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Changes in Urine Microflora in Children with Community-Acquired Urinary Tract Infection Admitted to Hospital Between 1990 and 2015: a Retrospective Full-Design Study of Case Series

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Background. *It is necessary to study the microbial spectrum of urine in order to determine the features of the urinary tract infection (UTI) course and to make the right choice of a therapeutic approach.* ***Objective.*** *Our aim was to study the structure of urine microflora in children with community-acquired UTI and its change in the period from 1990 to 2015.* ***Methods.*** *We carried out a continuous analysis of case histories of children admitted to hospital with UTI (pyelonephritis, cystitis, non-site specific urinary tract infection) in 1990, 2000, and 2015. We studied the results of triple (in succession) urine cultures. Shedding in a concentration of* $\geq 10^3$ *cfu/ml for primary pathogens,* $\geq 10^3$ *cfu/ml in boys and* $\geq 10^4$ *cfu/ml in girls for secondary pathogens,* $\geq 10^5$ *cfu/ml for doubtful pathogens considered to be a diagnostically significant one.* ***Results.*** *Members of the family Enterobacteriaceae were the main causative agents of the UTI in 1990 (found in 90.4% of 502 samples), 2000 (in 79.7% of 632 samples), and 2015 (in 67.6% of 801 samples, df =2,* $p < 0.001$*). Escherichia coli remained the most common microorganism, the isolation rate of which decreased from 79.9% in 1990 to 39.5% in 2015 (*$p < 0.001$*). In the period from 2000 to 2015, there was a decrease in the frequency of urine detection of Enterobacter spp. (from 5.9 to 2.5%;* $p < 0.001$*) and Citrobacter spp. (from 5.2 to 1%;* $p < 0.001$*) and, on the contrary, an increase in the isolation rate of Proteus spp. (from 7.8 to 11.7%;* $p = 0.005$*), Klebsiella spp. (from 2.8 to 12.9%;* $p < 0.001$*) and Enterococcus spp. (from 1.8 to 19.1%;* $p < 0.001$*); the latter two — due to more frequent shedding in boys (by 10.5 and 19.9%, respectively).* ***Conclusion.*** *The Enterobacteriaceae members, mainly E. coli and Enterococcus spp., remained the predominant UTI pathogens in children in 1990, 2000, and 2015. The isolation rate of E. coli has declined significantly in recent years, whereas that of Klebsiella spp. and Enterococcus spp. has increased.*

Key words: *children, urinary tract infection, urine, culture, microflora, Enterobacteriaceae.*

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Table 1. Diagnostic urine titres of the urinary tract infection pathogens [17]

Groups	UTI pathogens	Diagnostic titre
Primary pathogens (group I)	*Escherichia coli*, *Staphylococcus saprophyticus*, Leptospira, Salmonella, mycobacteria	$\geq 10^3$ cfu/ml
Secondary pathogens (group II)	*Enterobacter spp.*, *Klebsiella spp.*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Staphylococcus aureus*, *Citrobacter spp.*, *Morganella spp.*, *Serratia spp.*, *Haemophilus spp.*, *Streptococcus pneumoniae*, *Corynebacterium urealyticum*	Pure culture: men — $\geq 10^3$ cfu/ml, women — $\geq 10^4$ cfu/ml Mixed culture $\geq 10^5$ cfu/ml
Doubtful pathogens (group III)	Coagulase-negative staphylococci (with the exception of *S. saprophyticus*), *Streptococcus agalactiae*, *Acinetobacter spp.*, *Pseudomonas spp.*, *Stenotrophomonas maltophilia*	$\geq 10^5$ cfu/ml
Normal microflora of the urethra and genital organs	*Gardenella vaginalis*, *α*-streptococci, lactobacilli, bifidobacteria, diphtheroid bacilli	Urine isolation has no diagnostic value

Note. Primary UTI pathogens (group I) are able to independently cause damage to the urinary organs. Secondary UTI pathogens (group II) show pathogenic properties mainly against the background of other infections, weakening of the immune system, after invasive diagnostic and therapeutic procedures. Doubtful UTI pathogens (group III) hardly ever cause clinically significant UTIs. UTI — urinary tract infection.

Table 2. Characteristics of children with urinary tract infection and confirmed bacteriuria

Parameter	1990 *n* =502	2000 *n* =632	2015 *n* =801	p^1	p^2
Girls, abs. (%)	342 (68.1)	396 (62.7)	377 (47.1)	0.063	0.001
Children > 3 years, abs. (%)	124 (24.7)	175 (27.7)	437 (54.6)	0.287	0.001
UTI, abs. (%)					
• Pyelonephritis	338 (67.3)	441 (69.8)	624 (77.9)	0.414	0.001
• Cystitis	52 (10.4)	73 (11.6)	32 (4.0)		
• Other[3]	112 (22.3)	118 (18.7)	145 (18.1)		

Note. [1] — the results of a statistical comparison of children's characteristics in the samples of 1990 and 2000; [2] — the results of comparison in the samples of 1990, 2000, and 2015. (at *df* =2); [3] — non-site specific UTI. UTI — urinary tract infection.

