Antibiotic Resistance Phenotypes of Escherichia Coli Strains Isolated from Urinary Tract Infections in the Medical Biology Laboratory of Niamakoro FOMBA Hospital in Segou, Mali

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Summary

Introduction: In order to guide antibiotic therapy, most often probabilistic this study aimed to characterize the different phenotypes of antibiotic resistance of E. coli strains responsible for urinary tract infections. Materials and methods: This was a prospective cross-sectional study with descriptive purposes that took place from January to December 2020 at the medical biology laboratory of Niamakoro FOMBA Hospital in Ségou. Uriselect 4 Agar was used for urine culture followed by biochemical identification by API 20E gallery. The antibiogram was then performed by the disc method according to the 2019 recommendations of the antibiogram committee of the French Society of Microbiology. Results: During this study, 56 enterobacteriaceae were isolated and identified in urinary tract infections, including 43 strains of E. coli or 76.79%. Regarding resistance patterns, the ESBL phenotype was the most observed with 46.51% for the beta-lactam class. Aminoglycoside resistance affected 41.46% of strains resistant to all aminoglycosides tested. Quinolone resistance was identified with 88.10% of strains resistant to all quinolones. ESBL profiles were associated with resistance to aminoglycosides, fluoroquinolones and sulfamethoxazole + trimethoprim in 13.95% of cases. Conclusion: The present study on resistance phenotypes in E. coli isolates reports worrisome results for the main classes of antibiotics.

Keywords: Antibiotics; E. coli; urinary tract infection; resistance phenotypes
Introduction

According to the World Health Organization (WHO), urinary tract infections with *E. coli* are by far the most common in hospitals and communities [1]. *E. coli* is naturally sensitive to many antibiotics, the emergence and subsequent spread of different resistance mechanisms acquired within this species [2] represent a real threat to global public health [3]. In Togo in 2017 a study reported that 57.94% of *E. coli* strains isolated during urinary tract infections had the ESBL phenotype [4]. In Mali in 2019 in Bamako a study reported that 14.3% of *E. coli* strains isolated from urine had the extended-spectrum beta-lactamase phenotype (ESBL) [5]. *E. coli* UTIs are therefore a priority for antibiotic resistance surveillance given their high frequency and severity [6]. However, few studies have addressed the problem with the result of the existence of little data on antibiotic resistance phenotypes of *E. coli* strains isolated during UTIs, hence this study which aimed to characterize the different antibiotic resistance phenotypes of *E. coli* strains responsible for UTIs in order to guide antibiotic therapy, most often probabilistic.

Materials and Methods

This was a prospective cross-sectional study with descriptive purposes that took place from January to December 2020 at the medical biology laboratory of Niamakoro FOMBA Hospital in Ségou. Niamakoro FOMBA Hospital is a reference health facility for eight health districts with a hospitalization capacity of 198 beds. It includes inpatient services (medicine, paediatrics, surgery, gynaecology and obstetrics, urology, traumatology, cardiology and resuscitation), consultation services (ophthalmology, nephrology, odontology) and complementary examination services (laboratory, imaging).

The study population consisted of patients (adults and children) from the city of Ségou and surrounding communities received in the laboratory as part of routine diagnosis. Patients who met the following criteria were included in this study:

**Criterion 1:** all non-urinary catheter patients with an *E. coli* positive ECBU with bacteriuria greater than or equal to 103 CFU/ml associated with leukocyturia greater than or equal to 104 leukocytes/ml;

**Criterion 2:** All urinary catheter patients with an *E. coli* positive ECBU with bacteriuria greater than or equal to 105 CFU/ml.

Cytology of each urine sample was performed by direct examination on the Kova cell and gram staining. Uriselect 4 Agar was used for aerobic urine culture at 37°C for 24 hours followed by biochemical identification by API 20E gallery. The susceptibility test was then performed by the disc method according to the recommendations of the antibiogram committee of the French Society of Microbiology [7]. Data were collected from test reports and laboratory records and analyzed on epi info version 7.2.1.0 and Excel 2013.

Ethical considerations

This study is part of the national surveillance of antimicrobial resistance (AMR) and therefore submission to the ethics committee was not required. Each patient’s informed consent was obtained prior to inclusion in the study.

Results

During this study, 56 uropathogenic Enterobacteriaceae were isolated and confirmed from UTIs, including 43 non-repetitive strains of *E. coli*, representing an isolation frequency of 76.79%. Antibiotic resistance of isolated *E. coli* strains showed total resistance to amoxicillin (100%), significant resistance to sulfamethoxazole + trimethoprim (94.97%), ciprofloxacin (88.10%), ceftriaxone (79.07%), amoxicillin + clavulanic acid (66.67%) and gentamycin (57.50%). Regarding beta-lactam resistance, the extended-spectrum beta-lactamase phenotype (ESBL) is the most observed with 46.51% (n: 20) followed by high-level cephalosporinases (CHN) with 30.23% (n: 13) (Figure 1). Aminoglycoside resistance of *E. coli* strains showed a predominance of the resistant phenotype to all aminoglycosides tested with 41.46% (n: 17) followed by wild phenotypes with 36.59% (n: 15) (Figure 2). Quinolone resistance occurred in 88.10% (n: 37) of isolates (Figure 3). Phenotypes of resistance to other families were dominated by sulfamethoxazole + trimethoprim resistant with 94.87% (n: 37). ESBL profiles were associated with resistance to aminoglycosides, fluoroquinolones and sulfamethoxazole + trimethoprim in 13.95% (n: 6).
**ESBL**: Betalactamase extended spectrum; **CHN**: High-level cephalosporinase; **PBN**: Low-level penicillinase; **PHN**: High-level penicillinase; **BHRe**: Emerging highly resistant bacterium; **TRI**: Inhibitor-resistant TEM.

