Etiological Role of *Gardnerella vaginalis* in Children with Urinary Tract Diseases

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The objective of our study was to evaluate the role of *Gardnerella vaginalis* (in the etiology of urinary tract diseases (UTD) in children.

There are some publications on the prevalence of *Gardnerella vaginalis* in children's urogenital tract. But there are no data on the role of this organism in the etiology of UTD in children. Some children who present to our doctors with symptoms of urinary tract infection (dysuria and frequency) fail to yield a conventional uropathogen on standard culture. After this it seemed reasonable to verity whether fastidious microorganisms (*G. vaginalis*) might cause dysuria and possibly some of the other conditions in which conventional urine culture is negative.

One hundred and six children (91 girls and 15 boys) with UTD and 22 healthy controls were enrolled in the study. The mean age of children was 11 years (range, 5.4 to 15.1 years). The patients were divided into three groups: group I, children with history of dysuria, but negative urinary cultures (n = 38), group II, children with cystitis or pyelonephritis (n = 38), and group III, children with microhaematuria (n = 30). Urethral swab specimens from boys and vaginal or vulval swabs from girls were collected. The samples were cultured selectively for *G. vaginalis.* Samples collected from 13 of the 106 patients with UTD harbored *G. vaginalis*: seven samples obtained from 38 children in group I, 2 samples from 38 children in group II, and 4 samples from 30 children in group III. *G. vaginalis* was isolated from 6 prepubertal and 7 postpubertal girls. The organism was not recovered from boys with UTD and controls.

Our study suggests that dysuria with negative urinary cultures in children might be caused by an uncommon microorganism.

Key words: *Gardnerella vaginalis*, urinary tract diseases, children

INTRODUCTION

Urinary tract infections (UTI) are frequently encountered in both children and adults. *Escherichia coli* (*E. coli*) is the most common cause of UTI in children of all ages (1–3). Organisms encountered less frequently are *Enterobacter*, *Klebsiella*, *Proteus* species, coagulase-negative staphylococci, *Enterococcus*, *Pseudomonas aeruginosa* (2). However, there are some publications showing that other uncommon microorganisms such as *Gardnerella vaginalis* (*G. vaginalis*) can cause urinary tract diseases (UTD) (4–6). *G. vaginalis* was recovered from bladder aspiration urine of patients with reflux nephropathy and from subjects with acute symptoms of urinary tract infection (7, 4, 8). *G. vaginalis* was also associated with hemorrhagic cystitis (5), chronic pyelonephritis (6), and symptomatic bacteriuria (9, 10).

It is known that up to 50% of women and two-thirds of men with symptoms of acute urinary tract infection (dysuria and frequency) fail to yield a conventional uropathogen on standard culture (11). Abercrombie et al. (12) reported their findings for a patient with severe hemorrhagic cystitis. Multiple midstream urine samples for conventional uropathogens yielded no growth. However, when a bladder urine sample was examined for fastidious organisms, a pure growth of *G. vaginalis* was isolated. McDonald

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et al. (13) reported the recovery of *G. vaginalis*, frequently accompanied by *U.urealyticum*, from the bladder urine of 7 of 101 patients with acute symptoms of urinary tract infection. Loulerque et al. (14) isolated *G. vaginalis* from urine obtained directly from the obstructed renal calyx of a female patient with chronic pyelonephritis, whose routine preoperative urine culture was negative for any other organism. Petit and Mouton (15) recovered *G. vaginalis* from urine samples of 14 from 23 symptomatic kidney transplant patients.

Leopold first reported the isolation of a small nonencapsulated pleomorphic Gram-negative rod from the genitourinary tract of women with cervicitis in 1953 (16). Two years later, Gardner and Dukes (17) isolated this organism, named *Haemophilus vaginalis*, from 92% of 141 women with "bacterial vaginitis", from 20% of women with *Trichomonas vaginalis* infection and from none of 78 controls. Since then, numerous studies have confirmed the link between *G. vaginalis* and this syndrome, when normal vaginal flora (*Lactobacillus*) is replaced by a mixed flora including *G. vaginalis*, anaerobes, *Mobiluncus* spp., genital mycoplasmas (18, 19). Extravaginal infections with *G. vaginalis* are increasingly recognized using improved media and methods for the isolation and identification of bacteria (20).

