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Pediatric Stroke Among Hong Kong Chinese Subjects

Brian Chung, MRCPCH, and Virginia Wong, FHKAM, FHKC(Paed), FRCPCH, FRCP

ABSTRACT. *Background.* The incidence of pediatric stroke was estimated to be 2.5 to 2.7 cases per 100 000 children per year in North America and 13 cases per 100 000 children per year in France. Stroke is among the top 10 causes of death among children in the United States, with the highest incidence in the first 1 year of life. The annual mortality rate was 0.34 deaths per 100 000 person-years, with an average of 244 deaths per year. Interethnic differences have been demonstrated to be important in pediatric stroke. However, most population-based studies on pediatric stroke were from Europe or North America, and there was a lack of data on the incidence of stroke among Chinese or Asian children. Whether the etiologic patterns and risk factors for death and morbidity among Chinese children with stroke were similar to those described for other ethnic groups was unknown.

Objectives. To calculate the incidence of stroke among Chinese children in Hong Kong and to examine the clinical spectrum, causes, patterns, risk factors, and outcomes of pediatric stroke among Chinese subjects.

Methods. The population of Hong Kong was 6.7 million in 2001, and >98% of our population is Chinese in origin. In Hong Kong, public hospitals under the Hospital Authority provide >95% of the hospital service for the region. We identified children (>1 month to <15 years of age) who were admitted and given a discharge diagnosis of stroke from the Clinical Data Analysis and Reporting System, which is a centralized computerized database for all public hospitals. The discharge coding of stroke used codes from the *International Classification of Diseases, 9th Revision, Clinical Modification*. Only first admissions during the study period were included. We excluded any subsequent admissions by using multiple demographic characteristics of the patients. The incidence of pediatric stroke was estimated as the number of first hospitalizations divided by the person-years at risk.

Since 1991, we had been collecting a database on pediatric stroke (ages of 1 month to 16 years) from a single center (the university-affiliated pediatric unit). The clinical presentation, causes, risk factors, and outcomes for those in the Hong Kong Children's Stroke Registry with follow-up data for ≥ 2 years were analyzed.

Data on outcomes, in terms of survival and neurologic deficits, were studied. For survivors, neurologic deficits were defined as short-term if they resolved within 3 months and long-term if they persisted for >3 months. The severity of deficits was defined as mild when function was minimally affected and the patient remained independent in activities of daily living, moderate when the patient required supervision or partial assistance in activities of daily living or when the deficit caused delay in developmental milestones, and severe when the patient required total or near-total care in activities of daily living. Potential risk factors for death and poor neurologic outcomes, including gender, age at the time of stroke, clinical presentation, causes, and neuroimaging findings, were analyzed.

Results. Using projections from census data in 2001, the number of children <15 years of age in Hong Kong from 1998 to 2001 was estimated to be 1 104 100 to 1 158 800, resulting in 4 545 300 person-years. During the same period, 94 children with discharge coding of stroke were identified. Therefore, the estimated incidence of pediatric stroke between 1998 and 2001 was 2.1 cases per 100 000 children-years. The average number of new cases treated annually was 4.5 (0–15 cases/year). Fifty children (28 boys and 22 girls; male/female ratio: 1.27:1) were identified in the 11-year period. The mean age at presentation was 5.6 ± 4.9 years. Thirty-six strokes (72%) were ischemic and 14 (28%) were hemorrhagic. Despite evaluation for possible underlying causes, 12% (6 cases) remained idiopathic. Eighteen patients with ischemic strokes had cerebral thrombosis, whereas 15 had cerebral embolism. We did not observe any case of sinovenous thrombosis. The 36 cases of ischemic stroke were subtyped according to vascular territories. Eleven cases had infarction involving the middle cerebral artery territory; 2 were limited to the cortical region, 3 were limited to subcortical structures such as the basal ganglia or internal capsule or both, and 6 had complete middle cerebral artery involvement, with cortical and subcortical stroke. Involvement of the anterior cerebral artery occurred in 2 cases, with involvement of cerebellar/basilar artery territories in another 2 cases. The remaining 15 cases had multiple sites of infarction. Three patients experienced secondary hemorrhagic transformation after the initial thrombotic event. Of the 14 patients with hemorrhagic strokes, only 1 had subarachnoid hemorrhage. All others had intracerebral bleeding, at single ($N = 9$) or multiple ($N = 4$) loci. Important causes included complications related to congenital heart diseases ($N = 15$, 30%), vascular diseases ($N = 13$, 26%), and hematologic diseases ($N = 14$, 28%). Six cases had no determined causes. One case involved mitochondrial encephalopathy with lactic acidosis and stroke-like episodes and constituted the only case with a metabolic cause. For the 7 patients for whom prothrombotic screening was performed, findings were negative. Seizures (52%) and hemiplegia (34%) were the most common presenting features. Other presenting clinical features included headaches (22%), decreased con-

