Antibiotic Use and Resistance in Single Orthopedic Department, Egypt

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ABSTRACT

Antimicrobial use and subsequently antimicrobial resistance among bacterial pathogens is a global problem, but in Egypt data are sparse. Orthopedic departments reflect this problem because in them surgery constitutes the main manipulation and septic diseases constitute common complications, both need guided antimicrobial therapy otherwise antimicrobial resistance will emerge. To highlight these issues, we define the pattern and appropriateness of antibiotic use and identify the infecting micro-organisms and their resistance patterns in a prospective study carried out in Orthopedic Department, Tanta University Hospital, Egypt, within 9 months. High antimicrobial prescription rates (98.1%) with low rates of appropriateness (11.3%) were detected. Eighty-one percent of prescribed antimicrobial agents belong to cephalosporins and penicillins classes and 54.2% of all antimicrobial use consisted of cefotaxime (42.1%) and amoxicillin-flucloxacillin (12.1%). High rates of resistance were found in most of the bacteria studied. 53.3% of Staphylococcus aureus (S. aureus) and 66.7% of coagulase-negative staphylococcus (CNS) isolates were oxacillin resistant. Multi-resistant (MR) strains represented 48.6% of the isolated gram negative bacilli of which 29.2% were ESBL (Klebsiella 62.5% and E.coli 33.3%) while 19.4% were MR Pseudomonas and Acinetobacter isolates. Antibiotic treatment in our Orthopedic Department appears to be substantial. Increasing and justifying efforts are needed to improve appropriateness of antimicrobial therapy and minimize the development of antimicrobial resistance. We call for a nationwide surveillance programme to monitor microbial trends and antimicrobial resistance patterns in Egypt.

INTRODUCTION

Antibiotics are arguably the most important advance in the history of medicine and undoubtly; they are among medicine's most powerful tools.[1,2] The more frequently antibiotics are used, the more they promote the bacterial resistance.[2] Since problems associated with the development and spread of antibiotic resistance in hospitals have been increasing since the early 1960s and are currently viewed as a major threat to clinical practice with significant mortality and health care costs, many experts believe that inappropriate and overuse of antibiotics must be curtailed if we are going to reduce the prevalence of bacterial resistance. [3,4]

In hospitals, antibiotics are often classified by their use for treatment of documented infection, empiric therapy, and antibiotic prophylaxis (ABP).[3] In Orthopedic Departments, surgery constitutes the main manipulation and requires guided ABP. In addition to the usual nosocomial infections that commonly occur in surgical wards, specific septic diseases such as osteomyelitis, osteitis, spondylodiscitis, septic arthritis and prosthetic joint infection represent the worst complications[5] because their outcome can be devastating, resulting in total loss of joint function, re-operative intervention, amputation and, occasionally, death.[6] In general, successful treatment usually requires a combination of surgical debridement and antibiotic therapy. Only antibiotics with a high bioavailability in bone are suited for treatment, but they have to be administered in high dosage and for long terms, at least 4 to 6 weeks. Unfortunately, both high antibiotic doses and long term treatment favor the emergence of MR strains if the antibiotic therapy (empirical and specific) was not adequately guided.[5]

Knowledge of used antibiotics and local antimicrobial resistance patterns are essential to

guide empirical and pathogen-specific therapy. They are also critical for optimal decisions regarding infection control policies.[7] Furthermore, they may help assessing the magnitude of the resistance problem locally, nationally and internationally, monitoring changes in resistance rates and detecting the emergence and spread of new resistance traits. Unfortunately, these data are unavailable in many parts of the world, including the low income countries which are potentially disastrous because of the lack of resources for purchasing expensive second-line drugs.[8]

The present study was undertaken to define the pattern and appropriateness of antibiotic use, identify the infecting micro-organisms, determine the resistance patterns among the isolated bacteria and identify multi-resistant bacteria from different isolates, in Orthopedic Department as an example, aiming to highlight the present situation and the urgent need to design an antibiotic policy as a part of efficient infection control measures in our hospitals.

