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Surveillance of antimicrobial resistance in Lebanese hospitals: retrospective nationwide compiled data

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SUMMARY

Antimicrobial resistance is closely linked to antimicrobial use and is a growing concern worldwide. Antimicrobial resistance increases healthcare costs substantially in many countries, including Lebanon. National data from Lebanon have, in the most part, been limited to a few academic hospitals. The Lebanese Society of Infectious Diseases conducted a retrospective study to better describe the antimicrobial susceptibility patterns of bacterial isolates in Lebanon. Data were based on records retrieved from the bacteriology laboratories of 16 different Lebanese hospitals between January 2011 and December 2013. The susceptibility results of a total 20 684 Gram-positive and 55 594 Gram-negative bacteria were analyzed. The prevalence rate of methicillin-resistant *Staphylococcus aureus* was 27.6% and of vancomycin-resistant *Enterococcus spp* was 1%. *Streptococcus pneumoniae* had susceptibilities of 46% to oxacillin, 63% to erythromycin, and 98% to levofloxacin. *Streptococcus pyogenes* had susceptibilities of 94% to erythromycin and 95% to clindamycin. The mean ampicillin susceptibility of *Haemophilus influenzae*, *Salmonella spp*, and *Shigella spp* isolates was 79%, 81.3%, and 62.2%, respectively. The extended-spectrum beta-lactamase production rate for *Escherichia coli* was 32.3% and for *Klebsiella spp* was 29.2%. *Acinetobacter spp* showed high resistance to most antimicrobials, with low resistance to colistin (17.1%). *Pseudomonas spp* susceptibilities to piperacillin–tazobactam and imipenem were lower than 80% (79.7% and 72.8%, respectively). This study provides population-specific data that are valuable in guiding antimicrobial use in Lebanon and

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neighbouring countries and will help in the establishment of a surveillance system for antimicrobial resistance following the implementation of a nationwide standardization of laboratory methods and data entry.

1. Introduction

Antimicrobial resistance is a public health concern worldwide, particularly in developing nations, and is associated with many socio-cultural factors. Over the last 70 years, bacteria have become resistant to nearly all clinically relevant antibiotic agents. The United States Centers for Disease Control and Prevention (CDC) estimates that at least two million Americans become infected with antibiotic-resistant bacteria each year, with at least 23 000 people dying yearly as a direct result of these infections.[1] Countries in the Arabian Gulf including Saudi Arabia, the United Arab Emirates, Kuwait, Qatar, Oman, and Bahrain share a high prevalence of infections due to extended-spectrum beta-lactamase (ESBL)- and carbapenemase-producing Gram-negative bacilli.[2]

The single most important factor leading to antimicrobial resistance globally is the overuse/misuse of antimicrobials.[1] This is mainly due to incorrect diagnosis, the irrational use of antimicrobials, and irregular consumption, the latter due either to an incorrect prescription or to poor compliance. Up to 50% of all antimicrobials prescribed for patients are not needed or are not optimal as prescribed.[3] A core action to fight the spread of antimicrobial resistance is their improved use. The lack of implementation of adequate infection control measures has complicated this goal, necessitating urgent intervention.

Infections caused by antibiotic-resistant organisms continue to add considerable and avoidable costs to the already overburdened Lebanese healthcare system. The infections lead to complications that require additional therapeutic interventions, including indwelling catheters, sophisticated life support, intravenous fluid therapy, and prosthetic devices. They can also extend the hospital stay and the use of broad-spectrum antimicrobials appreciably, which in turn can increase the prevalence rate of multidrug-resistant pathogens.

The pattern of antimicrobial resistance changes with time and varies from country to country and also between hospitals within the same country. Therefore, data on the prevailing regional resistance and trends of clinically important bacterial isolates are helpful for physicians making decisions concerning the appropriate empirical treatment of various infections.

In Lebanon, the resistance trends of bacterial isolates have been reported in a few hospitals for several years. However, similar information does not exist at the national level. The Lebanese Society of Infectious Diseases (LSID) study group conducted the present study to better describe the national antimicrobial resistance patterns among clinically relevant pathogens. The LSID also intends to implement a database into which laboratories using standardized techniques can enter their data on a regular basis. This will allow the establishment of a surveillance system in Lebanon, which will help in combating antimicrobial resistance.

2. Methods

This retrospective study was based on the records of antimicrobial susceptibility tests performed on bacterial isolates in the bacteriology laboratories of 16 different tertiary care centres, representing 40.7% of all hospital beds in Lebanon. Hospitals and hospital bed distribution data are presented in Figures 1 and 2,

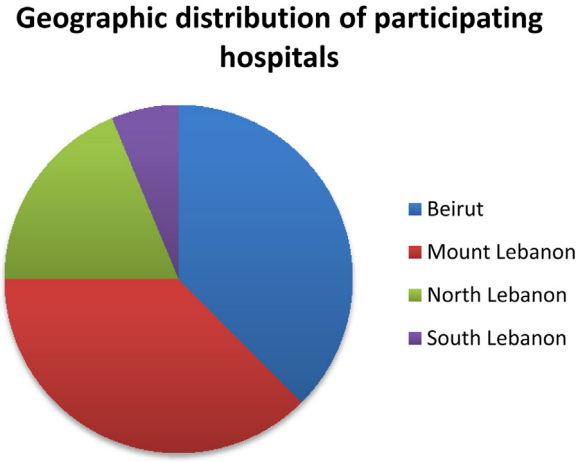

Figure 1. Geographic distribution of participating hospitals.

