Delay to Diagnosis in Acute Pediatric Arterial Ischemic Stroke

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Background and Purpose—For the clinician, the diagnosis of arterial ischemic stroke (AIS) in children is a challenge. Prompt diagnosis of pediatric AIS within 6 hours enables stroke-specific thrombolytic and neuroprotective strategies.

Methods—We conducted a retrospective study of prospectively enrolled consecutive cohort of children with AIS, admitted to The Hospital for Sick Children, Toronto, from January 1992 to December 2004. The data on clinical presentation, symptom onset, emergency department arrival, neuroimaging and stroke diagnosis were recorded. The putative predictors of delayed diagnosis were selected a priori for analysis.

Results—A total of 209 children with AIS were studied. The median interval from symptom onset to AIS diagnosis was 22.7 hours (interquartile range: 7.1 to 57.7 hours), prehospital delay (symptom onset to hospital arrival) was 1.7 hours (interquartile range: 49 minutes to 8.1 hours), and the in-hospital delay (presentation to diagnosis) was 12.7 hours (interquartile range: 4.5 to 33.5 hours). The initial assessment was completed in 16 minutes and initial neuroimaging in 8.8 hours. The diagnosis of AIS was suspected on initial assessment in 79 (38%) children and the initial neuroimaging diagnosed AIS in 47%. The parent’s help seeking action, nonabrupt onset of symptoms, altered consciousness, milder stroke severity, posterior circulation infarction and lack of initial neuroimaging at a tertiary hospital were predictive delayed AIS diagnosis.

Conclusion—In the diagnosis of AIS, significant prehospital and in-hospital delays exist in children. Several predictors of the delayed AIS diagnosis were identified in the present study. Efforts to target these predictors can reduce diagnostic delays and optimize the management of AIS in children. (Stroke. 2009;40:58-64.)

Key Words: delay ■ organized stroke care ■ pediatric stroke ■ predictors ■ stroke diagnosis

The diagnosis of arterial ischemic stroke (AIS) is based on both clinical suspicion and its differentiation from conditions that mimic stroke presentation. For the clinician, the recognition of AIS in children is a challenge because of several reasons. AIS is infrequent in children. The reported incidence ranges from 0.6 to 7.9 per 100 000 children per year.¹ The presentation is varied and nonspecific encompassing a broad differential diagnosis. In young children, AIS usually presents with seizures, irritability, or altered consciousness. Hemiparesis, although not uncommon, is often difficult to recognize in young children. Ischemic stroke presentation in children may be erroneously attributed to other conditions having similar presentations with which physicians are more familiar. These include migraine with aura, focal seizure, ictal or postictal Todd’s paresis, focal intracranial lesions such as hemorrhage, tumors, or demyelination. Cranial CT scan, the initial neuroimaging test for acute neurological presentations, may miss the early signs of infarction. These factors contribute to delays and inaccuracies in the diagnosis of pediatric AIS.² Pediatric AIS is associated with death in 12%, decreased quality of life in over 50%, and disability in over 60% of AIS survivors.¹³–⁶ Thrombolytic and neuroprotective strategies have improved the outcome from adult AIS.⁷–¹⁰ However, these must be instituted within a narrow therapeutic window (typically within 3 to 6 hours). This necessitates rapid diagnosis. Effective adult therapies can be tested for efficacy in children. However, the very significant delay in childhood stroke diagnosis must be reduced. The recognition of “stroke mimickers” is also paramount.

In adult AIS, delays still exist in presentation, evaluation, diagnosis, and treatment.¹¹ Limited literature is available in children on this topic.¹² We sought to systematically determine the components and predictors of delays associated with childhood AIS diagnosis.

Materials and Methods

Study Design

We conducted a retrospective chart review of a prospectively ascertained consecutive cohort of children with confirmed diagnosis of AIS admitted to The Hospital for Sick Children (HSC), from...
January 1992 to December 2004. The study was approved by the institution’s research ethics board.

