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Pediatric Stroke in the Southern Region of Iran: A Retrospective Prognostic Cohort Study

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Abstract

Objective

Childhood stroke is linked to high personal costs for affected children and their families since more than half of the survivors are impaired for a long time, hampering their normal development and lifestyle. Thus, the present study aimed to evaluate the neurological developmental outcomes of children admitted to Namazi hospital, Shiraz, Iran, for ischemic and hemorrhagic stroke with a five-year follow-up.

Ma a retrospective cohort study on children admitted to Namazi Hospital due to ischemic and hemorrhagic stroke during the past three years (2012-2015). The information was collected by reviewing the medical records and clinically visiting the patients on follow-up. The SPSS 21.0 software was used for statistical analysis.

Materials & Method

This is a retrospective cohort study on children admitted to Namazi hospital due to ischemic and hemorrhagic stroke during past three years (2012-2015). The information was collected by reviewing the medical records and clinically visiting the patients at the time of follow up. The SPSS 21.0 software was used for statistical analysis Settings.

Results

The patients' mean age at the time of stroke was 6.87 ± 4.60 years. The mean follow-up period was 3.5 ± 1.64 years. 53.1% of the children (N=17) were diagnosed with hemorrhagic stroke, and 46.9% (N=15) with ischemic stroke. The most frequent symptoms first presented by the study population were a decrease in the level of consciousness (LOC) (40.6%), headaches (37.5 %), and hand/arm/leg weakness (34.4%), respectively. The number of patients in the poor

and severe outcome group was 73.3% in the ischemic and 52.9% in the hemorrhagic group.

Conclusion

Hemorrhagic stroke was slightly more frequent than ischemic stroke, and stroke was more frequent in boys. A decrease in LOC and headaches were the most common symptoms upon admission. The left sensorimotor area was the most involved in both ischemic and hemorrhagic groups. In addition, trauma was the most common cause of stroke in this study population.

Keywords: Neurological development; Children; Stroke

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Introduction

Stroke, by definition, is the unexpected occlusion or rupture of cerebral arteries or veins leading to focal cerebral damage and clinical neurological deficits (1). Stroke is first categorized based on the simple distinction between ischemic and hemorrhagic stroke. Ischemic varieties are arterial ischemic stroke (AIS) and cerebral sinovenous thrombosis (CSVT). However, a hemorrhagic stroke occurs due to vascular rupture, characterized essentially by their intracranial location (1). A stroke should be considered a medical emergency in any age group; despite its importance, the diagnosis is frequently delayed with doubts regarding optimal management or treatment (2).

Reviewing the stroke epidemiology in pediatrics highlighted that childhood arterial ischemic stroke incidence has been variably reported (3-5). The incidence estimations range from 0.63 to 7.9 per 100,000 (6, 7). On the other hand, although 20% of adult strokes are hemorrhagic, this type accounts for approximately half of all childhood strokes (6, 7). Despite this relative over-representation, data on rates and risk factors for hemorrhagic or ischemic stroke in children are scarce (6, 7).

Many risk factors have been identified for stroke in children, divided into eight main groups suggested by the international pediatric stroke study (IPSS). They include arteriopathy, cardiac disorders, chronic systemic disorders and treatments, prothrombotic states, acute systemic conditions, chronic head and neck disorders, and atherosclerosis risk factors (8).

Pediatric neurological emergencies involve status epilepticus, stroke, acute raised intracranial pressure, traumatic brain injury, central nervous system infections, acute demyelinating disorders, and acute flaccid paralysis (9)—some of these conditions present with different states of consciousness. In contrast, others present with unexpected onset of focal neurological or “brain attack” symptoms, including weakness, speech disorders, sensory or visual disturbances, headache, or ataxia (9, 10). It is advised to suspect stroke in all cases of acute onset of focal neurological deficit (6, 7). A combination of focal neurological signs, hemiparesis or speech disturbance, altered consciousness, headache, and seizures are also