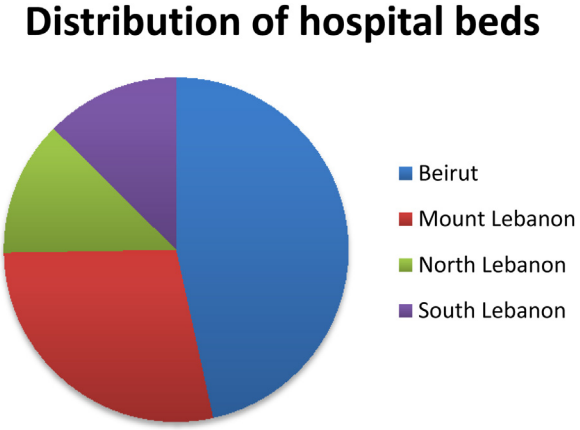

Figure 2. Distribution of hospital beds.

respectively. The only governorate that was not represented in this study was Bekaa.

The study team collected data related to tests performed between January 2011 and December 2013. The data collected were primarily qualitative (resistant, intermediate, or susceptible). Data were then tabulated in Excel spreadsheets. Most of the laboratories generated their data using WHONET software. In an attempt to standardize the selection criteria for bacterial isolates and avoid the duplication of isolates, laboratories not using WHONET software included only the first isolate from each patient with different antibiotic susceptibility profiles (criteria for selection set for WHONET). Six hospitals provided data for the year 2011, 12 provided data for 2012, and 13 provided data for 2013. Clinical specimens included urine, sputum, deep tracheal aspirates, blood, body fluids, central line tips, and others. The characteristics of the participating hospitals, as well as the testing methods and guidelines followed at each institution, are presented in Table 1. Non-automated tests with oxacillin and cefoxitin[4] and a double-disc synergy test[5] were used for the detection of methicillin-resistant *Staphylococcus aureus* (MRSA) and ESBL-producing bacteria, respectively.

Table 1
Demographics and testing guidelines related to the participating hospitals

Hospital	Region	Type	Beds	Method[a]	Guidelines
Abou Jaoude	Mount Lebanon	Community	110	DD	CLSI
AUBMC	Beirut	University	350	DD	CLSI
BMC	Mount Lebanon	University	110	DD	SFM
CHN	North Lebanon	University	200	DD	CLSI
Hammoud	South Lebanon	University	500	Automated	CLSI
HDF	Beirut	University	450	Automated	EUCAST
UMCRH	Beirut	University	90	DD	CLSI
Makassed	Beirut	University	200	DD	CLSI
Mazloum	North Lebanon	Community	180	DD + automated	CLSI + EUCAST
MEIH	Mount Lebanon	University	200	DD	SFM
MLH	Mount Lebanon	University	240	Automated	CLSI
NDS	Mount Lebanon	University	250	Automated	CLSI
NINI	North Lebanon	Community	120	DD	EUCAST
RHUH	Beirut	University	350	Automated	CLSI
SCH	Mount Lebanon	University	200	DD	EUCAST
SGH	Beirut	University	400	DD	CLSI

AUBMC, American University of Beirut Medical Center; BMC, Bellevue Medical Center; CHN, Centre Hospitalier du Nord; HDF, Hotel Dieu de France; UMCRH, University Medical Center Rizk Hospital; MEIH, Middle East Institute of Health; MLH, Mount Lebanon Hospital; NDS, Notre Dame des Secours; NINI; RHUH, Rafik Hariri University Hospital; SCH, Sacré Coeur Hospital; SGH, Saint Georges Hospital; DD, disc diffusion; CLSI, Clinical and Laboratory Standards Institute; SFM, Societé Française de Microbiologie; EUCAST, European Committee on Antimicrobial Susceptibility Testing.

[a] Automated microbial identification system: Vitek, BD Phoenix.

Antimicrobial susceptibility results were collected, entered into Microsoft Excel spreadsheets, verified, and analyzed using Microsoft Excel 2007. The rates of susceptibility to individual antimicrobials were calculated for every bacterial isolate by hospital, year of isolation, and region. The mean percentages of the susceptibility of each isolate to all tested antimicrobials were calculated. Yearly and regional comparisons were performed using the Chi-square test after checking the applicability conditions. A p-value of < 0.05 was considered significant. When comparing results from the three different years, $p < 0.05$ was considered statistically significant if at least one value was different from the others. In the case where the Chi-square test could not be applied because of an expected count in a cell of less than 5, the two-sided Fisher's exact test was used.

