

RESEARCH

Open Access



Exploring the causes of the prevalence of vancomycin-resistant *Enterococcus faecalis*

Yi-Chang Zhao^{1,2,3†}, Zhi-Hua Sun^{3,4†}, Jia-Kai Li^{1,2,3}, Huai-yuan Liu^{3,4}, Hua-Lin Cai^{1,2,3}, Wei Cao^{1,5}, Feng Yu⁴, Bi-Kui Zhang^{1,2,3*} and Miao Yan^{1,2,3*}

Abstract

Background Bacterial drug resistance represents a significant global concern, with vancomycin-resistant *Enterococcus faecalis* posing a particularly grave threat to contemporary healthcare systems. This study aims to reveal the reasons for the prevalence of VRE in China.

Methods This study collected data from the China Antimicrobial Resistance Detection System, China Statistical Yearbook, and China Meteorological Network. The collected data are meticulously organized and subjected to both single-factor and multi-factor analyses. An accurate multiple linear regression model was developed by utilizing this comprehensive dataset.

Results Single-factor analysis revealed significant regional variations in the resistance rate of vancomycin-resistant *Enterococcus faecalis* ($P=0.003$). Specifically, there were noteworthy disparities observed between regions experiencing temperate and monsoon climates ($P=0.029$; $P=0.005$). Furthermore, multi-factor regression analysis demonstrated a negative correlation between the drug resistance rate and both rainfall and rGDP, while a positive correlation was observed with nPI.

Conclusion We successfully established a prediction model for the VRE and found that the resistance rate was low in areas with high rainfall and high per capita economic income, but high in areas with many specialized public health institutions. This is critical for public health strategies and helps policymakers and healthcare practitioners tailor antibiotic resistance approaches to local geography, meteorology, economic conditions.

Keywords Drug resistance rate, Climate, Geographical distribution, Vancomycin-resistant *Enterococcus faecalis*, Mainland China

[†]Yi-Chang Zhao and Zhi-Hua Sun have contributed equally to this work and share first authorship.

*Correspondence:

Bi-Kui Zhang
505995@csu.edu.cn

Miao Yan
yanmiao@csu.edu.cn

¹ Department of Clinical Pharmacy, The Second Xiangya Hospital, Central South University, Changsha, Hunan, People's Republic of China 410011

² Department of Pharmacy, the Second Xiangya Hospital, Central South University, Changsha, Hunan, People's Republic of China 410011

³ International Research Center for Precision Medicine, Transformative Technology and Software Services, Hunan, China

⁴ China Pharmaceutical University, Nanjing, Jiangsu, People's Republic of China 210009

⁵ Department of Medical Laboratory, the Second Xiangya Hospital, Central South University, Changsha, Hunan, People's Republic of China 410011

Introduction

The increasing disease burden posed by antibiotic resistance is emerging as a significant challenge to global public health security [1–3]. The World Health Organization (WHO) estimates that in 2019, bacterial antimicrobial resistance (AMR) directly caused 1.27 million deaths and was linked to a total of 4.95 million deaths worldwide. Projections suggest that AMR could cause up to 10 million deaths annually by 2050, with an economic impact of \$100.2 trillion on global GDP [4, 5]. Enterococci are a group of bacteria that live in the intestines of humans and animals and are usually harmless. However, certain strains of *Enterococcus faecalis* (*E. faecalis*) can cause infections [6–8]. *E. faecalis* is an opportunistic pathogen. Infections caused by pathogenic include urinary tract infections, purulent abdominal infections, sepsis, endocarditis, diarrhea, fever, and other symptoms, which can cause infection in humans through food [9, 10].

Vancomycin is one of the important antibiotics used to treat these infections. However, over time, *E. faecalis* developed resistance to vancomycin [11, 12]. This may be caused by factors such as long-term abuse of antibiotics, irrational use, cross-infection, or genetic mutations [13]. This resistance makes it more difficult to treat the infection. According to the National Health care Safety Network (NHSN), in 2006–2007, approximately 33% of all enterococci were resistant to vancomycin [14]. Additionally, a recent analysis of NHSN data from 2014 reports that if all *Enterococcus* species were analyzed within their genus group, they would be considered the second-most common group of pathogens across all Healthcare-Associated Infections types, and the single-most common group of pathogens among central line-associated bloodstream infections [15]. Besides, vancomycin-resistant *E. faecalis* (VRE) bacteremia remains associated with an increased risk of in-hospital mortality and total hospital length of stay [16]. In the United States, data from the Centers for Disease Control and Prevention (CDC) for the year 2020 indicate that approximately 35,000 deaths occur annually due to infections caused by antibiotic-resistant bacteria or fungi, among which VRE are a common source of hospital-acquired resistant infections [1, 17–19], while in China, *E. faecalis* also exhibits an escalating trend towards antibiotic resistance. In certain regions, the prevalence of VRE ranged from 1.6 to 11% [20–23]. Hospitals and nursing facilities are important sites for the spread of vancomycin-resistant bacteria [24, 25]. Contact between patients, medical equipment, and medical personnel are all possible routes of transmission of vancomycin resistance, and studies have found that vancomycin-resistant enterococci strains are not only present in medical settings, but are also found in the environment [26–28]. Research conducted

