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Analysis of CAST in 9 Lebanese hospitals between 2008 and 2017

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ABSTRACT

Background: Cumulative Antibiotic Susceptibility Testing (CAST) plays a crucial role in providing knowledge about the evolution of bacterial resistance. The preparation of such report is however prone to many errors. This study investigated the variety of mistakes detected in the CAST of 9 Lebanese hospitals.
Methods: Nine Lebanese hospitals were involved, where 21 different errors were looked for and analyzed. The total number of errors in each year was calculated and averaged according to the number of hospitals. Obtaining the average number of errors per hospital per year allowed the comparison of each hospital individually.
Results: The average number of errors in 2008 was 38.75 and increased to 51.5 in 2012. The average number of errors then decreased to 37.89 by 2017. The most common error between 2008–2017 was the incoherent percentages. Superimposing these results allowed to determine if hospitals in general were following the trend of average errors. Some hospitals were constantly improving, others were making a variable number of errors over the years.
Conclusion: The percentages of errors found here are alarming, urging therefore educating microbiologists on preparing CAST correctly. Future studies should aim to study the physician's level of knowledge on the proper utilization of CAST.

Introduction

With the increasing worldwide incidence of antimicrobial resistance, controlling its emergence becomes not only a need, but also a must in hospitals as well as in communities [1]. Unfortunately, quantifying and reporting resistance remains a challenge which microbiologists aim to address; in this context, emphasis was put on this task by setting guidelines for antimicrobial stewardship [2]. Antimicrobial stewardship aims to set appropriate selection, route, and dosing of the primary empirical antimicrobial drug [3].

Testing antimicrobial susceptibility aims at supporting clinical decision making as well as infection-control activities through compiling them into antibiograms [1]. Clinicians use antibiograms in order to estimate the effectiveness of an antibiotic against bacterial agent [4]. Antibiograms therefore, assist physicians in reducing antibiotic overuse for a better clinical practice and a more judicious use of anti-infectives [4] and in decreasing undesirable effects such as increase in resistance and toxicity [3]. An additional goal is to decrease the healthcare financial burden while insuring a patient's health and safety [3]. Antibiograms also limit nosocomial morbidity and mortality whose leading cause is improper empirical treatment [3].

Compiling these antibiograms over the years forms Cumulative Antimicrobial Susceptibility Testing (CAST). CAST has two main purposes in hospitals. First, it is a useful tool in tracking resistance development throughout the years in the same institution which in turn will allow the comparison of antimicrobial susceptibility across different hospitals [2]. Second, it is essential to share the information provided by these CASTs to all the concerned hospital staff [2] including pharmacists, microbiologists, clinicians, and infection control officers [5]. In addition, CAST guides hospital decision in antibiotic formulary and its protocols with surgical prophylaxis and therapy guidelines [2]. However, in order for CASTs to be useful, different clinical laboratories should use standardized AST with standard, reliable and uniform reports [6].

Therefore, for an antibiogram to have a high impact, it should follow specific sets of guidelines and criteria. These recommendations highlight the importance of generating clinically and statistically useful data that decreases the overestimation of drug-resistance rates and the false impression of security given by the

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Table 1
Main Clinical and Laboratory Standards Institute recommendations for presentation of cumulative antibiogram.

Annual presentation of CAST
Include data when isolate *n* is >30
Include only diagnostic isolates and not those of surveillance and screening origin
Include the data for drugs that are routinely tested
Exclude environmental isolates
Exclude duplicate isolates
Exclude results that is only for laboratory statistics
Exclude results of isolates with intermediate susceptibility
Report separately *S. aureus* that is methicillin resistant vs. methicillin sensitive
Include susceptibilities of meningitis vs. non-meningitis *S. pneumoniae*

over-estimated drug-susceptibility rates [7]. The Clinical and Laboratory Standards Institute (CLSI) developed guidelines that health care facilities can use in order to develop an antibiogram that is both standardized and efficient (Table 1) [6,8].