PATIENTS, MATERIALS & METHODS

Study design:

This study is a prospective study conducted for 9 months from the start of January, 2008 to the end of September, 2008 on antibiotic use in Orthopedic Department, Tanta University Hospital, Egypt. The infection rate and prevalence of antimicrobial resistance among the possible isolated organisms was detected during the same period. This department, collectively, admit patients from all socioeconomic strata from Tanta and the surrounding rural areas. It is a 83-bed department containing 5 wards and 2 operation theaters with 3 operation's tables. The department doses not follow any definite antimicrobial protocols.

All cases who were admitted to this department during the study period are enrolled including both sexes and all ages. Approval of the local research ethics committee was obtained. One of the investigators, the microbiologist, visited the department at least 4 times a week and reviewed the patients' files. On each visit, the number of admitted patients was recorded as well as the number of patients receiving antibiotics. Demographic and clinical data of those patients were extracted and entered into patient-specific sheet. Obtained data included the patient's name, age, sex, past history, date of admission, date of discharge, diagnosis, details of operation (if any), details of infection, details of antibiotic used and baseline serum creatinine. For accurate microbiological diagnosis, samples were collected from infected cases and were subjected to standard microbiological examination.

Infections developed 72 h or more after admission were considered nosocomial infections. The indication of use of antibiotics was classified into prophylactic, empirical and therapeutic as well as randomly where antibiotics were given without evidence or suspicion of infection.[9] Antimicrobial use was evaluated according to indication of administration, source of infections, and appropriateness of treatment. Antimicrobial therapy was followed from initiation through possible adaptations, until discontinuation of treatment.

Microbiological examination: identification of infected cases and the study of the resistance pattern of bacterial isolates were done in Microbiology Department, Tanta faculty of medicine. The specimens were collected, stained and cultured and the bacterial isolates were identified using standard microbiological procedure.[10] The performance of antibiotic sensitivity test and the choice of disks for each isolated organism and the interpretation of zone diameters results were guided by CLSI guidelines.[11] Quality control strains were routinely utilized to ensure accurate assays. The isolates showing intermediate resistance were few and were grouped together with sensitive isolates for the purpose of data analysis. Methicillin resistance was detected by oxacillin disks. The diagnosis and conformation of ESBL was preliminary according to new and updated protocols for AST, 2005. [12]

Data analysis:

Data were collected and tabulated as numbers and percentages. Appropriateness of therapy used is evaluated according to WHO guidelines.[13] Prescription rate was calculated by dividing the number of antimicrobial agents prescribed in each category (prophylactic, empiric, *etc*) on the total number of antibiotics prescribed multiplied by 100. The appropriateness of therapy used was calculated by dividing the number of appropriate antimicrobial agents prescribed on the total number of antibiotics prescribed multiplied by 100.

RESULTS

Out of 671 patients who were admitted to the Orthopedic Department during the study period, 32 patients were excluded because their records were irretrievable. Of the 639 surveyed hospitalized patients, 627 were received antimicrobial therapy, with a percentage of 98.1% (Table 1).

Table 1: Antimicrobial consumption rate during the study period break down by the diagnosis categories.

Diagnosis category	*No. of patients included in the study*	*No. of patients receiving antibiotics*	*% of patients receiving antibiotics*
Surgical:	474	471	99.4
Conservative:	147	138	93.9
Infections:	18	18	100
Total	**639**	**627**	**98.1**

A total of 1119 antibiotics were given to 627 patients, of whom 258 (41.1%) were female and 369 (58.9%) male. Of the patients receiving antibiotics, 53.1% were ≥61 years old, 24.4% were 21–60 years and 22.5% were ≤20 years. Of notice, the infection rate was 13.1% where nosocomial infections represent the majority of the cases with a percentage of 10.3%, mainly in the form of SSI (4.7%) (Table 2).

