTE STROKE IN CHILDREN: AN OVERVIEW.

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Key words:-
stroke, childhood, etiology, clinical features, neuro-imaging.

Abstract

Objective: The aim of this study was to delineate the different characteristics of stroke in children and their outcome.
Method: Clinically diagnosed stroke in children patients underwent general, full neurological examination and radiological investigation with evaluation of severity by pediatric National institute of health scale of stroke (NIHSS) and outcome disability by using Modified Rankin Scale for children (mRS).
Results: The study was conducted on 60 patients with mean age ± standard deviation was (5.98 ± 5.65), median age 3.5 (1-18), 32 (53.3%) of them were male and 28 (46.7%) were female. Most of patients (83.3%) arrived to hospital after 12 hours from the stroke onset. Etiologically, 12 (20%) patients had congenital heart disease, 8 (13.3%) had hemorrhagic diseases, while 23 (38.3%) were cryptogenic. Ischemic stroke represent 83.3% of all patients. MRI brain imaging had better evaluation in patients with hemorrhagic stroke (2 of 6 patients (33.3%) revealed underlying pathology) rather than ischemic ones (only 2 of 44 ischemic stroke patients (4.5%) showed hemorrhagic transformation in one case and vascular anomaly in the other). Twenty (33.3%) patients had mild severity using pediatric NIHSS on admission, 35 (58.3%) were mild to moderate, 3 (5.0%) were sever and 2 (3.3%) were very sever. mRS for children after three months revealed 3 patients (5.0%) with complete recovery, 14 (23.3%) had no significant disabilities despite symptoms in clinical examination, 18 (30.0%) had slight disability, 10 (16.7%) with moderate disability, 2 (3.3%) had moderately severe disability while 13 (21.7%) patients died. There was significant weak positive correlation between severity of stroke at the onset and disability outcome three months later.
Conclusion: Etiological factors in childhood are quite different from those present in adulthood. Despite a careful investigation, some causes of stroke in children remain unidentified. MRI brain imaging is modality of choice in patients with hemorrhagic stroke.

Introduction:-

The word stroke is used to refer to a rapidly developing focal or global neurological deficit lasting more than 24 hours if it has a vascular basis. The term “children” is between one month and 18 years of age (1), (2). In adults,

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aetiology and outcome of stroke is well known, but it is quite few information about children especially in Egypt. The studies of stroke in children are few with variable results and under estimation of hemorrhagic stroke (3). The aim of this study was to delineate the different characteristics of stroke in children and their outcome.

Material and Methods:-

An informed consent was taken from at least one of each child parents. This study was conducted on sixty clinically diagnosed strokes in children patients obtained from Mansoura University Hospitals and other governmental hospitals in Mansoura from July 2011 till April 2016. With the following *Inclusion criteria*: stroke in children between one and 18 years of age, both hemorrhagic and ischemic strokes in children and both parenchymatous and non parenchymatous stroke in children. *Exclusion criteria:* includes stroke in the first year of life, in hospital stroke in children and hemorrhagic brain tumors in children. All patients were subjected to the following: Detailed history, including previous medical diseases and hospital delay duration in hours (<6 hours, 6-12 hours, 12-24 hours, 24-48 hours and >48 hours) according to Charlotte Martin et al. (4). General examination: with the following clinical items that should be considered in the diagnosis of stroke in children: Body mass index, measurement of head circumference, the skin should be examined for rash, signs of trauma, splinter haemorrhage or embolic skin rash and detailed cardiovascular examination including blood pressure. Neurological examination: Pediatric (NIHSS) at three points (on admission, on discharge and three months later) (5), funduscopic examination for papilloedema or hemorrhage and (mRS) for children at three points (on admission, on discharge and three months later) (6). Laboratory investigations and radiological examination: Chest x-ray, electrocardiogram, echocardiogram, brain computed tomography, brain magnetic resonance imaging. The study was approved by the institutional board review of Mansoura University, faculty of medicine.

Statistical Analysis Of The Data:-

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. Qualitative data were described using number and percent. Quantitative data were described using (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level. The used tests were Monte Carlo correction for categorical variables, to compare between different groups Correction for chi-square when more than 20% of the cells have expected count less than 5.

