

Etiological spectrum and antimicrobial resistance of most frequently isolated pathogens, associated with Urinary tract infections in ambulatory patients

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Background

Urinary tract infections (UTIs) are one of the most common infections both in the community and in the hospital setting. Adult women are 30 times more likely to develop a UTI than men, with almost half of them experiencing at least one episode of UTI during their lifetime. In addition to the gender and age, other risk factors for UTIs are pregnancy, urethral catheterization, diabetes and spinal cord injury. Regardless of the age group, the most important pathogen of UTIs is *E. coli*, followed by other representatives of order *Enterobacterales* (*Proteus*, *Klebsiella*, etc.), *Enterococcus* spp. and *Staphylococcus saprophyticus*.

Objective

The aim of this study is to investigate the etiological spectrum and antimicrobial resistance of most frequently isolated pathogens, associated with community - acquired UTIs in Varna city, Bulgaria during a seven-month period - October 2020 - April 2021.

Materials and methods

A total of 1600 urine samples, collected prospectively from ambulatory patients with symptoms of acute cystitis or UTI were studied. The following diagnostic criteria for UTIs were used: a microbial count of $> 10^5$ CFU/mL for clean catch midstream samples or any bacterial growth of a single pathogen for urine samples collected from patients with urethral catheterization. Gram microscopy was directly performed from the broth of all positive samples after screening on HM&L instrument (Alifax, Italy). Bacterial isolates were identified using routine biochemical identification and were confirmed by VITEK (bioMérieux, France). Antimicrobial susceptibility testing to set of antimicrobial agents (ampicillin, amoxicillin-clavulanate, cefuroxime, ceftriaxone, ceftazidime, trimethoprim/sulphomethoxazole, ciprofloxacin, levofloxacin, gentamicin, amikacin, meropenem, imipenem) was performed by VITEK 2 Compact System (bioMérieux) and for fosfomycin, 5-nitroxoline and nitrofurantoin by Kirby-Bauer disk diffusion method. The Double Disk Synergy Test (DDST) was used as a phenotypic confirmatory test for ESBL production. The results were interpreted according to EUCAST Guidelines 2021 (Version 11).

Results

A total of 127 urine samples (7.9%) were positive for bacterial growth by HM&L. From these samples, 127 bacterial pathogens were isolated: Gram negative bacteria were found in 62.2% (n=79) and Gram positive - in 37.8% (n= 48). *E. coli* was the predominant species, associated with UTIs in the studied group of patients (77%, n=61) (Figure 1). The Gram-positive bacteria accounted for 37.8 % (n= 48), with *E. faecalis* being the leading pathogen in this group (87.5%, n=42). *Staphylococcus saprophyticus* and *Streptococcus agalactiae* were diagnosed in 8% (n=4) and 4% (n=2) respectively (Figure 2). Antimicrobial susceptibility test results are presented in tables 1 and 2. The rate of 3rd generation cephalosporin resistance among the representative of order *Enterobacterales* in the study is between 13.9% for ceftriaxone and 10.1% for ceftazidime. The rates of ESBL-producing isolates, identified by the phenotypic DDST and Vitek 2 system, were as follows: 5% in *E. coli* (n=4) and 2.5% in *K. pneumoniae* (n=2) and *Enterobacter cloacae* (n=2).

Figure 1. Species distribution of Gram-negative isolates, associated with UTIs.

