Heliyon 9 (2023) e16851

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

The impact of antimicrobial management by clinical pharmacists in obstetrics and gynecology on antimicrobial indicators, bacterial resistance and drug costs from 2011 to 2021 in China

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ARTICLE INFO

Keywords:
Antibiotic management
Clinical pharmacist
Obstetrics and gynecology hospital
Antibiotic use prevention

ABSTRACT

Objectives: The goal of our study is to analyze the effectiveness and role of clinical pharmacists in antibiotic management through retrospective research from 2011 to 2021, depending on the current scenario of the antibiotic application in China.
Methods: We formed a team of pharmacists to carry out multifaceted intervention measures, such as forming a working group, developing a plan, establishing management rules via the pre-trial system, prescription comments, collaborating with the administrative department, implementing training and publicity, and so on. Antibiotic use was studied, bacterial drug resistance was determined, and antibiotic costs were computed.
Results: The pharmacist intervention and rectification of inappropriate antibacterial drug orders considerably enhanced the rational use rate of antibiotics and reduced the cost of antibiotics. Antibiotic use in clean surgery decreased from 90.22% to 11.14%, the use rate of antibiotics decreased from 63.82% to 30.26%, and antibiotic use intensity decreased from 42.75DDDs to 30.04DDDs. The types, timing, and course of antibacterials used in wards were all improved to varying degrees. Bacterial drug resistance improved noticeably, with resistance of *Escherichia coli* to cephalosporins, ciprofloxacin and carbapenems decreased in varying degrees. The use of antibacterial drugs has decreased significantly.
Conclusions: It is feasible and effective for pharmacists in gynecology and obstetrics to control antibiotic use, which plays a positive role in promoting the safe, effective, and cost-effective use of antibiotics and serves as a valuable reference for the antibiotic management.

1. Introduction

It is a serious public health issue globally, particularly in developing nations, as the overuse of antibiotics has placed a significant burden on the health system of many countries, increasing medication errors, medical costs, and mortality as well as having far-reaching effects like antibiotic resistance and patients' mistrust of the healthcare system [1,2,3,4,5,6,7]. The World Health Organization (WHO) started taking action to stop the spread of antibiotic resistance (AMR) in 2001, and they strongly recommended that governments of all nations to undertake antimicrobial stewardship (AMS). The AMS should include medical, infection, pharmacy,

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https://doi.org/10.1016/j.heliyon.2023.e16851
Received 25 September 2022; Received in revised form 28 May 2023; Accepted 31 May 2023
Available online 12 June 2023

clinical microbiology, hospital infection management, information, quality control, nursing, and other professionals. Pharmacists must create a catalog and prescription set of antibacterial drugs, monitor their clinical use, and advise clinical departments on antibiotic use. They must also train medical staff and subordinate medical institutions on antibiotic use. Increasing evidence suggests that AMS interventions can improve the rational use of antimicrobials in countries around the world, whether it is a high-income or low-income country. Governments and society have recognized the harm caused by inappropriate use of antibiotics, making the WHO's recommendation to combat drug resistance in 2011: "if we do not take action today, we will not be cured tomorrow" [8–15,].

In response to antibiotic resistance, the People's Republic of China's National Health and Family Planning Commission (NHFPC) issued the "national plan for special rectification activities on clinical application of antibiotics" in 2011, which officially carried out special rectification activities on clinical application of antibiotics nationwide. After that, a series of regulations were issued to further promote antibiotic management. The NHFPC's guiding principles for clinical application of antibiotics, published in 2004 and updated in 2015, proposed preventive antibiotic use in various operations, described the characteristics of various antibiotics and their appropriate use in the treatment and prevention of infectious diseases, and provided authoritative guidance for the rational use of antibiotics in China [16,17,18,19]. The NHFPC has established various goals for the clinical use of antibiotics, which are detailed below. The special management policy mostly applies to level II and level III public hospitals, which are required to provide antibiotic use data to the government on a monthly basis.

The rules and pertinent policies are crucial, but not all medical professionals are aware of their significance. At the same time, because to their diverse roles in clinical therapy, they focus more on patient efficacy and less on the rationality, dosage, and antibiotic drug resistance. The pharmacists organize the instruction and training on rational drug use, as well as examination and assessment of rational drug antibiotic use. The current focus of antibiotic management in Chinese hospitals continues to be on how to create a scientific and professional long-term antibiotic management mechanism, prevent rebound, optimize the anti-infection treatment plan, and improve the degree of medication therapy. Since 2001, we have taken numerous initiatives to limit unnecessary antibiotic use and improve medication treatment. The goal of this study is to share our effective management experience, identify current problems, and provide ways to control the rational use of antibiotics in hospitals, especially the preventive use of inpatients during perioperative.

