World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 4.223

SPECIMENS AND GRAM-NEGATIVE BACTERIA ETIOLOGIES OF INFECTIOUS DISEASES IN A SEMI-URBAN AREA IN WEST-CAMEROON: A TWELVE-MONTH RUNDOWN OF INFECTION SCREENING IN THE MEDICAL SCHOOL TEACHING HOSPITAL

Pierre René Fotsing Kwetche*[1,3,4], William Lelorel Nankam Nguekap[3,4], Christelle Domngang Noche[2,3,4], Anselme Michel Yawat Djogang[1,4], Sandrine Gamwo[1,3,4], Josué Simo Louokdon[1,3,4], Exupere Cheugoue Towo[1,4], Serge Honoré Tchoukoua[2,4], Jonas Kouamouo[1,3,4] and Kaba Kourouma[1,3,4]

[1]School of Pharmacy Higher Institute of Health Sciences, Université des Montagnes; Bangangté-Cameroon.
[2]School of Medicine Higher Institute of Health Sciences, Université des Montagnes; Bangangté-Cameroon.
[3]School of Medical Biology Higher Institute of Health Sciences, Université des Montagnes; Bangangté-Cameroon.
[4]Cliniques Universitaires des Montagnes; Bangangté-Cameroon Higher Institute of Health Sciences, Université des Montagnes; Bangangté-Cameroon.

***Corresponding Author: Pierre René Fotsing Kwetche**
School of Pharmacy Higher Institute of Health Sciences, Université des Montagnes; Bangangté-Cameroon.

Article Received on 18/12/2017 **Article Revised on 08/01/2018** **Article Accepted on 29/01/2018**

ABSTRACT

The present survey aimed at identifying the most frequent clinical specimens submitted for analyses and the related susceptibility/resistance profile of Gram-negative rods isolated over a twelve-month period (January 1st through December 31st 2016) at the Université des Montagnes Teaching Hospital, Bangangté, West-Cameroon. All specimen collection, identifications and susceptibility tests were conducted in the Laboratory of Microbiology according to standard protocols recommended by REMIC, 2015 and Eucast-SFM, 2015. Most frequent specimens recorded (87%) were urines, women genital secretions and pus from which close to 88 % of the isolates, overwhelmed by members of the *Enterobacteriaceae* family were recovered. The most frequent etiologies (*Escherichia coli*, *Enterobacter* spp., and *Klebsiella* spp.) typically predominated in the urine (50% of isolates), followed by the vaginal secretion and pus (19% and 18%, respectively). Overall, the resistance rates to common or related antibacterial agents were higher in *Enterobacteriaceae* (Ampicillin, 94%; Trimethoprim/Sulfamethoxazole, 64%; Nalidixic acid, 61% and Ciprofloxacin, 43%) while susceptibility ranged from 3% with Amoxicillin/Clavulanic acid to 72% with Imipenem. This trend was also similar in non-fermenting Gram-negative rods, consistent with previous reports. The successive findings could serve as useful clues for effective action towards antibiotic susceptibility/resistance stewardship. To be effective the intervention policy should simultaneously target policy makers, prescribers, and drug users with trained and committed human resources.

KEYWORDS: Antibacterial susceptibility/resistance, Gram-negative rods, clinical setting

INTRODUCTION

Infectious diseases (IDs) remain leading causes of morbidity and death in large numbers of countries throughout the world, especially in low-income communities. Owing to the fact that most are related to enabling factors related to human behavior like poor utilization of available resources and colonization by drug-tolerant microorganisms, the rates of most of these IDs can be mitigated. For several decades antimicrobial-resistant bacteria has been identified and invariably substantiated as undeniable cause of concern due to reduced efficacy of antimicrobial agents, primarily on known pathogenic micro-organisms.[1] Recent studies indicate, however, that non-pathogens are likely more involved in resistance selection and dissemination in the bacteria world than true pathogens; and that their impact which increases with resource limitation jeopardizes effective caretaking of known IDs. Accordingly, antibiotic-resistant bacteria strains are critical concerns in healthcare facilities where the use of antibiotics (ABs) is common and most importantly, in those where empiric and probabilistic antibacterial therapies are the rules.[2–4] In these settings in fact, non-pathogenic AB-resistant rods represent major etiologies of infections; favored by the low immunity of the hosts. In connection with their high potential in diffusing mobile genetic determinants in bacterial populations, the predictable natural phenotypes that would guide the probabilistic antibacterial therapy have been overwhelmed by multitude of stochastic

