

Limited Evaluation of Microscopic Hematuria in Pediatrics

Leonard G. Feld, MD, PhD*; Kevin E. C. Meyers, MB, BCh†; Bernard S. Kaplan, MB, BCh‡; and F. Bruder Stapleton, MD*

ABSTRACT. *Objective.* The purpose was to determine the value of the standard laboratory and radiologic evaluation of microscopic hematuria in children, and to determine the prevalence of idiopathic hypercalciuria in those children referred for evaluation of unexplained microscopic hematuria.

Methods. This was a retrospective study of 325 children referred from 1985 to 1994 for the evaluation of asymptomatic microscopic hematuria. The diagnostic studies reviewed included serum creatinine, blood urea nitrogen, serum electrolyte studies, serum complement concentration, antinuclear antibody, urinalysis, urine calcium to creatinine ratios, urinary protein to creatinine ratio and/or 24-hour urinary protein excretion, renal ultrasounds, intravenous pyelograms, voiding cystourethrograms, and historical information.

Results. All creatinine and electrolyte values were normal for age, and none of the biochemical tests obtained in the children with hypercalciuria was abnormal. Of the 325 patients with idiopathic microscopic hematuria, only 18 had abnormal renal ultrasound examinations and 9 voiding cystourethrograms showed low-grade reflux. Hypercalciuria was found in 29 patients. The family history was positive for urolithiasis in 16% of patients without hypercalciuria compared with 14% of patients with hypercalciuria. A positive family history of hematuria was reported in 25% of patients; 62 patients did not have hypercalciuria and 4 of the patients had hypercalciuria. Microscopic hematuria in children is a benign finding in the vast majority of children.

Conclusions. Our data demonstrate that a renal ultrasound, voiding cystourethrogram, cystoscopy, and renal biopsy are not indicated in the work-up of microscopic hematuria, and microhematuria in the otherwise healthy child is a minimal health threat, rarely indicative of serious illness. *Pediatrics* 1998;102(4). URL: <http://www.pediatrics.org/cgi/content/full/102/4/e42>; *proteinuria, hematuria, microscopic hematuria, renal ultrasound.*

ABBREVIATIONS. VCUG, voiding cystourethrogram; C₃, serum complement concentration.

Microscopic hematuria is a common finding on urine dipstick examination with a prevalence rate between 1% and 2% for two or more positive samples in children from 6 to 15 years of age.¹⁻³ If hematuria is defined as more than five red blood cells per high-power field on more than two occasions, then microscopic hematuria would be discovered in nearly one million children in the first 2 decades of life. Although there is a long list of causes of asymptomatic microscopic hematuria, the vast majority of cases are diagnosed as idiopathic or benign and are not indicative of significant kidney disease.

The laboratory and radiographic evaluation, as well as the indications for a renal biopsy in children with microscopic hematuria, are disputed.⁴⁻¹² The value of a comprehensive evaluation for microscopic hematuria in children has been challenged by Lieu et al.¹³ Because of the large number of referrals to pediatric nephrologists for microscopic hematuria, the appropriate cost-effective diagnostic evaluation by primary care physicians of this common clinical dilemma warrants further clarification.

For more than a decade, routine evaluation of nonglomerular hematuria in children has included screening for hypercalciuria.¹⁴⁻¹⁶ The association of hematuria with hypercalciuria has been reported predominantly in children from the southern United States.^{17,18} In the early reports, 27% to 35% of children with microscopic hematuria had hypercalciuria. The finding of hypercalciuria in a child with nonglomerular hematuria may identify up to 13% of patients at risk for developing urolithiasis.^{17,19} However, the value of screening children with unexplained hematuria for hypercalciuria has not been tested in different regions of the United States.

The purpose of this study was twofold: 1) to determine the value of the standard laboratory and radiologic evaluation of microscopic hematuria in children, and 2) to determine the prevalence of idiopathic hypercalciuria in those children referred for evaluation of unexplained microscopic hematuria in the northeastern United States.

METHODS

This study is a retrospective study of all children who were referred to the Pediatric Nephrology outpatient clinics at the Children's Hospital of Buffalo and the Children's Hospital of Philadelphia from 1985 to 1994 for the evaluation of asymptomatic microscopic hematuria. These two institutions serve as regional pediatric referral centers. Three hundred and twenty-five charts were reviewed. The mean age of the patients was 10.7 ± 0.8 years with a median of 9 years (Table 1). Microscopic hematuria was

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Received for publication Feb 10, 1998; accepted May 15, 1998.

