Published in final edited form as:

J Child Neurol. 2018 June ; 33(7): 463–467. doi:10.1177/0883073818767039.

Pediatric Stroke Rates over 17 Years: Report from a Population-Based Study

Laura L. Lehman, MD¹, Jane C. Khoury, PhD², J. Michael Taylor, MD³, Samrat Yeramaneni, PhD^{2,4}, Heidi Sucharew, PhD², Kathleen Alwell, RN, BSN⁵, Charles J. Moomaw, PhD⁵, Katrina Peariso, MD, PhD³, Matthew Flaherty, MD⁵, Pooja Khatri, MD⁵, Joseph P. Broderick, MD⁵, Brett M. Kissela, MD⁵, and Dawn O Kleindorfer, MD⁵

¹Department of Neurology, Boston Children's Hospital

²Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

³Division of Neurology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

⁴Center for Clinical Effectiveness, Baylor Scott & White Health, Dallas, TX

⁵Department of Neurology and Rehabilitation Medicine, University of Cincinnati, Cincinnati, OH

Abstract

We previously published rates of pediatric stroke using our population-based Greater Cincinnati Northern Kentucky Stroke Study (GCNK) for periods 7/1993–6/1994 and 1999. We report population-based rates from two additional study periods: 2005 and 2010. We identified all pediatric strokes for residents of the GCNK region that occurred in 7/1/93–6/30/94 and calendar years 1999, 2005, and 2010. Stroke cases were ascertained by screening discharge ICD-9 codes, and verified by a physician. Pediatric stroke was defined as stroke in those <20 years of age. Stroke rates by study period, overall, by age and by race, were calculated. Eleven children died within 30 days, yielding an all-cause case-fatality rate of 15.7% (95% CI 1.1, 26.4%) with 3 (27.3%) ischemic, 6 (54.5%) hemorrhagic and 2 (18.2%) unknown stroke type. The pediatric stroke rate of 4.4 per 100,000 in the GCNK study region has not changed over 17 years.

Keywords

stroke; children; pediatric; outcome; epidemiology

Introduction

Stroke is one of the top ten causes of childhood mortality in the United States.¹ From 1979 to 2010, pediatric stroke mortality has declined in the United States, with notable decrease in mortality in black children, compared with white children, thought to be in part due to the

CORRESPONDING AUTHOR: Name: Laura Lehman, MD Address: 300 Longwood Avenue Fegan 11 Boston, MA 02115, Telephone: 617-355-2758, Fax: 617-730-0285, Laura.Lehman@childrens.harvard.edu.

Conflicts of interest: No conflicts of interest for L.L.L., J.C.K, J.M.T, S.Y., H.S., K.A., C.J.M., K.P., M.F., J.P.B., B.M.K., D.O.K. P.K. discloses that University of Cincinnati Department of Neurology is paid by Genentech for her research effort as PRISMS PI

implementation of recommendations from the Stroke Prevention Trial in Sickle Cell Anemia (STOP trial).² Specific sub-populations are at greater risk for stroke. An increased stroke risk for black children cannot be completely explained by sickle cell anemia alone.³ Boys have been shown to be at greater risk for stroke, compared with girls.^{4, 5} Adolescents and infants also have increased risk of stroke.³

Estimates of pediatric stroke incidence in the United States range from 1.3 to 5.4 per 100,000 children.^{6–11} This range is in part due to the varying definition of stroke, the age range defined, geographical area of case capture, and method of case ascertainment. Temporal trends and case fatality have been previously examined both in the Greater Cincinnati/Northern Kentucky area as well as in New Jersey.^{6, 7, 12} In New Jersey the rates of stroke were examined from 1994 to 2007 in children; incidence rates initially decreased from 1994, with a nadir in 1999, and then increased through 2007. This is in comparison with our previously published findings of stable incidence of pediatric stroke in the Greater Cincinnati/Northern Kentucky area over a 12 year time period; 1989 to 1999.⁷ These observations both contrast the decade's long fall in adult stroke incidence attributed to better management of cardiovascular risk factors.