2. Method

2.1. Schedule

According to various management policies issued by the state, the guiding principles for the clinical application of antibiotics updated in 2015 are quite authoritative. Therefore, we divided the whole retrospective study into three stages. The first stage (2011.1–2014.12): the basic stage; The second stage (2015.1–2017.12): the control stage; The third stage (2018.1–2021.12): the consolidation stage [20].

2.2. Data collection

Antibiotic usage data are directly extracted from the hospital information system (HIS). The pre-trial system is used to acquire the

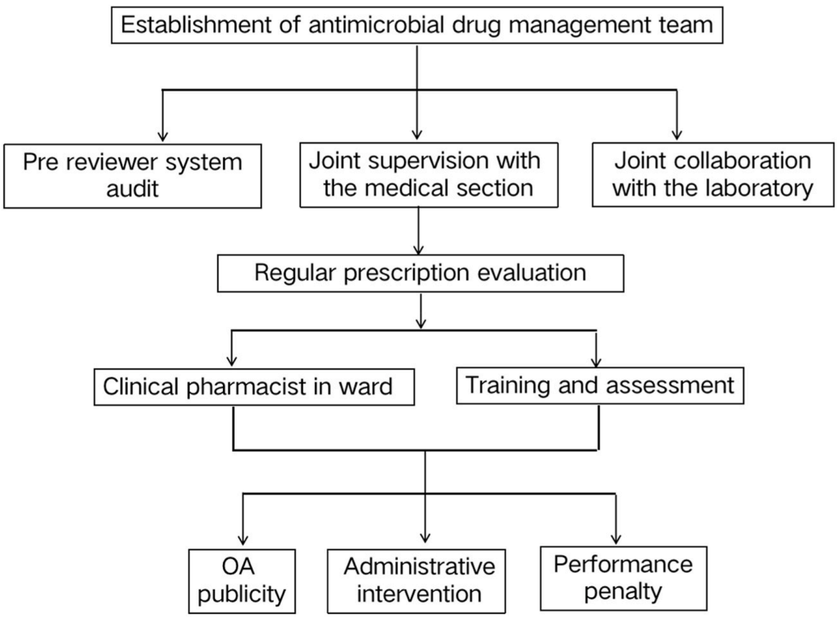


Fig. 1. Flow chart of antibiotics control.

appropriate intervention data. Data on bacterial resistance are obtained from the nosocomial infection and clinical microbiology departments.

2.3. Management and control (Fig. 1)

2.3.1. Establishment of the antimicrobial drug management team

AMS was established under the hospital pharmacy management and pharmacotherapeutics committee, which is comprised of management personnel, clinicians, infectious disease physicians, pharmacists, microbiologists, and information personnel, to clarify the responsibility system for the management of the clinical application of antibiotics. Clinical pharmacists are in the charge of the specialized work.

2.3.2. Pre-reviewer system audit

To limit the occurrence of pharmaceutical errors caused by personnel negligence, we implemented a pre-trial prescription system, built a rule foundation to examine the clinical use of drugs. The pre-reviewer system combines system and manual review. The system automatically reviews a doctor's prescription or order, finds no illogical questions, and enters the patient's paid medication process. Otherwise, a reasonable medication review reminder interface appears. Interface warning level has three categories: 1-interception: must be handled. Doctors can't click next. This mode applies to situations where usage must be forbidden, such as medication over 5 times the upper maximum dose, pharmaceuticals with special authorization or hospital management requirements, etc. 2-Severe warning, relevant to contraindications, severe interactions, allergies, pregnancy, lactation, and other special population medicine; 3-General warnings, applicable to most audit rules, including indications, usage and dose, caution, etc. If the doctor verifies no error and submits, both critical and general warnings can be clicked on Next. The pharmacists can evaluate patient data, medical history, and inspection reports on the review interface. The patient pays or clicks to start the physician-pharmacist interaction window. This interface offers a physician dispensing dual signature application [21].

2.3.3. Regular prescription evaluation

Clinical pharmacists regularly monitor and evaluate the clinical application of antibiotics, and they implement the antibiotic prescription comment system. Every month, the clinical application of antibiotics at the hospital and department levels was investigated. Supervise and inspect the prescription, history, indicators, and ranking of antibacterial drugs, make correction and improvement suggestions for irrational drug use, and report to relevant functional departments.

2.3.4. Joint supervision with the medical section

The pharmaceutical and medical departments collaborated in the development of the rules for the review of hospital practices, and antibiotic use was dynamically monitored based on prescriptions review. Make statistics and follow-up monitoring on the number and amount of drugs used each month, establish a monitoring mechanism for abnormal growth of medical expenses by using HIS, and focus on monitoring and evaluating the varieties and doctors' prescriptions with abnormal growth or high ranking.