In Lebanon, 15 to 20 years ago, the Microbiology labs of 2 major hospitals began to produce the yearly cumulative antibiograms and to distribute them to the medical staff. Gradually, it became a common practice to prepare and distribute these yearly statistics as flyers in many hospitals. By itself, this constituted a major improvement since it increased knowledge about the institutional as well as local epidemiology of resistance, and raised awareness about the drawbacks and collateral damage associated with the overuse of antibiotics. However, in many cases, these brochures of cumulative antibiograms showed limited commitment to the guidelines [2]. They presented a source of error in view of lack of appropriate analysis and/or proper interpretation [2]. This can be misleading when reporting the level of resistance and eventually affect the clinical decision making [2].

Therefore, the purpose of this work was to analyze the CASTs produced by Lebanese hospitals in order to assess the percentage of errors present in each one, and whether there is an improvement in their number throughout the years. Hence, we obtained and studied 65 CASTs from 9 hospitals in Lebanon, and we assessed the accuracy and appropriateness of these brochures from microbiological, statistical, and scientific perspectives.

Table 2
List of errors found in the 65 antibiograms that were collected and analyzed.

Errors in natural resistance
Non suitable AMA tested for the bacterium
Reporting a number that is only for lab statistics
Duplicate isolates
Number analyzed isolates<30
Environmental isolates
Carriage of Multi-Drug-Resistant-Organisms (MDROs)
Interpretation based on diameter where MIC is needed
Old interpretation breakpoints
%R consistent with correspondent MDRO
Logical cross resistance
Unusual resistant/not reported before in Lebanon (other than natural resistance)
Reporting and AST of normal flora
Data not divided into species
Incoherent percentages
Calculation errors
Errors due to cascade algorithm
Misleading or dangerous combinations
Special organisms not taken into account
Mixing inappropriately several criteria (CLSI, EUCAST, etc.)
Scientific typos

AMA: antimicrobial agent; MDRO: multi-drug resistant organism; MIC: Minimum Inhibitory Concentration; AST: Antibiotic Susceptibility Testing, CLSI: Clinical and Laboratory Standards Institute; EUCAST: European Committee on Antimicrobial Susceptibility Testing.

Methods

Collection of data

The flyers reporting the CASTs of 9 Lebanese hospitals were retrospectively gathered over 5 (2013–2017) and 10 years (2008–2017), depending on the activity of each hospital. For this purpose, the flyers prepared by these hospitals and distributed to clinicians and staff and communicated between different hospitals were considered as public information since they were made available with no restrictions. The respective hospitals were located in different areas of Lebanon (5 in Greater Beirut, 3 in Mount Lebanon, and 1 in the north). 3 hospitals that produced less than 3 successive flyers were excluded from the study. There was no demographic or regional representation since the study included hospitals producing annual cumulative antibiograms, the 9 hospitals (referred here to as hospitals 1–9) were the only ones publishing annual susceptibility data. These CASTs were thoroughly analyzed and consequently the errors as per the "Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data" proposed by the CLSI were detected, classified, and categorized.

The CASTs were produced on routine basis by compiling individual patient culture and sensitivity results over a year into an aggregate picture of the bacterial isolates and their susceptibility profiles to different antibiotics. We examined these data over 5–10 years depending on the activity of each hospital, and a total of 65 data sets were analyzed (4 hospitals with data over 10 years, and 5 hospitals with data over 5 years). All the flyers were examined for different types of errors including: conceptual, microbiological, statistical, as well as transcriptional. In some cases, contacts were done with the laboratories in order to obtain information about specific points such as interpretation guidelines used (CLSI, EUCAST, ASM), statistical elimination of duplicate isolates, etc.

Statistical analysis

The prevalence of errors in each hospital over the 5 and 10 years; in addition to the average number of errors per hospital per year were calculated using IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA).

Results

The average number of errors was 38.75 in 2008 and increased to 51.1 in 2012. After 2012, there was a decrease to an average of 37.89 errors in 2017. In hospitals 1, 7, and 8, incoherent percentages was the most common type of error. In hospitals2, 5, and 9, the prevalent error was error due to cascade algorithm. Duplicate isolates was the main error in hospital 3; whereas errors in natural resistance was in hospital 6. In hospital 4, both incoherent percentages and duplicate isolates were the most common error.

