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Correlation Between Asymptomatic Persistent Microscopic Hematuria and Reflux Nephropathy

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Abstract

Background: Asymptomatic persistent microscopic hematuria is one of the common symptoms in children with kidney disorders and may be one of the most important signs of glomerular damage. Vesicoureteral reflux (VUR) also is one of the common disorders in children that causes scarring, secondary lesions, and subsequent problems, including hypertension, chronic renal failure, and end-stage renal disease (ESRD).
Methods: This is a case-control study that was conducted on 100 children with VUR (50 children with reflux nephropathy as the case group and 50 children without reflux nephropathy as the control group) at Amirkabir Hospital, Arak, Iran. The frequency of asymptomatic persistent microscopic hematuria was evaluated in both groups of children.
Results: The mean age of the children in the case group was 2.93 $\pm$ 2.30 and in the control group was 3.46 $\pm$ 2.68 years old (P = 0.268). Thirty-four percent of the case group and 14% of the control group were males (P = 0.019). In addition, 22% of children in the case group and only 8% of children in the control group showed asymptomatic persistent microscopic hematuria (P = 0.049).
Conclusions: According to the results of this study, it seems that the asymptomatic persistent microscopic hematuria is more in children with reflux nephropathy.

Keywords: Hematuria, Reflux Nephropathy, Children

1. Background

Asymptomatic persistent microscopic hematuria is one of the common symptoms in children with kidney disorders. Its prevalence is 1 to 2 percent (1, 2). There is a long list of the causes related to this condition most of which are benign conditions (3, 4). However, hematuria may be one of the most important signs of glomerular damage, especially if hematuria is persistent. The American Academy of Pediatrics recommends screening for urine analysis at the age of entrance to the school and during adolescence (5). Despite the high prevalence of this disorder, the exact nature of this condition is not precisely defined (6, 7).

The incidence of vesicoureteral reflux (VUR) is 1% in asymptomatic children and 25% to 40% in symptomatic children and shows itself with urinary tract infection (8, 9). Urinary tract infections are one of the most important factors associated with vesicoureteral reflux that causing scarring, secondary lesions, and subsequent problems, including hypertension, chronic renal failure, and end-stage renal disease (ESRD) (10, 11). It has been observed that 30% - 49% of the patients have parenchymal scars at the time of diagnosis (12, 13).

2. Objectives

In the current study, we have investigated the association between asymptomatic persistent microscopic hematuria and reflux nephropathy.

3. Methods

This is a case-control study that was conducted on 100 children with VUR at Amirkabir Hospital, Arak, Iran. Fifty children with reflux nephropathy as the case group and 50 children without reflux nephropathy as the control group enrolled in this study. The patients were enrolled in the study based on inclusion and exclusion criteria.

Diagnosis of reflux was done based on VCUG and diagnosis of nephropathy was done based on DMSA criteria. The grading of the reflux was done according to the VCUG and by the pediatric nephrologist (14-16).

Table 1. General Characteristics of the Studied Children[a]

Parameter	Group		P Value
	Case	Control	
Age, y (mean ± SD)	2.93 ± 2.30	3.46 ± 2.68	0.268
Gender, No. (%)			0.019*
Male	17 (34)	7 (14)	
Female	33 (66)	43 (86)	

[a] Values are expressed as No. (%) unless otherwise indicated.

Table 2. Gestational Factors of the Studied Children[a]

Parameter	Group		P Value
	Case	Control	
Birth weight, g			0.009*
< 1000	3 (6)	0 (0)	
1000 - 1500	3 (6)	1 (2)	
1500 - 2500	26 (52)	15 (30)	
2500 - 4000	17 (34)	34 (68)	
> 4000	1 (2)	0 (0)	
Gestational age			0.001*
Pre-term	31 (62)	14 (28)	
Term	19 (38)	33 (66)	
Post-term	0 (0)	3 (6)	
Feeding			0.420
Breast-feeding	39 (78)	34 (68)	
Milk powder	10 (20)	13 (26)	
Both	1 (2)	3 (6)	
Parity			0.139
First	33 (66)	24 (48)	
Second	9 (18)	17 (34)	
3rd and more	8 (16)	9 (18)	
Mother's age at pregnancy, (mean ± SD)	25.68 ± 4.65	27.56 ± 4.78	0.049*

[a] Values are expressed as No. (%) unless otherwise indicated.

For all children in the study, urine analysis was performed in 3 consecutive times and cases with asymptomatic persistent microscopic hematuria were recorded.