Table 2
Gram-positive and Gram-negative isolates

Gram-positive isolates	Total number collected	Proportion (Gram-positive)
Coagulase-negative Staphylococcus	8194	39.6%
Staphylococcus aureus	4890	23.6%
Enterococcus spp	4145	20%
Streptococcus agalactiae	1386	6.7%
Streptococcus pyogenes	1059	5.1%
Streptococcus pneumoniae	648	3.1%
Streptococcus viridans group	362	1.8%
Total Gram-positive	20 684	100%
Gram-negative isolates	**Total number collected**	**Proportion (Gram-negative)**
Escherichia coli	30 411	54.7%
Pseudomonas aeruginosa	7897	14.2%
Klebsiella spp	7883	14.2%
Acinetobacter spp	3409	6.1%
Enterobacter spp	2207	4.0%
Salmonella spp	877	1.6%
Citrobacter spp	738	1.3%
Morganella morganii	675	1.2%
Haemophilus influenzae	552	1.0%
Serratia spp	480	0.9%
Shigella spp	164	0.3%
Proteus spp	162	0.3%
Moraxella catarrhalis	139	0.2%
Total Gram-negative	55 594	100%
Total Gram-positive and Gram-negative isolates	76 278	

3. Results

The susceptibility results of 20 684 Gram-positive and 55 594 Gram-negative bacteria collected from 16 different hospitals in Lebanon (3950 beds) between January 2011 and December 2013 were analyzed. The isolates are summarized in Table 2. The most common Gram-negative species isolated was *Escherichia coli*, followed by *Pseudomonas aeruginosa* and *Klebsiella spp*.

A total 4890 *S. aureus* isolates were collected in the 16 hospitals. The prevalence of MRSA extrapolated based on resistance to oxacillin and cefoxitin was 27.6%. The susceptibility of *S. aureus* isolates to erythromycin and clindamycin was stable (mean 76% and 83.2%, respectively). Mean susceptibilities to the most relevant antimicrobials are presented in Table 3. The vancomycin-non-susceptible isolates from 2012 were not independently confirmed; the data were thus considered as only presumptive, requiring further investigation. This finding suggests the need for greater vigilance in the process of detecting and reporting this important type of resistance.

The mean susceptibility results for the 648 isolates of *Streptococcus pneumoniae* and 986 isolates of *Streptococcus pyogenes* are presented in Table 3. *S. pneumoniae* isolates displayed low susceptibility to oxacillin (46.2%). A statistically significant decreasing trend in erythromycin susceptibility was noted, from 69.4% in 2011 to 58.7% in 2013. High susceptibilities were evident to levofloxacin (98%) and ceftriaxone (95%).

The susceptibility of *Enterococcus spp* to ampicillin was 84.4%, with a decreasing trend, from 91.1% in 2011 to 81.6% in 2013. Vancomycin-resistant enterococci (VRE) were reported from six centres, with a rate of 1% (Table 3). Some hospitals reported *Enterococcus faecalis* and *Enterococcus faecium* separately, while others made no distinction between *Enterococcus* species. The data reported here are for all *Enterococcus* species.

The mean susceptibilities of *Haemophilus influenzae* did not differ from 2011 to 2013. The mean susceptibility to ampicillin was 79%. The susceptibility to both levofloxacin and ciprofloxacin was a mean of 93% (Table 4).

Salmonella spp showed a mean susceptibility of 81.3% to ampicillin and 95% to ciprofloxacin. The susceptibility to trimethoprim–sulfamethoxazole decreased in 2013 to about 88%, but this decrease was not statistically significant. Susceptibility to ceftriaxone remained high at 97.3% (Table 4). Nalidixic acid susceptibility, which was reported from one centre only, was 75% ($n = 4$) for *Salmonella* Typhi and 11% for non-Typhi *Salmonella* ($n = 28$).

Shigella spp showed 62.2% susceptibility to ampicillin, 99% to ciprofloxacin, and 28% to trimethoprim–sulfamethoxazole. Susceptibility to ceftriaxone remained high at 89.1% (Table 4).

The mean susceptibilities of *E. coli* isolates are presented in Table 5. The average ESBL production was found to be 32.3% during the study period. In the years 2011, 2012, and 2013, the ESBL production rates were 32.0%, 30.8%, and 33.6%, respectively. *E. coli* showed the least resistance to imipenem (mean resistance of 0.7%), and this was stable over the 3-year study period. Resistance to nitrofurantoin and tigecycline was low (4% and 1.8%, respectively). Susceptibility to most cephalosporins showed a statistically significant decreasing trend. Susceptibility to ciprofloxacin also decreased from 2011 to 2013, with mean values of 57.4% in 2011 and 52.0% in 2013. Among the aminoglycosides, *E. coli* was more susceptible to amikacin than gentamicin, with mean susceptibilities of 97.2% and 71.7%, respectively, and these were stable during the study period (Table 5).

