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INCREASED RATE OF EXTENDED-SPECTRUM BETA-LACTAMASE (ESBL)-PRODUCING INTESTINAL *Enterobacteriaceae* AMONG HOSPITALIZED PATIENTS IN THE SURGICAL DEPARTMENTS OF THREE HEALTH FACILITIES IN THE NDE DIVISION, WEST-CAMEROON

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ABSTRACT

The increasing rates of therapeutic failure imposed by resistance to antibacterial agents has become a global health challenge endowed with community specificities. One of the most common traits in bacteria is related to the expression of extended spectrum beta-lactamases (ESBL), a large group of determinants that inhibit ranges of β-lactam's antibiotics and represent serious threats to public health. The present study aimed at investigating the influence of hospitalization in the overall bacterial susceptibility and more specifically, the interplay between hospital stay and ESBL rates within the surgery departments of three health facilities in West Cameroon. When all administrative and ethical requirements were met, rectal swabs (or stools) were collected for bacterial screening and Susceptib-ility testing. Prior to specimen collection, a record was made on drug administration during hospital stay for each respondent. All laboratory procedures were conducted according to

standard protocols (CAS-SFM 2019; REMIC; 2018) with focus on *Enterobacteriaceae*. Data analyses revealed that beta-lactams were commonly used. A total of 104 specimens were collected from which 241 isolates were recovered (131 recovered on admission and 110 at discharge). Most common isolates were *E. coli*, *Proteus* spp., and *Klebsiella* spp. Susceptibility tests indicated higher resistance rates at discharge than on admission, with significant difference observed with β-lactams, unlike fluoroquinolones and aminoglycosides. Moreover, the detection rates of ESBL were significantly higher at discharge and was found to be strongly associated with hospitalization. Altogether, these results represented reliable indicators of a break between stakeholders in the caretaking chain. They therefore, highlighted the need to promote policies aiming at increasing the turn-over in order to reduce the risk of colonization by multidrug-resistant bacteria during hospitalization. Trained and committed human resources were thought to be primordial in designing and implementing sustainably, health policies that could meet current and future challenges related to antibacterial resistance.

KEYWORDS: Hospitalization, ESBL, surgery patients, West-Cameroon.

INTRODUCTION

The hospital environment is a conducive ecological niche for the selection and dissemination of infectious agents[1–5] and hospital stay exposes patients to contaminations by these agents. Infectious agents can become etiologies of human conditions with varied amplitude. Effect of infectious diseases and related consequences are exacerbated by drug-resistant microorganisms for which infections reduce the likelihood of therapeutic success, commonly with available and affordable antimicrobial agents. Bacteria are among the most common infectious agents found in hospitals One of the most important factor that mastermind difficulties in the caretaking of infectious diseases due to bacteria is the expression of resistance traits through the production of extended spectrum β-lactamase (ESBL). Endowed with high flexibility in connection with the prokaryotic cellular organization and growth rates, bacteria have the ability to adapt and resist in stressful environments. This ability provides explanation to the growing phenomenon of antibiotic resistance throughout the world.[6–8] As foreseen by Alexander Fleming, the misuse of antibacterial agents actually accelerate the emergence of resistant strains.[9]

Investigations through bacterial resistance in hospitals have provided evidences on resistance traits development, on contamination by multidrug-resistant bacteria during hospitalization and their harmful consequences on patient's safety. Bacterial resistance is a natural phenomenon that occurs to provide fitness to these organisms. Their selection was for a long time thought to be typically associated with hospital environment. Recent and more inclusive paradigms identify human activities like animal husbandry and plant production as key systems from which selection of resistance traits could emerge and disseminate throughout hospital environments as well.[10] These selection and dissemination of resistance traits evolve in complex networks encompassing humans, animals and environments all of which are negatively affected in turn. Owing to this, microbial resistance has become a global concern and one of the biggest priority for the Global Health Security Agenda (GHSA) and One Health.[11,12] In addition, hospital stay appears to be associated with resistance selection and spread in bacteria.