**Figure 1**: Beta-lactam resistance phenotypes tested for *E. coli* strains.

*Missing strains*: amikacin was not tested and gentamycin showed resistance.

**Figure 2**: Aminoglycoside resistance phenotypes of *E. coli* strains.

*Missing strain*: ciprofloxacin was not tested and nalidixic acid showed resistance.

**Figure 3**: Quinolone resistance phenotypes tested for *E. coli* strains.
**Study Limitation**

ECBU availability limited to the first three days of each week.

**Discussion**

Urinary tract infection is a common pathology both in hospitals and in the community. In this work, E. coli dominated the uropathogenic flora with 76.79% of cases of enterobacteriaceae. This observation is shared by several authors with variable rates [8]. The ascending pathophysiology of UI as well as the strong colonization of the perineum by E. coli of digestive origin, associated with specific uropathogenicity factors such as adhesives capable of binding to the urinary epithelium could explain this predominance [9]. The study of antibiotic resistance showed total resistance of E. coli strains. coli with aminopenicillins (100%). The same result is reported in Mali by Kalambr et al. in 2019 (92.3%) and Madagascar by Rakotovao-Ravahatra et al. in 2017 (94.1%) [5.6]. This rate of total resistance can be explained by the over-prescription and self-medication of this molecule [9]. The present study showed significant resistance to ciprofloxacin (88.10%), ceftriaxone (79.07%) and gentamycin (57.50%). These high rates of resistance are higher than those reported by Sissoko in 2006 who found respectively 42.1%, 22.1% and 20% [10]. This situation is the consequence of selection pressure due to excessive prescription and the sometimes abusive use of broad-spectrum antibiotics both in hospitals and in the community (dispensing without prescription, self-medication, free sample,...), not to mention the impact of poorly controlled feeding and where more and more antibiotics are used in agriculture and livestock [11]. Regarding beta-lactam resistance phenotypes, the mechanism of resistance by production of extended-spectrum beta-lactamase (ESBL) is the most isolated with a frequency of 46.51%. This proportion is lower than that reported in Togo by Toudji et al. in 2017 which found 57.94% [4]. However, this rate of ESBL production by uropathogenic E. coli strains remains high and confirms the high secretion of ESBLs and the wide diffusion both in community and hospital settings [12]. This should draw our attention to the extent of the inevitable and worrying spread of these strains in the absence of control and prevention measures, especially since the majority of our patients (86.40%) were external consultants [9]. High-level cephalosporinase producing strains are observed with a frequency of 30.23%. This rate is much higher than that reported by Kalambr et al. in 2019 which found only 12.70% [5]. CHNs are probably related to the in-process selection of chromosomal cephalosporinase hyperproducing mutants in E. coli [13]. Also 11.63% of low-level penicillinase-producing strains (PBN) are observed. This rate is close to that reported by Gonsu Kamga et al. in 2014 which had found 13.60% [14]. High-level penicillinase-producing (PNH) strains were reported representing 4.65% of strains. This rate is slightly higher than that reported by Kalambr et al. in 2019 which found only 2.47% [5]. This resistance could be explained by a decrease in the activity of the beta-lactamase inhibitor (clavulanic acid) resulting from hyperproduction of penicillinase, or from the inactivation of the inhibitor itself [14]. The present study found 41.46% of phenotypes resistant to all aminoglycosides. This rate is higher than that reported by Rakotovao-Ravahatra et al. in 2017 which reported only 14.7% [6]. This high proportion could be explained by the current emergence of methyl transfersases of 16S RNA conferring a high level of resistance to all aminoglycosides used in practice [15]. Regarding quinolone and fluoroquinolone resistance phenotypes, 88.10% of strains were resistant to all quinolones. This proportion is higher than that reported by Rakotovao-Ravahatra et al. which showed only 40.20% [6]. This resistance could be explained by the fact that a probabilistic first-line treatment of a UTI, based on a fluoroquinolone is often used in our country [9]. It is now established that E. coli resistance to quinolones is correlated with ambulatory consumption of these molecules, at the state, hospital, general practice, and community levels [16]. Regarding phenotypes of resistance to other antibiotic families, 94.97% of strains were resistant to sulfamethoxazole+trimethoprim. Our results are slightly higher than those of El toumarri et al. in 2014 who reported respectively 55% [12]. The high rate of resistance of E. coli to sulfamethoxazole + trimethoprim is proof that this molecule should be avoided as a first line by our prescribers [9]. ESBL profiles were associated with resistance to fluoroquinolones, aminoglycosides and sulfamethoxazole + trimethoprim in 13.95% of cases. Tagajid et al. reported 2% in 2010, which is lower than our result [17]. This multiresistance could be explained by the fact that ESBL genes generally carried by plasmids, are often associated with antibiotic resistance genes including aminoglycosides, fluoroquinolones [12].
Conclusion

This prospective cross-sectional study identified several antibiotic resistance phenotypes of which extended-spectrum beta-lactamases were the most important. The study of resistance phenotypes in *E. coli* isolates reported worrisome results for the main classes of antibiotics. Monitoring of antibiotic prescribing within the framework of a multidisciplinary committee is required in the hospital.

References