Pediatric Neurology 45 (2011) 67–71

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Original Article

Prevalence of Congenital Hydrocephalus in California, 1991-2000

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ARTICLE INFORMATION

Article history:
Received 31 August 2010
Accepted 7 March 2011

ABSTRACT

In a population-based retrospective cohort of 5,353,022 California births from 1991 to 2000, 3,152 newborns were diagnosed with congenital hydrocephalus during the birth hospitalization. We compared demographic and clinical characteristics of infants with and without congenital hydrocephalus, and examined in-hospital fatality rates. The prevalence of congenital hydrocephalus was 5.9 per 10,000. During the study period, there was a decline in congenital hydrocephalus due to spina bifida (1.4 to 0.9 per 10,000), and an increase in congenital hydrocephalus due to obstructive hydrocephalus (0.5 to 1.0 per 10,000). Independent risk factors for congenital hydrocephalus were birth weight <1,500 g (odds ratio [OR] 51.6, 95% confidence interval [CI] 47.7-55.8) and birth weight 1,500-2,000 g (OR 14.1, 95% CI 12.4-16) compared to birth weight greater than 2,000 g, low socioeconomic status (OR 1.5, 95% CI 1.4-1.6), and male sex (OR 1.2, 95% CI 1.1-1.3). Asians had a decreased risk for congenital hydrocephalus (OR 0.7, 95% CI 0.6-0.8) when compared to whites. Thirteen percent of affected neonates died before hospital discharge.

Introduction

Congenital hydrocephalus is an important cause of neurologic morbidity and mortality in children. Although the widespread use of cerebrospinal fluid shunting has reduced mortality, children with hydrocephalus often face multiple surgical procedures resulting in significant morbidity [1,2]. The prevalence and demographics of congenital hydrocephalus remain poorly defined, in part because the definition of "congenital hydrocephalus" varies between studies; depending on the clinical criteria used to define congenital hydrocephalus, the prevalence has been reported between 1 and 32 per 10,000 live births [3-13]. Some studies have suggested that the prevalence of congenital hydrocephalus increased between the 1960s and 1990s [5,14,15], possibly as a result of the increased survival of extremely preterm infants. Others have found that the prevalence of congenital hydrocephalus diminished in recent years [8,12,14]. This more recent decline in diagnoses of congenital hydrocephalus has been thought to result from improved care of extremely preterm infants and the advent of folic acid enrichment of food, but it may also be due to an increasing rate of fetal termination after prenatal diagnosis of congenital hydrocephalus [14,16].

Previous studies of congenital hydrocephalus incidence have mostly been limited by small sample size [3,9,10,12,13,17,18]. Many studies have been hospital based [5,9,17,19], and population-based studies have typically lacked an appropriate control group to allow examination of demographic and other risk factors [7,11,15,20]. The prevalence of hydrocephalus has been best studied in European populations [3,10,12,13,15,18], and only one prevalence study has been reported in the United States within the past 15 years [8]. We report the prevalence of congenital hydrocephalus diagnoses among all infants born in California hospitals during a 10-year period. We examine time trends during this period and demographic and clinical risk factors, as well as in-hospital mortality rates among infants with congenital hydrocephalus.

Patients and Methods

The California Office of Statewide Health Planning and Development (OSHPD) collects discharge abstracts for all admissions to nonfederal hospitals in California. We searched the OSHPD hospital discharge database from January 1991 to December 2000 for all newborn infants with a discharge diagnosis of hydrocephalus, as defined by any of the following ICD-CM-9 (International Classification of Disease, Ninth Revision, Clinical Modification) codes: congenital hydrocephalus (742.3); spina bifida with hydrocephalus (741.0); communicating hydrocephalus (331.3); and obstructive hydrocephalus (331.4).

The prevalence of congenital hydrocephalus was calculated as the number of newborns discharged with a diagnosis of hydrocephalus during the 10-year period of study, divided by the total number of live births recorded in the OSHPD hospital

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doi:10.1016/j.pediatrneurol.2011.03.009

discharge data set during the study period. Only newborn infants with residency zip codes in California were included.

