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The impact of the COVID pandemic on the uropathogenic bacterial resistance profile: Experience of the bacteriology lab of the military hospital Avicenne in Marrakech

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Abstract

The aim of this study is to define the uropathogenic bacterial resistance and to clarify how the COVID 19 pandemic has affected the development of bacterial resistance.

Patients and methods: We conducted a retrospective analysis of the bacterial profile and antibiotic resistance status of the main isolates of uropathogens at the laboratory of microbiology at the military hospital Avicenne in Marrakech over the course of two time periods: the first was prior to COVID 19 (January 2019 to February 2020), and the second was one year later (January 2021 to February 2022).

Results: In the first phase of the study, out of 4000 ECBU intended for the bacteriology lab, 581 met the criteria for a urinary tract infection. In the second phase of the study, out of 4692 ECBU requested, 590 samples were found to be positive, with a rate of incidence of 15%. For the two times, the *Enterobacteries* made up 80% of all the isolated bacteria. The total number of multiresistant bacteria (BMR) discovered on the ECBU's isolats during the course of the two study periods is 153, or 6.5% of the total isolats.

Conclusion: This study made *Escherichia coli* the bacteria most implicated in the epidemiology of urogenital infections during the two periods. In the majority of cases, rates of resistance to various antibiotics increased during the COVID pandemic compared to the same time period two years earlier.

Keywords: Urinary infection; Uopathogenic bacteria; Antibiotic; Antibioresistance; COVID -19

1. Introduction

In the absence of other infectious sites, the association of a significant bactériurie and evocative symptoms is what constitutes a urogenital infection. This distinction from urinary colonizations, which are instead identified by a significant bactériurie without accompanying symptoms [1]. Urinary tract infections are common both in the community and in hospitals. Every year, the number of urinary tract infections around the world is estimated to be over 150 million. They are the first site of nosocomial infections and the second communicable bacterial infection site after the respiratory apparatus [2]. The bacteria that are most frequently blamed are enterobacteria, which are naturally occurring hosts of the environment and the intestine (*Escherichia coli*, *Proteus*, *Klebsiella*). *E. Coli* makes up 70 to 80 percent of the isolated bacteria seen in urogenital infections [3, 4, 5]. The main treatment is the administration of antibiotics, either empirically based on epidemiological data or under the direction of the findings of a cytobacterial examination of the urine. However, the failures associated with empirical treatment are become more concerning.

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Resistance's emergence and spread present a serious public health issue, and tackling it is difficult for medical professionals, microbiologists, hygienists, and public health authorities [6]. As a result, the microbiology lab is crucial to the diagnosis of urogenital infections and, more importantly, the selection of an appropriate antibiotherapy. Every effective therapeutic approach begins with the accurate identification of the involved microorganisms and the investigation of their susceptibility to antibiotics. And in order to clearly understand how the COVID 19 pandemic has affected the development of bacterial resistance, we conducted a retrospective analysis of the bacterial profile and antibiotic resistance status of the main isolates of uropathogens at the laboratory of microbiology at the military hospital Avicenne in Marrakech over the course of two time periods: the first was prior to COVID 19 (January 2019 to February 2020), and the second was one year later (January 2021).

2. Material and methods

We carried out a descriptive retrospective comparative study at the military hospital Avicenne in Marrakech (HMA). We included ECBU from patients who were admitted to various L'HMA of Marrakech services as well as patients who served as external consultants in the study. These two time periods are from January 2019 to February 2020 and from January 2021 to February 2022.

The Becton Dickinson PHOENIX M50 system carried out the biochemical identification and antibacterial susceptibility testing, which were completed by the EUCAST 2018-recommended method of using enriched diffusion disks.

3. Results

3.1. Distribution of cytobacterial urine examinations (ECBU)

The primary test performed at the laboratory of microbiology at the military hospital Avicenne in Marrakech is the examination of urine for cytobacterial contamination. In the first phase of the study, out of 4000 ECBU intended for the bacteriology lab, 581 met the criteria for a urinary tract infection. In the second phase of the study, out of 4692 ECBU requested, 590 prélèvements were found to be positive, with a rate of incidence of 15%. More than 85% of the positive ECBUs across the study's two periods came from outpatients (External/Urgent). However, we did not see a significant difference in the distribution of the sexes, with the sex ratio being almost 1.