Overall, hospitals 1 and 6 had a decrease in their errors throughout the years. Hospitals 5, 8 and 9 did not show any significant changes in their number of errors whereas hospitals 2,3, 4 and 7 had inconsistent number of errors. In 2008, incoherent percentages and percentage of resistance consistent with correspondent multidrug resistant organisms were the most prevalent type of errors. In 2009, 2010, 2013, 2015, and 2016, incoherent percentages were the most common one. In 2011 and 2012, the inclusion of duplicate isolates was the most common. In 2014, incoherent percentages and the inclusion of duplicate isolates were found to be the most prevalent. In 2017, the most common type of errors were incoherent percentages, errors in natural resistance, and the inclusion of duplicate isolate.

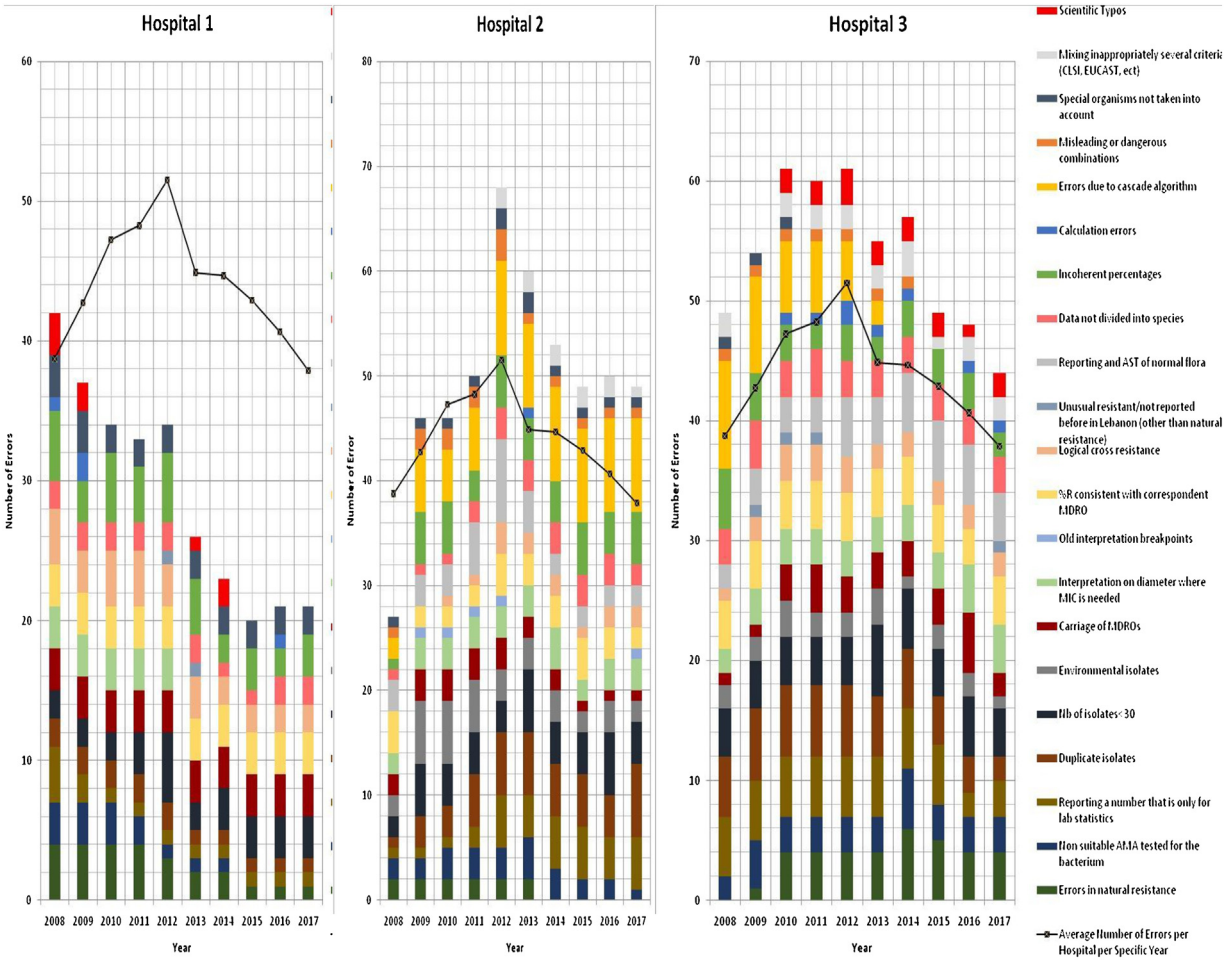

Fig. 1. The line graph shows the average number of errors per hospital per specific year. Each color in the bar graph shows the number of errors present in each criterion. The total number of errors of these criteria stacked represents the total number of error present in hospital 1 (H1), hospital 2 (H2), and hospital 3 (H3) each year.