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sciousness (30%), visual field defects (12%), dysphasia (10%), and lethargy (8%). Only 1 patient, with moyamoya disease, had a family history of stroke. The median follow-up time was 8.7 years (range: 2–12.4 years). Nine patients (18%) died, 5 with ischemic stroke and 4 with hemorrhagic stroke. Among the 5 cases of death with ischemic stroke, 3 involved hemorrhagic transformation before death. Seven patients (77%) died within 31 days (range: 2–31 days), whereas the other 2 died 6 months and 2.5 years after the episode. Recurrence occurred in 5 cases (10%). Long-term neurologic deficits occurred among 41% of survivors, including mental retardation ($N = 11$), epilepsy ($N = 7$), and hemiplegia ($N = 10$). The functional deficits were classified as severe in 7 cases, moderate in 3 cases, and mild in 7 cases, for patients with long-term neurologic deficits. Decreased levels of consciousness, hematologic causes, and hemorrhagic transformation (applicable only in ischemic stroke) were significant risk factors associated with high mortality rates. For the 41 patients who survived, the only significant risk factor for long-term neurologic deficits was seizures at the initial presentation. Other factors, such as gender, age, other clinical features, stroke type, vascular territory, other causes, and recurrence of stroke, were all insignificant for both death and long-term deficits. The 3 risk factors identified for death were analyzed in multivariate logistic regression analyses, with adjustment for the confounding variables, and only decreased levels of consciousness remained significant (odds ratio = 15.6).

Conclusions. The incidence of stroke among Chinese children was slightly lower than that in Europe or North America. The etiologic pattern was different in our cohort, and there was no sickle cell anemia, thrombophilia, or sinovenous thrombosis. Despite these differences, however, mortality and long-term neurologic deficit rates were similar. *Pediatrics* 2004;114:e206–e212. URL: <http://www.pediatrics.org/cgi/content/full/114/2/e206>; Chinese, children, stroke, incidence, hemorrhage, ischemic.

ABBREVIATIONS. CT, computed tomography; MRI, magnetic resonance imaging.

The incidence of pediatric stroke was estimated to be 2.5 to 2.7 cases per 100 000 children per year in North America^{1,2} and was reported to be as high as 13 cases per 100 000 children per year in France.³ Stroke is among the top 10 causes of death among children in the United States, with the highest incidence in the first 1 year of life.⁴ In a recent study in the United States, the annual mortality rate was 0.34 deaths per 100 000 person-years, yielding an average of 244 deaths per year.⁵ A report from the National Institute of Neurological Disorders and Stroke Workshop on Perinatal and Childhood Stroke noted that up to 10% of affected children died and more than one-half of those who survived experienced long-term neurologic or cognitive sequelae.⁶

Interethnic differences were demonstrated to be important in pediatric stroke. The studies by Fullerton et al.^{5,7} showed that black American children were at greater risk of both hospitalization for stroke treatment and death, compared with white children. However, most population-based studies on pediatric stroke were from Europe or North America,^{1–3} and there was a lack of data on the incidence of stroke among Chinese or Asian children. Whether

the etiologic pattern and risk factors for death and morbidity among Chinese children with stroke were similar to those described for other ethnic groups also was unknown.

This study aimed to study stroke among children in Hong Kong, a developed city in southern China in which >98% of the residents are Chinese in origin. Our objectives were to estimate the annual incidence of stroke among southern Chinese children and to determine the clinical spectrum, causes, outcomes, and prognostic risk factors for these patients.

METHODS

Definitions and Diagnostic Criteria

Stroke was defined as a sudden-onset, focal, neurologic deficit resulting from irreversible, focal, ischemic or hemorrhagic damage to the brain parenchyma secondary to a cerebrovascular disorder.⁸ Ischemic stroke was defined on the basis of the sudden onset of a neurologic deficit, localized to the brain, that lasted ≥ 24 hours, with accompanying computed tomography (CT) or magnetic resonance imaging (MRI) studies or autopsy results showing changes consistent with brain infarction or normal findings.² Intracerebral hemorrhage was defined on the basis of clinical history and examination findings consistent with intracerebral hemorrhage (sudden onset of headache, changes in the level of responsiveness, or focal neurologic deficit), accompanied by a focal collection of blood within the brain parenchyma on CT scans, on MRI scans, or at autopsy.² Subarachnoid hemorrhage was defined on the basis of nontraumatic subarachnoid hemorrhage on CT scans or at autopsy or clinical history and examination findings consistent with subarachnoid hemorrhage (sudden onset of severe headache or changes in responsiveness), with xanthochromia and many red cells in the cerebrospinal fluid.² Sinovenous thrombosis was defined on the basis of clinical history and examination findings consistent with sinovenous thrombosis (seizure, lethargy, or focal neurologic deficit), with evidence of thrombosis in cerebral veins or sinus on CT scans, on MRI scans, or at autopsy.⁹

Neonatal (from birth to 1 month of age) strokes and traumatic strokes were excluded from the study. Because of the information constraints with the census data, the incidence of stroke was calculated for children >1 month and ≤ 15 years of age. Children ≤ 16 years of age were included in this stroke registry, because all children <16 years of age with acute stroke were admitted to the pediatric unit.

