Incidence of Urinary Tract Infection Among Siblings of Children With Vesicoureteral Reflux

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Abstract

Background: Siblings of children with vesicoureteral reflux (VUR) are at elevated risk of VUR. Screening siblings may identify VUR before a clinical illness such as a urinary tract infection (UTI), but the benefit of screening has not been demonstrated. We sought to determine the incidence of UTI among siblings, and we hypothesized that the sibling UTI rate is similar between screened and unscreened siblings.

Methods: We performed a retrospective cohort analysis using insurance claims data (January 1, 2000, to December 31, 2009). Within each family, we identified the index VUR patient and siblings; we included siblings who were enrolled in the insurance plan from birth for at least 1 year. We identified siblings who were screened for VUR and/or had UTI. We investigated the association of screening and UTI, controlling for patient characteristics and clustering within families.

Results: Among 617 siblings (associated with 497 index patients), 317 (51%) were girls. Median insurance enrollment time was 53.0 months, with 424 enrolled ≥3 years. Among those with 1 or 3 years of enrollment, the proportions of siblings who experienced UTI was 8.4% (52 of 617) and 10.4% (44 of 424), respectively. Median age at initial UTI was 32.7 months. A total of 223 siblings (36.0%) underwent sibling screening. There was no significant difference in UTI between screened and unscreened siblings (odds ratio 1.57, 95% confidence interval 0.87–2.85; $P = .14$). In multivariate analysis, screening was not associated with sibling UTI incidence (odds ratio 1.33, 95% confidence interval 0.68–2.60; $P = .40$).

Conclusions: Although UTI is relatively common among siblings of VUR patients, there was no statistically significant difference in UTI incidence between screened and unscreened siblings.

Keywords: screening; siblings; urinary tract infection; vesicoureteral reflux

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What's New

The benefit of screening siblings for vesicoureteral reflux remains unproven. We determined sibling urinary tract infection (UTI) incidence, and we observed no difference in UTI risk between screened and unscreened siblings, suggesting that universal sibling screening may not reduce UTI risk.

IT HAS BEEN recognized for decades that vesicoureteral reflux (VUR) is common among relatives of patients with VUR, particularly siblings. Published studies report that 11% to 67% of screened siblings have VUR, with overall incidence using pooled data of 32%, and up to 46% among siblings <2 years old.[1–5] However, while it is clear that VUR is more common among siblings than among the general population (usually estimated at 1% to 2%),[6] the clinical significance of sibling VUR, as well as the potential benefit of screening siblings to identify it, remain uncertain.

Sibling screening for VUR has been widely promoted in the literature[7–9] and has in the past been common practice among pediatric urologists, as indicated in a 1998 survey.[10] However, it is unclear how widespread the practice is currently. Furthermore, the evidence in support of routine sibling screening is weak,[11] and the 2010 American Urological Association guidelines cited the lack of evidence in not recommending screening for VUR among siblings with normal renal ultrasound results.[12] Aside from VUR resolution rates in siblings with VUR,[2,13] few data exist regarding the long-term clinical outcomes of siblings. In particular, observational data on urinary tract infection (UTI) incidence among siblings (screened or unscreened) have not been reported. Because the primary benefit of sibling screening would be to prevent UTI (through identification of VUR and initiation of antimicrobial prophylaxis, surgery, or other interventions), knowledge of the incidence of UTI among the sibling population is needed if we are to assess the effectiveness of sibling screening.

In this study we sought to determine the incidence of UTI among siblings of children with VUR during the

sibling's first 3 years of life and to determine the association of screening for VUR with UTI among these siblings.

PATIENTS AND METHODS

DATA SOURCE

This study was a retrospective cohort analysis of health insurance claims data. The claims data were obtained from Harvard Pilgrim Health Care (HPHC), a large nonprofit health plan in New England, currently serving over 1 million members in Massachusetts, New Hampshire, and Maine. Claims files include ambulatory visits, hospitalizations, procedures completed, and medication dispensed to insured members. We examined claims over the time period of January 1, 2000, through December 31, 2009. Institutional review board approval was obtained from Boston Children's Hospital, to which HPHC ceded institutional review board oversight.