Table 2: Infection rate during the study period

Infection	**Infected cases**		**% of Infection rate (*n*= 639)**
	No	**%**	
Community acquired infection:	18	21.4	2.8
SSI	*15*	17.9	2.3
RTI	*3*	3.5	0.5
Nosocomial infection:	66	78.6	10.3
SSI	*30*	*35.7*	*4.7*
UTI	*18*	*21.4.*	*2.8*
RTI	*15*	*17.9*	*2.3*
Sepsis	*3*	*3.6*	*0.5*
Total	**84**	**100**	**13.1**

Infection rate = (number of infected cases/total number of patients included in the study)×100.
SSI: surgical site infection, UTI: urinary tract infection, RTI: respiratory tract infection

Twenty-one antimicrobial agents were prescribed as single agent (486 prescriptions) and as drug combinations (633 prescriptions in 273 combinations; double: 186 or triple: 87). The main duration of treatment was 12.4±10.9 with a range of 3-37 days. The most frequently prescribed antimicrobial classes are shown in figure 1 and the most frequently prescribed antimicrobial agents are shown in table 3.

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Eighty-one percent of prescribed antimicrobial agents belong to cephalosporins and penicillins classes and 54.2% of all antimicrobial use consisted of cefotaxime (42.1%) and amoxicillin-flucloxacillin (12.1%). Of the total of 1119 antimicrobial drug courses, 213 (19%) were entirely provided orally, 243 (21.7%) intramuscularly (I.M) and 663 (59.3%) intravenously (I.V)(Table 4)

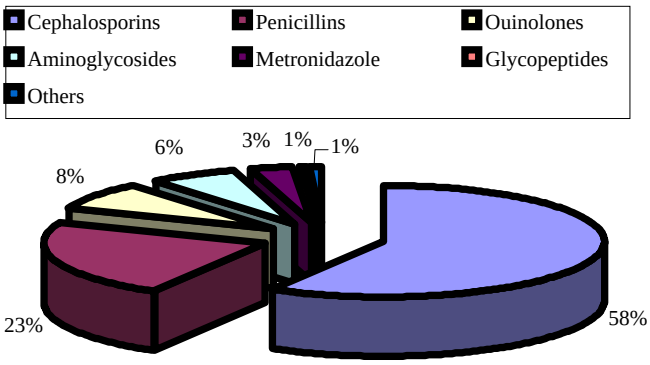

Fig 1: Prescription rate of different antimicrobial classes. *The most common prescribed classes of antimicrobial agent are Cephalosporins (58%), Penicillins (23%), Quinolones (8%), Aminoglycosides (6%), Metronidazole (3%) and Glycopeptides (1%).*

Table 3: Prescription rate of each prescribed antimicrobial agent.

Antimicrobial agent	Antimicrobial course						Prescription rate (*n*=1119)	
	Prophylactic		Random		Empiric/ therapeutic			
	No	%	No	%	No	%	No	%
Cefotaxime	342	72.6	69	14.6	60	12.7	**471**	**42.1**
Amoxicillin-flucloxacillin	105	77.8	15	11.1	15	11.1	**135**	**12.1**
Ampicillin-sulbactam	66	73.4	3	3.3	21	23.3	**90**	**8**
Ciprofloxacin	42	46.7	30	33.3	18	20	**90**	**8**
Cefipime	42	73.7	6	10.5	9	15.8	**57**	**5.1**
Cefradine	45	100	0.0	0	0.0	0	**45**	**4**
Amikacin	6	14.3	0.0	0	36	85.7	**42**	**3.8**
Others	99	52.4	42	22.2	48	25.4	**189**	**16.9**

Prescription rate = (the number of antimicrobial agents prescribed in each category /the total number of antibiotics prescribed) ×100

Table 4: Antimicrobial prescription rate break down by their rout.

