# A Novel Algorithm for Predicting Antimicrobial Resistance in Unequal Groups of Bacterial Isolates

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**Abstract:** Choosing antimicrobials is a common dilemma when the expected rate of bacterial resistance is high. The observed resistance values in unequal groups of isolates tested for different antimicrobials can be misleading. This can affect the decision to recommend one antibiotic over the other. We analyzed recalled data with the statistical consideration of unequal sample groups.

Data was collected concerning children suspected to have typhoid fever at Al Alwyia Pediatric Teaching Hospital in Baghdad, Iraq. The study period extended from September 2021 to September 2022. A novel algorithm was developed to compare the drug sensitivity among unequal numbers of Salmonella typhi (S. Typhi) isolates tested with different antibacterials.

According to the proposed algorithm, the predicted resistance values were more valid than the observed values. This proposed algorithm is expected to help the hospital antibiotic policy committee recommend the proper antibacterial agents for S. Typhi and further bacterial isolates.

**Keywords:** Unequal groups, ranking, salmonella drug resistant, predicted value, observed value.

## HIGHLIGHTS

- Isolates with different sample sizes of groups tested for antimicrobial sensitivity are difficult to analyze.
- A novel algorithmic method is developed to analyze the retrieved data of a sample of unequal groups of bacterial isolates tested for different antibacterial agents in order to rank these groups according to their degree of resistance.
- This method can be used in analyzing different unequal group sizes in general.

## 1. INTRODUCTION

Antimicrobial resistance (AMR) has emerged as a major public health problem all over the world. By 2018 *Salmonella typhi* (*S. Typhi*) had drug resistance to multiple antimicrobials including fluoroquinolones (FQ) [1]. Furthermore, there were many internationally transmitted reported cases of Extensively drug-resistant (XDR*)* S. Typhi strain from the United States, United Kingdom, Denmark, Germany, Canada; and Australia [2].

*S. Typhi, a* gram-negative bacilli that belongs to the species *S. enterica*, caused typhoid fever for an estimated 21.7 million illnesses and 216,000 deaths globally in 2000 [3-5].

Although the first outbreak of third-generation cephalosporin resistance was identified in Pakistan, resistant *S. typhi* strains have later been reported from India, Bangladesh, Philippines, Guatemala, Italy, and Iraq [6].

The first reported extended resistant *S. typhi* strain reported in Iraqi patients was back in 2008 [7]. Between 2002 and 2007, Multidrug -resistant (MDR) strains prevalence were 83% In Iraq [8].

Previous studies on Salmonella-resistant typhoid cases in Iraq showed a diversity of resistance patterns *S. typhi* among different institutions and geographical locations. Furthermore, these studies were not limited to a pediatric age group [8-10].

In Iraq and many other countries, there are limitations in using the national antimicrobial policy which include the local resistance problems which

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dictate the development of a system to rapidly detect and report resistant microorganisms within each institution. Institutional antimicrobial policy can give different solutions and different prescribing practices within a defined geographical region [11].

To be effective, this system also should revise the policy every year based on the antimicrobial susceptibility profiles [11-13]. Each healthcare institution should have its local antibiotic policy. Resistance surveillance to identify the current resistance rates and trends is essential to develop a local institutional antibiotic policy [14, 15].

According to statistical standards recommendations, data presentation and analyses of antibacterial resistance should adhere to a rigorous statistical standard by using equal sample sizes is the preferred method in statistical studies [16, 17]. Nevertheless, the literature sometimes expresses the proportions of *S. typhi* isolates in percentages despite unequal denominators [8, 18, 19].

Allocating equal group sizes of retrieved data of hospital isolates is sometimes difficult, and sometimes near impossible, especially when recalling resistance and sensitivity data is urgently needed. This can limit the use of such data for analysis and interpretation unless allocating equal groups of isolates.

In the context of existing data bias and distressing investigations of salmonella resistance and other bacterial isolates in Iraq [8, 10, 20], we designed this study to look for a valid method to deal with an unequal number of S. typhi isolates tested for different antibacterials to rank these groups according to best available evidence for drug resistance and sensitivity. This will fill the gap of knowledge in the unequal study groups, particularly among drug resistance isolates. This is crucial when no robust data is available for analysis and when urgent action is needed.

Here, we present evidence that with algorithmic treatment of different numbers of subgroups of the studied sample can gain a more powerful study than neglecting data with unequal groups.

Using this novel algorithm can help us to avoid the presentation of potentially misleading or confusing data. This is imperative because the tested number of isolates for antibiotics is not necessarily constant within a certain center and most often to be inconsistent across different centers.