Table 3
Susceptibility rates of Gram-positive organisms obtained from 16 Lebanese hospitals

	Percentage susceptibility to the antimicrobial agents (number of isolates)									
	Staphylococcus aureus					*Streptococcus pneumoniae*				
	2011 (790)	2012 (1717)	2013 (2383)	All years (4890)	*p*-Value	2011 (102)	2012 (230)	2013 (316)	All years (648)	*p*-Value
Oxacillin	76.4 (790)	72.1 (1717)	72.9 (2245)	73.3	0.066	50.5 (61)	44.3 (201)	46.7 (239)	46.2	0.205
Ceftriaxone						94.5 (94)	92.4 (92)	97.5 (81)	94.7	<0.05[a]
Tigecycline	100 (12)	98.8 (236)	100 (244)	99.4	<0.05[a,b]					
TMP–SMX	91.1 (595)	91.6 (1679)	90.5 (2330)	90.9	0.475	52.9 (17)	52.2 (160)	53.3 (119)	52.6	0.654
Levofloxacin	88.3 (300)	83.0 (1213)	84.0 (784)	84	<0.05[a]	98.5 (70)	96.6 (210)	99.6 (203)	98.1	<0.05[b]
Erythromycin	76.2 (790)	76.0 (1717)	75.9 (2383)	76	0.986	69.4 (102)	64.6 (230)	58.7 (212)	63.2	<0.05[b]
Clindamycin	85.8 (759)	81.5 (1535)	83.7 (2065)	83.2	<0.05[a]	82.0 (94)	73.0 (212)	76.4 (282)	76	0.183
Vancomycin	100 (790)	99.1 (1717)	100 (2383)	99.7	<0.05[a,b]					
	Streptococcus pyogenes					*Enterococcus spp*				
	2011 (60)	2012 (459)	2013 (467)	All years (986)	*p*-Value	2011 (538)	2012 (1666)	2013 (1941)	All years (4145)	*p*-Value
Penicillin	100 (60)	100 (459)	100 (160)	100						
Ampicillin						91.1 (518)	85.5 (1415)	81.6 (1914)	84.4	<0.05[a,b]
Tigecycline						100 (67)	99.0 (388)	100 (268)	99.4	<0.05[a,b]
Erythromycin	88.4 (60)	93.7 (459)	94.9 (467)	94	<0.05[a]					
Clindamycin	83.3 (30)	95.4 (450)	96.1 (419)	95.3	<0.05[a]					
Vancomycin						100 (538)	99.0 (1666)	98.8 (1941)	99	<0.05[a]
Teicoplanin						100 (538)	97.7 (1400)	98.8 (1941)	98.6	<0.05[a,b]

TMP–SMX, trimethoprim–sulfamethoxazole.
p-Value reports at least one significant difference between any percentages.
[a] *p*-value <0.05 between 2011 and 2012.
[b] *p*-value <0.05 between 2012 and 2013.

The mean susceptibilities of *Klebsiella spp* to the most relevant antimicrobials are presented in Table 5. In the years 2011, 2012, and 2013, the ESBL production rates in Klebsiella were 30.2%, 28.1%, and 29.9%, respectively (mean 29.2%). *Klebsiella spp* showed the highest susceptibility to imipenem (98%) and amikacin (95.7%), followed by tigecycline (87%). A low resistance to carbapenems, a relatively low susceptibility to trimethoprim–sulfamethoxazole, and a statistically significant decline in susceptibility to nitrofurantoin were noted.

Four hospitals reported the susceptibility to *Acinetobacter baumannii*, while all of the others reported the susceptibility of *Acinetobacter spp*. The mean susceptibilities of *Acinetobacter spp* are presented in Table 6. *Acinetobacter spp* showed high resistance to most of the antimicrobials and low resistance to colistin. The susceptibility to colistin was 77.1% in 2012 and 95.6% in 2013, with a mean of 82.9% (Table 6).

The mean susceptibilities of *Pseudomonas spp* are presented in Table 6. Susceptibility to ceftazidime ranged between 78.4% and 83.3%. Susceptibilities to both aztreonam and imipenem were lower than 80%, while ciprofloxacin was associated with susceptibility ranging between 74.8% and 80.3%.

4. Discussion

The first comprehensive report of the antimicrobial susceptibility of bacterial isolates in Lebanon was published in 1994 following an investigation by Araj et al. on the susceptibility patterns of clinical isolates at the American University of Beirut Medical Center (AUBMC) from March 1992 through June 1993. The overall antimicrobial resistance rates did not differ significantly from those reported in the Arabian Gulf countries and US medical centres.[6] The surveillance of bacterial susceptibility to antimicrobials was performed in selected, mainly academic hospitals in Lebanon. Each hospital reported its own data separately. The present study is the first to compile data generated by different hospitals representing most regions of the country.

S. aureus is a major pathogen in both the hospital environment and the wider community. It causes a wide variety of infections that are associated with considerable morbidity and significant mortality. The high prevalence of MRSA found in this study (27.6%) may reflect healthcare-associated infections that are difficult to control. The transmission of MRSA may occur during bed-making, changing of clothes, and sneezing, and may result from poor hygiene practices.[7,8] Many hospitals in Lebanon do not use contact isolation for patients with MRSA, which could be a cause of this high reported rate.

Among all resistant pathogens, MRSA is of particular concern because of its importance in causing various clinical conditions. MRSA prevalence differed among the hospitals, being low (<20%) in some and exceeding 30% in others, suggesting possible outbreaks in some of these centres.

