Modeling the antimicrobial resistance of enterobacteria responsible for Urinary Tract Infections in Benin: Another way to control Antimicrobial Resistance

DOUGNON Victorien (victorien.dougnon@gmail.com)
Universite d'Abomey-Calavi https://orcid.org/0000-0001-9047-7299
ASSOGBA Phenix
Universite d'Abomey-Calavi Faculte des Sciences de la Sante
JIBRIL Mohammed
Sokoine University of Agriculture Faculty of Veterinary Medicine
GNIMATIN Jean-Pierre
Research Unit in Applied Microbiology and Pharmacology of Natural Substances, University of Abomey-Calavi, Benin
AGBANKPE Jerrold
Universite d'Abomey-Calavi
KOUDOKPON Hornel
Universite d'Abomey-Calavi
DEGUENON Esther
Universite d'Abomey-Calavi
FABIYI Kafayath
Universite d'Abomey-Calavi
The Global Taskforce for AMR Control Consortium
university of abomey-calavi
MEDEGAN FAGLA Sèdami Romarique
Universite d'Abomey-Calavi
LOKO Yêyinou Laura Estelle
Universite Nationale des Sciences Technologies Ingenierie et Mathematiques
KOUKOUI Omédine
Universite Nationale des Sciences Technologies Ingenierie et Mathematiques
DJOGBENOU Luc
Universite d'Abomey-Calavi
DOUGNON Jacques
Universite d'Abomey-Calavi
BANKOLE Honoré
Universite d'Abomey-Calavi
BABA-MOUSSA Lamine
Universite d'Abomey-Calavi

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Abstract

Background: Infectious diseases are serious public health issue both in developing countries and industrialized nations. In developing countries, they are the main cause of high mortality rates. In the second group, existing resistance strains to antibiotics is developing and growing at an alarming rate. The purpose of this study was to produce data of national interest to implement sustainable control program against the spread of antimicrobial resistance strains in Benin.

Methods: One hundred and ninety (190) urine samples were collected in selected hospitals in Benin from patients with urinary tract infection. After getting the informed consent from the patients, samples collections were performed under aseptic conditions and cultured for further analysis in the laboratory. The resistance profile of the bacterial strains was established. The search for beta-lactamase production by the isolates was performed using the synergy test for amoxicillin/clavulanic acid and cephalosporins. Mathematical modeling for predicting the development of resistance of the strains by the year 2024 was carried out employing the compartmental deterministic models.

Results: Two hundred and thirty (230) strains were identified from the urine samples. Male individuals were the most affected by urinary tract infections. Individuals between the ages of 21-30 were predominantly infected. *E. coli* was the most isolated species (32.43%) in the urine samples, followed by *K. pneumoniae* (26.85%) and *E. cloacae* (25.92%). The susceptibility testing of isolates showed a high resistance to amoxicillin (91.82%). Whereas the lowest resistance was to imipenem (2%). The beta-lactamase was produced by 24.03% of the strains. *Escherichia coli* (32.43%) was the most productive of broad spectrum beta-lactamase, followed by *K. pneumoniae* (31.03%). The mathematical modeling revealed a rampant rise in resistance development of the strains to the tested antibiotics.

Conclusions: These results provide important data for developing new preventive strategies against the evolution of bacterial resistance to antibiotics. It therefore, further deserves a constructive advocacy so that more actions are taken against the rampant spread of antimicrobial resistance strains in our health facilities as well as in the communities.

1. Introduction

Infectious diseases are a serious public health issue both in developing countries, where they are the main cause of high mortality rates, and in industrialized nations where resistance to existing antibiotics is growing at an alarming rate [1]. Infection of the urinary tract is one of the most common diseases in the hospital and the community.. This infection covers various clinical realities such as uncomplicated acute cystitis, asymptomatic bacteriuria; it can lead to worse conditions including pyelonephritis, prostatitis, urethritis or infection complicating uropathy [4]. The urinary tract infection is extremely frequent among elderly and the symptoms are polymorphous such as asthenia, anorexia, recent incontinence or urgency without urgency [4]. With an incidence between 150–250 million people worldwide [5], urinary tract infections are also more prevalent in women as compared to male. In the community population, bacteriuria is very common, thirty times more in women than in men, with a prevalence of up to 3.5% on a population scale, increasing almost linearly with age. Before the age of 24, 30% of women will have a UTI, and almost 50% of women will have a UTI during their lifetime. In this for institutionalized patients, bacteriuria can reach up to 24%. Urinary tract infection is the most common bacterial infection in hospitalized patients. Urinary tract infections account for 40% of all nosocomial infections. The use of urinary drainage catheters represents the most important risk factor and is the responsible factor in 80% of urinary tract infection acquired in hospital settings. The incidence of urinary tract infections is increasing in certain populations, including: pregnant women, people with spinal cord injuries, patients with multiple sclerosis and those with HIV and AIDS [1, 3, 4, 5].

According to several reports, Enterobacteriaceae are the most isolated bacteria in urinary infections and E. coli is the leading cause of such infection [5].

The poorly controlled use of antibiotics has led to phenomena of bacterial resistance. Bacterial resistance to antimicrobial agents is a problem of increasing importance in medical practice. Dissemination of resistant bacteria is responsible for a considerable increase in mortality, morbidity and cost of treatment [8].