2.3.5. Cooperate with laboratory

The pharmaceutical department's laboratory division jointly collaborated on bacterial drug resistance monitoring and devised an early warning mechanism for bacterial drug resistance. Combined with the monitoring results of our hospital, we put forward suggestions on the selection of antibacterial drugs for the treatment of various pathogenic bacteria and optimized the antibacterial drug treatment scheme.

2.3.6. Pharmacist in ward

According to the specific conditions of each ward, pharmacists regularly enter the key wards to discuss and communicate with the director of the ward about the unreasonable conditions found and formulate corresponding rectification measures to effectively solve the unreasonable application of drugs due to bad drug use habits.

With about 10 wards apiece, we specialise in obstetrics and gynecology. Each ward has 4–5 diagnosis and treatment groups with directors, supervising doctors, bed doctors, and continuing education doctors. Each diagnosis and treatment group has 5–8 doctors. Each ward averages 55–65 admitted patients.

2.3.7. Training and assessment of rational drug use

For at least twice a year, pharmacists conduct training and assessments on rational use of antibiotics, publicize popular knowledge of drug use, strengthen the concept of rational drug use, and promote rational drug use. Strictly limit antibacterial medicine prescribing rights at different management levels, ensure the implementation of the hierarchical management system. After the training passes the examination, the corresponding authority shall be granted.

2.3.8. Office automation publicity(OA)

OA is the hospital's working platform for the medical personnel. We will publicize antibiotic-related content on the in real time, such as publishing management documents, dynamic monitoring reports of antibiotics in each ward, top 10 drug announcements in terms of the amount and amount of antibiotics used, comment reports on antibiotics prescriptions, and so on.

2.3.9. Administrative intervention

The medical department will send comments and antibiotic use data to the functional departments, performance office, and ward department directors every month, incorporate the antibiotic rational use into the medical quality and comprehensive management objective assessment system, the annual assessment of departments and middle-level cadres, and increase the corresponding assessment weight for the most common problems of the previous year.

2.3.10. Performance penalty

Every year, hospital's director in charge of medical technology requires the clinical department directors to sign a letter of responsibility for assessment and use. Hospital leaders, directors of the medical department, quality control department and pharmaceutical department have updated the performance appraisal system for the use of antibiotics, defined the rewards and punishments, and the medical department is responsible for reviewing and handling such measures. We have listed the deduction in detail(Table 1).

2.4. Evaluation criterion

According to the policies, drug instructions, clinical medication guidelines for Chinese physician/pharmacists, authoritative guidelines for Chinese obstetrics and gynaecology, such as the American Association of Obstetricians and Gynecologists, the Canadian Association of Obstetricians and Gynecologists, and other relevant guidelines issued by the NHFPC, and based on the actual medication situation in our hospital, we evaluated the indications for medication, the selection of medications, and the administration of medications.

2.5. Statistical analysis

The database was established by Excel, and antimicrobial indexes from different periods were compared. The results were statistically analyzed by spss19.0 statistical software. $P < 0.05$ showed that the difference was statistically significant.

3. Result

3.1. Trend of antimicrobial monitoring indicators

In the ten years under our administration, the indicators tracked by the state have declined to varying degrees. The data can be found in Table 2. There are five indicators with upper limits among them. We have detailed the change trend in detail(Fig. 2). Indicators 2, 3 and 5 have achieved remarkable results performed admirably in the first stage and maintained low values in the second and third stages; indicators 1 and 4 met the requirements of national indicators after the first stage, but only recently entered the second stage with a rebound trend, which was the focus of the second stage control. We identified the wards with the greatest utilization rate and intensity using the information system and scheduled pharmacists to enter the wards for control. The third stage's final two indicators were greatly improved.

3.2. Trends of antimicrobial resistance monitoring indicators

According to our hospital's semi-annual bacterial resistance monitoring report since 2015, the most common gram-negative bacilli, gram-positive cocci, and fungi isolated from patients have been *Escherichia coli(E. coli)*, *Streptococcus agalactiae(SA),* and *Candida albicans*.

E. coli resistance to third-generation cephalosporins and ciprofloxacin decreased from 2015 to 2021, while carbapenems resistance did not change significantly. Resistance rates of *E. coli* to third generation cephalosporins and ciprofloxacin reduced by 6.3% and 7% (Tab le3–a) respectively. *SA* resistance rates to erythromycin and nitrofuranto in increased by 15.1% and at least 4.5% respectively, while tetracycline, clindamycin, and levofloxacin resistance rates decreased (Tab le3–b). Candida albicans resistance to 5-fluorocytosine and fluconazole decreased, but the resistance rate to itraconazole increased (Tab le3–c).

