Antibiotic prescribing patterns for children's outpatient department of primary care institutions in Southwest China

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Abstract

Background

The problem of inappropriate use of antibiotics in children is common in many countries. The purpose of the study was to explore patterns of antibiotic prescribing in children's outpatient clinics in primary care institutions.

Methods

We obtained prescription data from 75 primary care institutions in Guizhou province recorded by the hospital information system in 2020. The classification of incorrect spectrum of antibiotics, unnecessary use and combined use of antibiotics was based on the Guiding Principle of Clinical Use of Antibiotics (2015, China) and guidelines from the USA Centers for Disease Control and Prevention. Potential risk factors for inappropriate use of antibiotics were identified using a bivariate cross table. The generalized estimation equation was used to identify independent predictors controlling irrational use of antibiotics.

Results

A total of 158,267 antibiotic prescriptions were retrieved. Acute upper respiratory tract infections were the most common diseases, accounting for 74.9% of all prescriptions. The main antibiotic group used was penicillins (63.7%), followed by cephalosporins (18.8%). Of 137,284 visits, 30.2% of antibiotic prescriptions were appropriate and the percentage of unnecessary use, incorrect spectrum of antibiotics and combined use of antibiotics was 63.8%, 3.6% and 2.4%, respectively. Physicians with lower professional titles and more than 40 years of work duration were relatively more likely to prescribe inappropriate antibiotics.

Conclusion

The inappropriate use of antibiotics in children is still prominent in primary care institutions of China. The education and training of physicians and caregivers in these institutions should be strengthened.

Background

Antibiotic resistance (AMR) has become a major challenge in the field of global public health [1]. Inappropriate use of antibiotics not only leads to the development of AMR, but also increases various adverse reactions and the financial burden on health services [2]. In recent years, measures to control the irrational use of antibiotics have been implemented by health authorities, scientific research and medical institutions in many countries [3–8]. The prevalence of overuse and abuse of antibiotics has decreased [9–14]. However, the main pathogens of AMR in pediatric patients remain high [15, 16].

The appropriate use of antibiotics in children is critical because there are limited formulations of antibiotics suitable for this population [17, 18]. Studies of antibiotic prescribing patterns in primary care institutions for children in many countries have found inappropriate antibiotic use among children ranging from 19.6 to 79.8 percent [18–22]. However, children belong to special drug using groups and the organs and functions of their bodies are not fully developed. They have unique digestive characteristics, lack of liver and kidney metabolism, and incomplete blood-brain barrier function. Antibiotic absorption, distribution, metabolism and excretion are weaker than that in adults [23]. Therefore, more attention should be paid to the inappropriate use of antibiotics in this population.

This study reviewed the antibiotic prescription data of children in outpatient clinics of primary care institutions in Guizhou, southwest China in 2020. The objective of the study was to explore patterns of antibiotic prescribing in children's outpatient clinics in primary care institutions.

Materials And Methods

Ethics Approval

The study was approved by the Review Committee of Guizhou Medical University (Approval Certificate No. 2019(149)). All participants provided written informed consent to participate in the study.

Study design and setting

A retrospective study was conducted in Guizhou, one of China's poorest provinces. Antibiotic prescribing patterns for children in primary care institutions were quantified from January to December 2020. The main influencing factors of inappropriate use of antibiotics were explored.

This study has been authorized by the Information Center of Guizhou Provincial Health Commission. A data collection agreement was reached with the Guizhou LianKe Weixin Co., LTD. (LWTC), which developed the electronic Hospital Information System (HIS). The data was obtained through the data port of the information center with the help of the LWTC's technical staff.

Data sources

In 2020, there were 252 public primary care institutions using the aforementioned HIS system in Guizhou Province. Seventy-five hospitals were randomly selected for the study. The two selection criteria were: (1) more than 3 outpatient general practitioners, and (2) the physicians must be on duty year-round during 2020. One hundred and seventy-two primary care institutions met the above criteria and 75 primary care institutions were randomly selected. We derived outpatient antibiotic prescription related information and demographic information of patients from the HIS. The gender, age, education, title and working experience of physicians were provided by the Personnel Management Department of the primary care institutions.

People under 18 years of age who received antibiotics were included in our study, as defined by *the United Nations Convention on the Rights of the Child* [24]. The classification of diseases was based on *the 10th Edition of the International Classification of Diseases* (ICD-10) [25]. According to *the 2018 National Catalogue for Clinical Application of Antibacterial Drugs* (summarized in additional file S1), antibiotics were classified into penicillins, cephalosporins, macrolides, quinolones, lincoamides, nitroimidazoles and aminoglycosides. We focused on systemic antibiotics, and topical antibiotics such as eye drops and ointments were excluded.

