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FIVE YEAR NEURODEVELOPMENTAL OUTCOME OF NEONATAL DEHYDRATION

Gabriel J. Escobar, MD^{1,2}, Petra Liljestrand^{1,3}, Esther S. Hudes, PhD³, Donna M. Ferriero, MD^{4,5}, Yvonne W. Wu, MD, MPH^{4,5}, Rita J. Jeremy, PhD⁵, and Thomas B. Newman, MD, MPH^{1,3,5}

¹Kaiser Permanente Medical Care Program, Division of Research, Perinatal Research Unit, 2000 Broadway, 2nd floor, Oakland, California 94612, 510-891-3502, 510-891-3408 (fax), gabriel.escobar@kp.org

²Kaiser Permanente Medical Center, Department of Inpatient Pediatrics, 1425 S. Main St., Walnut Creek, California 94596

³University of California, San Francisco, Department of Epidemiology and Biostatistics, UCSF Box 0560, San Francisco, California 94143

⁴University of California San Francisco, Department of Neurology, Box 0663, 521 Parnassus Ave. C215, San Francisco, CA 94143-0663

⁵University of California San Francisco, Department of Pediatrics, Box 0105, 505 Parnassus Ave, San Francisco, CA 94143

Abstract

Objective—To determine the long-term outcome of neonatal dehydration.

Study design—We identified 182 newborns rehospitalized with dehydration (weight loss $\geq 12\%$ of birth weight and/or serum sodium ≥ 150 mEq/L) and 419 randomly selected controls from a cohort of 106,627 term and near-term infants ≥ 2000 g born from 1995 through 1998 in Northern California Kaiser Permanente hospitals. Outcomes data were obtained from electronic records, interviews, questionnaire responses, and neurodevelopmental evaluations performed in a masked fashion.

Results—Follow-up data to the age of at least two years were available for 173/182 children with a history of dehydration (95%) and 372/419 controls (89%) and included formal evaluation at a mean ($\pm$ SD) age of 5.1 ± 0.12 years for 106 children (58%) and 168 children (40%) respectively. None of the cases developed shock, gangrene, or respiratory failure. Neither crude nor adjusted scores on cognitive tests differed significantly between groups. There was no significant difference between groups in the proportion of children with abnormal neurologic examinations or neurologic diagnoses. Frequencies of parental concerns and reported behavior problems also were not significantly different in the two groups.

Conclusions—Neonatal dehydration in this managed care setting was not associated with adverse neurodevelopmental outcomes in infants born at or near term.

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Keywords

dehydration; neonatal; hypernatremia; neurodevelopmental outcome; breastfeeding

Long-term outcomes of neonatal dehydration, which in developed nations usually results from problems with establishing breastfeeding, are not known. In recent studies, rehospitalization for neonatal dehydration has been reported in 0.25 to 5.9/1000 live births.(1–6) Estimates of the risk of the long-term consequences of neonatal dehydration are based on either catastrophic cases(7) or the outcomes of hypernatremia following diarrheal dehydration. Infants with diarrheal dehydration have had high rates (8 to 16%) of long-term neurological damage.(8–11) In developed nations, neonatal dehydration is likely to develop more slowly than diarrheal dehydration, because it is most often due to insufficient fluid intake and/or abnormally high levels of sodium^[A1] in breast milk.(12–15) For this reason, long-term sequelae of neonatal dehydration in developed nations may be less frequent or less severe than previous case series would suggest.

In this report, we focus on non-diarrheal neonatal dehydration. We studied a cohort from the Northern California Kaiser Permanente Medical Care Program (KPMCP), a mature managed care organization with integrated information systems.(6,16–20) Given the pathophysiology of dehydration, which does not appear to affect any one particular part of the brain, we did not expect to find discrete neurological deficits among our cohort. We expected to find non-specific neurodevelopmental problems affecting multiple domains (i.e., decreases in performance across multiple areas measured).