Results:-

The study was conducted between 2011 and 2016 on 60 patients with (mean age ± standard deviation) (5.98 ± 5.65), median age 3.5 (1-18), 32 (53.3%) of them were male and 28 (46.7%) were female (Table.1). As regard distribution of studied patients according to their presenting complaints, lateralization was the most common presentation (in 44 (73.3%) patients), disturbed conscious level was found in 24 (40%) patients, convulsions in 21 (35%) patients, headache and/or vomiting in only 10 (16.7%) patients (Table.1). According to the hospital delay duration of studied patients, most of patients (56.7%) arrived to hospital within 12-48 hours, 16 (26.7%) patients were arrived after 48 hours while only 10 (16.7%) patients were arrived before 12 hours (Table.2). Twenty (33.3%) patients were mild severity using pediatric NIHSS on admission, 35 (58.3%) were mild to moderate, 3 (5.0%) were sever and 2 (3.3%) were very sever (Table.3). Cardiac evaluation of our cases revealed 12 (20%) patients with cardioembolic stroke (Table.4). Three cases had transposition of great arteries one of them associated also with patent ductus arteriosus (PDA) and atrial septal defect (ASD). Ventricular septal defect (VSD) proved in 2 patients. Infective endocarditis with VSD was seen in 2 cases. There was one case for each of the following: PDA, restrictive cardiomyopathy, mitral prolapse with mitral regurge, atrial myxoma with left atrial septal thrombosis and complex congenital heart disease (secondary to Down syndrome). Forty four (73.3%) patients were discovered ischemic stroke in CT brain imaging, however by MRI brain imaging, only 2 of them showed hemorrhagic transformation in one case and arteriovenous malformations (AVM) in the other, while 10 (6.7%) patients showed intracerebral hemorrhage (ICH) by CT brain imaging, 4 (6.7%) of them died before doing MRI brain imaging and 2 of the remaining 6 patients (33.3%) showed underlying pathology by MRI brain imaging (AVM and venous angioma) (Table.4).

The rest of the patients in our study were cryptogenic (38.3%), with 2 cases had AVM, 2 had moyamoya disease and one had venous angioma (Table.5).

Most of our cases (58.3%) showed no to mild disability after three months using mRS for children; three patients (5.0%) were completely recovered, 14 (23.3%) had no significant disabilities despite symptoms in clinical examination and 18 (30.0%) had slight disability. Moderate to severe disability was proved in (20%) of our patients;

10 (16.7%) patients showed moderate disability and 2 (3.3%) had moderate sever disability. The rest of patients (21.7%) died (mRS score 6) (Table.3). There was significant weak positive correlation between severity of stroke at the onset and disability outcome three months later (Table.3).

Table.1:- Age, gender and complaint

Age: Mean ± Standard deviation	5.98 ± 5.65
Gender: Number %	
• Male	32 (53.3%)
• Female	28 (46.7%)
Complaint: Number %	
• Lateralization	44 (73.3%)
• Disturbed conscious level	24 (40.0%)
• Headache/Vomiting	10 (16.7%)
• Convulsions	21 (35.0%)

Table.2:- Distribution of studied patients according to their hospital delay duration

	Studied patients n=60	
Hospital delay (hours)	N	%
<6	5	8.3%
6-12	5	8.3%
12-24	17	28.3%
24-48	17	28.3%
>48	16	26.7%

Table.3:- Distribution of studied patients according to NIH stroke scale on admission, on discharge and after 3 months

NIH	Studied patients n=60	
• On admission	N	%
Mild	20	33.3%
Mild to moderate	35	58.3%
Severe	3	5.0%
Very severe	2	3.3%
mRS	Studied patients n=60	
• After 3 months		
0	3	5.0%
1	14	23.3%
2	18	30.0%
3	10	16.7%
4	2	3.3%
5	0	0 %
6	13	21.7%
		mRS 3 months
NIHSS on admission	r	0.431
	p	0.001*

Table.4:- Distribution of studied patients according to the radiological investigations

Radiology	Studied patients n=60	
	N	%
ECHO		
• Negative	48	80.0%
• Positive	12	20.0%%
CT		
• Ischemic	44	73.3%
• Hemorrhagic	10	16.7%
• Hemorrhagic infarction	6	10%
MRI		
• Died (hemorrhagic stroke)	4	6.7%
• Ischemic	42	70%
• Hemorrhagic	4	6.7%
• Hemorrhagic infarction	7	11.7%
• Space occupying lesions	3	5.0%

Table.5:- Distribution of studied patients according to their etiology

Etiology	Studied patients n=60	
	N	%
1. Cryptogenic	23	38.3%
2. Vasculitis	4	6.7%
3. Congenital Heart Disease, Rheumatic Heart Disease	12	20.0%
4. Mitochondrial cytopathy*	2	3.3%
5. Hemorrhagic diseases	8	13.3%
6. Sinus thrombosis	4	6.7%
7. Diabetes Mellitus	2	3.3%
8. Vascular anomaly	5	8.3%