A survey conducted among malnourished children in Niger revealed that 94% of children that were negative for ESBL- *Enterobacteriaceae* on admission to hospital were positive at discharge.[7] Also, several others studies throughout the world, in West Cameroon and more specifically in the hospitals of the Ndé Division found that hospital environments (mainly surgeries) were conducive to the selection and dissemination of multidrug-resistant bacteria, favored by transfer of genetic traits amongst human's and environmental microbial flora.[8,13–15]

Management with antibiotics would become increasingly difficult as the length of hospital stay increases, but data remain scarce to address this issue sustainably. Otherwise, pieces of information that are useful in understanding this growing phenomenon of antibiotic resistance, which threatens patient's care are scarce around the world and particularly in developing countries where resources (human and financial) for research are limited. It is an imperative to master the chain of facts that promotes resistance growth in order to address the related morbidity and mortality in all settings. The present investigation was initiated in the global frame that encompasses containment and mitigation of microbial resistance in hospital. It focused on the effect that hospitalization could have on bacteria resistance. This effect was assessed based on the frequency rates of ESBL-positive enteric bacteria isolated amongst hospitalized patients in the surgery departments of three healthcare facilities in the Ndé Division, West-Cameroon. To date and knowledge, the present study was first of its kind in

Cameroon. The results of this work will guide probabilistic antibiotic therapy on admission and during hospitalization, will provide foundation for implementation and evaluation of useful policies and strategies that would focus reduction of bacteria resistant in patients during their hospital stays on one hand and the hospital community dissemination risk on the other.

MATERIAL AND METHODS

Ethical consideration, study site, populations and sampling

To carry out this survey, an ethical clearance referenced: 2019/236/UdM/PR/CIE was issued by the "Université des Montagnes (UdM)" legal Authority at the central level. This was followed by the research authorizations provided by the heads of the healthcare facilities in which specimen collection was conducted and signed inform consent by each the participants.

This study was conducted from February 1st through May 30th 2019 in three healthcare facilities in the Ndé Division, West-Cameroon. Namely they were the District Hospital of Bangangté, the Protestant Hospital of Bangwa and the Université des Montagnes Teachning Hospital. Pieces of information were collected in a follow-up strategy, from admission to discharge in each case.When all administrative and ethical requirements were met, rectal swabs (or stools specimen) performed according to standard procedures were collected, labelled then conveyed to the laboratory of Microbiology of the "Université des Montagnes" Teaching Hospital in refrigerated containers (≈4°-8°C) where they underwent bacteriological screening. Susceptibility tests were thereafter performed on selected *Enterobacteriaceae* bacteria isolates for overall susceptibility profile and phenotypic characterization of a few resistance mechanisms.

Bacterial isolation and identification

Specimens were plated on Mc Conkey agar and incubated at 37°C for 18 to 24 h. Other morphological and biochemical tests followed according to standard protocols recommended by REMIC (2018) for *Enterobacteriaceae* identification with API 10S gallery specification. Reference bacteria strains used throughout the process were *Escherichia coli* ATCC 25922 and *Klebsiella pneumonia* ATCC 700603.

Susceptibility testing

The susceptibility tests were performed by the disk diffusion method (Kirby-Bauer) on Mueller Hinton agar following standard procedures recommended by CASFM, 2019.[16] From a pure 24 h subculture at 37°C on nutrient agar, a bacterial inoculum was made in 5 mL sterile 0.9% physiological saline and adjusted to the density equal to that of the McFarland 0.5 turbidity standard as recommended by CASFM 2019 for non-stringent bacteria. The antibiotic tested in these essays were chosen from the list of the most common antibacterial agents that are commonly used. This list was provided by physicians and nurses that work for the target healthcare facilities. Overall, the 21 antibiotics selected from different drug's families included: The Amoxicillin (20 µg), Amoxicillin/ clavulanic acid (20/10 µg), Ticarcillin (75 µg), Cefalotin (30 µg), Cefuroxime (30 µg), Cefoxitin (30 µg), Ceftazidime (10 µg), Ceftriaxone (30 µg), Aztreonam (30 µg), Cefepime (30 µg), Imipenem (10 µg), Nalidixic acid (30 µg), Ciprofloxacin (5 µg), Gentamcin (15 µg), Tobramycin (10 µg), Netilmicin (10 µg), Amikacin (30 µg), Colistin (50 µg), Levofloxacin (5 µg), Norfloxacin (5 µg) and Ofloxacin (5 µg). For quality control, *Escherichia coli* ATCC 25922 was used as reference strain. All antibiotic disks, isolation and identification media were produced by Liofilchem® and were used according to standard guidelines.