by Emameini M et al. in Iran delineated a significant resistance across a diverse array of antibiotics within *E. faecalis*, notably identifying a substantial incidence of gentamicin resistance alongside the widespread presence of the *aac(6)-Ie-aph(2)-Ia* gene [29]. Concurrently, investigations by Xuan Huiyong et al. in China unveiled that *E. faecalis* strains originating from animals demonstrated pronounced resistance to critical antibiotics, signifying potential implications for human health [30]. Further elucidation of the mechanisms underlying resistance gene dissemination was provided by Jahan Musarrat et al., who expounded on the transmission pathways through the food chain, thereby underlining the hazard posed by food-derived *Enterococcus faecalis* as a reservoir for antibiotic resistance [31]. Additionally, Ali Liaqat et al. explicated the influence of environmental factors, such as eutrophication, on the resistance profiles of enterococci, illustrating the environmental dimension of antimicrobial resistance [32]. The work of Makarov Dmitry A et al. further explored the impact of antibiotic utilization practices on the resistance levels among enterococci from farm animals, shedding light on the interconnectedness of antibiotic use and resistance emergence [33]. The emergence of antibiotic resistance in *E. faecalis* strains presents a formidable challenge to global public health, encompassing a broad spectrum of contexts from clinical settings to agricultural domains and aquatic environments. This has raised concerns about the relationship between the environment and vancomycin resistance. China has a large population, a vast territory, and a diverse environment, which makes it very difficult to deal with *E. faecalis* infection.

In light of this, the main purpose of this study is to identify the key factors influencing the distribution and resistance patterns of VRE within China, taking into account the combined effects of environmental factors, levels of economic development, and public health facilities on the formation of VRE resistance. Through in-depth analysis of these key factors, this study aims to fill the current research gaps, providing a scientific basis for the development of targeted surveillance and control strategies, further developing effective prevention and control strategies to reduce the disease burden caused by *E. faecalis*, and ensuring public health safety.

Method

Data collection

The drug resistance rate of VRE was ascertained through meticulous analysis of data sourced from the authoritative China Antimicrobial Resistance Surveillance System (CARSS). Concurrently, data on meteorological factors, economics, medical, and other influencing factors are

collected from the China Statistical Yearbook and the China Meteorological Network.

Data classification

We systematically classified the 31 provinces and cities within China based on their geographical alignment with the Hu Huanyong Line, stratifying them into three distinct categories: those predominantly situated to the northwest of the Hu Line (NW), those intersected by the Hu Line itself (ON), and those primarily located to the southeast of the Hu Line (SE). Moreover, we employed a comprehensive climate typology encompassing six distinct categories: tropical, temperate, subtropical, plateau, continental, and monsoon, to further delineate the climatic diversity across our dataset.

Data analysis

The research findings underwent rigorous statistical analysis using SPSS software version 26.0. To assess data normality, the Shapiro–Wilk test was meticulously employed. We selected either the Mann–Whitney U test or the Kruskal–Wallis H test as appropriate. Additionally, a multivariate regression model was thoughtfully constructed to unravel intricate relationships within our dataset. We set the significance level for our tests at $\alpha=0.05$, with a two-sided P -value less than 0.05 indicating statistical significance.

Results

Distribution of drug resistance rates in different regions

Eight-year cumulative average drug resistance rate were ranked in the top three, featuring Beijing, Jilin, and

Gansu/Guizhou. Notably, Tibet’s average resistance rate remarkably stood at 0 (Fig. 1).

Geographic variations in *E. faecalis* resistance and detection rates

Utilizing the robust Kruskal–Wallis H test, our study unveiled significant variations in the resistance rates of VRE across different regions delineated by the Hu Huanyong Line. Specifically, the northwest region of the Hu Line, encompassing 36 samples, exhibited a median resistance rate of 0.20[0.00,0.48]. In contrast, along the Hu Line itself (with 24 samples), this rate increased to 0.60[0.23,0.80]. Meanwhile, the southeast region of the Hu Line (184 samples) showed a median resistance rate of 0.40[0.20,0.70]. These significant variations ($P=0.003$, Table 1) highlighted the profound impact of geographical location on the resistance dynamics of *E. faecalis*. However, there was no statistical difference in detection rates. The drug resistance rate had the highest value in the northwest of the Hu Huanyong Line, and the detection rate appeared in the southeast (Fig. 2).