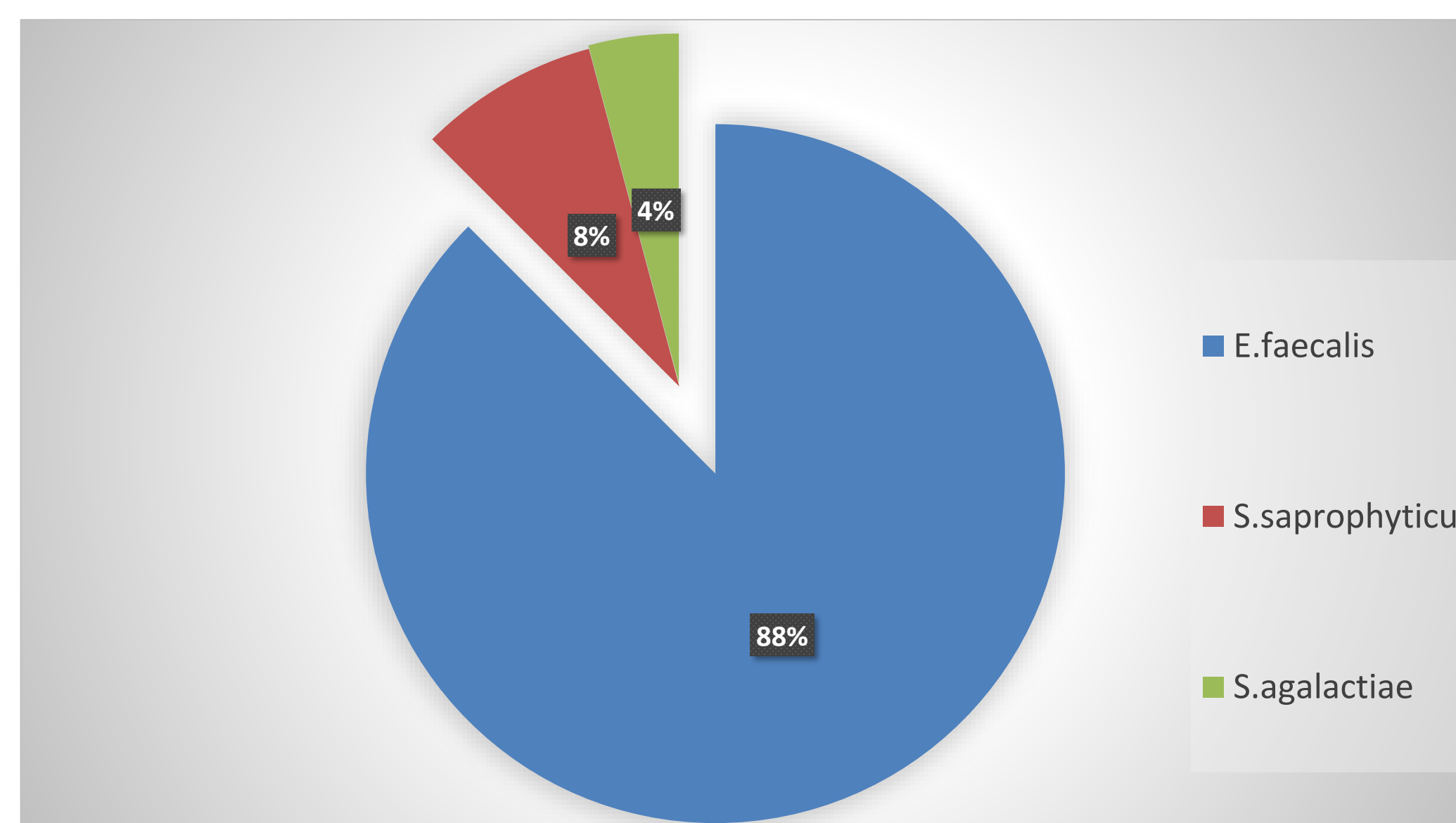
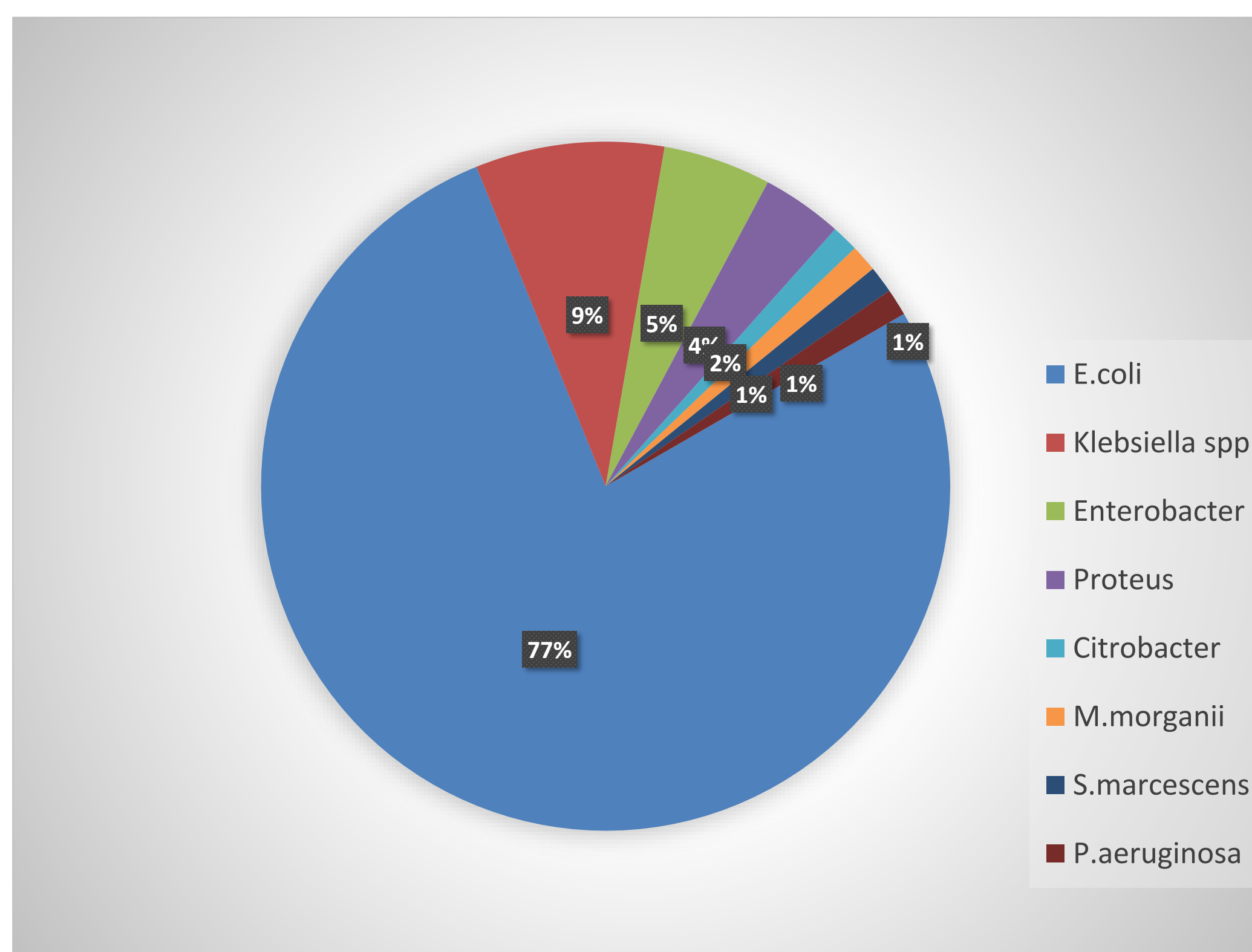