Table 1
Details of antimicrobial penalty.

Item	Content	Penalty
Deduct	Doctors issue unreasonable medical orders	50 CNY/outpatient prescription
	Doctors issue unreasonable prescriptions	100 CNY/inpatient order
Points deducted	Violating the use principle of antibiotics or using antibiotics unreasonably	Deduct 2 points
	No prescription right to use antibacterial drugs	Deduct 4 points
	10≤accumulated points deducted within two years<14	1 month off job training
	14≤accumulated points deducted within two years<18	2 months off job training
	accumulated points deducted within two years≥18	3 months off job training

Table 2
2011-2021Dynamic monitoring report of antibiotics in the affiliated obstetrics and Gynecology Hospital of Fudan University.

Antibiotic outcome measures	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Indicator1.Proportion of inpatients receiving antibiotics (≤60%)	63.82%	51.22%	48.89%	44.24%	43.43%	42.70%	39.71%	32.42%	31.67%	29.24%	30.26%
Indicator2.Proportion of outpatients receiving antibiotics (≤20%)	11.18%	6.97%	6.72%	6.61%	7.06%	6.99%	6.73%	7.06%	7.11%	5.85%	6.57%
Indicator3.Proportion of emergency receiving antibiotics (≤20%)	27.47%	7.25%	6.64%	5.82%	5.90%	4.85%	4.35%	5.04%	5.07%	3.68%	4.83%
Indicator4.Intensity of inpatients' antibiotic consumption (≤40DDD/ 100bed-days)	42.75	32.8	35.30	35.98	39.95	34.46	35.79	28.82	29.34	28.07	30.04
Indicator5.Proportion of antibiotic prophylaxis in patients receiving type I incision operations/clean operations (≤30%)	90.22%	27.90%	12.08%	16.40%	13.12%	11.60%	10.14%	10.22%	9.05%	9.09%	11.14%
Indicator6.Proportion of inpatients receiving special antibiotics	0.93%	0.47%	0.42%	0.18%	0.30%	0.27%	0.38%	0.34%	0.34%	0.35%	0.37%
Indicator7.Intensity of inpatients' special antibiotic consumption	0.82	0.34	0.35	0.21	0.34	0.40	0.54	0.51	0.95	1.06	1.12
Indicator8.Outpatient intravenous antimicrobial use	–	–	–	1414	3652	3166	3253	2674	1173	1031	922
Indicator9.Emergency intravenous antimicrobial use	–	–	–	207	616	731	722	628	355	332	460
Indicator10.Outpatient intravenous antimicrobial use rate	–	–	–	0.11%	0.13%	0.10%	0.08%	0.06%	0.01%	0.02%	0.02%
Indicator11.Emergency intravenous antimicrobial use rate	–	–	–	0.25%	0.38%	0.35%	0.40%	0.44%	0.33%	0.20%	0.30%

1. Statistics on indicators 8,9,10 and 11 began in August 2014.
2. DDD, defined daily dose.

3.3. Changes in drug costs

The overall cost of antibiotics decreased significantly between 2011 and 2021. We calculated the proportion of antibiotic costs in total drug costs and total hospitalization costs to conduct a thorough analysis of antibiotic costs. Antibiotic process has decreased significantly (Table 4, Fig. 3).

