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Incidence and Clinical Characteristics of Childhood Glaucoma: A Population-Based Study

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Abstract

Objective—To describe the incidence and clinical characteristics of childhood glaucoma in a defined population of the United States.

Methods—The medical records of all patients (< 20 years) meeting diagnostic criteria for glaucoma or glaucoma suspect, as residents of Olmsted County, Minnesota, from January 1, 1965, through December 31, 2004 were reviewed.

Results—Thirty children were diagnosed with glaucoma during the 40-year study period. The age- and sex-adjusted incidence of childhood glaucoma was 2.29 (95% CI: 1.47–3.12) per 100,000 residents < 20 years of age, with the following types and incidences: 19 acquired (1.46/100,000; 95% CI: 0.80–2.12), 6 secondary (0.45/100,000; 95% CI: 0.08–0.82) and 5 with primary glaucoma (0.38/100,000; 95% CI: 0.05–0.72). The birth prevalence of primary congenital glaucoma during the 40-year period was 1 in 68,254 births or 1.46 per 100,000 births (95% CI: 0.03–8.16). Twenty-four glaucoma suspects were also identified, yielding an incidence of 1.9 per 100,000 patients < 20 years of age (95% CI: 1.14–2.66).

Conclusion—The incidence of childhood glaucoma in this population was 2.29 per 100,000 or 1 in 43,575 for patients <20 years of age. Acquired and secondary forms of glaucoma were the most common while congenital and juvenile glaucoma were rare.

Childhood glaucoma is an uncommon pediatric condition often associated with significant visual loss.[1, 2] It consists in a heterogeneous group of diseases leading to optic neuropathy and visual field changes that can be categorized into primary, secondary and acquired subtypes.[3] Primary glaucoma in children is generally divided into primary congenital glaucoma, infantile primary open angle glaucoma (1 to 3 years old), and juvenile primary open angle glaucoma (4 years to early adulthood).[3, 4] Primary congenital glaucoma (PCG) has previously been reported as the most common type of glaucoma seen in childhood.[4,5,6] Secondary glaucoma is usually defined as including syndromic disorders or other medical conditions present at birth, such as aniridia, Axenfeld-Rieger's syndrome, retinopathy of prematurity, Rubinstein-Taybi syndrome, Sturge-Weber, persistent hyperplastic primary vitreous (PHPV) and congenital rubella.[3, 4] Acquired glaucoma, often classified as secondary glaucoma, is the result of other processes not present at birth, such as inflammation, drugs, trauma and surgery.[3]

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The incidence of childhood glaucoma within the United States, including primary congenital glaucoma (PCG), has not been reported. The purpose of this study is to describe the incidence and clinical characteristics of childhood glaucoma diagnosed over a 40-year period among patients < 20 years of age who were residents of Olmsted County, Minnesota.

Subjects and Methods

The medical records of all patients younger than 20 years of age who were residents of Olmsted County, Minnesota, when diagnosed with glaucoma between January 1, 1965, and December 31, 2004, were retrospectively reviewed. Although the term *childhood* typically excludes patients older than 18 years, we extended the age limit to < 20 years because juvenile glaucoma is an entity that has been diagnosed in patients up to the fourth decade of life.[7, 8] Institutional Review Board (IRB) approval was obtained for this study. Potential cases of glaucoma and glaucoma suspects were identified using the resources of the Rochester Epidemiology Project, a medical record linkage system designed to capture data on any patient–physician encounter in Olmsted County, Minnesota.[9]

The racial distribution of Olmsted County residents in 1990 was 95.7% Caucasian, 3.0% Asian-American, 0.7% African-American, and 0.3% Native American. The population is relatively isolated from other urban areas and virtually all medical care is provided to its residents by Mayo Clinic, Olmsted Medical Group, and their affiliated hospitals. Patients not residing in Olmsted County at the time of their diagnosis were excluded from the study.

Glaucoma was defined generally in this study as an optic neuropathy and/or a visual field change, frequently associated with elevated intraocular pressure (IOP). Clinical signs such as elevated IOP (>21 mmHg), optic nerve cupping, asymmetric or progressive disc cupping, visual field defects, or anterior segment changes such as enlarged corneas or Haab's striae, alone or in combination, were used to make the diagnosis of glaucoma. Primary congenital glaucoma included patients presenting with ocular signs of enlargement combined with 1 or more classic findings such as photophobia, epiphora, Haab's striae, corneal clouding, or optic nerve cupping, and ranging in age from birth to early childhood. Primary open angle glaucoma diagnosed between 1 and 3 years of age was defined as infantile glaucoma and referred as juvenile glaucoma if presenting between 4 and 20 years of age. Secondary glaucoma included patients with a systemic or ocular condition present at birth, while acquired glaucoma referred to those patients with secondary processes occurring after birth. No retrospective diagnosis of glaucoma was made and all patients included had been diagnosed by the ophthalmologists who participated in their care.