In Africa and particularly in Benin, urinary tract infections remain endemic and represent the highest reason for consultation or hospital visits. However, the etiology of the bacteria involved is not known at the national level. In addition, the majority of patients do not have access to medical laboratories and the management of infectious syndromes is still probabilistic. This practice encourages the spread of multidrug-resistant bacteria in the community and even more in hospitals. No studies have addressed the incidence of multidrug resistance enterobacteria based on the production of beta-lactamase and carbapenemase in urinary tract infections in Benin, and using mathematical modeling to predict how the population of this resistance strains may evolve in the next five years.. Modeling biological phenomena has several importance such as helping to describe and better understand certain biological phenomena, and also makes it possible to summarize and organize knowledge. The mathematical modeling makes it possibleto estimate key parameters, known or unknown [8]. The purpose of this article is to produce data of national interest to guide, prevent and predict the spread of antimicrobial resistance by the year 2024.

2. Material And Methods

2-1- Study design

A cross-sectional prospective and analytical study comprising all patients suffering from urinary tract infections was carried out. The study included patients from the following hospitals and Departmental Hospital Centers in Benin as shown in Table I.

The present study was conducted on 190 urine samples collected from patients diagnosed with urinary tract infections visiting these health facilities within the period of May and September 2019. Prior to admission to this study, a written consent was obtained from patients. This study received the approval of the ethics committee of the research unit. The consent forms are available from the corresponding author upon request. Total confidentiality was assured to the patients who participated in this study.

2-2- Methods

2-2-1- Collection of urine specimen and bacteriological examination

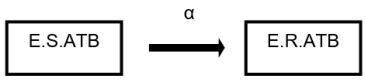
Urines samples were collected throughout Benin from the selected hospitals. For each patient who came to the hospitals for a cytobacteriological examination of urines, a sterile sampling tube was given. Patients were assisted with strict hygiene measures to ensure an aseptic sample. Once the samples were aseptically taken, they were transported to the Research Unit in Applied Microbiology and Pharmacology of natural substances in a cooler containing accumulator for diagnosis. Transport temperature was 2 °C to 4 °C. The samples have been collected at Bethesda's Area Hospital, Menontin's Area Hospital, Parakou-N'dali's Area Hospital, Padre-Pio's Area Hospital, HZ Tanguieta's Area Hospital, Departmental Hospital Center of Porto-Novo. Cytobacteriological examination of the urine was carried out on each sample in the following manner: macroscopic examination, microscopic examination (fresh state and gram stain) and cultivation. The cultivation took account of the gram results. Only the samples with gram negative bacilli were cultured as we were interested in enterobacteria. This process follows the procedures described by Hassan et al., and El bouamri et al., [8, 10]. Prior to the collection, a survey form was made available to capture patient's details. These details were related to socio-cultural characteristics.

2-2-2- Antibiogram

Antibiotic susceptibility was determined by the Mueller Hinton agar disk diffusion method [30]. The resistant enterobacteria that produced beta-lactamase were screened using the double synergy test as described by Inan et al., [11]. The production of ESBL appears in the form of a champagne cork on the agar as shown in figure S1. The table I shows the different antibiotics used with their concentrations.

2-2-3- Mathematical modeling of the resistance isolates

Following the determination of the antibiotic resistance profile, a mathematical modelisation was performed over six years period. The model used in this study is based on the compartmental model which describes the dynamics of colonization of members of a population by a bacterial strain constructed by Anderson et al., [31]. The population is divided into two compartments: colonized individuals and non-colonized or susceptible individuals. Individuals may be exposed to an antibiotic. The exposure to an antibiotic being homogeneously distributed among the study population. Our study took into account only colonized individuals, ie patients who came to the laboratory for the diagnosis of urinary tract infections. Within the population of colonized individuals, facing each antibiotic, the bacterial population is classified into 3 compartments: The compartment of sensitive strains (S), The compartment of strains with intermediate resistance (I) and the compartment of strains Resistors (R). The modeling in this case will allow us to estimate the evolution of resistance in the population of colonized individuals. The basic assumptions of the model are: The system is assumed to be closed, that is to say that births, deaths and migrations are not taken into account and the transition from one compartment to another is determined by fixed transfer rates. The purpose of this modeling was to predict an estimation of the spread of resistant population by the year 2024. For the resistance profiles not having intermediate resistance, the following model was used:



-E.S.ATB: Antibiotic-Sensitive Enterobacteria

-E.R.ATB: Antibiotic-Resistant Enterobacteria

Equations :

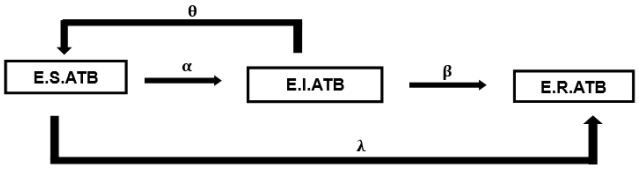
$$\dot{ESATB} = \frac{d(E.S.ATB)}{dt} = -\alpha E.S.ATB$$

$$\dot{ERATB} = \frac{d(E.R.ATB)}{dt} = \alpha E.S.ATB$$

Parameters:

α : Rate of $E.S.ATB$ becoming $E.R.ATB$

For resistance profiles with intermediate resistance, the following model was applied :



-E.S.ATB:Enterobacteria sensitive to antibiotic.

-E.I.ATB:Enterobacteria with Intermediate Antibiotic Resistance.

