

Prevalence of bacteriuria and bacterial resistance in adolescents from the center of the state of Tlaxcala, Mexico

Daniela Z. Méndez-Polonieski^{1,2}, Pablo Méndez-Hernández^{3,4*}, Olivier Barbier⁵, Manolo Ortega-Romero⁶, Juan C. Rubio-Gutiérrez⁵, Elodia Rojas-Lima⁷, Juana Narvaez-Morales⁵, Margarita Martínez-Gómez^{8,9}, Estela Cuevas-Romero^{2,8}, Rosalba Cerón-Meza³, and Mara Medeiros^{6,10}

¹Facultad de Ciencias de la Salud, Universidad Autónoma de Tlaxcala (UATx), Tlaxcala; ²Doctorado en Ciencias Biológicas, Centro Tlaxcala de Biología de la Conducta, UATx, Tlaxcala; ³Licenciatura en Naturopatía, Facultad de Agrobiología, UATx, Tlaxcala; ⁴Jefatura de Investigación del Hospital General Tlaxcala, Secretaría de Salud de Tlaxcala, Tlaxcala; ⁵Departamento de Toxicología, Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, Mexico City; ⁶Unidad de Investigación en Nefrología y Metabolismo Mineral Óseo, Hospital Infantil de México Federico Gómez, Mexico City; ⁷Unidad de Investigación en Salud en el Trabajo, Centro Médico Nacional "Siglo XXI", Instituto Mexicano del Seguro Social, Mexico City; ⁸Centro Tlaxcala de Biología de la Conducta, UATx, Tlaxcala; ⁹Instituto de Investigaciones Biomédicas, Departamento de Biología Celular y Fisiología, Unidad foránea Tlaxcala. Universidad Autónoma de México, Tlaxcala; ¹⁰Departamento de Farmacología, Facultad de Medicina. Universidad Autónoma de México, Mexico, City. Mexico

Abstract

Urinary tract infections and bacteriuria are common in the pediatric population, and antibiotic resistance is increasing significantly. Recurrent urinary infections, symptomatic or asymptomatic, are a risk factor for developing chronic kidney disease in adolescents and young adults. This study aimed to assess the prevalence of bacteriuria diagnosed by culture to identify the main causal agents and sensitivity to antibiotics in adolescents from the central region of the state of Tlaxcala. A cross-sectional study was carried out among 905 adolescents from 11 to 18 years old who lived in the central region of the state of Tlaxcala, Mexico. Bacteriuria was evaluated by positive nitrites and leukocyte esterase, and urine culture with antibiogram. Multivariate logistic regression models were executed to evaluate the risk of presenting bacteriuria, with a confidence level of 95%. A total of 31 participants had a positive urine culture, with a bacteriuria prevalence of 3.4%, of which 29 cases were asymptomatic. The most frequent agent was *Escherichia coli* in both sexes (28.6% in men and 29.7% in women) and regarding bacterial resistance: *E. coli* presented greater resistance to ampicillin, trimethoprim/sulfamethoxazol and ceftriaxone. The risk factors associated with bacteriuria were female sex, sexual activity, use of contraceptives, and greater consumption of sweetened beverages. Bacteriuria is common in this adolescent population, so its early identification is necessary to treat it, and to prevent its complications.

Keywords: Bacteriuria. Urinary tract infection. Adolescents. Bacterial resistance. Tlaxcala. Mexico.

Prevalencia de bacteriuria y resistencia bacteriana en adolescentes del centro del estado de Tlaxcala, México

Resumen

Las infecciones del tracto urinario y bacteriuria son comunes en la población pediátrica, y la resistencia a los antibióticos está aumentando significativamente. Las infecciones urinarias recurrentes, sintomáticas o asintomáticas, son un factor de riesgo para desarrollar Enfermedad Renal Crónica en adolescentes y adultos jóvenes. El objetivo de este estudio fue evaluar

*Correspondence:

Pablo Méndez-Hernández

E-mail: pmendezh@hotmail.com

1665-1146/© 2024 Hospital Infantil de México Federico Gómez. Published by Permanyer. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Date of reception: 03-05-2024

Date of acceptance: 12-09-2024

DOI: 10.24875/BMHIM.24000062

Available online: 21-11-2024

Bol Med Hosp Infant Mex. 2024;81(6):346-355

www.bmhim.com

la prevalencia de bacteriuria diagnosticada por cultivo, identificar los principales agentes causales y la sensibilidad a antibióticos, en adolescentes de la región centro del estado de Tlaxcala. Se realizó un estudio transversal en 905 adolescentes de 11 a 18 años de edad que vivían en la región centro del estado de Tlaxcala, México. La bacteriuria se evaluó mediante nitritos y esterasa leucocitaria positivas, y urocultivo con antibiograma. Se ejecutaron modelos de regresión logística multivariados para evaluar el riesgo de presentar bacteriuria, con un nivel de confianza del 95%. Un total de 31 participantes presentaron urocultivo positivo, siendo la prevalencia de bacteriuria del 3.4%, de los cuales 29 casos fueron asintomáticos. El agente que se presentó con mayor frecuencia fue *Escherichia coli* en ambos sexos (28.6% en hombres y 29.7% en mujeres), y respecto a la resistencia bacteriana: *E. coli* presentó mayor resistencia a Ampicilina, Trimetoprim/Sulfametoxazol y Ceftriaxona. Los factores de riesgo asociados a la bacteriuria fueron el sexo femenino, actividad sexual, uso de anticonceptivos y un mayor consumo de bebidas azucaradas. La bacteriuria es frecuente en esta población adolescente, por lo que es necesaria su identificación temprana para tratarlas y prevenir sus complicaciones.