common in children (6, 7). Timely diagnosis of stroke is essential to ensure appropriate acute management (11). Four recent pediatric studies have confirmed significant diagnostic delays in the prehospital setting attributed to lack of community awareness and after arrival at the hospital attributed to lack of recognition of stroke symptoms by attending physicians (9, 11). Diagnostic delays might be due to a lack of consideration of stroke as a diagnosis in children presenting with acute focal neurologic symptoms or headaches (9, 11). Childhood stroke is linked to high personal costs for affected children and their families since more than half of the survivors are impaired for a long time, hampering their normal development and lifestyle (12, 13). Strokes are less common in children than in adults. However, it is a significant cause of lifelong morbidity, leading to physical complications and a profound long-term impact on a child's rational, interactive, and psychosocial functioning and quality of life (12, 13). More studies have been dedicated to pediatric ischemic stroke recently. However, a few studies have investigated hemorrhagic strokes (6, 9, 10). According to recent estimations, few studies have examined (6, 9, 10). Subarachnoid and intracerebral hemorrhage might explain up to 45% of all childhood strokes, but research results on pediatric hemorrhagic stroke are lacking (14, 15). Only one study focused on the outcomes in survivors beyond 1-year post-stroke (16). Gathering more information on the outcomes of pediatric hemorrhagic stroke seems essential. Therefore, The current study aimed to evaluate the neurological developmental outcomes in children admitted to Namazi hospital, Shiraz, Iran, for ischemic and hemorrhagic stroke with a five-year follow-up.

Materials & Methods

This study is a retrospective prognostic cohort study of stroke in children admitted to Namazi hospital due to ischemic and hemorrhagic strokes (including intracranial hemorrhage or subarachnoid hemorrhage) during the past three years (2012-2015). All children aged one month to 18 years referred to the emergency department due to brain attacks from March 2012 to December 2015 were selected. The patients with ischemic and hemorrhagic strokes were enrolled and followed for one to five years after admission (at least one year after admission). The study exclusion criteria were as follows: patients with extradural or subdural hemorrhage or intraventricular hemorrhage, brain tumor, patients diagnosed with cerebral palsy, or patients having had any brain infections. The patients' medical records were reviewed to gather the following data: neuroimaging examinations, current age, age at the time of stroke, sex, underlying etiologies, initial clinical presentation, neurological signs at admission, diagnostic procedures, anatomic location, therapy, and neurological outcome. Different laboratory tests, such as biochemistry, hematology, immunology, genetics, and bacteriology/virology, were performed based on the patient's condition. Brain imaging such as MRI, MRA, and MRV was performed based on the specialist's opinion, and their findings were recorded. All patients were followed for five years after admission and examined for neurological signs or symptoms.

Outcome Study

A total score (maximum, 10) of the Pediatric Stroke Outcome Measure (PSOM) in all five spheres: right sensorimotor, left sensorimotor, language production, language comprehension, and cognitive and behavioral performances were

applied to assess the neurologic outcomes of a stroke. The neurologic outcomes were classified according to the Deficit Severity Score of the PSOM as normal (a score of 0, no impairment in all five spheres), good (a score of 0.5 in one sphere only), poor (a moderate deficit of 0.5 in two, three, or four spheres, a score of 1 in one sphere, 0.5 in one sphere, and 1 in one sphere only), and severe (a score of 0.5 in all five spheres, a score of 1 in one sphere, 0.5 in two spheres, 1 in at least two spheres, or 2 in at least one sphere).

Statistical analysis

The present study used SPSS 21.0 software for statistical analysis. Descriptive data were explained in tables and figures by frequency and Mean ± STD. The chi-square test, student T-test, and repeated measurements were used to examine the relationships between stroke types and other factors. $P < 0.05$ was considered statistically significant.

Results

This research reviewed 108 patients' records and based on inclusion and exclusion criteria, 32 patients were selected (Figure 1). These patients' files were studied. All patients have been visited once for clinical evaluation. Nineteen patients (59.4%) were male, and 40.6% (N=13) were female. The mean age of patients at the time of stroke was 6.87 ± 4.60 years (min = 3 months, max = 16 years). The mean follow-up period was 3.31 ± 1.30 years (min=1, max=5, Median=3), and 18 patients (56.3%) were followed for three or less than three years, while 14 patients (43.8%) were followed for more than three years.

Figure 1. Flow chart of the study population

Among the study population, 53.1% (N=17) were diagnosed with hemorrhagic stroke and 46.9% (N=15) with ischemic stroke. The frequency of the first reported signs and symptoms is shown in Table 1.

The mean length of hospital staywas 9.93 ± 8.16 days (min=1, max=38), and eight patients (25%) had ICU admission during their hospitalization. The mean Glasgow Coma Scale of patients admitted to ICU was 9.87 ± 2.1 (min=8 / max=13). All patients underwent brain CT scans, 34.4% (N=11) underwent MRI, and 18.8% (N=6) underwent MRA to confirm the ischemic or hemorrhagic stroke diagnosis and its etiology. The neuro-imaging findings based on stroke type classification are demonstrated in Table 2.