-E.R.ATB: Enterobacteria Resistant to Antibiotics.

Equations :

$$\dot{ES.ATB} = \frac{d(E.S.ATB)}{dt} = -(\alpha + \lambda)E.S.ATB + \theta E.I.ATB$$

$$\dot{EI.ATB} = \frac{d(EI.ATB)}{dt} = \alpha E.S.ATB - (\beta + \theta)E.I.ATB$$

$$\dot{ER.ATB} = \frac{d(ER.ATB)}{dt} = \beta E.I.ATB + \lambda E.S.ATB$$

Parameters :

α : E.S.ATB rate becoming E.I.ATB

β : E.I.ATB rate becoming E.R.ATB

λ : E.S.ATB rate becoming E.R.ATB

θ : E.I.ATB rate becoming E.S.ATB

2.2.4. Statistical analyzes

The data collected were coded and uploaded in a Microsoft Excel 2019 database. The graphs were developed using the GraphPad Prism 8 software. The proportions were compared using Chi square test.

3. Results And Discussion

3.1. Results

Figure 1 shows the percentage of samples received per center. Bethesda and Menontin hospitals received more patients for cytobacteriological examination of urine than others. The study revealed that more Female patients contracted urinary tract infections in Benin (Fig. 2a) with a positive proportion of 80% (115 positive samples out of 142) against 87.5% (35 positive samples upon 48) of male. However, this shows that population of female patients that visited the hospitals for diagnosis was far less compared to those of male patients.

The Fig. 2b shows the distribution of individuals according to age group. This figure revealed that individuals between the age groups of 20 and 30 years were the most infected.

Similarly, the distribution of the study population by age group and sex has shown that women are the most represented in the age group between 20 and 30 years (Fig. 2c). Macroscopic examination of the urine samples has several aspects with variable turbidity as indicated in Fig. 3. The table II shows the microscopic examination of the different elements detected in the study samples.

Figure 4a shows the frequency of the different bacterial species identified after the culturing. It shows that E. coli (32.43%) was the most isolated, followed by K. pneumoniae (26.85%) and E. cloacae (25.92%).

The sensitivity of the different bacterial isolates to the tested antibiotics are shown in Fig. 4b. Table III shows the resistance profile of these enterobacteria to each antibiotic.

Table IV shows the prevalence of the isolates detected for producing beta-lactamase enzyme. Here, E. coli (24/74) is the bacteria with the highest production of beta-lactamase followed by K. pneumonia (18/58)

MODELISATION OF THE RESISTANCE

The resistance of the different strains has been modeled to have an estimate of their population resistance by the year 2024. This study is the first in Benin. We therefore used the current data obtained during this study to predict the level of resistance on the 2024 scale. The results of this study are a basis for the use of Benin modeling. For all strains, high levels of resistance will be observed for all antibiotics and only imipenem will show low levels of resistance. However, M. morganii strains have surprisingly showed total resistance to imipenem (Fig. 5).

Modeling K. pneumoniae strains showed total resistance to some antibiotics by 2024, namely Amoxicillin, Ceftriaxone and Ciprofloxacin. Apart from Imipenem, which in 2024, a rate of 34.80% will be observed, all the other antibiotics tested will show high levels of resistance (Fig. 5a).

For strains of C. diversus, a 100% resistance will be observed for amoxicillin and ciprofloxacin. Imipenem and Aztreonam are the two antibiotics with relatively low levels of resistance (Fig. 5b).

Strains of E. aerogenes will show high resistance to most antibiotics tested. Only carbapenems will show moderately low resistance (Fig. 5c).

In 2019, high levels of resistance were already observed against all antibiotics tested in strains of M. morganii and in 2024, there would be complete resistance against all antibiotics (Fig. 5d).

In K. oxytoca, resistance against all the antibiotics tested will be 100% except for Imipenem which is 22% (Fig. 5e).

Strains of E. coli will also show high levels of resistance to Horizon 2024. However, Imipenem resistance rate remains low (Fig. 5f).

In 2024, the strains of E. cloacae will also show high levels of resistance against all the antibiotics tested except for Imipenem which will be 22.04% while it was zero in 2019 (Fig. 5g).

DISCUSSION

In a developing country such as Benin, bacterial infections such as urinary tract infection remain a major public health issue given their frequency and antimicrobial resistance [12]. Several bacterial species are involved as far as urinary tract infections are concerned. The general objective of this study was to determine the main enterobacteriaceae responsible for urinary tract infections in Benin and to evaluate the level of resistance of these uropathogenic bacteria to bata-lactamin and carbapenem classes of antibiotics and also to model how this population of antibiotic-resistant strains may evolve by the year 2014.This study was carried out in various health facilities across the country where clinical specimen where collected and analysed at the reference laboratory. The health facilities comprised district hospitals and Departmental Hospital Centers. These centers were chosen according to the geographical location in the country, the affluence in terms of microbiological diagnosis based on the availability of a bacteriological laboratory. Thus, a total of 190 urine samples were collected. On average, fifteen [13] urine samples are received per week in the surveyed hospitals. This influx would be justified by the public health threats posed by urinary tract infections in developing countries like Benin [14]. Several researchers have reported in various studies that these infections are the most common bacterial diseases in hospital and community settings [15, 16]. This state of affairs shows that urinary tract infections are endemic to Benin.