Calculation of the Incidence of Pediatric Stroke

The population of Hong Kong was 6.7 million in 2001,¹⁰ and >98% of the population is Chinese in origin. In Hong Kong, public hospitals under the Hospital Authority provide >95% of the hospital service for the region. Since 1997, inpatient data from all public hospitals under the Hospital Authority have been stored in a central computerized database; data from 1998 onward could be retrieved with the Clinical Data Analysis and Reporting System program.

We obtained data (stripped of identifiers) for children who were >1 month and <16 years of age and were given a discharge diagnosis of stroke in any discharge coding, using the following codes from the *International Classification of Diseases, 9th Revision, Clinical Modification*: for hemorrhagic stroke, code 431 (intracerebral hemorrhage) or code 430 (subarachnoid hemorrhage); for ischemic stroke, code 433 (occlusion and stenosis of precerebral arteries), code 434 (occlusion of cerebral arteries), code 436 (acute but ill-defined cerebrovascular disease), or code 437.6 (nonpyogenic thrombosis of an intracranial venous sinus). All data from all public hospitals in Hong Kong during the period from January 1998 to December 2001 were retrieved through the computerized database. Only first admissions during the study period were included; multiple demographic characteristics of patients were used to exclude any subsequent admissions.

The annual stroke rates were estimated as the number of first admissions with a diagnosis of stroke for that year. Person-years were defined as the average size of the population <15 years of age¹⁰ during the study period times the number of years of the study. The incidence of pediatric stroke was estimated as the

number of first hospitalizations divided by the person-years of risk.

Stroke Registry

From 1991 onward, all children (<16 years of age at the time of admission) who presented to the Department of Pediatrics and Adolescent Medicine, Queen Mary Hospital, with first strokes were recruited into our Pediatric Stroke Registry. We excluded neonatal strokes and traumatic hemorrhage, because they exhibited different etiologic patterns. The identities of patients recruited into the registry were cross-checked with the discharge database, to identify cases that might have been missed at admission.

Clinical information collected from these patients included family history of stroke, drug history (including use of recreational drugs), and presence of infection, head injury, or any associated systemic or neurologic diseases. Neuroimaging (either CT or MRI) of the brain was performed for each patient, either at our center or at the referring hospitals. Seven patients also underwent magnetic resonance angiography and 2 underwent digital subtraction angiography. All imaging studies were reviewed by the 2 pediatric radiologists at our hospital, and difficult cases were discussed with the pediatric neurologists and neurosurgeon during the monthly neuroradiology meeting. Patients who did not satisfy the clinical and radiologic diagnostic criteria for stroke were excluded from the study. We did not have any autopsy data, because Chinese parents are reluctant to have autopsies performed for deceased children. The cases of stroke were classified as ischemic or hemorrhagic type according to the diagnostic criteria described above.

There is no standard investigation protocol for pediatric stroke at our center, and our approach is guided by the clinical findings. On the basis of the clinical, radiologic, and laboratory findings, risk factors were classified into the following categories: cardiac, vascular, hematologic, or other, according to the underlying causes. Cases without an identifiable cause were defined as "stroke with no determined cause." Similar classifications of risk factors were used in other studies and reviews of pediatric stroke.^{6,8,11-15}

After discharge, patients were monitored regularly in our neurology clinic, at 3- to 6-month intervals. Closer follow-up schedules or admissions as "day-cases" were implemented for patients with seizures that were difficult to control or patients who required intensive rehabilitation. All patients were evaluated by the senior author (V.W.) during admission and outpatient follow-up monitoring.

Data on outcomes, in terms of survival and neurologic deficits, were studied. For survivors, neurologic deficits were defined as short-term if they resolved within 3 months and long-term if they persisted for >3 months. The severity of deficits was defined as mild when function was minimally affected and the patient remained independent in activities of daily living, moderate when the patient required supervision or partial assistance in activities of daily living or when the deficit caused delays in developmental milestones, and severe when the patient required total or near-total care in activities of daily living. Potential risk factors for death and poor neurologic outcomes, including gender, age at the time of stroke, clinical presentation, cause, and neuroimaging findings, were analyzed.

Summary statistics were presented as mean \pm SD and range. Student's *t* test was used for comparisons of age at onset as a risk factor for poor prognosis among different types of strokes. Fisher's exact test was used for the other categorical data. All significant risk factors identified were reanalyzed with multivariate logistic regression analysis. *P* < .05 was considered statistically significant.