Appropriate classification of antibiotic use

Our evaluation of the appropriateness of antibiotic prescription was mainly based on the following three aspects: 1) National Health Commission of China for *Guiding Principle of Clinical Use of Antibiotics* introduced in 2015 [17], 2) *the United States Centers for Disease Control and Prevention (CDC) Guidelines* for use of antibiotics [26], and 3) based on our previous research [27], we also added the opinions of experts familiar with the situation of domestic primary care institutions. Thus, antibiotic prescriptions in primary care institutions were divided into appropriate and inappropriate use. Appropriate use of antibiotics was further divided into two categories: 1) preferred medication: optimal drug, and 2) antibiotics can be used or substituted: available, not optimal. Inappropriate antibiotic prescribing was further divided into three categories: 1) Unnecessary use: prescribing antibiotics to prevent viral infections, 2) incorrect spectrum of antibiotics: prescribing aminoglycosides for gram-positive bacteria, and 3) combined use of antibiotics, more than one systemic antibiotic by injection or oral administration at a time by an outpatient physician without any indication, e.g. amoxicillin capsule and ceftazidime injection combined.

Data analysis

All prescriptions were linked to physicians and patients through coding identification, forming a database of medical service information. A physician can prescribe one or more antibiotics to a patient in a day, but multiple visits per patient per day count as only one visit. Antibiotic prescribing patterns were determined using a bivariate cross-tabulation between ICD-10 disease classification and antibiotic groups. Potential risk factors for inappropriate use of antibiotics were identified using a bivariate cross-tabulation. In order to explain the correlation between antibiotic prescriptions prescribed by the same physician and to

avoid possible confounding effects of other variables, the generalized estimation equation (GEE) was used to identify independent predictors controlling irrational use of antibiotics. All P-values were two-sided. R version 4.1.2 was used for all data management and analysis.

Results

During the study period, 158,267 antibiotics prescribed to 143,809 patients aged 18 years and under were obtained from the HIS. After excluding 823 antibiotic prescriptions labeled in other categories and 2,310 topical antibiotic prescriptions, there were 155,134 prescriptions remaining among 143,257 patients. For the purposes of this analysis, only patients who were diagnosed with any of the top 10 common systemic diseases were included in the study, resulting in a total of 150,133 antibiotic prescriptions (96.8%).

Figure 1 shows the number of antibiotic prescriptions per quarter in 2020. Throughout the year, penicillins were prescribed much more often than other antibiotics. The second most commonly prescribed antibiotic class was cephalosporins. More penicillins and cephalosporins were prescribed in the first or fourth quarter, while quinolones and nitroimidazoles showed little change in prescription fluctuations across the four quarters.

Table 1 shows the distribution of clinical diagnoses and antibiotic prescriptions. Diseases of the respiratory system accounted for 86.8% of all antibiotic prescriptions, followed by diseases of the digestive system (6.0%) and diseases of the skin and subcutaneous tissue (2.1%). The highest rate of inappropriate use was seen for symptoms, signs and abnormal clinical and laboratory finding not elsewhere classified (100%), diseases of the circulatory system (96.9%), and diseases of the skin and subcutaneous tissue (88.6%). Incorrect spectrum of antibiotic was common for children with diseases of the eye and adnexa (37.1%), certain infectious and parasitic diseases (13.2%), and diseases of the ear and mastoid process (6.1%). The unnecessary use of antibiotics for diseases of the ear and mastoid process and diseases of the eye and adnexa was 12.6% and 8.5%, respectively, and unnecessary use of antibiotics for the other eight systemic diseases was more than 50%. In terms of the appropriateness of the use of antibiotics for diseases, ear and mastoid process (81.3%), diseases of the eye and adnexa (54.5%) and injury, poisoning and certain other consequences of external causes (47.2%) were the top three ranked diseases.

Table 1
Distribution of antibiotic prescriptions stratified by clinical diagnosis and appropriateness of use.