The ratio of male to female has shown that males are the most affected by urinary tract infections. However, the study revealed that numbers of male patients were far less compared to female patients that visited the health facilities. Pregnant women are the most affected are the most affected as pregnancy is a physiological state that weakens the woman's immune system [17, 18 and 19]. In addition, among the population studied, individuals between the age group of 21 and 30 years are the most affected by this disease and among these, women are also the most represented. The female predominance is related to the anatomical configuration: shortness of the urethra, proximity of the genital and anal openings, insufficient hygiene practices, sexual intercourse and pregnancy. A study by Moutachakkir et al., [20] noted a similar result in his study on enterobacterial phenotypes responsible for community and nosocomial infections. However, urinary cytology showed epithelial cells, urinary crystals, kidney cells and leukocytes which were mostly high. These results corroborate those of Mshana et al., [21] in their study carried out on the resistance phenotypes of E. coli strains responsible for urinary tract infections in the laboratory of the University Medical Center of Befelatananain Antananarivo.

In the present study, 230 Enterobacteriaceae have been isolated and identified from the urine samples. Escherichia coli (32.42%) is the most isolated bacterial species, followed by K. pneumoniae (26.85%) and E. cloaceae (25.92%). This result corroborates several studies conducted by researchers from other countries that worked on enterobacteria responsible for urinary tract infections [22, 23, 24, 25, 26]. A study by Sbiti et al., [27] also obtained similar results. In addition to the commonly encountered species, other bacteria have also been isolated. These include K. oxytoca (6.94%), E. aerogenes (6.02%), M. morganii (0.92%) and C. diversus (0.92%). The involvement of these bacteria in the case of urinary tract infection has been demonstrated by other studies [28]. Indeed, most of these authors have shown that these bacteria are also responsible for urinary tract infections but with a very low proportion compared to the frequently isolated species.

The study of the sensitivity of isolated strains showed a high resistant to penicillins, Amoxicillin/clavulanic acid and amoxicillin. This result is similar to that of Zahir et al., [29], who researched on the evolution of the resistance of enterobacteria responsible for human infections at the Douala hospital. The different bacterial species isolated showed varying levels of resistance to the different antibiotics used. In the family of bet-alatamin, penicillins including amoxicillin (50.56%) and amoxicillin / clavulanic acid (91.82%) showed the most resistance. Cephalosporins such as cefotaxime (36.24%) and ceftriazone (45.58%) exhibited high level resistance as did aztreonam (35.81%). Imipenem (2.00%) showed very low resistance compared to ertapenem (36.07%) of the carbapenem class. In the aminoglycoside family, gentamicin showed a resistance of 33.74%, lower than the resistance level of ciprofloxacin (52.05%) in the quinolone family. The high level of resistance observed in the penicillin class has been demonstrated by other researchers [27, 18, 30]. The latter explained that this resistance is acquired and would be the consequence of the selection pressure linked to the excessive consumption of antibiotics in the developing countries. This result confirms that amino-penicillins are no longer recommended for treating urinary tract infections. The high resistance level of cephalosporins is similar to that of Chemlal et al., [4] but different from those of Kanadjigui et al., [15]. The latter found resistances a little lower than ours. This result could be justified by the fact that cephalosporins are the most used antibiotics [11]. Also in the context of our study, the samples were collected in Benin reference centers so patients often come from other health facilities where probabilistic treatments based on the use of these molecules have sometimes already been initiated. Self-medication and lack of infection management guidelines can also contribute to increased levels of resistance to these antibiotics in our context. Imipenem had good activity on enterobacterial strains. This trend has also been found in Spain [25]. The evolution of the resistance of uropathogenic enterobacteria to gentamicin and ciprofloxacin has also been demonstrated by this author.

In the current study, E. coli showed the highest resistance to amoxicillin and high sensitivity to imipenem (89.65%). These results are consistent with those obtained by Konaré [17]. For K. pneumoniae strains, the highest resistance was observed to Amoxicillin and the lowest resistance was to Imipenem (6.25%). These results are similar to those of Inan et al., [11] conducted in India. Klebsiella pneumoniae strains are naturally resistant to amino-penicillins due to the expression of Ambler class A chromosomal beta-lactamases (5), which could justify their high resistance to Amoxicillin. In Burkina Faso, Konaré [17] obtained a sensitivity rate for Imipenem that is similar to that obtained in this study.

The determination of the production of beta-lactamase by the double synergy test showed a general prevalence of 18. 44%. This prevalence is slightly below what was reported by Ahoyo et al., [1]. In fact, they worked on the bacteria responsible for nosocomial infections at the Zou-Colline Departmental Hospital Center. Strains of E. coli (34.61%) are the most producing beta-lactamase in our study followed by K. pneumoniae (30.77%). This resistance may be explained by a decrease in the activity of the beta-lactamase inhibitor (clavulanic acid), resulting from a penicillinase hyperproduction, or the inactivation of the inhibitor itself [14]. This is probably due to the often anarchic prescription of these molecules, especially in ambulatory medicine, pending ECBU results.