Table 3
List of most prevalent error(s) per year with their percentage.

2008	Incoherent percentages %R consistent with correspondent MDRO	9.032% (14 out of 155 total errors)
2009	Incoherent percentages	9.941% (17 out of 171 total errors)
2010	Incoherent percentages	8.994% (17 out of 189 total errors)
2011	Duplicate isolates	8.808% (14 out of 193 total errors)
2012	Duplicate isolates	9.223%(19 out of 206 total errors)
2013	Incoherent percentages	8.415% (34 out of 404 total errors)
2014	Incoherent percentages Duplicate isolates	7.462% (30 out of 402 total errors)
2015	Incoherent percentages	8.031% (31 out of 386 total errors)
2016	Incoherent percentages	8.197% (30 out of 366 total errors)
2017	Incoherent percentages Duplicate isolates Errors in natural resistance	7.624% (26 out of 341total errors)

Discussion

The 65 CASTs collected from 9 Lebanese hospitals were studied according to the guidelines set by the CLSI [8]. The analysis of these cumulative antibiograms revealed minor to major errors in the microbiological interpretation and reporting. Each of the recommendations adopted by the CLSI holds a clinical importance necessitating therefore a proper presentation of the cumulative antibiograms. Subsequently, several errors can result from not complying with the CLSI recommendations and guidelines [7]. As shown in our results, 21 categories of errors were identified (Table 2).

Incoherent percentages were the leading type of error present in every year with the exception of the years 2011 and 2012. Incoherent percentages are unreasonable susceptibility percentages of the same bacterium to two or more antibiotics; knowing that the one that is correlated to the lower susceptibility is known and proved to have a better antibacterial activity (i.e. activity of cefuroxime versus cefotaxime on *Escherichia coli*). In 2008, the most common errors present were percentage of resistance consistent with correspondent multidrug resistant organisms and incoherent percentages. In 2011, 2012, 2014, and 2017, the most prevalent type of error was reporting duplicate isolates which constitutes a bias yielding either false increased or decreased percentages of susceptibility/resistance. Statistical analysis should consider only the first isolate obtained from the same patient, same site of infection, and over a specific period of time [5]. Inclusion of duplicate isolates will further skew the results in favor of patients who have been cultured more frequently than others leading to a more biased resistance rate [6]. Guidelines suggest some recommendations to follow in such a case [6]. All the isolates of a specific species that have been collected during the same period of time should be analyzed equally irrespective of the body site taken [6]. However, certain reports indicate that cultures from a specific body site can report species with a higher percentage of resistance than others [6]. Therefore, due to the high variability of the methods to handle duplicate isolates (all isolates strategy, first isolate strategy, episode-based

strategy. . .), each CAST should specify the method of their choice for all public health surveillances in order to adjust accordingly [6]. As for 2017, this year exhibited a third type of error to be most prevalent in addition to incoherent percentages and duplicate isolates which is errors in natural resistance. This is represented by reporting a relatively high susceptibility percentage of an organism with intrinsic resistance to a specific antibiotic (Table 3).

It was also noticed that some hospitals inappropriately mixed several criteria (CLSI, EUCAST. . .) and/or used old interpretation breakpoints by missing the changes in the new guidelines [6]. Guidelines set by CLSI or EUCAST follow different rules in the way they interpret the antibiotic testing results [6]. Mixing both breakpoints and interpretative rules affects the resistance rates and makes comparison not feasible as well as monitoring of resistance over time. Errors due to cascade algorithm were also observed; these are represented by testing the bacterial susceptibility to a second line antimicrobial agent only when it is found to be resistant to the first line agent [9]. Although from a microbiological point of view this attitude is not considered a mistake, it leads to serious ambiguity if not taken into consideration when statistical analysis is done, since it divides the population of tested bacteria into two incomparable sub-populations. This issue yield for example a 68% susceptibility to cefuroxime and 42% susceptibility to cefotaxime of the same population of *E. coli*, a result that is totally erroneous [9] (Table 4).