Palabras clave: Bacteriuria. Infección urinaria. Adolescentes. Resistencia bacteriana. Tlaxcala. México.

Introduction

Urinary tract infection (UTI) is a significant public health problem worldwide, representing the second most common cause of infection in the general population¹. In Mexico, it is the third leading cause of morbidity in adolescents and adults². In addition, it is associated with high healthcare costs due to the misuse of antibiotics and antimicrobial resistance, which leads to the use of broader-spectrum and more expensive drugs³.

UTI has been considered a risk factor associated with renal malformations, chronic kidney disease (CKD), and hypertension. As a result, urine cultures have been routinely performed, often yielding positive results in apparently healthy and asymptomatic individuals, a characteristic termed asymptomatic bacteriuria (AB)⁴. Other studies have shown that AB has been associated with urinary symptoms such as nocturnal enuresis, urinary urgency, and foul-smelling urine in up to 70% of cases, which has been termed covert bacteriuria rather than asymptomatic⁵. AB has also been linked to urological abnormalities in 47% of cases, including vesicoureteral reflux (21-33%), renal scarring (10-26%), and bladder trabeculation (7-16%). However, other studies have reported a lower prevalence of urological abnormalities (renal malformations in 3-14% and reflux in 7-13% of cases), while some have found no differences between patients with AB and the general population⁴.

The AB prevalence is estimated at 3% in school-age children, 1% in preadolescent children⁵, and between 1.1 and 1.8% in adolescent females, while it is almost non-existent in males. Some studies report that AB is not associated with significant genitourinary tract malformations⁶. The bacteria isolated in patients with AB are primarily enterobacteria originating from the digestive system. *Escherichia coli* is the most frequent cause

of symptomatic UTIs and AB. However, other bacteria such as *Enterobacteriaceae*, *Pseudomonas aeruginosa*, *Enterococcus* species, and Group B *Streptococcus* can also be found. In males, *Enterococcus* species and Gram-negative bacilli are more common⁴.

UTIs, symptomatic and asymptomatic, are very common in the pediatric population. Over the past two decades, antibiotic resistance has been increasing significantly due to extended-spectrum beta-lactamase (ESBL) producing microorganisms⁷. *E. coli* is the microorganism with the highest antibiotic resistance in children and adolescents under 18-years-old: a meta-analysis in Organization for Economic Co-operation and Development (OECD) member countries showed a resistance prevalence of 53.4% for ampicillin, 23.6% for trimethoprim, 8.2% for amoxiclav, 2.1% for ciprofloxacin, and 1.3% for nitrofurantoin. Meanwhile, resistance in non-OECD countries was significantly higher: 79.8% for ampicillin, 60.3% for co-amoxiclav, 26.8% for ciprofloxacin, and 17% for nitrofurantoin⁸. In Mexico, it has also been shown that the susceptibility of many Gram-positive and Gram-negative uropathogens to widely used antibiotics has decreased, mainly due to prolonged and inappropriate use of these drugs⁹. Due to its frequency, *E. coli* has shown resistance to third-generation cephalosporins and quinolones, mainly due to the presence of ESBLs¹⁰. Likewise, *Enterococcus faecium* presents increasing resistance to vancomycin, *P. aeruginosa* to quinolones and third-generation cephalosporins, and *Enterobacter cloacae* and *Klebsiella pneumoniae* have shown multi-drug resistance¹¹.

Recurrent UTIs are one of the main risk factors for developing CKD in adolescents and young adults. It has been estimated that between 10 and 25% of children and adolescents with CKD have a history of chronic pyelonephritis¹². Furthermore, it has been reported that 10% of adolescents with recurrent UTIs developed CKD

after 25 years of follow-up¹³. This study aimed to evaluate the prevalence of bacteriuria, the main causative agents, and antibiotic sensitivity in adolescents from the central region of the state of Tlaxcala.

Materials and methods

A cross-sectional analytical study was conducted from September 2019 to March 2022 among students aged 11-18 years from public and private secondary and upper secondary schools in the municipalities of Tlaxcala, Chiautempan, and Apetatitlán in the state of Tlaxcala, Mexico. The sample size was calculated for cross-sectional studies, considering a 95% confidence level, 5% precision, an expected prevalence of 4.3%, a design effect of 2.0, and using the correction for diseases with prevalences below 10%: multiplying the precision by the expected prevalence¹⁴. A multi-stage sampling strategy was employed, stratified by education level (secondary or upper secondary) and proportional to the size of the strata (number of schools per municipality). Simple random sampling was used at each stage and in each selected school. Students who were taking antibiotics or non-steroidal anti-inflammatory drugs and female students who were menstruating or whose period had ended three or fewer days before the study were excluded from the study. This study was conducted following the Declaration of Helsinki, considering the ethical principles for medical research involving human subjects¹⁵. The study was approved by the research Ethics Committees of the Hospital Infantil de México and the Tlaxcala Health Ministry. Invited participants signed an assent form, and their parents provided informed consent.