For the purpose of this study, "high socioeconomic status" was defined as individuals with private or health maintenance organization insurances, while "low socioeconomic status" included those who have Medicaid or Medi-Cal, who are indigent, or who self-pay. Newborns were assigned to 1 of 3 birth weight strata on the basis of hospital discharge diagnoses: very low birth weight (<1,500 g), low birth weight (1,500-1,999 g), or normal birth weight (≥2,000 g). "Race/ethnicity" was defined by mother's reported race/ethnicity in the OSHPD hospital discharge record. Details regarding the discharge diagnostic codes used to determine birth weight strata have been previously described in detail [21].

Congenital hydrocephalus prevalence rates stratified by sex, race/ethnicity, birth weight, and insurance status were compared in univariate analyses by calculating odds ratios (OR) and 95% confidence intervals (95% CI) by the Cornfield method [22]. Multivariate odds ratios and 95% CI were calculated by a logistic regression model. Because congenital hydrocephalus is rare, ORs approximate the relative risk. In our multivariate analysis, we adjusted for all available demographic variables including sex, race/ethnicity, birth weight, and socioeconomic status. Case fatality rates, defined as the percentage of infants with congenital hydrocephalus who died before hospital discharge, were compared in univariate and multivariate analyses. The change in prevalence rates and case fatality rates over the 10 years of the study was analyzed by the Cochran-Armitage trend test [23].

All statistical analyses were performed with SAS software, version 8.2 [23]. The OSHPD administrative data set contains no personal identifiers. This study was approved by the institutional review board at the University of California, San Francisco.

Results

Among 5,353,022 newborns, we identified 3,152 infants who were diagnosed with congenital hydrocephalus during the birth hospitalization, providing an overall population prevalence of 5.9 per 10,000 live births. Although this prevalence decreased slightly from 6.0 to 5.7 per 10,000 live births during the 10-year study period, this did not represent a statistically significant decline ($P = 0.06$). The prevalence of hydrocephalus related to spina bifida declined significantly, however, from 1.4 to 0.9 per 10,000 live births ($P = 0.01$), while the prevalence of obstructive hydrocephalus increased significantly, from 0.5 to 1.0 per 10,000 live births ($P < 0.0001$).

Several demographic factors were independently associated with increased risk of congenital hydrocephalus (Table 1), including very low birth weight (OR 51.6, 95% CI 47.7-55.8) and low birth weight (OR 14.1, 95% CI 12.4-16.0) when compared to normal birth weight; lower socioeconomic status (OR 1.5, 95% CI 1.4-1.6); blacks/Hispanics when compared to whites (OR 1.7/1.2, 95% CI 1.5-1.9/1.1-1.3); and male sex (OR 1.2, 95% CI 1.1-1.3). Asians demonstrated a decreased risk of congenital hydrocephalus when compared to whites (OR 0.7, 95% CI 0.6-0.8).

Several other congenital anomalies were also frequently diagnosed in children with congenital hydrocephalus. Among normal birth weight infants, 27% had spina bifida and 12% had congenital heart disease (Table 2). Congenital heart disease was even more common among low birth weight infants (49%). Other conditions that were more common among low birth weight infants with congenital hydrocephalus than in normal birth weight infants were intracranial hemorrhage (64% vs 8%) and delivery by cesarean section (12% vs 3%).

Thirteen percent of infants with congenital hydrocephalus died before hospital discharge. This rate did not change over the 10-year study period (data not shown). As expected, very low birth weight (OR 2.4, 95% CI 1.9-2.9) and low birth weight (OR 1.9, 95% CI 1.3-2.7) infants with congenital hydrocephalus exhibited an increased risk of mortality when compared to normal birth weight infants in multivariate analysis (Table 3). Although boys demonstrated a higher risk for developing congenital hydrocephalus, boys with congenital hydrocephalus were at lower risk for in-hospital death than girls (OR 0.8, 95% CI 0.6-0.9).