3.2. Global Bacterial Isolation Distribution

For the two times, the Entérobacterias made up 80% of all the isolated bacteria. *Escherichia coli* (71%), *Klebsiella pneumoniae* (5%), *Enterobacter cloacae* (10%), and *Proteus mirabilis* (3%), with no other species accounting for more than 3% of their total population. The BGN non fermentative make up 5% of the isolated bacteria. They are mostly represented by the *Pseudomonas aeruginosa*, which is by far the most prevalent species (65%), and by *Acinetobacterbaumannii* (35%). The cocci make up 15% of isolated bacteria and are distributed as follows: 20% of them are *Staphylococcus aureus*, and 20% are *Staphylococcus* with negative coagulase.

3.3. The germs' resistance to antibiotics

Enterobacterias

The analysis of the potential for enterobacterial resistance to tested antibiotics is the subject of the table 1.

Escherichia coli

According to our findings, *E. Coli* has a high rate of resistance to aminopenicillins, with frequencies of 65.3% in 2019 and 70% in 2021 for ampicillin/amoxicillin. This resistance appears to be overcome by the addition of clavulanic acid, which reduces the rate of resistance to 43.5% for the first period of the study and to 46% for the second period. Contrarily, the C3G are quite active against this bacteria, with resistance percentages of little more than 9.5% during the first period and 10.9% during the second (entered for Ceftriaxone). When it comes to carbapenemas, the percentages of 0.1 for imipenemas and 1.0 for ertapenems allow us to consider them to be the compounds most active against *E. coli*.

Our study demonstrates that aminosides are among the antibiotics that are most effective against *E. coli*, with resistance rates that do not exceed the value of 2.9% for amikacine. In contrast, resistance to gentamicine has increased, although it still exhibits good activity (10.3% vs. 12.8%). In our study, isolated urine samples showed significant fluoroquinolone resistance rates during the first period (Ciprofloxacine 30.4% and Lévofloxacine 21.3%), with a notable increase during the second period (Ciprofloxacine 32.1% and Lévofloxacine 24.5%).According to our study, the resistance rate for the combination of trimethoprim and sulfamethoxazole was 40% during the first period and 43% during the second. For the two periods, there is no resistance to colistine.

Klebsiella Pneumoniae

51.7% of the *Klebsiella pneumoniae* species in our study are resistant to amoxicillin and clavulanic acid. Regarding third-generation cephalosporine resistance, there has been a slight increase from 22% in the first period to 23.4% in the second. The carbapénèmes continue to be among the most effective antibiotics for treating *Klebsiella*, with resistance percentages of 2.5% for Imipénème and 8.8% for Ertapénème. With 2.7% resistance to amikacine and 18.2% resistance to gentamicine, respectively, *Klebsiella* sores are shown to be weakly resistant to aminosides. According to our study, the resistance rate for the combination of trimethoprim and sulfamethoxazole was 40% during the first period and 43% during the second. During the two periods, there is no colistine resistance. This demonstrates the significance of fluoroquinolones in the treatment of urethral infections as ciprofloxacine was 72.6% and levofloxacine was 75.8% effective against *Klebsiella* souches. For the colistine, there is no resistance over the two periods.

Enterobacter cloacae

In our series, *Enterobacter cloacae* exhibited high C3G oral resistance (Céfixime 70%), but only low C3G injectable resistance (no more than 35%) during the course of the two periods. Amikacine (1.6%) and imipenem (4.9%) have very good activity against *enterobacter*, placing them at the top of the list of antibiotiques that are most effective against this pathogen. On the tested sores, a significant increase in resistance to Cotrimoxazole (from 41% during the first period to 45% during the second period) and to ciprofloxacine (from 45.1% to 47%) was seen. For colistine, there is no resistance at all.