Route	Antimicrobial course						Prescription rate (*n*=1119)	
	Prophylactic		Random		Empiric/therapeutic			
	No	%	No	%	No	%	No	%
Oral	102	47.9	78	36.6	33	15.5	**213**	**19**
I.M	174	71.6	66	27.2	3	1.2	**243**	**21.7**
I.V	471	71	21	3.2	171	25.8	**663**	**59.3**

Prescription rate = (the number of antimicrobial agents prescribed in each category /the total number of antibiotics prescribed) ×100
I.M: Intramuscular, I.V: Intravenous

Antibiotics were given for prophylaxis continued post-operatively (483; 77%), for infections (84; 13.4%: community 18; 2.9% and hospital 66; 10.5%) and randomly (138; 22%). The antimicrobial prescription rate for these groups was 66.8%, 18.5% and 14.7% respectively. Of notice, there was an overlap in antibiotic courses as 12 out of 18 patients who were admitted with infections have received empirical/therapeutic then prophylactic antibiotic courses. Similar overlap occurred in the 66 nosocomially infected patients. Antimicrobial prescription rate in community acquired and nosocomial infections was 4.3% and 14.2%, respectively (Tables 5).

Table 5: Antimicrobial prescription rate break down by the indication of use.

Course	% of patients receiving antibiotics (*n*=627)	/ Total Prescription (*n*= 1119)	
		No	**%**
Prophylactic	**77**	**747**	**66.8**
Random	**22**	**165**	**14.7**
Empiric/therapeutic:	**13.4**	**207**	**18.5**
Community acquired infections	***2.9***	***48***	***4.3***
-SSI	2.4	35	3.1
-RTI	0.5	13	1.2
***Nosocomial infection*:**	***10.5***	***159***	***14.2***
-SSI	4.8	69	6.2
-UTI	2.9	45	4
-RTI	2.4	33	2.9
-Sepsis	0.5	12	1.1

Prescription rate = (the number of antimicrobial agents prescribed in each category /the total number of antibiotics prescribed) ×100
SSI: surgical site infection, UTI: urinary tract infection, RTI: respiratory tract infection

The overall appropriateness of treatment was 11.3%, with a range of 4.8–71.9% per course. Of notice, 165 prescriptions were given randomly without any indication. The appropriateness of ABP, empiric and therapeutic antibiotics used were 4.8%, 18.9% and 71.9%, respectively. All ABP were given by intravenous rout. The appropriateness of ABP (36; 4.8%) was based on its type (45; 6%), duration (69; 9.2%) and timing (93; 12.4%) while the appropriateness of empiric (21; 18.9%) and therapeutic (69; 71.9%) antibiotic therapies were based mainly on the source of infection (34; 30.6% and 73; 76%, respectively), age of the patient (59; 53.2% and 89; 92.7%, respectively) and underlying kidney diseases (74; 66.7% and 81; 84.4%, respectively). Interestingly, the rate of appropriateness varied among different sources and sits of infections (Table 6).

Table 6: Appropriateness of empiric and therapeutic antimicrobial therapy in different sources and types of infection.

Infection	Total empiric	Appropriate	Total theraputic	Appropriate
	n	%	*n*	%
Community acqu. Infection:	27	22.2	21	90.5
SSI	22	22.7	15	86.7
RTI	5	20	8	75
Nosocomial infection:	84	17.9	75	66.7
SSI:	*36*	*16.7*	*33*	*78.8*
UTI	*24*	*25*	*21*	*66.7*
RTI	*18*	*16.7*	*15*	*40*
Sepsis	*6*	*0.0*	*6*	*66.7*
Total	111	18.9	96	71.9

The appropriateness of therapy used = (the number of appropriate antimicrobial agents prescribed / the total number of antibiotics prescribed) ×100.

In order to address the relationship between misuse of antibiotics and the development of resistant bacterial strains, all infected cases were subjected to standard microbiological examination of different isolates with analysis of their antibiograms. Ninety-three isolates were recovered from 84 infected patients. The majority of isolates were gram negative (77.4 %) which are represented by 5 bacterial types (Table 7). The rate of oxacillin resistance was nearly similar among both *S. aureus* and CNS isolates, at 53.3% and 66.7%, respectively. All isolates of staphylococci were susceptible to vancomycin (Table 8). Resistance rates of ≥50% to ceftazidime and/or cefotaxime were detected especially in *Acinetobacter, Klebsiella*, *Pseudomonas and E. coli* strains. Noticeably, susceptibility to imipenem for gram negative bacilli was >80% (Table 9).