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TABLE 1. Study Population With Microscopic Hematuria

Patients	Buffalo	Philadelphia	Total
Number	210	115	325
Ages (y)	7.5 ± 0.3 Median = 7	16.0 ± 1.9 Median = 14	10.7 ± 0.8 Median = 9
Gender (male/female)	74/136	61/54	135/190
Family history of hematuria	47 (22%)	19 (16%)	66 (20%)
Family history of kidney stones	21 (10%)	20 (17%)	41 (13%)

defined as five or more red blood cells per high-power field in a fresh centrifuged urine specimen and/or as a positive dipstick test of the urine. Patients were excluded from the study if they also had nonorthostatic proteinuria (>+1 on a urinary dipstick, or urinary protein to creatinine ratio >0.2), previous urolithiasis, documented urinary tract infection, acute or chronic glomerulopathies (Henoch-Schönlein purpura, systemic lupus erythematosus, postinfectious glomerulonephritis), sickle cell disease, or a known bleeding diathesis. Children with chronic systemic illness, with or without growth failure, were also excluded. The diagnostic studies that were reviewed included serum creatinine, blood urea nitrogen, serum electrolyte studies, serum complement concentration (C₃), antinuclear antibody, urinalysis, urine calcium to creatinine ratios, urinary protein to creatinine ratio and/or 24-hour urinary protein excretion, renal ultrasounds, intravenous pyelograms, voiding cystourethrograms (VCUG), and hearing tests (audiograms or historical information). Hypercalciuria was defined as a urinary calcium excretion of >4 mg/kg/24 h, or two random urinary calcium to creatinine ratios >0.21. Studies were included in the evaluation if they were obtained by the referring physician before the examination at the referral center. Patient records were reviewed for family histories, laboratory, and radiologic data.

The cost of the evaluations to patients and insurers was calculated from the current outpatient laboratory and radiology charges at the Children’s Hospital of Buffalo.

All data were prepared in Microsoft Excel and statistical analysis was performed on Minitab (State College, PA).

RESULTS

The results of the diagnostic studies are included in Table 2. Laboratory work up of microscopic hematuria included serum chemistries (creatinine and electrolytes) obtained in 254 (78%) patients. All values were normal for age in every patient. Similarly, none of the biochemical tests obtained in the children with hypercalciuria was abnormal. Twelve percent of patients had an initial urine protein to creatinine ratio or positive dipstick result that exceeded normal limits. In each instance, the urine protein value normalized on repeat testing allowing the final diagnosis of asymptomatic microscopic hematuria. Serum complement concentrations (C₃) were obtained in 157 (48%) of patients. Nineteen serum C₃ concentrations were low, although only 2 were more than 10% below the lower limit of normal. Despite this finding, the work-up was unremarkable for proteinuria, hypertension, or impaired renal function. The final di-

agnosis in each patient was idiopathic microscopic hematuria.

Of the 325 patients with idiopathic microscopic hematuria, 283 had a renal ultrasound and 90 had VCUG studies. Of the 18 abnormal renal ultrasound examinations, no finding was clinically significant (Table 3). Thirty-eight percent of the ultrasounds and 59% of the VCUGs were ordered by a private physician or a urologist before the nephrology evaluation. At The Children’s Hospital in Buffalo, 43% of ultrasounds were ordered by private physicians or urologists compared with 32% at the Children’s Hospital of Philadelphia. For VCUG, 72% of the studies in Buffalo were ordered before the nephrology consult. None of the VCUG’s performed in Philadelphia was done before the renal visit, although the total number of studies was small (n = 14). Nine VCUGs showed low grade reflux (I or II).

Urinary calcium/creatinine ratios were obtained in 263 (81%) of the patients with microscopic hematuria. Hypercalciuria was found in 29 (11%) of these patients. Mean age of the patients with hypercalciuria was not significantly different (8.9 ± 4.0 years vs 10.0 ± 5.7 years, P = .2). There was no gender difference in this small number of patients. Sixteen percent (41/263) of patients had a family history of renal stones. The family history was positive for urolithiasis in 16% (37/234) of patients without hypercalciuria compared with 14% (4/29) of patients with hypercalciuria. A positive family history of hematuria was reported in 25% (66/263) of patients; 62 (26%) patients did not have hypercalciuria and 4 (14%) of the patients had hypercalciuria.

The estimated cost for a consultation with a pediatric nephrologist, renal ultrasound examination, and a limited biochemical evaluation is at least \$500 per patient. With additional biochemical tests and a VCUG the cost escalates to \$1000 per patient. For the 325 patients in our study the total cost was ~\$175 000 or \$540 per patient.

TABLE 2. Diagnostic Studies*

Diagnostic Study	Normal Result—No. of Patients (No. of tests not performed)	Abnormal Result— No. of Patients	No. of Studies Performed by Referring MD
Serum creatinine	254 (71)	0	—
Urine protein/creatinine ratio or dipstick positive	285 (0)	40	—
Serum complement	138 (168)	19	—
Renal ultrasound	265 (42)	18	113
VCUG	81 (235)	9	52
Urine calcium/creatinine ratio	234 (62)	29	—

Abbreviation: VCUG, voiding cystourethrogram.