**Patient Population**

**Patient Identification**
The study subjects were identified from the Canadian Pediatric Ischemic Stroke Registry, Toronto site. The Canadian Pediatric Ischemic Stroke Registry is a consecutive cohort registry of prospectively enrolled children with ischemic stroke. Case ascertainment is supplemented by medical records searches applying International Classification of Diseases, 9th Revision discharge codes for stroke. The validation of the diagnosis consisted of review of the hospital records, including neuroimaging.

Exclusion criteria were (1) transient ischemic attacks or recurrent AIS; (2) AIS diagnosed on screening neuroimaging (asymptomatic infarction); (3) unclear neuroimaging; (4) unavailable medical chart; eg, medicolegal reasons, missing chart; and (5) missed diagnosis (not confirmed by the review of neuroimaging (CT and/or MRI). Exclusion criteria were (1) transient ischemic attacks or recurrent AIS; (2) AIS diagnosed on screening neuroimaging (asymptomatic infarction); (3) unclear neuroimaging; (4) unavailable medical chart; eg, medicolegal reasons, missing chart; and (5) missed diagnosis (not suspected for 14 or more days before diagnosis).

**Definition of Terms**

**Diagnosis of Arterial Ischemic Stroke**
Diagnostic criteria for AIS were an acute neurological deficit (focal or diffuse) or seizures with CT or MRI evidence of a focal infarct conforming to an established cerebral arterial territory consistent with the patient’s clinical presentation.

**Out-of-Hospital Arterial Ischemic Stroke**
Out-of-hospital AIS is stroke occurring at home or places other than a hospital.

**In-Hospital Arterial Ischemic Stroke**
In-hospital AIS is stroke occurring in a hospital while admitted for other reasons.

**Total Delay in Diagnosis**
Total delay in diagnosis was the time interval from symptom onset to the confirmed AIS diagnosis, which was set at the confirmation of the presence of acute AIS on review of neuroimaging.

**Delay in Initial Assessment**
Delay in initial assessment was the time interval between symptom onset to being seen by the first health professional.

**Delay in Initial Neuroimaging**
Delay in initial neuroimaging was the time interval from symptom onset to the start of the initial neuroimaging.

**Prehospital Delay**
Prehospital delay was the time interval from symptom onset to hospital arrival (first presentation to a hospital with symptoms that may represent AIS and was the earliest documented time in the hospital charts).

**In-Hospital Delay**
In-hospital delay was the time interval from presentation (arrival in a hospital for out-of-hospital AIS and symptom onset for in-hospital AIS) to the confirmed AIS diagnosis.

**Data Collection**
A standardized structured data form was completed from review of the medical charts. Data were collected from the objective documentation in the emergency medical services, emergency department (ED) and clinical documents, admission and progress notes of nurses/physicians, neuroimaging requests and images, and initiation and completion time from the radiology procedure log book. When exact time of symptom onset was unavailable, a time was estimated based on all available information. These data were supplemented with relevant data from the Canadian Pediatric Ischemic Stroke Registry and the Pediatric Stroke Outcome Measure parental questionnaire. The Pediatric Stroke Outcome Measure includes specific questions regarding delay to diagnosis. Stroke severity was assessed using the Pediatric National Institute of Health Stroke Scale (Ped-NIHSS), a pediatric modification of the National Institute of Health Stroke Scale. Background data included age at AIS event, gender, ethnicity, geographic location of event, transport method (ambulance versus caregiver’s vehicle), parent’s help-seeking action (ED versus clinic visit, and referral history. The geographic location was dichotomized by Canada postal codes as central Ontario (where our hospital is located) or other regions.