Table 1 The enterobacterial resistance during the two periods of the study

Bacteria	***E. coli***		***K. pneumoniae***		***E. cloacae***	
Period	2019	2021	2019	2021	2019	2021
Amoxicilline	65%	70%	100%	100%	100%	100%
Amoxicilline +acideclavulanique	43.5%	46%	22%	23.4%	100%	100%
Ceftriaxone	9.5%	10.9%	22%	23.8%	34.5%	34.4%
Imipineme	0.1%	0.1%	2.5%	2.1%	4.9%	4.8%
Amikacine	2.9%	2.3%	2.7%	2.1%	1.6%	1.5%
Levofloxacine	21.3%	23.4%	25%	25.1%	44%	47%
Ciprofloxacine	30.4%	32.1%	27.4%	26%	45%	47%
Sulfamethoxazole+trimethoprime	40%	43%	25%	23.9%	22.4%	21%

Gram-positive cocci: Staphylococcus aureus

S. aureus isolated sores exhibit a high level of sensitivity to the majority of tested antibiotics. More than 90% of *S. aureus* strains tested during the two study periods have a resistance to penicilline *G*. This demonstrates the *staphylocoques'* strong resistance to beta-lactams. Only 17.5% of the samples in our study have the phenotype Meti R (oxacilline resistance) of *Staphylococcus aureus* (SARM). The macrolides were effective against our germ. The most studied molecules in this class of antibiotics are erythromycin and clindamycin, which produce positive results because their resistance rates have decreased to 10,5% and 4,3%, respectively. In our study, aminosides were effective against this species (gentamicine: 28.9%). Low levels of resistance to ciprofloxacin (less than 10%). With a 10% infection resistance rate for Cotrimoxazole, it continues to have good activity against *S. aureus*. Vancomycine is not resistant to anything.

Gram-negative non fermentative bacteria

Acinetobacter Baumanii

The antibacterial marker most indicative of this species' multi-resistance appears to be resistance to ticarcilline. Thus, more than 70% . In our study are multiresistant. This multi-resistance is a result of beta-lactamase synthesis.

Additionally, a high resistance rate to numerous molecules is noted: According to our findings, aztreonam had a high resistance (96.7%). It should be noted that this taux is the highest in comparison to other antibacterials.Céfépime (70%), ceftazidime (65.4%), and cefotaxime (62.5%) are the céphalosporines.Lévofloxacine (66.7%) and Ciprofloxacine (60%) are among the fluoroquinolones. Cotrimoxazole (Le): (51.5%).The activity of aminosides has been found to be partially preserved, with resistance levels of no more than 21,9% for amikacine, 33.3% for tobramycine, and 35.3% for gentamicine. The chemicals that are most effective against this species are carbapenemas. We were able to achieve an 18.2% resistance rate for the impenem. The substance that continues to successfully inhibit this germ is colistine, which has zero resistance and is effective against all isolated sores.

Pseudomonas Aerogginosa

There is a 60% resistance rate to aminopenicillins as well as a 54.54% resistance rate to the combination of ticarcilline and clavulanic acid. Additionally, with regard to cephalosporines, ceftazidime and cefépime have good activity against this species; the resistance rates are, respectively, 8.8% and 15.3%. Regarding aminosides, our research revealed that our germ was only moderately resistant to tobramycine (15.4%), amikacine (19.1%), and gentamicine (23.8%). Some fluoroquinolones under study, such as ciprofloxacine (38.2%) and levofloxacine (60%) were less effective against *Pseudomonas aeruginosa*. Theimipene is quite effective against this germ, with a resistance level of about 3.3%. For colistine, there is no resistance at all.

3.4. Evolution Multiresistant bacteria (BMR)

The total number of multiresistant bacteria (BMR) discovered on the ECBU's isolats during the course of the two study periods is 153, 6.5% of the total isolats. The analysis of these data reveals that the most frequently isolated bacteria are those that produce BLSE (N=136), followed by *Pseudomonas aeruginosa* resistant to ceftazidime PARC (n=7), *Staphylococcus aureus* resistant to meticilline SARM (n=5), and *Acinetobacterbaumanii* resistant to imipenem (n=5).