Evaluation of bacteriuria and bacterial sensitivity to antibiotics

Bacteriuria was assessed using a first-morning urine sample (midstream), with the Clinitek Status Plus equipment using Multistix 10sg reagent strips, considering the parameters of bacteriuria, leukocyte esterase, and nitrites as suggestive of bacteriuria or UTI^{16,17}. In case of a positive parameter, a urine culture was performed. Uncentrifuged urine was inoculated using a calibrated loop on Blood Agar, MacConkey Agar, Biggy Agar, and Mannitol Salt Agar culture media. The inoculated plates were incubated at $37 \pm 0.5^\circ\text{C}$ for 72 h with daily review based on the literature¹⁸. After observing bacterial growth, differential staining and biochemical tests were

performed to identify genus and species. Finally, an antibiogram was conducted using the Kirby-Bauer method¹⁹. The diagnosis of AB was based on the Mexican Clinical Practice Guideline on "Diagnosis and treatment of uncomplicated UTI in individuals under 18 years of age in primary and secondary care levels". The criteria for a clean midstream urine sample in patients without permanent catheters were the presence of significant bacteriuria without clinical manifestations and two positive cultures. Significant bacteriuria refers to the isolation of a recognized urinary pathogen in a urine culture, collected aseptically, with a colony-forming unit (CFU) count that varies according to the urine collection method: spontaneous micturition, transurethral catheterization, or suprapubic puncture²⁰. In this study, the isolation of at least 100,000 CFU per mL of the same bacterial species was considered significant. In addition, since some authors recommend that in the case of males, the diagnosis of AB can be made with a single culture^{21,22}, and due to logistical difficulties in collecting a second sample in different schools, this study only cultured one urine sample for both males and females.

Evaluation of urinary symptoms

The assessment of urinary symptoms was conducted using the following questions: in the past year, have you experienced burning or pain while urinating? While urinating, do you feel the need to urinate more but cannot? Do you frequently feel an urgency to urinate more than usual? Has a doctor ever diagnosed you with an UTI?

Evaluation of family socioeconomic characteristics and sugary drink consumption in participants

A self-administered questionnaire was used for parents or guardians, consisting of 154 questions divided into sections: personal and pathological history, family environmental exposure, and occupational data. In addition, the following aspects were evaluated in the participants: pathological history, family medical history, medical care, hygienic-dietary habits, urinary history and symptoms, sexuality, substance use, quality of life, and physical examination.

The socioeconomic level was assessed according to the Mexican Association of Market Intelligence and Public Opinion Agencies (AMAI, for its Spanish acronym)²³, which classifies into seven social strata. However,

Table 1. Sociodemographic, anthropometric, and clinical characteristics of participants, by sex

Variables	Sex		p value
	Male (n = 415) (45.9%)	Female (n = 490) (54.1%)	
Age, years (mean \pm SD)	13.8 \pm 1.7	13.8 \pm 1.6	0.641
Secondary school			
Public (%)	57.5	63.7	0.078
Private (%)	42.5	36.3	
Upper secondary (high school)			
Public (%)	45.4	68.1	0.001
Private (%)	54.6	31.9	
Socioeconomic level*			
Very low (%)	1.7	1.4	0.756
Low (%)	53.6	57.4	0.258
Medium (%)	44.7	41.2	0.290
Frequency of potable water supply to house*			
Daily (%)	51.8	54.1	0.477
Every third day (%)	37.3	35.8	0.649
Twice a week (%)	8.8	8.5	0.866
Once a week (%)	0.9	0.7	0.771
Occasionally (%)	0.6	0.6	0.801
Never (%)	0.6	0.3	0.447
Body mass index†			
Numerical, kg/m ² (mean \pm SD)	21.4 \pm 0.2	22.1 \pm 0.1	0.013
Underweight (%)	1.7	0.6	0.110
Normal (%)	56.2	58.6	0.439
Overweight (%)	23.2	28.5	0.068
Obesity (%)	18.9	12.3	0.004
Waist circumference, cm (mean \pm SD)	79 \pm 1.5	74 \pm 1.3	0.012
Abdominal obesity‡			
Normal	71.4	75.8	0.134
Risk of abdominal obesity	18.7	15.6	0.224
Abdominal obesity	9.9	8.6	0.486

*Information was provided by parents and/or guardians.

The socioeconomic level was assessed using items on maternal education, paternal education, electricity supply (public service, private plant, solar panel, no electrical service), type of flooring in the house (cement, tile, wood, dirt, other material), number of people living in the household, and type of drainage or sewage connection (public network, septic tank, pipe leading to a ravine, pipe leading to a river, no drainage); according to the Mexican Association of Market Intelligence and Public Opinion Agencies (AMAI, for its Spanish acronym)²³, socioeconomic level is classified into seven social strata, however, for this analysis only four categories are considered: very low (score 0-89), low (score 135-190), medium (score 191-204), and high (score > 205).

†BMI was calculated using the formula weight (kg)/height² (m), and depending on the child's sex, BMI, and age, it was categorized as underweight (< 3rd percentile), normal (3rd-84.9th percentile), overweight (85th-97th percentile), and obesity (> 97th percentile)²⁵.

‡The Abdominal Obesity Index was calculated based on waist circumference values and classified as normal (< 75th percentile), risk of abdominal obesity (75th-90th percentile), and abdominal obesity (> 90th percentile)²⁶.

SD: standard deviation.

in this study, they were condensed into four categories: very low (score 0-89), low (score 135-190), medium (score 191-204), and high (score > 205).

The intake of sugary drinks was quantified by the number of portions consumed per day, and the following beverages were included in the study: cola, flavored soft drinks, diet soft drinks, powdered flavored water, natural fruit juice, industrialized juice, industrialized tea, coffee with milk, coffee without milk, atole (a traditional hot corn-based beverage) with milk, atole without milk, hot chocolate with milk, and hot chocolate without milk²⁴.

Evaluation of body mass index (BMI) and abdominal obesity

Body mass index (BMI) was calculated using the formula weight (kg)/height² (m), adjusted for age and sex. Participants were categorized into underweight (< 3rd percentile), normal (3rd-84.9th percentile), overweight (85th-97th percentile), and obese (> 97th percentile)²⁵. Abdominal obesity was determined based on waist circumference values and classified as normal (< 75th percentile), at risk of abdominal obesity (75th-90th percentile), and abdominal obesity (> 90th percentile)²⁶.