RESULTS

Estimated Incidence of Pediatric Stroke in Hong Kong

Using projections from 2001 census data, the population \leq 15 years of age in Hong Kong was estimated to be 1 104 100 to 1 158 800 from 1998 to 2001.¹⁰ We included 4 545 300 person-years of observation in the period from 1998 to 2001. During the same period, 94 patients were identified from the central computerized hospital database as having

been discharged with the coding listed above. Therefore, the estimated incidence of pediatric stroke between 1998 and 2001 was 2.1 cases per 100 000 children-years.

Pediatric Stroke Registry

Patient Characteristics and Investigations

Fifty patients were identified in the 11-year period from 1991 to 2001. The average number of new cases treated each year was 4.5 (range: 0-15 cases/year). No obvious trend could be identified. There were 28 boys and 22 girls (male/female ratio: 1.27:1). The mean age at the time of presentation was 5.6 ± 4.9 years. Seizures (52%) and hemiplegia (34%) were the most common presenting features. Other presenting clinical features included headaches (22%), decreased consciousness (30%), visual field defects (12%), dysphasia (10%), and lethargy (8%). Only 1 patient, with moyamoya disease, had a family history of stroke.

The investigations were guided by clinical findings; there was no standardized protocol. The investigations performed included 1) neuroimaging (brain CT, brain MRI, magnetic resonance angiography, conventional cerebral angiography, digital subtraction angiography, or transcranial Doppler ultrasonography), 2) cardiac assessment (electrocardiography, 24-hour Holter study, or echocardiography), 3) hematologic tests (complete blood count, hematocrit level, clotting profile, hemoglobinopathy study, erythrocyte sedimentation rate, lupus anticoagulant assay, and coagulation panel, including protein C, protein S, antithrombin III, and factor V Leiden levels and prothrombin G20210A assessment), 4) immunologic tests (anticardiolipin, antinuclear antibody, rheumatoid factor, and complement levels), 5) infection screening (blood culture, cerebrospinal fluid biochemistry assay, microscopy, culture, and polymerase chain reaction assay), 6) toxicology screening, and 7) metabolic screening (blood glucose level, electrolyte levels, liver and renal function tests, blood and cerebrospinal fluid lactate levels, pyruvate level, serum amino acid and homocysteine levels, lipid profile, and lysosomal enzymatic assay).

Echocardiography was performed for 12 patients with ischemic stroke and 3 patients with hemorrhagic stroke. Prothrombotic screening, including assessment of antiphospholipid antibody, protein C, protein S, antithrombin III, and factor V Leiden levels and prothrombin G20210A mutation, was available only in the latter one-half of the study period and was performed for 7 patients (20%) with ischemic stroke.

Stroke Patterns and Causes

Thirty-six strokes (72%) were ischemic and 14 (28%) were hemorrhagic (Fig 1). Despite evaluations of possible underlying causes, 12% of cases remained idiopathic. Twenty-one patients with ischemic strokes had cerebral thrombosis, whereas 15 had cerebral embolism. No case of sinovenous thrombosis was seen in our cohort.

