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Article

Prevalence of urinary infection in children and adolescentes

Prevalência de infecção urinária em crianças e adolescentes

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ABSTRACT: Urinary tract infection (UTI) is one of the most common infections in children, especially among neonates, and it tends to recur. In this context, a quicker diagnosis of UTI in children and adolescents can aid in establishing early and effective therapy, thereby preventing long-term consequences. **OBJECTIVE**: To determine the prevalence of microorganisms found in positive urine samples of children and adolescents, as well as their resistance and sensitivity. **METHODS**: A cross-sectional study was conducted using urine samples from children and adolescents collected in 2019. Analyses were performed by the Carlos Chagas Laboratory, Grupo Sabin, in Cuiabá, MT. The data were subjected to descriptive statistical analysis. **RESULTS**: Among the 532 samples analyzed, 81.76% were enterobacteria, with *E. coli* being the most prevalent (64.13%). Females had a higher incidence across all age groups, particularly among those aged 0 to 2 years and 11 months. Age-wise analysis revealed that 57% of UTIs occurred in children aged 0 to 2 years and 11 months. The sensitivity profile of enterobacteria indicated high sensitivity to meropenem, ertapenem, ceftriaxone, and ceftazidime, while there was significant resistance to ampicillin, amoxicillin, and sulfamethoxazole/trimethoprim. **DISCUSSION**: The prevalence of *E. coli* as the causative agent of UTIs in children is consistent with previous studies. *E. coli* resistance to certain antibiotics underscores the need to consider alternative treatment options. **CONCLUSION**: It is concluded that *E. coli* is the primary microorganism responsible for UTIs in children, with a prevalence among females and the age group of 0 to 2 years and 11 months. Regarding sensitivity profiles, bacteria were more sensitive to carbapenems and aminoglycosides. Early diagnosis is crucial to prevent long-term complications associated with UTIs in children.

KEY WORDS: Bacteriuria; Urinary Tract Infection; Pyelonephritis; Urine.

RESUMO: A infecção do trato urinário (ITU) é uma das infecções mais comuns entre as crianças, sendo mais frequente entre os neonatos, além de muito recorrente. Neste contexto, maior agilidade em estabelecer o diagnóstico da ITU em crianças e adolescentes pode ajudar a estabelecer precocemente a terapêutica assertiva e prevenir consequências tardias. **OBJETIVO:** Verificar a prevalência dos microrganismos encontrados nas urinas positivas das crianças e adolescentes, bem como sua a resistência e sensibilidade. **MÉTODOS**: Foi conduzido um estudo transversal com amostras de urina de crianças e adolescentes coletadas em 2019. As análises foram realizadas pelo Laboratório Carlos Chagas Grupo Sabin em Cuiabá, MT. Os dados foram submetidos a análises estatísticas descritivas. **RESULTADOS**: Entre as 532 amostras analisadas, 81,76% foram enterobacteriales, sendo a *E. coli* a mais prevalente (64,13%). O sexo feminino apresentou maior incidência em todas as faixas etárias, sendo mais expressivo entre 0 a 2 anos e 11 meses. A análise por faixa etária revelou que 57% das ITUs ocorreram em crianças de 0 a 2 anos e 11 meses. O perfil de sensibilidade das enterobacteriales indicou alta sensibilidade a meropenem, ertapenem, ceftriaxona e ceftazidima, enquanto houve resistência significativa a ampicilina, amoxicilina e sulfametoxazol/trimetoprim. **DISCUSSÃO**: A prevalência da *E. coli* como agente causador de ITUs nas crianças é consistente com estudos anteriores. A resistência da *E. coli* a certos antibióticos destaca a necessidade de considerar opções alternativas de tratamento. **CONCLUSÃO**: Conclui-se que a *E. coli* é o principal microrganismo de ITUs em crianças, com prevalência no sexo feminino e faixa etária de 0 a 2 anos e 11 meses. Em relação ao perfil de sensibilidade as bactérias foram mais sensíveis aos carbapenêmicos e aminoglicosídeos. O diagnóstico precoce é crucial para prevenir complicações a longo prazo associadas à ITU em crianças.