Table 2. Results of urine cultures and etiological agents, by sex (n = 71)

Urine culture results and etiological agents	Sex	
	Male* (n = 7) (9.9%)	Female* (n = 64) (90.1%)
Negative cultures	n = 4 (57.1%)	n = 36 (56.3%)
Positive cultures	n = 3 (57.2%)	n = 28 (43.8%)
Etiological agent (%)		
<i>Escherichia coli</i>	28.6%	29.7%
<i>Staphylococcus epidermidis</i>	14.3%	17.2%
<i>Enterococcus faecalis</i>	14.3%	12.5%
<i>Lactobacillus</i>	-	9.3%

*Algunos participantes mostraron cultivos con más de un agente etiológico: 2 hombres y 16 mujeres. Negative culture: considered when bacterial growth was < 100,000 CFU/mL over a 72-h period; Positive culture: considered when AB when bacterial growth was greater than 100,000 CFU/mL²⁰⁻²². In the case of females, cultures with more than one etiological agent were observed.

Statistical analysis

In order to compare the sociodemographic, anthropometric and clinical characteristics by sex, comparisons of means were performed for numerical variables, using linear regression; and comparisons of percentages for nominal variables, using logistic regression. A comparison of bacterial resistance percentages of pathogens to each antibiotic was carried out. The presence of bacteriuria was compared against its absence across sociodemographic, anthropometric, and clinical characteristics. Furthermore, this study hypothesized that there was a higher risk of presenting AB in females compared to males. To test this, multivariate logistic regression models were executed with a 95% confidence level and adjusted for age, sex, sexual activity, contraceptive use, and sugary drink intake. Statistical tests were performed using STATA Version 15.0 software.

Results

Table 1 shows the sociodemographic, anthropometric, and clinical characteristics of the 905 participants. The average age was 13 years, 54.1% were female, about 60% were enrolled in public schools, and 55% were categorized as low socioeconomic status. Regarding nutritional status, 23.2% of males and 28.5% of females were overweight, while 18.9% of males and 12.3% of females were obese. In addition, 9.9% of males and 8.6% of females showed abdominal obesity.

Table 2 presents the results of the cultures and etiological agents by sex. Seventy-one urine cultures were performed on participants who showed suspicion of bacteriuria, that is, positive nitrite test, positive leukocyte esterase test, or moderate presence of bacteria in urine, resulting in 31 positive cultures (43.7%). The most frequent agent in both sexes was *E. coli* (28.6% in males and 29.7% in females), while *Staphylococcus epidermidis* was detected in 14.3% of males and 17.2% of females, and *Enterococcus faecalis* was isolated in 14.3% of males and 12.5% of females. Finally, *Lactobacilli* was found in 9.3% of the cultures from females, and 2 males and 16 females presented two etiological agents.

Table 3 shows the bacterial resistance of the etiological agents found in positive urine cultures. *E. coli* showed higher resistance to ampicillin, trimethoprim/SMX, and ceftriaxone; *S. epidermidis* demonstrated resistance to clindamycin and penicillin; and *E. faecalis* showed resistance to tetracycline and nitrofurantoin.

Table 4 presents the prevalence of bacteriuria and its associated risk factors. Thirty-one cases with positive urine cultures were identified, the prevalence of symptomatic or AB was 3.4%, AB was 3.5%, and the prevalence of AB was. The most common symptom was urinary urgency (3.2% in cases with bacteriuria and 1.5% without bacteriuria). Furthermore, females showed a significantly higher prevalence of bacteriuria compared to males (3.1% vs. 0.3%, respectively; $p = 0.0001$).

Regarding risk factors related to bacteriuria, a higher percentage of adolescents with sexual activity and contraceptive use showed a higher prevalence of bacteriuria (3.2%) compared to those who did not report these activities (0.1%; $p = 0.043$ in both cases). In addition, those who reported consuming an average of more portions of sugary drinks per day (3.4 portions) showed a higher prevalence of bacteriuria compared to those without bacteriuria (2.1 portions) ($p = 0.036$).

Table 5 shows the probability of presenting bacteriuria (symptomatic or asymptomatic) concerning female sex and other risk factors. In a bivariate analysis, females were 8.3 times more likely to present bacteriuria than males (95% confidence interval [CI] 2.5-27.7; $p = 0.001$). In the multivariate analysis, the probability of presenting bacteriuria in females increased to 9 times higher than in males (95% CI 2.6-31.2; $p = 0.000$).

Discussion

This study demonstrated that bacteriuria is common in this adolescent population from central Tlaxcala

Table 3. Bacterial resistance to antibiotics of etiological agents found in positive urine cultures (n = 31)

Antibiotic	Etiological agent found in positive urine cultures*			p value
	<i>Escherichia coli</i> (Gram-negative) (n = 17) (55%)	<i>Staphylococcus epidermidis</i> (Gram-positive) (n = 8) (26%)	<i>Enterococcus faecalis</i> (Gram-positive) (n = 6) (19%)	
Ampicillin (%)	58.8	0	11.1	0.0001
Amoxicillin/Clavulanic acid (%)	29.4	N/A [†]	11.1	0.319
Nitrofurantoin (%)	23.5	20	16.6	0.932
Trimethoprim/SMX (%)	52.9	N/A [†]	N/A [†]	0.003
Clindamycin (%)	N/A [†]	60	0	0.012
Tetracycline (%)	N/A [†]	30	55.5	0.228
Penicillin (%)	N/A [†]	60	11.1	0.021
Ceftriaxone (%)	50	0	0	0.0001

*Positive urine culture was considered as bacterial growth greater than 100,000 CFU/mL²⁰⁻²².