acquired resistance characteristics. High-income countries have enacted policies to address on regular basis the changes that might be observed in this light, in order to guide drug prescribers and other health personnel on the appropriate agents that could be used either in probabilistic antibacterial therapy in emergency or with the aid of susceptibility tests. In resource-limited areas, very few health institutions can afford proper identification and susceptibility tests prior to ABs therapy because of sets of factors including reduced educational potential (consistent with shortage of human resources) and other associated basic needs.[5,6] Beyond increased morbidity and mortality, the short run consequences of increased drug tolerance is the increase of the length of hospitalization, additional health cost with often more potent and costly drugs as part of the frame which sustains the vicious cycles of ambient poverty in poor communities. The control of the AB-resistance trend appeared as paramount target for medical laboratories, as part of the network that has to gather useful parameters in the database for initial and epidemiological resistance surveillance. In this regards, and with their high potential in disseminating resistance traits in bacterial world, the present work was initiated to address resistance/susceptibility (R/S) trends in Gram-negative rods isolated from clinical specimens for a twelve-month period of time in the Laboratory of Microbiology of the Université des Montagnes Teaching Hospital. The holistic data thereof could guide better usage of available resources and effective probabilistic antibacterial therapy in the short run and serve as reference mark in the R/S control in the health facility within a stewardship program in both the intermediate and the long runs.

MATERIAL AND METHODS

Ethical consideration, health amenities and Study population,

The go-ahead was obtained from the Head of the Cliniques Universitaires des Montagnes under reference number: Ref: 2018/008/CUM/LAM.

Typically semi-urban, Bangangté hosts a mixed population which shares sets of common social determinants like believes, purchasing power and scarce community outreach services. This scarcity extends to health institutions, human resources for health and basic amenities like safe drinking water. Resource shortage contrasts with the fast population growth favored by the development of several institutions of higher learning and flourishing trading. Most people rely on wells and streams that also commonly serve as rubbish dumps for local domestic wastes. Often, only serious cases of diseases are reported to the available health facilities because traditional medicine practices regarded by most as legacy predominate.

Sample collection and bacteria isolation

This was a cross-sectional descriptive study conducted on cryopreserved Gram-negative rods gathered over a 12-months period (January 1st through December 31st, 2016). Original pathologic specimens included pleural fluid, urethral and vaginal swabbing, pus, blood, stool, sperm and urine. All were collected according to standard procedures and conveyed without delay to the Laboratory of Microbiology of the Université des Montagnes Teaching Hospital for processing. All cultures, isolations and identifications were conducted according to REMIC recommendations throughout the year.[7] In short for the Gram-negative rods targeted, colony isolation was performed on McConkey, Cled and Hektoen agars. All identifications were conducted according to standard morphological and biochemical procedures by the same reference repository.