Table 1 Differences in drug resistance detection rates under different Hu Huanyong line distributions

Level	N	Resi	N	Dete
Hu Line				
Northwest	36	0.20[0.00,0.48]	6	2.64[2.49,2.86]
On	24	0.60[0.23,0.80]	6	2.75[2.25,3.09]
Southeast	184	0.40[0.20,0.70]	63	2.69[2.33,3.71]
P		0.003		0.908

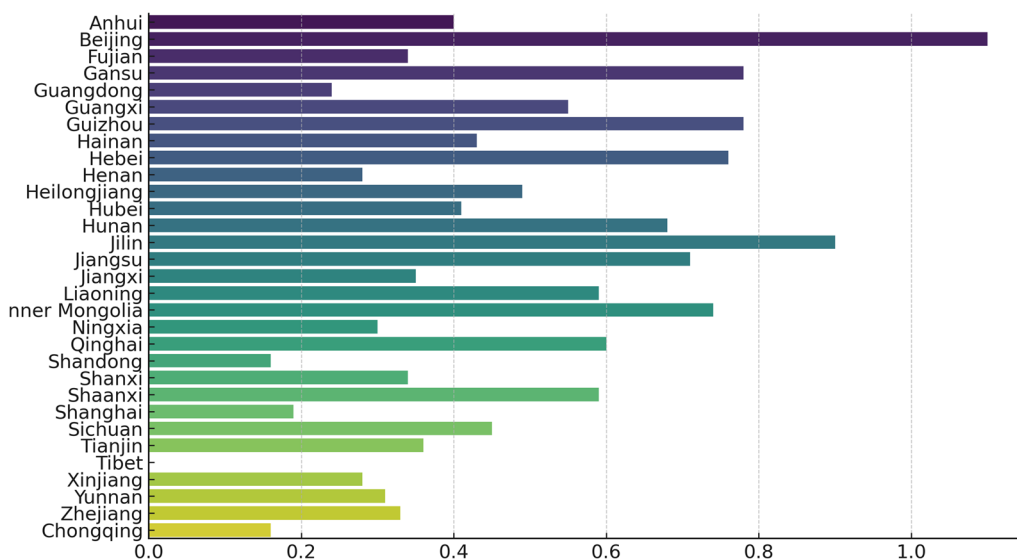


Fig. 1 Average distribution of drug resistance rates in various provinces (cities)

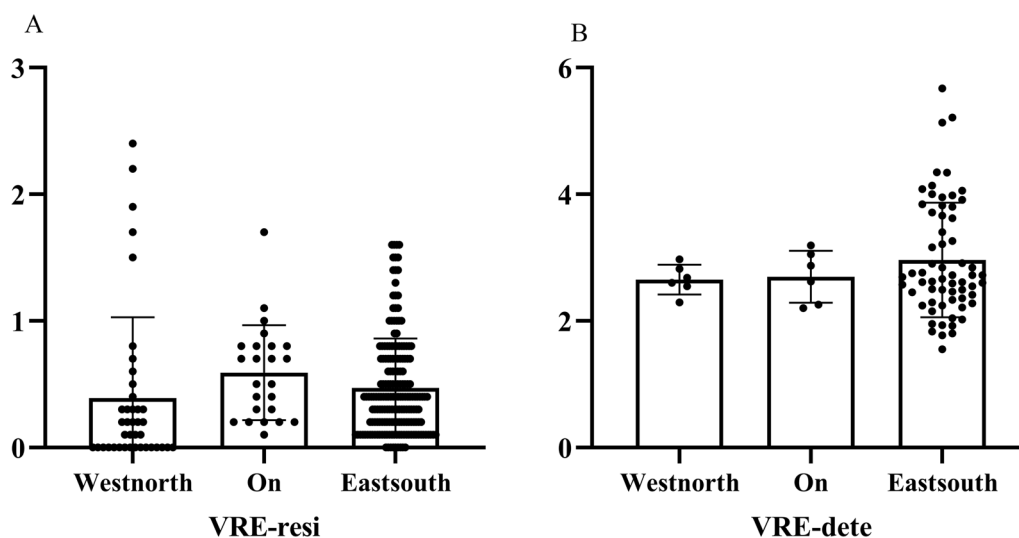


Fig.2 Histogram of the detection rate of drug resistance detection rate under different Hu Huanyong line distributions

Climatic differences in resistance and detection rates of *E. faecalis*

The relationship between resistance and detection rates of VRE under different climate categories was tested using Mann–Whitney U. The results showed that the resistance rate differed between temperate and monsoon climate types ($P=0.029$; $P=0.005$). Detection rates varied in temperate climates ($P=0.032$) (Table 2).

Multivariable regression analysis of meteorological, economic, medical, and other factors

Our analysis illuminated the significance of several variables in relation to VRE. It was found that the drug resistance rate is related to temperature, Tn,Rainfall, nPI, GDP,rGDP, temperate and monsoon (-0.179 to 0.202 , $p<0.05$). Similarly, the detection rate was correlated with Rainfall,H, nHI, nPI, temperate (-0.627 to 0.259 , $p<0.05$) (Table 3, Fig. 3).

Through rigorous stepwise linear regression models, we constructed comprehensive prediction models for drug resistance rates and detection, respectively (Table 4, Table 5).