In Benin, mathematical modeling has so far been rarely used in predicting the spread of antibiotic resistance population and therefore the literature on the latter is almost non-existent. In this study, mathematical modeling of bacterial resistance to the antibiotics tested showed a significant difference in the evolution of resistance at the 2024 scale. A rapid increase in resistance was observed in all bacterial species studied. It is only at the level of imipenem that a low level of resistance has been obtained at the 2024 scale. Indeed, in a report published in 2014, WHO refers to Africa and South-East Asia as the regions of the world without antimicrobial resistance surveillance systems [13]. It is in this perspective that the present study was carried out. The results of this study therefore open a perspective for an estimate of the resistance rates of these strains by the year 2024. Other more recent models have been developed in recent years for modeling applied to antimicrobial resistance. However, the complexity of these models (due to the fact that they were built in developed countries) prevents us from being able to apply them in Benin (a developing country).

Conclusion

The present study has highlighted enterobacteria responsible for urinary tract infections in Benin and the increasing evolution of bacterial resistance to an antibiotic which requires radical measures. Thus, before any suspicion of urinary tract infection, it is preferable to perform a cytobacteriological examination of urine with a mandatory antibiogram. Indeed, the antibiogram is above all a tool to help the therapeutic decision: by categorizing the sensitive bacteria, intermediate or resistant, it guides with predictability antibiotic therapy, contributing to a gain in morbi-mortality according to the severity of infections concerned. This will avoid the probabilistic or empirical treatment of the urinary tract infection which may lead to resistance. Similarly, self-medication should be avoided by controlling the supply of antibiotics at the community and hospital level. Standard and specific hygiene precautions should also be adhered to, so as to limit the spread and transmission of ESBLs. Awareness among health authorities, health professionals and the population is necessary for these measures to be understood and practiced appropriately.

Declarations

Ethics approval and consent to participate:

The study has been submitted to the Benin National Ethical Committee for Health Research. An approval has been issued under the number N°65/MS/DC/SGM/DRFMT/CNERS/SA. The approval letter is available upon requested from the corresponding author. The respondents gave their verbal consent to participate in the study.

Consent for publication:

All authors gave their consent for the publication of the manuscript.

Availability of data and material: All data generated or analysed during this study is included in this published article and supplementary information files.

Competing interests:

Authors declare no competing interest.**Funding:** The authors are very grateful to the Benin Center for Scientific Research and Innovation for the funding provided in this study. **Authors' contributions:**DV, AP, JM, GJ-P, AJ, KH, DE, KF and the Global Taskforce for AMR control consortium wrote the protocol, performed the study, designed the manuscript.DV, AP and GJ-P performed the statistical analyses.MFSR, LYE, KO, DL, DJ, BH, and LB-M reviewed the manuscript.

All authors have read and approved the manuscript.

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Authors' Information:

DOUGNON Victorien (victorien.dougnon@gmail.com),

ASSOGBA Phénix (esseconstant.assogba@gmail.com)

GNIMATIN Jean-Pierre (jeanpierre.gnimatin@gmail.com)

AGBANKPE Jerrold (agbankpejerrold@yahoo.fr)

KOUDOKPON Hornel (charleshornel@yahoo.fr)

DEGUENON Esther (misesther@yahoo.fr)

FABIYI[1] Kafayath, (kafayathfabiyi@yahoo.fr)

The Global Taskforce for AMR Control Consortium:

AGBENOMBA Adjoa Irma (agbenombairma2017@gmail.com),

AHOKPOSSI Merveille (merveilleahokpossi@gmail.com),

AHOLOU-GBEWA G. Richard (aholougbewaking1@gmail.com),

AHOUEKE Elvire, (ahouekeelvirehahouegnon@gmail.com),

AKOTEGNON Kafoui Rémi Espérantos (akotegnonk7@gmail.com),

ATACOLODLOU Jocelyne (urmaphaepac@hotmail.com),

BETE Mawuyéna Mélaine (mawuyenadjakpo@gmail.com),

BOKOSSA Donald (donaldbokossa09@gmail.com),

CODJIA Prixille (prixillecodjia@gmail.com),

COMLAN Gloria Lydie (comlanglorialydie@gmail.com),

DEGBEY Hermine Flora (degbeyhermineflora04@gmail.com),

GBESSOUA Ariane (arianeamigbessoua1@gmail.com),

GNANVI Marius (gnanvimarius@gmail.com),

GOUNOUKPEROU Solange (urmaphaepac@hotmail.com) ,

HOLOGAN Hermione (milenehologanl48@gmail.com),

HONFO Paterne (honfopaterne@gmail.com),

HOUDE Emmanuella (rubenelchou@gmail.com),

HOUNDEHESSI F. R. Gloria (rosaliehoundehessi364@gmail.com),

HOUNDONOUGBO Belvida (houndonougbobelvida@gmail.com),

HOUNKANRIN GbêmêhoManoir Pascal (manoirpascal@gmail.com),

IROUKORA Annick (annickiroukora0@gmail.com),

KINTIN Mélaine (melykint@gmail.com),

KOONON Christian (kochrist5@gmail.com),

KOUTANGNI Tatiana (tatikoutangni@gmail.com),

LANMATCHION Romuald (gladinlife95@gmail.com),

MIDINOUDEWA Yves Ornel (ornelyves@gmail.com),

MINDZIE NGOMO Rajeunie (urmaphaepac@hotmail.com) ,

OLOUDE Marielle (marielleoloude@gmail.com),

OWOLABI Marlène (marleneowolabi@gmail.com),

SALISSOU TOURE Yassimine (salissoutoureyassimine@gmail.com),

SANHONGOU Layombo (sanhongoufidele@gmail.com),

SESSOU Rémi Maquez (sessouremi@gmail.com),

TIDJANI Romziath (tidjani.romziath@gmail.com),

YATTA Paulette (yattpaulett@gmail.com),

ZIN Septuce Gaétan (septucemusset@gmail.com),

ZOUNON Daniella (gloriazounon6@gmail.com),

MEDEGAN FAGLASèdamiRomarique (medegansed@gmail.com),

LOKOYêyinouLaura Estelle (lokoestelle@yahoo.fr),

KOUKOUI Omédidine (omedine24@gmail.com),

DJOGBENOU Luc (ldjogbenou22002@yahoo.fr),

DOUGNONJacques (dougnonj@yahoo.fr),

BANKOLE Honoré (bahosour@yahoo.fr)

