

Inappropriate antibiotic prescriptions among pediatric inpatients in different type hospitals

Ruixue Miao, MMed^{a,b}, Chaomin Wan, MD, PHD^{a,b,*}, Zhiling Wang, MD^{a,b,*}, Yu Zhu, MD^{a,b}, Yun Zhao, MMed^c, Liling Zhang, MMed^c, Juan Liu, MMed^d, Jing Qin, MMed^e, Jialing Xia, MD^f, Huiqiong Yan, MMed^g

Abstract

To investigate the situation of antibiotic consumption and to assess the inappropriate use on pediatric inpatients of different types hospitals in Sichuan, China.

A cross-sectional survey of antibiotic prescriptions among hospitalized children aged 1 month -14years were conducted from April 2018 to June 2018 in southwestern China. Antibiotic prescriptions were extracted from electronic records during hospitalization of each inpatient in five different types hospitals.

In this study, the antibiotic prescription rate of hospitalized children was 66.9% (1176/1758). Compared with tertiary children hospital (TC) (46.1%), general hospitals and non-tertiary children hospitals has higher rate of antibiotic prescription (almost 85%) ($P < .001$). 93.4% of inpatients received parenteral antibiotic. Overall, the most common antibiotics were *Cefoperazone and enzyme inhibitor*, *Cefixime and Azithromycin*. Lower respiratory tract infection (LRTI) was the leading reason for antibiotic consumption in pediatric wards (56.8%), followed by upper respiratory tract infection (URTI) (22.2%). For children with LRTI, Cephalosporins were heavy prescribed, especially broad-spectrum third-generation Cephalosporins (60.3%). The antibiotic prescription proportion of URTI in general hospitals and non-tertiary children hospitals (more than 18%) was higher than TC (8.1%) ($P < .001$).

There was inappropriate use of antibiotic in hospitalized children including overuse of parenteral administration, overprescribing of antibiotic on URTI and misuse of third-generation Cephalosporins in pediatric inpatients with LRTI. Compared with tertiary freestanding children hospital, the irrational antibiotic prescription of general hospitals and non-tertiary children hospitals were more serious. Management strategy should be implementer on quality improvement of antibiotic use.

Abbreviations: ASP = Antimicrobial Stewardship program, ATC = Anatomical Therapeutic Chemical, CAP = community-acquire pneumonia, *Hi* = *Haemophilus influenzae*, Hospital PC = primary children hospital, Hospital SC = second children hospital, Hospital SG = second general hospital, Hospital TC = tertiary children hospital, Hospital TG = tertiary general hospital, LRTIs = lower respiratory infections, *SP* = *Streptococcus pneumoniae*, URTIs = upper respiratory infections.

Keywords: antibiotic prescriptions, appropriate, hospitalized children

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^a Department of Pediatrics, West China Second Hospital, Sichuan University, Chengdu, PR China, ^b Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, ^c Department of Pediatrics, Chengdu Children's Special Hospital, ^d Department of Pediatrics, Nanchong Central Hospital, ^e Department of Pediatrics, Dujiangyan Second People's Hospital, PR China, ^f Department of pediatrics, ^g Department of Pharmacy, Angel Children's Hospital Chengdu, PR China.

* Correspondence: Chaomin Wan, Zhiling Wang, Department of Pediatrics, West China Second Hospital, Sichuan University, No 20, 3rd section of Renmin South Road, Chengdu 610041, PR China (e-mail: wcm0220@126.com, wang_zhi_ling@126.com).

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1. Introduction

Antibiotic resistance is a global threat to public health and it has been worsened by the inappropriate of antibiotic in the increasing number and types of resistant bacteria. When comes to resistant microorganism especially to those resistant to multi-drug, the potential of antibiotics is declined and infection become uncontrollable. In addition to the overgrowth of resistant microorganisms, inappropriate prescribing of antibiotics can lead to antibiotic-related toxicity and complications, gut-microbiome-mediated effects and immense healthcare expenditures.^[1] Inappropriate antibiotic prescriptions are common in pediatric like misuse in viral respiratory tract infections, overuse of broad spectrum antibiotic in respiratory tract infections and urinary tract infections.^[2-4] Reducing unnecessary use of antibiotics is an important step to decelerate antibiotic resistance. Rational Antimicrobial Stewardship program (ASP) should be forwarded based on the feedback of current inappropriate prescriptions and local resistance status to optimize the use of antibiotic and minimize bacteria resistance. Regional ASPs were implemented and have been proved effective in optimizing antibiotics use in children.^[5-6] The majority of survey on pediatric antibiotic use were conducted in tertiary children's hospitals. However, there are plentiful underlying patients in pediatric wards of general hospital and secondary or primary children hospitals (Hospital PC). Study reported that there existed distinction in children guideline-

concordant prescribing between different type hospitals.^[7] Therefore, conducting a comprehensive survey in different hospital helps to understand the actual situation of local antibiotics use. This study evaluated the quality of antibiotic prescription and analyzed inappropriate consumption in different types of hospitals among hospitalized children in southwestern China for optimizing antimicrobial use and reducing antibiotic resistance.

