Infection and Drug Resistance

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ORIGINAL RESEARCH

Impact of Antimicrobial Stewardship and Infection Prevention and Control Programmes on Antibiotic Usage and *A. baumannii* resistance: A 2016–2023 Multicentre Prospective Study

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Objective: This study assesses the efficacy of antimicrobial stewardship (AMS) and infection prevention and control programmes (IPCP) in guiding the use of antibiotics and the control of *A. baumannii* (AB) resistance at multiple medical centres.

Methods: We evaluated the effectiveness of the policy on antibiotic consumption and AB resistance by determining the relationship between the defined daily doses (DDD) for antibiotics – or alcohol-based hand gel (ABHG) consumption – and the incidence of carbapenem-resistant AB (CR-AB), multidrug-resistant AB (MDR-AB) and extensively drug-resistant AB (XDR-AB) at two medical centers from 2016–2023.

Results: In total, 4057 AB isolates were collected; 64.95% of the AB isolates were CR, 59.48% were MDR and 1.41% were XDR. The major categories of the AB clinical strains collected were extracted primarily from patients' respiratory tract specimens, the ICU wards and patients over 65 years old, accounting for 76.98%, 67.98% and 63.72%, respectively. The incidence of CR-AB, MDR-AB and XDR-AB based on AMS and IPCP measures ranged from 70.04% to 58.42% (P<0.0001), 64.26% to 52.16% (P<0.0001) and 2.27% to 0.60% (P=0.0167), respectively. The DDD of total antibiotics administered per 1000 patient days (PD) decreased significantly from 51.25±4.22 to 40.92±2.48 (P<0.0001), and ABHG consumption per 1000 PD increased significantly from 5.25 ±0.98 to 13.51±5.12 (P<0.0001). We found a statistically significant positive correlation between the DDD of antibiotic consumption and the incidence of CR-AB, MDR-AB and XDR-AB (r=0.9755 and P<0.0001, r=0.9571 and P=0.0002, r=0.9230 and p=0.0011, respectively). In addition, a statistically negative correlation was found between ABHG consumption and the incidence of CR-AB, MDR-AB, and XDR-AB (r=−0.9473 and P=0.0004, r=−0.9123 and P=0.0016, r=−0.9138 and P=0.0015, respectively).

Conclusion: Comprehensive AMS and IPCP intervention measures can successfully achieve a sustained amelioration in the resistance and transmission of CR-AB, MDR-AB and XDR-AB, which are regarding potential applicability to other hospitals.

Keywords: *Acinetobacter baumannii*, antibiotic resistance, antimicrobial stewardship, infection prevention and control programmes

Introduction

Antibiotics have played a major role in the treatment of critically infected patients, saving many lives. However, research findings have shown that the overuse, misuse and unreasonable use of antibacterial drugs lead to the emergence of antibiotic-resistant bacterial strains, which have been implicated in severely adverse patient outcomes.[1] The World Health Organization (WHO) reports that the proportion of hospital inpatients receiving antibiotic prescriptions in China (70%) was higher than the global average of 30% in 2011.[2] The findings of certain studies show that the incidence rate of antimicrobial-resistant *A.baumannii* (AB) in China has increased over the last two decades.[3] Data from the China Antimicrobial Surveillance Network (CHINET) indicate that the proportion of *A. baumannii* strains that are resistant to

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meropenem and imipenem increased from 30.1% and 39.0% in 2005 to 71.5% and 72.3%, respectively, in 2021.[4] *A. baumannii* is one of the most significant nosocomial opportunistic infection pathogens. It is listed as a critical priority pathogen by the WHO and is implicated in hospital-acquired infections and outbreaks, especially in critically ill patients.[5] Irrational use of antibiotics is a major cause of the growing antimicrobial resistance of *A.baumannii*,[5,6] and multidrug-resistant (MDR), carbapenem-resistant (CR) and, especially, extensively drug-resistant (XDR) *A. baumannii* are major public health problems.[6,7]

In 2011, the National Health and Family Planning Commission of the People's Republic of China issued nationwide guidelines for antimicrobial stewardship (AMS) to promote the rational use of antibiotics, reduce antibiotic use and reverse bacterial resistance.[8] Furthermore, the National Health and Family Planning Commission concurrently published the national Technical Guidelines for the Prevention and Control of Hospital Infection Caused by Multidrug-Resistant Bacteria.[7] AMS plays an important role in reducing the consumption of antibiotics and lessening antibiotic resistance in hospitals and is – to a certain extent – positively correlated with antibiotic consumption.[6–9] However, some previous studies have shown that AMS alone has had only limited effects on the control of *A.baumannii* resistance in hospitals, as the incidence of multidrug-resistant *A.baumannii*(MDR-AB) still remains high, underscoring the urgent need for highly effective infection prevention and control programmes (IPCPs) to reduce the transmission of resistant *A.baumannii* in hospitals.[3,7] Furthermore, one study found that both IPCPs and AMS are essential for controlling MDR-AB infection rates.[3] The findings of another set of studies indicate that combined AMS and IPCP interventions can produce a durative reduction in the spread and resistance rates of CR-AB in intensive care units (ICU).[5,10] However, the aforementioned studies are all single-centre studies; thus, further evaluation via multicentre studies is needed to determine the applicability of AMS and IPCP measures; however, multicentre research data is extremely limited in China. In addition, there are only a few studies on the long-term effects of AMS and IPCPs in China; hence, whether AMS and IPCP measures can achieve lasting effects still needs to be evaluated continuously.

Therefore, this prospective study assesses the efficacy of AMS and IPCPs in guiding the use of antimicrobial agents and the control of AB resistance at the First Affiliated Hospital of Hainan Medical University and the Fourth Affiliated Hospital of Harbin Medical University over an eight-year period, with the objective of uncovering and sharing successful management experiences and strategies. This study was conducted from January 2016 to December 2023 at the two medical centres.

Methods

The First Affiliated Hospital of Hainan Medical University is a 1500-bed teaching hospital located in the southernmost province of China. AMS and IPCP measures have been implemented at this hospital early, with strict adherence to the IPCP since 2014. The Fourth Affiliated Hospital of Harbin Medical University is a 3200-bed teaching hospital located in the northernmost metropolis in China. AMS and an IPCP have been implemented at this hospital early; the IPCP has been in strict implementation since 2013.