The formulas were as follows:

$$\text{Resistance rate} := -0.237\text{Rainfall} + 0.201\text{nPI}$$

$$-0.137\text{rGDP} + 0.529$$

$$\text{Detection rate} := -0.582\text{nPI} - 0.200\text{Rainfall} + 3.357$$

Here, Rainfall: average annual rainfall; nPI: number of specialized public health institutions in each province; rGDP: GDP growth rate. The final models for resistance and detection rates of *E. faecalis* present intriguing insights into how environmental and socioeconomic factors influence health outcomes. In the resistance rate

Table 2 Differences in drug resistance detection rates under different climate types

Level	N	Resi	N	Dete
Tropical				
No	228	0.40[0.20,0.70]	72	2.67[2.30,3.57]
Yes	16	0.35[0.13,0.50]	3	
P		0.632		0.871
Temperate				
No	132	0.30[0.10,0.58]	42	2.80[2.54,3.74]
Yes	112	0.40[0.20,0.80]	33	2.55[2.34,2.88]
P		0.029		0.032
Subtropical				
No	116	0.40[0.20,0.80]	33	2.60[2.24,2.91]
Yes	128	0.35[0.10,0.58]	42	2.74[2.48,3.74]
P		0.166		0.084
Plateau				
No	208	0.40[0.20,0.70]	69	2.62[2.29,3.64]
Yes	36	0.30[0.10,0.58]	6	2.92[2.66,3.09]
P		0.112		0.364
Monsoon				
No	20	0.10[0.00,0.48]	0	
Yes	224	0.40[0.20,0.70]	75	2.7[2.3,3.4]
P		0.005		
Mainland				
No	196	0.40[0.10,0.70]	60	2.72[2.42,3.57]
Yes	48	0.35[0.20,0.78]	15	2.60[2.20,2.97]
P		0.296		0.194

model, increased rainfall decreases resistance rates by 0.237 units for each unit increase in rainfall. Additionally, a rise in rGDP correlates with a 0.137 unit decrease in

Table 3 Correlation table between meteorological, economic, hygienic factors and drug resistance detection rate

Variable	Resi		Dete	
	Coefficients	P value	Coefficients	P value
Weather				
Temperature	-0.179**	0.005	0.142	0.224
minTemp12h	-0.141*	0.028	0.181	0.121
maxTemp12h	-0.102	0.113	0.192	0.098
Humidity	-0.054	0.399	0.110	0.349
Rainfall	-0.263**	<0.001	0.241*	0.037
Pressure	0.012	0.853	0.122	0.298
Level of medical care				
H	-0.116	0.070	-0.367**	0.001
nHI	-0.022	0.733	-0.444**	<0.001
nPI	0.202**	0.001	-0.596**	<0.001
Economic situation				
GDP (hundred million)	-0.171**	0.007	-0.065	0.581
iGDP (hundred million)	-0.120	0.061	0.017	0.883
rGDP (%)	-0.160*	0.013	0.098	0.404
Distributions by Hu Line	0.006	0.931	0.122	0.296
Distributions by climate				
Tropical	-0.066	0.305	-0.044	0.708
Temperate	0.145*	0.023	-0.229*	0.048
Subtropical	-0.134*	0.037	0.208	0.073
Plateau	-0.010	0.873	-0.008	0.944
Monsoon	0.087	0.174		
Mainland	0.077	0.228	-0.147	0.207

* $p < 0.05$; ** $p < 0.01$

resistance rates per unit, indicating that economic growth likely supports better healthcare infrastructure, which in turn helps in controlling resistant strains. Conversely, the nPI (coefficient=0.201) directly correlates with increasing resistance rates. In terms of detection rates, an increase in nPI significantly reduces detection capabilities by 0.582 units per unit increase. Moreover, each unit increase in rainfall leads to a 0.200 unit decrease in detection rates, which suggests that conditions during higher rainfall complicate the logistics or operations necessary for detecting VRE infections.

Discussion

Our results indicate that the resistance rate of *E. faecalis* is affected to a certain extent by economic, medical, climatic, factors. VRE is a highly resistant bacterium, and its ability to resist antibiotics makes it a threat to the medical industry and public health [34].

Economic level has a significant impact on the resistance rate of VRE. In low-income countries, health facilities and health care resources may be limited, which may result in inadequate infection control measures and the

spread of VRE more easily. Additionally, low-income populations may be more susceptible to infection because they may not have access to adequate health care, making the spread of VRE in these communities easier [35–37].

The rate of resistance to VRE in medical practice is huge. Medical facilities such as hospitals are the focus of transmission of VRE infections, especially patients who use broad-spectrum antibiotics. Overuse of antibiotics, improper use, and cleanliness of medical facilities can increase VRE resistance rates [38, 39]. In addition, improper implementation of hand hygiene and infection control measures can also aggravate the spread of VRE [40].

Climate change can affect the spread of VRE. Climatic factors such as temperature and humidity can affect the survival and spread of VRE in the environment [41]. High temperatures and humidity may help VRE survive in the environment longer, increasing the chance of spread. In addition, climate change may trigger extreme weather events, leading to outbreaks in densely populated areas and increasing the risk of VRE transmission.