Glaucoma suspect was defined according to the AAO guidelines[10]as an individual with open anterior-chamber angles by gonioscopy and one or more of the following clinical findings: 1) appearance of the optic disc or retinal nerve fiber layer that is suspicious for glaucomatous damage, 2) a visual field suspicious for glaucomatous damage, or 3) consistently elevated intraocular pressure (IOP) associated with normal appearance of the optic disc and retinal nerve fiber layer and with normal visual field test results. We included patients with an IOP greater than 21 mmHg for ≥ 6 months as satisfactorily meeting the third AAO clinical criteria. Patients not meeting the glaucoma suspect diagnosis guideline, as established by the AAO, were excluded. In addition, patients diagnosed simply with large physiologic cups or whose exam appeared to have isolated optic nerve cupping were also excluded. Other patients, with normal exams initially diagnosed as glaucoma suspects based on a positive family history of glaucoma, were also excluded. Except for patients with a 6-month history of elevated IOP, those who were no longer considered glaucoma suspects at their last follow-up exams were also excluded from the study. Only those patients who had at least two ophthalmologic exams with a diagnosis of glaucoma suspect were included in this study.

Continuous data is presented as a mean and categorical data is presented as counts and percentages. To determine the incidence of childhood glaucoma in Olmsted County, annual age- and sex-specific incidence rates were constructed using the age-and sex-specific population figures for this county from the US Census. Because primary congenital glaucoma (PCG) is often diagnosed within the first year of life, a birth prevalence for PCG was also calculated from the number of births occurring from January 1, 1965 through December 31, 2004, using the annual birth incidence for this county. The 95% confidence intervals were calculated using assumptions based on the Poisson distribution.

Results

A total of 30 patients < 20 years of age were diagnosed with glaucoma in Olmsted County, Minnesota, during the 40-year study period. This number corresponds to an age-and sex-adjusted incidence of 2.29/100,000 residents < 20 years of age (95% CI: 1.47–3.12). Twenty-one (70%) of the children were diagnosed in the second half of the study (Table 1). Fifty percent of the subjects had bilateral disease, affecting a total of 45 eyes. The incidence of primary congenital glaucoma and other forms of childhood glaucoma diagnosed in this population are shown in Table 2, while the clinical and demographic characteristics are shown in Table 3. There were 16 boys and 14 girls with the following ethnicities: 18 white (60%), 4 black (13.3%), 2 Asian (6.7%), 1 American Indian (3.3%) and 5 of unknown race (16.7%), diagnosed at a mean age of 10.4 years (range, 15 days to 19.7 years). A family history of glaucoma was present in 20% of the study patients while the mean presenting IOP and mean cup-to-disc ratio at the first visit were 30.8 mmHg (range, 14 to 56 mmHg) and 0.5 (range 0.1 to 1) in the glaucomatous eye.

Nineteen (63%) of the 30 children with glaucoma were diagnosed with acquired glaucoma at a mean age of 11.1 years (range, 3.0 to 18.8 years) and an incidence of 1.46 per 100,000 or 1 in 68,470 patients younger than 20 years of age (95% CI: 0.80–2.12). This group consisted of 12 boys and 7 girls, among which 14 developed glaucoma secondary to trauma or surgery, 4 from uveitis, and 1 following topical steroid use (Table 3). Seven (37%) of the 19 cases were bilateral and 1 (17%) had a family history of glaucoma. The average IOP and cup-to-disc ratio at presentation were 34.8 mmHg (range, 20 to 56 mmHg) and 0.4 (range, 0.1 to 1) in the affected eye.

Six (20%) of the 30 glaucomatous children were diagnosed with secondary glaucoma including 2 with Sturge Weber, 2 with neovascular glaucoma (1 patient with Coats disease and a second with ROP), and 1 each with Rubinstein-Taybi and cutis marmorata telangiectatica congenita, yielding an age-and sex-adjusted incidence of 0.45 per 100,000 or 1 in 221,877 patients < 20 years of age (95% CI: 0.08–0.82). The mean age at diagnosis for the 6 children was 6.4 years (range 2 months to 18. 4 years), with a mean initial IOP of 19.7 mmHg (range, 14 to 30 mmHg) in the glaucomatous eye. Fifty percent (3/6) of the secondary glaucoma cases were bilateral.