Discussion

By analyzing Californian statewide hospital discharge data, we found that overall prevalence of congenital hydrocephalus did not change during the previous decade, but the prevalence of

Table 1. Prevalence of congenital hydrocephalus among 5,353,022 births in California, 1991-2000, stratified by sex, ethnicity, birth weight, and socioeconomic status

Characteristic	N	%	Prevalence (1/10,000)	Univariate			Adjusted*		
				OR	(95% CI)	*P* Value	OR	(95% CI)	*P* Value
Hydrocephalus type									
Communicating	41	1.3	0.1	…	…	…	…	…	…
Obstructive	423	13.3	0.8	…	…	…	…	…	…
Spina bifida	544	17.2	1.0	…	…	…	…	…	…
Congenital	2,161	68.2	4.0	…	…	…	…	…	…
Birth weight (g)†									
>2,000	1,907	60.6	3.6	Ref	…	…	Ref	…	…
1,500-2,000	276	8.8	51.1	14.1	(12.4-16.0)	<0.001	13.9	(12.3-15.8)	<0.001
<1,500	964	30.6	184.2	51.6	(47.7-55.8)	<0.001	50.7	(46.8-54.8)	<0.001
Sex									
Female	1,423	45.1	5.4	Ref	…	…	Ref	…	…
Male	1,729	54.9	6.3	1.2	(1.1-1.3)	<0.001	1.2	(1.1-1.3)	<0.001
Ethnicity									
White	1,123	35.6	5.4	Ref	…	…	Ref	…	…
Black	328	10.4	9.1	1.7	(1.5-1.9)	<0.001	1.0	(0.9-1.1)	0.86
Hispanic	1,159	36.8	6.2	1.2	(1.1-1.3)	<0.001	1.1	(1.0-1.2)	0.11
Asian	182	5.8	3.7	0.7	(0.6-0.8)	<0.001	0.7	(0.6-0.8)	<0.001
Other	360	11.4	6.7	1.3	(1.1-1.4)	<0.001	1.1	(1.0-1.2)	0.19
Socioeconomic status‡									
High	1,289	40.9	4.8	Ref	…	…	Ref	…	…
Low	1,863	59.1	7.0	1.5	(1.4-1.6)	<0.001	1.3	(1.2-1.4)	<0.001

Abbreviations:
CI = Confidence interval
OR = Odds ratio
Ref = Reference

* Adjusted for sex, ethnicity, birth weight, and socioeconomic status

† Five cases did not have birth weight data and thus are excluded

‡ Socioeconomic status is determined by health insurance status. Lower socioeconomic status includes patients with government insurance, no insurance, or who are self-pay. Higher socioeconomic status includes patients with private or health maintenance organization insurance

Table 2. Conditions associated with increased risk of congenital hydrocephalus among 5,353,022 births in California, 1991-2000, stratified by birth weight

Condition	Birth Weight >2,000 g (n = 1,911)			Birth Weight <2,000 g (n = 1,240)		
	%*	OR†	95% CI	%	OR	95% CI
Congenital anomaly						
Spina bifida	26.7	54.8	(36.6-82.0)	3	2614.5	(2308.2-2961.5)
Congenital heart disease	11.8	5.1	(4.6-5.7)	49	19.7	(17.2-22.7)
Chromosomal anomaly	2.6	4.0	(2.6-6.0)	2	84.4	(58.8-120.9)
Multiple congenital anomalies	0.8	2.3	(0.8-6.2)	0	124.8	(74.3-209.8)
Intracranial hemorrhage						
Any	8.1	22.8	(20.3-25.6)	64	134.0	(113.1-158.9)
Intraventricular	5.5	20.9	(18.6-23.4)	53	267.9	(218.2-328.9)
Infection						
Meningitis	1.2	19.3	(14.5-25.8)	5	71.3	(46.6-109.1)
Cytomegalovirus	0.5	2.8	1.4-5.6)	1	119.2	(63.2-224.8)
Toxoplasmosis	0.3	3.0	(1.6-5.6)	1	8.5	(3.6-20.6)
Rubella	0.1	5.4	(0.7-40.5)	0	162.5	(39.1-675.2)
Birth characteristics‡						
Multiple gestation	4.4	0.7	(0.6-0.8)	17	2.5	(2.0-3.1)
Cesarean section	3.2	0.8	(0.6-0.9)	12	2.9	(2.3-3.8)
Birth asphyxia	2.7	2.1	(1.6-2.7)	5.0	6.8	(5.1-8.9)

Abbreviations:
CI = Confidence interval
OR = Odds ratio
Ref = Reference

* The percentage of infants with congenital hydrocephalus who also have the condition listed in the first column

† The odds of being diagnosed with congenital hydrocephalus if a newborn has the accompanying condition listed in column 1, compared to the odds of hydrocephalus among infants without this other condition

‡ Data from 3 additional patients with hydrocephalus and a brain tumor are not included here as a result of small numbers

congenital hydrocephalus due to spina bifida decreased. Low birth weight, low socioeconomic status, male sex, and black and Hispanic ethnicity were all related to an increased risk of congenital hydrocephalus; Asian ethnicity was associated with a lower risk for congenital hydrocephalus. Overall, 13% of affected neonates died before hospital discharge.