[†]For the selection of the antibiotic used for each etiological agent, the characteristics of the bacteria (whether they were Gram-positive or Gram-negative) were taken into account.

state, with enterobacterium *E. coli* being the most frequent causative agent, isolated in nearly half of the cultures. In addition, bacterial resistance to ampicillin, trimethoprim/sulfamethoxazole, and ceftriaxone was observed. Furthermore, the main risk factors identified were female sex, sexual activity, use of contraceptive methods, and higher consumption of sugar-sweetened beverages.

The prevalence of symptomatic (3.4%) or AB (3.2%) found in our study is higher than the prevalence reported in a meta-analysis and systematic review of 40 studies from various countries, which considered a population of 49,806 children and adolescents under 19 years of age, showing a bacteriuria prevalence of 0.37% in males and 0.47% in females. The highest prevalences were found in uncircumcised males under 1 year of age and in females over 2 years old; however, the prevalence of AB decreased in adolescent males to 0.08%²⁷. Another study evaluated the prevalence of asymptomatic urinary abnormalities in 2,500 adolescents using reagent strips and optical microscopy: adolescents with abnormal results were re-examined after 2 weeks, and those who had abnormal results twice underwent systemic clinical examinations and additional clinical and laboratory studies, detecting 23 cases of AB (0.9%), all of which were in females²⁸.

Asymptomatic urinary infections are generally caused by Gram-negative bacteria such as *E. coli*; however, bacterial strains associated with AB express fewer virulence factors than bacterial strains involved in febrile

UTIs. It has been discovered that these strains have different genes for the production of fimbriae, which are important for *E. coli*'s ability to ascend the urinary tract²⁹. The host response to AB is also altered, as interleukins (IL) 6 and 8 were found to be elevated in 63% and 76% of children under 6 years old with febrile UTIs, respectively; while no child with AB had elevated levels of IL-6, and only 30% had elevated levels of IL-8³⁰.

On the other hand, toll-like receptor 4 (TLR-4), an important transmembrane protein in cell signaling and activation of the innate immune system, has been observed to be reduced by almost 50% in children with AB. This could contribute to the weak mucosal immune response to bacteria in AB³¹. Analysis of the TLR-4 promoter sequence has shown that patients with AB have fewer genotype variants and reduced expression compared to patients with UTI symptoms, further supporting TLR-4 alterations at the genomic level in AB³². The combination of altered bacterial characteristics and host response in AB suggests that the phenomenon could represent a form of commensalism, a symbiotic relationship in which bacteria benefit while the human host normally neither gains benefit nor suffers harm³³. In fact, intravesical inoculations with a modified *E. coli* strain isolated from patients with AB have been successfully used to treat recurrent UTIs in the adult population^{5,34-36}.

Regarding the uropathogens isolated in our study, *E. coli* was the most frequent (55%), a finding that is

Table 4. Risk factors associated with the presence of asymptomatic bacteriuria in the participant population

Variables	Bacteriuria [‡]		p-value
	Absent (n = 874) (96.6%)	Present (n = 31) (3.4%)	
Age, years (mean ± SD)	13.7 ± 0.05	14.1 ± 0.31	0.305
Sex			
Male (%)	47.2	12.9	0.0001
Female (%)	52.8	87.1	
BMI*			
Underweight (%)	1.1	-	0.399
Normal (%)	57.4	54.8	0.781
Overweight (%)	26.3	19.4	0.371
Obese (%)	15.2	25.8	0.134
Socioeconomic level [†]			
Very low (%)	1.5	3.2	0.500
Low (%)	55.4	61.3	0.514
Medium (%)	43.1	35.5	0.307
Frequency of water supply to the house			
Daily (%)	53.6	43.3	0.266
Every third day (%)	36.1	46.7	0.242
Twice a week (%)	8.7	6.7	0.690
Once a week (%)	0.8	-	0.488
Occasionally (%)	0.6	-	0.558
Never (%)	0.2	3.3	0.076
Sexual activity			
Yes (%)	0.1	3.2	0.043
Use of contraceptives			
Yes (%)	0.1	3.2	0.043
Urinary symptoms in the last year [§]			
Asymptomatic	95.5	96.8	0.726
One or more symptoms (%)	4.5	3.2	0.726
Tenesmus (%)	2.3	0.0	0.236
Burning or pain when urinating (%)	1.2	0.0	0.401
Urinary urgency (%)	1.5	3.2	0.515
Water intake, number of glasses per day (mean ± SD)	5.2 ± 0.47	4.6 ± 0.08	0.247
Intake of sugary drinks, number of portions per day [¶] (mean ± SD)	2.1 ± 0.11	3.4 ± 0.62	0.036

*Body mass index was calculated using the formula weight (kg)/height² (m), and depending on the child's sex, BMI, and age, it was categorized as underweight (< 3rd percentile), normal (3rd - 84.9th percentile), overweight (85th - 97th percentile), and obesity (> 97th percentile)²⁵.

[†]The socioeconomic level was assessed using items on maternal education, paternal education, electricity supply (public service, private plant, solar panel, no electrical service), type of flooring in the home (cement, tile, wood, dirt, other material), number of people living in the household, and type of drainage or sewage connection (public network, septic tank, pipe leading to a ravine, pipe leading to a river, no drainage); according to the Mexican Association of Market Intelligence and Public Opinion Agencies (AMAI, for its Spanish acronym)²³, socioeconomic level is classified into 7 social strata, however, for this analysis only 4 categories are considered: very low (score 0-89), low (score 135-190), medium (score 191-204), and high (score > 205).

[‡]Positive Bacteriuria was considered in those participants whose urine cultures showed bacterial growth greater than 100,000 CFU/mL²⁰⁻²²

[§]Urinary symptoms in the last year. Participants were asked: In the last year, have you had burning or pain when urinating? Have you felt an urgency to urinate? Have you felt the need to urinate more, but you couldn't? Possible responses were: Always, Almost always, Almost never, and Never.