Lumbar puncture was performed for seven patients (21.8%) that was negative for infections in all samples; however, xanthochromia was seen in three cases (9.4%). The number of patients with abnormal specific laboratory results was found based on reference ranges of ANA, ACLA, C-ANCA, P-ANCA, and Anti-ds-DNA values. Two patients (6.3%) had abnormal C-ANCA, one patient (3.1%) had abnormal P-ANCA, and four patients (12.5%) had abnormal ANA titer.

During the hospital stay, 12 patients (37.5%) received ASA (11 patients with ischemic stroke and one with hemorrhagic stroke). No difference was found between the groups based on ASA consumption (P value < 0.238). Other drugs were not reviewed in this study.

The outcome results, separated by groups based on the PSOM, are recorded and described in Table 2. The differences between ischemic and hemorrhagic stroke outcomes have also been investigated in Table 3.

The neurologic outcomes were categorized according to the Deficit Severity of the PSOM; the results are shown in Table 4.

No difference was between the ischemic and hemorrhagic groups in outcome severity classification described in Table 4 (P value = 0.538). During the follow-up, 25 patients (78.1%) were under the supervision of a pediatric neurologist, and 53.1 % (N=17) were on specific neurological drugs. The etiology of hemorrhagic and ischemic stroke in the study population was investigated, and the final diagnosis confirmed by specialists was reported (Table 5).

After hospitalization, programmed rehabilitation, including physiotherapy, was performed for 22 (68.8%) patients, consisting of 13 patients in the ischemic and nine in the hemorrhagic group. Statistical analysis shows a significant difference in outcome scores between patients who underwent rehabilitation and those who did not (P value = 0.019). Most patients who suffered from severe deficits underwent rehabilitation based on outcome measures.

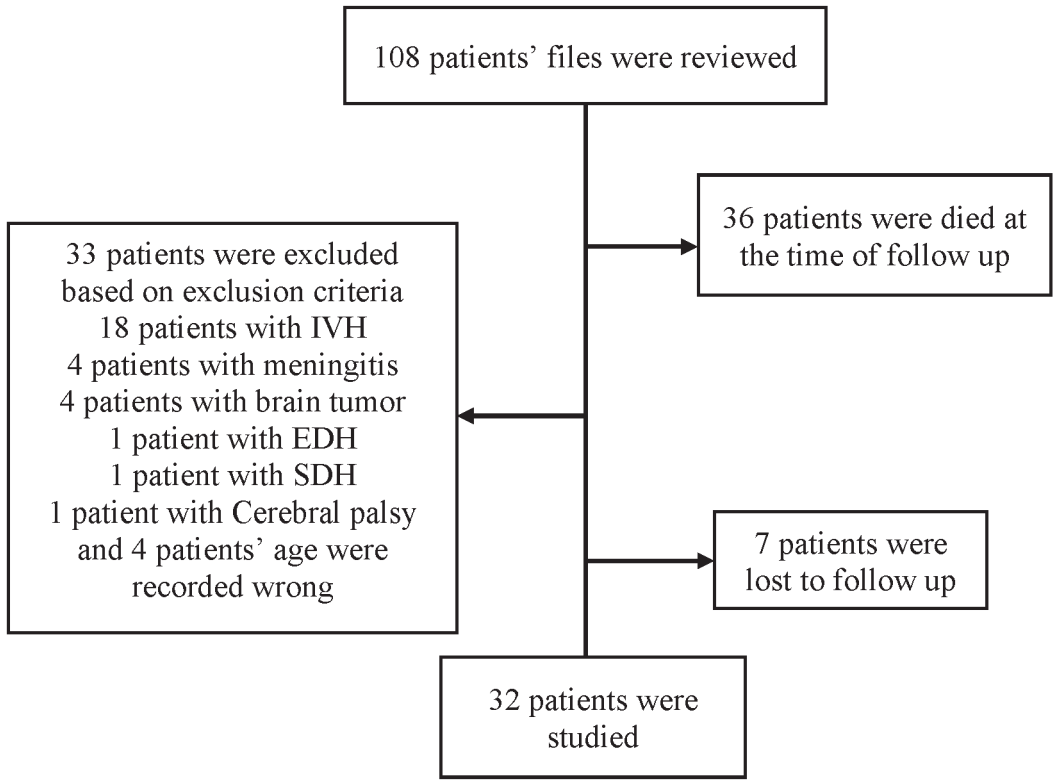

Figure 1. *Flow chart of study population*

Table 1. First recorded sign and symptoms frequency in study population

Title	Frequency % (N)	Title	Frequency % (N)	Title	Frequency % (N)
Headache	37.5% (12)	Vomiting	31.3% (10)	Decrease in LOC*	40.6% (13)
Focal weakness	6.3% (2)	Hand/Arm/Leg weakness	34.4% (11)	Facial weakness	9.4% (3)