Asymptomatic persistent microscopic hematuria was defined as repeated microscopic hematuria without any symptoms in 3 consecutive urine analysis (17). Finally, the data were collected through a checklist and the results of diagnostic tests were analyzed by SPSS software version 23.

Inclusion criteria consisted of children without any age limitation. In addition, both genders and any grade of VUR entered the study.

Exclusion criteria were comprised of children who had nephropathy due to congenital kidney disease. The children who had gross hematuria and asymptomatic hematuria were excluded from the study.

This study was approved by the Ethics Committee of Arak University of Medical Sciences with ethics code IR.ARAKMU.REC.1395.296. Written informed consent was obtained from all children's parents.

Eventually, collected data was statistically analyzed via the SPSS-23 software, using independent sample *t* test, and chi-square tests.

4. Results

The mean age of the total children was 3.20 ± 2.50 and 24% of them were boys and 76% of them were girls. More detailed information on their age and gender are summarized in Table 1. Also, the Gestational factors of the children are summarized in Table 2.

In the results of this study, it was observed that among children with reflux nephropathy, 22% of children had asymptomatic persistent microscopic hematuria while among children without reflux nephropathy, 8% of them had asymptomatic persistent microscopic hematuria (P = 0.049). Imaging and laboratory factors of children are summarized in Table 3.

5. Discussion

The recent study aimed to investigate the association between asymptomatic persistent microscopic hematuria and reflux nephropathy among children with VUR.

The results of this study showed that boys were significantly more likely to have reflux nephropathy than girls (reflux nephropathy were seen in 70.83% of the boys and 43.42% of the girls). Wennerstrom et al. reported that renal scar was seen in 86% of the males and 30% of the females (18). It is observed that the results of their study are similar to our study. This confirms the role of the gender in the development of reflux nephropathy.

The results of this study showed that low birth weight and pre-term labor (less than 37 weeks) had a significant effect on the incidence of reflux nephropathy in children with VUR. In another study that was done by Yousefichaijan et al. it was reported that pre-term labor had a relationship with reflux nephropathy in the children (19).

It was also observed in this study that high-grade VUR had a relationship with the incidence of reflux nephropathy. Shaikh et al. also reported that the higher grades of VUR are related to the incidence of reflux nephropathy (20).

In this study, we observed that asymptomatic persistent microscopic hematuria is more in children with reflux nephropathy. To the best of our knowledge, this is the first study that has studied the asymptomatic persistent micro-

Table 3. Imaging and Laboratory Factor of Children[a]

Parameter	Group		P Value
	Case	Control	
Age at diagnose time, y (mean ± SD)	1.27 ± 1.92	1.44 ± 1.84	0.687
Positive family history of VUR	1 (2)	2 (4)	0.513
VUR grading			0.001
I	1 (2)	12 (24)	
II	11 (22)	19 (38)	
III	19 (38)	18 (36)	
IV	12 (24)	0 (0)	
V	7 (14)	1 (2)	
VUR side			0.819
Right	15 (30)	14 (28)	
Left	12 (24)	10 (20)	
Both side	23 (46)	26 (52)	
Asymptomatic persistent microscopic hematuria	11 (22)	4 (8)	0.049

[a] Values are expressed as No. (%) unless otherwise indicated.

scopic hematuria in children with reflux nephropathy.

In this study, we encountered some limitations. First, the population of the experimental and control group was small. Second, some of the parents did not cooperate in the study. Third, Lack of prior research studies on the topic, thus it is recommended that future studies should be done with fewer restricting factors in this area.

5.1. Conclusions

Regarding the higher prevalence of reflux nephropathy in boys and pre-term infants, the attention should be paid to pre-term infants and boys with VUR and their follow-up with higher precision to prevent the development of nephropathy-related reflux. Also, regarding the higher frequency of asymptomatic persistent microscopic hematuria in children with reflux nephropathy, it is possible to improve the prognosis of the patients with VUR by taking this hematuria more seriously in patients with VUR and detecting and treating them at the right time.

However, this study requires more investigations. Similar studies with a higher proportion of samples at different centers are recommended in order to help these patients.

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Footnotes

Authors' Contribution: Study concept and design: Parsa Yousefichaijan and Manijeh Kahbazi. Analysis and interpretation of data: Yasaman Mirmoeini. Drafting of the manuscript: Ali Khosrobeigi. Critical revision of the manuscript for important intellectual content: Parsa Yousefichaijan, Manijeh Kahbazi, Yasaman Mirmoeini, Pezhman Parsa. Statistical analysis: Ali Khosrobeigi.

Conflict of Interests: None declared.

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