The interpretation of diameter where Minimum Inhibitory Concentration (MIC) is required was another common mistake for specific organisms such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, etc. In some cases, it is not enough to assess qualitatively whether the bacterium is susceptible or not to a specific antibiotic, quantitative determination of MIC is therefore a must [9]. Carriage of multidrug resistant organisms should be monitored diligently. Furthermore, illogical cross resistance refers to the usage of an antimicrobial agent with an incompatible agent leading to an inappropriate reported level of resistance/susceptibility.

Less frequent errors were also noted such as not dividing data into species or studying less than 30 isolates. Some cumulative antibiograms reported susceptibilities that are important only for the microbiology labs and not for the clinical setting. These antimicrobial agents are normally tested to detect a specific mechanism of resistance or to track epidemiological traits of resistance and should never be reported for clinical use.

Table 4
Average number of errors per specific year in all hospitals.

2008	38.75
2009	42.75
2010	47.25
2011	48.25
2012	51.5
2013	44.889
2014	44.667
2015	42.889
2016	40.667
2017	37.889

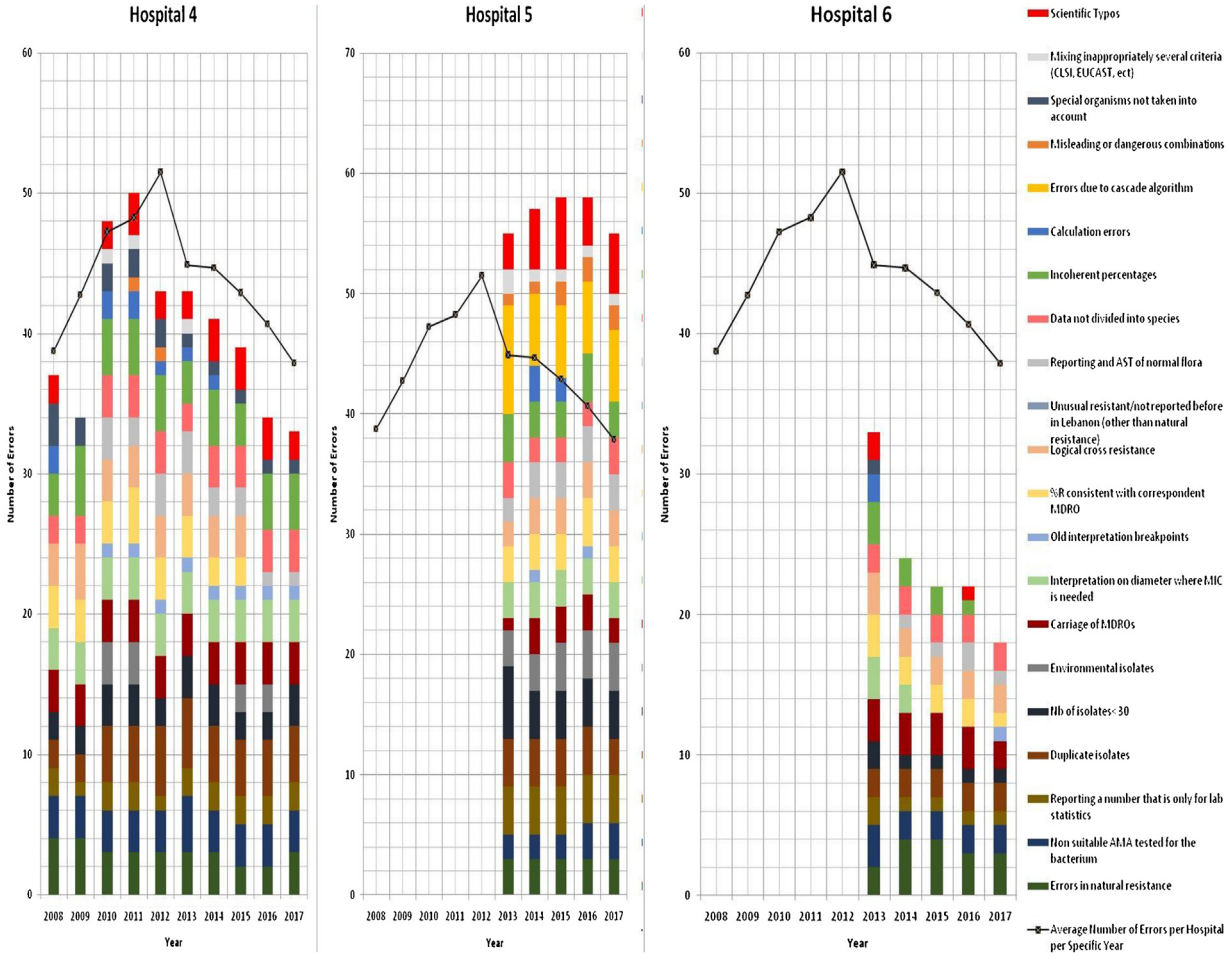

Fig. 2. The line graph shows the average number of errors per hospital per specific year. Each color in the bar graph shows the number of errors present in each criterion. The total number of errors of these criteria stacked represents the total number of error present in hospital 4 (H4), hospital 5 (H5), and hospital 6 (H6) each year.