Demographic factors such as population density, mobility, and health status also have an impact on VRE

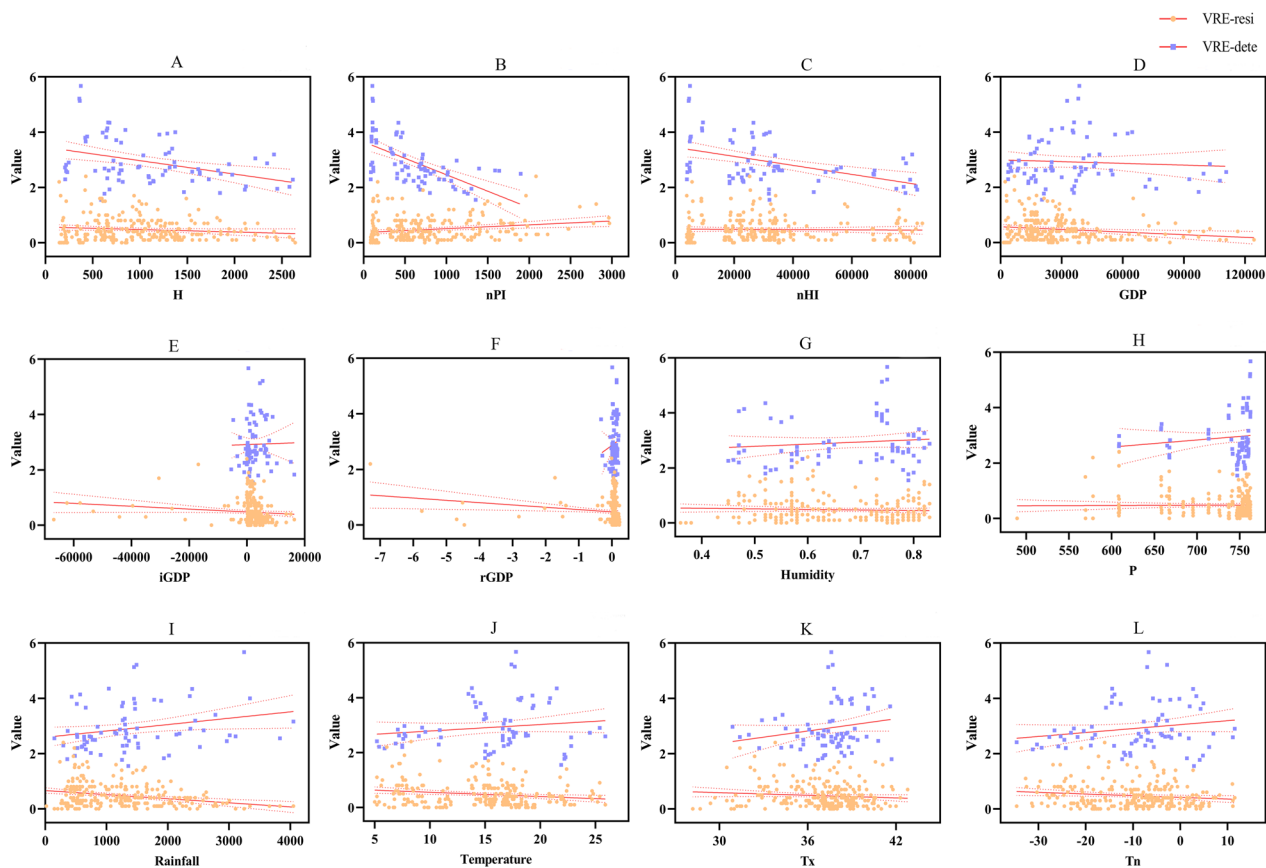


Fig. 3 Correlation combination chart. **A** Correlation between the number of hospitals in each province (H) and drug resistance rate; **B** correlation between the number of public health professional institutions in each province (nPI) and drug resistance rate; **C** correlation between the number of primary health care institutions (nHI) and drug resistance rates in each province; **D** correlation between gross national product (GDP) and drug resistance rate; **E** correlation between gross domestic product growth quantity (iGDP) and drug resistance rate; **F** correlation between GDP growth rate (rGDP) and drug resistance rate; **G** correlation between relative humidity and drug resistance rate; **H** correlation between average air pressure (P) and drug resistance rate; **I** correlation between average rainfall and drug resistance rate; **J** correlation between average temperature and drug resistance rate; **K** correlation between maximum temperature (Tx) and drug resistance rate; **L** correlation between minimum temperature (Tn) and drug resistance rate

Table 4 Resistance rate regression linear model

Variable	Unstandardized coefficients		Standardized coefficients	t	P value	VIF
	B	Std. error				
Rainfall	-1.33×10^{-4}	3.4×10^{-5}	-0.237	-3.892	<0.001	1.021
nPI	1.37×10^{-4}	4.1×10^{-5}	0.201	3.319	0.001	1.004
rGDP	-0.071	0.032	-0.137	-2.242	0.026	1.022
Constant	0.529	0.061		8.678	<0.001	
	F	11.430				
	R ²	0.125		Adjusted R ²	0.114	

resistance rates. Areas with high population density are more likely to spread infected pathogens, including VRE. Population mobility (such as international travel) can spread VRE to different regions and increase the spread

of drug-resistant strains. People in poor health are more susceptible to infection, aggravating the spread of VRE.

