Descriptive Epidemiology of Congenital Hydrocephaly in Hawaii, 1986-2000

Mathias B. Forrester BS and and Ruth D. Merz MS

Mathias B. Forrester BS

Ruth D. Merz MS

Authors:
Hawaii Birth Defects Program, Honolulu, HI 96817

This research was supported by a contract with the Hawaii State Department of Health Children With Special Health Needs Branch, and grants from the Centers for Disease Control and Prevention, Ronald McDonald's Childrens Charities, March of Dimes Birth Defects Foundation, George F. Straub Trust, Queen Emma Foundation, Pacific Southwest Regional Genetics Network, and Kamehameha Schools/Bishop Estate.

Correspondence to:
Ruth D. Merz MS
Administrator, Hawaii Birth Defects Program
76 North King Street, #208
Honolulu, HI 96817-5157
Tel: 808-587-4120
Fax: 808-587-4130
E-Mail: hbdp@crch.hawaii.edu

Abstract

Using data from a birth defects registry, this study examined the epidemiology of hydrocephaly in Hawaii during 1986-2000. There were 294 cases of hydrocephaly, resulting in a rate of 10.4 per 10,000 live births. The hydrocephaly rate was lower with increased maternal age and female sex and higher with lower birth weight, lower gestational age, and multiple gestation pregnancy.

Introduction

Congenital hydrocephaly, enlargement of the cerebral ventricles and excessive accumulation of cerebrospinal fluid (CSF) in the cranium, is one of the most common congenital central nervous system (CNS) defects. Its prevalence in the United States has been reported to be 7-15 per 10,000 births.[1-4]

Congenital hydrocephaly is heterogenous in etiology, occurring secondary to other CNS defects (spina bifida, Arnold-Chiari malformation, holoprosencephaly, hydranencephaly, cysts, and tumors); chromosomal abnormalities (trisomies 13 and 18, 9(p), and triploidy); other syndromes (Walker-Wardburg, Meckel, Smith-Lemli-Opitz, and achondroplastic dwarfism); congenital infections (toxoplasmosis, syphilis, cytomegalovirus, rubella); and intraventricular hemorrhage.[5-7] However, in a number of cases the cause of congenital hydrocephaly is not known. A large percentage of infants with hydrocephaly have other birth defects as well.[6,8-10]

There have been few population-based studies exclusively examining the descriptive epidemiology of hydrocephaly,[6,8,11-14] only one of which was performed in the United States.[3] However, these and other investigations that included hydrocephaly among other birth defects have reported hydrocephaly risk to be influenced by sex,[3,4,6,12,14-17] plurality,[16,18-20] gestational age,[6] birth weight,[6,16,21] time period,[11-13,16] race/ethnicity,[22,23] and maternal age.[11]

The purpose of this investigation was to examine the relationship between congenital hydrocephaly and a variety of diagnostic and demographic factors in Hawaii during a recent fifteen-year period.

Methods

Data were provided by the Hawaii Birth Defects Program (HBDP), an active, statewide birth defects surveillance registry.[24] Inclusion criteria for the HBDP consists of all infants and fetuses of all pregnancy outcomes (live births, fetal deaths, elective terminations) regardless of gestational age where the pregnancy ended in Hawaii and one or more reportable birth defects had been diagnosed between conception and one year after delivery. Trained HBDP staff review records at all birth and pediatric tertiary care hospitals, facilities that perform elective terminations secondary to fetal anomaly, cytogenetic laboratories, and genetic counseling centers and all but one of the prenatal ultrasound facilities in the state to identify eligible infants and fetuses and to collect diagnostic, demographic, and health information.

This study included as cases all pregnancy outcomes with congenital hydrocephaly delivered in Hawaii during 1986-2000. Diagnoses of congenital hydrocephaly included the following terminology: hydrocephaly, ventriculomegaly, (cerebral) ventricular dilation/dilatation, enlarged (cerebral) ventricles. Measurements of ventricular size or CSF pressure were not used for case criteria because such information was not readily found in the medical records available to the HBDP. Cases of hydrocephaly associated with spina bifida (n=77) were excluded from this analysis to be consistent with the definition of hydrocephaly included in the National Birth Defects Prevention Network annual report[25] and to allow for comparison with some of the literature which also excluded cases of hydrocephaly associated with spina bifida or neural tube defects.[6,13,14] Cases of hydranencephaly (n=13) were also excluded from the analyses, as were all cases where the hydrocephaly diagnosis was listed as "possible" or "probable" (n=18). The HBDP does not collect cases of hydrocephaly secondary to intraventricular hemorrhage.