The paper is organized as follows. In section 2, we present the data description. Section 3 describes the Presentation of the proposed algorithm. In section 4, we present the validity and reliability of algorithmic predictive values. Section 5 presents the predicted resistance and sensitivity according to the proposed algorithm.

Testing for Z values and ranking of findings are presented in section 6. A concluding discussion is given in section 7.

## 2. DATA DESCRIPTION

### 2.1. Sample Collection

Between September 2021 to September 2022, medical records and lab reports of all patients with confirmed typhoid fever at Al-Alwyia Pediatrics Teaching Hospital, Bagdad, Iraq, were reviewed. Confirmation was done by isolation of *S. typhi* from cultured blood samples.

Inclusion criteria included fever, > 1-month-old children, and positive isolate for *S. typhi*. We collected data on demographic characteristics, and results of microbiologic and sensitivity tests.

### 2.2. Laboratory Procedures

Blood samples were obtained from patients using aseptic means. Isolates were directly inoculated in BacT/ALERT culture or Brain-heart infusion bottles. Later on, subcultures were done on MacConkey and blood Agar and then incubated at 37 °C for 18-24 h. The sample was considered sterile if no bacterial growth was observed on the subculture after 7 days of incubation at 37 °C. Isolation and identification of the isolates were done by standard biotyping (colony morphology, staining reaction, biochemical characteristics; and serotyping). Some isolates were identified with the help of Vitek 2 (Biomerieux System).

MIC of the cultures was determined according to the guidelines provided by the Clinical and Laboratories Standards Institute (CLSI) by microdilution method (CLSI, 2020). The disk diffusion test was used. The antibacterial discs were: tetracycline (30 µg), ceftazidime (30 µg), cefepime (30 µg), TMP-SMX (1.25/23.75 µg), gentamicin (10 µg), meropenem (10 µg), ciprofloxacin (CIP) (5 µg), piperacillin-tazobactam (100/10 µg), ceftriaxone (30 µg), tobramycin (10 µg), amikacin (30 µg), piperacillin (100 µg), ceftriaxone (30 µg), minocycline (30 µg) and azithromycin (15 µg) (Hi-Media Laboratories).

## 3. PRESENTATION OF THE PROPOSED ALGORITHM

There were differences in the number of isolates tested for each antibacterial agent. 3 isolates were tested for minocycline, 27 for tetracycline, 23 for ceftazidime, 13 for cefepime, 17 for cefotaxime, 26 for ceftriaxone, 6 for tazocine, 4 for piperacillin, 11 for meropenem, 32 for CIP, 8 for gentamycin, 3 for tobramycin, 4 for amikacin; and 24 for azithromycin and TMP-SMX. In light of the different number of isolates tested for each antibacterial agent, it is not valid to get the order of resistance for antibacterial agents measured as an observed percentage. Instead of ranking antibacterial agents according to the observed (non-valid) percentage of resistant isolates/isolates tested for a certain agent, we proposed a technique for predicting a valid value for resistance and sensitivity (in percentage) with the following algorithmic steps:

1. The adoption of a total number of isolates which represents the highest number of isolates tested for a single antibacterial agent. This number was the number of isolates tested for CIP which was 32.

2. Calculate the percentage of the number of resistant isolates for each antibacterial agent to the adopted number of isolates referred to in the first step (i.e. 32). The same step is applied for sensitive isolates (calculating the percentage of the number of sensitive isolates for each antibacterial agent with the adopted number (32) which represents the isolates number referred to in the first step). An intermediate sensitivity isolate number was added to the sensitive isolates.

3. Finding the missing number of isolates for each antimicrobial agent by subtracting the total observed number (observed resistance and observed s sensitivity) from the adopted number (32).

4. Find the product of multiplying the outputs of the second step by the number of missing isolates obtained in step 3 for each of the resistance and sensitivity.

5. The results of the fourth step are added to the observed number of isolates for both resistance and sensitivity correspondingly. Then, the sum of these two new numbers together makes a new total.

6. This step depends on the assumption of a random distribution of the remaining number of isolates after excluding the output achieved in the fifth step, by adding half the number of remaining isolates to each of the resistance number and sensitivity number equally.

7. Obtaining Z value: The differences between the proportions of observed frequencies of the resistance/sensitivity and the corresponding predictive resistance/sensitivity values are tested under the null hypothesis.