When considering these factors comprehensively, we can see that they are interconnected. For example,

Table 5 Detection rate regression linear model

Variable	Unstandardized coefficients		Standardized coefficients	t	P value	VIF
	B	Std. error				
nPI	-0.001	1.83×10^{-4}	-0.582	-6.332	< 0.001	1.005
Rainfall	1.92×10^{-4}	8.8×10^{-5}	0.200	2.179	0.033	1.005
Constant	3.357	0.191		17.602	< 0.001	
	F	23.502				
	R ²	0.395		Adjusted R ²	0.378	

medical facilities in low-income areas may be poorer, which makes VRE more likely to spread. Climate change may cause natural disasters and further exacerbate the spread of infections. Therefore, solving the problem of VRE resistance requires comprehensive efforts from many aspects, including improving medical facilities, strengthening antibiotic management, improving medical standards, strengthening infection control measures, and responding to climate change. This will help reduce the spread of VRE and safeguard public health.

The study has limitations.

Due to the retrospective analysis of data, some information is missing. We will design more prospective experiments to verify this in the future. At the same time, the scope of research is expanded beyond China.

Conclusion

We successfully established a prediction model for the VRE and found that the resistance rate was low in areas with high rainfall and high per capita economic income, but high in areas with many specialized public health institutions. This is critical for public health strategies and helps policymakers and healthcare practitioners tailor antibiotic resistance approaches to local geography, meteorology, and economic conditions.

Data sharing statement

The datasets analyzed during the current study are publicly available at the China Antimicrobial Resistance Surveillance System (CARSS) ([http:// www.carss.cn/](http://www.carss.cn/)), and the National Bureau of Statistics (<http://www.stats.gov.cn/>).

Abbreviations

Resi	Vancomycin-resistant <i>E. faecalis</i> resistance rate
Dete	Vancomycin-resistant <i>E. faecalis</i> detection rate
Temperature / T	Atmospheric temperature 2 meters above the ground
minTemp12h / Tn	The lowest temperature in the past period
maxTemp12h / Tm	The highest temperature in the past period
H	Number of hospitals in each province
nHI	Number of primary health care institutions in each province
nPI	Number of specialized public health institutions in each province
GDP	Gross national product

iGDP	Gross domestic product growth quantity
rGDP	GDP growth rate
Humidity	Relative humidity 2 m above the ground
Rainfall	Average annual rainfall
Pressure	Weather station horizontal air pressure

Acknowledgements

The authors would like to thank all individuals who participated in this study.

Author contributions

Conceptualization, BKZ, MY, YCZ; methodology, YCZ and ZHS; software, JKL and HYL; validation, BKZ, MY, YCZ and ZHS; formal analysis, YCZ and ZHS; investigation, YCZ, WC and YCZ; resources, YCZ; data curation, ZHS; writing—original draft preparation, ZHS; writing—review and editing, MY, YCZ, HLC and BKZ; visualization, YCZ; supervision, MY, HLC, BKZ and FY; project administration, HLC, YF and MY; funding acquisition, MY. All authors have read and agreed to the published version of the manuscript.

Funding

This research was funded by the Hunan Medical Association [NO. HMA202001002] and the Health Commission of Hunan Provincial [NO. 202113012480]. It was also supported by the International Research Center for Precision Medicine, Transformative Technology, and Software Services, Hunan, China.

Declarations

Competing interests

All authors declare no competing interests.

Received: 18 February 2024 Accepted: 28 April 2024

Published online: 05 May 2024

References

- G. Atlanta (2019) Antibiotic Resistance Threats in the United States, 2019 (2019 AR Threats Report). Centers for Disease Control and Prevention-<https://www.cdc.gov/drugresistance/biggest-threats.html> <https://doi.org/10.15620/cdc:82532>
- Huemer M, Mairpady S, Brugger Shambat SD, Zinkernagel AS (2020) Antibiotic resistance and persistence—Implications for human health and treatment perspectives. EMBO Rep 21(12):e51034. <https://doi.org/10.15252/embr.202051034>
- W.H. Organisation (2023) Antimicrobial resistance. <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>
- D.M.A.D.L.A. DONNA SHALALA (2023) Antimicrobial resistance will be worse than COVID — we have to act now. <https://thehill.com/opinion/healthcare/4052215-antimicrobial-resistance-will-be-worse-than-covid-we-have-to-act-now>.
- GBD 2019 Antimicrobial Resistance Collaborators (2022) Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet (London, England) 400(10369):2221–2248. [https://doi.org/10.1016/s0140-6736\(22\)02185-7](https://doi.org/10.1016/s0140-6736(22)02185-7)