The total rate of hydrocephaly was calculated and the defect's distribution by pregnancy outcome determined. The proportion of cases with other major birth defects was identified and the distribution of other birth defects listed. The hydrocephaly rate by delivery year was computed and evaluated for secular trends. No attempt was made to adjust the year of delivery for elective terminations and fetal deaths should the

pregnancies have gone to term.

The hydrocephaly rate was calculated by maternal age, infant sex, plurality, gestational age (for live births alone), birth weight (for live births alone), residence at delivery, and maternal race/ethnicity. The rates among the various subgroups were then compared by calculating the rate ratio.

Residence at delivery was categorized as county and also whether the woman lived in metropolitan Honolulu (zip codes starting with 968) or the rest of Hawaii (zip codes starting with 967). Deliveries to non-Hawaii residents (n=11) were excluded from the analysis of residence. Maternal race/ethnicity was classified as white, Far East Asian (Japanese, Chinese, Korean), Pacific Islander (Hawaiian, Samoan, Guamanian), and Filipino. Maternal race/ethnicity listed as other (n=28) or unknown (n=11) was excluded from the analysis of race/ethnicity. Values were not always available for all of the variables, so the sums of the subgroups will not always equal the total number of cases.

Denominators were obtained from the Hawaii Department of Health Office of Health Status Monitoring as derived from birth certificates. Fetal death certificate information was not also used because the data were considered to be less complete. Ninety-five percent confidence intervals (CIs) were calculated by Poisson probability. Secular trends were analyzed by the Chi-square tests for trend.

Results

There were a total of 294 cases of congenital hydrocephaly identified in Hawaii among 1986-2000 deliveries. At the same time there were 281,866 total live births, so the resulting hydrocephaly rate was 10.4 per 10,000 live births (95% CI 9.3-11.7). Live births comprised 255 (86.7%) of the cases, while 21 (7.1%) were fetal deaths and 48 (16.3%) were elective terminations. If fetal deaths and elective terminations were excluded, the hydrocephaly rate was 9.1 per 10,000 live births (95% CI 8.0-10.2).

Of the total hydrocephaly cases, 86 (29.3%) were isolated and 208 (70.7%) had other major birth defects. A list of other birth defects diagnosed among hydrocephaly cases is provided in Table 1. The most common other structural birth defects were microcephaly, ventricular septal defect, and cleft lip with/without cleft palate. The results of a cytogenetic analysis was known for 135 (45.9%) of the cases. Chromosomal abnormalities were detected in 26 cases (8.8% of all of the cases or 19.3% of those cases with a cytogenetic analysis). The more common chromosomal abnormalities were trisomy 21, trisomy 18, trisomy 13, and Turner syndrome. An additional 26 (8.8%) of the cases had other syndromes, the most common of which were Sotos syndrome, Aicardi syndrome, amniotic band anomalad, and Pfeiffer syndrome.

Table 1.— Distribution of other major birth defects in congenital hydrocephaly cases, Hawaii, 1986-2000.