Table 7: The frequency of different isolated organisms

Organism	**Total *n* (%)**	**%Community acquired infection**	**% Nosocomial Infections**			
			SSI	**RTI**	**UTI**	**BSI**
Staphylococci:	21 (22.6)	28.6	42.8	14.3	0.0	14.3
S. aureus	*15(71.4)*	40	40	20	----	-----
CNS	*6*(28.6)	----	50	----	----	50
Gram –ve:	72 (77.4)	25	29.2	16.7	29.2	-----
klebsiella	24 (33.3)	37.5	12.5	25	25	-----
pseudomonas	21 (29.2)	28.6	42.9	14.3	14.3	-----
E. coli	18 (25)	----	33.3	16.7	50	-----
Proteus	6 (8.3)	50	----	----	50	-----
Acinetobacter	3(4.2)	----	100	----	------	-----

CNS: coagulase negative *Staphylococci.*
S. aureus : staphylococci aureus

Table 8: Percentage resistance of gram positive isolates

Staphylococci	**Penicillin G**	**Oxacillin**	**Erythomycin**	**Clindamycin**	**Cefoxitin**	**Gentamicin**	**Ceftriaxone**	**Oxytetracyclin**	**Co-trimoxazole**	**Vancomycin**
	% resistance									
S. aureus (n = 15)	86.7	53.3	100	86.7	60	80	33.3	73.3	86.7	0.0
CNS (n =6)	100	66.7	83.3	66.7	66.7	83.3	50	66.7	83.3	0.0
Total (*n*=21)	**90.5**	**57.1**	**95.2**	**81**	**61.9**	**81**	**38.1**	**71.4**	**85.7**	**0.0**

CNS: coagulase negative *Staphylococci.*
S. aureus : staphylococci aureus

Table 9: Percentage resistance of gram negative isolates

Gram negative (n =72)	**Amikacin**	**Ampicillin**	**Amoxacillin-clavulanate**	**Pipracillin**	**Cephalothin[1]**	**Cefoxitin**	**Cefotaxime**	**Ceftazidime**	**Azteronam**	**Imipenem**	**Gentamicin**	**Co-trimoxazole**	**Ciprofloxacin**	**Nitrofurantoin[2]**	**Tobramycin**	**Carbencillin[3]**
	% resistance															
Klebsiella (n=24)	**12.5**	**100**	**75**	**62.5**	**87.5**	**87.5**	**75**	**62.5**	**62.5**	**0.0**	**62.5**	**75**	**37.5**	**75**	**75**	
Pseudomonas (n=21)	**57.1**			**57.1**				**57.1**	**57.1**	**14.3**			**71.4**		**71.4**	**57.1**
E. coli (n =18)	**16.7**	**83.3**	**66.7**	**33.3**	**66.7**	**66.7**	**50**	**50**	**33.3**	**0.0**	**66.7**	**33.3**	**16.7**	**66.7**	**50**	
Proteus (n=6)	**0.0**	**50**	**50**		**50**	**0.0**		**0.0**			**50**	**100**	**0.0**	**50**	**0.0**	
Acinetobacter (n=3)	**66.7**	**100**	**100**	**100**	**100**	**100**	**66.7**	**66.7**	**66.7**	**0.0**	**100**	**100**	**66.7**		**100**	

[1] *Cephalothin or Cefazolin* [2] *For urinary isolates only* [3] *For pseudomonas isolates only*

Prevalence of antimicrobial multi-resistance in different isolates is shown in Table 10. Methicillin resistance was detected in 57.1% of Staphylococcal isolates with MRSA prevalence of 38.1% (8/21 isolates). Multi-resistant strains represented 48.6% (35/72) of the isolated gram negative strains. ESBLs were identified in 21/72; 29.2% of those isolates with percentages of 62.5% and 33.3% in *Klebsiella* and *E.coli* isolates, respectively. Of notice, 57.1% and 66.7% of *Pseudomonas* and *Acinetobacter* isolates (19.4% of gram negative isolates) were resistant to amikin, ciprofloxacin and ceftazidime.