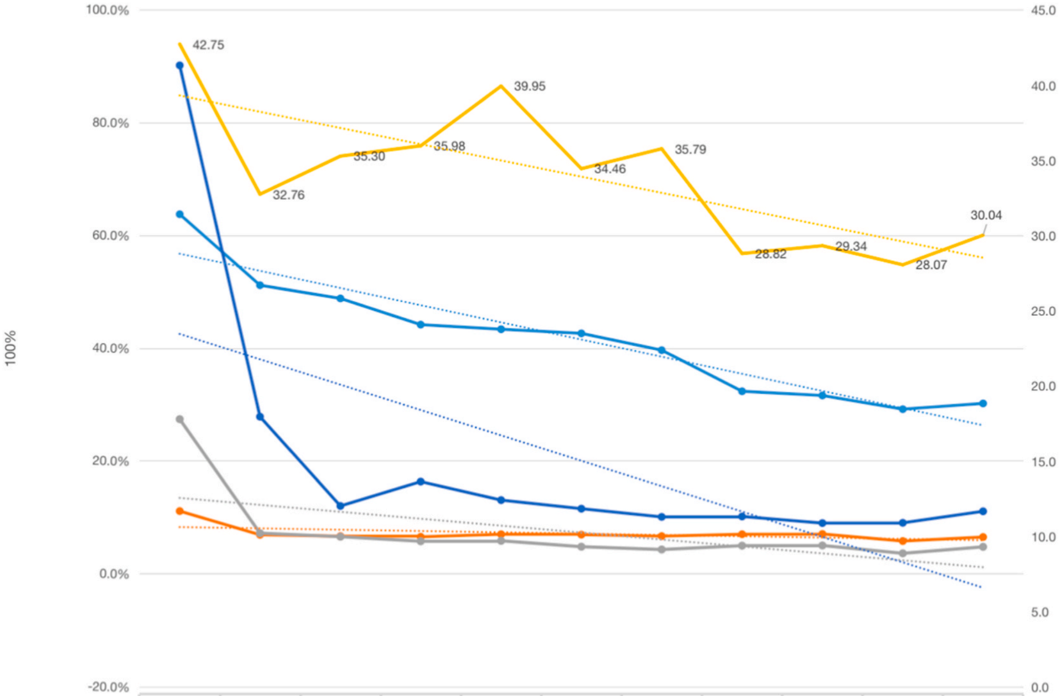
4. Discussion

4.1. Decreased use of antibiotics

After ten years of antibacterial drug control, antibiotic use has improved significantly, and all indicators have reached the standard. In addition to the traditional management methods (such as pre-trial interception, clinical pharmacists' comments, publicity, education, training, and assessment, etc), we also emphasize hospital-level management and the importance of collaboration with administrative and auxiliary departments to form a joint force and common control.

Prophylactic antibiotic use during the perioperative period is a very useful entry point for reducing antibiotic use in the hospital [22,23,24]. Strict control is exercised in accordance with the basic principles. For example, class I incision surgery generally does not prevent the use of antibiotics. When it is really necessary to use antibiotics, it is necessary to strictly master the indications, drug selection, start and duration of medication [25]. We strengthen the management of class I incision surgery without antibiotics.

There is no indication in the ward for the antibiotic use in class I incision surgery, such as ovarian cyst exfoliation, which could be due to the doctors' fear of postoperative infection or their habit of using preoperative preventative medication. The clinical pharmacist also found during the review of the doctor's order that some patients still used antibiotics over time when their body temperature and white blood cell count were normal after hysteromyoma removal. Considering the large scope of operation and the high risk of postoperative infection, the clinicians thought that the time of preventive medication needed to be extended. However, the Chinese guidelines stipulated that the time of preventive medication for clean surgery and clean pollution surgery was 24 h. After full



	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Indicator 1	63.82%	51.22%	48.89%	44.24%	43.43%	42.70%	39.71%	32.42%	31.67%	29.24%	30.26%
Indicator 2	11.18%	6.97%	6.72%	6.61%	7.06%	6.99%	6.73%	7.06%	7.11%	5.85%	6.57%
Indicator 3	27.47%	7.25%	6.64%	5.82%	5.90%	4.85%	4.35%	5.04%	5.07%	3.68%	4.83%
Indicator 5	90.22%	27.90%	12.08%	16.40%	13.12%	11.60%	10.14%	10.22%	9.05%	9.09%	11.14%
Indicator 4	42.75	32.76	35.30	35.98	39.95	34.46	35.79	28.82	29.34	28.07	30.04

Fig. 2. Change trend of antimicrobial index.

communication between clinical pharmacists and doctors [21], the proportion of prophylactic use of antibiotics and the time of prophylactic use of antibiotics in class I incision of the ward have decreased significantly, and the role of clinical pharmacists has been recognized, which is consistent with the research of Tefera GM [26].

Clinical pharmacists will uncover items that are not clearly specified in the guidelines or reference policies during the intervention, where clinical pharmacists can play a practical role, in addition to referring to the specific clinical problems contained in the guidelines. For example, some patients combine oral antibiological bowel preparation (OABP) with mechanical bowel preparation (MBP).

It is useful to use extraintestinal medicines to avoid infection when such patients have intestinal surgery [27]. There is little evidence that MBP will lower the risk of infection further, and the addition of oral antibiotics can exacerbate nausea, vomiting, and abdominal pain, thus it is not recommended [28,29]. The overall incidence rate of laparoscopic surgery was 9.4%, of which 0.4% was attributed to intestinal injury. In vaginal surgery, these percentages were 8.7% and 0% respectively [30]. The readmission rate and overall infection rate of the two operations were equally low (minimally invasive surgery 0.9% and 0.89%, vaginal surgery 1.3% and 0.9%). In other reviews, the incidence of gastrointestinal injury caused by laparoscopy was even reported as low as 0.13%, and the incidence of intestinal perforation was only 0.22% [31]. According to the suggestions of clinical pharmacists, doctors should strengthen the indication control of preoperative oral use of antibiotics for intestinal preparation, not only to avoid unnecessary use of antibiotics, but also to reduce adverse drug reactions and slow down the occurrence of bacterial drug resistance. Some studies suggest that MBP and OABP should be used together only when colectomy is planned, or even oral antibiotics should be used alone [32,33].