Diagnosis	Number	%
Anencephaly	2	0.7
Encephalocele	7	2.4
Holoprosencephaly	5	1.7
Microcephaly	25	8.5
Anophthalmia/Microphthalmia	8	2.7
Cataract	2	0.7
Glaucoma	1	0.3
Anotia/microtia	2	0.7
Truncus arteriosus	2	0.7
Transposition of great arteries	3	1.0
Tetralogy of Fallot	4	1.4
Single ventricle	1	0.3
Ventricular septal defect	22	7.5
Atrial septal defect	11	3.7
Endocardial cushion defect	1	0.3
Pulmonary valve atresia and stenosis	6	2.0
Aortic valve stenosis	2	0.7
Coarctation of aorta	3	1.0
Interrupted aortic arch	1	0.3
Choanal atresia or stenosis	4	1.4
Cleft palate	6	2.0
Cleft lip with/without cleft palate	17	5.8
Esophageal atresia and/or tracheoesophageal fistula	3	1.0
Pyloric stenosis	3	1.0
Small intestinal atresia/stenosis	3	1.0
Rectal and large intestinal atresia/stenosis	4	1.4
Malrotation of intestines	1	0.3
Hypospadias and epispadias	8	2.7
Renal agenesis/hypoplasia	1	0.3
Cystic kidney	7	2.4
Obstructive genitourinary defect	10	3.4
Congenital hip dislocation	4	1.4
Polydactyly	3	1.0
Syndactyly	11	3.7
Reduction deformity of upper limbs	4	1.4
Reduction deformity of lower limbs	1	0.3
Craniosynostosis	10	3.4
Diaphragmatic hernia	3	1.0
Omphalocele	3	1.0
Gastroschisis	1	0.3
Chromosomal abnormalities	26	8.8
Trisomy 21	6	2.0
Trisomy 13	2	0.7
Trisomy 18	6	2.0
Turner syndrome	2	0.7
Other syndromes	22	7.5
Aicardi syndrome	2	0.7
Amniotic band anomalad	2	0.7
Apert syndrome	1	0.3
Beare-Stevenson syndrome	1	0.3
Caudal regression syndrome	1	0.3
CHARGE association	1	0.3
Crouzon syndrome	1	0.3
Fryn syndrome	1	0.3
Neu-Laxova syndrome	1	0.3
Pallister-Killian syndrome	1	0.3
Pena-Shokeir syndrome	1	0.3
Pfeiffer syndrome	2	0.7
Prader-Willi syndrome	1	0.3
Sotos syndrome	3	1.0
Sturge-Weber syndrome	1	0.3
Waardenburg syndrome	1	0.3
Warburg syndrome	1	0.3
Total	**294**	

The list of birth defects is not intended to be comprehensive but to include those defects associated with infant mortality and morbidity, are easily diagnosed, or require health care intervention.

Table 2.— Rate per 10,000 live births of congenital hydrocephaly by various demographic and clinical factors, Hawaii, 1986-2000.

Demographic factor	Total live births	No.	Rate	Rate ratio	95% CI[a]
Maternal age (years)					
≤19	28,492	34	11.9	1.01	0.70-1.41
20-24	73,325	76	10.4	0.87	0.69-1.09
25-29	79,250	94	11.9	ref	
30-34	63,803	53	8.3	0.70	0.52-0.92
35-39	30,472	28	9.2	0.78	0.51-1.12
≥40	6,065	8	13.2	1.11	0.48-2.19
Maternal age (years) - chromosomal abnormalities excluded	28,492	33	11.6	1.01	0.69-1.42
≤19	73,325	69	9.4	0.82	0.64-1.04
20-24	79,250	91	11.5	ref	
25-29	63,803	47	7.4	0.64	0.47-0.85
30-34	30,472	24	7.9	0.69	0.44-1.02
35-39	6,065	3	4.9	0.43	0.09-1.26
≥40					
Race/Ethnicity	74,236	77	10.4	ref	
White	51,264	39	7.6	0.73	0.52-1.00
Far East Asian	78,396	88	11.2	1.08	0.87-1.33
Pacific islander	51,795	51	9.8	0.95	0.71-1.25
Filipino					
Geographic area	223,318	210	9.4	ref	
Honolulu	31,856	33	10.4	1.10	0.76-1.55
Hawaii County	27,548	29	10.5	1.12	0.75-1.61
Maui County	13,562	11	8.1	0.86	0.43-1.54
Kauai County					
Metropolitan Honolulu	84,949	69	8.1	0.74	0.58-0.94
Rest of Hawaii	195,843	215	11	ref	
Sex					
Male	144,835	157	10.8	ref	
Female	136,597	129	9.4	0.87	0.73-1.04
Birth weight (live births)					
<2,500 grams	19,752	101	51.1	11.12	9.06-13.51
≥2,500 grams	258,730	119	4.6	ref	
Gestational age (live births)					
<38 weeks	43,151	136	31.5	7.94	6.66-9.40
≥38 weeks	224,321	89	4.0	ref	
Plurality					
Singleton	274,512	275	10.0	ref	
Multiple birth	5,723	19	33.2	3.31	2.00-5.18

[a]CI, confidence interval.