## 4. ALGORITHMIC VALIDITY AND RELIABILITY

As far as there is always random variability, sample data can't be expected to be perfectively represent reality when measured in percentage, especially when samples are small. The expression of bacterial resistance in percentage while denominators differs among compared results deviates an observed value of an element of a statistical sample from the actual value. Biased observational data is a possible cause of invalid findings, unreliable conclusions, and recommendations in different studies.

The validity of the algorithm was assessed through the person correlation coefficient (r). Correlation coefficients were +0.901 for observed and predicted resistance, and + 0.885 for observed and predicted sensitivity (strong direct correlation).

Kolmogorov-Smirnov test also proved that the distribution function of percentages' values was normal, indicating that parametric statistical methods are applicable (Table **1**).

Furthermore, comparing statistical significance differences between observed and predicted results for resistant and sensitivity values were reported as not significant at P>0.05 (Table **2**). Since no significant differences are accounted for between values of resistant, and sensitivity criteria independently, we conclude that the proposed algorithm has a high reliability and confidence.

## 5. PREDICTED RESISTANCE AND SENSITIVITY ACCORDING TO THE PROPOSED ALGORITHM

The observed resistance (%) among isolates was reported as following descending percentages: 100 for ceftazidime, cefotaxime, tobramycin; and amikacin, 96.15 for ceftriaxone, 92.30 for cefepime, 87.5 for gentamycin, 75.0 for piperacillin, 33.33 for tazocine,

**Table 1: One-Sample Kolmogorov-Smirnov Test**

| One-Sample Kolmogorov-Smirnov Test | | | | | |
|---|---|---|---|---|---|
| **Parameters** | | **Resistance Observed** | **Resistance Predictive** | **Sensitive Observed** | **Sensitive Predictive** |
| No. | Statistics | 15 | 15 | 15 | 15 |
| Normal Parameters | Mean | 55.73 | 51.0447 | 42.9847 | 48.9613 |
| | Std. Deviation | 43.4758 | 32.5981 | 42.0354 | 32.5968 |
| Most Extreme Differences | Absolute | 0.234 | 0.121 | 0.233 | 0.121 |
| | Positive | 0.192 | 0.121 | 0.233 | 0.105 |
| | Negative | -0.234 | -0.105 | -0.18 | -0.121 |
| Kolmogorov-Smirnov Z | | 0.907 | 0.469 | 0.9 | 0.469 |
| Asymp. Sig. (2-tailed) | | 0.383 | 0.98 | 0.392 | 0.98 |
| Test distribution is Normal. | | | | | |

SPSS output.
NS: Non Significant at P>0.05.

**Table 2: Statistical Significance Differences between Observed and Predicted Results for Resistant and Sensitivity**

| **Paired** | **Paired Differences** | **Mean** | **Std. Dev.** | **Std. Error Mean** | **95% Conf. Interval of the Diff.** | | **t-test** | **df** | **Sig. level** |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | **Lower** | **Upper** | | | |
| Pair 1 | Resistance Observed - Resistance Predicated | 4.685 | 19.996 | 5.16 | -6.39 | 15.76 | 0.908 | 14 | 0.379 NS |
| Pair 2 | Sensitive Observed - Sensitive Predicated | -5.977 | 20.1 | 5.19 | -17.1 | 5.16 | -1.15 | 14 | 0.269 NS |

SPSS output.
NS: Non Significant at P>0.05.

25.92 for tetracycline, 9.09 for meropenem, 8.33 for TMP-SMX and azithromycin, 0 for minocycline and CIP.

According to the proposed algorithm by using the highest number of isolates tested for single antibacterial agents (N=32), the predicted resistance among isolates was reported in the following descending percentages: 96.88 for ceftriaxone and ceftazidime, 93.75 for cefotaxime, 78.13 for cefepime, 65.63 for gentamycin and amikacin, 59.38 for tobramycin, 56.25 for piperacillin, 43.75 for tazocine, 40.63 to minocycline, 25 for tetracycline and meropenem, 9.38 for TMP-SMX and azithromycin; and 0 for CIP (Table **3**).

## 6. TESTING FOR Z VALUES AND RANKING OF FINDINGS

To be accepted values, the z values should be not significant (at P>0.05) for all studied isolates.

All Z values were less than 1.96 and were not significant (at P>0.05) (Table **3**).

At the top of the observed resistance order were ceftazidime, cefotaxime, tobramycine, and amikacin with an order of 2.5, while at the top of the predicted order was reported for cefotaxime. At the bottom of observed resistance order were CIP and minocycline with an order of 14.5. The observed resistance order for trimethoprim/sulfamethoxazole was 12.5.