The 36 cases of ischemic stroke were subtyped

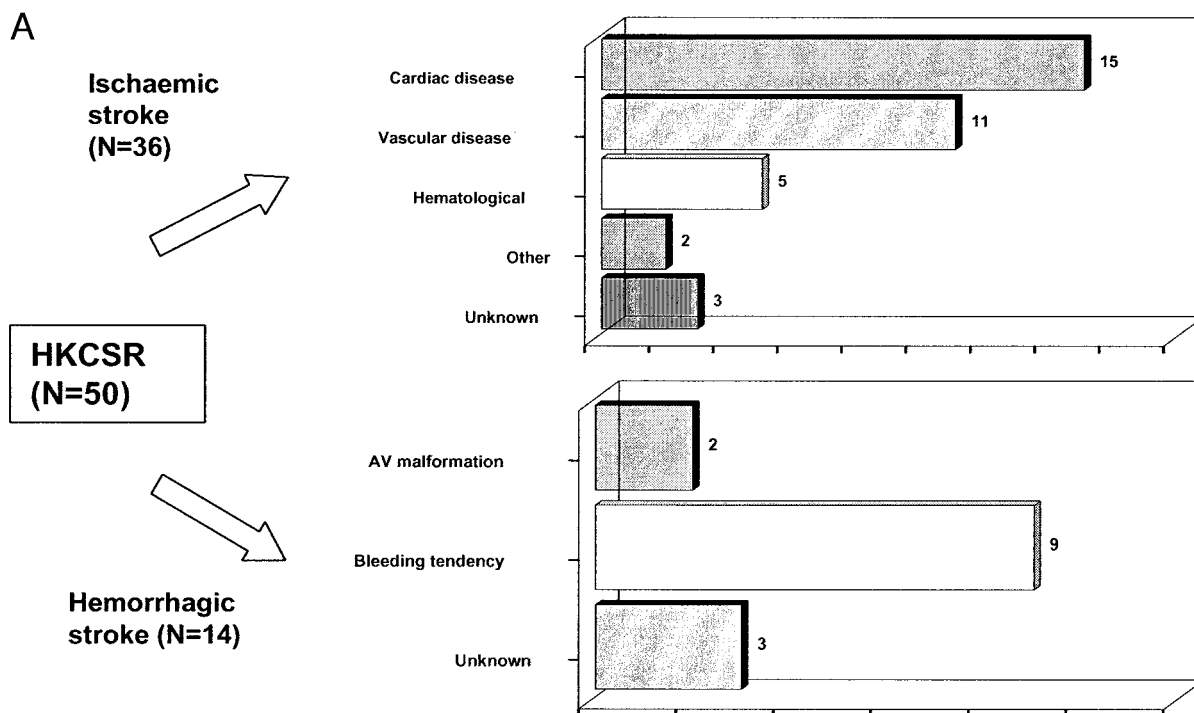


Fig 1. Classification of the Hong Kong Children Stroke Registry according to the type of stroke (A) and the underlying cause (B, next page).

according to vascular territories. Seventeen cases had infarction involving the middle cerebral artery territory, ie, 2 limited to the cortical region, 3 involving subcortical structures such as the basal ganglia, internal capsule, or both, and 6 involving the complete middle cerebral artery, with cortical and subcortical stroke. Neuroimaging from the other 6 patients could not be retrieved, but their radiology reports state that there was evidence of middle cerebral artery infarction. Involvement of the anterior cerebral artery occurred in 2 cases, and involvement of the cerebellar/basilar artery territories occurred in another 2 cases. The remaining 15 cases had multiple sites of infarction. Three patients experienced secondary hemorrhagic transformation after the initial thrombotic event. Of the 14 patients with hemorrhagic strokes, only 1 had subarachnoid hemorrhage. All others experienced intracerebral bleeding at a single site ($N = 9$) or at multiple loci ($N = 4$).

Fifteen patients (30%) had underlying cardiac disorders, whereas 14 (28%) had hematologic disorders predisposing them to either thrombosis (5 patients) or bleeding (9 patients). Thirteen patients (26%) had angiographically established vascular abnormalities, with all cases except 2 cases of arteriovenous malformations involving ischemic strokes. One patient had mitochondrial encephalopathy with lactic acidosis and stroke-like episodes, representing the only case with a metabolic cause. Six cases had no determined causes. For the 7 patients for whom prothrombotic screening was performed, all findings were negative.

Outcomes

The median follow-up time was 8.7 years (range: 2.0–12.4 years). Nine patients (18%) died, including 5

with ischemic strokes and 4 with hemorrhagic strokes. Of the 5 patients with ischemic stroke who died, 3 experienced hemorrhagic transformation before death. Seven patients (77%) died within 31 days (range: 2–31 days), whereas the other 2 died 6 months and 2.5 years after the episodes.

Recurrence occurred for 5 patients (10%), including 1 with Wiskott-Aldrich syndrome, 1 with mitochondrial encephalopathy with lactic acidosis and stroke-like episodes, and 3 with moyamoya disease. The patient with Wiskott-Aldrich syndrome experienced recurrent intracerebral hemorrhage, whereas the other patients experienced ischemic strokes.

Seventeen patients (41%) had long-term neurologic deficits, mainly epilepsy ($N = 7$), mental retardation ($N = 11$), and hemiplegia ($N = 10$). Eight patients (19.5%) had ≥ 1 neurologic problem. The functional deficits were classified as severe for 7 patients, moderate for 3 patients, and mild for 7 patients with long-term neurologic deficits.

Risk Factors and Clinical Outcomes

The relationships of stroke types and subtypes, clinical presentations, and causes to clinical outcomes were statistically analyzed. Decreased levels of consciousness ($P = .004$), hematologic causes ($P = .04$), and hemorrhagic transformation (applicable only in ischemic stroke cases) ($P = .01$) were significant risk factors associated with high mortality rates. Among the 41 patients who survived, the only significant risk factor for long-term neurologic deficits was seizures at the initial presentation ($P = .04$). Other factors, such as gender, age, other clinical features, stroke type, vascular territory, other causes, and recurrence of stroke, were all insignificant with