METHODS

This report covers two of the three cohorts in the **Jaundice and Infant Feeding** ("JIFee") study, a follow-up study of infants with neonatal jaundice or dehydration and randomly selected controls. We identified subjects born in 1995–96 in previous nested-case-control studies.(6, 19,21) Study participants were drawn from 1995–98 KPMCP live births (N=106,627) with birth weights of at least 2000 grams and gestational age of at least 36 weeks (1995–96 cohorts) or 34 weeks (1997–98 cohorts). Eligible subjects had to meet the dehydration definition given below (cases) or were randomly selected from the 1995–96 and 1997–98 birth cohorts (controls) (Figure). We excluded subjects who had died (N=1), whose primary care provider declined contact (N=3), or who were diagnosed with a genetic or congenital disorder likely to affect neurodevelopment (N=20). Outcomes in the hyperbilirubinemia cohort have been previously reported.(22) The study was approved by the Institutional Review Boards for the Protection of Human Subjects of the KPMCP, the University of California San Francisco, and the State of California. Parents or guardians provided written informed consent for examinations.

Definition of Dehydration

Macaulay's studies(8,9) defined hypernatremia as a serum sodium ≥ 150 mEq/L, although Maisels's work supports the notion that losing $\geq 12\%$ of birth weight is excessive.(23) To be included as a case in our study, infants had to meet the following criteria: 1) rehospitalized within 15 days of discharge from the birth hospitalization; 2) diagnosis of dehydration by the treating physician; and 3) weight loss $\geq 12\%$ of birth weight or serum sodium ≥ 150 mEq/L. To identify possible cases, we scanned the KPMCP hospitalization database for the following International Classification of Diseases (ICD)(24) diagnosis codes: 276.0 (hyperosmolality and/or hypernatremia), 276.5 (volume depletion), 276.9 (electrolyte and fluid disorders not elsewhere classified), 775.5 (other transient electrolyte disturbance), 778.4 (disturbances of temperature regulation, which includes dehydration fever), 779.3 (feeding problems), 783.2

(abnormal weight loss), 783.3 (feeding difficulties/mismanagement), 784.4 (lack of normal physiologic development), 785.50 (shock, unspecified), and 785.59 (shock, other).

Predictor variables

We obtained perinatal data on eligible subjects from mothers' and infants' medical records (6,21) and additional data on potential confounding variables from caregivers, including assessment of parental depression using the Center for Epidemiologic Studies Depression Scale (CES-D).(25) The CES-D is a 20 item self-administered questionnaire designed for screening for depression in the general population; higher scores indicate increased presence of symptoms. We used birth certificate data to categorize parent race and education (linked for 96%) and 2000 U.S. census data on median household income in census tracts (linked for 95%) when these variables were missing from questionnaires.

Outcome variables

Overview—Neurodevelopmental evaluations were performed at a mean age of 5.1 years by examiners masked to study group. Parents who declined formal evaluations were provided a questionnaire-only study option. We also searched KPMCP electronic records for these ICD neurological diagnosis codes: 320–360 (nervous system disorders); 378–378.9 (strabismus); 389.1, 389.2 (hearing loss), 773.4, 774.7 (kernicterus); 780.5 (sleep disturbance); 781, 781.2, 781.3, 781.9, (movement, gait, coordination, or posture problems); 794–794.19 (abnormal brain imaging); and 796.1 (abnormal reflexes).

Neurodevelopmental Evaluations—Licensed child psychologists administered the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R)(26), and the Beery-Buktenica Developmental Test of Visual-Motor Integration-Fourth edition (VMI-4).(27) Child neurologists and a child neurology clinical nurse specialist (2 examinations) conducted standard neurological examinations and entered an overall impression on a 5-point scale: 1: “normal”; 2: “normal/questionable”; 3: “abnormal with minimal functional disability”; 4: “abnormal with moderate functional disability”; 5: “abnormal with severe functional disability.” To maximize sensitivity, neurologists were instructed to select “normal/questionable” for anything slightly suspicious on examination. Research assistants assessed motor skills using the Motor Performance Checklist (MPC), a validated 12-item screening instrument that includes items such as throwing a ball and putting beans in a bottle; each is scored pass (0) or fail (1).(28)