- The majority of the isolates of BLSE-associated bacteria are *E. Coli* (n=73), followed by *Klebsiella pneumoniae* (n=31), *Enterobacter cloacae* (n=22), and other BLSE-associated bacteria with a maximum of 10 isolats.
- Of all isolated enterobacteria, the frequency of BLSE outbreaks is 14%.
- 10% of the *E. Coli* strains tested using cefotaxime that were tested as a whole produced BLSE.
- 15% of the *Pseudomonas aeruginosa* colonies are *Pseudomonas aeruginosa* resistant to ceftazidime (PARC, N=7) (49 isolats).
- Of the 27 isolated *Acinetobacter baumannii*, 5 were imipenem-resistant.
  15% of the *Staphylococcus aureus* strains are resistant to the antibiotic methicillin.

4. Discussion

The colonization of urinary tracts is determined by uropathogens, which also cause infection and inflammation at various levels. Urinary tract infections afflict millions of people annually, regardless of gender or age, and are a major cause of morbidity. Compared to men, women have a higher prevalence of urogenital infections, with over 80% of cases worldwide among women; recurrence is also more common among women. The level of resistance of uropathogenic bacteria can be precisely assessed by a number of international surveillance programs. However, in order to better understand the dynamics of the resistance status, local data must be gathered. To ascertain if the trends are positive or whether a thorough examination of antibacterial resistance is still required, it is necessary to monitor how sensitivity and resistance change over time. Additionally, preliminary data suggest that the COVID -19 pandemic affected the resistance mechanisms of several bacteria as a result of the excessive use of free-to-the-public antibiotics.

4.1. Global division of isolated bacteria

The most common uropathogenic bacteria found in urine samples are Gram-negative, with *Escherichia coli* accounting for the majority (65.3%%). In fact, almost all studies have found that this enterobactéria is the most common uropathogen across all continents, accounting for various percentages:

Switzerland, Europe center: 74.6% [7], Al-Kharj, Saoudite: 70.4% [8], Seoul, South Corea: 87.3% [9], United States, North America: 72% [10], KwaZulu-Natal, Africa: 81.25 % [11]. *Klebsiella* spp. are the second most common Gram-negative bacteria, accounting for 17.25% of all samples. Regional results for Hongry [12] showed that *Klebsiella spp.* accounted for 13.4% of all urine samples from hospitalized patients, which was comparable to results from other countries in the Middle East, such as Turkey [13]. *Pseudomonas spp*. and *Proteus spp*. are in third and fourth place, respectively, in terms of the frequency of uropathogens; this study shows *Proteus* spp. to be more common, accounting for 5.54% compared to *Pseudomonas spp.* 2.59% ; however, this finding is not consistent with other findings. Recently, Jan Hrbacek et al. published a paper analyzing urine sample collections over a nine-year period and found that *P. aeruginosa* soured more frequently (7.3%) than *Proteus spp*. (6.2%) [14]. *Staphylococcus spp*. and Enterococcus spp. had the highest rates of occurrence among Gram-positive bacteria, with the former accounting for 11.54% and the latter for just 2.1% of the total number of infections, respectively.

4.2. Enterobacterial Resistance Evolution

Current data on antibiotic resistance trends in European countries [14,15,16] indicate discouraging results regarding the proportion of *E. Coli* resistant to aminopenicillins, fluoroquinolones, and trimethoprim/sulfamethoxazole; promising profiles of sensitivity have been noted for aminoglycosides, carbapenemas, and cephalosporines. Additionally, *Klebsiella* species has been a Gram-negative first-line uropathogen with high céphalosporin, fluoroquinolone, and nitrofurantoin resistance as well as a robust overall response to polymyxin B, colistine, and carbapenemas. *Proteus spp*., the most significant urea-producing bacteria involved in urogenital infections, accounts for slightly more than 5% of all cases but has a significant morbidity. Similar findings were reported in Brazil [17] in a study of 92 recently published articles that included more than 3385 female urine test positive samples. The drugs involved were fluoroquinolones (Ciprofloxacine R = 21.56%, Amoxicilline-Clavulanic Ac. R = 25.49%), cephalosporines (Cefuroxime R = 19.69%, and ceftiaxone R = 18.3%).