Table 10: Prevalence of antimicrobial multi-resistance in different isolates

Type of resistant organism	Total number of organism isolated	% of resistant strains
MRSA♦	21	57.1
ESBL*	72	29.2
Klebsiella	24	62.5
E. coli	18	33.3
Multi-resistance*	14	19.4
Psedomonas	21	57.1
Acinetobacter	3	66.7

♦ *Methicillin resistant Staphylococci* **Total gram –ve isolates includes 6 Proteus isolates*

DISCUSSION

Much concern has been voiced in the last two decades about the widespread use of antimicrobial agents, including broad-spectrum antibiotics, leading to emergence of multiple-drug-resistant organisms. In addition, it has been repeatedly demonstrated that 40–70% of use of these agents is inappropriate, with consequent waste of resources. Many hospitals have attempted to modify these worrying trends by supervising use of certain antimicrobial agents, with various degrees of success. Drug use evaluations have been shown to complement these efforts, and may provide such valuable information. [(14)]

The purpose of the current study is to generate up-to-date information on antimicrobial use in orthopedic department, indications for use, source of infections, utilization of the clinical microbiology laboratory, appropriateness of use and the prevalence of multi-resistant bacterial strains in order to spot light on the situation in our hospital and to establish an effective antibiotic policy.

The first major finding of this study is that 98.1% of the surveyed hospitalized patients received antibiotics, with a range of 93.9–100% per diagnostic class category. About seventy percent of these antibiotics were used as ABP. Little is known about the antibiotic usage in orthopedic departments. However, a European study from the early 1990s in the five largest European countries reported that antibiotic usage ranged from 42%-55% with the largest usage of antibiotics was for orthopedic surgical procedures where antibiotic usage as prophylaxis by the surgical specialties consistent 75% of therapy days.[(15)] Similar Results were obtained by a prospective survey of 3 months in 10 acute care hospitals in Lebanon.[(16)] In contrary, Raveh *et al* (2001) using a prospective longitudinal method to assess their hospital, found that 62% of admitted patients and 19% of orthopedic patients had received an antimicrobial on evaluation. They explain this difference by the presence of case mix variation as well as the use of different methodology.[(14)] Moreover, we believe that our high percentage reflects that there is not only misuse but also overuse of antimicrobial agents as 22% of our patients received random antibiotics.

The second major finding of this study is that of 1119 prescribed antibiotics, 159(14.2%) were given for infections acquired in the hospital. The most frequent are infections of surgical wounds. This figure is considerably higher than that reported in from other countries and from an Egyptian study involving the surgical wards and 7 ICUs in two hospitals (0.34%).[(17)] Similar to our results, European studies suggest a nosocomial infection rate in the range of 9–12% in countries such as England (9%), Belgium (10%) and Denmark (12%) as well as Greek and Tunisian studies. [(15,18,19)] In contrary, Raveh *et al.*, (2001) reported a higher ratio (34%).[(14)] There may be several explanations for these different figures. First, as previously mentioned, there may be considerable differences in case mix between hospitals. Second, the difference in definition of nosocomial infections that may possibly have led to inadvertent inclusions of community-acquired infections or to the exclusion of nosocomial infections which only manifest after discharge, such as certain surgical wound infections. Third is the failure of hospital hygiene.[(14)]