**Clinical Data**
Clinical presentations were classified as (1) focal neurological (speech, paresis, visual, other deficits); (2) nonfocal neurological symptoms (altered consciousness, headache); and (3) seizures. For focal neurological deficits, mode of onset was classified as previously defined “Abrupt” defined onset with progression to maximum deficit within 30 minutes or fixed deficits on awakening and “nonabrupt” as all others. Neurological examination findings at presentation were documented. Stroke severity was graded by retrospective review of the initial neurological examination from the health records. For children aged 4 months to 18 years, PedNIHSS was applied. Scores ranged from zero (no deficit) to 42 (maximal deficit). For children <4 months, a simple 2-point neurological deficit severity scale, the “Simple Severity Score” was designed and applied. One point each was scored for altered consciousness and motor deficits (focal or generalized). Children with normal examination were scored zero and with both deficits scored 2. Children were classified by stroke etiology as (1) previously healthy with or without intercurrent common childhood illnesses; (2) comorbid disorder not associated with risk for AIS; and (3) comorbid disorder known to be associated with AIS (cardiac disease, prothrombotic states, sickle cell anemia, cranial trauma, surgery, tumor, vasculopathy).

Radiological data included (1) neuroimaging type: CT, MRI, or ultrasound (both initial and first diagnosing AIS); (2) neuroimaging interpretation: confirmed AIS, unclear or suspicious for AIS, abnormal but not AIS, normal or misread normal scan; (3) patient location preceding test (ED, outpatient, inpatient); and (5) infarct characteristics: number, location, and circulation.

Treatment types, including intravenous or intra-arterial thrombolytic, anticoagulant, and antiplatelet therapy, were noted.

**Outcome Data**
The primary outcome was total delay in AIS diagnosis. This was bisected into prehospital delay (applicable to out-of-hospital AIS) and in-hospital delay (applicable to both out-of-hospital and in-hospital AIS). Symptom onset was defined as time when symptoms or signs that suggest AIS were first reported or recognized by the patient or caregiver (including symptoms identified on awakening). If the patient was found or woke with symptoms, a note was made of the time last seen without symptoms, but this was not considered as the time of symptom onset. The completion time of the neuroimaging test that made the diagnosis was taken as the time of diagnosis. Other studied intervals included delay to initial assessment and neuroimaging. Reasons for neuroimaging delay, including sedation requirement and patient instability, were noted.

**Statistical Analysis**
For all time intervals, median, means, range, interquartile range, skewness, and kurtosis were calculated. Median and interquartile ranges are reported because the data distribution was skewed.
Comparisons used Pearson’s χ² for nominal and Wilcoxon rank sum test for continuous variables.

Putative predictors of delay were selected a priori based on clinical relevance. These included age, gender, ethnicity, geographic location at the time of index AIS, parent or caregiver’s help-seeking action (not brought directly to the ED), nonambulance transport, seizures at onset, altered consciousness, less severe symptoms, nonabrupt symptom onset, absence of symptoms on awakening, absence of focal motor signs, lack of known risk factors for AIS, infarct characteristics, and lack of stroke suspicion and initial neuroimaging at the HSC ED. Associations of predictors and outcomes were assessed using phi correlation for categorical and Pearson’s correlation for continuous variables.

Because the distribution of the outcome variables was skewed, logarithmic transformation was performed. One-way analysis of variance for categorical and linear regression for continuous variables was performed. Predictors with significance or trend toward significance on univariate analysis (P<0.2) were retested with multivariate analysis (multiple regression). A probability value <0.05 was considered significant. Analyses were performed using SAS statistical software package (Version 9.1.3; SAS Institute, Cary, NC).

Results
A total of 209 children with acute AIS (132 out-of-hospital and 77 in-hospital) and symptom onset within 14 days were included.

Patient Demographics
The mean age was 6 years with 125 males. Most children (80%) were from central Ontario with 58% from Toronto. In 80% (106 of 132), parents brought children to an ED. One third (35 of 132) were brought directly to the HSC ED. In 26% (34 of 132), parents contacted emergency medical services (30 emergency medical services, 4 private ambulances).

Clinical Data
The exact time of symptom onset was available for 149 (71%) children, estimated in 40 (19%), and missing in 20 (9%) children. Twenty-four percent of children awoke with symptoms (overnight sleep 50%, daytime nap 8%, and sedation such as postanesthesia 42%). Most children (51%) with in-hospital AIS were admitted for cardiac reasons.