PALAVRAS-CHAVE: Bacteriuria; Infecção Trato Urinário; Pielonefrite; Urina.

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INTRODUCTION

Urinary tract infection (UTI), according to the Brazilian Society of Pediatrics, is most common among children and the most common among newborns. Studies indicate that recurrence (two or more infectious episodes in six months or at least three episodes in one year) occurs significantly more in patients under 2 years of age and females. There is a 50% prevalence of recidivism in girls during the first year and 75% in the following two years. In relation to boys, it was noticed that the presence of an intact foreskin increases the risk of recurrence[1] between 3.7 and 11 times.

In general, UTIs in pediatrics are established from the same pathological process that occurs in adults. In more severe cases, the pathogen continues its upward course until it reaches higher structures, causing infection and renal inflammation known as pyelonephritis[2]. However, although there is this similarity in the course of the disease, UTI in childhood has some relevant peculiarities linked to the anatomy of the childhood urinary tract, which results in a range of restricted etiologies and sequelae typical of this age group. Furthermore, according to the literature, there is a prevalence of UTI in males up to the third month of life. However, in the pediatric universe this clinical difference is more linked to the patient's age group than to the severity of the condition.[3].

Non-specific and systemic signs and symptoms, such as high fever, irritability, gastrointestinal tract disorders, reduced general health and reduced eating, are more commonly found in children under 2 years of age[4]. In older children, a more typical semiology of low UTI appears, such as dysuria, increased urinary frequency and changes in the appearance of urine[5]. Although, in most cases, the clinical manifestation is sufficient to establish the diagnosis of the disease, complementary tests are important to confirm the hypothesis, define the pathogen and its sensitivity profile, with urine and urine culture tests being the most requested[6].

Regarding to adolescents, there is a connection between the occurrence of urinary infections and hormonal changes, characteristic of this stage of life, although it is not yet well understood. It seems to be related to the lack of hygiene after urination and sexual intercourse, as it facilitates the moving of bacteria that live in the urethra and anal region. UTI has a peak incidence in childhood in young children during the learning phase of self cleaning. Its prevalence increases again in adolescence, when hormonal changes favor vaginal colonization by nephritogenic bacteria that, migrating to the periurethral area, can ascend through the urinary tract, causing urinary tract infection. During this period, infections caused by Staphylococcus saprophyticus stand out, particularly in sexually active adolescents[7].

Furthermore, the success of therapy in children and adolescents largely depends on promptly seeing a doctor and the correct choice of antimicrobial therapy. However, clinicians face a dilemma during diagnosis while trying to distinguish asymptomatic bacteriuria from urinary tract infections (UTIs) in these children, since the asymptomatic bacteriuria is not associated with the development of kidney scarring and therefore does not require antibiotic treatment[8].

In this context, many clinicians rely on the combination of urinalysis (UA) results and the presence or absence of symptoms to determine when to initiate antibiotic treatment in children with bacteriuria[9].

Therefore, given the lack of current Brazilian studies on the subject, especially in adolescents, this research aims to verify the prevalence of microorganisms found in the positive urine of children and adolescents, as well as their resistance and sensitivity. The purpose is, therefore, to offer scientific basis so that there is greater agility in establishing the diagnosis of UTIs in childhood and adolescence, and to indicate the best antibiotic to be used empirically to, thus, prevent late consequences.

MATERIAL E METHODS

A cross-sectional study was carried out with urine samples from children and adolescents between 1 month and 15 years of age. The samples were collected from the Shift system databases of the Carlos Chagas Grupo Sabin Laboratory in Cuiabá – MT for the year 2019.

The study included only records of urine samples collected and received in the Laboratory of the Cuiabá and Várzea Grande (MT) units from female and male patients, aged between 1 month and 15 years. Data that did not present information consistent with the study and without a confirmed diagnosis of urinary tract infection were excluded.