Each of CIP and trimethoprim/sulfamethoxazole had a lower predicted resistance order of 14.5. The predicted resistance order was up to 10 (Table **4**).

The highest adjusted value % was 90.6 which was reported for minocycline and tobramycin which had the lowest number for tested isolates.

## 7. CONCLUSIONS AND RECOMMENDATIONS

We put here a novel algorithm to analyze the results of the retrieved resistance and sensitivity data with statistical considerations of unequal groups of isolates to be considered by the antibiotic policy committee as valid results instead of neglecting such available data.

**Table 3: Distribution of Antimicrobial Resistance According to Observed and Predicted (Up to 32 Isolates) and Z Values**

| Main Classification of Antibiotic | Sub Classification of Antibiotic | Resistance | | | | Sensitivity | | | | Intermediate sensitivity (%) | Total observed number | $Z_{.value}$ * |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Observed | | Predicted (out of 32) | | Observed | | predicted out of 32 | | | | |
| | | No. | % | No. | % | No. | % | No. | % | | | |
| A – Tetracycline | Tetracycline | 7 | 25.92 | 8 | 25.00 | 19 | 70.37 | 24 | 75.00 | 1 (3.7) | 27 | 0.116 |
| | Minocycline | 0 | 0.00 | 13 | 40.63 | 3 | 100 | 19 | 59.38 | - | 3 | 1.392 |
| B – Cephalosporin | Ceftazidime | 23 | 100 | 31 | 96.88 | 0 | 0.00 | 1 | 3.13 | - | 23 | 0.856 |
| | Cefepime | 12 | 92.30 | 25 | 78.13 | 1 | 7.69 | 7 | 21.88 | - | 13 | 1.128 |
| | Cefotaxime | 17 | 100 | 30 | 93.75 | 0 | 0.00 | 2 | 6.25 | - | 17 | 1.052 |
| | Ceftriaxone | 25 | 96.15 | 31 | 96.88 | 1 | 3.85 | 1 | 3.13 | - | 26 | 0.150 |
| C- Penicillins | Tazocine (Piperacillin/Tazobactam) | 2 | 33.33 | 14 | 43.75 | 4 | 66.7 | 18 | 56.25 | - | 6 | 0.474 |
| | Piperacillin | 3 | 75.0 | 18 | 56.25 | 1 | 25.0 | 14 | 43.75 | - | 4 | 0.717 |
| D - TMP-SMX | | 2 | 8.33 | 3 | 9.38 | 22 | 91.67 | 29 | 90.63 | - | 24 | 0.135 |
| E- Meropenem | | 1 | 9.09 | 8 | 25.00 | 10 | 90.91 | 24 | 75.00 | - | 11 | 1.119 |
| F- Ciprofloxacin (CIP) | | 0 | 0.00 | 0 | 0.00 | 27 | 84.38 | 32 | 100 | 5 (15.6) | 32 | 0.000 |
| G- Aminoglycosides | Gentamycin | 7 | 87.5 | 21 | 65.63 | 1 | 12.5 | 11 | 34.38 | - | 8 | 1.208 |
| | Tobramycin | 3 | 100 | 19 | 59.38 | 0 | 0.00 | 13 | 40.63 | - | 3 | 1.392 |
| | Amikacin | 4 | 100 | 21 | 65.63 | 0 | 0.00 | 11 | 34.38 | - | 4 | 1.407 |
| H- Azithromycin | | 2 | 8.33 | 3 | 9.38 | 22 | 91.7 | 29 | 90.63 | - | 24 | 0.135 |

*Non Significant at P>0.05.

**Table 4: Antimicrobials Sensitivity and Resistance Ranking According to Observed Resistance Order and Predicted Sensitivity Order**