Detection of ESBL- producing bacteria: Double-Disk Synergy Test (DDST)

Extended β-lactamase-positive isolated were detected by the double-disk synergy test. All tests and test interpretations were conducted when above overall susceptibility/resistance were assessed as done in Fosting-Kwetche et al (2015) and Simo-Louokdom et al. (2018).[4,17,18] Briefly, Cefepime (30µg), Ceftriaxone (30µg) and Aztreonam (30µg) were deposited at 30 mm each time from the Amoxicillin/clavulanic acid combination. *Escherichia coli* ATCC 25922 and *Klebsiella pneumoniae* ATCC 700603 were used as negative and positive controls, respectively.

Statistics

Microsoft Excel 2016 and StatView5 were thereafter used for statistics. Descriptive analyses were carried out on the study variables, which included computation of addition and frequencies. The Chi-square test was used to compare the susceptibility profiles and frequency of ESBL recorded on admission and at discharge. Logistic regression analyses was used to identify determinants of ESBL production in *Enterobacteriaceae.* Logistic regression analyses (uni-variable and multi-variable) were used to identify determinants of ESBL

production in *Enterobacteriaceae*. All tests were conducted at 95% confidence interval (5% degree of significance).

RESULTS

Features of study participants

Throughout the study period, 52 participants were enrolled and followed. Their ages ranged from 5 through 79 years (mean age 40.77 years). Hospital stay was found between 3 and 22 days (average 7.58 days). Additional details on the study population were summarized as displayed in Table I.

Table I: Participant's characteristics.

Variables		Number	Frequency (%)
Sex	Males	37	71.15
	Females	15	28.85
Type of surgery	Visceral	38	73.08
	Orthopedic	14	26.92
Antibiotics	**β-lactams**	**43**	**82.69**
	Ampicillin	21	40.38
	Ceftriaxone	29	55.77
	Cefixime	9	17.31
	Cefuroxime	2	3.85
	Amoxicillin/Clavulanic Acid	4	7.69
	Cloxacillin	1	1.92
	Fluoroquinolone	**15**	**28.85**
	Ciprofloxacin	15	28.85
	Aminoside	**17**	**32.69**
	Gentamicin	17	32.69
	Nitro-5-imidazoles	**46**	**88.46**
	Metronidazole	46	88.46
	Macrolide	**1**	**1.92**
	Clarithromycin	1	1.92

It appeared that men accounted for almost 3/4 of the population. Similarly, visceral surgery was the most frequent type of surgery (3/4). Finally, the antibiotics most commonly used belonged in decreasing order to imidazole, β-lactams, fluoroquinolones and macrolides groups. Beta-lactams were most diversified but metronidazole was the most frequently administered antibacterial agent.

Distribution of bacterial isolates

From admission to discharge, 104 specimens were collected and submitted laboratory screening. Isolation and identification resulted in the detection of 241 isolates, members of the *Enterobacteriaceae* family. A closer look on their distribution revealed that 131 were recovered on admission 110 at discharge. Fig 1 summarizes overall distribution of these isolates.