B		
Cardiac diseases (N=15)	HOCM MS* MR ASD** Right isomerism, PS DORV, VSD,AS TGA, VSD, hypoplastic RV TGA, PAVSD TOF * TOF** PS * PS VSD* PA VSD* PA IVS and Ebstein abnormaly*	1 1 1 2 1 1 1 1 1 1 1 1 1 1
Vascular diseases (N=13)	Moya-moya disease Vascular dysplasia in NF-1 Fibromuscular dysplasia Post-infectious/vaccination vasculitis - Hemophilus influenzae - Streptococcus pneumoniae - Recurrent Herpes simplex encephalitis - Post-pertussis vaccination - Post- MMR vaccination AV malformation	3 2 1 5 2
Hematological disease (N=14)		
(A) Thrombosis (N=5)	ALL (1 with asparaginase therapy) AML Beta-thalassaemia intermedia Beta-thalassaemia /Hb E post BMT	2 1 1 1
(B) Bleeding tendency (N=9)	Aplastic anemia (1 post-BMT) Hemophilia Wiskott Aldrich syndrome AML (1 with E. coli sepsis) ALL PAVSD* and streptokinase infusion	2 2 1 2 1 1
Others (N=2)	MELAS Gastroenteritis with severe dehydration	1 1

HOCM indicates hypertrophic obstructive cardiomyopathy; MS, mitral stenosis; MR, mitral regurgitation; ASD, atrial septal defect; PS, pulmonary stenosis; DORV, double outlet right ventricle; VSD, ventricular septal defect; AS, aortic stenosis; TGS, transposition of great artery; PA, pulmonary atresia; TOF, tetralogy of Fallot; IVS, intact ventricular septum; NF-1, neurofibromatosis type 1; MMR, mumps, measles, rubella; ALL, acute lymphoid leukemia; AML, acute myeloid leukemia; Hb E, hemoglobin E; BMT, bone marrow transplant; MELAS, mitochondrial encephalopathy with lactic acidosis and stroke-like syndrome. *Postcatheterization. **Postsurgery.

Fig 1. Continued.

respect to both mortality and long-term deficit rates. When the 3 identified risk factors for death were analyzed in a multivariate logistic regression analysis with adjustment for the confounding variables, only decreased levels of consciousness remained significant (odds ratio: 15.6; $P = .005$).

DISCUSSION

The incidence of pediatric stroke was 2.1 cases per 100 000 children-years for Chinese children in Hong Kong. The rate was similar to or slightly less than those reported for North America (2.3 cases per 100 000 children-years in a California study,⁷ 2.5 cases per 100 000 children per year in a Rochester study,² and 2.7 cases per 100 000 children per year in

a Cincinnati study¹) but much less than that reported for Europe (13 cases per 100 000 children per year in France⁶).

To our knowledge, this is the first report of the incidence of pediatric stroke among Chinese children. The incidence of stroke among Asian children was investigated by Fullerton et al⁷ in a population-based study in the United States. Those authors reported an incidence of 1.9 cases per 100 000 person-years among Asian Americans, which ranked third, compared with 4.22 cases per 100 000 person-years for black subjects, 1.99 cases per 100 000 person-years for white subjects, and 1.50 cases per 100 000 person-years for Hispanic subjects. Therefore, on the basis of the findings of the 2 studies, the incidence of pedi-

atric strokes among Asian races is probably in the range of 1.9 to 2.1 cases per 100 000 children-years.

We excluded neonatal stroke in the present study, for reason previously stated. Knowing that neonatal stroke had an incidence of 28 cases per 100 000 live births¹¹ and constituted up to one-fourth of all childhood strokes,⁹ we would expect a higher incidence if neonatal cases were included; this would potentially have some implications for interethnic comparisons of our findings with studies that included both neonatal and pediatric strokes.

Our small series of 50 Chinese children with strokes, collected prospectively during an 11-year period, demonstrated a different profile, compared with other ethnic groups. In comparison with data from North America, there were similarities in the stroke patterns. As observed by our counterparts,^{6,12,13,16-19} the majority of our patients had thromboembolism, rather than hemorrhage, and underlying heart disease was the most important cause of pediatric strokes.

We observed some differences, however, in comparison with other ethnic groups. We did not observe any cases of sickle cell disease, which is known to increase the risk of stroke 200- to 400-fold⁶ and is accountable for 35% of deaths among black children with strokes in the United States.⁵ Sickle cell disease is rare among southern Chinese subjects; at our center, we have not observed a single case of sickle cell disease among our Chinese patients. The most common hemoglobinopathy in Hong Kong is thalassemia syndrome, and our carrier rates of α - and β -thalassemia were 5% and 3.4%, respectively.²⁰ In our cohort, there were 2 thalassemic patients who experienced ischemic strokes, 1 of whom was described previously.²¹ Moratelli et al²² reported that the prevalence of thromboembolic accidents among thalassemic patients, with or without additional risk factors, was ~5.2% in Italy.