6. Miller WR, Murray BE, Rice LB, Arias CA (2020) Resistance in vancomycin-resistant enterococci. *Infect Dis Clin North Am* 34(4):751–771. <https://doi.org/10.1016/j.idc.2020.08.004>
7. Fiore E, Van Tyne D, Gilmore MS (2019) Pathogenicity of enterococci. *Microbiol Spectr*. <https://doi.org/10.1128/microbiolspec.GPP3-0053-2018>
8. Reyes K, Bardossy AC, Zervos M (2016) Vancomycin-resistant enterococci: epidemiology, infection prevention, and control. *Infect Dis Clin North Am* 30(4):953–965. <https://doi.org/10.1016/j.idc.2016.07.009>
9. Fernández-Hidalgo N, Escolà-Vergé L, Pericàs JM (2020) Enterococcus faecalis endocarditis: what's next? *Future Microbiol*. <https://doi.org/10.2217/fmb-2019-0247>
10. Kao PHN, Kline KA (2019) Dr. Jekyll and Mr. Hyde: How enterococcus faecalis subverts the host immune response to cause infection. *J Mol Biol* 431(16):2932–2945. <https://doi.org/10.1016/j.jmb.2019.05.030>
11. Wilhelm MP (1991) Vancomycin. *Mayo Clin Proc* 66(11):1165–1170. [https://doi.org/10.1016/s0025-6196\(12\)65799-1](https://doi.org/10.1016/s0025-6196(12)65799-1)
12. Mühlberg E, Umstätter F, Kleist C, Domhan C, Mier W, Uhl P (2020) Renaissance of vancomycin: approaches for breaking antibiotic resistance in multidrug-resistant bacteria. *Can J Microbiol* 66(1):11–16. <https://doi.org/10.1139/cjm-2019-0309>
13. Peterson E, Kaur P (2018) Antibiotic resistance mechanisms in bacteria: relationships between resistance determinants of antibiotic producers, environmental bacteria, and clinical pathogens. *Front Microbiol*. <https://doi.org/10.3389/fmicb.2018.02928>
14. Hidron AI, Edwards JR, Patel J, Horan TC, Sievert DM, Pollock DA, Fridkin SK (2008) NHSN annual update: antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National healthcare safety network at the centers for disease control and prevention, 2006–2007. *Infect Control Hosp Epidemiol* 29(11):996–1011. <https://doi.org/10.1086/591861>
15. Weiner LM, Webb AK, Limbago B, Dudeck MA, Patel J, Kallen AJ, Edwards JR, Sievert DM (2016) Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the national healthcare safety network at the centers for disease control and prevention, 2011–2014. *Infect Control Hosp Epidemiol* 37(11):1288–1301. <https://doi.org/10.1017/ice.2016.174>
16. Prematunge C, MacDougall C, Johnstone J, Adomako K, Lam F, Robertson J, Garber G (2016) VRE and VSE bacteremia outcomes in the era of effective VRE therapy: a systematic review and meta-analysis. *Infect Control Hosp Epidemiol* 37(1):26–35. <https://doi.org/10.1017/ice.2015.228>
17. F.D.o.H.D.o.D.C.H. Protection (2020) Guidelines for Prevention and Control of Infection Due to Antibiotic Resistant Organisms. <https://www.floridahealth.gov/diseases-and-conditions/health-care-associated-infections>.
18. Li X, Song L, Zhu S, Xiao Y, Huang Y, Hua Y, Chu Q, Ren Z (2019) Two Strains of lactobacilli effectively decrease the colonization of VRE in a mouse model. *Front cell infect microbiol*. <https://doi.org/10.3389/fcimb.2019.00006>
19. Zhu S, Li X, Song L, Huang Y, Xiao Y, Chu Q, Kang Y, Duan S, Wu D, Ren Z (2021) Stachyose inhibits vancomycin-resistant enterococcus colonization and affects gut microbiota in mice. *Microb patho*. <https://doi.org/10.1016/j.micpath.2021.105094>
20. Liling H, Liu V, Xiaoyan M, Lin F, Ying D, Ge E, Yalin B, Wanjuan D, Guangbo Z (2021) Distribution of pathogenic bacteria and drug resistance analysis in critical care medicine, 2016–2019. *Chin Exp Diagn* 25(12):1794–1799
21. Wee L, Bo Z, Yuan L, Feng X, Xiuzhen Z, Yunjian H, Yufen J, Zhidong H, Jianhong Z, Shiyang P, Huayin L, Yunsong Y, Yan L, Liu W, Lau A, Cherry F, Zhiyong L, Xiuli X, Fengyan P, Ling M, Ping J, Jin T, Huiqun F, Radium Z, Shan W, Jia Z, Qing W, Liu YY (2022) China bacterial drug resistance monitoring study 2019–2020 gram-positive bacteria monitoring report. *Chin J Clin Pharmacol* 38(04):369–384. <https://doi.org/10.13699/j.cnki.1001-6821.2022.04.018>
22. Wee L, Bo Z, Feng X, Xiuzhen Z, Yunjian H, Yufen J, Jianhong Z, Shiyang P, Wei G, Feng Z, Yunsong Y, Xuan C, Liu W, Liu A, Cherry F, Jiayun L, Fengyan P, Ling M, Ping J, Jin T, Kai X, Radium Z, Cunwei C, Heping X, Shan W, Lanqing C, Jia Z, Liu YY (2023) China bacterial resistance surveillance study (CARST) 2021–2022 gram-positive bacteria surveillance report. *Chin J Clin Pharmacol* 39(23):3509–3524. <https://doi.org/10.13699/j.cnki.1001-6821.2023.23.036>