The initial presentation was focal neurological deficits in 131 (63%) children with abrupt onset in 89 (67%). Other presentations were seizures in 53 (25%) and nonfocal neurological symptoms in 25 (12%). Fourteen children had transient ischemic attacks before the index AIS. The initial physician suspected AIS in 79 (38%) of children. The median PedNIHSS score in 186 children (10 prospective, 176 retrospective) was 7 with scores 5 in 29% and >15 in 11%. The median Simple Severity Score in 23 infants (<4 months) was 1. Prior risks for AIS were definable in 108 (52%) children with the most common being cardiac disease (Table 1).

In most children (96%), CT scan was the initial neuroimaging study. Of 127 children brought to an ED, 107 (84%) completed initial neuroimaging in the ED. The initial neuroimaging diagnosed AIS in only 110 (53%) and was reported as suspicious for AIS in 17 (8%) children.

### Table 1. Clinical Characteristics of All Study Patients

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>All AIS</th>
<th>Out-of-Hospital AIS</th>
<th>In-Hospital AIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>4.7</td>
<td>5.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Male sex</td>
<td>125 (60%)</td>
<td>79 (60%)</td>
<td>46 (60%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>95 (45%)</td>
<td>67 (51%)</td>
<td>28 (36%)</td>
</tr>
<tr>
<td>Black</td>
<td>20 (10%)</td>
<td>15 (11%)</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>Aboriginal</td>
<td>3 (1.5%)</td>
<td>2 (1%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>South Asian</td>
<td>32 (15%)</td>
<td>21 (16%)</td>
<td>11 (14%)</td>
</tr>
<tr>
<td>Central/South American</td>
<td>2 (1%)</td>
<td>2 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>2 (1%)</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Mixed ethnicity</td>
<td>3 (1.5%)</td>
<td>2 (1%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Not specified</td>
<td>52 (25%)</td>
<td>23 (17%)</td>
<td>29 (38%)</td>
</tr>
<tr>
<td>PedNIHSS score*</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
</tr>
<tr>
<td>Simple severity score*</td>
<td>1.0</td>
<td>1.0</td>
<td>NA</td>
</tr>
<tr>
<td>Transport by ambulance</td>
<td>34 (26%)</td>
<td>34 (26%)</td>
<td>NA</td>
</tr>
<tr>
<td>Mode of onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal motor abrupt</td>
<td>89 (43%)</td>
<td>60 (46%)</td>
<td>29 (38%)</td>
</tr>
<tr>
<td>Focal motor nonabrupt</td>
<td>42 (20%)</td>
<td>39 (30%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Nonfocal motor</td>
<td>25 (12%)</td>
<td>13 (10%)</td>
<td>12 (15%)</td>
</tr>
<tr>
<td>Seizures</td>
<td>53 (25%)</td>
<td>20 (15%)</td>
<td>33 (43%)</td>
</tr>
<tr>
<td>Prior risk for AIS</td>
<td>108 (52%)</td>
<td>46 (39%)</td>
<td>62 (80%)</td>
</tr>
<tr>
<td>Infarct characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single infarct</td>
<td>130 (62%)</td>
<td>94 (71%)</td>
<td>36 (47%)</td>
</tr>
<tr>
<td>Unilateral infarct</td>
<td>166 (79%)</td>
<td>112 (85%)</td>
<td>54 (70%)</td>
</tr>
<tr>
<td>Anterior circulation infarction</td>
<td>144 (69%)</td>
<td>100 (76%)</td>
<td>44 (57%)</td>
</tr>
<tr>
<td>Location of infarct</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical</td>
<td>93 (45%)</td>
<td>38 (29%)</td>
<td>55 (72%)</td>
</tr>
<tr>
<td>Subcortical</td>
<td>61 (29%)</td>
<td>54 (41%)</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>Brainstem</td>
<td>7 (3%)</td>
<td>6 (4%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Cortical/subcortical</td>
<td>48 (23%)</td>
<td>34 (26%)</td>
<td>14 (18%)</td>
</tr>
<tr>
<td>Treatment initiated</td>
<td>132 (63%)</td>
<td>103 (78%)</td>
<td>29 (38%)</td>
</tr>
<tr>
<td>None</td>
<td>62 (30%)</td>
<td>28 (21.3%)</td>
<td>34 (44%)</td>
</tr>
<tr>
<td>Antithrombotic therapy†</td>
<td>96 (46%)</td>
<td>74 (56%)</td>
<td>22 (29%)</td>
</tr>
<tr>
<td>Antiplatelet therapy</td>
<td>36 (17%)</td>
<td>29 (22%)</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>With prior treatment</td>
<td>15 (7%)</td>
<td>14 (11%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