In this largest population-based study of congenital hydrocephalus yet reported in the United States, the prevalence of congenital hydrocephalus in California was 5.9 per 10,000 live births from 1991 to 2000. This finding falls within the range of previously reported prevalence rates from recent studies performed in developed countries (2.5 to 10.4 per 10,000 live births) [4,8,10,12,13,15,24].

Similar to previous findings from other studies in the United States [8] and Sweden [12], the prevalence of congenital hydrocephalus decreased during our study period, with the strongest decline observed in hydrocephalus related to spina bifida. Possible etiologies for this decline include implementation of folic acid supplementation, improved care of extremely preterm infants, and improved prenatal diagnosis leading to pregnancy termination.

The recent decline in the overall rate of neural tube defects including spina bifida in the United States has been attributed to increased folic acid supplementation [25]. The US Public Health Service first recommended folic acid supplementation in 1992, and the Institute of Medicine followed in 1998. A meta-analysis of studies from 1965 to 2005 found a modest decrease in risk of overall congenital hydrocephalus with multivitamin and folate supplementation [26]. Our study confirmed a decrease in the prevalence of spina bifida-related congenital hydrocephalus during the time period of increased multivitamin supplementation. Of note, even in countries where folic supplementation has not been implemented, improved prenatal diagnosis leading to pregnancy termination is thought to have decreased the prevalence of hydrocephalus related to spina bifida [4,12]. In the United States, although several states reported elective terminations in about 30% of total cases of neural tube defects [8,27,28], the decline in the overall rate of neural tube defects was observed before widespread availability of prenatal diagnostic services [29].

Similar to a previous study [12], we also found a trend of increasing prevalence of obstructive congenital hydrocephalus during the past decade (Fig 1). It is well documented that low birth weight infants have an increased risk of congenital hydrocephalus [3,8-10]. This occurrence is not surprising, given the increased risk of intracranial hemorrhage in premature infants, leading to obstructive hydrocephalus. A prior population-based study of congenital hydrocephalus in Sweden found that the prevalence of intracranial hemorrhage in premature infants was roughly double that of term

Table 3. In-hospital mortality rates among 3,152 newborn infants with congenital hydrocephalus in California, 1991-2000

Characteristic	% Died	Univariate			Adjusted*		
		OR	95% CI	*P* Value	OR	95% CI	*P* Value
Birth weight (g)							
>2,000	9.6	Ref	…	…	Ref	…	…
1,500-2,000	16.7	1.9	(1.3-2.6)	0.00	1.9	(1.3-2.7)	<0.001
<1,500	20.0	2.4	(1.9-2.9)	<0.001	2.4	(1.9-3.0)	<0.001
Sex							
Female	15.2	Ref	…	…	Ref	…	…
Male	12.2	0.8	(0.63-0.9)	0.01	0.8	(0.6-0.9)	0.01
Ethnicity							
White	11.2	Ref	…	…	Ref	…	…
Black	16.5	1.6	(1.1-2.2)	0.01	1.4	(1.0-2.1)	0.05
Hispanic	14.4	1.3	(1.0-1.7)	0.02	1.4	(1.0-1.8)	0.02
Asian	14.8	1.4	(0.9-2.2)	0.15	1.4	(0.9-2.2)	0.14
Socioeconomic status†							
High	13.2	Ref	…	…	Ref	…	…
Low	13.8	1.1	(0.9-1.3)	0.61	1.0	(0.8-1.2)	0.87

Abbreviations:
CI = Confidence interval
OR = Odds ratio
Ref = Reference

* Adjusted for sex, ethnicity, birth weight, and socioeconomic status

† Socioeconomic status is determined by health insurance status. Lower socioeconomic status includes patients with government insurance, no insurance, or who are self-pay. Higher socioeconomic status includes patients with private or health maintenance organization insurance