Lack of consensus on the taxonomic status of *G.vaginalis* added to the uncertainty surrounding the microorganism. In 1980, Greenwood and Pickett resolved the issue by proposing a new genus, *Gardnerella*, "to include catalase and oxidase-negative, Gram-negative to Gram-variable bacteria with laminated cell walls, which produce acetic acid as the major end product of fermentation" (21).

Over half women of reproductive age without vaginal infections are usually colonized by *G. vaginalis* (22). In contrast, prepubertal girls have a low prevalence of *G. vaginalis* in their urogenital tract (23).

G. vaginalis has been implicated as the etiologic agent in bacterial vaginosis by numerous investigators (19, 24, 25). However, the role of this bacterial species in urinary tract diseases has attracted comparatively little attention.

Some children who present to our doctors with symptoms of urinary tract infection (dysuria and frequency) fail to yield a conventional uropathogen on standard culture. After this it seemed reasonable to verify whether fastidious microorganisms (*G. vaginalis*) might cause dysuria and possibly some of the other conditions in which conventional urine culture is negative.

The aim of this study was to evaluate the role of *G. vaginalis* in the etiology of urinary tract diseases (UTD) in children.

MATERIALS AND METHODS

One hundred and six children (91 girls and 15 boys) with UTD and 22 healthy controls (21 girls and 1 boy) were enrolled in the study. The patients were treated at Vilnius University Children Hospital and Vilnius Çeçkine outpatient departament in 1999–2002. The mean age of children was 11 years (range, 5.4 to 15.1 years). Their age, gender, presenting symptoms, laboratory data (blood analysis, urinalysis, urine culture) and ultrasonography (renal and bladder) were assessed. The patients were divided into three groups:

1. Children with history of dysuria, but negative urinary cultures (n = 38; group I).
2. Children with cystitis or pyelonephritis (n = = 38; group II). The most frequent clinical presentations were chronic cystitis (n = 30), acute cystitis (n = 6) and chronic pyelonephritis (n = 2).
3. Children with microhaematuria (n = 38; group III).

Questionnaires were given about children complaints, the beginning and duration of disease, previous antibiotic usage. Adolescents were asked about their sexual intercourse.

Midstream urine samples were cultured on cystine lactose electrolyte deficient (CLED) agar for conventional uropathogens.

All children underwent renal and bladder ultrasonography.

Vaginal or vulval swabs from girls and urethral swab specimens from boys were collected. Gramstained vaginal and urethral smears were examined under oil immersion. The samples were cultured selectively for *G. vaginalis* (Columbia blood agar media, Oxoid). Vaginal and urethral swab specimens were cultured from 8 girls at the same time. *G. vaginalis* was identified on the basis of production of diffuse beta-hemolysis on agar medium, a Gram stain showing small gram-negative to gram-variable bacilli, and by biochemical identification (BBL Crystal identification systems, Becton Dickinson).

Permission of Ethics Committee and informed consents of parents and/or participating children were received.

RESULTS AND DISCUSSION

In 1998–2002, 106 patients (age range from 5.4 to 15.1 years with an average of 11 years) diagnosed with UTD were treated in Vilnius University Children's Hospital, Centre of Paediatrics and in Vilnius Šeškinė outpatient clinic.

Distribution of children into groups I, II, III and in control group (CG) by their age and gender is shown in Table 1.

Table 1. **Distribution of patients into groups I, II, III and CG by age and gender**

Groups	Age		Gender	
	mean	range	female	male
Group I (n = 38)	12	6.1–15.1	32	6
Group II (n = 38)	9.1	5.3–15.3	36	2
Group III (n = 30)	11.3	5.3–15.6	23	7
CG (n = 22)	11.1	5.5–15.4	21	1

The findings showed that females were affected more often than males. Based on community studies, investigators believe that UTI is more prevalent in girls than in boys after the first year of life (26).

Blood analysis, urinalysis, urine culture and ultrasonography (renal and bladder) were assessed.

Thirty seven patients had normal blood analysis in group I, 30 – in group II. Erythrocyte sedimentation rate was elevated in one patient of group I. In group II, elevated count of white blood cells was found in 6 patients and elevated erythrocyte sedimentation rate in 2 patients. Analysis data in group III were normal.

The results of urinalysis in groups I, II, III and CG are shown in Table 2.