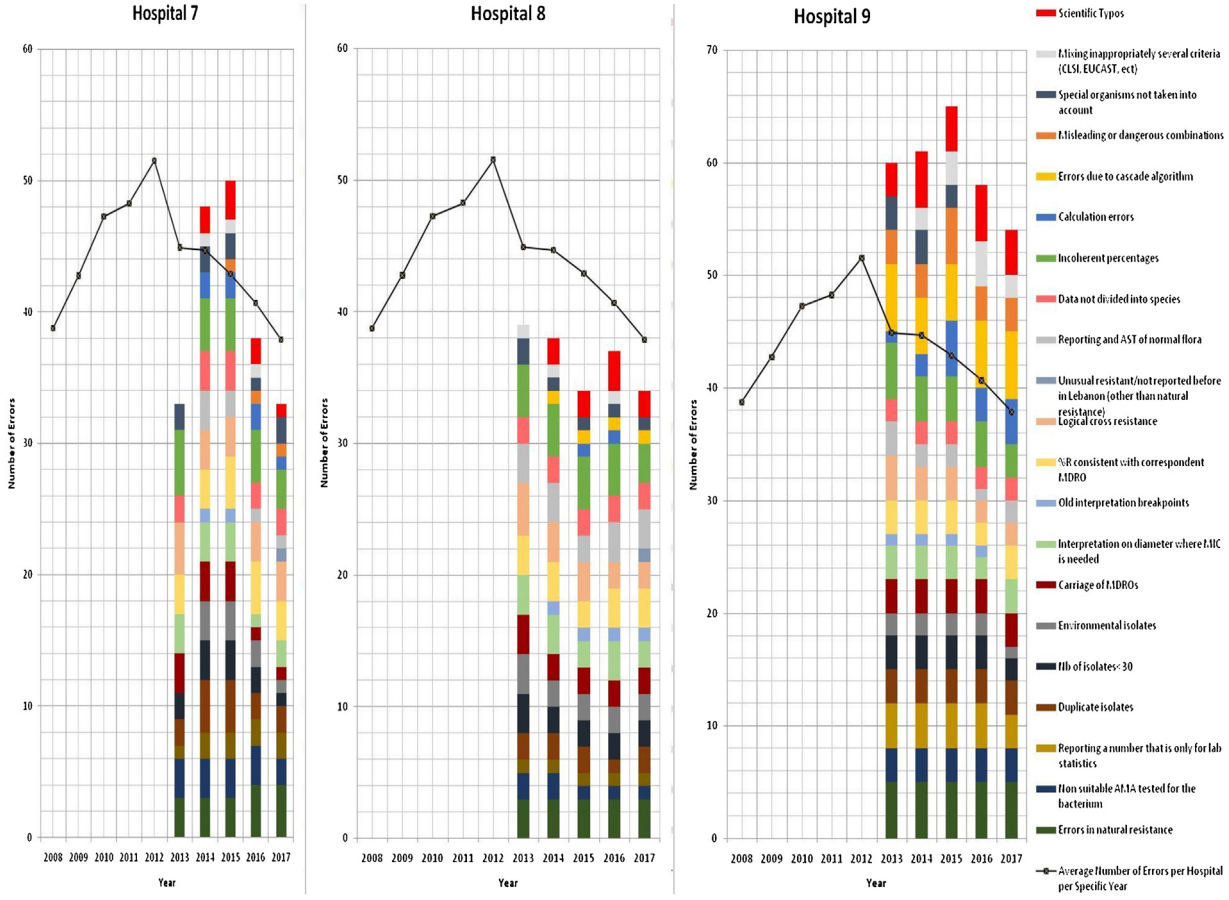

Fig. 3. The line graph shows the average number of errors per hospital per specific year. Each color in the bar graph shows the numbers of errors present in each criterion. The total number of errors of these criteria stacked represents the total number of error present in hospital 7 (H7), hospital 8 (H8), and hospital 9 (H9) each year.

On the other hand, the inclusion of surveillance isolates from patients or the environment in the statistical analysis of clinical isolates can lead to major misrepresentations in susceptibility [7].

In addition to some typing and calculation errors [7], some hospitals tested some bacteria with a non-suitable or with a dangerous combination of antibiotics. Others reported environmental isolates or normal flora, and were not taking special bacteria into account. Reporting unusual resistance not present in Lebanon previously was also detected.

The number of errors in each hospital varied with the number of errors per year in a specific hospital. The average number of errors in the Lebanese Hospitals followed an escalating pattern starting in 2008 with an average of 38.75 to reach a peaking average of 51.5 in 2012. Following 2012, there was a marked decrease to a mean of 37.89 errors in 2017. This trend was probably due to the statistical variation between each individual hospital over the years. The yearly number of errors per hospital followed 3 different patterns, depending on the hospital. Some hospitals exhibited a decline in this number (H1—Fig. 1 and H6—Fig. 2); some showed a relatively constant number (H5—Fig. 2, H8—Fig. 3, and H9—Fig. 3), while others displayed a fluctuating pattern (H2—Fig. 1, H3—Fig. 1, H4—Fig. 2, and H7—Fig. 3). Comparing these hospitals to the trending curve (mean of all hospitals), H3 (Fig. 1), H5 (Fig. 2), and H9 (Fig. 3) were constantly above the curve; H6 (Fig. 2) and H8 (Fig. 3) were constantly below the curve, and H1 (Fig. 1), H2 (Fig. 1), H4 (Fig. 2), and H7 (Fig. 3) had an inconsistent pattern with some years above the curve and others below it.