Parent Questionnaires—Parents completed the Parent Evaluation of Developmental Status (PEDS)(29) and the Child Behavior Checklist (CBCL)(30) questionnaires, either as part of the formal evaluation or the questionnaire-only arm of the study (Figure). The PEDS is a 10-item instrument that asks whether parents have any concerns about areas of their child's development; answers are “No,” “Yes,” and “A little.” The CBCL is a checklist of 120 problem behaviors grouped into syndrome scales. Its ‘Internalizing score’ summarizes ‘Withdrawn,’ ‘Somatic Complaints,’ and ‘Anxious/Depressed’ syndrome scales and its ‘Externalizing score’ summarizes ‘Delinquent’ and ‘Aggressive Behavior’ syndrome scales.

Statistical analysis—We assessed bivariate associations using chi-square, Fisher's exact, rank sum or t-tests; only 2-tailed P values are reported. To test for interactions between study group and study participation, we included interaction terms in linear or logistic regression models.

For multivariate analyses of outcomes we used backward stepwise multiple regression with P to remove 0.10, with the main predictor variable (dehydration case status) forced into all models. Additional candidate predictor variables, selected based upon biological plausibility

or previous studies, included maternal and paternal race and education level, household income, maternal age, maternal smoking, gestational age, sex, small for gestational age (below 10th percentile), 5-minute Apgar score, initial exclusive breastfeeding, parental depression, and examiner. We imputed missing values for income for multivariate analyses in 7 subjects. In addition to summary scores on each of the main instruments, we looked for differences on each of the subtests of the WPPSI-R, and each item of the MPC, PEDS, and CBCL.

To address the possibility that neurological examination results might be biased due to preferential participation of controls whose parents were concerned about their child's development, we repeated analyses of neurological examinations, stratifying on whether the parents had concerns about motor problems on the PEDS.

We hypothesized that one subgroup of infants might be at increased risk of adverse outcome – those who either had a serum sodium ≥ 160 mEq/dL or weight loss $\geq 15\%$. We compared the outcomes of this group with the outcomes of the controls in separate analyses.

All statistical analyses were performed using Stata 8 (StataCorp, College Station, TX).

RESULTS

Eligibility and Enrollment

A full examination, completed parental questionnaire, or record of an outpatient visit at age 2 years or older was available on 95 percent of the dehydration group and 89 percent of the control group (Figure; $P=0.06$). Among those not formally evaluated, the age at time of the last follow-up visit (mean $\pm$ standard deviation) was 4.8 ± 2.6 years. Subjects in the dehydration group were more likely than controls to consent to formal evaluations (58 percent versus 40 percent; $P<0.001$).

We first compared demographic and clinical characteristics of the subjects with and without formal evaluations within each group. In the dehydration group, formally evaluated subjects had higher birth weights than those who were not formally evaluated (3511 vs. 3337 grams, $P=0.015$) and a lower average weight loss (12.8% vs. 14.0% of birth weight, $P=0.05$). There were no differences between dehydrated infants who were and were not formally evaluated with respect to sex, gestational age, mother's age, percent with serum sodium measured, mean serum sodium level, dehydration diagnoses, exclusive breastfeeding at the time of discharge from the birth hospitalization, number of prenatal visits, maternal education, or poverty indicators. Among controls, there were no significant differences among formally evaluated and non-evaluated infants with respect to any of the predictor variables, except for a statistically significant but clinically trivial (1 day) difference in gestational age.

Table I shows the clinical and demographic characteristics of cases and controls with and without formal evaluations. There was no evidence of bias due to refusal of formal evaluation. For example, although cases with formal evaluations were slightly more likely to have been exclusively breastfed at the time of discharge from the birth hospitalization than were cases without an evaluation (92% vs. 88%), a similar difference (64% vs 58%) was evident among controls, and neither this nor any of the other interaction terms was significant (i.e., there was no evidence of differential participation of cases and controls by any of the predictor variables).