Prothrombotic disorders were reported to be important for both ischemic strokes and sinovenous thrombosis,¹⁴ either alone or in association with other risk factors (eg, cardiac disorders).²³ DeVeber et al²⁴ reported that 38% and 50% of their patients with cerebral thromboembolism and sinovenous thrombosis, respectively, had coagulation abnormalities. However, inherited thrombophilia is rare in Chinese populations.²⁵⁻²⁸ In our study, 7 patients (20%) with thromboembolism were screened for inherited thrombophilia since these tests became available locally in the late 1990s; all results were negative (including antiphospholipid antibody, protein C, protein S, antithrombin III, factor V Leiden, and prothrombin G20210A mutation assays). To date, evidence of the effects of these prothrombotic factors on the pathogenesis of stroke among Chinese children is lacking. However, data on adult Chinese stroke patients²⁹ and the role of these factors indicated less importance, compared with that for white subjects. The absence of these coagulation abnormalities might also explain the lack of sinovenous thrombosis in our registry. In fact, in the centralized computerized database, there was no case of nonpyogenic thrombosis of an intracranial venous sinus (code

437.6), which confirmed the observations from our own database.

Despite a different stroke pattern, our mortality rate of 18% was comparable to those reported for white subjects (23%³⁰ and 20%⁸). Moreover, our neurologic outcomes, with 41% persistent neurologic deficits, were comparable to the rates of 54% reported by Higgins et al³⁰ and 45% reported by Lanthier et al.⁸

Previous studies identified multiple but inconsistent poor prognostic factors for childhood stroke, including younger age at onset,^{5,19} female¹⁹ or male⁵ gender, black ethnic origin,⁵ underlying cardiac diseases,¹⁸ associated neurologic disorders,¹⁵ multiple risk factors,⁸ recurrent stroke,⁸ arterial stroke (compared with venous stroke),¹⁵ hemorrhagic stroke,³⁰ persistent hemiparesis,¹⁹ altered level of consciousness,³⁰ seizures,¹⁵ cortical infarction (compared with subcortical infarction),^{9,31} and hemorrhagic transformation.³² In our study, altered levels of consciousness, seizures, hematologic causes, and hemorrhagic transformation (in cases of ischemic stroke) were predictors of poor outcomes. Hematologic causes of stroke as a poor survival predictor is a unique finding for our cohort. This is probably related to our referral pattern, because a large proportion of cases with "hematologic causes" actually involved underlying medical conditions with high mortality rates (eg, acute leukemia) or recent bone marrow transplants. Only decreased levels of consciousness remained significant in the multivariate analysis. Additional studies, either with large sample sizes or with newer methods for prognostication, should be conducted, to determine and confirm the genuine predictors of poor outcomes among pediatric stroke patients.

The incidence of stroke among children in Hong Kong was estimated to be 2.1 cases per 100 000 children-years. Our sample of 50 cases of stroke among southern Chinese children demonstrated different patterns of causes and risk factors, compared with those for other ethnic groups. Our stroke pattern was unique, because there were no strokes associated with sickle cell anemia, inherited thrombophilic disorders, or sinovenous thrombosis. Despite the different causes, our patients exhibited similar clinical outcomes, compared with children in North America. We found that underlying hematologic diseases, clinical presentation with altered levels of consciousness or seizures, and secondary hemorrhage were significant predictors of poor outcomes. However, because other risk factors for stroke were reported recently,³³ we need international, collaborative, multiethnic, stroke studies among children, using standard protocols, to identify risk factors and to determine the modalities of treatment.

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REFERENCES

1. Schoenberg BS, Mellinger JF, Schoenberg DG. Cerebrovascular disease in infants and children: a study of incidence, clinical features, and survival. *Neurology*. 1978;28:763-768

