ZIBELINE INTERNATIONAL™ PUBLISHING

ISSN: 2521-0858 (Print)
ISSN: 2521-0866 (Online)
CODEN: SHJCAS

Science Heritage Journal (GWS)

DOI: http://doi.org/10.26480/gws.02.2021.44.48

RESEARCH ARTICLE

ANTIMICROBIAL RESISTANCE (AMR)-FORECAST FOR 30 COUNTRIES IN EUROPE

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ARTICLE DETAILS

Article History:

Received 20 October 2021
Accepted 23 November 2021
Available online 25 November 2021

ABSTRACT

Antimicrobial resistance (AMR) has emerged among the most serious public health issues, prompting the creation of worldwide implementation strategies. In this study, the application of seasonal or time-series approaches was suggested for forecasting the unknown percentages of resistance towards other microbial groups for seven microorganisms. Annual data between 2012 and 2019 were acquired from European Centre for Disease Prevention, and Control (ECDC) reports. Microsoft Excel's function, 'FORECAST.ETS', was used for prediction purposes. Then, a brief analysis was done on the forecasted results. Forecasting AMR's percentage makes it possible to develop a strategy for dealing with any situation that may emerge.

KEYWORDS

Antimicrobial resistance; Antimicrobials; Forecasting

1. INTRODUCTION

Antimicrobial resistance (AMR) refers to a microorganism's capability to withstand the effects of one antimicrobial agent or more (European Centre for Disease Prevention and Control (ECDC, 2018). Antimicrobial resistance arises once a microbe develops tolerance toward a substance designed to eradicate or slow it down (VanOeffelen et al., 2021). It is among the most severe health issues confronting current civilizations (Broom et al., 2021). Since a lot of strains are immune to nearly all current antibacterial drugs, combating diseases caused by resistant pathogens is typically challenging. Resistance has advanced significantly throughout circumstances and countries in the decades since it was first discovered in the developmental stages of antimicrobials (Nieuwlaat et al., 2021). Antimicrobial monitoring research is crucial for determining patterns in microorganism AMR and detecting new pathogens worldwide. This knowledge allows for the creation of tailored AMR management strategies (Masterton, 2008). Monitoring of particular organisms over a period could be used to evaluate the development of new strains or species, as well as differences in the pathogens' antibiotic tolerance characteristics (Fuhrmeister and Jones, 2019).

2. MATERIALS AND METHODS

2.1 Antimicrobial Analyzed

This analysis looks at seven microbial: Acinetobacter spp., Escherichia coli, Enterococcus faecium, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, and Streptococcus pneumoniae. Their resistance in Europe was forecasted for the years 2020 and 2021 based on available data.

2.2 Thrips rearing and preparation

Antimicrobial resistance (AMR) data were collected and extracted from European Centre for Disease Prevention and Control (ECDC) reports (European Centre for Disease Prevention and Control (ECDC, 2019). The AMR data for 30 countries in Europe were then organized according to the antimicrobials to be analyzed. All the data were taken as percentages of resistance towards other groups of microbial. Periods of eight years were used to analyze the resistance of the seven microbial of interest, depending on the available data from ECDC.

2.3 Forecasting of AMR

Microsoft Excel was used to forecast the percentage of AMR of the organisms analyzed for the countries in Europe. The data for each of the microbial were organized by country and year in Excel. Then, with the available information, the function 'FORECAST.ETS' was used to forecast the percentage of resistance for the years 2020 and 2021 for every country using the data from 2012 until 2019. The function predicts a value given past values with a seasonal pattern, and in this case, the pattern is annual. The AMR's percentages were predicted using a 95% confidence interval.

3. RESULTS AND DISCUSSION

The analysis involved 30 countries in Europe with data of AMR's percentages for *Acinetobacter* spp., *Escherichia coli, Enterococcus faecium, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus,* and *Streptococcus pneumoniae.* The percentages of AMR for the countries for the years 2020 and 2021 were predicted, and the results were presented in the tables below.

From Table 1, it can be seen that 16 out of 30 countries show an increasing percentage of combined resistance to fluoroquinolones, aminoglycosides and carbapenems for *Acinetobacter* spp. In comparison, four countries don't have enough data to forecast the AMR's rates for 2020 and 2021. AMR in *Acinetobacter* spp., such as in prior years, differed throughout Europe, with relatively high resistance percentages recorded from the Baltic nations, along with southern and south-eastern of Europe.

Quick Response Code	Access this article online	
	Website: www.jscienceheritage.com	**DOI:** 10.26480/gws.02.2021.44.48

Table 1: Forecasted AMR's percentage for Acinetobacter spp.