ICD-10	Diseases	Total, n (%)	Appropriate use, n (%)		Inappropriate use, n (%)	
			Preferred medication	Antibiotic can be used or substituted	Incorrect spectrum of antibiotics	Unnecessary use
1Diseases of the respiratory system		**130371 (86.8)**	**10779 (8.3)**	**30767 (23.6)**	**6630 (5.1)**	**82195 (63.0)**
J06	Acute upper respiratory infections of multiple and unspecifed sites	76478	0 (0.0)	0 (0.0)	0 (0.0)	76478 (100.0)
J20	Acute bronchitis	19766	0 (0.0)	17522 (88.7)	2244 (11.3)	0 (0.0)
J03	Acute tonsillitis	17849	9257 (51.9)	5607 (31.4)	2985 (16.7)	0 (0.0)
J40	Bronchitis, not specifed as acute or chronic	6257	0 (0.0)	5280 (84.4)	977 (15.6)	0 (0.0)
J98	Other respiratory disorders	2122	0 (0.0)	0 (0.0)	0 (0.0)	2122 (100.0)
J39	Other diseases of upper respiratory tract	1756	0 (0.0)	0 (0.0)	0 (0.0)	1756 (100.0)
J02	Acute pharyngitis	1638	1023 (62.4)	473 (28.9)	142 (8.7)	0 (0.0)
J18	Pneumonia, organism unspecifed	1554	0 (0.0)	1378 (88.7)	176 (11.3)	0 (0.0)
J00	Acute nasopharyngitis [common cold]	1442	0 (0.0)	0 (0.0)	0 (0.0)	1442 (100.0)
J21	Acute bronchiolitis	562	0 (0.0)	478 (85.1)	84 (14.9)	0 (0.0)
J31	Chronic rhinitis, nasopharyngitis and pharyngitis	397	0 (0.0)	0 (0.0)	0 (0.0)	397 (100.0)
J22	Unspecifed acute lower respiratory infection	316	289 (91.5)	15 (4.7)	12 (3.8)	0 (0.0)
J04	Acute laryngitis and tracheitis	234	210 (89.7)	14 (6.0)	10 (4.3)	0 (0.0)
2Diseases of the digestive system		**9047 (6.0)**	**2000 (22.1)**	**1218 (13.5)**	**388 (4.3)**	**5441 (60.1)**
K52	Other noninfective gastroenteritis and colitis	4360	0 (0.0)	0 (0.0)	0 (0.0)	4360 (100.0)
K05	Gingivitis and periodontal diseases	1365	998(73.1)	289(21.2)	78(5.7)	0(0.0)
K29	Gastritis and duodenitis	1177	789 (67.0)	167 (14.2)	221 (18.8)	0 (0.0)
K30	Functional dyspepsia	776	0 (0.0)	0 (0.0)	0 (0.0)	776 (100.0)
K12	Stomatitis and related lesions	686	0 (0.0)	600 (87.5)	86 (12.5)	0 (0.0)
K04	Diseases of pulp and periapical tissues	218	161 (73.8)	56 (25.7)	1 (0.5)	0 (0.0)
K13	Other diseases of lip and oral mucosa	85	0 (0.0)	0 (0.0)	0 (0.0)	85 (100.0)
K81	Cholecystitis	85	12 (14.1)	71 (83.5)	2 (2.4)	0 (0.0)
K08	Other disorders of teeth and supporting structures	76	0 (0.0)	0 (0.0)	0 (0.0)	76 (100.0)
K35	Acute appendicitis	50	15 (30.0)	35 (70.0)	0 (0.0)	0 (0.0)

ICD-10	Diseases	Total, n (%)	Appropriate use, n (%)		Inappropriate use, n (%)	
			Preferred medication	Antibiotic can be used or substituted	Incorrect spectrum of antibiotics	Unnecessary use
K14	Diseases of tongue	48	0 (0.0)	0 (0.0)	0 (0.0)	48 (100.0)
K59	Other functional intestinal disorders	34	0 (0.0)	0 (0.0)	0 (0.0)	34 (100.0)
K11	Diseases of salivary glands	31	0 (0.0)	0 (0.0)	0 (0.0)	31 (100.0)
K92	Other diseases of digestive system	31	0 (0.0)	0 (0.0)	0 (0.0)	31 (100.0)
K36	Other appendicitis	25	25 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
3Diseases of the skin and subcutaneous tissue		**3220 (2.1)**	**350 (10.9)**	**18 (0.5)**	**60 (1.9)**	**2792 (86.7)**
L08	Other local infections of skin and subcutaneous tissue	1556	0 (0.0)	0 (0.0)	0 (0.0)	1556 (100.0)
L23	Allergic contact dermatitis	556	0 (0.0)	0 (0.0)	0 (0.0)	556 (100.0)
L04	Acute lymphadenitis	443	0 (0.0)	0 (0.0)	0 (0.0)	443 (100.0)
L03	Cellulitis	257	214 (83.3)	14 (5.4)	29 (11.3)	0 (0.0)
L02	Cutaneous abscess, furuncle and carbuncle	159	125 (78.6)	4 (2.5)	30 (18.9)	0 (0.0)
L30	Other dermatitis	159	0 (0.0)	0 (0.0)	0 (0.0)	159 (100.0)
L24	Irritant contact dermatitis	32	0 (0.0)	0 (0.0)	0 (0.0)	32 (100.0)
L50	Urticaria	29	0 (0.0)	0 (0.0)	0 (0.0)	29 (100.0)
L70	Acne	17	0 (0.0)	0 (0.0)	0 (0.0)	17 (100.0)
L01	Impetigo	12	11 (91.7)	0 (0.0)	1 (8.3)	0 (0.0)
4Symptoms, signs and abnormal clinical and laboratory fndings not elsewhere classifed		**2609 (1.7)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2609 (100.0)**
R10	Abdominal and pelvic pain	1827	0 (0.0)	0 (0.0)	0 (0.0)	1827 (100.0)
R05	Cough	161	0 (0.0)	0 (0.0)	0 (0.0)	161 (100.0)
R59	Enlarged lymph nodes	146	0 (0.0)	0 (0.0)	0 (0.0)	146 (100.0)
R50	Fever of other and unknown origin	140	0 (0.0)	0 (0.0)	0 (0.0)	140 (100.0)
R04	Haemorrhage from respiratory passages	93	0 (0.0)	0 (0.0)	0 (0.0)	93 (100.0)
R07	Pain in throat and chest	70	0 (0.0)	0 (0.0)	0 (0.0)	70 (100.0)
R51	Headache	63	0 (0.0)	0 (0.0)	0 (0.0)	63 (100.0)
R22	Localized swelling, mass and lump of skin and subcutaneous tissue	42	0 (0.0)	0 (0.0)	0 (0.0)	42 (100.0)
R21	Rash and other nonspecifc skin eruption	38	0 (0.0)	0 (0.0)	0 (0.0)	38 (100.0)
R11	Nausea and vomiting	29	0 (0.0)	0 (0.0)	0 (0.0)	29 (100.0)