Clinical Characteristics of the Formally Evaluated Subjects

Cases and controls with formal evaluations were similar with respect to gestational age, sex, maternal race, maternal education, father's education, and income. Cases were more likely to have mothers over age 25 (87% versus 74%, $P=0.02$) and were more likely to have been exclusively breastfed at the time of discharge (Table I). No infant had an ICD code for shock

(785.50 or 785.59). Chart review confirmed that no infant experienced shock, gangrene, or respiratory failure.

All but 15 of the 106 formally evaluated cases had a serum sodium measured, 20 (19%) had a level <150 mEq/L, 64 (60%) had a level of 150–159 mEq/L, and 7 had a level of 160–167 mEq/L. Only one of these 106 cases did not have a weight obtained at time of hospitalization, 34 (32%) had weight loss $<12\%$, 49 (46%) had weight loss of 12–14.9%, and 22 (21%) had weight loss of 15–32%. A total of 49 of the cases, or 27 (25.5%) of those with full exams, had more severe dehydration, with a serum sodium ≥ 160 mEq/L or weight loss $\geq 15\%$.

OUTCOMES

There were no significant differences between the cases and controls on the WPPSI-R or VMI-4 (Table II). Table III provides comparisons of key dichotomous outcomes and shows that children in the dehydration group were not more likely to have neurological examination scores of 2 (“questionable”) or worse (20.8% versus 28.6%; $P=0.3$), and that they were about as likely to have neurological examinations rated 3 (“abnormal with minimal disability”) or worse (7.6% vs. 7.1%, $P=0.8$). Stratifying on motor concerns on the PEDS did not alter the results. On the MPC, neither the mean total score, nor the proportion of children with scores of 4 or worse or 5 or worse differed significantly between the groups. Only one of the 12 individual items differed between the two groups; children in the dehydration group were more likely to fail the ‘copy shapes’ item (a test of fine motor skills) (40% versus 30%; $P=0.04$).

Results on the CBCL and PEDS were available for a slightly larger group of children ($N=126$ in the dehydration group and $N=239$ in the control group). On the CBCL, there were no significant differences in “Total Internalizing” or “Total Externalizing” behavior scores or on any of the eight composite scales. Of the 120 specific characteristics and behaviors addressed in the CBCL, three were statistically significantly more commonly reported for children in the dehydration group (P from rank sum test): ‘disability’ (15% vs. 7%, $P=0.019$), ‘allergy’ (42% vs. 23%, $P<0.001$), and ‘shyness’ (63% vs. 52%, $P=0.05$).

Parents of children in both groups reported an average of 1.5 concerns on the PEDS and the proportions with 1 or more concerns were also similar (21% vs. 23%; $P=0.6$). There were no differences in proportions answering “Yes” or “A little” on any item except for one. Parents of children with dehydration were more likely to report a concern about their child’s speech (26% vs. 18%; $P=0.017$). To further evaluate possible speech pathology, we looked for indications of speech problems noted by the psychologist or the neurologist; rates did not differ significantly between the groups (11% vs. 16%, $P=0.40$).

Results of outpatient visits at ≥ 2 years of age were available for 173/182 (95%) of the cases and 372/419 (89%) of the controls. Eight (4.4%) of the children in the dehydration group had any neurological diagnoses (e.g., gait abnormality), compared to 18 (4.3%) of controls (risk difference, 0.1%; 95% CI, -3.5 to $+3.7$; $P=0.96$).

We separately compared outcomes among the 27 children whose dehydration had been more severe (serum sodium ≥ 160 mEq/L and/or weight loss $\geq 15\%$) with those of controls. The outcome pattern for the entire cohort held for this subset, with a slight trend toward better scores for cases that did not persist in multivariate models. The baby with the highest serum sodium in our cohort (167 mEq/L), who experienced 23% weight loss, had some of the highest IQ scores in the sample (e.g., verbal IQ = 121, visual VMI = 130). (Table 4; available at www.jpeds.com)

DISCUSSION

In this study with prospective neurodevelopmental assessment of children who experienced neonatal dehydration, we found little evidence of adverse effects. Although our results cannot be generalized to catastrophic dehydration, they do provide reassurance that the more common possible adverse effects of dehydration, such as mild cognitive, behavioral, or motor impairment, are unlikely to occur in the type of dehydration usually seen by primary care physicians.