Primary childhood glaucoma was diagnosed in 4 children with juvenile glaucoma and 1 child with primary congenital glaucoma (PCG). This corresponds to incidences of 0.38 (95% CI: 0.08–0.82), 0.31 (95% CI: 0.08–0.82) and 0.07 (95% CI: 0.08–0.82) per 100,000 patients less than 20 years of age for primary childhood glaucoma, juvenile glaucoma and primary congenital glaucoma, respectively. In addition, since PCG occurs during the first year of life, its birth prevalence was also calculated as 1 in 68,254 births or 1.46 per 100,000 births. Three of the four children with juvenile glaucoma were girls, 2 (50%) had a positive family history of glaucoma, and all were diagnosed between 13 and 19 years of age with bilateral ocular involvement. The mean IOP for juvenile glaucoma at presentation was 28.6 mmHg (range, 16 to 45 mmHg), with a mean cup-to-disc ratio of 0.7 (range, 0.1 to 1) in the glaucomatous eye.

Twenty-four additional children were diagnosed as glaucoma suspects, generating an incidence of 1.90 per 100,000 patients < 20 years of age (95% CI: 1.14–2.66) (Table 4). Twelve of the 24 children were glaucoma suspects on the basis of elevated intraocular pressure greater than 21 for at least six months. Five patients were considered suspects based on C/D asymmetry and one due to varying disc cupping, who was stable at final follow-up with a normal visual field and IOP. Six additional suspects were identified based on other factors, including one patient with pigmentary dispersion syndrome, and others with different combinations of unusual disc appearance, suspicious visual fields, cupping and elevated IOP. The mean age at diagnosis for the 24 patients was 13.7 years (range, 6.7 to 19.7 years), with a mean initial intraocular pressure of 18.9 mmHg (range, 14 to 30 mmHg) in the affected eye. All glaucoma suspects included in the study were still considered suspects at the final follow-up by their ophthalmologist and had not developed glaucoma.

Discussion

Childhood glaucoma was diagnosed in 30 children or 1 in 43,575 patients less than 20 years of age as residents of Olmsted County, MN during the 40-year study period. Among this heterogeneous group, 19 were diagnosed with acquired glaucoma, 6 with secondary glaucoma, 4 with primary juvenile glaucoma and 1 with primary congenital glaucoma. The birth prevalence of primary congenital glaucoma (PCG) in this population was 1 in 68,254 or 1.46 in 100,000 births (95% CI: 0.03–8.16). The clinical characteristics of these patients, by glaucoma type, were consistent with prior reports.

The incidence of primary congenital glaucoma in this population is lower than all prior reports. The highest reported prevalence has been in Slovakian Gypsies (1:1250)[11]and Saudi Arabians (1:2500).12 Although the incidence of PCG in Western countries has been estimated at 1 in 10,0003, 13, 14 to 1 in 12,5005 in previous reports, a recent population-based study conducted in the United Kingdom reported an incidence of diagnosis of PCG in Great Britain to be 5.41 in 100,000 (1/18,500) and 3.31 in 100,000 (1/30,200) in the Republic of Ireland.[4] In addition, a birth prevalence of 2.85 per 100,000 (1 in 38,000) was recently reported in Spain,15 which was similar to an incidence of 1 in 30,000 births found in an Australian study.16

This study, to our knowledge, is the first population-based report on the incidence of childhood glaucoma and PCG in the United States. The difference in incidence between this and other studies may be due to a number of reasons. First, some of the reported incidences are not population-based and are likely to have been artificially elevated due to referral bias.[5, 14] Secondly, the diagnostic classification and inclusion criteria for childhood glaucomas have been inconsistent between studies.[17,18] For example, some reports define PCG as occurring within the first year of life,[4] while others include children up to the age of 4 years.[5,19] However, just one additional case of PCG in Olmsted County would have doubled the birth prevalence from 1 in 68,254 births to 1 in 34,127 births, a rate more consistent with the recent studies from Ireland, Spain and Australia. A more likely explanation is the relative homogeneous nature of the Olmsted County, Minnesota population. The British Infantile and Childhood Glaucoma eye study, in addition to reporting an incidence of 1/18,500, demonstrated significant differences in the incidence of PCG among different ethnic groups. The incidence of PCG in white British children < 16 years of age was found to be 0.28/100,000 and that of British children of Pakistani origin of the same age was 2.46/100,000, almost nine times that of Caucasians.[4] The elevated rates in some populations may be partially due to a greater incidence of consanguinity.[5]

Acquired glaucoma was the most prevalent type of childhood glaucoma diagnosed in Olmsted County, comprising more than 63% of cases and occurring in 1 in 68,470 patients < 20 years of age. The relative predominance of males in this glaucoma subtype likely reflects the higher

rate of traumatic glaucoma among males (10 males and 3 females). The incidence of traumatic hyphema from the same population was 12 in 100,000, with a male-to-female ratio of 5:1.[20] Fourteen of the 19 children with acquired glaucoma had either traumatic or iatrogenic causes for the development of their glaucoma. The larger proportion of traumatic and aphakic cases in this study highlights the importance of protective eyewear and limiting the glaucomatous effects of anterior segment surgery.