Title	Frequency % (N)	Title	Frequency % (N)	Title	Frequency % (N)
Right side weakness	15.6% (5)	Left side weakness	15.6% (5)	Hand/Arm sensory Disturbance	3.1% (1)
Leg sensory Disturbance	3.1% (1)	Left side sensory Disturbance	3.1% (1)	Seizure	15.6%
Visual Disturbance	6.3% (2)	Ataxia	18.8% (6)	Fever	25% (8)
Dysphasia	15.6% (5)	Abnormal eye movement	3.1% (1)	Pupillary Abnormality	15.6% (5)
Behavioral change	3.1% (1)	Vertigo	9.4% (3)	Hemiplegia	12.5% (4)

Table 2. The findings of neuro-imaging in study population

Stroke type	Neuro imaging findings (N/%)	Stroke type	Neuro imaging findings (N/%)
Ischemic	Lacunar INF (1/7.1%)	Hemorrhagic	Ant Temporal Lobe H (5/29.4%)
	MCA INF (6/ 42.9%)		Inf frontal Lobe H (4/23.5%)
	Partial ACA INF (6/42.9%)		Post Temporal Lobe H (3/17.6%)
	CSVT (1/7.1%)		Frontal Lobe H (4/23.5%)
			Occipital Lobe H (1/5.9%)

INF: Infarction, MCA: Middle cerebral artery, ACA: Anterior cerebral artery, CSVT: Cerebral sinus venous thrombosis, Ant: Anterior, H: Hemorrhage, Inf: Inferior.

Table 3. The classified outcome results in ischemic and hemorrhagic group patients

Spheres	Ischemic Stroke	Hemorrhagic Stroke	Total	P
Right Sensorimotor	0.46 ± 0.61	0.50 ± 0.70	0.48 ± 0.65	0.888
Left Sensorimotor	0.56 ± 0.72	0.64 ± 0.84	0.60 ± 0.78	0.776
Language Production	0.40 ± 0.68	0.26 ± 0.56	0.32 ± 0.61	0.545
Language Comprehension	0.30 ± 0.70	0.26 ± 0.56	0.28 ± 0.62	0.876
Cognitive and behavioral performance	0.26 ± 0.70	0.26 ± 0.56	0.26 ± 0.62	0.993

Table 4. The Deficit Severity classification results in study population

Diagnosis	Severity				P value
	Normal	Good	Poor	Severe	
Ischemic	2 (13.3%)	2 (13.3%)	9 (60%)	2 (13.3%)	0.538
Hemorrhagic	5 (29.4%)	3 (17.6%)	6 (35.3%)	3 (17.6%)	
Total	7 (21.9%)	5 (15.6%)	15 (46.9%)	5 (15.6%)	

Table 5. The etiology of hemorrhagic and ischemic stroke in study population

Title	Ischemic group	Hemorrhagic group	Total
Trauma	3 (20%)	7 (41.2%)	10 (31.3%)
Rheumatologic disease	3 (20%)	0	3 (9.4%)
Vasculitis	1 (6.7%)	3 (17.6%)	8 (25%)
Hematologic disease	6 (40%)	2 (11.8%)	3 (9.4%)
Heart disease	1 (6.7%)	2 (11.8%)	3 (9.4%)
AVM	0	3 (17.6%)	3 (9.4%)
Unknown	1 (6.7%)	0	2 (6.3%)

Discussion

This retrospective study focused on the neurocognitive outcomes in children with childhood strokes. As far as we know, few studies have focused on the neurocognitive outcomes of childhood stroke retrospectively (6, 7, 10, 11). however, long-term follow-up was first used in our study. The present study found that both ischemic and hemorrhagic strokes mainly occurred in school-aged children, and the most frequent symptoms first presented by the study population were a decrease in the level of consciousness (40.6%), headaches (37.5 %), and hand/arm/leg weakness (34.4%), respectively.

In this study, the most affected areas in the ischemic group were MCA and partial ACA, and the most common findings in the hemorrhagic group were anterior temporal lobe, frontal lobe, and inferior frontal lobe hemorrhage in the hemorrhagic group, retrospectively.

Both ischemic and hemorrhagic strokes impact the cortical and subcortical areas in which the sensorimotor systems are located (17, 18). Several studies have reported the prevalence of motor impairment and hemiparesis in 30-60% of children with stroke (17, 18).