BABA-MOUSSALamine (laminesaid@yahoo.fr)

Additional File

Figure S1: Appearance of champagne corks on MH agar; **Figure S2:** Variation of resistance among *Escherichia coli* strains between 2019 and 2024; **Figure S3:** Variation of resistance among *Citrobacterdiversus* strains between 2019 and 2024; **Figure S4:** Variation of resistance among *Enterobacteraerogenes* strains between 2019 and 2024; **Figure S5:** Variation of resistance among *Enterobacter cloacae* strains between 2019 and 2024; **Figure S6:** Variation of resistance among *Klebsiellaoxytoca* strains between 2019 and 2024; **Figure S7:** Variation of resistance among *Klebsiellapneumoniae* strains between 2019 and 2024; **Figure S8:** Variation of resistance among *Morganellamorganii* strains between 2019 and 2024

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Tables

Table I: List of antibiotics used in the study and their corresponding charges

Antibiotics	Abbreviations	Charge in µg
Amoxicillin + Clavulanic Acid	AMC	30
Amoxicillin	AMX	25
Cefotaxim	CTX	30
Aztreonam	AT	30
Ertapenem	ETP	10
Ciprofloxacin	CIP	5
Gentamicin	GEN	10
Ceftriazone	CRO	30
Imipenem	IMP	10

Table II: Microscopic aspects of the elements present in the samples.

	Appreciations				
Elements	**Rare**	**Many**	**Numerous**	**Very Numerous**	**TOTAL**
Epithelial cells	12%	30%	40%	18%	100%
Kidney cells	70%	20%	10%	00%	100%
Crystals	45%	35%	15%	05%	100%
Leukocytes	7%	10%	35%	48%	100%

Table III: Resistance profile of different bacterial species to different antibiotics used.

Bacteria	Interpretation of the inhibition diameters	Class of Antibiotics								
		Beta lactams							Aminosides	Quinc
		Penicillins		Cephalosporins		Monobactams	Carbapenems			
		Amoxiclav	Amoxicillin	Cefotaxim	Ceftriazone	Aztreonam	Imipenem	Ertapenem	Gentamicin	Ciprof
		AMC	AMX	CTX	CRO	AT	IMP	ETP	GEN	CIP
E. coli	Resistant (%)	58.63	91.37	37.28	41.37	31.03	3.44	10.34	36.20	58.18
	Intermediate (%)	00	00	12.06	13.8	17.24	6.90	12.06	8.62	3.45
	Susceptible (%)	41.37	8.63	50.66	44.83	51.73	89.66	77.6	55.18	38.37
K. pneumoniae	Resistant (%)	62.5	93.75	29.2	44.7	27.1	6.3	31.2	27.1	41.7
	Intermediate (%)	00	00	10.4	6.3	31.2	4.1	10.4	2.1	20.8
	Susceptible (%)	37.5	6.25	60.4	24	41.7	89.6	58.3	70.8	37.5
E. cloaceae	Resistant (%)	50	82.6	50	43.5	30.4	00	43.5	23.9	50
	Intermediate (%)	00	00	17.4	6.5	32.6	6.5	6.5	6.5	10.9
	Susceptible (%)	50	17.4	32,6	50	37	93.5	50	69.6	39.1
K. oxytoca	Resistant (%)	53.3	100	66.7	60	66.7	00	33.4	46.7	60
	Intermediate (%)	00	00	00	00	00	00	13.3	6.6	13.3
	Susceptible (%)	46.7	00	33.3	40	33.3	100	53.3	46.7	26.7
E. aerogenes	Resistant (%)	54.5	100	45.5	54.5	45.5	00	9.1	27.3	54.5
	Intermediate (%)	00	00	00	9.1	18.1	00	00	18.2	9.1
	Susceptible (%)	45.5	00	55.5	36.4	36.4	100	90.9	54.5	36.4
M. morganii	Resistant (%)	50	100	00	50	50	00	100	50	50
	Intermediate (%)	00	00	100	00	00	50	00	00	50
	Susceptible (%)	50	00	00	50	50	50	00	50	00
C. diversus	Resistant (%)	25	75	25	25	00	00	25	25	50
	Intermediate (%)	00	00	00	00	00	00	00	00	00
	Susceptible (%)	75	25	75	75	100	100	75	75	50

Table IV: Prevalence of the enterobacteria producing betalactamase.