*Median value.
†Including one child who received intra-arterial tissue plasminogen activator.
NA indicates not applicable.

Specific AIS treatment was initiated at diagnosis in 132 (63%) children. Fifteen children were already receiving antithrombotic therapy for other reasons.

Analysis of Delay in Arterial Ischemic Stroke Diagnosis
The median delay in diagnosis for all children was 22.7 hours. Prehospital delay (for out-of-hospital children) was 1.7 hours and in-hospital delay (for all) was 12.7 hours (Table 2; Figure). Only 10% were diagnosed within 3 hours and 20% within 6 hours. In children with out-of-hospital AIS, 61 (58%)
presented within 3 hours and 12 (11%) between 3 and <6 hours. The median interval from symptom onset to initial assessment was 16 minute and to initial neuroimaging was 8.8 hours.

For children seen in the ED, the median time from hospital arrival to contact with the ED physician was 20 minutes (interquartile range, 10 to 40 minutes) at the HSC ED and 11 minutes (interquartile range, 1 to 18 minutes) at other EDs. The median interval from hospital arrival to initial neuroimaging was 3.7 hours (interquartile range, 2.5 to 5.4 hours) at the HSC ED compared with 2.3 hours (interquartile range, 1 to 10 hours) for other EDs (Table 2).

Out-of-hospital AIS had a significantly longer delay in diagnosis (**P**= 0.0007) and time to initial physician assessment (**P**= 0.001) compared with in-hospital AIS. However, in-hospital delay (**P**= 0.95) and time to initial neuroimaging from symptom onset (**P**= 0.88) were not significantly different.

### Analysis of Predictors of Delay in Arterial Ischemic Stroke Diagnosis

#### Prehospital Delay
In univariate analysis, predictors of longer prehospital delay included parent’s help-seeking action (not brought directly to the ED), nonambulance transport, lower PedNIHSS score, presence of focal deficits, absence of seizures, nonabrupt onset, and altered consciousness (Table 3). In multivariate analysis, parent’s help-seeking action (**P**=0.0001), lower PedNIHSS score (**P**=0.039), and nonabrupt onset (**P**=0.046) were predictive. The overall prediction of the model was good (F=9.4; **P**<0.0001; adjusted $R^2$=0.425). Because only one PedNIHSS was missing, analysis with Simple Severity Score was not performed.

#### In-Hospital Delay
In both univariate and multivariate analysis, only less severe PedNIHSS score was predictive of longer in-hospital delay (F=2.85; **P**=0.0082; adjusted $R^2$=0.082). A trend toward significance was noted for posterior circulation and right...
hemispheric infarction. For in-hospital delay, 63 observations were missing, including 41 with insufficient data and 22 with no PedNIHSS in infants <4 months of age. On analysis, both with and without Simple Severity Score, only posterior circulation infarction was predictive.

**Total Diagnostic Delay**

In univariate analysis, the predictors of longer total delay included young age, parent’s help-seeking action, nonambulance transport, less stroke severity, nonabrupt onset, and absence of altered consciousness (Table 3). In multivariate, lower PedNIHSS score ($P=0.0003$), location outside central Ontario ($P=0.05$), and lack of initial neuroimaging at the HSC ($P=0.041$) predicted longer delays ($F=5.00; P<0.0001$; adjusted $R^2=0.328$). Because only one PedNIHSS observation was missing, analysis with Simple Severity Score was not performed.