[¶]Sugary drink intake was quantified by the number of portions consumed per day and included the following beverages: cola, flavored soda, diet soda, powdered flavor water, natural fruit juice, industrialized juice, industrialized tea, coffee with milk, coffee without milk, atole with milk, atole without milk, chocolate with milk, chocolate without milk²⁴.

SD: standard deviation.

below what was found in a Mexican study in adults, where *E. coli* was reported in 93.7% of cases³⁵ and in 60.3% of 1,045 cultures performed in Spanish children under 2-years-old³⁷. Our finding is similar to that of a study conducted in adults from Monterrey and Colombia, which reported *E. coli* in 47.1%³⁸ and 62.6%³⁹ cultures, respectively.

Regarding bacterial resistance of etiological agents to antibiotics, in this study, *E. coli* showed 58% resistance to trimethoprim-sulfamethoxazole and 52% to ampicillin, while in a Colombian study, *E. coli* showed 43% resistance to trimethoprim-sulfamethoxazole and 51% to ampicillin³⁹. Other studies in adults have reported that *E. coli* is the microorganism that presents the highest

Table 5. Risk of presenting asymptomatic bacteriuria in adolescent females in central Tlaxcala

Variables	Risk of UTI* (Odds ratio)	Confidence interval 95%	p-value
Bivariate analysis			
Males (reference category)	1.0		
Females	8.3	(2.5-27.7)	0.001
Multivariate analyze			
Females	8.3	(2.5-27.6)	0.001
Adjusted for age			
Females	8.8	(2.6-30.2)	0.000
Adjusted for age, sexual activity, and contraceptive use			
Females	9.0	(2.6-31.2)	0.000
Adjusted for age, sexual activity, contraceptive use, and sugary drink intake			

*UTI: urinary tract infection.

The p-value was calculated using multivariate logistic regression models, with a 95% confidence level, and adjusted for age, sex, sexual activity, contraceptive use, and sugary drink intake.

resistance to ampicillin, trimethoprim-sulfamethoxazole, and ceftriaxone^{36,39}. In the pediatric population of Ecuador, resistance to ampicillin was observed in 92% of cases, trimethoprim in 61%, and nalidixic acid in 68%; in Colombia, in 2007, resistance to ampicillin was shown in 79.7% and to trimethoprim in 52.8% of participants^{40,41}. In the Spanish pediatric population, it was reported that *E. coli* showed resistance in 61% of cases treated with ampicillin and in 48% of cases treated with trimethoprim-sulfamethoxazole³⁷.

Scientific literature has reported that the main risk factors associated with the prevalence of UTIs and AB in adolescents are female sex, urinary tract malformations, history of kidney disease, poor hygiene, sexual activity, menstruation, and circumcision, among others⁴. In our study, as in others, the prevalence of AB in females was found to be significantly higher than in males (5.7% and 0.7% respectively). These differences may be due to anatomical characteristics, estrogen concentration, pH variations, and inadequate hygiene, as indicated in other investigations²¹. Similarly, sexual activity and the use of contraceptives are related to the prevalence of UTIs due to chemical alterations and loss of vaginal microbiota⁴².

Some studies have shown that the most frequent UTI symptoms are dysuria, tenesmus, suprapubic pain, fever, and urinary urgency, although its asymptomatic form is very common^{24,43}. In our study, almost a third of the participants with AB diagnosed by culture also reported having experienced burning or pain while urinating in the last year, and almost a fifth reported tenesmus. The Newcastle AB Research Group reported that, out of 13,464 girls between 4 and 18 years of age, the prevalence of AB was 1.9%, while among 1,595 boys

from 5 to 18 years, the prevalence was 0.2%. Of the participants with AB, 21.4% had vesicoureteral reflux, and 15.4% had renal scars⁴⁴.

Our study identified that another risk factor related to AB is the higher intake of sugar-sweetened beverages. A 5-year longitudinal study conducted in the United States of America showed that participants who drank a greater quantity of soft drinks or who increased their consumption during the time period were 1.29-1.75 times more likely to report progression or onset of UTI symptoms⁴⁵. Another study conducted on British women under 40 years of age found that drinking at least one serving of soft drinks per day was associated with the presence of UTIs, overactive bladder, and urinary incontinence^{45,46}.

The main limitation of this study is its cross-sectional design, as it cannot establish temporality in the cause-effect relationship. Moreover, this study only represents adolescents in high schools and secondary schools, both private and public, in three municipalities of the central region of Tlaxcala state. In addition, there could be a memory bias regarding urinary symptomatology, measured over the last year.

Conclusions

AB is common in adolescents and represents an important risk factor for the development of long-term complications, such as CKD. In this study, the prevalence of bacteriuria was higher than the national average and more than double that reported in Latin America. The uropathogens and bacterial resistance found are similar to those reported in the scientific literature. Furthermore, to avoid complications, it would

be appropriate to identify the causes of bacteriuria in young populations, as these may be associated with genitourinary tract malformations and inappropriate use of antibiotics.

Acknowledgment

We thank the *Secretaría de Salud* of Tlaxcala and the *Secretaría de Educación Pública* of Tlaxcala for the facilities provided for the execution of this research.

Funding

The present work has been funded by the *Consejo Nacional de Humanidades, Ciencias y Tecnologías* (CONAHCYT) (project number 2017-01-6613) and Fondos Federales (HIM/2019/025); additionally, DZMP is a beneficiary of a CONAHCYT scholarship (CVU # 842641) and by funds from the *Facultad de Ciencias de la Salud* from the *Universidad Autónoma de Tlaxcala*.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author has this document.