Since the stroke incidence previously reported by our group was stable and unfortunately there have not been significant advances in stroke prevention in children our research question was; is the incidence of stroke stable over our study period. We re-examine the temporal trends in incidence, overall stroke rate, and 30-day all-cause case-fatality for the period 7/1993–6/1994 and for calendar years 1999, 2005, and 2010; these are the specific periods examined in the population-based Greater Cincinnati Northern Kentucky Stroke Study (GCNK). To ensure consistency of methodology we did not include 1988–1989 data as only strokes in children <15 years of age were captured in that period. Attention is given to age and race to examine temporal trends in stroke rates and fatality in children within the Greater Cincinnati/Northern Kentucky population, a region overall representative of the United States with respect to the demographic characteristics; percent white (79.8% vs. 78.1%), and percent female (51.4% vs. 50.8%), as well as the socioeconomic characteristics; median household income (\$53.2K vs. \$52.8K), percent below poverty (13.5% vs. 14.3%) and percent of high school graduates (87.9% vs. 85.4%), in Cincinnati 5-county area versus the US population, respectively.¹³

Methods

We ascertained all strokes (ischemic and hemorrhagic) among residents of the Greater Cincinnati/Northern Kentucky region of 1.3 million people, as part of the Greater Cincinnati/Northern Kentucky Stroke Study. The population is defined as all residents of two southwest Ohio counties and three northern Kentucky counties separated by the Ohio River.

Stroke events for the four discrete one-year periods, July 1, 1993 to June 30, 1994, and calendar years 1999, 2005 and 2010, within the pre-defined 5-county Greater Cincinnati area, were identified. Study research nurses screened the medical records of all inpatients with primary or secondary stroke-related discharge diagnoses (International Classification of

Disease, Version 9, codes 430–436) from all acute-care hospitals in the study region. To ensure complete capture of pediatric strokes, ICD-9 codes 437 and 438 (which have been shown to have a very low yield for identifying strokes in adults), as well as 325, 671.5, 674.xx, 747.8x, and 997.02 were also screened at Cincinnati Children's Hospital. In addition, hospital emergency departments, outpatient clinics and a sample of nursing homes and physician's offices were screened. The methodology has been described in detail elsewhere.⁶

Once a potential case was identified, a study nurse collected information from medical records in a case report form, including demographics, stroke symptoms, past medical and surgical history, time of symptom onset and arrival in the emergency department, neurologic evaluation, and diagnostic test results. Mortality was documented to 30-days post stroke, according to hospital records or state death indices. A study physician reviewed every case report form, along with all available neuroimaging studies, to verify the occurrence of a stroke and determine stroke type and mechanism.

Stroke onset was determined to be the time the child was noted to have any focal neurological deficit. For children this was typically based on parental report of when the child was last seen "normal." Patients younger than 20 years old with stroke onset within any of the study periods, except for traumatic intracerebral and germinal matrix hemorrhages of prematurity, were eligible for this analysis. Institutional Review Boards at all participating hospitals approved this study.

Demographic continuous variables are reported as median and range. Categorical variables are reported as number and percentage. Stroke rates were calculated by using the number of physician-confirmed cases as the numerator and the study period-specific age race and sex categories of county data as the denominator as provided by the US Census Bureau.¹⁴ In addition, in order to compute rates for neonates <29 days old the denominator used was county-specific residential live births within each study period.¹⁵ Overall stroke rates and stroke rates for those 29 days and older were standardized to the 2000 census adjusted for race, sex, and age as appropriate. Rates and associated standard errors were estimated assuming a Poisson distribution. Rates were not presented for categories in which the sample size was less than 5, and rates estimated for categories with fewer than 20 subjects should be interpreted with caution. Case-fatality rate was calculated as the number dead by 30 days post stroke onset divided by total number of strokes. Bivariate analyses were performed using Fisher's exact test or Wilcoxon rank sum exact test due to small numbers. Proportions and exact 95% confidence interval (CI) are reported; adjusted proportions and CI are estimated using a generalized linear model, assuming a binomial distribution and log link. Trends over time for rates were tested using a general linear model, assuming a Poisson distribution with a logit link and using an offset of the log of the population count. SAS®, version 9.4 (SAS Institute, Cary NC) was used for data management and analysis. A p-value <0.05 was considered statistically significant.

Results

A total of 70 pediatric strokes occurred over the four study periods. Ischemic stroke predominated with 41 events (58.6%) compared with 27 hemorrhagic strokes (38.6%); 2 strokes were coded as unknown. The overall stroke rate was 4.4 (95% CI; 3.4, 5.4) per 100,000 and 4.1 (3.1, 5.1) per 100,000 for first ever stroke, or stroke incidence; rates were adjusted by age, race and sex to 2000 US population. The children ranged in age from 0 days to 19 years; 34% were black, 59% were female, and 8.6% had a recurrent stroke. Ascertainment at hospitals in the region other than Cincinnati Children's Hospital found seven additional cases, one in 1993/94, two in 1999, three children in 2005, and one in 2010 for a total of 70 cases. The seven children were aged 19 years, 18 years, 16 years, 15 years, 1 day old, and two were 17 years old. Demographic information on childhood stroke cases is shown in Table 1.