**Discussion**

The presence of significant morbidity and mortality in children with AIS drives the need for acute thrombolytic and neuroprotective therapies. Consideration of these acute treatments is, however, dependent on prompt and accurate diagnosis. In a large consecutive cohort study, we demonstrate significant delays in childhood AIS diagnosis both before and after arrival to the hospital. We also found predictors of this delay in diagnosis.

The delay to AIS diagnosis we observed (median, 29 hours) is comparable to that reported in another study of 18 children with AIS (median, 20 hours). However, the proportion of children in our study diagnosed within 6 hours was 20% compared with nearly 50% (7 of 18) in the Gabis study. The Gabis study included recurrent strokes, which are likely diagnosed more rapidly than index strokes, possibly explaining this difference. Interestingly, the prehospital delay we observed is similar to that reported in adults. With organized acute stroke care in adults, the prehospital delays range from 30 minutes to 6 hours. Depending on the study, between 6% and 47% of adults with AIS present within 3 hours. However, in our study, a relatively higher proportion of children (68%) reached the hospital within 3 hours. Possible reasons for faster arrival in children include increased supervision and time under observation by parents, a greater sense of urgency in parents to bring a sick child to medical attention, increased presentation with seizures in children with stroke and at our center, periodic local media coverage of childhood stroke, and the HSC Children’s Stroke Program during the study. In contrast to children, adults frequently live alone. The resultant lack of in-home assistance for identification of the acute illness and subsequent transportation to a hospital could result in slower arrival times.

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Prehospital Delay (N=106)</th>
<th>In-Hospital Delay (N=168)</th>
<th>Total Delay (N=116)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F Value</td>
<td>P</td>
<td>F Value</td>
</tr>
<tr>
<td>Age*</td>
<td>0.270</td>
<td>0.976</td>
<td>0.976</td>
</tr>
<tr>
<td>PedNIHSS score*</td>
<td>&lt;0.0001</td>
<td>0.001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Simple severity score*</td>
<td>0.0002</td>
<td>0.302</td>
<td>0.0002</td>
</tr>
<tr>
<td>Outside central ontario</td>
<td>0.13</td>
<td>0.717</td>
<td>NA</td>
</tr>
<tr>
<td>Parent’s help-seeking action†</td>
<td>40.95</td>
<td>&lt;0.0001</td>
<td>NA</td>
</tr>
<tr>
<td>Nonambulance transport</td>
<td>12.17</td>
<td>0.0007</td>
<td>NA</td>
</tr>
<tr>
<td>Absence of symptoms on awakening</td>
<td>0.50</td>
<td>0.480</td>
<td>0.01</td>
</tr>
<tr>
<td>Presence of focal motor deficit</td>
<td>5.94</td>
<td>0.016</td>
<td>0.29</td>
</tr>
<tr>
<td>Absence of seizures</td>
<td>6.18</td>
<td>0.014</td>
<td>0.75</td>
</tr>
<tr>
<td>Nonabrupt onset</td>
<td>17.02</td>
<td>&lt;0.0001</td>
<td>1.95</td>
</tr>
<tr>
<td>Lack of altered consciousness</td>
<td>16.07</td>
<td>0.0001</td>
<td>1.77</td>
</tr>
<tr>
<td>Absence of heart disease</td>
<td>0.43</td>
<td>0.515</td>
<td>0.71</td>
</tr>
<tr>
<td>Stroke not suspected</td>
<td>0.21</td>
<td>0.646</td>
<td>1.18</td>
</tr>
<tr>
<td>Initial neuroimaging at non-HSC ED</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Presence of multiple infarcts</td>
<td>0.03</td>
<td>0.861</td>
<td>7.98</td>
</tr>
<tr>
<td>Laterality of infarct</td>
<td>2.76</td>
<td>0.067</td>
<td>1.79</td>
</tr>
<tr>
<td>Circulation</td>
<td>0.17</td>
<td>0.846</td>
<td>2.91</td>
</tr>
</tbody>
</table>

*Linear regression: Pearson correlation.
†Not brought directly to ED.
NA indicates not applicable.