| Main Classification of Antibiotic | Sub Classification of Antibiotic | Number of tested isolates (observed) | Resistance | | Sensitivity | | Adjusted Value %** |
|---|---|---|---|---|---|---|---|
| | | | Observed resistance order | Predicted resistance order | Observed sensitivity order* | Predicted sensitivity order | |
| A – Tetracycline | Tetracycline | 27 | 10 | 11.5 | 6 | 4.5 | 15.6 |
| | Minocycline | 3 | 14.5 | 10 | 1.5 | 6 | 90.6 |
| B – Cephalosporin | Ceftazidime | 23 | 2.5 | 1.5 | 12.5 | 14.5 | 28.1 |
| | Cefepime | 13 | 6 | 4 | 10 | 12 | 59.4 |
| | Cefotaxime | 17 | 2.5 | 3 | 12.5 | 13 | 50 |
| | Ceftriaxone | 26 | 5 | 1.5 | 11 | 14.5 | 18.7 |
| C- Penicillins | Tazocine (Piperacillin/Tazobactam) | 6 | 9 | 9 | 7 | 7 | 81.2 |
| | Piperacillin | 4 | 8 | 8 | 8 | 8 | 87.5 |
| D - Trimethoprim / Sulfamethoxazole (TMP-SMX) | | 24 | 12.5 | 14.5 | 3 | 2.5 | 25 |
| E- Meropenem | | 11 | 11 | 11.5 | 5 | 4.5 | 65.6 |
| F- Ciprofloxacin(CIP) | | 32 | 14.5 | 14.5 | 1.5 | 1 | 0 |
| G- Amino Glycosides | Gentamycin | 8 | 7 | 5.5 | 9 | 10.5 | 27 |
| | Tobramycin | 3 | 2.5 | 7 | 12.5 | 9 | 90.6 |
| | Amikacin | 4 | 2.5 | 5.5 | 12.5 | 10.5 | 87.5 |
| H- Azithromycin | | 24 | 12.5 | 13 | 4 | 2.5 | 25 |

*Including intermediate results.
**adjusted value %: denotes the proportion of the added number of adjustments / 32 %.

By introducing of this method of analysis, the antibiotic policy will be able to recognize emerging micro-organisms and be able to recommend locally effective antibacterial guidelines based on the best available evidence.

This method can help greatly in avoiding bias created by unequal groups in bacterial resistance studies as well as other studies. Therefore, data with unequal groups are useful for powerful studies instead of neglecting these data. This method will be time-consuming, statistically valid especially for small numbers, and indeed cost effective.

A novel algorithmic method has been presented to obtain predicted values for drug resistance towards bacterial isolates across studied unequal groups. By this method, a valid data sorting was presented which involved arranging the data into a meaningful order that is easy to understand, analyze, and visualize. The valid drug resistance and sensitivity values and orders will help antibiotic policy committees and other decision-makers to recommend one drug over another on a more solid basis. The predicted order of resistant or sensitive antibiotics generated by this new algorithmic method replaces the non-valid order of the observed values.

The novel algorithmic data management adopted in this study can be used in a wide variety of studies dealing with unequal groups.

## DECLARATIONS

### Ethics Approval and Consent to Participate

All steps were carried out by relevant guidelines and regulations. The study plan and the conduction of the study approval were obtained from the Al-Rusafa Health Directorate Research Ethical Committee.

### Authors' Contributions

All the authors have accepted responsibility for the entire content of this submitted manuscript and approved the submission.

### Consent for Publication

Not applicable.

### Availability of Data and Materials

All data underlying the results are available as part of the article and no additional source data are required.

### Competing Interests

The authors declared that no conflicts of interest exist.

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### Consent for Publication

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## ABBREVIATIONS

AMR = Antimicrobial resistance

CIP = Ciprofloxacin

CLSI = Clinical and Laboratories Standards Institute

FQ = fluoroquinolones

MDR = Multidrug -resistant

*S. typhi* = *Salmonella typhi*

TMP-SMX = Trimethoprim / Sulfamethoxazole

XDR = Extensively drug-resistant

## REFERENCES

[1] Barkume C, Date K, Saha SK, Qamar FN, Sur D, Andrews JR, *et al*. Phase I of the Surveillance for Enteric Fever in Asia Project (SEAP): an overview and lessons learned. J Infect Dis 2018; 218(Suppl_4): S188-S194. https://doi.org/10.1093/infdis/jiy522

[2] Chatham-Stephens K, Medalla F, Hughes M, Appiah GD, Aubert RD, Caidi H, Angelo KM, Walker AT, Hatley N, Masani S, Nash J, Belko J, Ryan ET, Mintz E, Friedman CR. Emergence of Extensively Drug-Resistant Salmonella Typhi Infections Among Travelers to or from Pakistan - United States, 2016-2018. MMWR Morb Mortal Wkly Rep 2019; 68(1): 11-13. https://doi.org/10.15585/mmwr.mm6801a3

[3] Typhoid Fever, Paratyphoid Fever, and Typhoidal Fevers in: Jason R. Andrews, Jason B. Harris and Edward T. Ryan. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 100, 1365-1379.e3