The hydrocephaly rate varied widely over the time period, and no secular trend was identified (p=0.101). However, if the fifteen-year period is divided into three five-year periods (1986-1990, 1991-1995, 1996-2000), the hydrocephaly rate in 1991-1995 was higher than the rate in 1986-1990 (rate ratio 1.05, 95% CI 0.86-1.26). The hydrocephaly rate in 1996-2000 was lower than the rate in 1986-1990 (rate ratio 0.83, 95% CI 0.66-1.03) and significantly lower than the rate in 1991-1995 (rate ratio 0.79, 95% CI 0.63-0.98).

The hydrocephaly rate by various demographic and clinical factors is presented in Table 2. Hydrocephaly rates tended to be lower for the older maternal age groups, particularly when those cases with a known chromosomal abnormality are excluded. This is more clear when maternal age is grouped as less than 30 years and 30 years or greater. In these circumstances, the hydrocephaly rate is substantially lower among the older maternal age group for all cases (rate ratio 0.79, 95% CI 0.63-0.97) and for cases without known chromosomal abnormalities (rate ratio 0.69, 95% CI 0.54-0.87).

The rate of hydrocephaly varied among the four racial/ethnic groups, but the differences were not statistically significant. Hydrocephaly rates did not differ significantly by county of residence but were substantially lower in metropolitan Honolulu when compared with the rest of the state. Although the hydrocephaly rate was higher among males than females, the difference was not statistically significant. The rate of hydrocephaly was markedly higher among multiple births and live births with lower birth weight and gestational age.

Discussion

This population-based study examined the descriptive epidemiology of congenital hydrocephaly during a recent fifteen-year period. Although other population-based studies in the United States have examined hydrocephaly, in addition to a number of other birth defects, with respect to one or several potential risk factors, there is only one other known population-based investigation in this country that focused on hydrocephaly and a variety of demographic and clinical variables.[3]

The total hydrocephaly rate identified in this study (10.4 per 10,000 live births) is higher than that reported for New York (7.8),[1] California (7.6),[2] and Utah (7.0),[3] and lower than the rate for Alabama (15.2).[4] However, hydrocephaly rates appear to vary widely within the United States.[25] The differences in rates may reflect differences in case definition, ascertainment (active, passive), and types of pregnancy outcomes included (live births, fetal deaths, elective terminations).

Over 70% of the hydrocephaly cases in the current investigation had other major birth defects. This is higher than the 40%-55% rates reported in other studies,[6,8-10] although it is consistent with the 70%-80% rate presented in a review article.[5] The differences in rates between the present study and the literature may be due to differences in thoroughness of identification of additional birth defects or definition of additional birth defect. The chromosomal abnormality rate for hydrocephaly was higher than the 5% reported in another study[6] but consistent with the 8-10% mentioned in others.[8,12] The more common types of chromosomal abnormalities observed among the hydrocephaly cases (trisomies 21, 13, and 18) had been reported in the literature.[2,5,6]

The hydrocephaly rate varied widely over time, and no clear secular trend was identified. However, the rate in the last five-year period of the study was lower than in the previous time periods. While several previous investigations had reported a decline in hydrocephaly rates,[11,13] others reported an increase[12,16] or no change.[3,26] The recent decline in hydrocephaly rates in Hawaii is not believed to be due to decreased ascertainment of diagnosed cases because the ascer-

tainment procedures have not changed. There may have been a decline in the diagnosis of hydrocephaly, particularly of the more mild cases; however, there is no way to examine this potential explanation with the information available in the HBDP. A recent decline in the rate of neural tube defects has been tentatively linked to increased folic acid supplementation and fortification.[27] Several studies have suggested that multivitamin and folic acid use may reduce risk of hydrocephaly,[28-30] although the reduction observed in the studies was modest.