Antimicrobial Susceptibility testing

Susceptibility tests were carried out by disk diffusion (Kirby-Bauer) with 22 conventional antibacterial agents that are commonly used in Cameroon. In short, this was conducted on 24 h bacterial pure culture obtained by streaking bacterial isolates on fresh nutrient agar and allowing for an overnight aerobic incubation at 37 °C. From the resulting bacterial population, a suspension to the density of a McFarland 0.5 turbidity standard prepared in 0.9% saline was adjusted to the final opacity recommended for susceptibility tests by agar diffusion technique on Mueller Hinton agar. Test procedures and interpretations were done according to the standard guidelines recommended by the Comité de l'Antibiogramme de la Société Française de Microbiologie.[8] The antibiotic disks tested included: Amoxicillin/clavulanic acid (20/10 µg), Amoxicillin (25 µg), Ampicillin (10 µg), Ceftazidime (30 µg), Ceftriaxone (30 µg), Cefixime (30 µg), Nitrofurantoin (300 µg), Chloramphenicol (30 µg), Cefoxitin (30 µg), Aztreonam (30 µg), Cefotaxime (30 µg), Cefuroxime (30 µg), Imipenem (10 µg), Gentamicin (15 µg), Ciprofloxacin (5 µg), Ofloxacin (5 µg), Levofloxacin (5 µg), Trimethoprim/sulfamethoxazole (1.25/23.75 µg), Colistin sulphate (10 µg). For identification and susceptibility tests, *E. coli* ATCC 2922 was the reference bacterial strain used for quality control.

RESULTS

Distribution of specimens

From January 1st through December 31st 2016, a total of 720 cultures were performed. Overall, 179 strains of Gram-negative rods were isolated from the related clinical specimens. Their distribution per specimen category was assessed and summarized as shown in Figure 1.

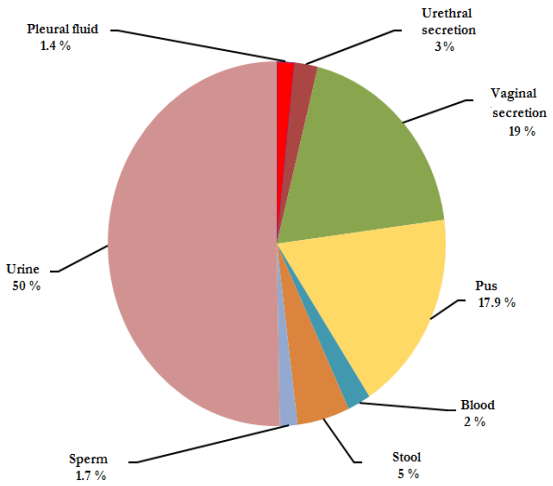

Figure 1: Distribution of specimen's type

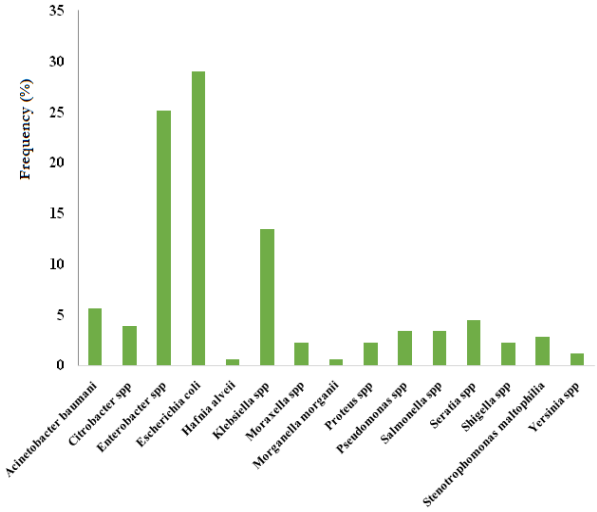

Figure 2: Distribution of bacterial species

It appears that in decreasing order, the most frequent sample types submitted for laboratory analyses were urine, women genitalia secretions and pus. Overall, they represented about 87 % of the total conveyed to the laboratory.

Bacterial types recovered

From the 179 isolates submitted to susceptibility testing, 84% were members of the *Enterobacteriaceae* family. Figure 2 further displays the detailed distribution of isolates subsequent isolation and identification.

Within the *Enterobacteriaceae* family and in decreasing order, most common were *Escherichia coli*, *Enterobacter* spp., and *Klebsiella* spp., representing an overall rate of about 67.6%, while the least were *Hafnia* and *Morganella* (≈ 0.6% each).

Distribution of bacteria isolates according to clinical specimens

With reference to clinical specimens, bacteria isolates were distributed as shown in Table 1.