AB Isolates and Antimicrobial Sensitivity and Resistance

In this study, AB was isolated from the patient's clinical case and identified infection from clinician. Clinical samples were obtained from patients with various AB infections, including blood, urinary tract, wound surface(postoperative, pressure sores, ulcers) and respiratory tract infections(BAL, sputum), other samples(bile, abdominal secretions). The AB isolates were identified using a double identification method that employed a VITEK II automated system (bioMerieux, Marcy-l'Étoile, France). Confirmation tests were conducted using Etest assays alongside the Kirby–Bauer method. Antimicrobial susceptibility testing was performed using a VITEK II automated system (bioMerieux, Marcy-l'Étoile, France). The strains were tested for seven types of antibiotic agents: β-lactam–β-lactamase inhibitor combinations (piperacillin–tazobactam and cefoperazone–sulbactam), aminoglycosides (gentamicin and amikacin), polypeptides (colistin), cephalosporins (ceftazidime), carbapenems (imipenem and meropenem), fluoroquinolone (ciprofloxacin) and tetracyclines (tigecycline). Colistin resistance was confirmed using broth microdilution (ComASP Colistin 0.25–16 μg/mL, Diagnostic Liofilchem Inc., Zona Industriale, Roseto degli Abruzzi, Italy), which was performed and interpreted as directed by the manufacturer. The broth microdilution method was used to determine the minimum inhibitory concentrations (MICs) to evaluate in vitro activity.[7]

The MIC test was performed in accordance with the guidelines of the Clinical and Laboratory Standards Institute (CLSI).[4] The interpretive standards for the MICs of the antibiotics were determined using CLSI breakpoints.[7] Clinical strains were defined as *resistant, intermediate* or *susceptible* to antimicrobial drugs.

Clinical isolates of *A.baumannii* were classified as CR-AB if resistant to imipenem or meropenem, while classification as MDR-AB or XDR-AB was based on the European Committee on Antimicrobial Susceptibility Testing (EUCAST) expert rules.[7] As previously mentioned,[11] MDR was defined as non-susceptibility to more than one agent in three or more classes of antibiotics and XDR was defined as non-susceptibility to one or more agents in all but one or two classes.

Infection Prevention and Control Programmes (IPCPs)

Based on the Technical Guidelines for the Prevention and Control of Hospital Infection Caused by Multidrug-Resistant Bacteria issued by the National Health and Family Planning Commission,[7] comprehensive IPCPs are being implemented at the First Affiliated Hospital of Hainan Medical University and the Fourth Affiliated Hospital of Harbin Medical University, as follows:

(1) *IPCP team*. A professional IPCP committee was established in each hospital and is the highest leadership body in the organisation. In addition, an IPCP department was founded to formulate specific infection control measures directly. The IPCP department of each hospital has a designated infection control doctor and nurse. The infection control doctor and nurse of the IPCP department are responsible for executing the stipulated measures.

(2) *Education, training, assessment and improvement plan for hand hygiene*. Alcohol-based hand gels (ABHGs) with a concentration of 70% ethanol were installed at the door and at the bedside of each patient's room. ABHGs are also available at all bedsides in the ICUs to promote fundamental hygiene. Staff education and training on hand hygiene and the principles of nosocomial transmission of CR-AB, MDR-AB and XDR-AB were conducted monthly. Education of the medical personnel and assessment of items meant to increase hand hygiene adherence were also conducted, with medical personnel education on hand hygiene and the principles of the nosocomial spread of CR-AB, MDR-AB and XDR-AB conducted monthly. Training on hand hygiene included all five evidence-based key moments per WHO recommendations.[12] Bacterial cultures and isolates from the hands of medical personnel who cared for infected patients were analysed at three time points during the patients' ICU stay. When necessary, bacterial culture and isolation from the environment were analysed to assess cross-infection and transmission routes. Each training session included feedback reports on existing problems regarding infection control to improve medical personnel practices in various departments and in the ICU. During these sessions, solutions and measures for improvement were discussed in detail. All the aforementioned measures were also applied to the cleaning staff at both hospitals. The infection control nurses directly observed and improved the operational procedures of the clean teams. Consistent with the literature,[7,13] ABHG consumption was defined as the number of litres per 1000 patient days (PD) and was measured as a standard value in adherence to IPCP rules.

(3) Introduction *of practices aimed at reducing environmental contamination outside the ICU*. These included practices such as restricting the transport of patients unless urgently required. The cleaning and disinfection of the medical equipment were implemented promptly after use on an infected patient. Healthcare workers and visitors were restricted from the ICU to prevent secondary infections. Nurses were tasked with monitoring healthcare workers and visitors during the day. Manual cleaning and disinfection operations were performed on the ICU, followed by air disinfection with a 1% hydrogen peroxide solution after the patient was discharged. Furthermore, the environmental sites of hospital were cleaned and the results recorded daily. Illustrations of guidelines for contact with and the seclusion of patients infected with CR-AB, MDR-AB and XDR-AB were provided, and the illustrations were not removed until the elimination of CR-AB, MDR-AB and XDR-AB infections or colonisation was achieved. Positive surveillance for CR-AB, MDR-AB and XDR-AB infection and colonisation was performed routinely.

(4) *Environmental cleaning*. An environmental cleaning programme was established; hypochlorite-based disinfectants were used. The doctors' offices were equipped with ultraviolet disinfection equipment, which allowed for one hour of daily exposure. A disinfection record form was compulsorily filled out and signed by the clean staff after performing a sterilisation procedure twice daily; the compliance rate was analysed weekly. The rooms and bedsides of patients with CR-AB, MDR-AB and XDR-AB infections underwent terminal cleaning after the patient was discharged. Hand cultures

from ICU medical personnel were obtained – and the culture results assessed – weekly. ICU environmental cultures were performed monthly for different sites in the ICU room, including blood pressure cuffs, infusion pumps, stethoscopes, suctioning equipment, washbasins, computer keyboards, surrounding curtains, bedrails, bedside tables, respiratory equipment ventilator tubes and monitors.