Because dehydrated newborns tend to be hypernatremic(1,31) the pathophysiology relevant to neonatal dehydration relates to hypernatremic states and to problems resulting from the intravenous fluid correction of such states.(7,12,13,31–34) If dehydration persists long enough, the adverse effects are similar to those mediated by acidosis and hypovolemic shock(34). However, we did not find any significant differences between cases and controls. We did not find such differences even when restricting the comparisons to the group of newborns with the greatest degree of dehydration.

Important limitations of our study must be noted. First, it is possible that favorable parent-infant interactions might be masking deficits due to the adverse effects of dehydration. Second, none of our study subjects had shock, respiratory failure, infarcts, or gangrene during their dehydration episode. Thus, our findings apply to cases of neonatal dehydration that is detected before these catastrophic events and cannot be generalized to cases of severe dehydration that have end organ damage. Third, we had a higher participation rate among dehydrated subjects than among controls. This is not surprising, because the research questions for the study were inherently less interesting for parents of the control children. If children in the participant control group were at higher risk of bad outcome than the control group as a whole, this could introduce a bias that would make the outcome among participating controls appear worse than it would have been with a more representative sample, and thus make the outcomes in the dehydration group look better in comparison. Based upon data from perinatal medical records and birth certificates, we have little evidence that this occurred. It is also reassuring that means on standardized tests in the dehydration group were uniformly and solidly average compared to national norms. Fourth, 5 years is still a young age. If non-catastrophic dehydration has subtle effects on higher cortical function, which would be manifested in difficulties with more complex tasks, assessment at 5 years might be too early to detect such effects.

Findings from our study may not be generalizable to different populations in developed nations. Our sample came from an insured population with a fairly high education level as well as a high rate of breastfeeding. These families had ready access to a number of support services (follow-up clinics and phone advice banks staffed by registered nurses) and no barriers to prompt rehospitalization.

In conclusion, our findings support current American Academy of Pediatrics recommendations for the follow-up of newborns, which specify the need to assess newborn hydration.(35) They also suggest that parents of infants who experienced rehospitalization for dehydration in the newborn period can be reassured that the episode is unlikely to have had significant adverse neurological effects.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Lee KS, Perlman M, Ballantyne M, Elliott I, To T. Association between duration of neonatal hospital stay and readmission rate. *J Pediatr* 1995;127(5):758–766. [PubMed: 7472833]
2. Edmonson MB, Stoddard JJ, Owens LM. Hospital readmission with feeding-related problems after early postpartum discharge of normal newborns. *JAMA* 1997;278(4):299–303. [PubMed: 9228435]
3. Liu L, Clemens C, Shay D, Davis R, Novack A. The safety of newborn early discharge. *JAMA* 1997;278:293–298. [PubMed: 9228434]
4. Lock M, Ray JG. Higher neonatal morbidity after routine early hospital discharge: are we sending newborns home too early? *CMAJ* 1999;161(3):249–253. [PubMed: 10463045]
5. Oddie S, Richmond S, Coulthard M. Hypernatraemic dehydration and breast feeding: a population study. *Arch Dis Child* 2001;85(4):318–320. [PubMed: 11567942]
6. Escobar G, Gonzales V, Armstrong M, Folck B, Xiong B, Newman T. Rehospitalization for neonatal dehydration: a nested case-control study. *Arch Pediatr Adol Med* 2002;156:155–161.
7. Cooper WO, Atherton HD, Kahana M, Kotagal UR. Increased incidence of severe breastfeeding malnutrition and hypernatremia in a metropolitan area. *Pediatrics* 1995;96(5 Pt 1):957–960. [PubMed: 7478844]
8. Macaulay D, Blackhall M. Hypernatraemic dehydration in infantile gastro-enteritis. *Arch Dis Child* 1961;36:543–550. [PubMed: 14467733]
9. Macaulay D, Watson M. Hypernatraemia in infants as a cause of brain damage. *Archives of Disease in Childhood* 1967;42(225):485–491. [PubMed: 6070260]
10. Morris-Jones PH, Houston IB, Evans RC. Prognosis of the neurological complications of acute hypernatraemia. *Lancet* 1967;2(7531):1385–1389. [PubMed: 4170055]
11. Chambers TL. Hypernatraemia: a preventable cause of acquired brain damage? *Developmental Medicine and Child Neurology* 1975;17(1):91–94. [PubMed: 1123126]
12. Rowland TW, Zori RT, Lafleur WR, Reiter EO. Malnutrition and hypernatremic dehydration in breast-fed infants. *JAMA* 1982;247(7):1016–1017. [PubMed: 7057575]
13. Peters JM. Hypernatremia in breast-fed infants due to elevated breast milk sodium. *Journal of the American Osteopathic Association* 1989;89(9):1165–1170. [PubMed: 2793539]
14. Morton JA. The clinical usefulness of breast milk sodium in the assessment of lactogenesis. *Pediatrics* 1994;93(5):802–806. [PubMed: 8165082]
15. Laing IA, Wong CM. Hypernatraemia in the first few days: is the incidence rising? *Arch Dis Child Fetal Neonatal Ed* 2002;87(3):F158–F162. [PubMed: 12390982]
16. Selby JV. Linking automated databases for research in managed care settings. *Ann Intern Med* 1997;127(8 Pt 2):719–724. [PubMed: 9382386]
17. Go AS, Hylek EM, Chang Y, Phillips KA, Henault LE, Capra AM, et al. Anticoagulation therapy for stroke prevention in atrial fibrillation: how well do randomized trials translate into clinical practice? *Jama* 2003;290(20):2685–2692. [PubMed: 14645310]