ICD-10	Diseases	Total, n (%)	Appropriate use, n (%)		Inappropriate use, n (%)	
			Preferred medication	Antibiotic can be used or substituted	Incorrect spectrum of antibiotics	Unnecessary use
5Injury, poisoning and certain other consequences of external causes		**1685 (1.1)**	**723 (42.9)**	**73 (4.3)**	**15 (0.9)**	**874 (51.9)**
T14	Injury of unspecifed body region	748	0 (0.0)	0 (0.0)	0 (0.0)	748 (100.0)
S01	Open wound of head	576	520 (90.3)	46 (8.0)	10 (1.7)	0 (0.0)
S00	Superfcial injury of head	177	164 (92.7)	13 (7.3)	0 (0.0)	0 (0.0)
T11	Other injuries of upper limb, level unspecifed	126	0 (0.0)	0 (0.0)	0 (0.0)	126 (100.0)
T13	Other injuries of lower limb, level unspecifed	58	39 (67.2)	14 (24.2)	5 (8.6)	0 (0.0)
6Diseases of the genitourinary system		**891 (0.6)**	**202 (22.7)**	**151 (16.9)**	**41 (4.6)**	**497 (55.8)**
N39	Other disorders of urinary system	359	0 (0.0)	0 (0.0)	0 (0.0)	359 (100.0)
N34	Urethritis and urethral syndrome	194	160 (82.5)	22 (11.3)	12 (6.2)	0 (0.0)
N48	Other disorders of penis	138	0 (0.0)	0 (0.0)	0 (0.0)	138 (100.0)
N73	Other female pelvic infammatory diseases	116	24 (20.7)	84 (72.4)	8 (6.9)	0 (0.0)
N47	Redundant prepuce, phimosis and paraphimosis	84	18 (21.4)	45 (53.6)	21 (25.0)	0 (0.0)
7Diseases of the circulatory system		**669 (0.5)**	**20 (3.0)**	**1 (0.1)**	**8 (1.2)**	**640 (95.7)**
I88	Nonspecifc lymphadenitis	589	0 (0.0)	0 (0.0)	0 (0.0)	589 (100.0)
I84	Haemorrhoids	42	0 (0.0)	0 (0.0)	0 (0.0)	42 (100.0)
I00	Rheumatic fever without mention of heart involvement	21	18 (85.7)	1 (4.8)	2 (9.5)	0 (0.0)
I67	Other cerebrovascular diseases	9	0 (0.0)	0 (0.0)	0 (0.0)	9 (100.0)
I40	Acute myocarditis	8	2 (25.0)	0 (0.0)	6 (75.0)	0 (0.0)
8Diseases of the ear and mastoid process		**603 (0.4)**	**410 (68.0)**	**80 (13.3)**	**37 (6.1)**	**76 (12.6)**
H66	Suppurative and unspecifed otitis media	468	395 (84.4)	39 (8.3)	34 (7.3)	0 (0.0)
H65	Nonsuppurative otitis media	44	0 (0.0)	0 (0.0)	0 (0.0)	44 (100.0)
H60	Otitis externa	43	3 (7.0)	38 (88.4)	2 (4.6)	0 (0.0)
H61	Other disorders of external ear	32	0 (0.0)	0 (0.0)	0 (0.0)	32 (100.0)
H70	Mastoiditis and related conditions	16	12 (75.0)	3 (18.8)	1 (6.2)	0 (0.0)
9Certain infectious and parasitic diseases		**590 (0.4)**	**1 (0.2)**	**185 (31.4)**	**78 (13.2)**	**326 (55.2)**

ICD-10	Diseases	Total, n (%)	Appropriate use, n (%)		Inappropriate use, n (%)	
			Preferred medication	Antibiotic can be used or substituted	Incorrect spectrum of antibiotics	Unnecessary use
A09		207	0 (0.0)			0 (0.0)
	Other gastroenteritis and colitis of infectious and unspecifed origin			145 (70.1)	62 (29.9)	
B00	Herpesviral [herpes simplex] infections	137	0 (0.0)	0 (0.0)	0 (0.0)	137 (100.0)
A08	Viral and other specifed intestinal infections	101	0 (0.0)	0 (0.0)	0 (0.0)	101 (100.0)
B08	Other viral infections characterized by skin and mucous membrane lesions, not elsewhere classifed	88	0 (0.0)	0 (0.0)	0 (0.0)	88 (100.0)
A04	Other bacterial intestinal infections	57	1 (1.7)	40 (70.2)	16 (28.1)	0 (0.0)
10Diseases of the eye and adnexa		**448 (0.3)**	**37 (8.3)**	**207 (46.2)**	**166 (37.0)**	**38 (8.5)**
H16	Keratitis	135	2 (1.5)	1 (0.7)	132 (97.8)	0 (0.0)
H01	Other infammation of eyelid	128	0 (0.0)	103 (80.5)	25 (19.5)	0 (0.0)
H00	Hordeolum and chalazion	88	14 (15.9)	66 (75.0)	8 (9.1)	0 (0.0)
H10	Conjunctivitis	59	21 (35.6)	37 (62.7)	1 (1.7)	0 (0.0)
H02	Other disorders of eyelid	38	0 (0.0)	0 (0.0)	0 (0.0)	38 (100.0)
Total prescriptions		**150133**	**14522 (9.7)**	**32700 (21.8)**	**7423 (4.9)**	**95488 (63.6)**