Antimicrobial Stewardship (AMS)

To evaluate the impact of the AMS strategy at the two hospitals based on the nationwide guidelines for AMS stipulated by the National Health and Family Planning Commission,[7] we utilised the following quantitative metrics to measure the consumption of antimicrobial drugs: defined daily dose (DDD) and a detailed calculation method elucidated in two previous studies.[2,7] Data on antimicrobial drug consumption were obtained from the pharmacy departments of the hospitals. Due to the comprehensive AMS measures implemented at the First Affiliated Hospital of Hainan Medical University and the Fourth Affiliated Hospital of Harbin Medical University, antibiotic usage was strictly restricted during the study period, and clinicians were mandatorily trained and appraised before they were granted various levels of antimicrobial prescribing authorisation annually. Based on the AMS guidelines,[2,7] antibacterial drug classification management was performed stringently, with antibiotics classified as follows: special use, restricted use and non-restricted use. Various levels of antibiotic prescription privileges were assigned to all physicians: only chief physicians can prescribe special-use antibiotics (eg, colistin); attending physicians can prescribe non-restricted-use antibiotics and restricted-use antibiotics(eg, piperacillin/tazobactam); while resident physicians can only prescribe non-restricted-use antibiotics, such as first-generation cephalosporins.

Clinical pharmacists retrospectively estimated antibiotic prescriptions for inpatients monthly. Inappropriate and irrational prescriptions were captured in a monthly antibiotic monitoring report that was made available to all medical personnel. Non-compliant doctors were fined according to the severity and frequency of inappropriate and irrational prescriptions. Clinical pharmacists instantaneously monitored antibiotic prescriptions for outpatients and contacted the prescribing doctor to modify inappropriate and irrational prescriptions.

Data Analysis

The data analyses in this study were performed using the Statistical Package for the Social Sciences (SPSS) software, version 19.0. A chi-square test was performed to contrast the categorical variables, while a one-way analysis of variance (ANOVA) was performed to analyse the continuous variables. A *t* test was used to contrast the variations in ABHG consumption and DDD of antibiotic consumption. The relationship between CR-AB, MDR-AB and XDR-AB incidence rates vis-à-vis ABHG consumption and DDD of antibiotic consumption were determined using a Pearson correlation coefficient. All tests were two-tailed, and $P < 0.05$ was considered statistically significant.

Results

Between January 2016 and December 2023, a total of 4057 AB clinical isolates were collected for this study. Detailed data on the two hospitals are presented in Figure 1. Overall, 64.95% (2635) of the AB clinical isolates collected were CR-AB, 59.48% (2413) were MDR-AB and 1.41% (57) were XDR-AB. The number of AB clinical isolates obtained annually varied between 415 and 671.

Table 1 shows that the AB clinical strains were primarily separated from the patient's respiratory tract specimen, ICU ward, and patients over 65 years old, accounting for 76.98% (3123), 67.98% (2758), and 63.72% (2585), respectively.

Data on the antimicrobial susceptibility and resistance of the AB clinical isolates obtained from patients at the two hospitals are presented in Table 2. One hundred percent and 99.80% of the isolated AB strains exhibited susceptibility to colistin and tigecycline in vitro, respectively. The data on the isolated AB strains indicate non-resistance to colistin, while 0.20% of the isolated AB strains exhibited resistance to tigecycline in vitro. Therefore, the data indicate that colistin and tigecycline were the most effective antibiotics assessed. In contrast, 5.40% and 9.40% of the isolated AB strains exhibited susceptibility to ceftazidime and ciprofloxacin, respectively, in vitro, and 77.40% and 78.20% showed resistance to ceftazidime and ciprofloxacin, respectively. Therefore, the least effective antimicrobial drugs were ceftazidime and ciprofloxacin. Susceptibility to colistin and tigecycline in vitro were as follows: 100% and 99.70%,

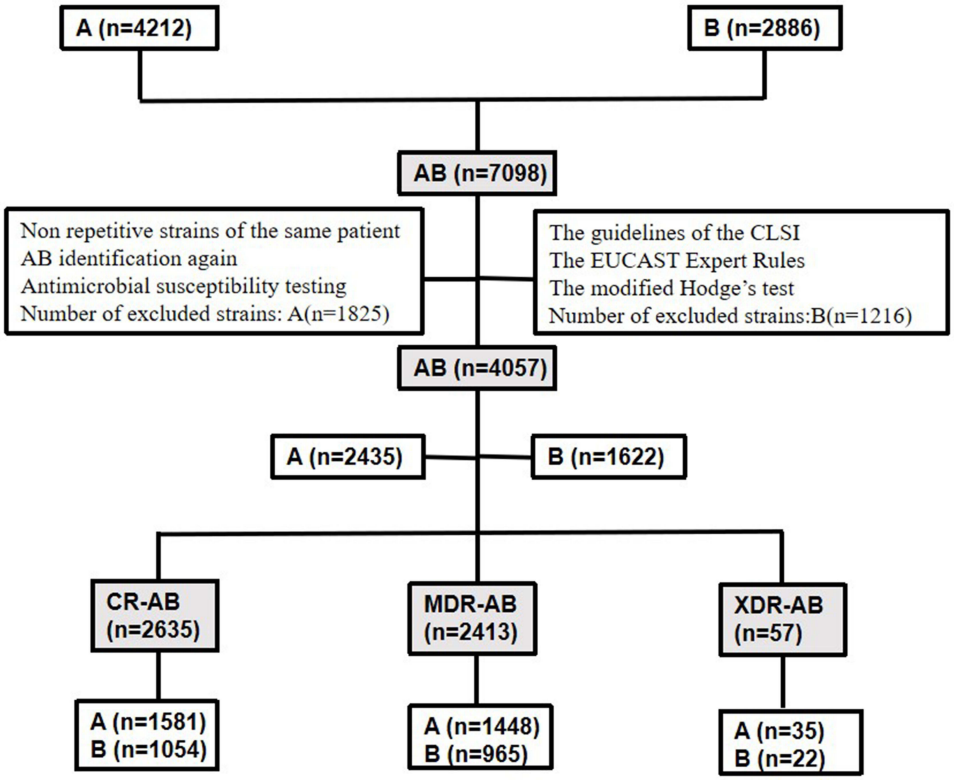

Figure 1 Collection of clinical samples and selection of *Acinetobacter baumannii* strains.
Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee for Antimicrobial Susceptibility Testing. A, The Fourth Affiliated Hospital of Harbin Medical University; B, The First Affiliated Hospital of Hainan Medical University; CR, carbapenem resistant; MDR, multidrug resistant; XDR, extensively drug resistant; AB, *Acinetobacter baumannii.*

respectively, for the isolated CR-AB strains; 100% and 99.67%, respectively, for the isolated MDR-AB strains; and 100% and 85.96%, respectively, for the isolated XDR-AB strains. Therefore, the data on the isolated CR-AB, MDR-AB and XDR-AB strains indicate that colistin and tigecycline remain the most effective antimicrobial drugs.