18. Hylek EM, Go AS, Chang Y, Jensvold NG, Henault LE, Selby JV, et al. Effect of intensity of oral anticoagulation on stroke severity and mortality in atrial fibrillation. *N Engl J Med* 2003;349(11):1019–1026. [PubMed: 12968085]
19. Newman T, Escobar G, Gonzales V, Armstrong M, Gardner M, Folck B. Frequency of neonatal bilirubin testing and hyperbilirubinemia in a large health maintenance organization. *Pediatrics* 1999;104(5 Pt 2):1198–1203. [PubMed: 10545573]
20. Escobar GJ, Joffe SJ, Gardner MN, Armstrong MA, Folck BF, Carpenter DM. Rehospitalization in the first two weeks after discharge from the Neonatal Intensive Care Unit. *Pediatrics* 1999;104(e2):1–9. [PubMed: 10390252]
21. Newman TB, Xiong BX, Gonzales VM, Escobar GJ. Prediction and prevention of extreme neonatal hyperbilirubinemia in a mature health maintenance organization. *Arch Pediatr Adol Med* 2000;154(11):1140–1147.
22. Newman T, Liljestrand P, Jeremy R, Ferriero D, Wu Y, Hudes E, et al. Outcomes among newborns with total serum bilirubin levels of 25 mg per deciliter or more. *N Engl J Med* 2006;354(18):1889–1900. [PubMed: 16672700]
23. Maisels MJ, Gifford K. Breast-feeding, weight loss, and jaundice. *Journal of Pediatrics* 1983;102(1):117–118. [PubMed: 6848709]
24. PMIC (Practice Management Information Corporation). ICD-9-CM (International Classification of Diseases, 9th Revision) Clinical Modification. 4th Edition. 1995.
25. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement* 1977;1(3):385–401.
26. Wechsler, D. The Wechsler Preschool and Primary Scale of Intelligence - Revised. San Antonio, Texas: The Psychological Corporation; 1989.
27. Beery, K. The Beery-Buktenica Developmental Test of Visual-Motor Integration - 4th Edition, Revised. Parsippany, NY: Modern Curriculum Press; 1997.
28. Gwynne K, Blick B. Motor Performance Checklist for 5-year-olds: a tool for identifying children at risk of developmental co-ordination disorder. *J Paediatr Child Health* 2004;40(7):369–373. [PubMed: 15228565]
29. Glascoe, F. Collaborating with parents: Using parent's evaluations of developmental status to detect and address developmental and behavioral problems. Ellsworth & Vandemeer Press Ltd; 1998.
30. Achenbach, T. Child Behavior Checklist /4–18 and 1991 Profile. Burlington, VT: University of Vermont, Dept. of Psychiatry; 1991.
31. Heldrich FJ, Shaw SS. Case report and review of literature: hypernatremia in breast-fed infants. *Maryland Medical Journal* 1990;39(5):475–478. [PubMed: 2185394]
32. Comay SC, Karabus CD. Peripheral gangrene in hypernatraemic dehydration of infancy. *Archives of Disease in Childhood* 1975;50(8):616–619. [PubMed: 1200677]
33. Roddey OF Jr, Martin ES, Swetenburg RL. Critical weight loss and malnutrition in breast-fed infants. *American Journal of Diseases of Children* 1981;135(7):597–599. [PubMed: 7246485]
34. Finberg, L.; Kravath, R.; Hellerstein, S. Water and electrolytes in pediatrics. Physiology, pathology and treatment. Philadelphia: W. B. Saunders Co.; 1993. Chapter 15: Hypernatremic dehydration; p. 124–134.
35. American Academy of Pediatrics Committee on Fetus and Newborn. Hospital stay for healthy term newborns. *Pediatrics* 1995;96(4 Pt 1):788–790. [PubMed: 7567351]