Table 2 shows the distribution of antibiotic prescriptions stratified by antibiotic group and appropriateness of use. Penicillins were used the most, accounting for 63.7% of the total prescriptions, cephalosporins (18.8%) and lincosamides (5.8%) followed. The proportion of inappropriate use of antibiotics in all groups exceeded 55.0%.

Table 2
Distribution of antibiotic prescriptions stratified by antibiotic group and appropriateness of use.

Antibiotic group	Total, n (%)	Appropriate use, n (%)		Inappropriate use, n (%)	
		Preferred medication	Antibiotic can be used or substituted	Incorrect spectrum of antibiotics	Unnecessary use
Penicillins	95604 (63.7)	13533 (14.2)	17237 (18.0)	85 (0.1)	64749 (67.7)
Cephalosporins	28272 (18.8)	577 (2.0)	11899 (42.1)	166 (0.6)	15630 (55.3)
Macrolides	7446 (5.0)	52 (0.7)	3010 (40.4)	27 (0.4)	4357 (58.5)
Quinolones	1054 (0.7)	8 (0.8)	239 (22.7)	11 (1.0)	796 (75.5)
Lincosamides	8763 (5.8)	17 (0.2)	109 (1.2)	3443 (39.3)	5194 (59.3)
Nitroimidazoles	1853 (1.2)	334 (18.0)	203 (11.0)	456 (24.6)	860 (46.4)
Aminoglycosides	7141 (4.8)	1 (0.0)	3 (0.0)	3235 (45.3)	3902 (54.6)
Total	**150133**	**14522 (9.7)**	**32700 (21.8)**	**7423 (4.9)**	**95478 (63.6)**

Table 3 compares the distribution of patterns of antibiotics use by physicians' and patients' characteristics. In column 5, "Combined use of antibiotics" refers to combined use of antibiotics, in which a physician prescribes two or more groups of antibiotics for the same patient in the same visit. The percentage of different antibiotic prescription types decreased compared to Table 1 and Table 2, as two or more antibiotics prescribed to the same patient on the same day were considered a single visit. As shown in Table 3, the proportions of "preferred medication", "antibiotic can be used or substituted", "combined use of antibiotics", "incorrect spectrum of antibiotics" and "unnecessary use" were 9.5%, 20.7%, 2.4%, 3.6% and 63.8%, respectively. Bivariate analysis showed that the different variables were statistically significant (all $P < 0.001$). Therefore, all variables were included in the multivariate analysis.

Table 3
Factors associated with inappropriate use of antibiotics on bivariate analysis.

Characteristic	Total, N (%)	Appropriate use, n (%)		Inappropriate use, n (%)			Chi-square test	
		Preferred medication	Antibiotic can be used or substituted	Combined use of antibiotics	Incorrect spectrum of antibiotics	Unnecessary use	χ^2	P value
Total	137284	12991 (9.5)	28419 (20.7)	3361 (2.4)	4901 (3.6)	87612 (63.8)		
Physician characteristics								
Sex							175.78	< 0.001
Female	43202 (31.5)	4642 (10.7)	8431 (19.5)	1041 (2.4)	1389 (3.2)	27699 (64.1)		
Male	94082 (68.5)	8349 (8.9)	19988 (21.2)	2320 (2.5)	3512 (3.7)	59913 (63.7)		
Age group (years)							282.97	< 0.001
[23, 32]	48348 (35.2)	5042 (10.4)	10351 (21.4)	1418 (2.9)	1643 (3.4)	29894 (61.8)		
(32,40]	46024 (33.5)	4390 (9.5)	9557 (20.8)	930 (2.0)	1673 (3.6)	29474 (64.0)		
(40,65]	42912 (31.3)	3559 (8.3)	8511 (19.8)	1013 (2.4)	1585 (3.7)	28244 (65.8)		
Professional title							398.05	< 0.001
Associate chief physician	5601 (4.1)	646 (11.5)	1604 (28.6)	82 (1.5)	221 (3.9)	3048 (54.4)		
Attending physician	16559 (12.1)	1496 (9.0)	3392 (20.5)	291 (1.8)	455 (2.7)	10925 (66.0)		
Resident physician	115124 (83.9)	10849 (9.4)	23423 (20.3)	2988 (2.6)	4225 (3.7)	73639 (64.0)		
Education							751.21	< 0.001
College	57121 (41.6)	5907 (10.3)	10945 (19.2)	1231 (2.2)	1383 (2.4)	37655 (65.9)		
Junior college	57979 (42.2)	5333 (9.2)	12987 (22.4)	1549 (2.7)	2502 (4.3)	35608 (61.4)		