This study found that hydrocephaly rates were lower among older maternal age groups. This varies from several other investigations, which had reported either no association between maternal age and hydrocephaly risk[6,31] or increased risk with a maternal age of 37 years or greater.[11] The racial/ethnic variation in hydrocephaly rates observed in the present study were not statistically significant. Although several investigations had noted differences in hydrocephaly rates by race/ethnicity,[22,23] others had not.[4,6,17,32]

Hydrocephaly rates were significantly lower in metropolitan Honolulu than the rest of Hawaii. Another study reported no relationship between hydrocephaly and residence.[6] That hydrocephaly was slightly more common in males was consistent with the literature.[3,4,6,12,14-17]

The observation that hydrocephaly risk was elevated with lower gestation age and birth weight and with multiple gestation pregnancies had also been reported by other investigations.[6,16,18-21,33] Multiple gestation pregnancies generally have lower birth weights and shorter gestations; thus some of the association between hydrocephaly risk and plurality may reflect the relationship between hydrocephaly and these other factors. Hydrocephaly rates may be higher with lower birth weight and gestational age because if the hydrocephaly is prenatally diagnosed the physician may plan to deliver the infant early to minimize trauma during birth. Alternatively, the hydrocephaly may be a consequence of preterm delivery or both hydrocephaly and preterm delivery may be associated with another factor.

One limitation of the investigation is the relatively small number of cases, particularly when divided among subgroups. However, a number of statistically significant results were observed. Another restriction of this study was the classification of hydrocephaly. Due to the nature of the data available to the HBDP, classification of hydrocephaly could not be based on size of the cerebral ventricles or excessive accumulation of CSF. Cases were included if the data sources reported a diagnosis of hydrocephaly or described enlargement of the cerebral ventricles (ventriculomegaly, dilated cerebral ventricles, etc.). As a result, a portion of the cases included in the study may not be considered "true" cases of hydrocephaly. However, considering birth defects registries in the United States use similar data sources,[24] it is likely that hydrocephaly investigations based on data from other registries will have similar problems. Moreover, the results of this investigation were generally consistent with that of other studies, the majority of which did not indicate their inclusion criteria for hydrocephaly.

In conclusion, this population-based investigation in Hawaii found the hydrocephaly rate and relationship between the defect and maternal race/ethnicity, infant sex, birth weight, gestational age, and plurality to be consistent with the literature. However, the associations of hydrocephaly with maternal age and residence at delivery had not been previously reported.

Acknowledgements

We wish to thank Dr. Laurence N. Kolonel for serving as program principal investigator, Edward R. Diaz for computer assistance, A. Michelle Weaver and Amy M. Yamamoto for data collection, the staff of the Office of Health Status Monitoring at the Hawaii Department of Health for providing data for determining denominators, and the 33 participating Hawaii health facilities who allowed us access to their patient data.