2. Broderick J, Talbot GT, Prenger E, Leach A, Brott T. Stroke in children within a major metropolitan area: the surprising importance of intracerebral hemorrhage. *J Child Neurol.* 1993;8:250–255
3. Giroud M, Lemesle M, Gouyon KB, Nivelon JL, Milan C, Dumas R. Cerebrovascular disease in children under 16 years of age in the city of Dijon, France: a study of incidence and clinical features from 1985 to 1993. *J Clin Epidemiol.* 1995;48:1343–1348
4. National Center for Health Statistics. Health, United States, 1994. Available at: www.cdc.gov/nchs/index.htm. Accessed June 21, 2004
5. Fullerton HJ, Chetkovick DM, Wu YW, Smith WS, Johnston SC. Deaths from stroke in US children, 1979–1998. *Neurology.* 2002;59:34–39
6. Lynch JK, Hirtz DG, DeVeber G, Nelson KB. Report of the National Institute of Neurological Disorders and Stroke Workshop on Perinatal and Childhood Stroke. *Pediatrics.* 2002;109:116–123
7. Fullerton HJ, Wu Y, Zhao S, Johnston SC. Risk of stroke in children: ethnic and gender disparities. *Neurology.* 2003;61:189–194
8. Lanthier S, Carmant L, David M, Larbrisseau A, DeVeber G. Stroke in children: the co-existence of multiple risk factors predicts poor outcome. *Neurology.* 2000;54:371–378
9. DeVeber GA, MacGregor D, Curtis R, Mayank S. Neurologic outcome in survivors of childhood arterial ischaemic stroke and sinovenous thrombosis. *J Child Neurol.* 2000;15:316–324
10. Census and Statistics Department, Hong Kong Special Administrative Region. *Population Data from Census 2001, Hong Kong.* Available at: www.info.gov.hk/censtatd. Accessed 2002
11. DeVeber G. Stroke and the child's brain: an overview of epidemiology, syndromes and risk factors. *Curr Opin Neurol.* 2002;15:133–138
12. Butler IJ. Cerebrovascular disorders of childhood. *J Child Neurol.* 1993;8:197–200
13. Reila AR, Roach S. Etiology of stroke in children. *J Child Neurol.* 1993;8:201–220
14. Roach ES. Etiology of stroke in children. *Semin Pediatr Neurol.* 2000;7:244–250
15. Delsing BJP, Ctasman-Berrevoets CE, Appel IM. Early prognostic indicators of outcome in ischemic childhood stroke. *Pediatr Neurol.* 2001;24:283–289
16. Kerr LM, Anderson DM, Thompson JA, Lyver SM, Call GK. Ischaemic stroke in the young: evaluation and age comparison of patients six months to thirty-nine years. *J Child Neurol.* 1993;8:266–270
17. Takeshita M, Kagawa M, Izawa M, Kitamura K. Hemorrhagic stroke in infancy, childhood and adolescence. *Surg Neurol.* 1986;26:496–500
18. Chabrier S, Husson B, Lasjaunias P, Landrieu P, Tardieu M. Stroke in childhood: outcome and recurrence risk by mechanism in 59 patients. *J Child Neurol.* 2000;15:290–294
19. Hurvitz EA, Baele L, Ried S, Nelson VS. Functional outcome of paediatric stroke survivors. *Pediatr Rehabil.* 1999;3:43–51
20. Lau YL, Chan LC, Chan YY, et al. Prevalence and genotypes of α - and β -thalassaemia carriers in Hong Kong: implications for population screening. *N Engl J Med.* 1997;336:1298–1301
21. Wong V, Yu YL, Liang RH, Tso WK, Li AM, Chan TK. Cerebral thrombosis in β -thalassaemia/hemoglobin E disease. *Stroke.* 1990;21:812–816
22. Moratelli S, De Sanctis V, Gemmati D, et al. Thrombotic risk in thalassaemic patients. *J Pediatr Endocrinol Metab.* 1998;11(suppl 3):915–921
23. Strater R, Vielhaber H, Kassenbohmer R, von Kries R, Gobel U, Nowak-Gottl U. Genetic risk factors of thrombophilia in ischaemic childhood stroke of cardiac origin: a prospective ESPED survey. *Eur J Pediatr.* 1999;158(suppl 3):S122–S125
24. DeVeber G, Monagle P, Chan A, et al. Prothrombotic disorders in infants and children with cerebral thromboembolism. *Arch Neurol.* 1998;55:1539–1543
25. Lim LC, Tan HH, Lee TH, Tien SL, Abdul Ghafar A. Activated protein C resistance: a study among 60 thromboembolic patients in the Singapore population. *Ann Acad Med Singapore.* 1999;28:252–255
26. Lin JS, Shen MC, Tsay W. The mutation at position 20210 in the 3'-untranslated region of the prothrombin gene is extremely rare in Taiwanese Chinese patients with venous thrombophilia [letter]. *Thromb Haemost.* 1998;80:343
27. Ho CH, Chau WK, Hsu HC, Gau JP, Chih CM. Prevalence of factor V Leiden in the Chinese population. *Zhonghua Yi Xue Za Zhi (Taipei).* 1999;62:875–878
28. Shen MC, Lin JS, Tsay W. Factor V Arg 306 to Gly mutation is not associated with activated protein C resistance and is rare in Taiwanese Chinese. *Thromb Haemost.* 2001;85:270–273
29. Chang JH, Zhang GS. Frequency of prothrombin gene G20210A variant in the 3'-untranslated region in Chinese people with ischaemic stroke. *Hunan Yi Ke Da Xue Xue Bao.* 2000;25:36–38
30. Higgins JJ, Kammerman LA, Fitz CR. Predictors of survival and characteristics of childhood stroke. *Neuropediatrics.* 1990;22:190–193
31. Powell FC, Hanigan WC, McCluney KW. Subcortical infarction in children. *Stroke.* 1994;25:117–121
32. Keidan I, Shahar E, Barzilay Z, Passwell J, Brand N. Predictors of outcome of stroke in infants and children based on clinical data and radiologic correlates. *Acta Paediatr.* 1994;83:762–765
33. Ganesan V, Prengler M, McShane MA, Wade AM, Kirkham J. Investigation of risk factors in children with arterial ischemic stroke. *Ann Neurol.* 2003;53:167–173

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