Characteristic	Total, N (%)	Appropriate use, n (%)		Inappropriate use, n (%)			Chi-square test	
		Preferred medication	Antibiotic can be used or substituted	Combined use of antibiotics	Incorrect spectrum of antibiotics	Unnecessary use	χ^2	P value
Technical secondary school	22184 (16.2)	1751 (7.9)	4487 (20.2)	581 (2.6)	1016 (4.6)	14349 (64.7)		
Work duration (years)							3162.59	< 0.001
≤ 5	30322 (22.1)	3046 (10.0)	6553 (21.6)	1014 (3.3)	1422 (4.7)	18287 (60.3)		
6–10	50214 (36.6)	4906 (9.8)	8672 (17.3)	903 (1.8)	896 (1.8)	34837 (69.4)		
11–20	22207 (16.2)	2225 (10.0)	6056 (27.3)	579 (2.6)	1145 (5.2)	12202 (54.9)		
21–30	21077 (15.4)	1782 (8.5)	4055 (19.2)	489 (2.3)	1022 (4.8)	13729 (65.1)		
31–39	10364 (7.5)	840 (8.1)	2800 (27.0)	354 (3.4)	344 (3.3)	6026 (58.1)		
≥ 40	3100 (2.3)	192 (6.2)	283 (9.1)	22 (0.7)	72 (2.3)	2531 (81.6)		
Patient characteristics								
Sex							79.72	< 0.001
Female	63023 (45.9)	5659 (9.0)	12940 (20.5)	1439 (2.3)	2108 (3.3)	40877 (64.9)		
Male	74261 (54.1)	7332 (9.9)	15479 (20.8)	1922 (2.6)	2793 (3.8)	46735 (62.9)		
Age group (years)							833.37	< 0.001
[0,1]	8417 (6.1)	445 (5.3)	1771 (21.0)	251 (3.0)	515 (6.1)	5435 (64.6)		
(1,2]	13806 (10.1)	989 (7.2)	2950 (21.4)	330 (2.4)	593 (4.3)	8944 (64.8)		
(2,5]	38485 (28.0)	3486 (9.1)	8760 (22.8)	875 (2.3)	1439 (3.7)	23925 (62.2)		
(5,11]	46863 (34.1)	4894 (10.4)	9677 (20.6)	1142 (2.4)	1386 (3.0)	29764 (63.5)		

Characteristic	Total, N (%)	Appropriate use, n (%)		Inappropriate use, n (%)			Chi-square test	
		Preferred medication	Antibiotic can be used or substituted	Combined use of antibiotics	Incorrect spectrum of antibiotics	Unnecessary use	χ^2	P value
(11,18]	29713 (21.6)	3177 (10.7)	5261 (17.7)	763 (2.6)	968 (3.3)	19544 (65.8)		
Quarter							1587.33	< 0.001
Q1	32611 (23.8)	3194 (9.8)	7592 (23.3)	1185 (3.6)	1912 (5.9)	18728 (57.4)		
Q2	22901 (16.7)	2249 (9.8)	4117 (18.0)	510 (2.2)	667 (2.9)	15358 (67.1)		
Q3	28002 (20.4)	3050 (10.9)	5221 (18.6)	614 (2.2)	93 (3.3)	18180 (64.9)		
Q4	53770 (39.2)	4498 (8.4)	11489 (21.4)	1052 (2.0)	1385 (2.6)	35346 (65.7)		
Antibiotic route							27448.57	< 0.001
Injection	25099 (18.3)	1442 (5.7)	5427 (21.6)	2499 (10.0)	4540 (18.1)	11191 (44.6)		
Oral	112185 (81.7)	11549 (10.3)	22992 (20.5)	862 (0.8)	361 (0.3)	76421 (68.1)		
Insurance							1075.73	< 0.001
Fully out-of-pocket	18394 (13.4)	1952 (10.6)	3334 (18.1)	782 (4.3)	1265 (6.9)	11061 (60.1)		
New rural cooperative medical system	118890 (86.6)	11039 (9.3)	25085 (21.1)	2579 (2.2)	3636 (3.1)	76551 (64.4)		

Table 4 shows factors associated with inappropriate antibiotic use on multivariate analysis. As shown in Table 4, for physicians, being male, older than 32 years, having a lower professional title, and having a lower level of education were associated with a higher likelihood of inappropriate antibiotic use. In terms of work duration, we found that physicians with 6 to 10 years of service and those with more than 40 years of work duration were more likely to prescribe inappropriate antibiotics. For patients, the antibiotic treatment received by girls and patients aged 0–1 years was more likely to be inappropriate. Physicians were more likely to prescribe inappropriate antibiotics in the other three quarters than in the first quarter of 2020. We also found that antibiotics prescribed intravenously were more likely to be inappropriate than oral antibiotics. In addition, insurance had nothing to do with whether the physicians were prescribing properly.