Bacteria	Nomber of bacteria identified	Number of ESBL Bacteria	Total
Escherichia coli	75	24	24/75
Klebsiella pneumoniae	60	18	18/60
Enterobacter cloaceae	58	8	8/58
Klebsiella oxytoca	18	2	2/18
Enterobacter aerogenes	15	1	1/15
Morganella morganii	02	0	0/2
Citrobacter diversus	02	0	0/2
Total	**230**	**53**	**53/230**

Figures

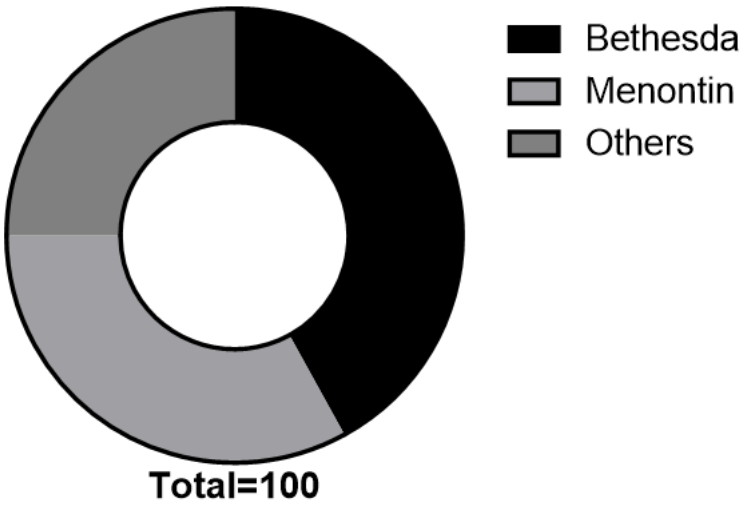

Figure 1

Percentage of urine samples according to the hospitals

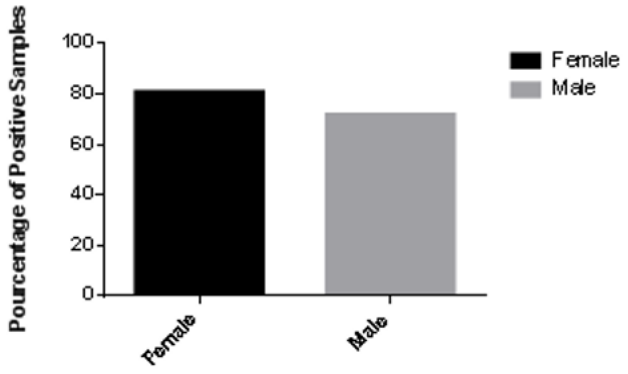

Figure 2a: Distribution of positive samples according the gender.

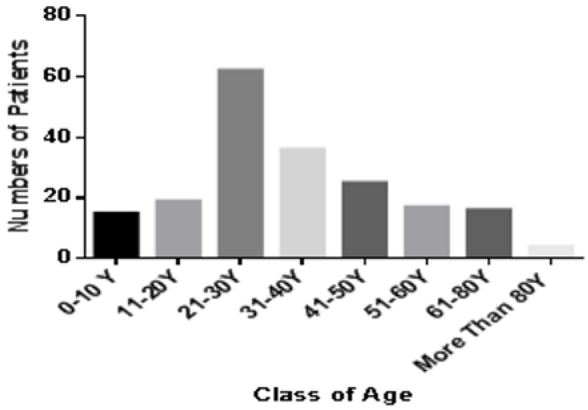

Figure 2b: Distribution of patients according the age.

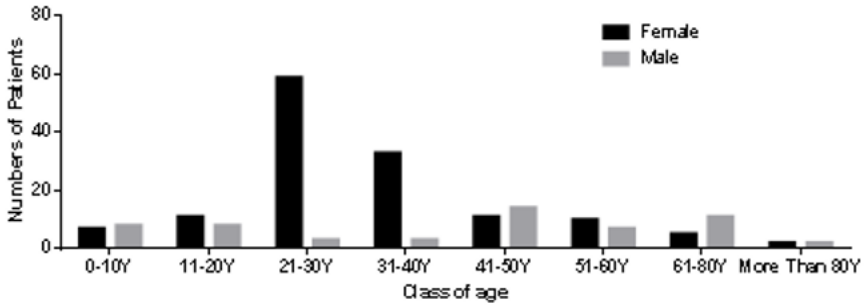

Figure 2c: Distribution of the study population following age group and gender.