* Some studies were not performed in all patients; see text for details.

TABLE 3. Renal Ultrasound Abnormalities

Duplication of ureter (3)*
Increased echogenicity (5)
Ectopic kidney
Kidney size discrepancy (6)
Bifid collecting system
Extrarenal pelvis (2)

* Number of abnormalities in parentheses.

DISCUSSION

We have found no major renal or bladder disorders on biochemical or imaging studies in 325 children referred to our nephrology centers from primary care physicians and pediatric urologists with the diagnosis of microscopic hematuria. In a small number of patients, the initial testing for low grade proteinuria was positive, although subsequent testing and evaluation resulted in the diagnosis of isolated or idiopathic microscopic hematuria. A similar conclusion was reached for those patients with a mildly depressed serum C_3 concentration. In those patients with a markedly depressed C_3 , the most likely diagnosis was postinfectious (or poststreptococcal) acute glomerulonephritis. Less frequent causes of a low serum C_3 include systemic lupus erythematosus, membranoproliferative glomerulonephritis, bacterial endocarditis, shunt nephritis, or cryoglobulinemia. Our findings compare with other studies in which a comprehensive evaluation of microscopic hematuria resulted in a low rate of positive findings and favorable prognosis.^{3,4,5} Based on our cohort of patients with the final diagnosis of idiopathic or benign microscopic hematuria, there is limited value in a biochemical work-up in all patients in whom blood is found in the urine during a routine test.

No surgically correctable abnormalities were noted on radiologic evaluation in our analysis. The expressed concern of missing a significant lesion such as a Wilms' tumor or rhabdomyosarcoma of the bladder seems unjustified for patients with microscopic hematuria. The history, physical examination, family history, and a complete urinalysis (examination for casts, differentiation of dysmorphic [renal bleeding] from nondysmorphic [nonrenal] red blood cells) should dictate the extent of the diagnostic evaluation in an individual child.

Familial occurrence of persistent microscopic hematuria (absence of proteinuria, progressive renal failure, and hearing deficit) was found in ~25% of our patients with microscopic hematuria. A positive family history for hematuria is almost twice as common in patients without hypercalciuria compared with those with increased calcium excretion. Similar to idiopathic or benign (nonfamilial) microscopic hematuria, the short-term and long-term prognosis is excellent.^{4,9} Because both familial microscopic hematuria and hereditary nephritis (Alport syndrome) may present in the early stages of the disease with only microscopic hematuria, urine dipstick testing for proteinuria should be performed on a periodic basis (every 1 to 2 years) in all patients with microscopic hematuria.^{20,21}

Hypercalciuria has been associated with hematuria in children from Spain, Brazil, and the southern United States.^{18,22} We found only an 11% prevalence of hypercalciuria in patients evaluated for microscopic hematuria. Of note, a family history of renal stones is similar in patients with or without the finding of hypercalciuria. Only 14% of our hypercalciuric patients had a positive family history of urolithiasis compared with 46% to 77% of hypercalciuric patients in the studies published from centers in the southwestern United States.^{17,18} Thus, the association of hypercalciuria and hematuria may be more common in regions with a high prevalence of urolithiasis. This report is the first to determine the prevalence of hypercalciuria in children with idiopathic microscopic hematuria in the northeastern United States. In our study, a family history of urolithiasis in the nonhypercalciuric patients (16%) was similar to the 18% of normocalciuric patients in the Southwest Pediatric Nephrology Study Group, and to the 15% of normocalciuric patients reported by Stapleton et al.^{17,18} Despite the extensive work-up of the patients with hypercalciuria, there was no evidence of nephrolithiasis on renal ultrasound and no patient developed a renal stone during a minimum of 24 months of follow-up. In this patient population, we were unable to confirm previous findings that 13% to 17% of children with hypercalciuria develop urinary stones within a 12- to 40-month follow-up period.^{17,19}

Based on our study, we suggest that the initial evaluation of microscopic hematuria should include a first morning urinalysis with microscopic examination. If the urinalysis demonstrates absence of proteinuria and red blood cell or white blood cell casts, serum chemistries, a renal ultrasound examination and a VCUG are not routinely indicated. There seems to be no indication for a cystoscopy or renal biopsy in children with microscopic hematuria. If there is a family history of hematuria, urolithiasis, or large numbers of crystals on a urinalysis, it would be appropriate to obtain a urinary calcium/creatinine ratio. As we have reported previously, pediatric nephrologists²³ and life insurance companies²⁴ do not favor an invasive approach for microscopic hematuria. In fact, life insurance companies request a commitment to a diagnosis and medical follow-up, rather than additional testing.

