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Original article

Clinical presentation, etiology, and outcome of stroke in children: A hospital-based study

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Abstract

Aim: To describe clinical presentations, etiologies, and outcomes of stroke in Jordanian children.

Patients and methods: We retrospectively reviewed the medical records of children diagnosed with ischemic stroke who presented to our clinic from January 2001 to June 2014. Patients with onset of stroke in the neonatal period were excluded.

Results: Twenty-four children (12 boys and 12 girls, with a male to female ratio of 1:1) were included in this study. The follow-up period ranged from 1 month to 9 years. Age at onset of the first stroke ranged from 1 month to 13 years. The most common initial clinical presentation was hemiparesis (58.3%). A known etiology was identified in 58.3% of patients. The most common etiologies were metabolic disorders, such as mitochondrial encephalopathy lactic acidosis and stroke (MELAS) and homocystinuria (25%), cardiac disorders (17%), and coagulopathy, such as a homozygous mutation in the MTHFR gene and a factor V Leiden mutation (17%). Recurrence of both clinical and silent strokes occurred in 46% of patients, residual motor weakness occurred in 58.3%, and residual epilepsy occurred in 29.2%.

Conclusion: Metabolic disorders, cardiac disorders, and coagulopathy are the causes of strokes in Jordanian children. Our results emphasized the importance of inherited disorders in Jordan.

Keywords: Stroke; Children; Jordan; Neurometabolic diseases; MTHFR gene

1. Introduction

Stroke is defined as any acute neurologic event, including seizures associated with an acute radiological abnormality and evidence of ischemia. However, stroke in children is extremely rare, with an estimated annual incidence of 2–3 cases/100,000 in children aged >5 years and 8–13 cases/100,000 in children aged 5–14 years [1]. Stroke in children differs from that in adults, as approximately half of pediatric cases are ischemic in comparison to 80–85% of adult cases [2]. Furthermore, the etiology of stroke in children differs significantly from that in adults. While the most common causes of stroke in adults are hypertension, diabetes, and atherosclerosis, causes in children include cardiac, hematological, infection, vascular/vasculitic, traumatic, and metabolic disorders [3,4]. However, there are a limited number of reports of pediatric stroke in the literature, and most are from developed countries. Reports are particularly rare from Arabic countries, including Jordan, and because of the high rate of consanguineous marriages, etiologies of stroke in children

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in middle-eastern countries might be unique. Hereditary autosomal recessive disorders, including neurometabolic disorders, are not uncommon in Jordan. In a study on the etiologies of global developmental delay in children, these diseases were the second major identified cause contributing to global developmental delay in children [5]. In another study on consanguinity and genetic disorders in Jordan, first cousin marriages constituted 69% of marriages among families with autosomal recessive conditions; this study concluded that approximately 30% of sporadic undiagnosed cases of mental retardation, congenital anomalies, and dysmorphism in Jordan may have an autosomal recessive etiology, with risks of recurrence in future pregnancies [6].

The aim of the present study was to describe the etiologies, clinical presentations, and outcomes of stroke in children presenting to the Child Neurology Clinic at Jordan University Hospital (Amman, Jordan).

2. Patients and methods

We retrospectively reviewed the records of children (aged one month to 18 years) who were diagnosed with ischemic stroke and who presented to our child neurology clinic over a 13.5 year period (January 2001 to June 2014). The data collected included patient demographics, age at onset of first stroke, number of recurrences, etiologies/risk factors, presenting symptoms/signs, incidence of seizures/epilepsy, and outcomes. Patients with onset of stroke in the perinatal or neonatal period were excluded.

3. Definitions

Known etiologies were defined as etiologies previously reported in the literature as known risk factors for stroke [4].

In our study, *probable etiologies* were defined as the etiologies that most likely caused stroke in patients who were in a heterozygous state. In our study, we defined them as probable because these etiologies were reported in the literature to cause stroke in the homozygous state [4].

Children were diagnosed with stroke based on a clinical picture and the results of brain neuroimaging (brain MRI or CT scan).

The usual investigations for stroke in our clinic included coagulopathy disorders methylenetetrahydrofolate reductase (MTHFR C677T) gene mutations, factor V Leiden mutation, protein S and C levels, and the antithrombin III level, in addition to cardiac evaluation. Investigations for neurometabolic disorders were only performed if there was an indicator in the patient's history, physical examination, or brain neuroimaging that suggested a metabolic disorder. Gene analyses for neurometabolic disorders were not performed in this study.

The study was approved by the institutional review board and the ethical committee of Jordan University Hospital.

4. Results

Of 24 children (12 boys and 12 girls, with a male to female ratio of 1:1), the total follow-up period ranged from 1 month to 9 years (median: 2 years). The age at onset of the first stroke ranged from 1 month to 13 years (median: 5 years). Onset in the first 6 years of life occurred in 16 (67%) patients, between 7 and 10 years in 5 (21%) patients, and after 10 years in 3 (12.5%) patients. The most common initial clinical presentation was hemiparesis in 14 (58.3%) patients. Other presentations included monoparesis of the upper limb (4/24, 17%), monoparesis of the lower limb (2/24, 8.3%), seizures (2/24, 8.3%), headache (1/24, 4.2%), or loss of vision with unilateral decreased facial sensation (1/24, 4.2%).

All patients underwent a cardiac evaluation and coagulopathy profile measurement, including a measurement of the protein C and S and antithrombin III level. Gene analyses for MTHFR and factor V Leiden mutations were performed for 14/24 patients.

Investigations for neurometabolic disorders, including serum lactate and amino acids, urinary organic acids, and the homocystine, level were performed for 13/24 patients.

A known etiology for stroke was identified in 14 (58.3%) patients. The most common known etiologies were metabolic disorders, namely, mitochondrial encephalopathy lactic acidosis and stroke (MELAS) and homocystinuria, which occurred in 6 (25%) patients. The second most common known etiologies were cardiac disorders (4/24, 17%) and coagulopathy disorders (4/24, 17%), namely, a homozygous mutation in the MTHFR gene or a factor V Leiden mutation. One very rare disorder, microcephalic osteodysplastic primordial dwarfism type II (MOPD2)-associated stroke, was identified in one patient. A probable etiology was found in 3 (12.5%) patients: two with a heterozygous MTHFR mutation and one with a combined heterozygous MTHFR and heterozygous factor V Leiden mutation. The etiology was not identified in 7 of the 24 (29.2%) patients. Multiple etiologies were found in one patient (cardiac and coagulopathy). The disease etiologies and outcome are summarized in Table 1. Recurrence of both clinical and silent strokes occurred in 11 (46%) patients. Of these, 6 (25%) were clinical recurrences in patients with an underlying metabolic disorder (MELAS, 3 and homocystinuria, 2) and in one patient with an unknown etiology. Five (21%) were silent multiple strokes revealed by brain magnetic resonance imaging (MRI),