Incident and overall stroke rates by study period standardized to the 2000 Census for neonates and children are shown in Table 2. Raw numbers by study year and age group are also shown. Stroke rates were similar across all four study periods. Both ischemic and hemorrhagic stroke subtypes exhibited this stable pattern over time. The overall ischemic stroke rate was 2.7 (1.9, 3.5) and the hemorrhagic rate was 1.7 (1.1, 2.4), both per 100,000. The incidence of neonatal stroke was 23.7 (14.1, 33.2) cases per 100,000 live births over the time period; similar rates were found in 1993/4 and 2010 but rates were not estimated in the intervening study years due to the low number of recorded cases. Figure 1 shows that incidence of pediatric stroke across age groups forms a U-shaped distribution. Racial trends are reviewed in Table 2, which shows that a consistently higher incidence of childhood stroke is observed in the black population compared with the white population over the past 2 decades. Nevertheless, the rate of stroke within black children appears to have been falling over time from 1999 to 2010.

Stroke etiology was investigated in all cases. For children, acute head and neck disorders (10 cases) and arteriopathy (7 cases) were the most common categories of ischemic stroke risk factors (Table 3). The most frequently identified ischemic stroke etiologies are arterial dissection, sickle cell disease, and meningitis – 4 cases each. No definite etiology was identified in 11 ischemic stroke cases (26%). Hemorrhagic stroke was found in 28 cases of children, with 12 attributable to AVM rupture and 3 due to aneurysmal subarachnoid hemorrhage. In 8 hemorrhagic cases, an underlying lesion or etiology was not identified on chart review.

All-cause case-fatality at 30 days over all four study periods was 11/70; 15.7%. (95%CI: 8.1%, 26.4%). After adjusting for age and race the case fatality rate was 16.0% (6.6%, 25.5%). Neonates are observed to have a higher all-cause case-fatality rate in this cohort, as shown in Table 4. The majority of deaths; 9 (81.8%) occurred within 6 days of stroke; however, cause of death was not collected. Three (27.3%) of the deaths were ischemic and 6 (54.5%) were hemorrhagic and 2 (18.2%) were unknown stroke type. These translate into rates of 7.3% (95% CI 1.5, 19.9%) for ischemic strokes and 22.2% (95% CI 8.6, 42.3%) for hemorrhagic stroke.

Discussion

To our knowledge this report is the first population-based study to examine temporal trends in incidence and 30-day all-cause case-fatality, within a population similar socio-demographically to the United States, over nearly two decades. The temporal trend of incidence in both neonatal and childhood stroke appears stable which is in contrast to the decrease in stroke incidence in adults within the same population.¹⁶ Unfortunately, stroke prevention in children has not significantly changed except for the recommendations of the STOP trial which is in contrast to prevention in adults. Although the temporal trend of stroke incidence in black children appears to be decreasing from 1999 to 2010 which is in contrast to the stable stroke incidence in black adults within the same population, the raw numbers are small so we did not report statistical significance. We also cannot comment on possible explanations for this decrease due to small numbers of events once subdivided by etiology.¹⁶

Our finding that the incidence of stroke in infants and adolescents is greater than the incidence for 1 to 14-year-olds is similar to what has been reported previously.^{3, 5} This may be due in part to the difference in etiologies of perinatal and adolescent stroke. Further research examining the etiologies by age is needed.

We found no significant difference in the 30-day all-cause case-fatality rate in the children over our 17 year study period. Of note, adolescents and neonates made up the majority of 30-day case fatality. Similar to previously reported data that 64%–74% of stroke deaths are due to hemorrhagic stroke, we found 54.5% of deaths in our cohort were in children with hemorrhagic stroke.^{2, 12}

Limitations of the study include small sample size and use of ICD-9 codes to screen for cases. We are limited by the small number of childhood strokes; we did not do a power calculation a priori and are admittedly underpowered as we are limited by sampling of this specific population. Assuming these rates in order to detect the difference observed between 1993/4 and 2010 as statistically significant we would require nearly 2000 childhood strokes overall. However, unlike other studies using ICD-9 codes, each case was reviewed by a study nurse and adjudicated by a stroke neurologist. Previous studies have shown the limitations of using ICD-9 codes alone to describe pediatric strokes.^{10, 13, 17} We are also limited by the large confidence intervals. Small numbers also limit our ability to perform subgroup analyses, and draw statistically substantiated conclusions on specific portions of the population.