Data on the antimicrobial resistance of the isolated AB strains obtained from patients at the two hospitals, stratified by study year, are presented in Table 3 and Figure 2. The resistance rates of the isolated AB strains against piperacillin/tazobactam, cefoperazone/sulbactam, gentamicin, amikacin, ceftazidime, imipenem, meropenem and ciprofloxacin decreased significantly over the eight-year study period. However, the resistance rates for colistin and tigecycline were steady and were the lowest among the antibiotics.

Table 1 Patients Characteristics of 4057 AB Clinical Isolates From 2016 to 2023

Characteristics	**Rate% (n=4057)**	**CR-AB** $^{\alpha}$ **Rate% (64.95%, n=2635)**	**MDR-AB** $^{\beta}$ **Rate% (59.48%, n=2413)**	**XDR-AB** $^{\gamma}$ **Rate% (1.41%, n=57)**
Samples				
Respiratory tract	76.98(3123)	74.99(1976)	74.97(1809)	84.22(48)
Wound surface	9.02(366)	8.99(237)	10.36(250)	5.26(3)
Blood	3.75(152)	4.59(121)	5.18(125)	1.75(1)
Urinary tract	3.50(142)	4.44(117)	3.48(84)	3.51(2)
Other	6.75(274)	6.99(184)	6.01(145)	5.26(3)

(*Continued*)

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Table 1 (Continued).

Characteristics	Rate% (n=4057)	CR-AB [α] Rate% (64.95%, n=2635)	MDR-AB [β] Rate% (59.48%, n=2413)	XDR-AB [γ] Rate% (1.41%, n=57)
Wards				
General ward	16.07(652)	12.71(335)	11.69(282)	3.51(2)
ICU	67.98(2758)	74.99(1976)	77.04(1859)	92.98(53)
Surgery department	15.95(647)	12.30(324)	11.27(272)	3.51(2)
Outpatient department	0(0)	0(0)	0(0)	0(0)
Emergency department	0(0)	0(0)	0(0)	0(0)
Age, 64.5(40–99)year				
≤17	0(0)	0(0)	0(0)	0(0)
18–64	36.28(1472)	35.48(935)	35.02(845)	33.33(19)
≥65	63.72(2585)	64.52(1700)	64.98(1568)	66.67(38)
Sex				
Female	40.03(1624)	40.11(1057)	40.41(975)	35.09(20)
Male	59.97(2433)	59.89(1578)	59.59(1438)	64.91(37)

Notes: [α]CR=carbapenem resistant. [β]MDR=multidrug resistant. [γ]XDR=extensively drug resistant.

Table 2 Antimicrobial Susceptibility of AB Clinical Isolates Obtained From Patients at Two Hospital Centers in China, 2016–2023

Antimicrobial Agents	All Isolates (n=4057)							CR-AB [b] (n=2635)	MDR-AB [c] (n=2413)	XDR-AB [d] (n=57)
	MIC (μg/mL)		Range of Values		Breakpoint Interpretations[a]					
	MIC_{50}	MIC_{90}	Min	Max	%R	%I	%S	%S	%S	%S
Ciprofloxacin	0.25	4	≤0.06	>16	78.20	12.40	9.40	1.37(n=36)	1.16(n=28)	0(n=0)
Ceftazidime	4	32	≤0.25	>32	77.40	17.20	5.40	7.13(n=188)	6.71(n=162)	0(n=0)
Amikacin	4	16	≤1	>64	62.50	5.20	32.30	20.23(n=533)	19.98(n=482)	0(n=0)
Meropenem	0.5	8	≤0.03	>32	60.80	7.10	32.10	23.04(n=607)	20.18(n=487)	0(n=0)
Gentamicin	2	8	≤0.5	>32	60.40	4.90	34.70	22.35(n=589)	21.84(n=527)	0(n=0)
Piperacillin/ Tazobactam	4	64	≤1	>128	79.30	5.10	15.60	3.87(n=102)	3.23(n=78)	0(n=0)
Cefoperazone/ Sulbactam	4	64	≤1	>128	38.70	16.90	44.40	28.88(n=761)	25.82(n=623)	0(n=0)
Imipenem	0.5	8	≤0.03	>32	63.10	6.60	30.30	20.08(n=529)	17.99(n=434)	0(n=0)
Tigecycline	1	2	≤0.06	>16	0.20	0	99.80	99.70(n=2627)	99.67(n=2405)	85.96(n=49)
Colistin	1	2	≤0.06	>16	0	0	100.00	100.00(n=2635)	100.00(n=2413)	100.00(n=57)

Notes: [a]%S=%susceptible,%I=%intermediate,%R=%resistant; Breakpoint Interpretation: Amikacin S≤16μg/mL, I=32μg/mL, R≥64μg/mL, Ceftazidime S≤8μg/mL, I=16μg/mL, R≥32μg/mL, Ciprofloxacin S≤1μg/mL, I=2μg/mL, R≥4μg/mL, Colistin S≤2μg/mL, I=4μg/mL, R≥8μg/mL, Gentamicin S≤4μg/mL, I=8μg/mL, R≥16μg/mL, Meropenem S≤2μg/mL, I=4μg/mL, R≥8μg/mL, Piperacillin/ Tazobactam S≤16/4μg/mL, I=32/4μg/mL, R≥128/4μg/mL, Cefoperazone/ Sulbactam S≤16/4μg/mL, I=32/4μg/mL, R≥128/4μg/mL, Imipenem S≤2μg/mL, I=4μg/mL, R≥8μg/mL, [b]CR=carbapenem resistant. [c]MDR=multidrug resistant. [d]XDR=extensively drug resistant.