References

1. Sekhobo JP, Druschel CM. An evaluation of congenital malformations surveillance in New York State: an application of Centers for Disease Control and Prevention (CDC) guidelines for evaluating surveillance systems. Public Health Rep. 2001;116:296-305.
2. Torfs CP, Christianson RE. Anomalies in Down syndrome individuals in a large population-based registry. Am J Med Genet. 1998;77:431-438.
3. Blackburn BL, Fineman RM. Epidemiology of congenital hydrocephalus in Utah, 1940-1979: report of an iatrogenically related "epidemic". Am J Med Genet. 1994;52:123-129.
4. Finley WH, Gustavson KH, Hall TM, Hurst DC, Barganier CM, Wiedmeyer JA. Birth defects surveillance: Jefferson County, Alabama, and Uppsala County, Sweden. South Med J. 1994;87:440-445.
5. Schrander-Stumpel C, Fryns JP. Congenital hydrocephalus: nosology and guidelines for clinical approach and genetic counselling. Eur J Pediatr. 1998;157:355-362.
6. Stoll C, Alembik Y, Dott B, Roth MP. An epidemiologic study of environmental and genetic factors in congenital hydrocephalus. Eur J Epidemiol. 1992;8:797-803.
7. Vintzileos AM, Ingardia CJ, Nochimson DJ. Congenital hydrocephalus: A review and protocol for perinatal management. Obstet Gynecol. 1983;62:539-549.
8. Christensen JH, Hansen LK, Garne E. Medfodt hydrocephalus - forekomst og prognose. Ugeskr Laeger. 2003;165:466-469.
9. Stoll C, Alembik Y, Dott B, Roth MP, Finck S. Evaluation of prenatal diagnosis by a registry of congenital anomalies. Prenat Diagn. 1992;12:263-270.
10. Castilla EE, Lopez-Camelo JS. The surveillance of birth defects in South America: I. The search for time clusters: epidemics. In: *Advances in Mutagenesis Research*. Springer-Verlag, New York. 1990;pp. 191-210.
11. Sipek A, Gregor V, Horacek J, Masatova D. Vrozeny hydrocefalus v obdobi 1961-2000 - vyskyt, prenatalni diagnostika a prevalence podle veku matky. Ceska Gynekol. 2002;67:360-364.
12. Glinianaia SV, Rankin J. Congenital hydrocephalus: occurrence and outcome. A population-based study in the North of England, 1985-1996. Eur J Pediatr Surg. 1999;9 Suppl 1:46.
13. Stone DH, Womersley J, Sinclair T, Evans L. Declining prevalence of hydrocephalus. Eur J Epidemiol. 1989;5:398-399.
14. Fernell E, Uvebrant P, von Wendt L. Overt hydrocephalus at birth - origin and outcome. Child's Nerv Syst. 1987;3:350-353.
15. Lary JM, Paulozzi LJ. Sex differences in the prevalence of human birth defects: a population-based study. Teratology. 2001;64:237-251.
16. Riley MM, Halliday JL, Lumley JM. Congenital malformations in Victoria, Australia, 1983-95: an overview of infant characteristics. J Paediatr Child Health. 1998;34:233-240.
17. Lowry RB, Thunem NY, Silver M. Congenital anomalies in American Indians of British Columbia. Genet Epidemiol. 1986;3:455-467.
18. Ramos-Arroyo MA. Birth defects in twins: study in a Spanish population. Acta Genet Med Gemellol (Roma). 1991;40:337-344.
19. Kallen B. Congenital malformations in twins: a population study. Acta Genet Med Gemellol (Roma). 1986;35:167-178.
20. Layde PM, Erickson JD, Falek A, McCarthy BJ. Congenital malformation in twins. Am J Hum Genet. 1980;32:69-78.
21. Mili F, Edmonds LD, Khoury MJ, McClearn AB. Prevalence of birth defects among low-birth-weight infants. A population study. Am J Dis Child. 1991;145:1313-1318.
22. Shaw GM, Carmichael SL, Nelson V. Congenital malformations in offspring of Vietnamese women in California, 1985-97. Teratology. 2002;65:121-124
23. Chavez GF, Cordero JF, Becerra JE. Leading major congenital malformations among minority groups in the United States, 1981-1986. Mor Mortal Wkly Rep CDC Surveill Summ. 1988;37:17-24.
24. National Birth Defects Prevention Network. State birth defects surveillance programs directory. Teratology. 2002;66:S59-S128.
25. National Birth Defects Prevention Network. Birth defects surveillance data from selected states, 1995-1999. Teratology. 2002;66:S129-S211.
26. Gucciardi E, Pietrusiak MA, Reynolds DL, Rouleau J. Incidence of neural tube defects in Ontario, 1986- 1999. CMAJ. 2002;167:237-240.
27. Williams LJ, Mai CT, Edmonds LD, Shaw GM, Kirby RS, Hobbs CA, Sever LE, Miller LA, Meaney FJ, Levitt M. Prevalence of spina bifida and anencephaly during the transition to mandatory folic acid fortification in the United States. Teratology. 2002;66:33-39.
28. Werler MM, Hayes C, Louik C, Shapiro S, Mitchell AA. Multivitamin supplementation and risk of birth defects. Am J Epidemiol. 1999;150:675-682.
29. Czeizel AE. Prevention of congenital abnormalities by periconceptional multivitamin supplementation. BMJ. 1993;306:1645-1648.
30. Czeizel AE, Toth M, Rockenbauer M. Population-based case control study of folic acid supplementation during pregnancy. Teratology. 1996;53:345-351.
31. Hollier LM, Leveno KJ, Kelly MA, McIntire DD, Cunningham FG. Maternal age and malformations in singleton births. Obstet Gynecol. 2000;96:701-706.
32. Leck I, Lancashire RJ. Birth prevalence of malformations in members of different ethnic groups and in the offspring of matings between them, in Birmingham, England. J Epidemiol Community Health. 1995;49:171-179.
33. Doyle PE, Beral V, Botting B, Wale CJ. Congenital malformations in twins in England and Wales. J Epidemiol Community Health. 1991;45:43-48.