Our hospital's doctor generally consider 37.5 °C to be a fever index. If the patient's temperature rises above 37.5 °C one day after surgery, the doctor will either continue antibiotics or switch to high-level drugs. The intensive care unit sets the fever as the body temperature reaches or exceeds 38.3 °C [34]. Fever is defined as a body temperature > 38 °C or ≥38.8 °C for the treatment after gynecological surgery, and it is considered that 50% ~ 92% of the fever after gynecological surgery is caused by non-infectious factors, which can usually subside spontaneously [35,36]. As postoperative fever can also be a manifestation of serious complications, it is necessary to conduct individualized evaluation according to the patient's symptoms and signs. It is suggested that clinicians should consider relaxing the indication of postoperative fever, raising the temperature threshold of fever, and deciding whether to use antibiotics after evaluating whether patients have infection symptoms.

Tab3-A

Trend changes in antimicrobial resistance of *Escherichia coli* to antimicrobial drugs from 2015 to 2021 Resistance rate(%),semiannually.

Antibiotic	First half of 2015	Second half of 2015	First half of 2016	Second half of 2016	First half of 2017	Second half of 2017	First half of 2018	Second half of 2018	First half of 2019	Second half of 2019	First half of 2020	Second half of 2020[a]	First half of 2021[b]	Second half of 2021[b]
Three generations of cephalosporins: Cefotaxime	49.40%	36.40%	49.40%	51.10%	35.40%	34.40%	37.00%	38.70%	43.80%	38.80%	42.90%	43.10%	1.80%	2.80%
Ciprofloxacin	43.00%	46.40%	44.00%	41.50%	37.40%	38.60%	41.10%	39.80%	40.20%	37.50%	42.40%	39.50%	44.70%	36.00%
Imipenem	1.30%	0.00%	0.30%	1.00%	0.40%	0.00%	0.00%	0.40%	0.50%	0.20%	0.50%	0.00%	0.20%	0.00%
Meropenem	0.00%	6.80%	3.40%	4.20%	0.70%	0.80%	0.80%	0.00%	0.00%	1.00%	0.80%	0.00%	0.00%	0.00%

[a] Drug resistance rate in antimicrobial resistance of Escherichiacoli to Cefatriaxone

[b] Drug resistance rate in antimicrobial resistance of Escherichiacoli to Ceftazidime

Tab3-B

Trend changes in antimicrobial resistance of Streptococcus agalactiae to antimicrobial drugs from 2015 to 2021 Resistancerate(%),semiannually.

Antibiotic	First half of 2015	Second half of 2015	First half of 2016	Second half of 2016	First half of 2017	Second half of 2017	First half of 2018	Second half of 2018	First half of 2019	Second half of 2019	First half of 2020	Second half of 2020	First half of 2021	Second half of 2021
Tetracycline	88.00%	87.80%	84.10%	81.30%	75.80%	76.70%	81.10%	75.90%	78.90%	76.70%	81.50%	74.50%	75.10%	80.90%
Erythromycin	52.20%	42.50%	60.00%	55.60%	70.80%	74.70%	71.50%	69.00%	75.30%	71.10%	65.50%	68.20%	75.20%	67.30%
Clindamycin	53.40%	44.70%	48.70%	41.30%	46.40%	54.50%	37.60%	44.40%	56.10%	50.70%	42.80%	45.10%	45.30%	45.20%
Levofloxacin	39.50%	37.50%	37.10%	31.70%	35.50%	39.00%	38.50%	39.40%	39.10%	43.30%	29.20%	35.80%	39.60%	30.30%
Macrodantin	<10%	<10%	<15%	<10%	6.20%	12.60%	13.70%	15.50%	13.10%	13.40%	17.50%	13.50%	15.70%	14.50%

Tab3-C
Trend changes in antimicrobial resistance of Saccharomycesalbicans to antifungal agents from 2015 to 2021 Resistancerate(%),semiannually.