Table 1: Distribution of bacteria isolates according to clinical specimens

Bacteria	Clinical specimens type							
	Urine (n=90)		Vaginal swab (n=34)		Pus (n=32)		Others[a] (n=23)	
	n	%	n	%	n	%	n	%
Acinetobacter baumannii	4	4.44	1	2.94	3	9.38	2	8.7
Citrobacter spp.	3	3.33	2	5.88	1	3.13	1	4.35
Enterobacter spp.	23	25.56	9	26.47	10	31.25	3	13.04
Escherichia coli	29	32.22	15	44.12	5	15.63	3	13.04
Hafnia alvei	1	1.11	0	0	0	0	0	0
Klebsiella spp.	14	15.56	5	14.71	3	9.38	2	8.7
Moraxella spp.	2	2.22	0	0	2	6.25	0	0
Morganella morganii	0	0	0	0	0	0	1	4.35
Proteus spp.	1	1.11	0	0	2	6.25	1	4.35
Pseudomonas spp.	2	2.22	0	0	2	6.25	2	8.7
Salmonella spp.	1	1.11	0	0	0	0	5	21.7
Serratia spp.	5	5.56	2	5.88	1	3.13	0	0
Shigella spp.	2	2.22	0	0	0	0	2	8.7
Stenotrophomonas maltophilia	1	1.11	0	0	3	9.38	1	4.35
Yersinia spp.	2	2.22	0	0	0	0	0	0

n: frequency; [a] Urethral swab, pleural fluid, blood, stools; sperm.

The most frequent (*Escherichia coli*, *Enterobacter* spp., and *Klebsiella* spp.) typically predominated in the urine (50% of isolates), followed by vaginal secretion and pus (19% and 18%, respectively). These three major bacteria types were recovered from all categories of biological specimens while *Salmonella* was most frequent in the "other" category. It could also be observed that the predominating bacteria isolated from pus belonged to the genus *Enterobacter*.

Antimicrobial susceptibility profile of isolates

Susceptibility tests on *Enterobacteriaceae* and non-fermenting Gram-negative generated the sets of information presented in Table 2 and Table 3.

Table 2: *Enterobacteriaceae* susceptibility/resistance profile

Antibiotic	Frequency[a]	Phenotype (%)		
		Susceptible	Intermediate	Resistant
Nalidixic acid (30 µg)	54	30	9	61
Amoxicillin/clavulanic Acid (20/10 µg)	140	3	11	86
Amoxicillin (25 µg)	116	14	8	78
Ampicillin (10 µg)	35	6	0	94
Aztreonam (30 µg)	57	42	0	58
Cefixime (30 µg)	113	11	14	75
Cefotaxime (30 µg)	70	51	7	42
Cefoxitin (30 µg)	20	30	5	65
Ceftazidime (30 µg)	106	13	29	58
Ceftriaxone (30 µg)	123	40	3	57
Chloramphenicol (30 µg)	5	60	0	40
Ciprofloxacin (5 µg)	144	54	3	43
Co-trimoxazole (1.25/23.75 µg)	74	28	8	64
Colistin (10 µg)	28	18	0	82
Cefuroxime (30 µg)	46	13	0	87
Gentamicin (15 µg)	126	45	9	46
Imipenem (10 µg)	128	72	25	3
Levofloxacin (5 µg)	12	50	0	50
Nitrofurantoin (300 µg),	118	70	1	29
Norfloxacin (5 µg)	47	28	9	63
Ofloxacin (5 µg)	59	40	15	45
Tetracycline (30 UI)	58	31	0	69

[a]:Number of tests performed with the antibiotic

Overall susceptibility rates varied from 3% with Amoxicillin/Clavulanic acid to 72% with Imipenem. Amongst beta-lactams, the highest susceptibility rate was recorded with Cefotaxime (51%). In addition, susceptibility rates higher or equal to 50% were observed for 23% of antibacterial agents used. Further details revealed frequent intermediate phenotypes with Aztreonam, Imipenem and Ofloxacin.