References

- Schappert SM, Rechtsteiner EA. Ambulatory medical care utilization estimates for 2006. Natl Health Stat Report. 2008;8:1-29.
- Soto-Estrada G, Moreno-Altamirano L, Pahua-Díaz D. Panorama epidemiológico de México, principales causas de morbilidad y mortalidad. *Reva Fac Med*. 2016;59:8-22.
- Guajardo-Lara CE, González-Martínez PM, Ayala-Gaytán JJ. Resistencia antimicrobiana en la infección urinaria por *Escherichia coli* adquirida en la comunidad. ¿Cuál antibiótico voy a usar? *Salud Publica Mex*. 2009;51:157-61.
- Alarcón-Alacio MT, Justa-Roldán ML. Bacteriuria asintomática. *Protoc Diagn Ter Pediatr*. 2014;1:109-17.
- Dahiya A, Goldman RD. Management of asymptomatic bacteriuria in children. *Can Fam Physician*. 2018;64:821-4.
- Nicolle LE, Gupta K, Bradley SF, Colgan R, DeMuri GP, Drekonja D, et al. Clinical practice guideline for the management of asymptomatic bacteriuria: 2019 update by the infectious diseases society of America. *Clin Infect Dis*. 2019;68:e83-110.
- Hanna-Wakim RH, Ghanem ST, El Helou MW, Khafaja SA, Shaker RA, Hassan SA, et al. Epidemiology and characteristics of urinary tract infections in children and adolescents. *Front Cell Infect Microbiol*. 2015;5:45.
- Bryce A, Hay AD, Lane IF, Thornton HV, Wootton M, Costelloe C. Global prevalence of antibiotic resistance in paediatric urinary tract infections caused by *Escherichia coli* and association with routine use of antibiotics in primary care: systematic review and meta-analysis. *BMJ*. 2016;352:i939.
- López-Martínez B, Calderón-Jaimes E, Olivar-López V, Parra-Ortega I, Alcázar-López V, Castellanos-Cruz MD, et al. Susceptibilidad antimicrobiana de microorganismos causantes de infección de vías urinarias bajas en un hospital pediátrico. *Bol Med Hosp Infant Mex*. 2014;71:339-45.
- Castanheira M, Simner PJ, Bradford PA. Extended-spectrum β -lactamases: an update on their characteristics, epidemiology and detection. *JAC Antimicrob Resist*. 2021;3:dlab092.
- Gupta K, Bhadelia N. Management of urinary tract infections from multi-drug-resistant organisms. *Infect Dis Clin North Am*. 2014;28:49-59.
- Kassir K, Vargas-Shiraishi O, Zaldivar F, Berman M, Singh J, Arrieta A. Cytokine profiles of pediatric patients treated with antibiotics for pyelonephritis: potential therapeutic impact. *Clin Diagn Lab Immunol*. 2001;8:1060-3.
- Jacobson SH, Eklöf O, Eriksson CG, Lins LE, Tidgren B, Winberg J. Development of hypertension and uraemia after pyelonephritis in childhood: 27 year follow up. *BMJ*. 1989;299:703-6.
- Naing L, Winn T, Rusli BN. Practical issues in calculating the sample size for prevalence studies. *Medical statistics*. *Arch Orol Facial Sci*. 2006;1:9-14.
- World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310:2191-4.
- Bermejo-Hernández YE, Pimentel-Cruz A. Sensibilidad y especificidad del examen general de orina como prueba de escritorio para infección de vías urinarias en pacientes con diabetes mellitus sin síntomas urinarios. *Residente*. 2011;6:160-4.
- Subcommittee on Urinary Tract Infection. Reaffirmation of AAP clinical practice guideline: the diagnosis and management of the initial urinary tract infection in febrile infants and young children 2-24 months of age. *Pediatrics*. 2016;138:e20163026.
- Lopardo DH. Urocultivo: procesamiento, criterios de interpretación e informe. *Rev Sanid Mil Argent*. 2018;84:1-24.
- IDEXX. Guía Microbiológica para Interpretar la Concentración Mínima Inhibitoria (CMI); 2018. Available from: <https://www.idexx.es/files/mic-gui%CC%81a-microbiolo%CC%81gica-es.pdf> [Last accessed on 2024 Mar 22].
- Diagnóstico y Tratamiento de la Infección de Vías Urinarias no Complicada en Menores de 18 Años en el Primer y Segundo Niveles de Atención. Guía de Práctica Clínica: Evidencias y Recomendaciones. México: CENETEC; 2021. Available from: <https://www.cenetec-difusion.com/cmppc/gpc-ss027-21/er.pdf>
- Piñero-Pérez R, Cilleruelo-Ortega MJ, Ares-Álvarez J, Baquero-Artigao F, Silva-Rico JC, Velasco-Zúñiga R, et al. Recomendaciones sobre el diagnóstico y tratamiento de la infección urinaria [Recommendations on the diagnosis and treatment of urinary tract infection]. *An Pediatr (Engl Ed)*. 2019;90:400.e1-9.
- Kaufman J, Temple-Smith M, Sanci L. Urinary tract infections in children: an overview of diagnosis and management. *BMJ Paediatr Open*. 2019;3:e000487.
- Asociación Mexicana de Agencias de Inteligencia de Mercado y Opinión. Nivel Socioeconómico AMAI 2022. Nota Metodológica; 2021. Available from: https://amai.org/descargas/nota_metodologico_nse_2022_v5.pdf [Last accessed on 2024 May 17].
- Hernández-Avila M, Romieu I, Parra S, Hernández-Avila J, Madrigal H, Willett W. Validity and reproducibility of a food frequency questionnaire to assess dietary intake of women living in Mexico City. *Salud Publica Mex*. 1998;40:133-40.
- Organización Mundial de Salud. Patrones de Crecimiento de Escolares y Adolescentes Entre 5 Años 1 Mes y 19 Años; 2007. Available from: <https://www.who.int/growthref/en> [Last accessed on 2024 May 17].
- Fernández JR, Redden DT, Pietrobello A, Allison DB. Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents. *J Pediatr*. 2004;145:439-44.
- Shaikh N, Osio VA, Wessel CB, Jeong JH. Prevalence of asymptomatic bacteriuria in children: a meta-analysis. *J Pediatr*. 2020;217:110-17.e4.
- Fouad M, Boraie M. Prevalence of asymptomatic urinary abnormalities among adolescents. *Saudi J Kidney Dis Transpl*. 2016;27:500-6.
- Yun KW, Kim HY, Park HK, Kim W, Lim IS. Virulence factors of uropathogenic *Escherichia coli* of urinary tract infections and asymptomatic bacteriuria in children. *J Microbiol Immunol Infect*. 2014;47:455-61.
- Benson M, Jodal U, Agace W, Hellström M, Mårdal S, Rosberg S, et al. Interleukin (IL)-6 and IL-8 in children with febrile urinary tract infection and asymptomatic bacteriuria. *J Infect Dis*. 1996;174:1080-4.
- Samuelsson P, Hang L, Wullt B, Irljala H, Svanborg C. Toll-like receptor 4 expression and cytokine responses in the human urinary tract mucosa. *Infect Immun*. 2004;72:3179-86.