The Carlos Chagas Grupo Sabin laboratory routinely collects samples from patients by qualified and properly trained technicians and professionals. Urine samples were collected by spontaneous urination and by urinary catheter. The entire technical, analytical and post-analytical process was carried out by trained and qualified microbiologists who work in the Laboratory's microbiology sector. All data is recorded and stored in its own database. This laboratory recommends collecting the urine sample as described by Kunin[10]. In addition, urine collection, packaging and transportation also follow biosafety standards. Sensitivity profile analyzes were standardized according to the Clinical and Laboratory Standards Institute[11].

This study was approved by the Research Ethics Committee of UNIVAG – Centro Universitário under protocol number 5,990,417. The collected data were listed in Excel with descriptive statistical analysis with frequency, percentages and prevalence measurements.

RESULTS

Between January and December 2019, 532 urine samples were collected from children and adolescents. Among the microorganisms found, 81.76% (435) were Gram-negative Bacilli (Enterobacteriales – glucose fermenters), followed by 12.03% (64) Gram-positive and only 6.2% (33) were Gram-negative Bacilli (Non-glucose fermenters – Pseudomonas aeruginosa), as demonstrated in table 1. Among Gram-positive, the prevalence was *Enterococcus faecalis*, representing 81.25% (52) of group. In the group of enterobacteria, the most common microorganism found was *Escherichia coli* (E. coli), representing 64.13% (279) of cases, followed by *Proteus mirabilis* with 15.8% (69) (Table 1).

TABLE 1 – Microorganisms found in urine samples from children and adolescents by group and species

Group		
Bacteria	**N**	**%**
Enterobacteria	435	81,7
Non-glucose fermenters (Pseudomonas aeruginosa)	33	6,2
Gram-positive	64	12
Total	532	100
Species		
Gram-positive Bacteria	N	%
Enterococcus faecalis	52	81,2
Streptococus agalactiae	7	10,9
Staphylococus saprophyticus	5	7,8
Enterobacteria	N	%
Escherichia coli	279	64,1
Proteus mirabilis	69	15,8
Citrobacter freundii	13	2,9
Enterobacter aerogenes	13	2,9
Proteus vulgaris	7	1,6
Citrobacter diversus	7	1,6
Klebsiella pneumoniae	41	9,4
Escherichia coli + Citrobacter freundii	1	0,2
Morganella morganii	3	0,6
Serratia rubideae	1	0,2
Klebsiella pneumoniae + Escherichia coli	1	0,2

Table 2 shows the most affected sex for each age group. The female sex stood out at all ages in the researched sample in relation to the male, and the age range was greater between 0 and 2 years and 11 months.

TABLE 2 – Number of children and adolescents comparing sex and age group

Sex	Age							
	0 to 2 years and 11 months		3 to 5 years and 11 months		6 to 10 years and 11 months		11 to 15 years and 11 months	
	N	%	N	%	N	%	N	%
Female	165	55	76	68	64	75	26	63
Male	134	45	35	32	21	25	15	37
Total	299	100	111	100	85	100	41	100

According to the data shown in Table 3, among girls, there was a growth of some Enterobacteriaceae in 83.5%. Within this group, 63% (208) of the cases presented *E. coli* and 8.7% (29) presented *Klebsiella pneumoniae*. In males, enterobacteria represented 78.2% (158) of the sample, 35.1% (71) of *E. coli* and 23.2% (47) of *Proteus mirabilis*.

In the *Pseudomonas aeruginosa* group, 51.5% (17) of cases were female. In Gram+, girls represented 56.2% (36) of cases. Among the enterobacteria, 63.6% (277) of the samples were female. Within this group, 69.1% (47) of the urines with *Proteus mirabilis* were male (Table 3).