IDENTIFICATION OF INDEX PATIENTS, FAMILY UNITS, AND SIBLINGS

The initial step was to identify all HPHC-enrolled patients born after January 1, 1995, with VUR, defined as presence of both an ICD-9 diagnostic code for VUR (593.7, 593.70, 593.71, 593.72, 593.73) and a CPT procedure code for cystography (74455 or 78740), at any time during the enrollment period. Each patient meeting this definition was assigned a diagnosis date that was based on the earliest date that a VUR ICD-9 code appeared in the claims data. We then excluded those with secondary VUR (concurrent codes for neurogenic bladder and spina bifida [ICD-9 596.5, 741], posterior urethral valves [ICD-9 753.6], bladder exstrophy [ICD-9 753.5], renal transplant [ICD-9 V42], and prune belly syndrome [ICD-9 756.71]). We further identified (but did not exclude) those patients with VUR who had a history of prenatal hydronephrosis (ICD-9 code 591, appearing within 6 months of date of birth). VUR patients were then grouped into family units, defined as all those enrolled under a single enrollment identification number (usually that of 1 parent). In family units with only 1 VUR patient, that patient was identified as the index patient. In family units with $\geq$2 VUR patients, the index patient was the one with the earliest chronological VUR diagnosis date. All other enrolled patients within the family unit born after January 1, 2000 (with or without VUR diagnosis), were defined as siblings. The diagnosis date for the index patient was considered the index diagnosis date for all other siblings in that family.

To further validate the sample, the medical records of index patients who underwent imaging at our institution (n = 407) were reviewed to confirm that the claims-based diagnosis of VUR was accurate; the review included medical records within our institution but not outside records (unless these were incorporated into our records).

CHARACTERIZATION OF SIBLINGS

Siblings were included in the analysis if they were continuously enrolled in HPHC for at least 1 year after birth, and sibling follow-up time included the entire period of continuous enrollment, from birth to the end of enrollment. Siblings were considered enrolled from birth if their enrollment date was within 90 days of birth, and at least one medical claim was filed within 45 days of life. As is common in claims-based studies, we ignored apparent gaps of <45 days in determining continuous enrollment. Siblings born before the index patient's diagnosis date were called pre-dx-sibs and could be categorized on the basis of their age at the time of the index date. Siblings born after the index diagnosis date were called post-dx-sibs (and therefore had no age at the index date). We excluded siblings with evidence of prenatal hydronephrosis or diagnoses associated with secondary VUR because both of these groups have reasons for undergoing cystography other than sibling screening. Siblings were further characterized by gender, index patient age at diagnosis, and socioeconomic status (using census geocoding based on median household income).

Diagnosis of VUR among siblings was based on appearance of a new diagnosis code for VUR (ICD-9 593.7, 593.70, 593.71, 593.72, 593.73) *and* cystography (CPT 74455 or 78740) less than 90 days apart. Occurrence of surgical treatment for VUR among siblings was assessed by open surgical (CPT 50780, 50780, 50782, 50785, 50783), laparoscopic (CPT 50947, 50948), or endoscopic codes (CPT 52327). Utilization of antimicrobial prophylaxis was defined as dispense records for 2 or more 30-day antibiotic prescriptions (or four 14-day prescriptions for penicillins or cephalosporins, as these classes typically require refills every 14 days). Antibiotics were grouped into 5 categories: trimethoprim/sulfonamides, penicillins, cephalosporins, antiseptics (nitrofurantoin and methenamine mandelate), and other (macrolides, quinolones, and tetracyclines). For purposes of analyzing the association of prophylaxis utilization with UTI, only siblings who initiated prophylaxis before their first UTI diagnosis were considered to have been provided prophylaxis.

CHARACTERIZATION OF SIBLING SCREENING

Pre-dx-sibs were considered to have undergone sibling screening for VUR if they underwent initial cystography (voiding cystourethrogram [VCUG] CPT 74455 or radionuclide cystogram [RNC] CPT 78740) within 12 months after the index patient diagnosis date, *and* if they did not have a UTI in the 6 months before the cystogram. Post-dx-sibs were considered to have undergone sibling screening for VUR if they underwent initial cystography (VCUG CPT 74455 or RNC CPT 78740) within 12 months after the sibling's date of birth, *and* if they did not have a UTI in the 6 months before the cystogram.

DEFINITION OF UTI

UTI (for outpatient encounters) was defined by the combined presence of 3 separate elements: 1) ICD-9 UTI diagnosis codes (590.0, 590.1, 590.2, 590.3, 590.8, 590.9, 595.0, 595.2, 595.9, 599.0, or 771.82); 2) performance of urine culture (CPT codes 87086, 87088); and 3) presence