These trends may be affected by the type of hospitals from which these cumulative antibiograms were taken, such as governmental hospitals, private hospitals, and university hospitals. Other parameters include the size of the hospital, its geographic location, the prescription habits, etc... [2]. University hospitals have well established antimicrobial stewardship programs and educational component. In this context, they organize trainings and conduct awareness activities to promote the judicious use of antibiotics. These involve special chapters about the appropriate detection and reporting, as well as reading of antibiograms and CASTs. Other obstacles could be related to the lack of specialized professionals such as clinical microbiologists who are responsible for the elaboration of such reliable reports [2].

Our study has a unique element of pinpointing the errors over the span of a certain period of time (5–10 years). This will allow future studies to assess the clinical relevance of yearly cumulative antibiotic testing, and to build strategic plans for a sustainable antimicrobial stewardship program [2]. Moreover, this is the only study to showcase the evolution of cumulative antibiogram reporting in Lebanese (and probably Arab) hospitals, what makes it a good analysis prototype to follow for a better assessment of such a clinical and educational activity

Conclusions

Summing up, collecting data is easy; however, collecting the correct data and using it appropriately is a more complex and difficult process. Lebanon is a small country with a high number of hospitals and medical centers. 15 years ago, only 2 hospitals used to analyze and publish their annual data. As a positive influence, many hospitals followed and this became a routine practice of microbiology labs. However, as it was shown in our study, the numbers

of errors in reporting these cumulative susceptibilities is still high and needs appropriate interventions. The concerned scientific societies, as well as the Lebanese official public health authorities have the obligation of addressing and following up on this important issue.

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Competing interests

None declared.

Ethical approval

Not required.

Authors contributions

All authors were involved in the collection of data, statistical analysis and drafting of the manuscript.

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