Between 2003 and 2005, the ARMed (Antibiotic Resistance Surveillance and Control in the Mediterranean Region) project reported an MRSA rate of 39% among the susceptibility test results of 5000 invasive isolates of *S. aureus* obtained from blood cultures in 62 hospitals located in Algeria, Cyprus, Egypt, Jordan, Lebanon, Malta, Morocco, Tunisia, and Turkey.[9] Lebanon appears to have a lower MRSA rate.

In the study conducted by Araj et al., there was a significant increase in the prevalence of MRSA from 3% in 1971 to 38% in 1999.[6] However, rates at AUBMC have been around 20% in the last decade. Vancomycin-intermediate *S. aureus* and vancomycin-resistant *S. aureus* strains were not reported.[10] The present nationwide data collected from 16 hospitals over a period of 3 years indicate an MRSA rate of 27.6%.

Previously reported rates of penicillin resistance of *S. pneumoniae* isolates in Lebanon between 1990 and 1996 were 13% in AUBMC and 12% in Makassed General Hospital.[11,12] A study conducted from 2000 to 2004 in a Beirut hospital reported that only 40.6–50% of *S. pneumoniae* isolates were susceptible to penicillin G, with a decreasing trend in the susceptibility to clindamycin and erythromycin.[13] The pattern of resistance of *S. pneumoniae* was assessed again in 2011; 48% of isolated species were susceptible to penicillin, 50% were intermediate, and 1.6% were fully resistant to this antibiotic.[14] Other data from Lebanon and the region have indicated *S. pneumoniae* susceptibility rates of

Table 4
Susceptibility rates of *Haemophilus influenzae*, *Salmonella spp*, and *Shigella spp* obtained from 16 Lebanese hospitals

	Percentage susceptibility to the antimicrobial agents (number of isolates)													
	Haemophilus influenzae					*Salmonella spp*				*Shigella spp*				
	2011 (91)	2012 (232)	2013 (244)	All years (552)	*p*-Value	2011 (151)	2012 (331)	2013 (395)	All years (877)	*p*-Value	2011 (8)	2012 (101)	2013 (55)	All years (164)	*p*-Value
Ampicillin	85.3 (73)	77.7 (201)	78.0 (215)	79	0.39	85.6 (113)	80.0 (285)	81.0 (386)	81.3	0.39	NA (0)	63.2 (98)	60.0 (44)	62.2	0.63
Amox–Clav	92.3 (91)	94.7 (232)	94.4 (234)	95.1	0.67	93.0 (151)	96.0 (209)	93.7 (183)	94.4	0.31	100 (8)	78.7 (19)	91.0 (11)	86.7	0.3
Cefuroxime	100 (8)	96.9 (131)	98.7 (165)	97.9	0.48										
Cefotaxime						100 (34)	99.4 (248)	98.5 (291)	99	0.41	100 (8)	84.6 (100)	85.3 (55)	85.6	0.49
Ceftriaxone	100 (73)	97.0 (99)	99.2 (215)	98.8	0.17	97.5 (127)	98.2 (215)	96.7 (348)	97.3	0.63	NA (0)	90.1 (30)	88.4 (44)	89.1	0.85
Cefepime	100 (8)	100 (14)	100 (6)	100	NA	97.9 (151)	99.4 (303)	98.7 (395)	98.8	0.45	100 (8)	96.2 (89)	94.6 (55)	95.8	0.69
Gentamicin	100 (18)	97.9 (50)	93.0 (29)	97.5	0.33										
TMP–SMX	46.4 (73)	59.8 (198)	63.1 (229)	59.3	<0.05[a]	95.0 (151)	94.8 (331)	87.9 (378)	91.8	<0.05	13 (8)	24.6 (95)	36.7 (55)	28.2	0.17
Ciprofloxacin	96.0 (83)	85.8 (49)	93.2 (70)	93	0.07	86.6 (151)	97.2 (331)	95.8 (395)	94.8	<0.05[a]	100 (8)	97.9 (100)	100 (55)	98.7	0.52
Norfloxacin						NA (0)	98.0 (216)	95.7 (233)	96.8	0.13	NA (0)	100 (98)	100 (44)	100	NA
Levofloxacin	100 (8)	91.6 (73)	93.3 (155)	93	0.65										
Azithromycin	87.5 (8)	100 (57)	100 (6)	98.6	<0.05[a]										
Tetracycline	89.0 (18)	88.1 (50)	96.6 (60)	92.1	0.20										

Amox–Clav, amoxicillin–clavulanic acid; TMP–SMX, trimethoprim–sulfamethoxazole; NA, not applicable.
p-Value reports significant difference between any percentages.
[a] *p*-value <0.05 between 2011 and 2012.