Data on the antimicrobial susceptibility of the isolated AB strains obtained from patients at the two hospitals, stratified by study year, are presented in Table 4 and Figure 3. The susceptibility of the isolated AB strains to piperacillin/ tazobactam, cefoperazone/sulbactam, gentamicin, amikacin, ceftazidime, imipenem, meropenem and ciprofloxacin increased significantly over the eight-year study period. However, the susceptibility rates for colistin and tigecycline remained steady and were highest among the antibiotics. Excluding colistin and tigecycline, the susceptibility of the

Table 3 Antimicrobial Resistance of AB Clinical Isolates

Antimicrobial Agents	Resistance % (n=4057)								P value [β]
	2016 (n=484)	2017 (n=508)	2018 (n=489)	2019 (n=415)	2020 (n= 449)	2021 (n=448)	2022 (n=593)	2023 (n=671)	
Ciprofloxacin	86.36(418)	85.43(434)	83.84(410)	81.45(338)	79.96(359)	78.57(352)	76.73(455)	75.26(505)	<0.0001
Ceftazidime	88.02(426)	88.98(452)	84.87(415)	83.86(348)	80.85(363)	79.91(358)	78.92(468)	77.94(523)	<0.0001
Amikacin	74.59(361)	75.39(383)	71.17(348)	69.16(287)	69.04(310)	66.96(300)	64.92(385)	63.93(429)	<0.0001
Meropenem	70.45(341)	70.08(356)	69.12(338)	67.95(282)	65.92(296)	64.06(287)	63.24(375)	61.40(412)	0.0014
Gentamicin	70.66(342)	69.88(355)	67.89(332)	66.02(274)	66.37(298)	64.96(291)	62.06(368)	60.51(406)	0.0004
Piperacillin/ Tazobactam	84.09(407)	85.83(436)	84.87(415)	82.41(342)	81.96(368)	79.91(358)	77.91(462)	74.96(503)	0.0002
Cefoperazone/ Sulbactam	56.40(273)	55.12(280)	53.99(264)	51.81(215)	50.11(225)	49.78(223)	47.89(284)	46.05(309)	0.0005
Imipenem	72.93(353)	71.85(365)	70.96(347)	69.88(290)	67.93(305)	66.96(300)	65.94(391)	63.04(423)	0.0005
Tigecycline	0.41(2)	0.20(1)	0.21(1)	0.24(1)	0.22(1)	0.22(1)	0.17(1)	0(0)	NS
Colistin	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	NS

Note: [β]value represent the difference of sensitive rate between year 2016 and year 2023.
Abbreviation: NS, not significant.

isolated AB strains to piperacillin/tazobactam, cefoperazone/sulbactam, gentamicin, amikacin, ceftazidime, imipenem, meropenem and ciprofloxacin were significantly improved after the AMS and IPCP interventions.

Data on the correlations between the isolation rates for CR-AB, MDR-AB, and XDR-AB vis-à-vis DDD of antibiotic consumption and ABHG consumption are presented in Table 5 and Figure 4.

As seen in Table 5, the study findings show that the incidence rate for the isolated CR-AB strains decreased significantly from 70.04% in 2016 to 58.42% in 2023 ($P < 0.0001$). Furthermore, the incidence rate for the isolated MDR-AB strains decreased significantly from 64.26% in 2016 to 52.16% in 2023 ($P < 0.0001$). In particular, the incidence rate for the isolated XDR-AB strains decreased significantly, from 2.27% in 2016 to 0.60% in 2023 ($P = 0.0167$). Similarly, it can be seen in Table 5 that the DDD per 1000 PD of total antibiotics decreased significantly from 51.25 ± 4.22 in 2016 to 40.92 ± 2.48 in 2023 ($P < 0.0001$), and ABHG consumption per 1000 PD increased significantly from 5.25 ± 0.98 in 2016 to 13.51 ± 5.12 in 2023 ($P < 0.0001$).

The relationships between the incidence rates for CR-AB, MDR-AB and XDR-AB vis-à-vis DDD of antibiotic consumption and ABHG consumption are outlined in Table 5 and Figure 4. Over the eight-year study period, the incidence rates for CR-AB were positively correlated with the DDD of antibiotic consumption ($r = 0.9755$, $P < 0.0001$).

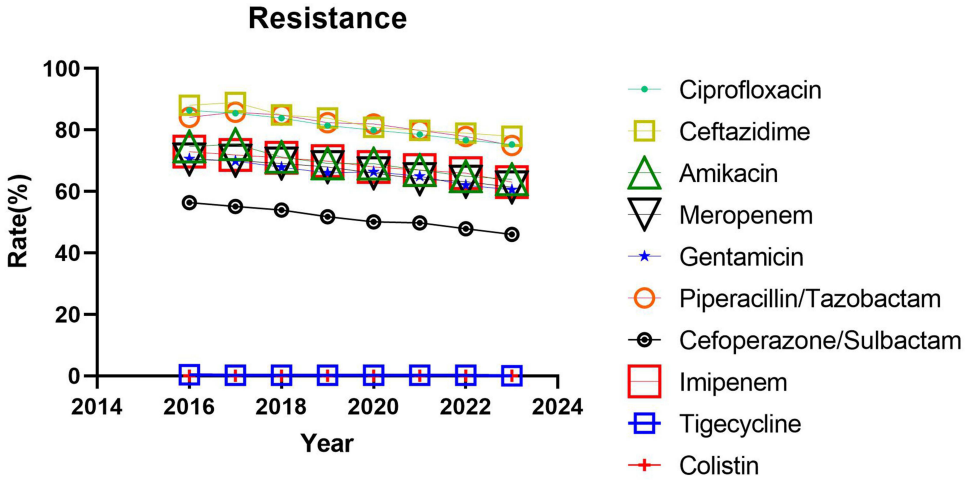

Figure 2 Antimicrobial resistance of AB clinical isolates obtained from patients at two hospital centers in China, 2016–2023.