Secondary glaucoma was found in 6 children, for an incidence of 0.45 per 100,000 or 1 in 221,777 patients < 20 years of age (95% CI: 0.08–0.82). In the British Infantile and Childhood Glaucoma study, 52 of 99 glaucomatous children < 16 years of age were diagnosed with "secondary" glaucoma, a classification that included "lens-related" cases as well as other medical or syndromic diseases. In our population-based study, secondary and acquired glaucoma cases would also consist of a majority of glaucoma cases seen. Although the distinction between secondary and acquired glaucomas was not made in prior studies, our population-based report shows that secondary glaucoma presented earlier than acquired glaucoma, possibly because of the association of other disorders present at birth.

Glaucoma suspect was diagnosed in 24 patients or 1.90 per 100,000 patients less than 20 years in this study. We are unaware of any other population-based incidence rate of glaucoma suspect among children. However, the incidence rate reported in this study is very likely an underestimation given the asymptomatic nature of the disease. None of the children with glaucoma suspect in this study were known to develop visual field loss characteristic of glaucoma during their follow-up. Interestingly, patients with cup-to-disc asymmetry were identified earlier than other glaucoma suspects and were more likely to have a positive family history.

There are several limitations to the findings in this study. The retrospective design is limited by non-standardized and incomplete data collection. The pressure measurements and other clinical findings were not all performed by a single examiner or a glaucoma specialist, potentially introducing the uncertainty of examiner error. In addition, some forms of glaucoma are asymptomatic or otherwise unrecognized by the patient or outside observer, particularly juvenile glaucoma and glaucoma suspect. As a result, the incidence of these forms, unlike that of PCG, is likely to be underestimated in this population. Similarly, the apparent increase in the incidence of glaucoma and glaucoma suspect in this cohort during the later years of the study is most likely due to an improved understanding and recognition of the disease.[21] Moreover, although a relatively isolated community, some glaucomatous residents of Olmsted County may have sought care outside the region, leading to a further underestimation of disease in this population. Finally, the low incidence of childhood glaucoma in this population makes it difficult to extrapolate the findings of the various subtypes of glaucoma. The generalization of data from this study is further limited by the demographics of Olmsted County, a relatively homogeneous semi-urban white population.

This study provides population-based incidence rates for childhood glaucoma diagnosed over a 40-year period. Childhood glaucoma was found in 1 in 43,575 patients less than 20 years of age. The most common type of glaucoma was acquired glaucoma (traumatic, surgical, uveitic or drug-induced), accounting for 63% of glaucoma patients, while secondary and primary forms were less common. Primary congenital glaucoma was diagnosed in 1 of 68,254 births (1.46/100,000 births), a rate that is lower than that reported in the Spanish, British or Australian general population.

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Table 1

Number of Olmsted County Residents < 20 Years Diagnosed with Glaucoma and Glaucoma Suspects by Decade from 1965 to 2004

Year*	Number of Residents <20 years of age	Decade	Number of Children <20 diagnosed with Glaucoma (% total glaucoma patients)	Number of Glaucoma Suspects <20 years of age (% total glaucoma suspects)
1965	30,423	**1965–1974**	3 (10%)	0(0%)
1975	32,346	**1975–1984**	6 (20%)	2 (8%)
1985	31,186	**1985–1994**	12 (40%)	5 (21%)
1995	34,269	**1995–2004**	9 (30%)	17 (71%)
2004	39183	**N/A**	N/A	N/A

*Population under 20 years of age is given for year noted.