The rate of appropriateness of antimicrobial drug usage in this study was 11.3%, with a

range of 4.8–71.9% per course. In ABP, both the type and the duration of the chosen antimicrobial agents were responsible for such inappropriateness. Although, the corresponding of antimicrobial agent to the age and kidney conditions had some influence on the failure of antimicrobial therapy, the main factor for the inappropriateness in empirical antimicrobial therapy was the unsuitability of the antimicrobial agent to the site of infection while the main factor for the inappropriateness in therapeutic antimicrobials was inappropriateness of the used antibiotic sensitivity test. Of notice, out of 84 infected cases, 27 cases (32.1%) were received repeated empirical courses with the same or different antimicrobial agents and in 18 cases (21.4%) the antibiotic sensitivity test was not requested before the start of antibiotic therapy. Also, there was an overlap in antibiotic courses as 12 out of 18 patients who were admitted with infections have received empirical/therapeutic then prophylactic antibiotic courses. Also, 66 patients who have developed nosocomial infections were received empirical / therapeutic courses which were preceded by either prophylactic or random courses.

Various studies published in the last three decades indicate that, using disparate criteria and methods, 40–70% of antibiotic use is inappropriate a percentage which is lower than that detected in this study.[20] However, our results are similar to that of *El-Kholy et al.*, 2003 where it was found that > 80% of hospitalized patients were given antibiotics on no sound ground within whom >30% had received repeated courses, with no apparent reasons for doing so.[7] The reason of these dissimilar rates may be related to whether or not an antibiotic policy is applied. However, we are not aware of any studies that compare rates of appropriate antibiotic use between similar departments, one with well-organized protocols and one without.

The striking finding in this work is the high degree of antimicrobial resistance among the isolates studied. Resistance among Gram-positive cocci and Gram-negative bacilli was widespread in our department. We do not have epidemiological or clinical data to evaluate further the extent to which these resistance patterns reflect endemic antimicrobial resistance within the community, versus nosocomial spread of resistant organisms within and between various hospitals. Nevertheless, we believe that these data highlight the fact that widespread antimicrobial resistance exists in our hospitals.

Staphylococcal isolates were highly resistant to all antimicrobials tested, except vancomycin. In similar studies, resistance rates in the USA and Canada were 26.2% and 2.7%, respectively. Compared with our isolates, the Canadian isolates of *S. aureus* were also more susceptible to gentamicin, macrolides and co-trimoxazole.[21] However, our resistant rates were not only similar to those reported in other Egyptian studies but also those reported from other geographical areas. [7, 17,19]

About two thirds of those bacilli are the two virulent organisms *Klebsiella* and *Pseudomonas*. Antimicrobial resistance among Gram-negative bacilli was common in the present study comparable to reports from other parts of the world.[22] Susceptibility of *Klebsiella, Proteus and Acinetobacter* to ampicillin, ampicillin–sulbactam, and to co-trimoxazole were low. On the other hand, imipenem, aminoglcosides and ciprofloxacin retained activity against most of these isolates.

Multi-resistant strains represented 48.6% of our gram negative isolates. Twelve of such strains are *Pseudomonas* isolates resistant to aminoglycosides, ceftazidime and fluoroquinolones. Of notice, ceftazidime, cefotaxime and/or aztreonam resistance among *Klebsiella* and *E. coli* isolates was high. Resistance to these antibiotics is a marker for the presence of ESBL.[12] We did not perform confirmation tests or genetic analyses to confirm the presence of ESBL enzymes in these isolates but the combined resistance pattern suggests that ESBL enzymes are endemic in our department. Of notice, the prevalence of ESBL enzymes has been increasing in many parts of the world. [23]

In summary, our data suggest that antimicrobial resistance among Gram-positive cocci and Gram-negative bacilli is common and significant in orthopedic department. An inappropriate scheme of antibiotic usage present in our hospitals may be responsible. Particularly alarming are the high rates of ESBL enzymes. The present results have important implications for practicing physicians in the region, as well as for authorities involved in hospital formulary decisions, to develop policies regarding antibiotic utilization and infection control. Our results call for further epidemiological studies to define whether ESBL are highly endemic in the community and, on a larger scale, for the implementation of a regional and nationwide

surveillance system to monitor antimicrobial resistance trends in our hospital and in Egypt. Till this is complete, prescription of antibiotics should be limited.

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