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Table 4 Antimicrobial Susceptibility of AB Clinical Isolates

Antimicrobial agents	Susceptibility % (n=4057)								P value [β]
	2016 (n=484)	2017 (n=508)	2018 (n=489)	2019 (n=415)	2020 (n=449)	2021 (n=448)	2022 (n=593)	2023 (n=671)	
Amikacin	22.31(108)	22.64(115)	24.74(121)	25.78(107)	27.39(123)	27.23(122)	31.53 (187)	32.94(221)	<0.0001
Ceftazidime	9.92(48)	9.84(50)	10.63(52)	11.81(49)	13.81(62)	14.29(64)	15.35(91)	15.05(101)	0.01
Ciprofloxacin	9.71(47)	10.04(51)	10.22(50)	10.36(43)	11.58(52)	11.16(50)	11.47(68)	13.86(93)	0.0356
Colistin	100(484)	100(508)	100(489)	100(415)	100(449)	100(448)	100(593)	100(671)	NS
Tigecycline	99.59(482)	99.80(507)	99.79(488)	99.76(414)	99.78(448)	99.78(447)	99.83(592)	100(671)	NS
Gentamicin	28.51(138)	27.17(138)	29.24(143)	31.57(131)	32.74(147)	32.59(146)	36.93(219)	38.30(257)	0.0005
Meropenem	25.62(124)	25.79(131)	25.36(124)	28.67(119)	30.07(135)	31.47(141)	33.05(196)	34.58(232)	0.0012
Piperacillin/ Tazobactam	14.88(72)	13.78(70)	14.52(71)	16.87(70)	17.59(79)	19.64(88)	21.75(129)	23.25(156)	0.0004
Cefoperazone/ Sulbactam	40.50(196)	42.91(218)	41.72(204)	41.20(171)	42.76(192)	43.75(196)	45.53(270)	49.63(333)	0.0023
Imipenem	21.07(102)	23.43(119)	24.13(118)	24.82(103)	26.06(117)	26.34(118)	28.16(167)	30.70(206)	0.0003

Note: [β]value represent the difference of resistance rate between year 2016 and year 2023.
Abbreviation: NS, not significant.

However, we found that the incidence rates for CR-AB were negatively correlated with ABHG consumption (r = −0.9473, P = 0.0004). Furthermore, the incidence rates for MDR-AB were positively correlated with the DDD of antibiotic consumption (r = 0.9571, P = 0.0002) but negatively correlated with ABHG consumption (r = −0.9123, P = 0.0016). Similarly, the incidence rates for XDR-AB were positively correlated with the DDD of antibiotic consumption (r = 0.9230, P = 0.0011) and negatively correlated with ABHG consumption (r = −0.9138, P = 0.0015).

Discussion

A.baumannii is one of the most common and resistant hospital-acquired infection pathogens; once an individual is infected, it is difficult to remove AB infection.[14] The occurrence of CR-AB, MDR-AB and XDR-AB clinical isolates are becoming major threats to human health,[1,7,11] and it is difficult to achieve the desired results regarding controlling the CR-AB, MDR-AB and XDR-AB stains in an ICU,[11,14] which may be related to the insufficient regulation of antibiotic use.[5,6] Various studies have shown that the DDD of antibiotic consumption is linked to the incremental resistance rates of AB in hospitals, and nosocomial transmission of drug-resistant AB has been linked

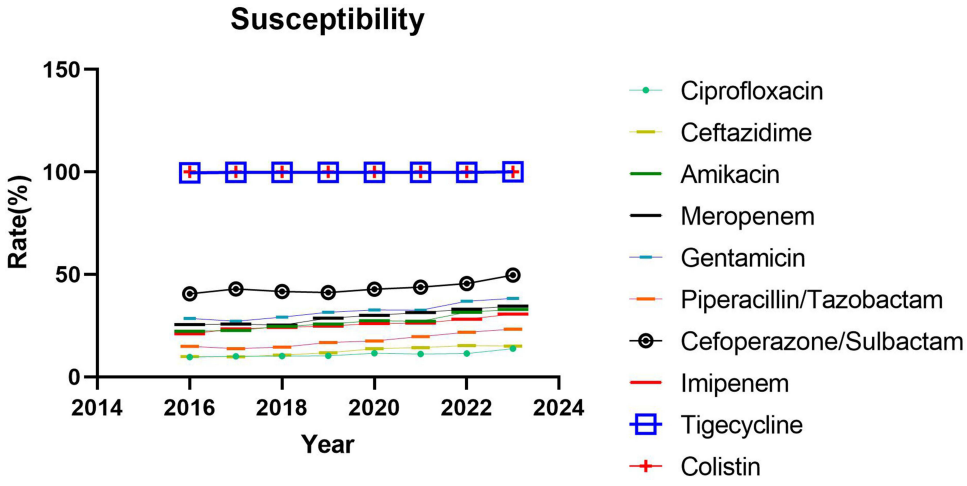

Figure 3 Antimicrobial susceptibility of AB clinical isolates obtained from patients at two hospital centers in China, 2016–2023.

Table 5 DDD, ABHG and the Rate of CR-AB, MDR-AB and XDR-AB From 2016 to 2023

	2016 (n=484)	**2017 (n=508)**	**2018 (n=489)**	**2019 (n=415)**	**2020 (n=449)**	**2021 (n=448)**	**2022 (n=593)**	**2023 (n=671)**	**P^1**	**P^2**	***r***
CR rate (%)	70.04 (339)	69.09 (351)	69.53 (340)	67.95 (282)	64.59 (290)	62.50 (280)	60.88 (361)	58.42 (392)	<0.0001	p_1= <0.0001 p_2= 0.0004	r_1= 0.9755 r_2= −0.9473
MDR rate (%)	64.26 (311)	63.98 (325)	63.80 (312)	61.93 (257)	59.91 (269)	57.59 (258)	55.82 (331)	52.16 (350)	<0.0001	p_1= 0.0002 p_2=0.0016	r_1= 0.9571 r_2= −0.9123
XDR rate (%)	2.27 (11)	1.77 (9)	1.84 (9)	1.45 (6)	1.34 (6)	1.34 (6)	1.01 (6)	0.60 (4)	0.0167	p_1= 0.0011 p_2=0.0015	r_1= 0.9230 r_2= −0.9138
DDD (g/1000 PD)	51.25±4.22	50.62±3.90	48.77±3.45	48.52±3.67	44.38±3.25	43.54±2.98	42.35±2.63	40.92±2.48	<0.0001		
ABHG (L/1000 PD)	5.25±0.98	6.67±2.08	6.82±2.15	8.55±3.24	12.45±4.86	12.18±4.35	13.29±4.98	13.51±5.12	<0.0001		

Notes: P^1: value represent the difference of isolation rate between year 2016 and year 2023. P^2: value represent the correlation of rates with DDD and ABHG. r_1: the correlation of rates with DDD. r_2: the correlation of rates with consumption of ABHG. P_1: value represent the correlation of rates with DDD. P_2: value represent the correlation of rates with consumption of ABHG.