Figure. Selection, Enrollment, and Follow-up of Study Subjects

See text for complete description of dehydration criteria.

TABLE I
Demographic Characteristics of Subjects and Their Parents by Evaluation Status

Characteristic	No formal evaluation		P	Formal evaluation		P	P for interaction of dehydration by formal evaluation status
	Cases (Dehydrated) N = 76	Controls N = 251		Cases (Dehydrated) N = 106	Controls N = 168		
Gestational age <38 weeks (%)	15%	10%	0.27	17%	14%	0.52	.69
N (%) with sodium ≥ 160 mEq/L or weight loss $\geq 15\%$	22 (28.9%)	n/a	n/a	27 (25.5%)	n/a	n/a	n/a
Maternal age ≥ 25 years (%)	82%	72%	<0.09	87%	74%	<0.02	.58
Exclusive breast-feeding at initial discharge	88%	58%	<0.001	92%	64%	<0.001	.66
Breast fed for at least 6 months*	56%	50%	0.68	52%	45%	0.26	.92
Mother's race/ethnicity [†]			0.001			0.49	
White	34%	42%	0.24	54%	46%	0.20	.08
Black	5%	12%	0.11	3%	11%	<0.02	.46
Asian	34%	24%	0.09	17%	16%	0.84	.34
Hispanic	12%	19%	0.16	21%	23%	0.72	.39
Other/Missing	15%	4%	<0.01	6%	4%	0.57	.11
Mother any college [‡]	83%	61%	<0.001	90%	86%	0.35	.14
Father any college [‡]	78%	59%	<0.01	77%	74%	0.51	.11
Median household income for census tract of residence (\$) Median age at last recorded outpatient visit	70,417	57,349	<0.001 [§]	66,471	62,073	0.48 [§]	.09
Follow-up (visits, exams or questionnaires) to age ≥ 2 yr	5.6	5.5	0.51	6.5	6.0	0.08	.67
	88%	81%	0.16	100%	100%	n/a	n/a

^fCases were infants rehospitalized with dehydration with serum sodium ≥ 150 mEq/L and/or weight loss $\geq 12\%$ of birth weight. See text for details

* From questionnaire; available for only 68 controls and 18 cases for those without formal evaluations.

[†]From mother's self-report at the time of admission for delivery. P-values in this row are for overall chi-squared; in next 5 rows P-values are for the comparison of each race with all others.

[‡]From birth certificate for subjects who did not complete questionnaires.

[§]Rank sum test.