[4] Ashurst JV, Truong J, Woodbury B. Salmonella Typhi. [Updated 2022 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519002/

[5] Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. Bull World Health Organ 2004; 82(5): 346-53

[6] Pustake M, Giri P, Tambolkar S, Nayak S. Extensively Drug-Resistant Typhoid Fever: A Call to Action. Indian J Community Med 2022; 47(1): 153-154. https://doi.org/10.4103/ijcm.ijcm_1008_21

[7] Pfeifer Y, Matten J, Rabsch W. Salmonella enterica Serovar Typhi with CTX-M β-Lactamase, Germany. Emerging Infectious Diseases 2009; 15(9): 1533-1535. https://doi.org/10.3201/eid1509.090567

[8] Rahman BA, Wasfy MO, Maksoud MA, Hanna N, Dueger E, House B. Multi-drug resistance and reduced susceptibility to ciprofloxacin among Salmonella enterica serovar Typhi isolates from the Middle East and Central Asia. New Microbes New Infect 2014; 2(4): 88-92. https://doi.org/10.1002/nmi2.46

[9] Habeeb Rasool K, Hammood Hussein N, Mahamed Taha B. Molecular Detection of *gyrA* Gene in *Salmonella enterica* serovar Typhi Isolated from Typhoid Patients in Baghdad. Pak J Biol Sci 2020; 23(10): 1303-1309. https://doi.org/10.3923/pjbs.2020.1303.1309

[10] Asreah R, Atta S, SarKo S. Clinical Characteristics and Antibiotics Sensitivity of Culture Positive Typhoid Fever Patients in Baghdad Teaching Hospital – A Single Center Study. Open Access Maced J Med Sci [Internet] 2022 Jul. 17 [cited 2022 Oct. 21]; 10(B): 1846-5. https://doi.org/10.3889/oamjms.2022.9336

[11] World Health Organization -Regional Office for South-East Asia. Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines 2011.

[12] Cisneros JM, Pérez-Moreno MA, Gil-Navarro MV. Política de antibióticos. Comisión de Infecciones y uso de antimicrobianos [The antibiotic policy. The Infection Committee and antimicrobial use]. Enferm Infecc Microbiol Clin 2014; 32(8): 533-6. Spanish. https://doi.org/10.1016/j.eimc.2014.01.008

[13] Keuleyan E, Gould IM. Key issues in developing antibiotic policies: from an institutional level to Europe-wide. European Study Group on Antibiotic Policy (ESGAP), Subgroup III. Clin Microbiol Infect 2001; 7(Suppl. 6): 16-21. https://doi.org/10.1046/j.1469-0691.7.s6.4.x

[14] Hawser S. Surveillance programmes and antibiotic resistance: worldwide and regional monitoring of antibiotic resistance trends. Handb Exp Pharmacol 2012; (211): 31-43. https://doi.org/10.1007/978-3-642-28951-4_3

[15] World Health Organization. WHO strategic and technical advisory group for antimicrobial resistance (STAG-AMR): report of the first meeting, 22-24 June 2021 2021. P 5. https://apps.who.int/iris/handle/10665/350002

[16] Rosenbaum PR and Rubin DB. Constructing a control group using multivariate matched sampling methods that incorporate the propensity score. The American Statistician. 1985; 39(1): 33-38. https://doi.org/10.1080/00031305.1985.10479383

[17] Oldfield, F. Unequal sample sizes and the use of larger control groups pertaining to power of a study -Published by Ministry of Defence UK Paper: DSTLTR92592 P2PP2R-2016-02-23T13. https://doi.org/10.4269/ajtmh.20-0258

[18] Marchello CS, Carr SD, Crump JA. A Systematic Review on Antimicrobial Resistance among *Salmonella* Typhi Worldwide. Am J Trop Med Hyg 2020; 103(6): 2518-2527.

[19] Browne AJ, Kashef Hamadani BH, Kumaran EAP, Rao P, Longbottom J, Harriss E, *et al*. Drug-resistant enteric fever worldwide, 1990 to 2018: a systematic review and meta-analysis. BMC Med 2020; 18(1): 1. https://doi.org/10.1186/s12916-019-1443-1

[20] Raham TF, Abood AM. Bacterial Profile and Antimicrobial Susceptibility in Neonatal sepses, Al -Alwyia Pediatric Teaching Hospital in Baghdad. AL-Kindy College Medical Journal 2019; 13(2): 21-25. https://doi.org/10.47723/kcmj.v13i2.32

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https://doi.org/10.6000/1929-6029.2023.12.26