Country	2020	2021
Austria	6.99	7.21
Belgium	1.29	1.35
Bulgaria	75.99	81.85
Croatia	92.30	94.29
Cyprus	84.40	88.16
Czech Republic	33.15	36.82
Denmark	0.05	0.00
Estonia	-	-
Finland	0.00	0.00
France	8.22	8.83
Germany	0.00	0.66
Greece	89.49	91.10
Hungary	46.74	47.38
Iceland	-	-
Ireland	0.31	0.00
Italy	72.81	72.10
Latvia	60.39	48.50
Lithuania	83.18	85.84
Luxembourg	-	-
Malta	-	-
Netherlands	1.35	4.43
Norway	0.16	0.00
Poland	64.54	77.95
Portugal	11.38	5.04
Romania	86.51	89.73
Slovakia	44.27	47.00
Slovenia	65.51	72.19
Spain	47.66	45.49
Sweden	1.82	1.43
United Kingdom	1.10	1.08

* Not enough data for forecasting

Table 2: Forecasted AMR's percentage for Escherichia coli

Country	2020	2021
Austria	3.35	3.44
Belgium	3.11	3.20
Bulgaria	20.75	21.34
Croatia	10.36	11.39
Cyprus	8.34	7.42
Czech Republic	6.83	7.10
Denmark	1.56	2.11
Estonia	2.24	2.26
Finland	1.80	1.99
France	3.21	3.18
Germany	3.50	3.56
Greece	8.45	8.22
Hungary	10.51	10.52
Iceland	1.85	0.89
Ireland	6.25	6.53
Italy	11.81	11.50
Latvia	9.69	10.18
Lithuania	5.26	5.73
Luxembourg	4.55	4.78
Malta	5.03	4.88
Netherlands	2.40	2.26
Norway	1.89	1.86
Poland	11.46	11.04
Portugal	5.67	5.26
Romania	6.97	5.95
Slovakia	14.49	14.39
Slovenia	8.14	8.54
Spain	6.23	6.31
Sweden	2.75	2.86
United Kingdom	4.46	4.49

Table 2 shows the forecasted percentage with combined resistance to fluoroquinolones, third generation cephalosporins and aminoglycosides for *Escherichia coli* (*E. Coli*) for the years 2020 and 2021. The majority of the countries show a slightly increasing trend in the percentage of AMR.

Table 3: Forecasted AMR's percentage for Enterococcus faecium

Country	2020	2021
Austria	2.19	0.46
Belgium	1.75	1.80
Bulgaria	13.89	15.60
Croatia	30.98	34.50
Cyprus	66.13	66.10
Czech Republic	21.65	23.33
Denmark	13.48	12.95
Estonia	6.52	7.43
Finland	0.77	1.42
France	0.81	1.13
Germany	27.94	29.60
Greece	44.08	40.15
Hungary	43.44	53.32
Iceland	0.00	0.00
Ireland	38.05	37.17
Italy	23.33	25.71
Latvia	45.80	50.83
Lithuania	46.02	51.92
Luxembourg	0.39	0.20
Malta	26.25	4.86
Netherlands	1.06	1.04
Norway	2.21	2.36
Poland	49.44	48.22
Portugal	0.53	0.00
Romania	43.12	48.09
Slovakia	40.20	44.61
Slovenia	0.84	0.80
Spain	1.87	1.92
Sweden	1.41	1.16
United Kingdom	24.61	25.61

Table 3 recorded the forecasted percentage with resistance to vancomycin for *Enterococcus faecium* in 2020 and 2021. The prediction of AMR's rates for 17 countries shows an increasing trend, while the others are falling.

Table 4: Forecasted AMR's percentage for *Klebsiella pneumoniae*

Country	2020	2021
Austria	2.88	2.76
Belgium	8.75	9.99
Bulgaria	51.14	52.97
Croatia	32.14	32.30
Cyprus	32.37	35.27
Czech Republic	39.80	39.71
Denmark	1.66	1.48
Estonia	5.41	4.93
Finland	3.52	3.18
France	19.77	19.57
Germany	4.65	4.45
Greece	50.07	49.43
Hungary	25.61	24.61
Iceland	0.00	0.00
Ireland	6.42	6.53
Italy	28.98	27.82
Latvia	16.53	13.30
Lithuania	36.07	35.83
Luxembourg	11.15	10.05
Malta	33.18	34.87
Netherlands	4.74	4.99
Norway	4.06	4.35
Poland	44.88	44.20
Portugal	27.23	27.86
Romania	53.94	55.00
Slovakia	43.79	42.16
Slovenia	13.24	12.73
Spain	15.07	16.73
Sweden	3.47	3.74
United Kingdom	6.08	6.50

Forecasted percentage with combined resistance to fluoroquinolones, third generation cephalosporins and aminoglycosides for *Klebsiella pneumoniae* in 2020 and 2021 were presented in Table 4. There were significant inter-country differences, with the southern and eastern Europe's regions reporting greater resistance rates than northern Europe.