Figure 2. Species distribution of Gram - positive isolates, associated with UTIs.

Conclusions

- ✓ The etiological spectrum of UTIs in Varna ambulatory patients was dominated by *E. coli*, followed by *Enterococcus faecalis*.
- ✓ In the group of Gram negative uro-pathogens, high resistance rates to ampicillin, trimethoprim/sulphomethoxazole and quinolones were detected, but relatively low resistance rate for 3rd generation cephalosporins was found.
- ✓ Fosfomycin, nitrofurantoin and nitroxoline retained very good activity and are adequate choice for antimicrobial treatment of uncomplicated community acquired UTIs or UTIs when other alternatives are lacking.
- ✓ The study highlights the importance of the periodic surveillance of the resistance rates to most commonly used antimicrobial agents in the ambulatory practice in Varna, Bulgaria to guide the empiric treatment recommendations.
- ✓ The good medical practice should always include microbiological examination of the urine sample in patients with suspected UTIs to identify the pathogen and to determine its susceptibility to antimicrobial agents.

Table 1. Antimicrobial susceptibility of 79 Gram negative isolates, obtained from urine samples of ambulatory patients with UTIs.

Antimicrobial agent	Susceptible n (%)	Resistant (R+) n (%)
ampicillin	28 (35,5)	51 (64,5)
amoxicillin/clavulanic acid	57 (72,2)	22 (27,8)
cefuroxime	62 (78,5)	17 (21,5)
ceftriaxone	68 (86,1)	11 (13,9)
ceftazidime	71 (89,9)	8 (10,1)
ciprofloxacin	56 (70,9)	23 (29,1)
levofloxacin	62 (78,5)	17 (21,5)
trimethoprim/sulphamethoxazole	51 (64,6)	28 (35,4)
nitrofurantoin	74 (93,7)	5 (6,3)
5-nitroxoline	75 (95,0)	4 (5,0)
fosfomycin	69 (87,4)	10 (12,6)
gentamicin	74 (93,7)	5 (6,3)
amikacin	79 (100)	0
meropenem	79 (100)	0
imipenem	79 (100)	0

Antimicrobial agent	Susceptible N (%)	Resistant(R+) N (%)
amoxicillin	41 (97,6)	1 (2,4)
gentamycin HLAR	32 (76,2)	10 (23,8)
ciprofloxacin	30 (71,4)	12 (28,6)
levofloxacin	34 (81)	8 (19)
nitrofurantoin	40 (95,2)	2 (4,8)
vancomycin	42 (100)	0
teicoplanin	42 (100)	0

Table 1. Antimicrobial susceptibility of 42 Enterococcus faecalis isolates, obtained from urine samples of ambulatory patients with UTIs.

References;

1. Wagenlehner, F.; Schmiemann, G. In Epidemiology, Diagnosis, Treatment Prevention and Management of Uncomplicated, Bacterial, Community-Acquired Urinary Tract Infections in Adult Patients, Langversion 1.1-2 AWMF-Register-Nr. 043/044; AWMF: Düsseldorf, Germany, 2017.
2. Chao YS, Farrah K. Fluoroquinolones for the Treatment of Urinary Tract Infection: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019 Apr 26
3. Surveillance of antimicrobial resistance in Bulgaria--a synopsis from BulSTAR 2018. Available at [https:// bam-bg.net/](https://bam-bg.net/)
4. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis. 2016; 62(10): e51-77.

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