Table 3: Non-fermenting Gram-negative susceptibility/resistance profile summary

Antibiotic	Frequency	Phenotype (%)		
		Susceptible	Intermediate	Resistant
Aztreonam[a] (30 µg)	7	14	57	29
Ceftazidime (30 µg)	17	41	0	59
Ciprofloxacin (5 µg)	24	67	4	29
Co-trimoxazole[b] (1.25/23.75 µg)	2	0	0	100
Colistin[b] (10 µg)	3	0	0	100
Gentamycine (15 µg)	21	52	0	48
Imipenem (10 µg)	22	**77**	14	9
Levofloxacin[a] (5 µg)	1	0	0	100
Norfloxacin[a] (5 µg)	4	50	0	50
Ofloxacin (5 µg)	9	33	11	56
Rifampicin (30 µg)	2	0	0	100
Tetracycline[b] (30UI)	10	50	0	50

[a] Tested on *Pseudomonas* spp., and *Moraxella* spp.; [b] Tested on *Stenotrophomonas maltophilia* and *Acinetobacter baumannii*.

For most frequent tests (with Ciprofloxacin, Gentamicin, Imipenem and Tetracycline), susceptibility rates were globally higher while intermediate phenotype was highest with Aztreonam. Overall, close to 34% of antibiotics susceptibility rates were equal or larger that 50%. Similarly, 100% resistance was observed for 34% of the antibacterial agents used.

DISCUSSION

From the present investigation, the most frequent clinical specimen types were urine, vaginal secretion, and pus. Urine was also identified as the most frequent clinical specimens during a recent similar survey conducted in Yaoundé (70 %).[9] With regards to bacteria etiologies, common type recovered (*E. coli*, *Enterobacter and Klebsiella*) were also identified as commonly in cause in

infections of the urinary tract and women genitalia.[4,10] These bacteria are members of the *Enterobacteriaceae* family; a group which encompasses a broad diversity of Gram-negative non-fastidious human mutualists and environmental microbial flora. In these three bacteria types, potent virulence factors like capsule can facilitate their translocation from the digestive to the urinary tract. If colonization of sterile bodily sites like the urinary tract can occur in hosts in communities and in hospitals, hospitalized people are more prone to overt infections and disease.[11] According to Uzunovic-Kamberovic *et al.* (2009)[12], strains from the *Enterobacteriaceae* family are associated with more than 70% of urinary tract infections (UTIs), in agreement with the results from the present survey. In particular, these authors observed that *E. coli* accounted for 80% of the cases. They further observed that in decreasing order the rate of isolation of *E. coli* was followed by that of *Proteus* spp., *Enterococcus faecalis, Enterobacter* spp., *Pseudomonas* spp., and *Klebsiella* spp. Similar reports were published by others authors from different settings.[13,14] Higher rates of isolation represent critical health threat in healthcare facilities[11] were bacteria definitely take advantage of the weakened host and operate as opportunistic, exacerbated by inappropriate hygiene and sanitation in the living environment.[15] With a glance at the range of consequences associated with UTIs caused by these bacteria, they will include beyond physical discomfort, higher morbidity, and others like genital infection and infertility.

Further data analysis from the present survey indicated that *Pseudomonas* and *Yersinia* were least frequent. Though rarely isolated, these bacteria types should be regarded as real cause of concern, especially in clinical environment. Originally non-pathogenic to human like *Pseudomonas, Yersinia* can represent a potent health hazard with on the high genetic flexibility that provides ability to acquire foreign genetic determinants.[16] In fact, *Yesinia* can undergo transduction by the filamentous bacteriophage "YpfF" and express pathogenicity in connection with various host conditions including gastroenteritis, UTIs, skin and eyes infections in immune-depressed hosts.[17–19] This bacteriophage belongs to a large family of filamentous viruses that mostly transform Gram-negative common rods into pathogenic strains and may explain, at least in part the frequent genetic modifications in bacteria populations. Another example of viral particle with similar ability from this group is that of the CtxΦ bacteriophage which is responsible for the *CtxAB* toxin gene transduction in *Vibrio* and *E. coli*.[20,21]