Table 5: Forecasted AMR's percentage for *Pseudomonas aeruginosa*

Country	2020	2021
Austria	4.98	4.45
Belgium	4.11	3.62
Bulgaria	34.19	35.51
Croatia	19.72	19.02
Cyprus	12.35	12.48
Czech Republic	17.78	17.50
Denmark	1.05	0.95
Estonia	3.44	3.64
Finland	1.27	1.65
France	8.63	7.06
Germany	5.68	4.39
Greece	35.00	34.86
Hungary	18.27	18.19
Iceland	2.54	2.91
Ireland	4.82	4.37
Italy	11.64	10.08
Latvia	26.22	28.11
Lithuania	11.18	10.80
Luxembourg	1.44	0.81
Malta	2.71	7.80
Netherlands	1.81	1.73
Norway	1.66	1.50
Poland	27.19	28.05
Portugal	15.30	15.02
Romania	51.93	51.79
Slovakia	34.32	38.53
Slovenia	16.51	13.56
Spain	11.92	11.92
Sweden	3.13	3.10
United Kingdom	3.14	3.32

From Table 5, 20 out of 30 countries were predicted with decreasing percentage resistance to piperacillin and tazobactam for *Pseudomonas aeruginosa*, and only ten countries display rising rates of AMR. There were notable intercountry inconsistencies, with the south and east of Europe having higher resistance than the north of Europe.

Table 7 illustrates the forecasted percentage resistance to penicillin for *Streptococcus pneumoniae* in 2020 and 2021. Half of the countries in Europe indicate increasing AMR's percentage, while one country, Greece, can't be forecasted for its AMR's percentage due to lack of data. Excel's linear trendline was used to analyze the data of antimicrobial resistance for every country of each species of the seven microbial. Best fit's line, or trendline, is a graphing term for a curved or non-curved line that represents the overall trend or data's orientation. This technique is commonly utilized to demonstrate data patterns or the association or correlation between two factors throughout a particular period.

From the trendline's tool, R-squared values can also be obtained, and values of 0.8 or higher are considered as a good fit and have lesser residuals. Although higher values of R-squared are commonly preferred, it's fine to use linear models with low R-squared values for certain areas of research that have a higher level of unexplained variance than others. In this analysis, although almost all R-squared values are low and many residuals are observed, the R-squared values obtained are acceptable as values lesser than 50% are common in research attempting to explain microorganisms' behavior. This is because organisms are more difficult to anticipate than physical systems.

Table 6: Forecasted AMR's percentage for Staphylococcus aureus

Country	2020	2021
Austria	4.85	3.97
Belgium	4.10	3.07
Bulgaria	13.77	13.01
Croatia	26.99	27.70
Cyprus	37.73	38.05
Czech Republic	13.15	13.14
Denmark	2.83	1.91
Estonia	2.44	1.99
Finland	2.09	2.10
France	10.10	8.98
Germany	5.50	4.32
Greece	36.75	36.28
Hungary	21.01	20.53
Iceland	4.55	2.66
Ireland	10.71	9.27
Italy	34.30	34.23
Latvia	6.76	6.38
Lithuania	9.12	9.02
Luxembourg	6.36	4.46
Malta	26.45	23.27
Netherlands	1.21	1.57
Norway	1.06	1.06
Poland	14.37	13.31
Portugal	32.92	30.48
Romania	37.47	39.83
Slovakia	15.02	25.48
Slovenia	11.64	8.83
Spain	22.56	22.35
Sweden	2.05	2.22
United Kingdom	3.94	2.68

The predicted percentage resistance to methicillin for *Staphylococcus aureus* for the years 2020 and 2021 was displayed in Table 6. The majority of the countries show a decreasing trend, where the percentage of AMR for 23 out of 30 countries were predicted to fall in 2020 and 2021.