*****One case proved by biopsy and other proved by high lactate level with stroke, myopathy and diabetes Mellitus

Discussion:-

Estimates of the incidence of stroke in the general population of children vary widely, ranging from 2.5 to 13 cases per 100,000 children per year (7). It frequently has the sequelae of cognitive and motor impairment, as well as epilepsy (8), (9). In adults the frequency of cerebral stroke is more in males than females and this has been attributed to neuroprotective effects of estrogen in females (10). Our study revealed that the frequency of stroke in children is also more common in males than females (53.3% versus 46.7%). The same trend has been clarified in other worldwide childhood stroke studies (10), inspite of absence of estrogen predominance before puberty (11). Severity of stroke in most of our children (91.7%) measured by pediatric NIHSS was mild and mild to moderate with lateralization as the most common presenting complaint in (73.3%) of patients. In a study by Del Balzo about stroke in children: inherited and acquired factors and age-related variations in the presentation of 48 pediatric patients, lateralization was the most common presenting stroke manifestation (12). Signs of lateralization were early picked only by neurologist and this might explain the hospital delay of stroke in children as showed by Zacharias et al., (13). On the other hand disturbed conscious level proved in 24 (40%) patients and convulsions in 21 (35%) patients. These were agreed with Brian Chung et al., (14). Coma and convulsions were the higher warning signs for stroke in children diagnosis and helps to early hospitalization and rapid management (15). Hospital delay duration in our study was mostly (83.3%) after 12 hours. However in multiple researches most of patients about (35%) arrived early before 6 hours of the disease onset (16), (17). The reasons for delay of our studied cases were diverse but typically included underestimation of the disease severity by the parents or healthcare providers of first or second referral, especially less than 40% of our patients presented with the higher warning signs; coma and/or convulsions. These reasons were matched with results from similar societies in India and Taiwan (18), (19), which raise the attention to increase the public awareness of early stroke symptoms and signs. Heart disease and stroke statistics-2016 update

revealed that there is no major difference between ischemic strokes percentage in adults compared to children (about 85% of all strokes) (20). In our study, most of patients had ischemic insults (83.3%). MRI brain imaging is superior than CT brain imaging in diagnosis of hemorrhagic stroke secondary to vascular malformations (21). The use of MRI brain in our hemorrhagic stroke patients showed that 2 of 6 patients (33.3%) revealed underlying pathology while only 2 of 44 ischemic stroke patients (4.5%) showed hemorrhagic transformation in one case and vascular anomaly in the other. This highlights the importance of MRI brain in patients with hemorrhagic stroke. In adults, ischemic stroke is often associated with the atherosclerosis while major etiology in hemorrhagic stroke is hypertension (22), (23), but in childhood, ischemic stroke has various causes, such as blood diseases, sickle cell anemia and heart diseases while hemorrhagic stroke main etiology is coagulopathy (3), (24). Seven different causes of stroke in our series had been found. Cardiac diseases and hemorrhagic blood diseases were common in the studied patients. Congenital heart disease is one of the leading causes of stroke in children, accounting for 15-30% (25). Cardiac evaluation of our cases was not different from them, revealed 12 (20.0%) patients with cardioembolic stroke. Our study also showed 8 (13.3%) cases with hemorrhagic blood diseases. Another recognizable cause of stroke in children worldwide is sickle cell disease (SCD) (26), (27). Our study revealed no proved SCD cases using hemoglobin electrophoresis in anemic patients. This could be explained by genetic and racial differences as it is not frequent in Egypt along the Nile Valley (28), and HbS gene is almost nonexistent except in the Oases where the carrier rate varies from 9 to 22% (29). In pediatric stroke the cause is often unidentified. The clinical presentation is often subtle and early radiological investigation may reveal normal findings (30). While most of our patients were secondary to various causes, 38% were cryptogenic. In a systemic review in stroke in children: Lindsey Barst Gumer et al., the cryptogenic etiology were only 14% with no recognizable risk factors (23). The mismatching of our study could be explained by short follow up time in our research, because some etiologies needs longer period to diagnose like mitochondrial cytopathies and other metabolic inherited disorders (31). Also fund limitation restricted investigations needed to detect other rare causes incriminated in the pathogenesis of stroke in children. Assessment of the stroke survivors after three months in our case study showed significant improvement in severity and disability. This could be explained by the high neuroplasticity and regeneration in children brain cells (32), (33), (34). In conclusion, diagnosis of stroke in children proves challenging, because symptoms are often unspecific in nature which reflected on hospital delay time, etiology is diverse and different from those present in adulthood. MRI brain imaging proved more efficacious in patients with hemorrhagic stroke rather than ischemic ones. Our limitations were the unawareness of the disease and short follow up time. Our study was unfunded to clarify the various and rare genetic causes seen in stroke in children and highlight the need of specialized stroke management teams at pediatric hospitals, with rapid transport, specific neuroimaging protocols, early therapeutic strategies that have improved outcomes.

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