Urine cultures were negative in groups I, III and CG. In group II, *E. coli* in counts greater than 10,000 colony-forming units per milliliter of urine was isolated in 35 samples, *Proteus* – in two samples. *Streptococcus pyogenes* was isolated from one sample.

Ultrasonography was normal in groups I, III and CG. In group II, ultrasound examination revealed thick mucous membrane of the bladder in 13, increased residual urine in 3 and nephrosclerosis in two of the children.

To investigate the role of *G. vaginalis* in urinary tract diseases in children, we examined vaginal or vulval and urethral samples from 106 patients. Gram-stained vaginal and urethral smears obtained from 13 patients revealed small gram-negative to gram-variable rods (Figure).

G. vaginalis was recovered by culture from the same 13 patients (Table 3).

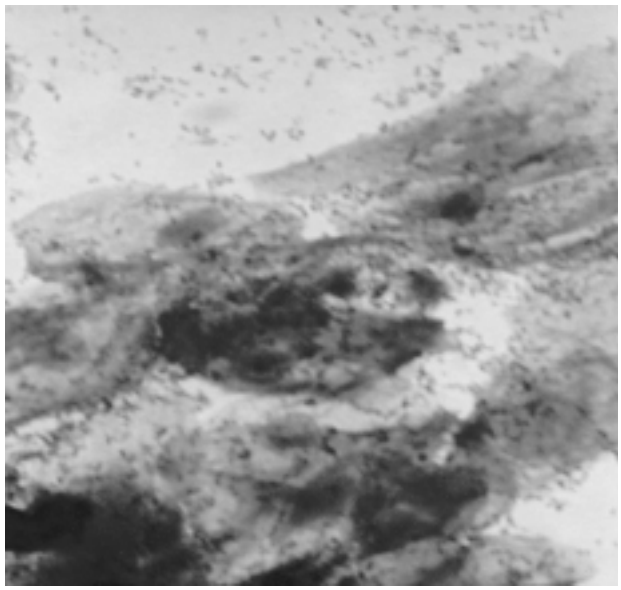

Figure. Prevalence of *Gardnerella vaginalis* in children's urogenital tract

Table 3. **Prevalence of *G. vaginalis* in groups I, II, III**

Groups	*G. vaginalis* (n = 13)	*p* value
Group I (n = 38)	7	0.03
Group II (n = 38)	2	0.2
Group III (n = 30)	4	0.1
CG (n = 22)	–	

Table 2. **Results of urinalysis in groups I, II, III and CG**

Groups	Urinalysis			
	Pyuria*	Bacteriuria	Microhaematuria**	Normal
Group I (n = 38)	5	–	5	29
Group II (n = 38)	34	28	17	4
Group III (n = 30)	1	–	28	2
CG (n = 22)	–	–	–	22
Total	**40**	**28**	**50**	**57**

* is defined as the presence of more than 10 white blood cells per high power field visualized by light microscopy in a centrifuged urinary sediment (27).
** > 5/μl red blood cells in fresh uncentifuged midstream urine (27).

This organism was isolated more frequently in children (n = 7) with history of dysuria and negative urinary cultures than in those (n = 2) with proven urinary tract infection or persistent or transient microhematuria (n = 4). The prevalence of *G. vaginalis* in group I was significantly higher (p = 0.03) than in controls. But there was no difference in the prevalence of *G. vaginalis* in group II (p = 0.2) and group III (p = 0.1) compared with control group. Although the preva-

lence of this organism was higher in children with history of dysuria but negative urinary cultures, there was no statistically significant difference between groups I, II, and III ($p > 0.05$).

Children who harbored *G. vaginalis* in their urogenital tract had clinical signs: dysuria (n = 7), frequency (n = 8), vaginal discharge (n = 8), abdominal pain (n = 4).

Vaginal and urethral swab specimens were cultured from 8 girls at the same time. Four females harbored *G. vaginalis* in their urethra and vagina at the same period. The other four were negative in both sites. Lam et al. (28) recovered *G. vaginalis* from female urine samples and their vaginas. The investigators showed that all culture-positive females also harbored *G.vaginalis* in their vaginas. Since the studies showed that *G. vaginalis* was recoverable from both genital and urinary tracts, the transfer of organisms probably occurred between the genital and urinary tract. The finding that a greater prevalence was observed in the genital tract than in the urinary tract suggests that the transfer of *G. vaginalis* took place from the genital tract to the urinary tract. Although anatomical proximity should allow easy transfer of *G. vaginalis* from the genital tract to the urinary tract, to date only some investigators have examined the role of *G. vaginalis* in urinary tract infections and renal diseases (4–10). All of these researchers have recovered this microorganism from urine samples and other body sites (vagina, urethra).