Outstanding findings on S/R revealed high resistance rates to drugs from the penicillins cephalosporins and sulfamides (Trimethoprim/Sulfamethoxazole) subgroups, with broad ranges of multiple resistances. These drugs are not only available and affordable, but also, most are easy to administer (orally) and/or recommended as first line in probabilistic therapy and in prophylaxis (for immune deficient hosts, for instance), then common in hospital environment as part of the regiment of antibacterial agents in force.[22] In agreement with several previous investigations, the role of fake drugs in resistance selection can, also explain the high rates recorded.[22–24] Fake drugs and other misuse appear as a global phenomenon in low-income communities of several nations worldwide. In Lebanon for instance, Moghnieh *et al.*(2014)[25] reported high rates of resistance in strains of *Klebsiella* incriminated in community-acquired infections. These authors further observed that resistances phenotypes were mainly associated with drugs that are recommended in empiric antibacterial therapy at the international level, then consistent with drug usage that does not rely on any holistic data. In Antananarivo (Madagascar), it was reported that rates of fluoroquinolone-resistant *E. coli* isolated from UTIs were higher than those recorded in Morocco.[26] In the present survey, these rates were also very high, highlighting the necessity of sensitization at all levels (from sellers to users and members of the regulatory bodies).

An investigation conducted in Sarajevo (Bosnia and Herzegovina) revealed high resistance rates of *E. coli* against Ampicillin (84.14 %), Trimethoprim/ Sulfamethoxazole (41.46 %) and Nalidixic acid (17.07 %); and improved strain susceptibility with Ciprofloxacin (95.12 %) and Gentamicin (87.80%).[27] Overall, the resistance rates were higher in the present investigation for *Enterobacteriaceae* in general (Ampicillin, 94%; Trimethoprim/Sulfamethoxazole, 64%; Nalidixic acid, 61% and Ciprofloxacin, 43%). Invariably and consistent with reports from former related studies conducted in West Cameroon, these high rates were also observed with non-*Enterobacteriaceae*.[22,24] Especially with Trimethroprim/ Sulfamethoxazole which is recommended for prophylaxis in HIV-positive patients in Cameroon, the certain degree of activity that remains despite the massive use is probably due to the double mutation required for effective resistance against this drugs combination.

The consequences of resistance that extend to non-pathogenic bacteria discussed in the present paper and other common environmental strains which highly contribute to the dissemination of genetic traits in the bacterial world globally associate with undermined attempts for therapeutic initiatives in case of infection by true pathogens at first glance; but in reality mostly (because they are larger in their number) by opportunistic bacteria in immune-compromised hosts. The number of this category of host increases with the poor living conditions engendered by war, famine, social exclusion, social discrimination, increased poverty that accompany unfair resource sharing and climate changes amongst others.

These successive findings are clues and should motivate effective actions towards antibiotic S/R stewardship in Cameroon. Key to this is the capacity building of community outreach services like laboratories and motivated human resources as observed by Abduzaimovic *et al.*, (2016).[28] Such intervention strategies must be inclusive and simultaneously target policy makers, drug prescribers and users. Other health facilities should also be provided with minimal resources for the screening of at least the most frequent clinical specimens represented by urine and women genitalia secretions; acknowledging that currently, less than 4% of clinical laboratory throughout the country perform identification and susceptibility tests.

CONCLUSION

The present survey revealed that urine was the most frequent sample type submitted for analysis, and that members of the *Enterobacteriaceae* family (overwhelmed by *E. coli*) were most incriminated in bacterial infections. In addition and invariably in both the fermenting and non-fermenting, susceptibility rates were low in general, especially with available and affordable antibacterial agents. These findings were consistent with previous surveys framed otherwise in other low-income settings, and should serve as useful indicators for effective action towards antibiotic susceptibility/resistance stewardship. But any effective intervention policy should simultaneously target policy makers, drug prescribers and users.