Figure 2

Socio-demographic characteristics of the population

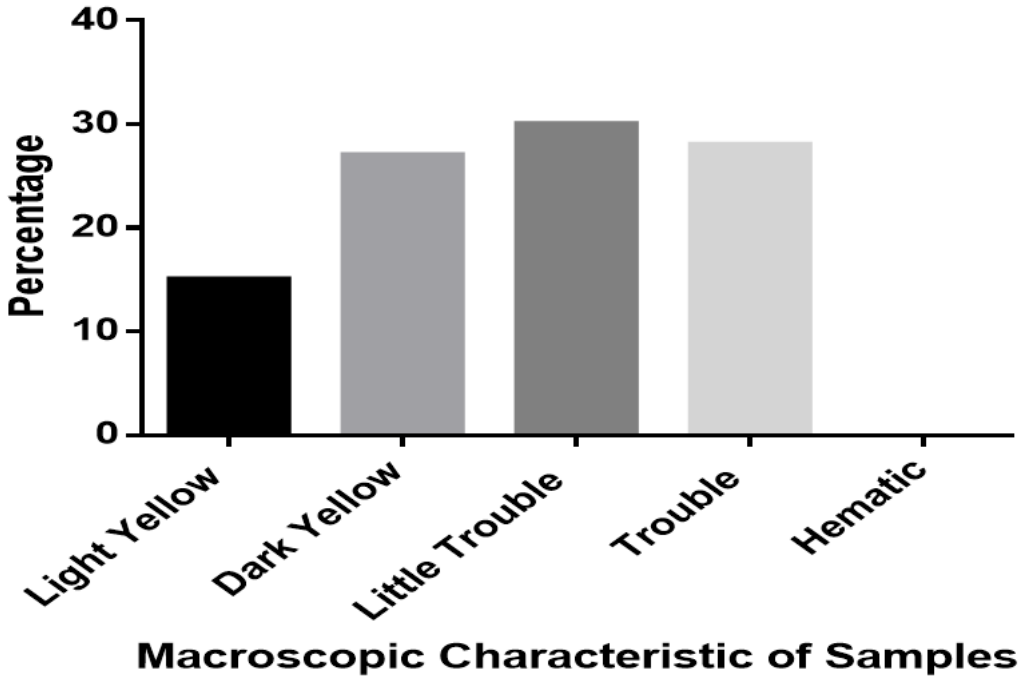

Figure 3

Macroscopic aspects of the samples collected

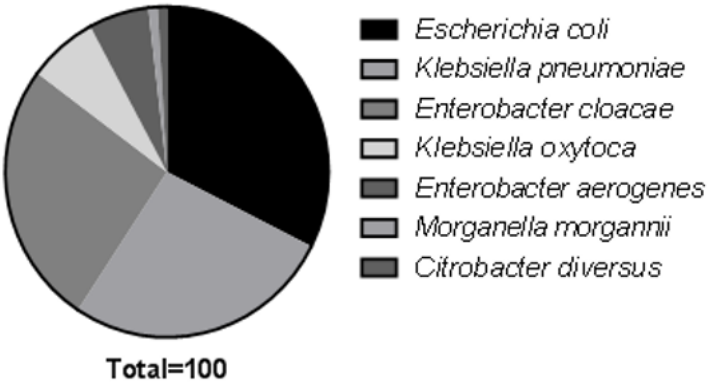

Figure 4a: Frequency of species identified

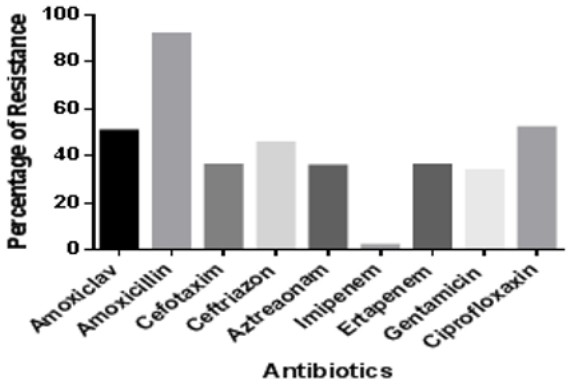

Figure 4b: Global Resistance percentage of the enterobacteria to the antibiotics

Figure 4

Bacteriological characteristics of enterobacteria

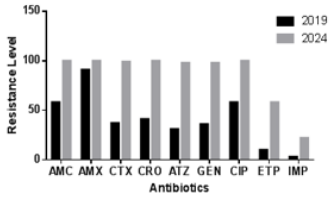

Figure 5a: Evolution of the resistance of *Escherichia coli*

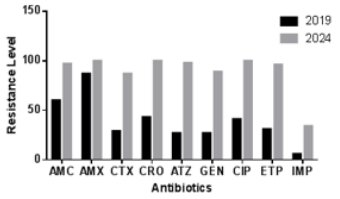

Figure 5b: Evolution of the resistance of *Klebsiella pneumoniae*

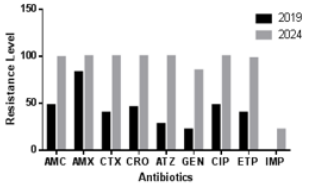

Figure 5c: Evolution of the resistance of *Enterobacter cloacae*

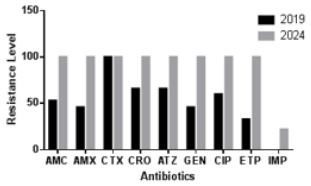

Figure 5d: Evolution of the resistance of *Klebsiella oxytoca*

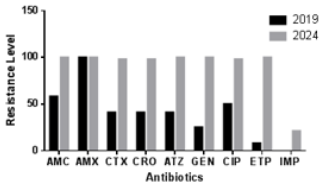

Figure 5e: Evolution of the resistance of *Enterobacter aerogenes*

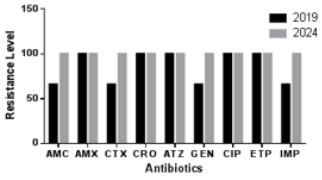

Figure 5f: Evolution of the resistance of *Morganella morganii*

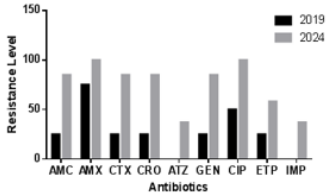

Figure 5g: Evolution of the resistance of *Citrobacter diversus*

Figure 5

Evolution of the resistance among enterobacteria till 2024 through a modelisation approach

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