We isolated this fastidious microorganism from 5 of 42 prepubertal and 7 of 69 postpubertal girls. This difference was not statistically significant ($p = 0.7$). Three adolescent girls had had sexual intercourse. The studies show that prepubertal girls have a low frequency of *G. vaginalis* (23). There may be an association between sexual activity and colonization of the lower genital tract in young girls (29). However, 10 to 31% of sexually inexperienced adolescent girls have had positive vaginal cultures for *G. vaginalis* (30).

We have not recovered *G. vaginalis* from male patients and controls. Some publications suggest that *G. vaginalis* is not an organism that commonly colonizes the urogenital tract in asymptomatic prepubertal boys (31). Sexually active adolescent males were found to habor this organism in their urethra (32).

The natural history of *G. vaginalis* is unknown and the significance of these findings is unclear. Holst (33) recovered *G. vaginalis* from rectums of females, males and children. The findings suggest that the organism is not spread sexually but colonizes the vagina from an endogenous intestinal tract site. Routine culturing for

G. vaginalis is not recommended as part of a sexual abuse workup.

The present study has clearly shown that colonization of the urethra and vagina by *G. vaginalis* is a phenomenon of females. Of the 128 children, *G.vaginalis* was isolated in 10% of children's urogenital tract. *G. vaginalis* was the most prevalent in group I ($p = 0.03$). Our study suggests that dysuria with negative urinary cultures in children might be caused by an uncommon microorganism. After this it seemed reasonable to investigate the role of *G. vaginalis* and other fastidious microorganisms in the etiology of dysuria and possibly some of the other conditions in which conventional urine cultures are negative.

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GARDNERELLA VAGINALIS VAIDMUO VAIKŲ ŠLAPIMO ORGANŲ LIGŲ ETIOLOGIJOJE

S a n t r a u k a

Darbo tikslas – nustatyti *Gardnerella vaginalis* paplitimą vaikų urogenitalinėje sistemoje bei įvertinti jos vaidmenį šlapimo organų ligų etiologijoje.

Literatūroje randama daug šaltinių, kurie atskleidžia *G. vaginalis* reikšmę suaugusiųjų urogenitalinių ligų etiologijoje. Tačiau nėra aišku, kaip dažnai urogenitalinės mikoplazmos sukelia vaikų šlapimo organų ligas. Mūsų patirtis rodo, kad yra nemažai vaikų, kurie skundžiasi skausmingu bei dažnu šlapinimusi. Jiems įtariama šlapimo organų infekcija, tačiau šlapime bakterijos neišauga. Tokių vaikų šlapimo tyrime kartais randame leukociturią. Gydant antibakteriniais vaistais (pvz., nitrofuranais), klinikiniai simptomai išlieka.

Ištyrėme 106 ligonius ir 22 sveikus vaikus (112 mergaičių ir 16 berniukų) kurių vidutinis amžius buvo 11 metų (5,4–15,11 metai). Ligoniai suskirstyti į tris grupes: I grupėje – vaikai, kuriems buvo dizurija be cistitui būdingų laboratorinių pakitimų (n = 38), II grupėje – sergantys cistitu ar pielonefritu (n = 38) ir III grupėje – mikrohematuria (n = 30). *G. vaginalis* nustatyta bandinius sėjant į selektyvią mitybinę terpę.

Ištyrę 128 vaikus, *G. vaginalis* radome 13 bandinių. Kontrolinėje grupėje ir tarp berniukų bakterijų neradome. Iš 38 pirmos tiriamosios grupės vaikų, *G. vaginalis* rasta 7 bandiniuose. II ir III grupėse šis mikroorganizmas aptiktas atitinkamai 2 ir 4 bandiniuose. Manome, kad *G. vaginalis* gali būti vaikų neaiškios kilmės dizurijos priežastimi.

Raktažodžiai: *Gardnerella vaginalis*, šlapimo organų ligos, vaikai