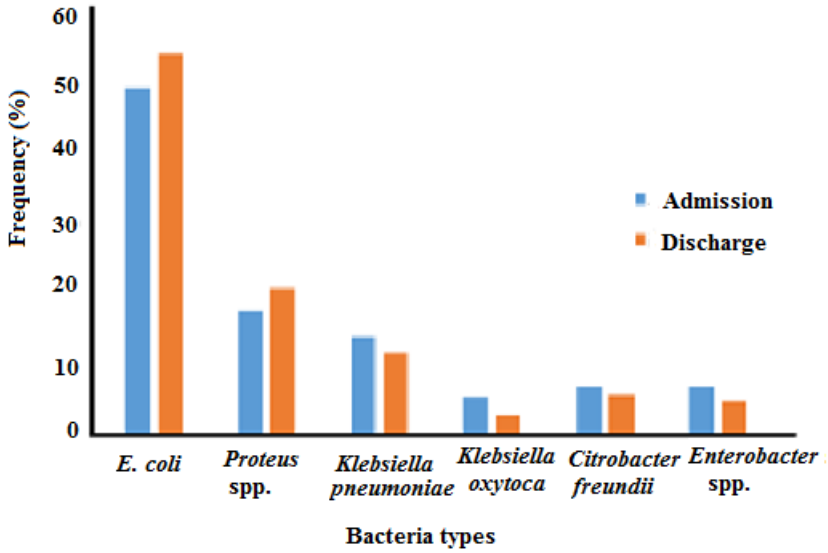

Figure 1: Distribution of bacterial isolates.

It indicated that the isolates recovered consisted in decreasing rates of *Escherichia coli*, *Proteus* spp., *Klebsiella peumoniae*, *Klebsiella oxytoca*, *Citrobacter freundii* and *Enterobacter* spp. Rate of *E. coli* detection was almost three time that of *Proteus* spp. Further details on *E. coli* indicated that they represented almost half of the total number of isolates at both major detection times. Overall, however, the rates of isolation for each bacterial type were almost similar on admission and at discharge.

Antibiotic susceptibility/resistance profiles of isolated from patients: admission *versus* discharge

Subsequent to isolation and identification, susceptibility tests on isolates recovered on admission on one hand and at discharge on the other yielded subtle pieces of information that were synthesised and reported in Table II and Table III.

Table II: Susceptibility profiles of isolates to β-lactam's.

Antibiotic	n (admission %)	n (discharge %)	χ^2	*p-value*
Amoxicillin				
S	12(9.16)	4(3.64)	2.94	0.0862
I	0(0.00)	0(0.00)		
R	119(90.84)	106(96.36)		
AMX/Clavulanic Acid				
S	33(25.19)	13(11.82)	11.00	0.0041
I	4(3.05)	0(0.00		
R	94(71.76)	97(88.18)		
Ticarcillin				
S	24(18.32)	9(8.18)	9.08	0.0107
I	4(3.05)	0(0.00)		
R	103(78.63)	101(91.82)		
Cefalotin				
S	7(5.34)	1(0.91)	3.73	0.1548
I	15(11.45)	12(10.91)		
R	109(83.21)	97(88.18)		
Cefuroxime				
S	21(16.03)	6(5.45)	6.72	0.0347
I	1(0.76)	1(0.91)		
R	109(83.21)	103(93.64)		
Cefoxitin				
S	60(45.80)	70(63.63)	9.16	0.0103
I	4(3.05)	5(4.55)		
R	67(51.15)	35(31.82)		
Ceftazidime				
S	47(35.88)	9(8.18)	39.88	<0.0001
I	17(12.98)	3(2.73)		
R	67(51.14)	98(89.09)		
Ceftriaxone				
S	41(31.30)	7(6.36)	33.52	<0.0001
I	10(7.63)	1(0.91)		
R	80(61.07)	102(92.73)		
Aztreonam				
S	66(50.38)	24(21.81)	22.88	<0.0001
I	7(5.35)	4(3.64)		
R	58(44.27)	82(74.55)		
Cefepime				
S	62(47.33)	10(9.09)	46.04	<0.0001
I	14(10.69)	9(8.18)		
R	55(41.98)	91(82.73)		
Imipenem				
S	114(87.02)	50(45,45)	48.72	<0.0001
I	11(8.40)	48(43,64)		
R	6(4.58)	12(10,91)		

S: susceptible; I: intermediate; R: resistant; AMX: amoxicillin; n: number

Table III: Susceptibility profiles of isolates to fluoroquinolones, aminoglycosides and colistin.