Antibiotic	First half of 2015	Second half of 2015	First half of 2016	Second half of 2016	First half of 2017	Second half of 2017	First half of 2018	Second half of 2018	First half of 2019	Second half of 2019	First half of 2020	Second half of 2020	First half of 2021	Second half of 2021
5-Fluorocytosine	<5%	<5%	<5%	<3%	3.10%	2.60%	3.20%	3.30%	3.60%	4.10%	4%	2.80%	1.90%	3.40%
Fluconazol	<5%	<5%	<2%	<3%	3.40%	6.80%	7.10%	23.10%	11.20%	14.60%	15.30%	12.40%	6.40%	3.80%
Itraconazole	<25%	<30%	<20%	<15%	24%	27.40%	26.80%	39.50%	34.70%	43.20%	37.70%	44.10%	34.40%	33.60%

4.2. Change of bacterial drug resistance

The main purpose of rational use of antibiotics is to reduce the prevalence of drug resistance. Our findings indicate that third-generation cephalosporins, fluoroquinolones, carbapenems resistance in *E coli* has decreased to varying degrees, suggesting that limiting the standard use of, these drugs may be able to *E coli* resistance. The decline in fluoroquinolones drug resistance is comparable previous studies [21,37]. However, our hospital's drug resistance to carbapenems and other antibiotics contradicts some reports [38]. Despite the severe carbapenems and other drugs resistance rate in China, *E coli* drug resistance to carbapenems has not increased significantly, which may be related to our antibiotic control. At the same time, compared with the three other comprehensive hospitals, the gynecological and obstetric hospitals are relatively less likely to accept severe infectious diseases.

SA, as a conditional pathogen, is frequently found in women's reproductive tracts and rectum. It is a common cause of neonatal bacteremia and meningitis. Drug resistance has remained high in recent year, with a slow upward trend year after year, and the erythromycin resistance rate is increasing [39,40,41]. The clindamycin resistance induced by it is also increasing. *SA* resistance rates to erythromycin and nitrofurantoin increased by 15.1% and at least 4.5% respectively, while tetracycline, clindamycin, and levofloxacin resistance rates dropped. It has been reported that GBS is resistant to clindamycin/erythromycin. Drug resistance rates vary greatly

Table 4
Trends in antimicrobial drug costs and proportions.

Time	Cost of antibacterial drugs (RMB)	Cost of drugs (RMB)	Costs of hospitalization (RMB)	Cost of antibacterial drugs/ Cost of drugs	Cost of antibacterial drugs/Cost of hospitalization
2011	12,030,432.19	74,601,595.74	321,201,347.26	16.13%	3.75%
2012	8,110,233.02	69,654,481.92	336,068,086.37	11.64%	2.41%
2013	7,766,084.29	74,828,902.15	372,944,679.81	10.38%	2.08%
2014	8,176,378.04	84,424,175.23	462,815,273.61	9.68%	1.77%
2015	8,811,833.64	92,923,777.15	501,538,055.20	9.48%	1.76%
2016	8,821,452.15	115,995,597.08	606,944,150.44	7.60%	1.45%
2017	7,938,039.74	102,727,295.64	623,849,133.58	7.73%	1.27%
2018	7,903,291.64	106,573,037.77	662,707,037.74	7.42%	1.19%
2019	8,467,761.48	130,878,625.40	762,010,204.11	6.47%	1.11%
2020	6,973,150.42	128,839,673.94	724,619,107.42	5.41%	0.96%
2021	6,178,454.29	155,272,814.98	896,392,644.99	3.98%	0.69%

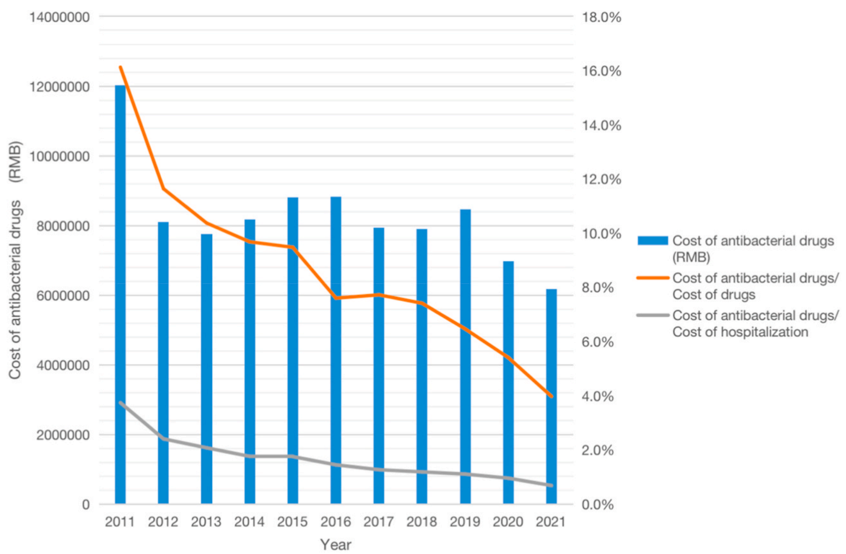


Fig. 3. Trends in antimicrobial drug costs and proportions.

across regions, ranging from 0.7% to 51.3% for erythromycin and 1.7% to 50% for clindamycin [42,43,44]. our hospital has a greater rate of erythromycin resistance than the literature. It is required to tighten erythromycin application control. Erythromycin as a preventive and therapeutic agent against *SA* infection will be limited. This may be related to the special characteristics of gynecology and obstetrics. Penicillin or ampicillin is recommended for the prevention of *SA* infection in women giving delivery in our hospital. Pregnant women who are severely allergic to penicillin will, nevertheless, undergo drug sensitivity testing on erythromycin and clindamycin and choose appropriate antibiotics.