Table 3. The urine isolation rate of microorganisms in children with urinary tract infection during the periods of 1990, 2000, and 2015

Microorganisms	**1990** ***n*** **=502**	**2000** ***n*** **=632**	**2015** ***n*** **=801**	***p*[1]**	***p*[2]**
Gram-negative, abs. (%)					
Enterobacteriaceae, total	454 (90.4)	504 (79.7)	541 (67.6)	0.001	0.001
• *E. coli*	401 (79.9)	332 (52.5)	316 (39.5)	0.001	0.001
• *Enterobacter spp.*	N/A	37 (5.9)	20 (2.5)	-	0.001
• *Citrobacter spp.*	N/A	33 (5.2)	8 (1.0)	-	0.001
• *Klebsiella spp.*	14 (2.8)	14 (2.2)	103(12.9)	0.671	0.001
• *Proteus spp.*	39 (7.8)	88 (13.9)	94 (11.7)	0.002	0.005
• *P. aeruginosa*	19 (3.8)	25 (4.0)	38 (4.7)	0.995	0.643
Gram-positive, abs. (%)					
Staphylococcus, total	15 (2.9)	35 (5.5)	35 (4.4)	0.054	0.115
• *S. epidermidis*	15 (2.9)	35 (5.5)	34 (4.3)	0.054	0.111
• *S. aureus*	N/A	N/A	1 (0.1)	-	-
Enterococcus spp.	9 (1.8)	31 (4.9)	153 (19.1)	0.008	0.001
Other[3], abs. (%)	5 (1)	37 (5.9)	34 (4.2)	0.001	0.001

Note. [1] — the results of a statistical comparison of the isolation rate of microorganisms in children in the samples of 1990 and 2000; [2] — the results of comparison in the samples of 1990, 2000, and 2015 (at *df* =2); [3] — *Morganella spp.*, *Acinetobacter spp.* and *Streptococcus spp.* N/A — no data available on the microorganism detection.

Table 4. The urine isolation rate of microorganisms in children with urinary tract infection aged over 3 years in 2000 and 2015

Microorganisms	**2000** ***n*** **=457**	**2015** ***n*** **=364**	***p***
Gram-negative, abs (%)			
Enterobacteriaceae, total	348 (76.2)	239 (65.7)	0.002
• *Escherichia coli*	258 (56.2)	167 (45.9)	0.004
• *Enterobacter spp.*	21 (4.6)	8 (2.2)	0.098
• *Citrobacter spp.*	22 (4.8)	2 (0.5)	0.001
• *Klebsiella spp.*	9 (2.0)	21 (5.8)	0.008
• *Proteus spp.*	38 (8.3)	41 (11.3)	0.193
P. aeruginosa	20 (4.4)	16 (4.4)	0.875
Gram-positive, abs (%)			
Staphylococcus, total	32 (7.0)	27 (7.4)	0.926
• *S. epidermidis*	32 (7.0)	1 (0.3)	0.001
• *S. aureus*	0	26 (7.1)	0.001
Enterococcus spp.	28 (6.1)	58 (15.9)	0.001
Other*, abs (%)	29 (6.3)	24 (6.6)	1.000

Note. * — *Morganella spp.*, *Acinetobacter spp.* and *Streptococcus spp.*

Table 5. The urine isolation rate of microorganisms in boys in 2000 and 2015

Microorganisms	**2000** ***n*** **=236**	**2015** ***n*** **=424**	***p***
Gram-negative, abs. (%)			
Enterobacteriaceae, total, incl.	180 (76.3)	253 (59.7)	0.001
• *Escherichia coli*	66 (27.9)	107 (25.2)	0.502
• *Enterobacter spp.*	20 (8.5)	13 (3.1)	0.005
• *Citrobacter spp.*	15 (6.4)	3 (0.7)	0.001
• *Klebsiella spp.*	5 (2.1)	53 (12.6)	0.001
• *Proteus spp.*	74 (31.4)	77 (18.1)	0.001
P. aeruginosa	20 (8.4)	27 (6.4)	0.395
Gram-positive, abs. (%)			
S. epidermidis	12 (5.1)	15 (3.5)	0.450
S. aureus	0	1 (0.2)	1.000
Enterococcus spp.	12 (5.1)	106 (25.0)	0.001
Other*, abs (%)	12 (5.1)	22 (5.2)	0.900

Note. * — *Morganella spp., Acinetobacter spp.* and *Streptococcus spp.*

FINANCING SOURCE

Not specified.

CONFLICT OF INTERESTS

Not declared.