ACKNOWLEDGEMENTS

The authors are thankful to Professor Lazare Kaptué, Head of the "Cliniques Universitaires des Montagnes" for the invaluable support provided during this survey. They are also highly indebted to the "Association pour l' Education et le Développement" (AED) for the literature resources and laboratory equipments; and to Dr Marie-Christine Fonkoua (Centre Pasteur du Cameroun) for providing advices and reference strains.

REFERENCE

1. Chougouo Kengne RD, Fotsing Kwetche PR, Kouamouo J, Domum Tchouanche B, Somo Moyo R, Kaptué L. Antibacterial and Antifungal Activity of the Essential Oil Extracted by Hydro-distillation from Artemisia annua Grown in West-Cameroon. Br. J. Pharmacol. Toxicol, 2013; 4(3): 89–94.
2. Bennett PM. Plasmid encoded antibiotic resistance: acquisition and transfer of antibiotic resistance genes in bacteria. Br. J. Pharmacol, 2008; 153(S1): S347–S357
3. Tagoe NA, Baidoo SE, Dadzie I, Tengey D, Agede C. Potential sources of transmission of hospital acquired infections in the Volta Regional Hospital in Ghana. Ghana Med. J, 2011; 45(1): 22-26.
4. Kouamouo J, Fotsing Kwetche PR, Yangoue D, Mbaya P, Simo Louokdom J, Nsangou A *et al.* Female genital tract infections and engines of antibiotic resistance in fast-growing populations of Bangangté, West-Cameroon. Int. J. Pharm. Biomed. Res, 2013; 4(3): 181–186.
5. Yongsi HBN. Suffering for water, suffering from water: access to drinking-water and associated health risks in Cameroon. J. Health Popul. Nutr, 2010; 28(5): 424-435.
6. Nguendo-Yongsi HB. Microbiological evaluation of drinking water in a sub-Saharan urban community (Yaounde). Am. J. Biochem. Mol.Bio, 2011; 1(1): 68–81.
7. Société Française de Microbiologie |. Rémic 2 volumes: Société Française de Microbiologie: 9782878050325 Societe francaise de microbiologie, Microbiologie . 4ème éditi. Societe Francaise De Microbiologie, editor. Paris, 2016; 370.
8. Microbiologie SFDE. Societe Francaise de Microbiologie . Paris, 2015; 117.
9. Longla E, Lyonga-Mbamyah E, Kalla C, Baiye W, Chafa A, Gonsu H. Evolution Profile of *Escherichia coli* Resistance from January 2009 – April 2013 to Antibiotics at the Yaounde University Teaching Hospital, Cameroon. Br. Microbiol. Res. J, 2016; 17(5): 1–9.
10. Toukam M, Lyonga EE AM, Fokunang CN, Atashili J KA, Gonsu HK, Mesembe M *et al*. Quinolone and fluoroquinolone resistance in *Enterobacteriaceae* isolated from hospitalised and community patients in Cameroon. J. Med. Med. Sci, 2010; 1(10): 490–494.
11. Rakotovao-Ravahatra Z D, Randriatsarafara F M, Rasoanandrasana S, Raverohanta L, Rakatavao AL. Phénotypes de résistance des souches d' *Escherichia coli* responsablesd'infection urinaire au laboratoire du Centre Hospitalo-Universitaire de Befelatanana Antananarivo. Pan African Medical Journal, 2017; 26(166): 1–10.
12. Uzunović-Kamberović S, Tina Zorman , Ingrid Berce , Lieve Herman SSM. Comparison of the frequency and the occurrence of antimicrobial resistance among *C. jejuni* and *C. col*i isolated from human in- fections, retail poultry meat and poultry in Zenica-Doboj Canton, Bosnia and Herzegovina. Med. Glas, 2009; 6(2): 173–180.
13. Abdallah HB, Sahnoun O, Romdhane FB, Loussaief C, Noomen, S, Bouzouaia N. Profil de sensibilité aux antibiotiques des entérobactéries uropathogènes isolées dans la région de Monastir. Rev. Tun. Infectiol, 2008; 2(2): 5-8.
14. ZAHIR H. L'infection urinaire chez l'enfant au CHU de Marrakech : écologie microbienne et sensibilité aux antibiotiques, Thesis N° 163, Faculté de Médecine et de Pharmacie, Marrakech, 2017; 109.
15. Osman KM, Mustafa AM, Elhariri M, AbdElhamed G S. Identification of serotypes and virulence markers of *Escherichia coli* isolated from human stool and urine samples in Egypt. Ind. J. of Med. Microbiol, 2012; 30(3): 308-313.
16. Lister PD, Wolter DJ, Hanson ND. Antibacterial-resistant *Pseudomonas aeruginosa*: clinical impact