23. Kaki R, Yu Y, O'Neill C, Lee C, Mertz D (2014) Vancomycin-resistant enterococcus (VRE) transmission and risk factors in contacts of VRE carriers. *Infect Control Hosp Epidemiol* 35(7):876–879. <https://doi.org/10.1086/676864>
24. Fernando SA, Gray TJ, Gottlieb T (2017) Healthcare-acquired infections: prevention strategies. *Intern Med J* 47(12):1341–1351. <https://doi.org/10.1111/imj.13642>
25. Mitchell BG, Hall L, White N, Barnett AG, Halton K, Paterson DL, Riley TV, Gardner A, Page K, Farrington A, Gericke CA, Graves N (2019) An environmental cleaning bundle and health-care-associated infections in hospitals (REACH): a multicentre, randomised trial. *Lancet Infect Dis* 19(4):410–418. [https://doi.org/10.1016/s1473-3099\(18\)30714-x](https://doi.org/10.1016/s1473-3099(18)30714-x)
26. Messi P, Guerrieri E, de Niederhäusern S, Sabia C, Bondi M (2006) Vancomycin-resistant enterococci (VRE) in meat and environmental samples. *Int J Food Microbiol* 107(2):218–222. <https://doi.org/10.1016/j.jifoodmicro.2005.08.026>
27. Berglund B (2015) Environmental dissemination of antibiotic resistance genes and correlation to anthropogenic contamination with antibiotics. *Infect Ecol Epidemiol*. <https://doi.org/10.3402/iee.v5.28564>
28. Dungan RS, Bjorneberg DL (2021) Antimicrobial resistance in escherichia coli and enterococcal isolates from irrigation return flows in a high-desert watershed. *Front Microbiol*. <https://doi.org/10.3389/fmicb.2021.660697>
29. Emameini M, Khoramian B, Jabalameli F, Beigverdi R, Asadollahi K, Taherikalani M, Lari AR (2016) Prevalence of high-level gentamicin-resistant Enterococcus faecalis and Enterococcus faecium in an Iranian hospital. *J Prev Med Hyg* 57(4):E197–e200
30. Xuan H, Yao X, Pan R, Gao Y, Wei J, Shao D, Liu K, Li Z, Qiu Y, Ma Z, Li B, Xia L (2021) Antimicrobial resistance in Enterococcus faecium and Enterococcus faecalis isolates of swine origin from eighteen provinces in China. *J Vet Med Sci* 83(12):1952–1958. <https://doi.org/10.1292/jvms.21-0413>
31. Jahan M, Zhanel GG, Sparling R, Holley RA (2015) Horizontal transfer of antibiotic resistance from Enterococcus faecium of fermented meat origin to clinical isolates of E. faecium and Enterococcus faecalis. *Int J Food Microbiol*. <https://doi.org/10.1016/j.jifoodmicro.2015.01.013>
32. Ali L, Wang YQ, Zhang J, Ajmal M, Xiao Z, Wu J, Chen JL, Yu D (2016) Nutrient-induced antibiotic resistance in Enterococcus faecalis in the eutrophic environment. *J Global Antimicrob Resist*. <https://doi.org/10.1016/j.jgar.2016.07.014>
33. Makarov DA, Ivanova OE, Pomazkova AV, Egoreva MA, Prasolova OV, Lenev SV, Gergel MA, Bukova NK, Karabanov SY (2022) Antimicrobial resistance of commensal Enterococcus faecalis and Enterococcus faecium from food-producing animals in Russia. *Veterinary world* 15(3):611–621. <https://doi.org/10.14202/vetworld.2022.611-621>
34. Huskins WC (2007) Interventions to prevent transmission of antimicrobial-resistant bacteria in the intensive care unit. *Curr Opin Crit Care* 13(5):572–577. <https://doi.org/10.1097/MCC.0b013e3282efc30e>
35. Fishman N (2006) Antimicrobial stewardship. *Am J Med*. <https://doi.org/10.1016/j.amjmed.2006.04.003>
36. Goff DA (2011) Antimicrobial stewardship: bridging the gap between quality care and cost. *Curr Opin Infect Dis*. <https://doi.org/10.1097/01.qco.0000093484.17894.05>
37. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, Goossens H, Laxminarayan R (2018) Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci U S A* 115(15):E3463–e3470. <https://doi.org/10.1073/pnas.1717295115>
38. Davis E, Hicks L, Ali I, Salzman E, Wang J, Snitkin E, Gibson K, Cassone M, Mody L, Foxman B (2020) Epidemiology of vancomycin-resistant enterococcus faecium and enterococcus faecalis colonization in nursing facilities. *Open Forum Infect Dis*. <https://doi.org/10.1093/ofid/ofz553>
39. Linden PK (2002) Treatment options for vancomycin-resistant enterococcal infections. *Drugs* 62(3):425–441. <https://doi.org/10.2165/00003495-200262030-00002>
40. Farsi S, Salama I, Escalante-Alderete E, Cervantes J (2023) multidrug-resistant enterococcal infection in surgical patients what surgeons need to know. *Microorganisms*. <https://doi.org/10.3390/microorganisms11020238>
41. Blanch AR, Caplin JL, Iversen A, Kühn I, Manero A, Taylor HD, Vilanova X (2003) Comparison of enterococcal populations related to urban and hospital wastewater in various climatic and geographic European regions. *J Appl Microbiol* 94(6):994–1002. <https://doi.org/10.1046/j.1365-2672.2003.01919.x>

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.