Abbreviations: CR, carbapenem resistant; MDR, multidrug resistant; XDR, extensively drug resist; DDD, daily defined doses per 1000 patient-days; ABHG, alcohol-based hand gel liters per 1000 patient-days; PD, patient-days.

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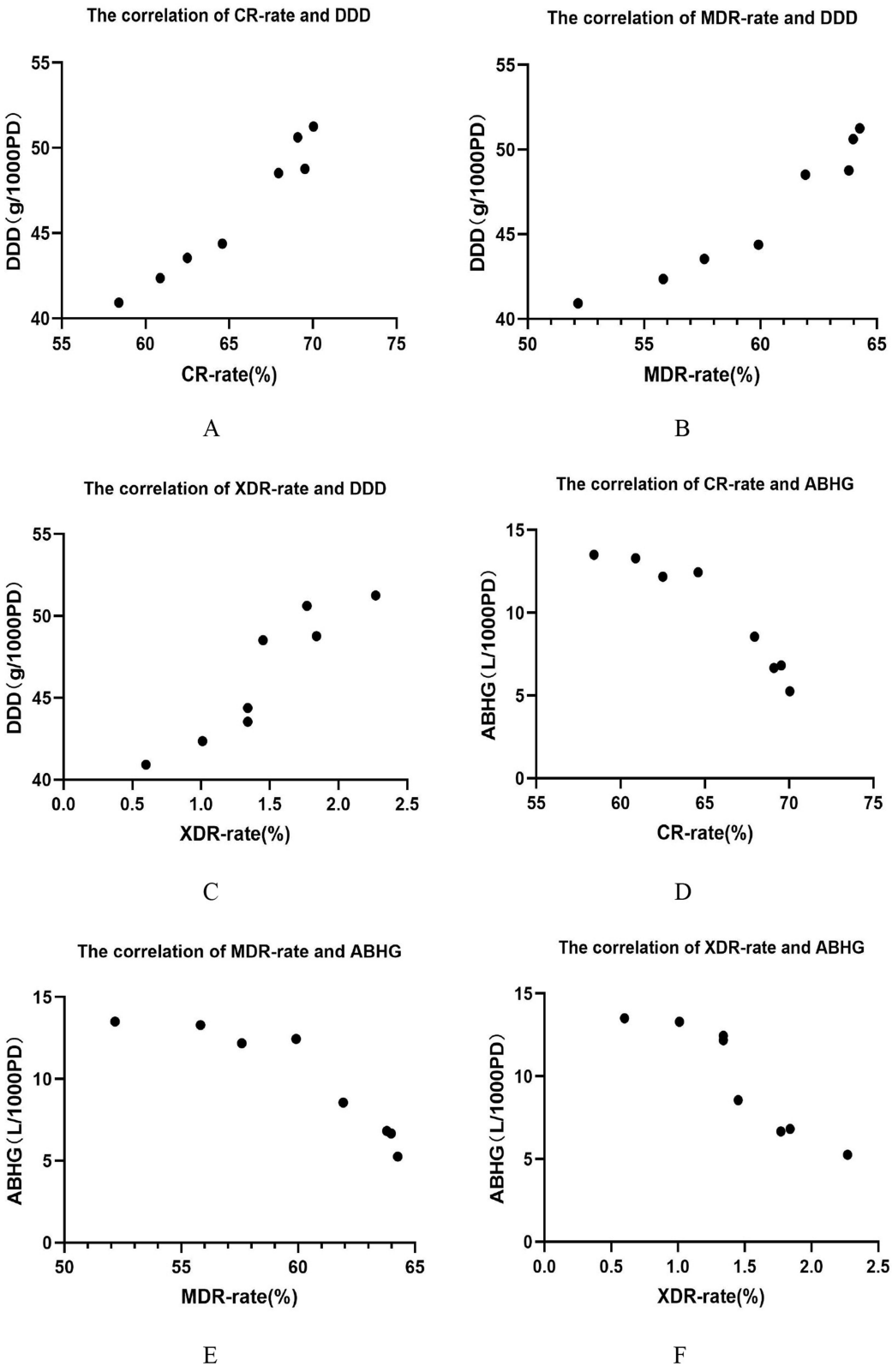

Figure 4 The correlations of isolation rates of CR-AB, MDR-AB, and XDR-AB with DDD and ABHG. (**A**–**C**) show a statistically significant positive correlation; (**D**–**F**) show a statistically significant negative correlation.

Abbreviations: CR, carbapenem resistant; MDR, multidrug resistant; XDR, extensively drug resistant; AB, *Acinetobacter baumannii*; DDD, defined daily doses; ABHG, alcohol-based hand gel.

to environmental contamination and invasive procedures in ICUs.[15] In particular, the unreasonable use of antimicrobial drugs is primarily responsible for the growing drug resistance of AB.[6,15] AMS aimed at reducing the unreasonable use of antimicrobial drugs has been recommended to decrease the incidence of drug-resistant AB infections in ICUs.[16] A study reports that the incidence of MDR-AB was reduced by curtailing the abuse of carbapenems and inappropriate antimicrobial treatment durations.[17] Although various studies have demonstrated the effectiveness of AMS, the incidence rate of hospital-acquired drug-resistant AB infections remains high.[7] In a study, evidence from environmental cultures obtained from ICUs show that the wards were contaminated with MDR-AB colonies.[18] In another study, the wards – especially the ICU – revealed that drug-resistant AB have a high potential for dissemination among patients, which may explain the spread of AB in ICUs.[19] However, the crucial question is how to solve this problem. Through the efforts of various researchers, study findings have revealed that infection control measures are effective in curtailing the dissemination of drug-resistant AB in ICUs, especially hand hygiene and environmental sanitation.[3,7] Our previous single-centre study confirmed that AMS and infection control measures may be some of the best and most effective for simultaneously addressing the growing incidence of MDR-AB and XDR-AB.[7] However, there are very few studies reporting on the effectiveness of combined AMS and IPCP interventions in controlling the resistance of CR-AB, MDR-AB and XDR-AB clinical isolates in China. Furthermore, there are only a few studies on the long-term impact of AMS and IPCP. In particular, single-centre research has limitations and cannot solve all the challenges faced by every hospital, and there are very few multicentre studies in this area. Therefore, it is imperative to undertake multi-centre research projects to evaluate the impact of AMS and IPCPs on the CR-AB, MDR-AB and XDR-AB infection rates.