and complex regulation of chromosomally encoded resistance mechanisms. Clin. Microbiol. Rev, 2009; 22(4): 582–610.
17. Bottone EJ. Atypical *Yersinia enterocolitica*: Clinical and epidemiological parameters. J. Clin. Microbiol, 1978; 7(6): 562–567.
18. Chouikha I, Charrier L, Filali S, Derbise A, Carniel E. Insights into the infective properties of YpfΦ, the *Yersinia pestis* filamentous phage. Virology, 2010; 407(1): 43–52.
19. Reuter S, Connor TR, Barquist L, Walker D, Feltwell T, Harris SR *et al*. Parallel independent evolution of pathogenicity within the genus *Yersinia*. Proc. Natl. Acad. Sci, 2014; 111(18): 6768–6773.
20. Waldor MK, Tschäpe H, Mekalanos JJ. A new type of conjugative transposon encodes resistance to sulfamethoxazole, trimethoprim, and streptomycin in *Vibrio cholerae* O139. J. Bacteriol, 1996; 178(14): 4157–4165.
21. Davis BM, Waldor MK. Filamentous phages linked to virulence of *Vibrio cholerae*. Curr. Opin. Microbiol, 2003; 6(1): 35–42.
22. Simo Louokdom J, Fotsing Kwetche PR, Kouamouo J, Kengne Toam AL, Gamwo Dongmo S, Tchoukoua SH. High Antibiotic Resistance in Bacteria from a Healthcare Setting : Case in the Surgery Wards of the Regional Hospital of Bafoussam. J. Chem. Biol. Phys. Sci, 2016; 6(4): 1297-1307.
23. Ouedraogo AS, Jean Pierre H, Banuls AL, Ouedraogo R, Godreuil S. Emergence and spread of antibiotic resistance in West Africa : contributing factors and threat assessment. Médecine et Santé Tropicales, 2017; 27(2): 147-154.
24. Noukela Noumi DP, Fotsing Kwetche PR, Kouamouo J, Simo Louokdom J, Gamwo Dongmo S, Kengne Toam AL *et al*. *Bacillus* spp . and *Staphylococcus* spp .: Potential Reservoirs of Resistance Traits in a Healthcare Facility ? J. Chem. Bio. Phy. Sci, 2017; 7(1): 37–48.
25. Moghnieh R A, Abdallah DI, Fawaz I A, Hamandi T, Kassem M, El-Rajab N, *et al*. Prescription Patterns for Tigecycline in Severely Ill Patients for Non-FDA Approved Indications in a Developing Country: A Compromised Outcome. Front. Microbiol, 2017; 8(497): 1-13.
26. Benhiba I, Bouzekraoui T, Zahidi J, Noureddine E, Ait Said L, Warda KKZ. Epidemiology and antibiotic resistance *Enterobacteriaceae* urinary of adults. Uro'Andro, 2015; 1: 166–171.
27. Vranic S, Zatric N, Rebic V, Aljicevic M, Abdulzaimovic A. The Most Frequent Isolates from Outpatients with Urinary Tract Infection. Mater. Socio. Medica, 2017; 29(1): 17.
28. Abduzaimovic A, Aljicevic M, Rebic V, Mahmutovic Vranic S, Abduzaimovic K, Sestic S. Antibiotic resistance in urinary isolates of *Escherichia coli*. Mater. Sociomed, 2016; 28(6): 416–419.