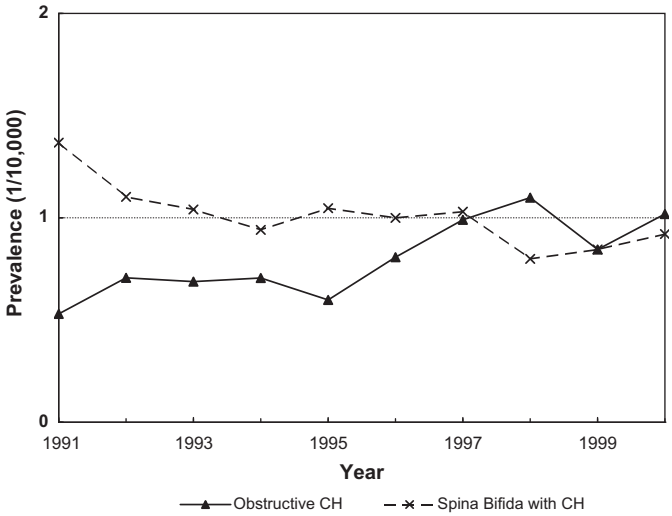

Figure 1. Trends in prevalence of obstructive hydrocephalus and hydrocephalus with spina bifida in California, 1991-2000.

infants (31% vs 12%) [6,7]. In our study, this effect was even more pronounced (63.7% vs 8.1%), which may be reflective of the increased survival of extremely premature infants over the last 2 decades.

The only prior study examining socioeconomic status as a predictor for congenital hydrocephalus found a similar result to our study [17]. Why low socioeconomic status is associated with increased risk of congenital hydrocephalus is unknown. Although women with low socioeconomic status are at higher risk of having an infant with low birth weight [30], the association between socioeconomic status and congenital hydrocephalus persisted after adjusting for birth weight. Whether genetic stressors or environmental factors such as access to prenatal counseling might affect the risk of congenital hydrocephalus independently from the risk of low birth weight in the setting of low socioeconomic status deserves further study.

In our study, we were able to confirm a male predominance, which has been noted in other studies of congenital hydrocephalus [3,6,8,12,15,17,31] but only achieved statistical significance in one [3]. Although X-linked aqueductal stenosis occurs only in boys, it is extremely rare (1 per 30,000 births) and does not fully explain the sex association we observed.

Within California's large multiethnic population, we found that Asians have a decreased prevalence of congenital hydrocephalus when compared to whites. The US Centers for Disease Control and Prevention published a report describing a decreased prevalence of spina bifida in the Asian population [29]. The lowest reported prevalence of congenital hydrocephalus in the literature (1 per 10,000) was reported in China [32]. However, a more recent study from China reported an overall prevalence rate of 7 per 10,000 [11], which is similar to rates found in white countries. Furthermore, a study in Hawaii of 244 cases of congenital hydrocephalus did not find a statistical difference between white, Far East Asian, Pacific Islander, and Filipino ethnicities [8].

Death by 1 year of age occurs in 14-51% [3,9,15,17,19] of infants with congenital hydrocephalus. Our case fatality rate was lower (13%), as we did not follow newborns after hospital discharge.

A major limitation of our study, as in any study that uses administrative data, is the variability with which hospital discharge diagnosis coding is performed. That is, the discharge diagnostic criteria used to determine the presence of congenital hydrocephalus may differ between hospitals and individual coders, and it is difficult to know the degree to which this variation may be associated with other sources of variation, such as infant's race/ethnicity or socioeconomic status. Thus, it is possible that some of the findings could result from ascertainment bias. In addition, our database only includes cases of congenital hydrocephalus that were determined at the time of birth hospitalization.

Despite this limitation, our large sample size and population-based control data allowed us to determine demographic risk factors for congenital hydrocephalus, which has been difficult to evaluate in previous case series. Although the prevalence of congenital hydrocephalus due to spina bifida decreased in the previous decade, spina bifida only accounted for 9% of all cases. Thus, a further understanding of the underlying risk factors and causes of congenital hydrocephalus is needed to develop improved preventative and treatment strategies.

YW was funded in part by NIH K02 NS46688. MW was funded in part by the Lewis Chair in Brain Tumor Research, and NIH grants R01CA52689 and P50CA097257. NG was supported by NIH K08 NS055061.

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