In summary, over the past 17 years the incidence and 30-day case-fatality rate of pediatric stroke has appeared stable, including neonatal and pediatric stroke incidence. The stable incidence of pediatric stroke, in the context of decreasing stroke incidence in adults within the same population indicates that there is a great need for research for determination of stroke prevention in this population.¹⁶ Interestingly, there may be a decline in the incidence of stroke in black children over time. A conservative estimate based on our data is that approximately 3,700 children < 20 years of age will have a stroke in 2017 in the United States.

Acknowledgments

Funding: NIH/NINDS R01 NS030678

References

1. Kochanek KDXJ, Murphy SL, Minino AM, Kung H. Deaths: Final Data for 2009. Natl Vital Stat Rep. 2011; 60(3):1–167.
2. Lehman LL, Fullerton HJ. Changing Ethnic Disparity in Ischemic Stroke Mortality in US Children After the STOP Trial. JAMA Pediatr. 2013:1–5.
3. Fullerton HJ, Wu YW, Zhao S, Johnston SC. Risk of stroke in children: ethnic and gender disparities. Neurology. 2003; 61:189–94. [PubMed: 12874397]
4. Golomb MR, Fullerton HJ, Nowak-Gottl U, Deveber G. Male predominance in childhood ischemic stroke: findings from the international pediatric stroke study. Stroke. 2009; 40:52–7. [PubMed: 18787197]
5. Lo W, Stephens J, Fernandez S. Pediatric stroke in the United States and the impact of risk factors. J Child Neurol. 2009; 24:194–203. [PubMed: 19182157]
6. 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; 8:250–5. [PubMed: 8409267]
7. Kleindorfer D, Panagos P, Pancioli A, et al. Incidence and short-term prognosis of transient ischemic attack in a population-based study. Stroke. 2005; 36:720–3. [PubMed: 15731465]
8. Schoenberg BS, Mellinger JF, Schoenberg DG. Cerebrovascular disease in infants and children: a study of incidence, clinical features, and survival. Neurology. 1978; 28:763–8. [PubMed: 567292]
9. Earley CJ, Kittner SJ, Feaser BR, et al. Stroke in children and sickle-cell disease: Baltimore-Washington Cooperative Young Stroke Study. Neurology. 1998; 51:169–76. [PubMed: 9674798]
10. Fullerton HJ, Wu YW, Sidney S, Johnston SC. Risk of recurrent childhood arterial ischemic stroke in a population-based cohort: the importance of cerebrovascular imaging. Pediatrics. 2007; 119:495–501. [PubMed: 17332202]
11. Zahuranec DB, Brown DL, Lisabeth LD, Morgenstern LB. Is it time for a large, collaborative study of pediatric stroke? Stroke. 2005; 36:1825–9. [PubMed: 16100029]
12. Gandhi SK, McKinney JS, Sedjro JE, et al. Temporal trends in incidence and long-term case fatality of stroke among children from 1994 to 2007. Neurology. 2012; 78:1923–9. [PubMed: 22649219]
13. U.S. Census Bureau. [Accessed January 6, 2017] Available at: https://quickfacts.census.gov/qfd/download_data.html
14. U.S. Census Bureau. [Accessed January 6, 2017] Available at: <https://census.gov>
15. Kid's Count Data Center. [Accessed January 6, 2017] Available at <https://datacenter.kidscount.org>
16. Kleindorfer DO, Khoury J, Moomaw CJ, et al. Stroke incidence is decreasing in whites but not in blacks: a population-based estimate of temporal trends in stroke incidence from the Greater Cincinnati/Northern Kentucky Stroke Study. Stroke. 2010; 41:1326–31. [PubMed: 20489177]
17. Golomb MR, Garg BP, Saha C, Williams LS. Accuracy and yield of ICD-9 codes for identifying children with ischemic stroke. Neurology. 2006; 67:2053–5. [PubMed: 17159120]

Figure 1.
Incidence/100,000, with the 95% confidence interval, of childhood stroke stratified by age group