Table 4
Factors predicting inappropriate use of antibiotics on multivariate analysis.

Characteristic	Adjusted OR (95% CI)	P value
Physicians		
Sex: ref = Female		
Male	1.07 (1.04, 1.10)	<0.001
Age: ref = [23, 32] **years (years)**		
(32,40]	1.35 (1.31, 1.40)	<0.001
(40,65]	2.30 (2.16, 2.45)	<0.001
Professional title: ref = Associate chief physician		
Attending physician	2.50 (2.31, 2.70)	<0.001
Resident physician	2.35 (2.19, 2.52)	<0.001
Education: ref = College		
Junior college	0.93 (0.90, 0.95)	<0.001
Technical secondary school	1.07 (1.03, 1.12)	<0.01
Work duration: ref = ≤ 5 (years)		
6–10	1.11 (1.08, 1.15)	<0.001
11–20	0.53 (0.50, 0.56)	<0.001
21–30	0.59 (0.55,0.64)	<0.001
31–39	0.39 (0.36, 0.42)	<0.001
≥ 40	1.73 (1.50, 1.98)	<0.001
Patient		
Sex: ref = Female		
Male	0.95 (0.93, 0.98)	<0.001
Age: ref [0,1] (years)		
(1,2]	0.88 (0.83, 0.94)	<0.001
(2,5]	0.76 (0.72, 0.80)	<0.001
(5,11]	0.77 (0.73, 0.81)	<0.001
(11,18]	0.85 (0.81, 0.90)	<0.001
Quarter: ref Q1		
Q2	1.32 (1.27, 1.37)	<0.001
Q3	1.23 (1.19, 1.28)	<0.001
Q4	1.23 (1.19, 1.26)	<0.001
Route: ref = Injection		
Oral	0.77 (0.74, 0.79)	<0.001

OR: Odds ratio; CI: Confidence interval; Ref: Reference group

Characteristic	Adjusted OR (95% CI)	P value
Insurance: ref = Fully out-of-pocket		
New rural cooperative medical system	0.98 (0.94, 1.01)	0.1845
OR: Odds ratio; CI: Confidence interval; Ref: Reference group		

Discussion

In this retrospective study, 75 primary care institutions in Guizhou Province were selected to describe the prescription patterns of antibacterial drugs among children in 2020. Overall, the rate of antibiotic prescriptions was highest in the fourth quarter, followed by the first quarter. Among them, penicillins and cephalosporins were the most commonly used antibiotics in outpatient primary care institutions. Sixty-nine percent of antibiotic prescriptions were inappropriate. The most common childhood diseases were the diseases of the respiratory system (86.8%), followed by diseases of the digestive system (6.0%) and diseases of the skin and subcutaneous tissue (2.1%). Penicillins (63.6%) and cephalosporins (18.8%) were the most commonly used antibiotics. Physicians with lower professional titles and more than 40 years of work duration were relatively more likely to prescribe inappropriate antibiotics.

Acute upper respiratory infections (J06, J03, J02, J00, J04) was the most common disease associated with antibiotic prescribing in children, accounting for 74.9%. In addition, although penicillins (63.7%) and cephalosporins (18.8%) accounted for a large proportion, the inappropriate rate of aminoglycosides (99.9%) and lincosamides (98.6%) was the highest. The top two diseases corresponding to aminoglycosides and lincosamides were *acute upper respiratory infections of multiple and unspecifed sites*, J06 (30.5%, 45.7%), and *acute tonsillitis*, J03 (18.3%, 17.0%) (additional file S2). Another study from China reported an antibiotic prescription rate for *acute upper respiratory tract infections* in children of 77.6% while other countries reported rates ranging from 28.7% (Japan) – 76.2% (Albania) [28–32]. However, the guidelines for the clinical application of antibiotics in China [17] and the United States CDC [26] state that *acute upper respiratory tract infections* are the most common community-acquired infections, most commonly caused by rhinoviruses, coronaviruses, influenza viruses, parainfluenza viruses, adenoviruses, and sometimes enteroviruses. Its course of disease is self-limited, generally do not require antibiotic treatment, and symptomatic treatment can be cured, especially in children. Hence, the use of antibiotics for *acute upper respiratory tract infections*, let alone lincosamides and aminoglycosides, was inappropriate because it may trigger allergies, infections, and even endanger the child's life [33]. This scenario likely to lead to AMR in children. The use of antibiotics in children is more likely to kill susceptible strains, leading to proliferation of resistant strains and replacement of susceptible strains, resulting in a sharp increase in drug resistance of bacteria [34].