32. Ragnarsdóttir B, Samuelsson M, Gustafsson MC, Leijonhufvud I, Karpman D, Svanborg C. Reduced toll-like receptor 4 expression in children with asymptomatic bacteriuria. *J Infect Dis.* 2007;196:475-84.
33. Ragnarsdóttir B, Jönsson K, Urbano A, Grönberg-Hernandez J, Lutay N, Tammi M, et al. Toll-like receptor 4 promoter polymorphisms: common TLR4 variants may protect against severe urinary tract infection. *PLoS One.* 2010;5:e10734.
34. Köves B, Salvador E, Grönberg-Hernández J, Zdziarski J, Wullt B, Svanborg C, et al. Rare emergence of symptoms during long-term asymptomatic *Escherichia coli* 83972 carriage without an altered virulence factor repertoire. *J Urol.* 2014;191:519-28.
35. Gallardo MG, Magaña M, Andrade HJ, Jiménez MJ, Sánchez K, Fragoso LE. Resistencia a fármacos empleados en infección de vías urinarias en pacientes de primer contacto en una unidad de medicina familiar del IMSS. *Enf Inf Microbiol.* 2008;28:13-8.
36. Fariña N, Sanabria R, Laspina F, Samudio M, Figueredo L, Miño de Kaspar H. Actividad *in vitro* de fluoroquinolonas en bacilos gramnegativos aislados de urocultivos de pacientes ambulatorios. *Mem Inst Investig Cienc Salud.* 2007;3:15-8.
37. Sorlózano-Puerto A, Gómez-Luque JM, Luna-Del-Castillo JD, Navarro-Marí JM, Gutiérrez-Fernández J. Etiological and resistance profile of bacteria involved in urinary tract infections in young children. *Biomed Res Int.* 2017;2017:4909452.
38. Villalobos-Ayala JL, Castillo B, Licea-Serrato D. Urinary tract infection etiology and antimicrobial sensitivity in a Mexican hospital from 2010 to 2015. *Rev Mex Urol.* 2017;77:97-105.
39. Gómez-Escobar CP, Plata-Salazar M, Sejnau JE, Luz-Rico C, Stella-Vanegas B. Resistencia de la *E.coli* en urocultivos de pacientes con sospecha de infección urinaria intr y extra-hospitalaria en la Fundación Santa Fe de Bogotá. *Rev Urol Colomb.* 2009;18:53-8.
40. Restrepo de Rovetto C. Infección del tracto urinario: un problema prevalente en Pediatría. *Bol Med Hosp Infant Mex.* 2017;74:241-2.
41. Mendieta-Tello I, Amao-Noboa A, Calderón-Robalino D, Gea-Izquierdo E. Análisis retrospectivo de perfil microbiológico y resistencia antimicrobiana en infección urinaria pediátrica de hospitales públicos de Quito-Ecuador. *Salud Uninorte.* 2023;39:95-108.
42. Salas CP, Barrera BP, González CC, Zambrano OP, Salgado DI, Quiroz L, et al. Actualización en el diagnóstico y manejo de la infección urinaria en pediatría. *Rev Chil Pediatr.* 2012;83:269-78.
43. Lino-Villacreses WA, Luzuriaga-Moncada MC, Zúñiga-Román IC, Jumbo-Chuquimarca GM. Bacteriuria Asintomática. *Recimundo.* 2019;3:1354-83.
44. Newcastle Asymptomatic Bacteriuria Research Group. Asymptomatic bacteriuria in schoolchildren in Newcastle upon Tyne. *Arch Dis Child.* 1975;50:90-102.
45. Maserejian NN, Wager CG, Giovannucci EL, Curto TM, McVary KT, McKinlay JB. Intake of caffeinated, carbonated, or citrus beverage types and development of lower urinary tract symptoms in men and women. *Am J Epidemiol.* 2013;177:1399-410.
46. Dallosso HM, McGrother CW, Matthews RJ, Donaldson MM, Leicestershire MRC Incontinence Study Group. The association of diet and other lifestyle factors with overactive bladder and stress incontinence: a longitudinal study in women. *BJU Int.* 2003;92:69-77.