Table 3. Univariate Analysis of Predictors of Delay in the Diagnosis of Childhood AIS

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Despite early presentation to the hospital, compared with adults and children in the Gabis study, we observed a much longer in-hospital delay (median, 12.9 versus 2.7 hours in adults and 1 hour in the Gabis study).\textsuperscript{11,12} The net result was that only 20\% were diagnosed within 6 hours. Obstacles to timely diagnosis once at a child’s hospital include the lack of experience with stroke in the ED, frequent nonfocal presentations of stroke in children (37\% in our series), a wider differential diagnosis for focal deficits in childhood, and the poor sensitivity of acute CT scanning for the diagnosis of pediatric AIS (only 53\% in our series).

Although children with in-hospital AIS were medically assessed earlier than out-of-hospital AIS, their delay to neuroimaging and diagnosis was not significantly different. This was contrary to our postulation that patients already in a hospital would have faster access to subspecialty consultation and neuroimaging. In-hospital evaluation for inpatient strokes requires an increased awareness and urgency.

The predictors of delayed presentation we observed were expected and closely linked to each other as has been reported in adults.\textsuperscript{24,26,28–30} In adults, these include absence of transport by ambulance, living alone status, and the presence of deficit on awakening.\textsuperscript{20–22,31,32} A lack of ambulance use in our cohort predicted prehospital delay on univariate but not multivariate analysis.

In our study, lower PedNIHSS score and posterior circulation infarction predicted in-hospital delays. Milder neurological deficits, including visual field defects, account for this observation. Right-sided infarction predicted delay on univariate but not multivariate analysis. In adults, increased diagnostic delays are observed with right hemispheric infarction.\textsuperscript{33} This is attributed to the lack of speech abnormalities compared with left hemispheric infarction.\textsuperscript{33} Young children have incomplete hemispheric differentiation reducing the impact of this factor.

Location of a child with AIS further from HSC was significant for total delay; however, it was not significant for prehospital delay. Although children living at distant and remote locations have access to medical care (early presentation), they needed to be transported to a children’s hospital for the full evaluation and urgent care (later diagnosis).

Another predictor of delayed diagnosis was initial neuroimaging at a non-HSC ED. Although the time to initial neuroimaging was decreased in children at a non-HSC ED (2.3 versus 3.7 hours), the proportions of misread CT scans at those centers was increased. The regional non-HSC hospitals were more frequently staffed by adult radiologists. It would be expected that pediatric neuroimaging would be more accurately interpreted by pediatric neuroradiologists available at HSC, a tertiary pediatric hospital.

Our study had several limitations related mainly to the retrospective design. Despite comprehensive Canadian Pediatric Ischemic Stroke Registry database and International Classification of Diseases, 9th Revision discharge code search for case ascertainment, there may still be patients with AIS that were missed. Because MRI was not widely available in the earlier study years, some children with stroke may not have come to diagnosis because they underwent only CT scanning. The data on timing of events were collected retrospectively. Although an exact symptom onset was available for over 70\%, this measure is susceptible to error. In 19\%, the symptom onset could only be estimated. For other time points, notably initial assessment, the time was estimated in 40\%. This may have resulted in either over- or underestimation. The PedNIHSS was scored retrospectively for the majority. Although the PedNIHSS has been validated for retrospective scoring, the validation of the prospectively scored PedNIHSS is pending.

**Summary**

In children with AIS, we have identified significant challenges to timely diagnosis. Some factors causing delayed diagnosis are nonmodifiable, including clinical and radiographic presenting characteristics. However, others are modifiable. Efforts are needed to increase public and physician awareness about childhood stroke. There is a need for institution of specialized stroke care teams at pediatric hospitals, including rapid transport, clinical consultation, and rapid and specific neuroimaging protocols for suspected stroke. These measures will facilitate rapid diagnosis of stroke in children and access to thrombolytic and neuroprotective strategies that have improved outcomes in adults as they become clinically available. However, like in adults, these efforts will require collaborative efforts and prioritization of healthcare funding at institutional, provincial, and national levels.

**Disclosures**

None.

**References**


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