Table 7: Forecasted AMR's percentage for *Streptococcus pneumoniae*

Country	2020	2021
Austria	2.57	2.47
Belgium	0.00	0.00
Bulgaria	0.00	0.00
Croatia	4.02	1.68
Cyprus	18.52	48.16
Czech Republic	0.18	0.11
Denmark	0.49	0.53
Estonia	1.04	1.12
Finland	0.70	0.76
France	2.27	2.59
Germany	0.79	1.32
Greece	-	-
Hungary	3.59	3.72
Iceland	0.00	1.23
Ireland	0.54	0.08
Italy	1.27	0.73
Latvia	1.62	0.96
Lithuania	3.56	9.81
Luxembourg	7.92	8.51
Malta	8.19	8.96
Netherlands	0.63	0.67
Norway	1.53	1.59
Poland	7.41	8.61
Portugal	5.39	5.04
Romania	16.49	14.64
Slovakia	0.00	0.00
Slovenia	0.00	0.00
Spain	16.02	14.69
Sweden	0.00	0.00
United Kingdom	1.53	1.67

*Not enough data for forecasting

Figure 1 and Figure 2 show the predicted level of antimicrobial resistance in 2020 and 2021 for the countries in Europe. The color's indicator for AMR percentage varies from green to dark brown depending on the antimicrobial resistance's level. Both of the figures do not show any significant difference, and just as in the previous years, it can be seen that Europe's south and east regions have greater AMR rates than the north of Europe.

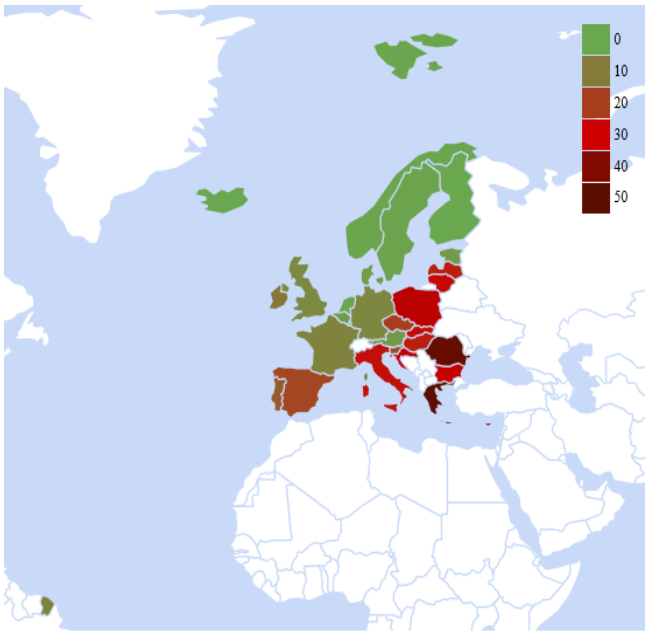

Figure 1: Average forecasted AMR's percentage for all analyzed microbial species in 2020

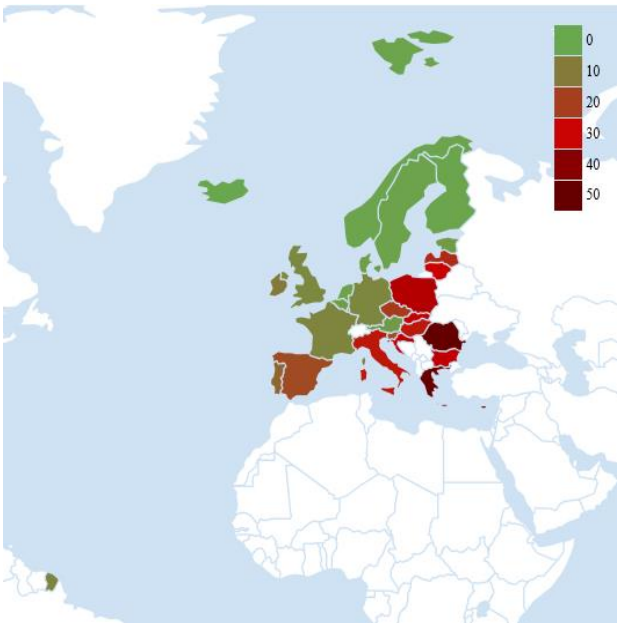

Figure 2: Average forecasted AMR's percentage for all analyzed microbial species in 2021

Based on the data obtained from ECDC and predicted percentages for 2020 and 2021, generally, AMR rates increased from 2019 to 2021. The beginning of the antimicrobial breakthrough occurred in the twentieth century, and antimicrobial resistance is currently a growing problem (Elisa et al., 2020). Ireland's Department of Health also publishes a report in 2021 stating that AMR is on the rise due to the extensive application of various antimicrobials in living organisms throughout the earth. Resistance to antibiotics is worsened by the incorrect and excess usage of antimicrobial medications.

4. Conclusion

The forecast's result of the percentages of antimicrobial resistance for the years 2020 and 2021 can be beneficial and crucial as it can be used to plan for the appropriate actions to overcome any problem that may arise. This is because the effective and efficient treatment of antimicrobial drugs begins with the analysis of AMR in organisms. Although yearly observed data seems adequate to develop a reliable antimicrobial resistance prediction model, the predicted data can still be used as precautions to prepare for what can happen.

Acknowledgement

Thank you Universiti Putra Malaysia.

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