Table 2

Incidence of Glaucoma and Glaucoma Suspect among Patients < 20 years of Age Diagnosed as Residents of Olmsted County, MN from 1965 to 2004

		Number of Cases	Incidence per -- /100,000 patients less than 20	Incidence 1 in ---- patients less than 20
All Glaucoma Patients		**30**	**2.29**	**43,575**
Primary glaucoma	**All 1° Glaucoma**	**5**	**0.38**	**260,688**
	Primary congenital glaucoma	1	0.07	
	Juvenile glaucoma	4	0.32	
Secondary glaucoma	**All 2° Glaucoma**	**6**	**0.45**	**221,877**
	Sturge Weber	2	0.14	
	Cutis marmorata	1	0.07	
	Rubenstein Taybi	**1**	**0.07**	
	Retinopathy of Prematurity	**1**	**0.08**	
	Coates disease	**1**	**0.10**	
Acquired glaucoma	**All Acquired Gl**	**19**	**1.46**	**68,470**
	Traumatic/Surgical	14	1.09	
	-Trauma	8		
	-Surgery	6		
	Uveitic	4	0.30	
	Drug-Induced	1	0.07	
Glaucoma Suspects		**24**	**1.90**	**52,579**

Table 3

The Clinical and Demographic Characteristics of 30 patients < 20 years diagnosed with Glaucoma as Residents of Olmsted County, MN, 1965 to 2004

	Number	Bilateral Cases N (%)	Mean age at Diagnosis in years (Range)	Sex		Family History of Glaucoma, N (%)	Mean Initial IOP in mmHg* (Range)	Mean Initial C/D* (Range)
				M	F			
All Glaucoma types	**30**	**15 (50)**	**10.4 (0.04–19.7)**	**6**	**14**	**6 (20)**	**30.8 (14–56)**	**0.5 (0.1–1.0)**
Primary glaucoma	**5**	**5 (100)**	**12.3 (0.04–19.7)**	**2**	**3**	**2 (40)**	**28.6 (23.5–32.5)**	**0.7 (0.45– 1.0)**
1° congenital glaucoma	1	1 (100)	15 days (N=1)	1	0	0 (0)	32.5 (N=1)	0.45 (N=1)
Juvenile glaucoma	4	4 (100)	15.4 (12.7–19.7)	1	3	2 (50)	27.6 (23.5–31.0)	0.85 (0.7–1.0)
Secondary glaucoma	**6**	**3 (50)**	**6.4 (0.1–18.4)**	**2**	**4**	**1 (17)**	**19.7 (14–27.5)**	**0.35 (N=1)**
Sturge Weber	2	0 (0)	3.2 (0.1–6.3)	1	1	0 (0)	14.0 (N=1)	N/A
Cutis marmorata (CMTC)	1	1 (100)	2 months (N=1)	0	1	0 (0)	27.5 (N=1)	0.35 (N=1)
Rubenstein Taybi	1	1 (100)	7 months (N=1)	0	1	0 (0)	16.0 (N=1)	N/A
Retinopathy of Prematurity	1	1 (100)	12.8 (N=1)	0	1	1 (100)	20.0 (N=1)	N/A
Coates disease	1	0 (0)	18.4 (N=1)	1	0	0 (0)	21.0 (N=1)	N/A
Acquired glaucoma	**19**	**7 (37)**	**11.1 (3–18.8)**	**2**	**7**	**3 (16)**	**34.8 (20–56)**	**0.4 (0.1–1.0)**
Traumatic/surgical	14	3 (21)	12 (3–18.8)	1	3	2 (14)	35.5 (20–56)	0.5 (0.2–1.0)
Uveitic	4	3 (75)	9.7 (5–17.3)	1	3	1 (25)	34.6 (26.5–54)	0.25 (0.1–0.5)
Drug-Induced	1	1 (100)	4.2 (N=1)	0	1	0 (0)	26.0 (N=1)	0.35 (N=1)

*Measurements reported are from the affected eye. If both eyes were affected then the mean OD & OS measure was used.

Table 4

The Clinical and Demographic Characteristics of 24 patients < 20 years diagnosed with Glaucoma Suspect as Residents of Olmsted County, MN, 1965 to 2004

	Number of Patients	Mean age at diagnosis (yrs) (Range)	Gender		Family History of Glaucoma N (%)	Mean Initial IOP in mmHg* (Range)	Mean Initial C/D* (Range)
			M	F			
All Glaucoma Suspects	**24**	**13.7 (6.7–19.7)**	**8**	**16**	**13 (54)**	**20.1 (8.0 – 26.0)**	**0.42 (0.10 – 0.85)**
Elevated IOP > 6 months	12	14.5 (9.4–19.7)	3	9	5 (42)	16.8 (12.0 – 22.5)	0.49 (0.30 – 0.70)
C/D asymmetry/anomaly	6	10.7 (6.7–14.5)	1	5	4 (67)	23.5 (21.0 – 26.0)	0.26 (0.10 – 0.55)
Glaucoma suspects-other	6	14.8 (7.3–17.2)	4	2	4 (67)	16.6 (8.0 – 23.0)	0.59 (0.25 – 0.85)

* Measurements reported are from the affected eye. If both eyes were affected then the mean OD & OS measure was used.