Antibiotic	n (admission %)	n (discharge %)	χ^2	*p-value*
Nalidixic acid				
S	50(38.17)	34(30.91)	1.39	0.2388
I	0(0.00)	0(0.00)		
R	81(61.83)	76(69.09)		
Norfloxacin				
S	77(58.78)	67(60.91)	0.44	0.8028
I	10(7.63)	10(9.09)		
R	44(33.59)	33(30.00)		
Ciprofloxacin				
S	61(46.56)	50(45.45)	0.82	0.6636
I	5(3.8)	7(6.37)		
R	65(49.62)	53(48.18)		
Ofloxacin				
S	40(30.53)	37(33.63)	3.71	0.1562
I	43(32.83)	24(21.82)		
R	48(36.64)	49(44.55)		
Levofloxacin				
S	111(84.73)	87(79.09)	1.33	0.5136
I	3(2.29)	3(2.73)		
R	17(12.98)	20(18.18)		
Gentamicin				
S	98(74.81)	73(66.36)	2.11	0.3486
I	5(3.82)	5(4.55)		
R	28(21.37)	32(29.09)		
Tobramycin				
S	88(67.18)	69(62.73)	0.72	0.6959
I	9(6.87)	7(6.36)		
R	34(25.95)	34(30.91)		
Netilmycin				
S	117(89.31)	86(78.18)	8.79	0.0123
I	9(6.87)	8(7.27)		
R	5(3.82)	16(14.55)		
Amikacin				
S	121(92.37)	98(89.09)	1.65	0.4392
I	0(0.00)	1(0.91)		
R	10(7.63)	11(10.00)		
Colistin				
S	84(64.12)	65(59.09)	0.64	0.4232
I	0(0.00)	0(0.00)		
R	47(35.88)	45(40.91)		

S: susceptible; I: intermediate; R: resistant; AMX: amoxicillin; n: number

Overall picture from above tables (II and III) showed that the resistance rates recorded at discharge were generally higher than those documented on admission. In a few cases, significant differences were reported between the susceptibility profiles on admission and at discharge. These significant differences were common with beta-lactam antibacterial agents (individually and collectively). These included carbapenem (Imipenem), 3rd generation cephalosprins (Ceftriaxone and Ceftazidime), 4th generation cephalosporin (Cefepime) and monobactam (Aztreonam). The significant difference observed for 3rd generation cephalosprins', 4th generation cephalosporins' and monobactam were twice higher at discharge than on admission to the healthcare facility. A bigger gap was observed with carbapenem intermediate phenotype (≈ 5 times larger at discharge than on admission).

Distribution of ESBL-positive and ESBL-negative: admission *versus* discharge

Systematic ESBL-dependent distribution was conducted and subtle clues on their occurrence were recorded (Table IV).

Table IV: ESBL-dependent isolate distribution between admission and discharge.

Phenotype	**n (admission %)**	**n (discharge %)**	χ^2	***p-value***
ESBL+	35(26.72)	79(71.82)	48.79	<0.0001
ESBL-	96(73.28)	31(28.18)		

n (admission): number at admission; n (discharge): number at discharge; ESBL+: positive Extended Spectrum β-lactamase; ESBL-: negative Extended Spectrum β-lactamase

Table IV revealed that the overall rate of ESBL-positive isolates was three times larger at discharge that the value documented on admission ($p<0.0001$).

ESBL associate risk factors

With a subtle glance on putative, but most likely engines that could promote acquisition of ESBL the data recorded and documented were summarized as shown in Table V.

Table V: Distribution of ESBL-positive isolates (multivariate analysis).