TABLE 3 – Microorganisms found in children and adolescents urine samples in relation to males and females

Microrganism	Female		Male	
	N	**%**	**N**	**%**
Pseudomonas aeruginosa	17	5,1	16	7,9
Gram +	36	10,9	28	13,8
Enterococcus faecalis	26	7,8	26	12,8
Streptococcus agalactiae	6	1,8	1	0,4
Staphylococcus saprophyticus	4	1,2	1	0,4
Enterobacteriales	277	83,5	158	78,2
Escherichia coli	208	63	71	35,1
Proteus mirabilis	21	6,3	47	23,2
Citrobacter freundii	9	2,7	4	1,9
Enterobacter aerogenes	5	1,5	8	3,9
Proteus vulgaris	2	0,6	5	2,4
Citrobacter diversus	1	0,3	6	2,9
Klebsiella pneumoniae	29	8,7	12	5,9
E. coli + citrobacter freundii	0	0	1	0,4
Morganella morganii	0	0	3	1,4
Serratia rubideae	0	0	1	0,4
Klebsiela pneumoniae + E. coli	1	0,3	0	0
Total	330	100	202	100

Regarding age group, 251 out of the 435 patients (57%) in whom enterobacteria were found occurred in the age group of 0 to 2 years and 11 months. The second most prevalent age group was 3 to 5 years and 11 months, with 20% (88). 30 out of 64 patients with Gram-positive bacteria, approximately 50% also occurred in younger children. 18 out of the 33 cases of Pseudomonas aeruginosa (54%) occurred in the age group of 0 to 2 years and 11 months, followed by the group aged 3 to 5 years and 11 months with half the value (Table 4).

In all age groups, the most common bacteria found was E. coli, being more affected in younger children (0 to 2 years and 11 months) and 3 years and 5 months, respectively, at 52% (156), 49.5 % (55), as explained in Table 4.

TABLE 4 – Microorganisms found in children and adolescents urine samples in relation to age

Microorganism	0 to 2 years and 11 months		3 to 5 years and 11 months		6 to 10 years and 11 months		11 to 15 years and 11 months	
	N	%	N	%	N	%	N	%
Pseudomonas	18	6	9	8,1	5	5,8	1	1,4
Gram +	30	10	14	12,6	14	16,2	6	8,8
Enterococcus faecalis	27	9	12	10,8	10	11,6	3	4,4
Streptococcus agalactiae	0	0	2	1,8	5	5,8	0	0
S. saprophyticus	0	0	3	2,7	2	2,3	0	0
Enterobacteria	251	83,9	88	79,2	67	77,9	29	42,6
Escherichia coli	156	52,1	55	49,5	49	56,9	19	27,9
Proteus mirabilis	39	13	21	18,9	5	5,8	4	5,8
Citrobacter freundii	9	3	3	2,7	1	1,1	0	0
Enterobacter aerogenes	10	3,3	0	0	3	4,4	0	0
Proteus vulgaris	1	0,3	0	0	1	1,1	0	0
Citrobacter diversus	3	1	1	0,9	2	2,3	1	1,4
Klebsiella pneumoniae	23	7,6	7	6,3	6	6,9	5	7
E. coli + C. freundii	1	0,3	0	0	0	0	0	0
Morganella morganii	3	1	0	0	0	0	0	0
Serratia rubideae	1	0,3	0	0	0	0	0	0
K. pneumoniae + E. coli	1	0,3	0	0	0	0	0	0
Total	299	56,2	111	20,8	86	16,1	68	12,7

Frame 1 presents the sensitivity profile of enterobacteria. The antibiotics to which these bacteria were most sensitive were meropenem and ertapenem, with 434 patients sensitive (99.7%). In addition to these, the antibiotics with more than 90% sensitivity in the sample were, in descending order: amikacin (99.3%), gentamicin (97.1%), imipinem (94.4%), cefepime (94.2%), ceftriaxone (93.7%) and ceftazidime (93.5%). The most resistant antibiotics were: ampicillin (29.16%), amocixillin (33.4%) and sulfamethoxazole/trimethoprim (35.48%).