The obtained results demonstrated a similar poor sensorimotor outcome in both strokes; the left sensorimotor impairment was insignificantly more frequent in hemorrhagic strokes. 36.6% of patients with ischemic stroke represented a moderate motor deficit, and 10% represented a severe motor deficit. On the other hand, 26.4% of patients in the hemorrhagic group had a moderate motor deficit, and 14.7% had a severe motor deficit.

In addition, kolk et al. (19) study reported that neuromotor impairment was evident in 62% of children with neonatal strokes and 70% of children with childhood strokes. Compared to control subjects, children with strokes had worse attention, language, memory, and sensorimotor functions (19).

In the current study, the sensorimotor system was the main impaired neurocognitive area in ischemic and hemorrhagic strokes. Manual motor sequences were the primary impaired neurocognitive skills due to problems with speed processing. Consistent with this study, Pavlovic et al.'s study reported that poor performance skills were observed in children with neonatal and childhood stroke (20). Based on their results, the sensorimotor system impairments were more frequent in the ischemic group, but motor deficits were more severe in the hemorrhagic group.

Regarding the language production skill, more patients in the ischemic group had moderate to severe disorders (26.6% moderate, 13.3% severe), while in the hemorrhagic group, 17.6% of patients had moderate, and 5.8% had severe language production impairments. On the other hand, moderate to severe language comprehension was more frequent in the hemorrhagic group (23.4%).

Studying the cognitive and behavioral performances revealed that cognitive impairment was more frequent in the hemorrhagic group than in the ischemic group (23.5 % Vs. 13.3%). The results showed that the severity of language and cognition impairment was not attributed to sensorimotor impairment. Consistent with the current study's findings, Westmacott et al. found that motor impairment severity was not linearly connected to cognitive impairment (21). However, Chevignard et al. (22) studied the language, cognitive, and school outcomes following childhood stroke. They reported that only 34% of the children followed the normal curriculum with no adaptations or postponement, and 28% took part in special education programs after a median follow-up of 9 months. They concluded that childhood strokes cause severe language and cognitive impairments, negatively impacting academic achievements (22). However, Yvon et al. (23) study reported that after a median follow-up of 43 months, 40% received special education. Requiring special education was predicted by persistent motor deficits, but IQ was the only substantial predictor of special education requirement when full-scale IQ was considered. (23).

In this study, mixed ischemic and hemorrhagic stroke was not found in any patient; however, there were several mixed-type strokes in the study population, excluded due to mentioned type of hemorrhagic stroke in the study method (IVH, SAH, SDH, and EDH). On the other hand, in the ischemic group, 14 patients (93.3%) had an arterial stroke, and only one had CSVT.

Finally, the Deficit Severity classification results showed that the overall outcome was more frequent and more severe in the ischemic group; the number of patients in the poor and severe outcome group was 73.3% in the ischemic and 52.9% in the hemorrhagic group. However, the difference between groups was not statistically significant.

As expected, patients with severe disabilities needed longer and more intense rehabilitation. Therefore, the outcome was more severe in patients who underwent rehabilitation in the study population. However, due to the limited sample size in our study, this research could not define the role of rehabilitation in children's stroke outcomes.

This study has some limitations: Reviewing the etiology of the strokes based on the patients' files was challenging because the neuroimaging reports were explicitly mentioned in the patients' files, and the parents were aware of the final diagnosis. Hence, the researchers classified stroke etiology based on clinical and para-clinical reports in patients' files. However, several patients' specified etiology was definitely mentioned in their records. Therefore, the most frequent etiology was trauma (31.3%) and vascular disease (25%) in both the ischemic and hemorrhagic groups.

The small number of patients who remained in the study population based on inclusion and exclusion criteria was another limitation. Nonetheless, the study involved most of the available children with stroke as a sample representative.

In Conclusion

hemorrhagic stroke was slightly more frequent than ischemic stroke, and strokes were more common in boys. A decrease in LOC and headaches were the most common symptoms on admission. The left sensorimotor area was the most severely involved in both ischemic and hemorrhagic groups. Moreover, trauma was the most common cause of stroke in the study population.

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Author's Contribution

The first/corresponding author (Hamid Nemati) Designed and conceptualized the study; analyzed the data; drafted and revised the manuscript.

The others (Leila Behrad, Hossein Esmaeil Zadeh, Nima Mahdizadegan, and Mohammad Paktinat) Collected the data and revised the manuscript.

Conflict of interest

The authors declared no conflict of interest.

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