Variable	**OR**	**OR 95%CI**	***p-value* (Ref)**
Admission/discharge			
Admission	1		
Discharge	0.17	[0.03-0.97]	0.0456
Duration of hospitalization			
	1.04	[0.91-1.19]	0.5569
Metronidazole			
No	1		
Yes	0.80	[0.17-3.89]	0.7851

Ceftriaxone			
No	1		
Yes	0.61	[0.24-1.58]	0.3113
Ciprofloxacin			
No	1		
Yes	1.69	[0.57-5.03]	0.3452
Gentamicin			
No	1		
Yes	1.03	[0.38-2.75]	0.9555
Ampicillin			
No	1		
Yes	1.08	[0.42-2.75]	0.8770
Cefixime			
No	1		
Yes	2.03	[0.49-8.39]	0.3297
AMX/Clavulanic acid			
No	1		
Yes	2.53	[0.24-26.23]	0.4362

AMX: Amoxicillin

It appears that in multivariate analysis only hospitalization (OR: 0.17 (95% CI; [0.03-0.97]) remained significantly associated with ESBL (p=0.0456).

DISCUSSION

The present investigation aimed at assessing the influence of hospitalization on *Enterobacteriaceae* susceptibility on patients in surgery. It provided sets of findings related to caretaking policies that could be useful in mitigating bacterial resistance and promoting the turn-over rates in hospitals.

Most participants were male (3/4), consistent with the fact that they are also most frequently involved in accident-prone activities. Also, their activities often require lots of physical efforts that eventually result in overt or discrete harms which require invasive medical procedures for correction. The number and proportion of visceral interventions for hernia could attest tis view, at least partially. Other causes that were not clearly anticipated from the present investigation but most likely at the origin of debriding in surgical departments of healthcare facilities include road accidents and accidents associated with other high-risk professions.

Data analysis indicated that β-lactams and nitro-5-imidazol represented more than 90% of all antibacterial agents that were common in routine processes. Two sets of reasons might justify

their rates of use: first, these antibacterial agents act on broad ranges of bacteria, diffuse optimally throughout body's tissues, are generally cost-effective and available; second, side effects are very rarely reported upon administration. These reasons could provide additional justifications for their frequent choice in preventing and managing infectious diseases.[19] This development is supported in the present piece of research by the rates of use recorded with macrolides, for instance, which are lower, certainly in connection with their spectrum of action that is limited to Gram-positive bacteria and their relatively higher toxicity.[19]

E. coli overwhelmed isolation's on admission and at discharge. But basically, isolates consisted of *Escherichia coli*, *Proteus* spp., *Klebsiella peumoniae*, *Klebsiella oxytoca*, *Citrobacter freundii* and *Enterobacter* spp., with almost similar rates on admission and at discharge. These bacteria isolates from asymptomatic patients are members of the endogenous microbial flora, which could evolve as opportunistic pathogens in immune-depressed hosts. Immune-depression is common issue in hospitalized patients and, most likely in those who undergo invasive procedures. The predominance of *Escherichia coli* observed in the present work was documented in previous surveys conducted in other settings[20,21] and could be justified by their affinity with molecular oxygen which naturally regulates bacteria distributions within and amongst ecological systems. In fact, as facultative anaerobe *E. coli* represents the majority of the aerobic flora in the human gut[7] and could easily spread under low hygiene standards. The above common members from the *Enterobacteriaceae* family of bacteria might be crucial in selecting and disseminating genetic traits throughout related and phylogenetically-distant groups of bacteria populations in the gastrointestinal tract. They are therefore liable putative engines for resistance phenotypes dissemination on which investigations on bacteria resistance from the gut might sustainably enroot.

With a focus on bacteria susceptibility, it appeared that the overall resistance rates at discharge were higher than those observed on admission. This result was in line with the above development on the selection and spread of genetic traits, favoured by the pressure imposed by broad spectrum antibacterial agents and the inherent flexibility of the bacterial genome. The range of antibacterial agents indicated that beta-lactams were most common in the routine practice. The same factors were alleged to justify the frequent multiple resistance phenotypes documented during previous studies within related frames.[8,9,11–14]