TABLE II

Results of Testing with the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) Test and the Beery-Buktenica Developmental Test of Visual-Motor Integration, 4th edition (VMI-4)

TEST	Cases	Controls	Adjusted Difference (95% CI) [*]	P Value
WPPSI-R [†]				
Verbal IQ				
No. of subjects	104	162		
Mean score	102.7	101.1	0.2 (−3.3 to 3.7)	0.9
Performance IQ				
No. of subjects	104	165		
Mean score	106.8	106.0	−0.8 (−4.1 to 2.6)	0.7
Full-scale IQ				
No. of subjects	104	162		
Mean score	105.3	104.0	−0.7 (−4.0 to 2.6)	0.7
VMI-4 [‡]				
Visual-motor integration				
No. of subjects	103	165		
Mean score	103.0	102.2	−0.8 (−4.0 to 2.5)	0.7
Visual perception				
No. of subjects	102	164		
Mean score	106.7	105.9	−1.0 (−5.4 to 3.4)	0.7
Motor coordination				
No. of subjects	102	165		
Mean score	101.8	100.4	−0.9 (−4.9 to 3.0)	0.6

^{*} Multiple linear regression. Models varied; most included paternal race and education.

[†] Scores on the WPPSI-R are distributed with a mean of 100 and standard deviation of 15. The range in this study was 46 to 149.

[‡] Scores on the VMI-4 are distributed with a mean of 100 and standard deviation of 15. The range in this study was 45 to 150.

Table III

Outcomes According to Neurologic Examination, Motor-Performance Checklist, Parent Evaluation of Developmental Status (PEDS) Questionnaire, and Child Behavior Checklist (CBCL).*

OUTCOME	Dehydrated group	Control group	Adjusted Odds Ratio (95% CI)	P value
Neurologic examination				
Normal	84/106 (79.3%)	120/168 (71.4%)	N/A	
Normal or questionable	14/106 (13.2%)	36/168 (21.4%)	N/A	
Abnormal with minimal disability	6/106 (5.7%)	10/168 (6.0%)	N/A	
Abnormal with moderate disability	1/106 (0.9%)	2/168 (1.2%)	N/A	
Abnormal with severe disability	1/106 (0.9%)	0/168 (0%)	N/A	
Normal or questionable, or worse	22/106 (20.8%)	48/168 (28.6%)	0.73 (0.39 – 1.36)	0.3
Abnormal with minimal disability, or worse	8/106 (7.6%)	12/168 (7.1%)	1.13(0.43 – 2.94)	0.8
Motor performance checklist (MPC) [†]				
Score >5	31/106 (29.3%)	58/167 (34.7%)	0.83 (0.48 – 1.45)	0.5
PEDS questionnaire				
At least 1 answer of "yes" [‡]	27/126(21.4%)	56/239 (23.4%)	0.86 (0.50 – 1.48)	0.6
CBCL preclinical or clinical total score [§]				
Internalizing behavior	17/123 (13.8%)	24/226(10.6%)	1.45 (0.74 – 2.87)	0.3
Externalizing behavior	13/123 (10.6%)	24/226 (10.6%)	1.06 (0.51 – 2.19)	0.9
Outpatient follow-up to age of >2yr	164/182 (90.1%)	349/419 (83.3%)	1.84 (1.04 – 3.25)	0.04
>1 Neurologic diagnosis	8/182 (4.4%)	18/419 (4.3%)	1.02 (0.44 – 2.40)	0.96

* Odds ratios and P values were calculated with the use of multiple logistic-regression analyses. The covariates included in each model are available from the investigators. CI denotes confidence interval.

[†] Higher scores indicate worse function; a score of 4 or more was considered abnormal for slightly older children (mean age 5.5 years).

[‡] A response of "yes" indicates a parent concern regarding the child's development.

[§] The internalizing score summarizes the syndrome scales for 'withdrawn,' 'somatic complaints,' and 'anxious/depressed.' The externalizing score summarizes the syndrome scales for 'delinquent behavior' and 'aggressive behavior.' A T score is classified as preclinical if it is at least 60 (approximately 1SD above the mean), and clinical if it is at least 70 (approximately 2 SD above the mean)