FRAME 1 – Enterobacteria sensivity profile

Medicine	Sensitive		Resistant	
	N	%	N	%
Imipenem	411	94,4	24	5,6
Amikacin	430	99,3	3	0,7
Amoxicillin	259	66,5	130	33,4
Ampicillin	306	70,83	126	29,16
Ciprofloxacin	368	85,58	62	14,41
Ceftriaxone	407	93,77	27	6,22
Ceftazidime	408	93,57	28	6,42
Cefuroxime	371	89,39	44	10,6
Cefepime	409	94,02	26	5,97
Gentamicin	422	97,01	13	2,98
Sulfamethoxazole/trimethoprim	280	64,5	154	35,48
Meropenen	434	99,77	1	0,22
Ertapenem	433	99,77	1	0,22
Nitrofurantoin	229	24,62	13	5,37
(tested for E. coli only)	270	97,82	6	2,17

Pseudomonas aeruginosa was sensitive to all antibiotics tested: amikacin, ciprofloxacin, cefepime, ceftazidime, gentamicin, levofloxacin, piperacillin-tazobactan, meropenem and imipenem.

Regarding Gram-positives, Staphylococcus saprophyticus was sensitive to all tested antibiotics ciprofloxacin, nitrofurantoin and sulfamethoxazole/trimethoprim. Enterococcus faecalis were sensitive to all tested antibiotics: ampicillin, nitrofurantoin and levofloxacin. Streptococcus agalactiae was sensitive to all tested antibiotics: ampicillin, nitrofurantoin, levofloxacin, penicillin.

DISCUSSION

In this study, the prevalence of 64% of E. coli and approximately 16% of P. mirabilis was noted in the analyzed samples, which was compatible with data presented by Silva and Oliveira[3], where the first episode of UTI in 90% of girls and 80% of boys has E. coli as the predominant pathogen.

That fact can be explained by the ability of this pathogen to attack the endothelium of the urinary tract[3]. The literature says that E. coli is the etiological agent in approximately 80 to 90% of cases in the first episode of UTI in life[12,13]. Another review showed similar results, where E. coli was responsible for 80 to 90% of UTIs in children, then Enterobacter aerogenes, Klebsiella pneumoniae and Proteus mirabilis[14]. Infection with an organism different from E. coli is associated with a greater probability of final results, as Shaikh et al. [15], found in a meta-analysis of more than 1,200 children that those infected with non-E. coli had an increased risk of kidney scarring by 120%.

In the age group 0 to 2 years and 11 months, more than half of the cases are female, with a small prevalence observed, which increased as age increased, reaching 83% of cases in the group aged 11 to 15 years and 11 months. It is believed that this pattern of female predominance in cases of urinary tract infections is due to anatomical characteristics of female bodies. In women, the urethral orifice is closer to the anal ostium and the urethra is shorter, favoring upward bacterial migration. It is also worth highlighting the role of incorrect cleaning habits, such as not using running water to clean after a bowel movement, cleaning the region with movements in the anus-urethra direction and taking too long to change diapers after a bowel movement[16].

Regarding the causes, Singh-Grewal et al.[17], demonstrated that uncircumcised male babies with fever have a prevalence of urinary tract infection eight times higher than those who are circumcised. Another meta-analysis revealed that uncircumcised male newborns, younger than 3 months old, had a higher prevalence of UTI compared to both male and female babies. In[18] addition to those peculiarities common to all pediatric patients, the relationship between congenital malformations of the urinary tract and infection is well established in the literature. Among the most common anomalies are neurogenic bladder, urethral duplication, pelvic kidney and, more rarely, pancake kidney. Generally, the anomalous anatomical condition favors infection by generating significant vesicourethral reflux (VUR), which carries bacteria upward throughout the urinary tract, which can result in recurrent urinary infections[3,19].

Most of the available data in the literature suggests that there is a decreasing prevalence of UTI with age, both in girls and circumcised and uncircumcised boys, significantly decreasing after 6 or 12 months of age. In this study, the first age group, 0 to 2 years and 11 months was noticed to be the most prevalent among the analyzed cases.