Significant differences were observed ($p<0.0001$) in the susceptibility rates between admission and discharge for β-lactams that included Imipenem, Ceftriaxone Ceftazidime, Cefepime and Aztreonam. Those seen for Ceftriaxone, Ceftazidime, Cefepime and Aztreonam were founded on the resistance rates (twice higher at discharge) while intermediate phenotypes were salient with Imipenem (five times higher at discharge). Acknowledging that antibiotics from this large group of antibacterial agents are also most commonly recommended by healthcare authorities, easily found in parallel markets, cost-effective thus frequent in infectious disease control, this effect of resistance for some and intermediate phenotypes for the others (most potent last-line'), tends to jeopardize future initiatives with available drugs. This result could be explained by the fact that β-lactams were the most widely used antibiotics, once again indexing the selection pressure discussed above in connection with specific phenotypic markers. These include expression of ESBL ($p<0.0001$) and provide explanation to the rates for 3^{rd} , 4^{th} generations of cephalosporins and monobactam used at discharge that were higher than those of Cefoxitin, an antibacterial that resists hydrolysis by ESBLs.[13] In fact, the rate of ESBL-positive isolates was 3 times higher at discharge. Similar findings were reported by Woether in Niger, where 94% of children who were negative for ESBL on admission carried ESBL-positive isolates at discharge.[7]

These resistances represent a real management challenge in case of bacterial infections. They therefore, highlight the need for proper diagnosis and appropriate susceptibility tests prior to drug administration (personalized management) with available and affordable antibiotics in the healthcare farcicalities were the present investigations were conducted. But generalized protocols and trained committed human resources are paramount and represent urgent priorities.

Insignificant differences between admission and discharge might at first glance suggest a reduced selection pressure. But in reality, and based on all the results recorded throughout this study, this hypothesis is not acceptable, especially since cross-resistance and co-resistance (known phenomena) are governed by similar laws, which regulate the horizontal transfer of mobile genetic determinants through stochastically complex support (plasmid, integrons, transposons).[19,22] ESBL encoded by these mobile genetic traits are powerful arguments that could be used to describe for a clearer view on the evolution of resistance

traits in bacteria. However, owing to the stochastic property of genetic supports and stressors that cause selection, this arguments are not sufficient to provide comprehensive explanation.

With univariate analysis, factors that were significantly associated with the production of ESBLs by *Enterobacteriaceae* included hospitalization (admission/discharge: $p<0.0001$), duration of hospitalization ($p<0.0001$), Metronidazole ($p<0.0001$), Ceftriaxone ($p=0.0002$), Ciprofloxacin ($p=0.0005$), Gentamicin ($p=0.0029$), Ampicillin ($p=0.0040$) and Cefixime ($p=0.018$). In multivariate analysis, only the hospitalisation remained significantly associated ($p=0.046$) with ESBL-positivity. This does not preclude the role that any of these factors might play individually in the overall ESBL-positivity recorded, and does not rule out the influence that other resistance mechanisms (not investigated and not discussed in the present work) might have in the global challenge for antimicrobial resistance. This further highlights the role of routine antimicrobial's in probabilistic therapy.

Altogether these results elucidate, at least partially (though yet to be fully investigated), the frequent rates of therapeutic failures that occurs during management by routine protocols. Selection and dissemination of resistance traits in hospitals is an indirect indicator of additional healthcare cost. Provided that the standard of living and the related purchasing power is low, this resistance growth would be seen as a factor that further aggravates poverty through prolonged hospital stay and the connected financial incidence. Taking into account overall susceptibility at the patient's entry could be a major asset for drug management using antibiotics. Interestingly, turn over in healthcare facilities appears to be paramount priority in the struggle against this resistance selection.

CONCLUSION

Key pieces of information from the present survey were recorded as follows: beta-lactams and nitro-5-imidazol were most common antibacterial agents. *E. coli*, *Proteus* and *Klebsiella* were also the most common with similar rates on admission and at discharge. While overall susceptibility profiles was globally linked to β-lactams with significant differences between admission and discharge, ESBL-expression appeared to be strongly associated with hospitalization. Like the overall susceptibility profile, the rates of their expression was higher at discharge than on admission. These findings indicate the necessity to design and implement sustainable policies that increase the turnover in all healthcare facilities (to shorten the length of hospital stay).

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