Candida albicans can invade all parts of the human body and has a good sensitivity to fluconazole, although it can develop resistance to 5-fluorocytosine fast. Generally, it is rarely used alone in our hospital, and itraconazole resistance is on the rise. Candida albicans had a resistance rate to azoles of less than 6.25%. Many studies around the world have also revealed that azoles have good in vitro activity against Candida albicans isolated from vulvovaginal candidiasis(VVC) [45,46,47,48]. Our hospital's drug resistance rate to fluconazole and 5-fluorocytosine is similar with the literature [49]. However, the drug resistance rate to itraconazole is high, which is not consistent with the relevant literature. The relevant reasons need to be further explored.

4.3. Cost change

Data from many years shows that as medical technology progresses, the total cost of hospitalization and medication for patients increases, whereas the cost of antibiotics decreases year after year. Drug cost control is a significant activity for hospitals in China, with the promotion of zero mark-up of drugs in public hospitals. A teaching hospital in China's Zhejiang Province has also confirmed the significance of clinical pharmacists in antimicrobial drug cost containment [50]. We have decreased not only the unneeded usage of antimicrobial drugs, but also the cost of antimicrobial drugs, decreasing the medical burden of patients, through our monitoring and control of rational use of antimicrobial drugs. This is consistent with the literature [51].

It should be mentioned that there are several limitations to this study. First of all, our study is a retrospective observation study without a contemporaneous control group, and the bias can not be effectively controlled, which is not as convincing as the prospective control study design. The good effect can be attributed not only to the pharmacist assistance, but also to many other factors. Secondly, because AMS has been carried out for many years, various clinical pharmacists have participated in the evaluation of the use of prophylactic antibiotics. We should formulate clinical application criteria for antibiotics for common diseases based on their unique characteristics in each clinical department, and set individualized indicators and services. The evaluation results may be slightly affected by individual differences. Finally, antibiotic data monitoring is closely tied to help from the information department. When AMS was implemented in our hospital, the data extraction module was embedded into HIS following discussions between clinical pharmacists and information personnel. The pre-trial system also includes an automatic prescription screening system, which can intercept inappropriate prescriptions, such as repetitive use or unreasonable combination. However, our system has not yet realized the entire closed-loop management process online. For example, the results of prescription feedback cannot be sent online to the doctor, and there is no real-time online assessment for the time being. These will be the focus of our follow-up work.

AMS, such as audit, feedback, education, implementation of a protocol, and a computer-assisted decision support methodology, appear to be effective in promoting adherence to surgical antibiotic prophylaxis protocols, reducing surgical site infection rate with a positive economic impact [52]. Similar management techniques in China have also been successful in other countries and regions, such as in Nigeria [24], in Italy [53], in Britain [54], in Greece [55], in Australia [56], in South Africa [57], in Pakistan [58], in Spain [59], in Iran [60], in India [61], to name but a few.

5. Conclusions

This study shows that AMS at our hospital can reduce and optimize antibiotic use, enhance several antibiotic indicators, decrease bacterial drug resistance, and lower antibiotic costs. Pharmacists have been played an essential role in increasing antibiotic stewardship, but hospital infection prevention and control strategies, as well as national policy guidelines, have also been helpful. Our findings point to several potential ways to bacterial epidemic control. AMR is on the rise throughout the world. As a result, it is critical for the ongoing efforts of AMS in large hospitals, grass-roots hospitals, and community hospitals.

Author contribution statement

Jing Jin: Conceived and designed the experiments: Wrote the paper.
JiaLei Zhu: Analyzed and interpreted the data; Wrote the paper.
Jing Tang: Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

Data included in article/supp. material/referenced in article.

Funding

This work was supported by the grants from National Natural Science Foundation of China (No. 82104148), Shanghai Sailing Program (No. 21YF1403600), Shanghai "Rising Stars of Medical Talent" Youth Development Program (No. 076478684Q/2022-

00033), China Medical Education Association (No. 2022-ZXKT041-07), and project of China Pharmaceutical Association (No. CMEI2022KPYJ00545).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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