A study carried out at the Hospital Universitário da Universidade de São Paulo (HU-USP) demonstrated that the highest prevalence of infections was concentrated in the two-year-old-and-younger[5] group. According to Korbel et al.[20]. UTI has a bimodal age of onset, with the first peak being in the first year of life and the second between 2 and 4 years-old, the age that corresponds to the beginning of the practice of self-hygiene. It is worth mentioning that even though the general prevalence of infections decreases in both sexes, recurrence rates can reach 50% in 5 years among girls, whereas in boys it will rarely happen after 1 year of age[21].

Some reasons may be linked to a lower prevalence of urinary tract infections in older children, such as changes in anatomy, increasing the length of the urethra and reducing bacterial growth, better hygiene and better bladder control, in addition to a better immunological response to pathogen attacks[22].

Except for acute unfavorable repercussions that a UTI triggers in children, studies indicate that, due to the recurrent inflammatory and healing process triggered by each infection, recurrent urinary tract infections in children increase the occurrence of renal scarring, which can culminate in chronic renal failure, poor renal growth, systemic arterial hypertension and proteinuria[3]. Around 6% to 13% of children with kidney scars will develop high blood pressure, and in 5% to 10% they are the cause of chronic renal failure proteinuria[23]. This risk is increased with late diagnosis, which reinforces the importance of carrying out an early diagnosis[3].

Regarding the sensitivity profile, greater sensitivity was observed to meropenem, ertapenem, ceftriaxone and ceftadizime. In those tested only for E. coli, the greatest sensitivity was observed in pósitomycin (97.82%) and nitrofurantoin (24.62%). A study carried out in Porto Alegre showed a high sensitivity of E. coli to nitrofurantoin and nalidixic acid[24]. E. coli was highly resistant to sulfamethoxazole/trimethoprim and ampicillin, antimicrobials that for many years were the first choice for treatment. In the study by Swei Lo et al.[5], E. coli also showed greater resistance to ampicillin (61.3%) and sulfamethoxazole/trimethoprim (45%). A study carried out in Turkey between 2009 and 2014 demonstrated that E. coli resistance during the period increased by more than 20% in relation to ampicillin and more than 10% in relation to sulfamethoxazole/trimethoprim[25]. Recent studies demonstrate that E. coli, when compared to other pathogens, was the pathogen with the greatest resistance to antibiotics, with the production of extended-spectrum β-lactamases (ESBLs) being the most common cause of this phenomenon[26].

According to North American studies, 24% of Escherichia coli strains were resistant to sulfamethoxazole/trimethoprim and 45% to ampicillin. In relation to cephalosporins, amoxicillin-clavulanic acid, ciprofloxacin and nitrofurantoin, the results were more encouraging, showing resistance[27] of around less than 10%.

Vazourasa et al.[28], demonstrated that Pseudomonas

aeruginosa did not show resistance to ceftazidime, aminoglycosides or quinolones, since they are not multi-resistant bacteria, a result that is similar to those in this study. Furthermore, quinolones are low-cost and easily accessible antibiotics, facilitating home treatment for the patient, without the need of hospitalization[28].

In this study, Enterococcus faecalis did not demonstrate high resistance, being sensitive to all tested antibiotics, a different result from a study carried out in Amapá in which Enterococcus faecalis was the most resistant to the antibiotics ciprofloxacin, ampicillin and gentamicin, with 35.7%[29]. Both studies did not show resistance to vancomycin, which is a really worrying fact since patients who have bacterial infections presenting such resistance have to be isolated when hospitalized, especially with anal colonization, in order to prevent the spreading of the focus.

The authors are aware of the limitations for this study, such as the restricted age range up to 15 years-old, the non-separation of samples into outpatient and hospital samples; as well as it was not possible to quantify the urinary catheter samples collected from spontaneous urination collection, since they were secondary data.

CONCLUSION

It is concluded that urinary infections affect children under 2 years and 11 months, predominantly females. *E. coli* is the most present microorganism in those infections. Regarding the sensitivity profile, the bacteria were more sensitive to carbapenems and aminoglycosides.

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