50% to penicillin and 25% to erythromycin between 2003 and 2005,[15] with markedly higher rates of penicillin resistance (60–72%) reported at AUBMC between 2000 and 2011.[10]

Penicillin resistance of *S. pneumoniae* has been correlated with the nationwide use of penicillin.[16] The Lebanese Inter-Hospital Pneumococcal Surveillance Program was established to determine the burden of invasive pneumococcal disease and the prevalent serotypes. The first nationwide data from the program published in 2012 indicated a penicillin resistance rate of 17.5% using the new Clinical and Laboratory Standards Institute (CLSI) breakpoints.[17] This is markedly less than the present resistance rate of 53.8%. The discrepancy may be due to the use of the older, pre-2008 CLSI breakpoint in most of the centres, or may be because of the use of 'meningitis' or 'non-meningitis' or 'oral' breakpoints. Information on the breakpoint used by the microbiology laboratories was not available. It is believed that the rate of susceptibility to penicillin is closer to that reported by the Pneumococcal Surveillance Program. On the other hand, the susceptibility of *S. pneumoniae* to erythromycin was low (63%), possibly because of the overuse of this class of antimicrobial in Lebanon, since all oral antimicrobials are available over the counter. *S. pneumoniae* susceptibility to levofloxacin remained high (98%). *S. pyogenes* remained sensitive to ampicillin during the study period. This finding is universal.

In an earlier study conducted at AUBMC, the rate of ampicillin susceptibility of *Enterococcus spp* ranged from 95% to 84% and VRE rates were low.[10] In the present study, the rate of *Enterococcus spp* susceptibility to ampicillin was similar at 84.4% and the VRE rate was low (1%). The data reported here are for all *Enterococcus* species, as not all hospitals made a distinction between the *Enterococcus* species.

A prior evaluation of *H. influenzae* isolates at a Beirut hospital revealed resistance to amoxicillin–clavulanate, ceftriaxone, ciprofloxacin, and rifampicin, with more than 92% of isolates showing susceptibility to cefuroxime, chloramphenicol, erythromycin, and tetracycline.[13] The high susceptibility of *H. influenzae* to the aforementioned antimicrobials was found to have continued in the present study (>92%).

Araj et al. reported high susceptibility of Salmonella and Shigella in 2012.[10] In the present study, Salmonella and Shigella susceptibilities to ampicillin were 81% and 62%, respectively. Susceptibilities to trimethoprim–sulfamethoxazole were lower, at 88% and 28%, respectively. High susceptibilities to ciprofloxacin and ceftriaxone were reported during the 3 years of the study. Resistance of *Shigella spp* to third-generation cephalosporins was first detected in Lebanon in 2005; this subsequently increased, and ESBL-producing strains were revealed.[18,19]

In 2003, the rate of ESBL-producing *E. coli* was found to be 2.0% in a large hospital in Beirut.[20] Later studies chronicled increased rates of ESBL-producing *E. coli* isolates from about 4% in 2000 to about 30% in 2011.[10,21] An investigation of the susceptibility profiles of *E. coli* at one centre between 2000 and 2009 revealed an increase in the prevalence of ESBL-producing isolates from 2.3% to 16.8%, with the least susceptibility to piperacillin and ampicillin and 100% susceptibility to imipenem.[21] Araj et al. found *E. coli* susceptibility to imipenem to be 99.9% to 100% in their 2012 study.[10] In the present study, the mean prevalence of ESBL-producing *E. coli* isolates was 32.3%; quinolone resistance was about 55% and imipenem resistance was 0.7%. As a result of these findings, the empirical use of quinolones as first-line therapy in the treatment of urinary tract infections is now avoided. This will be reflected in guidelines that are in preparation for publication.

The prevalence of ESBL-producing *Klebsiella pneumoniae* isolates was 20.0% in a study conducted in 2003 in a large hospital in Beirut and 28% in a study performed at AUBMC in 2011.[10,20] The

Table 5
Susceptibility rate of *Escherichia coli* and *Klebsiella spp* obtained from 16 Lebanese hospitals