4.3. The evolution of bacterial resistance Gram-positive

The most uncommon strain of Gram positive bacteria and uropathogens found in urine échantillons was *Staphylococcus spp*. Amikacine's resistance decreased from 3.03 percent to 0%, Trimethoprim/from Sulfamethazole's 18.18 % to 5.26 %, and others.

In contrast to our findings, the Chinese article revealed a critical level of pénicilline resistance between R = 95.2% and R = 96.9% from 2013 to 2017. They also presented high rates of resistance to the antibiotics triméthoprim/sulfaméthoxazole R = 27.1% and the fluoroquinolones ,ciprofloxacine R = 25.6% and amikacine R = 14.2% [18].

4.4. The evolution of Gram-negative non-fermenting bacteria's resistance

Pseudomonas aeruginosa has demonstrated a somewhat high sensitivity to piperacilline/tazobactam, aminoglycosides, and carbapenemas. Our study showed that *Pseudomonas spp.* had the highest resistance rates, with the strongest increases in all uropathogens; From R = 30.3% to R = 77.41%, lévofloxacine leads the resistance race, followed by ceftazidime, imipenem, meropénem, and amikacine. According to a study conducted in the Czech Republic over nine years, the rates of resistance to all antibacterial agents tested for this Gram-negative strain were lower, as follows: Imipénème R = 15.6%, Méropénem R = 31.8%, Ciprofloxacine R = 38.1%, Ceftazidime R = 18.7%, Imipénème R = Amikacine R = 9.3 %.

4.5. The role of COVID 19 in the resistance of uropathogenic bacteria

Coronavirus infection results in severe respiratory problems (SRAS-CoV 2), which puts a tremendous strain on the global healthcare industry. This public health initiative imposed several restrictions, including social distancing, wearing a disguise, avoiding overpopulated areas, active identification of infected individuals, and placement in quarantine. Therefore, these actions could have reduced the spread of the virus and protected people against other ailments such seasonal infections, the flu, and tuberculosis. However, COVID -19 may contribute to an increase in antibioresistance for a variety of reasons. First off, the increase in the automedication of antibiotics available for free sale leads to overconsumption, posing a higher risk of inappropriate doses and untimely cures of these drugs [19,20].

Second, despite the fact that some studies suggest that the prevalence of co-infection is low, antibiotic prescriptions are frequently used to rule out infectious bacterial diseases that mimic the symptoms of COVID infection [21,22].

Furthermore, unless there is a clear clinical symptom, the World Health Organization (OMS) advises against prescribing antibiotics in therapeutic or preventative doses to individuals who are in mild or moderate disease stages. Three-quarters of COVID patients who received antibiotics during the viral infection episode, according to a review of 154 studies estimating the prevalence of these drugs among patients with the disease [23]. This review included data from more than 30 000 individuals. A Belgian study last year on 164 COVID -positive patients found that 61% of them also received an antibacterial treatment, which ultimately did not lower the mortality rate (15.2% of whom were admitted to intensive care and 15.9% of whom passed away while hospitalized) [24].

5. Conclusion

This study made *Escherichia coli* the bacteria most implicated in the epidemiology of urogenital infections during the two periods, followed by *Klebsiella spp*. The most common Gram-positive bacteria was *Staphylococcus spp*. In the majority of cases, rates of resistance to various antibiotics increased during the COVID pandemic compared to the same time period two years earlier. With these findings, the empiric prescription of broad-spectrum antibiotics for COVID - 19 patients needs to be evaluated more carefully.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest

Statement of ethical approval

This is a perspective article and no ethical approval was required.

Statement of informed consent

The data collected retrospectively did not contain any personal information. For each patient, written informed consent was obtained.

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