Table 1

Demographic Characteristics by study period *

Study Period	1993/94	1999	2005	2010	Overall
Cases	14	24	15	17	70
Age	0.5 (0, 17)	11.5 (0, 19)	11.0 (0, 19)	4.0 (0, 18)	7.5 (0, 19)
Neonatal Strokes	6 (42.9%)	4 (16.7%)	2 (13.3%)	5 (29.4%)	17 (24.2%)
Female Sex	6 (42.9%)	17 (70.8%)	10 (66.7%)	8 (47.1%)	41 (58.6%)
Black Race	2 (14.3%)	11 (45.8%)	6 (40.0%)	5 (29.4%)	24 (34.3%)
Hemorrhagic Stroke	4 (28.6%)	11 (45.8%)	5 (33.3%)	7 (41.2%)	27 (38.6%)

* Data presented as median (range) or n (%)

Table 2

Childhood stroke rates (95% confidence interval)¹ and number of cases by age group in Greater Cincinnati/Northern Kentucky over two decades.

	1993/94	1999	2005	2010	TOTAL
Incidence (first ever stroke) rate (cases/100,000)	3.58 (1.69, 5.47)	5.19 (2.96, 7.42)	3.33 (1.51, 5.15)	4.12 (2.07, 6.16)	4.06 (3.06, 5.06)
Overall event rate (including recurrence) (cases/100,000)	3.58 (1.69, 5.47)	5.90 (3.53, 8.27)	3.85 (1.89, 5.80)	4.31 (2.23, 6.39)	4.41 (3.37, 5.45)
Neonatal event rate (cases/100,000 live births)	31.2 (20.2, 42.1)	NE (n=4)	NE (n=2)	31.2 (20.2, 42.1)	23.7 (14.1, 33.2)
29d to 19y event rate (cases/100,000)	2.14 (0.65, 3.62)	4.82 (2.70, 6.94)	3.32 (1.50, 5.13)	3.02 (1.28, 4.75)	3.32 (2.42, 4.22)
Age groups(cases)	Neonate	4	2	5	70 cases
	Infant	3	0	3	
	1–14 years	8	8	4	
	15–19 years	9	5	5	
Recurrent stroke (had a previous stroke)	0	3	2	1	6
Black Overall event rate (including recurrence) (cases/100,000)	NE (n=2)	14.16 (5.79, 22.54)	7.79 (1.56, 14.02)	5.40 (0.65, 10.14)	7.48 (4.48, 10.48)
White Overall event rate (including recurrence) (cases/100,000)	3.81 (1.65, 5.97)	4.21 (1.92, 6.48)	3.03 (1.05, 5.01)	4.08 (1.77, 6.38)	3.77 (2.68, 4.86)

NE denotes not estimable, i.e., we did not estimate rates for an N less than 5.

¹ rates adjusted by age (where appropriate), race, and sex to 2000 US population

Table 3

Etiologies of childhood stroke

		Category and Etiology (N=70)
Ischemic stroke	Arteriopathy	(7)
	Dissection	4
	Moyamoya	1
	Focal cerebral arteriopathy	1
	Cerebral arterial anomaly	1
	Cardiac	(2)
	Cardioembolic	1
	ECMO	1
	Acute Systemic Disease	(2)
	Chemotherapy	1
	Maternal Chorioamnionitis	1
	Chronic Systemic Disease	(5)
	Sickle cell anemia	4
	Sickle trait+dehydration	1
Hemorrhagic Stroke	Acute Head/Neck Disorder	(10)
	Meningitis	4
	CSVT	3
	AVM	2
	PRES	1
	Chronic Head/Neck Disorder	(3)
	Mitochondrial disease	2
	Venous anomaly	1
	Atherosclerosis	1
	Unknown	11
Hemorrhagic Stroke	AVM	12
	Aneurysm	3
	Cavernous hemangioma	1
	Thrombocytopenia	1
	Secondary to anticoagulation for	1
	ECMO	
	ITP PLT<10	1

		Category and Etiology (N=70)
	Unknown/Other	8
Unknown	Congenital heart	1
	Unknown	1

Table 4

30-day all-cause case-fatality by study period

	1993/94	1999	2005	2010	Case-Fatality (95%CI)
Neonates (n=17)	0 deaths/6 cases	1/4	1/2	3/5	29.4%
Infants and Children (n=53)	1/8	3/20	0/13	2/12	10.5%
Overall (n=70)	1/14 7.1% (0.2, 33.9%)	4/24 16.7% (4.7, 37.4%)	1/15 6.7% (0.2, 32.0%)	5/17 22.7% (7.8, 45.4%)	15.7% (8.1, 26.4%)

Data shown as exact counts; rate and 95% confidence interval are shown for overall