Parents, children, and physicians often become anxious when hematuria is discovered because of the association with malignancy or chronic renal disease in adults.²⁵ Microscopic hematuria in children is a benign nonurologic finding in the vast majority of children. Based on our study, a patient with microscopic hematuria can be followed in the primary care physician's office without an extensive nephrologic or urologic consultation. By implementing a limited biochemical testing and radiologic evaluation as described in Fig 1, there will be a cost savings of at least \$1000 per patient. Our data demonstrate that there is a negligible health care threat when a limited evaluation indicates a diagnosis of microscopic hematuria.

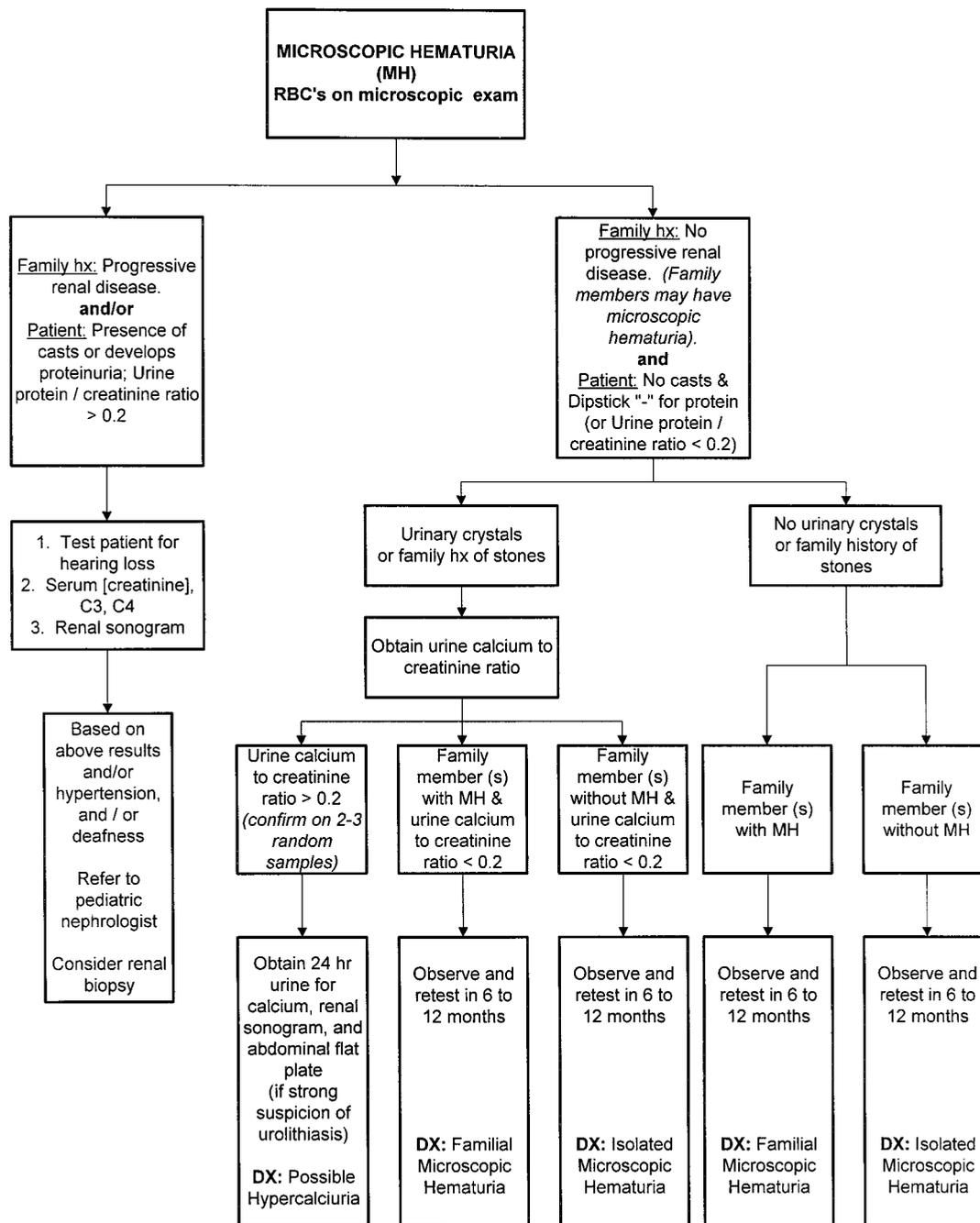


Fig 1. Evaluation of microscopic hematuria in children.

ACKNOWLEDGMENTS

We thank Jugta Kahai, MD, at the Children's Hospital of Buffalo and Ms S. Meyers at the Children's Hospital of Philadelphia for their careful review of the charts.

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Pediatrics 1998;102:e42

DOI: 10.1542/peds.102.4.e42

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