	Percentage susceptibility to the antimicrobial agents (number of isolates)									
	Escherichia coli					*Klebsiella spp*				
	2011 (4035)	2012 (12 003)	2013 (14 373)	*p*-Value	All years (30 411)	2011 (963)	2012 (3222)	2013 (3698)	*p*-Value	All years (7883)
Ampicillin	29.1 (1737)	23.6 (8704)	22.6 (12 544)	<0.05[a,b]	23.1	0.0 (227)	0.0 (1973)	0.0 (2366)		0
Amox–Clav	66.7 (4035)	63.3 (12 003)	58.5 (14 373)	<0.05[a,b]	61.4	71.1 (963)	68.2 (3222)	64.6 (3698)	<0.05[a,b]	66.8
Pip–Taz	89.2 (3466)	86.8 (11 437)	78.9 (13 836)	<0.05[a,b]	83.3	83.4 (872)	80.7 (3147)	79.5 (3599)	<0.05[a,b]	80.5
Cefoxitin	82.7 (2306)	88.7 (10 917)	86.8 (10 635)	<0.05[a,b]	87.3	81.0 (467)	88.0 (2754)	90.4 (2632)	<0.05[a,b]	88.5
Cefuroxime	69.5 (3591)	62.0 (11 572)	57.3 (9499)	<0.05[a,b]	59.2	71.4 (794)	63.1 (3074)	63.9 (2648)	<0.05[a]	64.4
Cefotaxime	73.6 (1390)	66.1 (8569)	61.5 (10 100)	<0.05[a,b]	64.3	75.9 (240)	65.0 (2113)	63.6 (2397)	<0.05[a,b]	64.8
Ceftazidime	75.6 (3591)	70.5 (11 572)	69.1 (13 567)	<0.05[a,b]	70.5	78.9 (794)	70.3 (3074)	68.7 (3467)	<0.05[a,b]	70.5
Cefixime	77.8 (821)	66.5 (5844)	68.7 (5798)	<0.05[a,b]	68.3					
Cefepime	85.2 (2278)	70.8 (11 006)	74.1 (13 030)	<0.05[a,b]	73.7					
Aztreonam	75.5 (2847)	63.3 (10 807)	66.7 (13 567)	<0.05[a,b]	66.3	80.3 (679)	66.7 (2938)	68.3 (3403)	<0.05[a,b]	68.8
Imipenem	99.5 (4035)	99.3 (12 003)	99.2 (14 373)	0.145	99.3	98.6 (963)	98.6 (3222)	97.3 (3698)	<0.05[b]	98
Gentamicin	66.7 (4035)	72.7 (11 491)	72.2 (13 801)	<0.05[a,b]	71.7	68.8 (963)	75.2 (3089)	75.6 (3549)	<0.05[a]	74.6
Amikacin	96.7 (3291)	97.5 (12 003)	97.0 (14 373)	<0.05[a]	97.2	94.2 (848)	96.7 (3222)	95.1 (3698)	<0.05[a,b]	95.7
TMP–SMX	49.4 (4035)	48.0 (12 003)	49.8 (13 651)	<0.05[a,b]	49	54.5 (963)	58.1 (3222)	55.8 (3524)	<0.05[a,b]	56.6
Ciprofloxacin	57.4 (3035)	57.0 (12 003)	52.0 (14 373)	<0.05[b]	54.7	72.2 (963)	71.8 (3222)	73.1 (3698)	0.372	72.5
Nitrofurantoin	95.4 (2306)	96.6 (7406)	95.6 (8710)	<0.05[a,b]	96	61.6 (467)	54.1 (1789)	48.4 (2100)	<0.05[a,b]	52.2
Tigecycline	100 (821)	97.3 (3795)	98.5 (5100)	<0.05[a,b]	98.2	100 (149)	84.9 (883)	86.9 (1211)	<0.05[a,b]	87
ESBL production rate	32	30.8	33.6	<0.05[a,b]	32.3	30.2	28.1	29.9	0.191	29.2

Amox–Clav, amoxicillin–clavulanic acid; Pip–Taz, piperacillin–tazobactam; TMP–SMX, trimethoprim–sulfamethoxazole; ESBL, extended-spectrum beta-lactamase.
p-Value reports significant difference between any percentages.
[a] *p*-value <0.05 between 2011 and 2012.
[b] *p*-value <0.05 between 2012 and 2013.

Table 6
Susceptibility rate of *Acinetobacter spp* and *Pseudomonas spp* obtained from 16 Lebanese hospitals.

	Percentage susceptibility to the antimicrobial agents (number of isolates)									
	Acinetobacter spp					*Pseudomonas spp*				
	2011 (242)	2012 (1704)	2013 (1463)	*p*-Value	All years (3343)	2011 (1105)	2012 (3294)	2013 (3498)	*p*-Value	All years (7897)
Pip–Taz	30.6 (242)	11.8 (1704)	11.1 (1397)	<0.05[a]	12.9	80.5 (1105)	78.1 (3294)	80.7 (3498)	<0.05[b]	79.6
Ceftazidime	24.7 (242)	11.6 (1704)	10.0 (1397)	<0.05[a]	11.8	78.4 (1105)	81.4 (3294)	83.3 (3498)	<0.05[a]	81.8
Cefepime	30.5 (242)	11.8 (1704)	12.5 (1463)	<0.05[a]	13.4	78.7 (1105)	82.6 (3294)	84.3 (3498)	<0.05[a]	82.8
Aztreonam	17.0 (219)	3.4 (1242)	9.0 (855)	<0.05[a,b]	6.7	71.5 (1059)	76.2 (3173)	77.9 (3251)	<0.05[a]	76.3
Imipenem	49.2 (242)	15.2 (1704)	15.1 (1463)	<0.05[a]	17.6	79.6 (1105)	70.9 (3294)	72.5 (3498)	<0.05[a]	72.8
Gentamicin	42.4 (242)	17.8 (1692)	15.5 (1450)	<0.05[a]	18.6	81.9 (1105)	82.5 (3210)	82.7 (3407)	0.673	82.5
Amikacin	33.3 (228)	14.0 (1704)	15.4 (1397)	<0.05[a]	15.9	89.2 (883)	87.1 (3294)	90.5 (3498)	<0.05[b]	88.9
TMP–SMX	35.5 (228)	17.2 (1440)	15.3 (1231)	<0.05[a]	17.8					
Ciprofloxacin	24.0 (242)	10.6 (1704)	10.5 (1433)	<0.05[a]	11.5	75.5 (1105)	74.8 (3294)	80.3 (3498)	<0.05[b]	77.3
Colistin	N/A	77.1 (552)	95.6 (254)	<0.05[b]	82.9					

Pip–Taz, piperacillin–tazobactam; TMP–SMX, trimethoprim–sulfamethoxazole.
p-Value reports significant difference between any percentages.
[a] *p*-value <0.05 between 2011 and 2012.
[b] *p*-value <0.05 between 2012 and 2013.

rate was found to be 29.2% in the present study. The mean imipenem susceptibility of *K. pneumoniae* was 98%.