The findings of various studies show that the department in which AB infections occur most frequently is the ICU, the most common infection site is the respiratory tract, and the most susceptible population is the elderly.[7,20] Our research findings are consistent with the findings of these published studies. A gender bias in AB infection rates has been reported in the literature;[21] however, this report is inconsistent with our research findings, and the observed gender bias may be explained by an insufficient sample size and/or the region and locale of the research site.

Our study data indicate that colistin and tigecycline are the most effective antibiotics against isolated AB strains, and the least effective antimicrobial drugs are ceftazidime and ciprofloxacin. The data indicate that colistin and tigecycline remained the most effective antimicrobial drugs against the isolated CR-AB, MDR-AB and XDR-AB strains throughout the study period. These results are consistent with reported findings in the literature.[7] However, our data on the isolated AB strains indicate non-resistance to colistin, which is inconsistent with an earlier report in the literature;[22] this discrepancy can be attributed to differences in AMS, IPCPs and the region and locale of the site.

Our study data show that colistin and tigecycline maintained steady susceptibility and had the highest susceptibility among the antibiotics assessed. The susceptibility of the isolated AB strains to piperacillin/tazobactam, cefoperazone/sulbactam, gentamicin, amikacin, ceftazidime, imipenem, meropenem and ciprofloxacin were significantly improved after the implementation of AMS and IPCP interventions over the eight-year study period. In particular, there was a decrease in the resistance rates for AB resistance to imipenem from 72.93% in 2016 to 63.04% in 2023, and for AB resistance to meropenem, the rates fell from 70.45% in 2016 to 61.40% in 2023. These findings are generally consistent with those reported in the literature.[7] Drug resistance research data lower than those predominantly reported in the literature[5] may be explained by the differences in the level of intensity of antibiotic use, the hospital departments studied and the regionality of bacterial resistance. A statistically significant reduction in the incidence of CR-AB, MDR-AB and XDR-AB was demonstrated in our study. Furthermore, a statistically significant negative correlation was confirmed between ABHG consumption and the incidence of CR-AB, MDR-AB and XDR-AB; concurrently, a positive correlation was confirmed between the DDD of antibiotic consumption and the incidence of CR-AB, MDR-AB and XDR-AB. These findings are consistent with the findings of single-centre studies reported in the literature.[5,7]

Our findings indicate that comprehensive AMS and IPCP intervention measures can successfully produce sustained amelioration in the resistance and transmission of AB in multiple medical centres. Furthermore, our study findings are encouraging as research reports are regarding multicentre research and potential applicability to

other hospitals. However, this study has a few limitations. First, susceptibility testing of the isolated AB strains was not performed for all antibiotics; therefore, local epidemiology should be considered to formulate the treatment strategies of CR-AB, MDR-AB and XDR-AB. Second, the scope of this study rules out investigating whether implementing other intervention methods may result in eliminating infection of CR-AB, MDR-AB and XDR-AB. Third, given that the Vitek and E-test methods were employed, it cannot be definitively concluded with 100% confidence that all these isolates are *A.baumannii* and not other members of the *Acinetobacter calcoaceticus-baumannii* complex. Furthermore, this study did not gather data to analyse the influence of our findings on patient outcomes, such as complications, length of hospital stay, quality of life, prognosis and mortality, as well as how long the impact of AMS and IPCP interventions are sustained. There is also an unaddressed question regarding the cumulative impact after the AMS and IPCP interventions. Further observation is needed to investigate these issues.

Conclusion

In total, 4057 isolated AB strains were obtained from patients, and 64.95% of these isolated AB strains were CR-AB, 59.48% were MDR-AB and 1.41% were XDR-AB. The department in which CR-AB, MDR-AB and XDR-AB occur most frequently is the ICU; the most common site of infection is the respiratory tract, and the most susceptible population is the elderly. Among the antibiotics assessed, colistin and tigecycline are the most effective against the isolated CR-AB, MDR-AB and XDR-AB strains. The resistance rates of the isolated AB strains against piperacillin/tazobactam, cefoperazone/sulbactam, gentamicin, amikacin, ceftazidime, imipenem, meropenem and ciprofloxacin were significantly improved after the AMS and IPCP interventions implemented over the eight-year period of this study. A statistically significant reduction in the incidence of CR-AB, MDR-AB and XDR-AB is demonstrated by our findings. In addition, a statistically significant negative correlation has been confirmed between ABHG consumption and the incidence of CR-AB, MDR-AB and XDR-AB; concurrently, a positive correlation has been confirmed between the DDD of antibiotic consumption and the incidence of CR-AB, MDR-AB and XDR-AB. Our data indicate that comprehensive AMS and IPCP intervention measures can successfully produce sustained amelioration in the resistance and transmission of AB in multiple medical centres. Furthermore, our study findings are encouraging, as research reports are regarding multicentre research, referential value and potential applicability to other hospitals.

Data Sharing Statement

The data will be made available to others on reasonable requests to the corresponding author. Availability of data and material also need to be approved by the institutional ethics board of the First Affiliated Hospital of Hainan Medical University and the Fourth Affiliated Hospital of Harbin Medical University.

Ethics and Consent Statement

This study was approved by the institutional ethics committee of the First Affiliated Hospital of Hainan Medical University and the Fourth Affiliated Hospital of Harbin Medical University which has waived the necessary for informed consent from participants because this was a retrospective observational study, involved very minimal risk to participants; this waiver does not adversely affect the rights and welfare of the participants. All relevant ethical safeguards have been met in line with the Declaration of Helsinki.

Consent for Publication

All authors have been personally and actively involved in substantive work leading to the report, and will hold themselves jointly and individually responsible for its content.

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Disclosure

The authors report no conflicts of interest in this work.

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