Overall, unnecessary use of antibiotics accounted for 63.6% of all antibiotic prescriptions. The unnecessary use of antibiotics was found in the top 10 systemic diseases. It should be noted that the 10 sub-diseases under *symptoms, signs and abnormal clinical and laboratory findings not elsewhere classified* (R10, R05, R59, R50, R04, R07, R51, R22, R21, R11) were all diseases for which antibiotics are unnecessary. The rate of inappropriate antibiotics use for these diseases often reached 100%. When treating such childhood diseases, physicians should make specific clinical diagnoses based on typical signs and symptoms [17, 26]. It is particularly important to stress that when physicians suspect a child has severe pneumonia according to typical signs and symptoms, the child should be transferred to a superior hospital in a timely manner [35]. According to National Health Commission of China for Guiding Principle of Clinical Use of Antibiotics introduced in 2015, there is a very limited range of antibiotics suitable for use by those aged 18 years and under [17]. Physicians should be more cautious about prescribing antibiotics for children as widespread use could exacerbate AMR.

We also found from those antibiotic prescriptions with incorrect spectrum of antibiotics accounted for 4.9% of all antibiotic prescriptions. Except for *the systemic disease of symptoms, signs and abnormal clinical and laboratory findings not elsewhere classified*, the other 9 systemic diseases all had the condition of incorrect spectrum of antibiotics. *Diseases of the eye and adnexa* had the highest proportion of incorrect spectrum of antibiotics (37.0%). The proportion of incorrect spectrum of antibiotics was highest in the *sub-disease (keratitis) of diseases of the eye and adnexa* (97.8%). Penicillins, cephalosporins,

macrolides, lincosamides and nitroimidazoles are the incorrect spectrum of antibiotics for these particular diseases. According to *Ophthalmology Clinical Guidelines of American Academy of Ophthalmology (2nd edition)* [36], *Ophthalmology of China (9th edition)* [37] and *National Health Commission of China for Guiding Principle of Clinical Use of Antibiotics introduced in 2015* [17], quinolones and aminoglycosides are the preferred medication for *keratitis* treatment, especially in children.

In this study, intravenous antibiotics were more likely to be inappropriate than oral antibiotics. Wang et al. [38] also showed similar results in intravenous antibiotics. In addition, it was easier to prescribe appropriate antibiotics in the first quarter than in the other three. This may be due to the high incidence of infectious diseases in winter and spring [39, 40]. However, most of them were viral infectious diseases.

In our study, the majority of inappropriate antibiotic prescriptions were prescribed by physicians older than 40 years, with lower professional titles (resident physician / attending physician) and more than 40 years of work duration. Their education was mostly non-undergraduate, and their professional knowledge and experience are often inadequate. Based on this result, it may be necessary to provide refresher courses in antibiotic prescribing for these primary care physicians [41, 42]. Training should emphasize avoiding incorrect and unnecessary use of antibiotic prescriptions in children.

We found that inappropriate antibiotic prescription in children may be correlated with gender of children. It may be related with the fact that left-behind children in rural areas of China are often cared for by poorly educated grandparents, as well as gender discrimination. In addition, children aged 0–1 are more likely than any other age group to be prescribed inappropriate antibiotics. This may be related to physicians using antibiotics recommended for children in China's antimicrobial guidelines (e.g., third-generation cephalosporins) instead of antibiotics prohibited (e.g., gentamicin in aminoglycosides) [43, 44]. A study by Elong et al [45] also reported that the main reason for children's inappropriate use of antibiotics was that their parents could not correctly understand the harm of antibiotics. Antibiotics are sometimes considered as a panacea. Therefore, more information about antibiotic use, such as easy-to-understand brochures and learning videos, should be provided to caregivers of children.

Our study has several limitations. First, the study subjects in primary care institutions may not fully represent the general population of children in China. Second, the time frame of the survey was only one year, thus we could not judge whether the prevalence of paediatric diseases and antibiotic use differed over several years [46, 47].

Conclusion

The inappropriate use of antibiotics in children is still prominent in primary care institutions in Guizhou, China. Unnecessary use of antibiotics for many diseases and the inappropriate use of lincosamides and aminoglycosides in children in primary care were the main clinical problems of rural children. The education and training of physicians and caregivers in primary care institutions should be strengthened.

Abbreviations

AMR: Antibiotic resistance

ICD-10: the 10th Edition of the International Classification of Diseases

CDC: Centers for Disease Control and Prevention

HIS: Hospital Information System

OR: Odds ratio

CI: Confidence interval

Ref: Reference group

Declarations

Ethics approval and consent to participate

The study was approved by the Review Committee of Guizhou Medical University (Approval Certificate No. 2019(149)). All participants provided written informed consent to participate in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

All authors made substantial contributions to the research, and read and approved the final manuscript. YC, XRZ, LW designed the research. WWJ drafted the manuscript, and WWJ and YC completed data extraction, statistical analysis and data interpretation. YC, STY, XH, and HNZ participated in the concept, data interpretation and manuscript revision. WWJ and YC is responsible for data integrity and accuracy of data analysis.

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Figures

Figure 1

Number of antibiotic prescriptions in each quarter in 2020 stratified by antibiotics classes.

Supplementary Files

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- Additionalfile1.pdf
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