Concerning Acinetobacter, an 80% susceptibility rate to imipenem was reported in 2010/11 from AUBMC.[10] The data of the present study revealed a marked decrease in the rate of Acinetobacter susceptibility to imipenem, from 49% in 2011 to 15% in 2013. Acinetobacter susceptibility to colistin was 83% in this study. A few hospitals reported susceptibility to tigecycline, with a mean of 58.3%; only one hospital reported tigecycline susceptibility in 2011. There was an appreciable drop in tigecycline susceptibility from 100% in 2011 to 39.6% in 2013. This could suggest outbreak patterns in some of these hospitals; outbreaks can easily be caused by this organism. In addition, these hospitals were probably overusing tigecycline because of prior outbreaks. It is also important to note that some hospitals only reported *A. baumannii*, so it is likely that the mean value reported has shifted towards *A. baumannii* susceptibilities. Previous studies investigating the basis of the carbapenem resistance of multidrug-resistant *A. baumannii* have found the resistance to be related to the production of carbapenem-hydrolyzing oxacillinase OXA-58 encoded by a plasmid-borne gene.[22,23] Such data were not available from the hospitals in the present study.

With regard to *Pseudomonas* species, high and variable multidrug resistance rates have been reported.[12] Mouawad et al. showed a trend of increasing resistance of *P. aeruginosa* to all antimicrobials in 2006 and 2009, with the highest resistance being to ciprofloxacin (33%).[24] In the present study, Pseudomonas susceptibility to imipenem and ciprofloxacin was 73% and 77%, respectively, less than the respective rates of 80% and 83% reported previously.[10,24] An increase in carbapenem resistance was noted in the present study, while susceptibility to ceftazidime and piperacillin–tazobactam was maintained at around 80% and to aztreonam at around 75%. Of note, most hospitals reported *P. aeruginosa* only, but others reported all *Pseudomonas* species. Imipenem resistance was reported more in the Beirut area, which could be a result of the increased use of carbapenems as a

consequence of the rise in ESBL-producing pathogens over the past few years in Lebanon. In addition, ciprofloxacin resistance was stable at around 23% during the study period.

There are some limitations to this study, mainly the biases associated with patient presentation to healthcare (often patients with prior treatment failure or complicated medical histories), patient sampling practices, and test practices. The main, largest hospitals reported the results by patient, avoiding duplicate isolates. A few hospitals were unable to do this. However, the number of isolates reported by these latter centres was low, with this limitation outweighed by the benefit of inclusion of the centres to provide a nationwide perspective. A further limitation is that, while most hospitals reported the bacterial susceptibility for inpatient and outpatient cultures together, one hospital reported only susceptibility for inpatient specimen cultures. Even for the hospitals reporting cultures from outpatients, the data obtained did not show prior recent admissions to the hospital or contact with recently hospitalized patients. This is expected in a non-clinical study such as the one presented here. This limitation is considered not to have considerably affected the results, since a comparison of inpatients and outpatients was not done. Another limitation is the different antibiotic susceptibility methods used in the different hospitals (Table 3). With regard to the use of European Committee for Antimicrobial Susceptibility Testing (EUCAST) and CLSI guidelines for the interpretation of resistance, EUCAST has published guidelines for the performance and interpretation of antibiotic susceptibility testing and has encouraged a change in the antibiotic susceptibility testing systems to facilitate the comparison of results. The CLSI updated its recommendations for the interpretation of in vitro drug susceptibility testing results in their 2010 and 2011 guidelines, based on clinical data, pharmacokinetic–pharmacodynamic properties, and minimal inhibitory concentration distributions, in part adopting the EUCAST strategies.[25] Since the present study period extended from 2011 to 2013, the differences in interpretation between the two recommendations were considered minimal; the majority of Lebanese hospitals were using the CLSI guidelines.[26,27] In addition, it is important to note that the differences between the EUCAST and CLSI systems after 2011 affect mostly intermediate resistance rather than susceptibility or resistance. Finally, the mean susceptibilities of all bacteria are presented in relation to the number of isolates tested, as mentioned in all of the tables. However, most of the standard antimicrobials used in determining the susceptibility patterns were reported.

In spite of these limitations, the data reflect the national pattern in an acceptable way. They are the only nationally compiled data available to date and constitute a platform for the future.

It is concluded that antimicrobial resistance is becoming a major problem in Lebanon. MRSA, penicillin- and erythromycin-resistant *S. pneumoniae*, and differentially resistant *Enterobacteriaceae*, Pseudomonas, and Acinetobacter are all important threats to the Lebanese population. A strategic plan is needed. The first step will be to establish a proper surveillance system after the standardization of microbiological methods. This study provides data that could assist clinicians in their daily practice and that may help in establishing prevention and treatment guidelines. Finally the results of this study could help direct further research efforts in the future.

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