2. Methods

A cross-sectional survey of hospitalized children antibiotic prescription was conducted in 5 different type hospitals from April 2018 to June 2018 in southwest China, in which several representative different levels hospitals were selected including: 1 tertiary children hospital (Hospital TC), 1 tertiary general hospital (Hospital TG), 1 second children hospital (Hospital SC), 1 second general hospital (Hospital SG), and 1 Hospital PC. Pediatric inpatients age with 1 months-14 years were adopted in the period of selected weeks from every month (April 1–7, May 8–14, June 15–21) and the data of inpatients with antibiotic consumption were extracted during hospitalization. Outpatients, day-case patients, pediatric surgery ward and neonatal ward were excluded.

Data were extracted from electronic medical record by clinical doctors and pharmacists anonymously during hospitalization including patient demographic details, indication for antibiotics, route of antibiotic administration and type of antibiotics. According to anatomic systems, diagnosis of infection was categorized as respiratory tract infections, central nervous system infections, gastrointestinal tract infections, urinary tract infections, skin/soft tissue infections and cardiovascular infections. Respiratory tract infections were sub-grouped into upper respiratory infections (URTIs include acute otitis media, sinusitis, pharyngitis, tonsillitis, and laryngitis) and lower respiratory infections (LRTIs including acute bronchitis and pneumonia). Sepsis and unexplained fever, infection with malignancy and prophylaxis also were classified separately. Antibiotic were coded as J01 according to WHO Anatomical Therapeutic Chemical (ATC) classification system. Anti-tuberculosis medications were excluded.

Data were collected and handled in excel form (Microsoft Office 2011) and were analyzed by the SPSS 22.0. The prevalence and route of antibiotic were compared across different hospital types by the chi-square tests. $P < .05$ were considered statistically significant.

This study was approved by the Ethical Committee of West Second University Hospital. Informed consent was obtained from guardian or older children.

3. Results

A total of 1758 inpatients were admission and 1176 (66.9%) were treated or prevented with antibiotic including 681 male and 495 female (1.38:1). The proportion of inpatients age with >1 month to <1 year, ≥ 1 year to <5 years, ≥ 5 years to <14 years were 20.1% (236), 54.3% (639), 25.6% (301), respectively. Table 1 shown the characteristics in hospitalized children treated with antibiotics in different types hospitals. There was obvious statistical difference about the rate of antibiotic among hospitals ($P < .001$), in which the percent of antibiotic use in TC (46.1%) was lower than that in general hospitals and non-tertiary children hospitals whose percent were more than 85%. Overall, 93.4% inpatients received parenteral antibiotics. Injected *Cefuroxime*, *Azithromycin*, *Amoxicillin* and *enzyme inhibitor* were used in Hospital TG, Hospital SC, Hospital SG, Hospital PG. During hospitalization, 1655 antibiotic prescriptions were prescribed in 1176 hospitalized patients with an average of 1.4 antibiotics per patient. The most prescriptions (8) was prescribed in a patient diagnosed as very severe pneumonia combined with respiratory failure in hospital TC. In addition, all patients with antibiotics were only prescribed in one antibiotic without combination and replacement during hospitalization of patients in Hospital SG and Hospital PG. The most common antibiotics were *Cefoperazone* and *enzyme inhibitor*, *Cefixime* and *Azithromycin*. Heterogeneity of antibiotic prescription were found among hospitals shown in Table 1.

According to ATC classification system, the composition of prescriptions was presented in Figure 1 including 15 antibiotic

Table 1
The proportion of antibiotic in hospitalized children among hospitals.

	N Admission patients	N patients with antibiotic	Proportion of antibiotic percent (95% ci)	Parenteral administration n (%)	N antibiotic Prescriptions (average prescription)	N antibiotic category	The 3 most common antibiotics
Hospital TC	881	406	46.1 (42.8–49.4)	375 (92.4)	635 (1.6)	14	Cefoperazone and enzyme inhibitor Mezlocillin and enzyme inhibitor Azithromycin
Hospital TG	323	285	88.2 (84.7–91.8)	284 (99.6)	338 (1.2)	7	Ceftazidime Cefathiamidine Cefuroxime
Hospital SC	382	334	87.4 (84.1–90.8)	288 (86.2)	531 (1.6)	6	Cefixime Cefoperazone and enzyme inhibitor Azithromycin
Hospital SG	127	108	85.0 (78.8–91.3)	108 (100)	108 (1)	2	Cefoxitin Cefsulodin
Hospital PC	45	43	95.6 (89.3–1.0)	54 (100)	43 (1)	4	Cefoperazone and enzyme inhibitor Cefoxitin Azithromycin
Total	1758	1176	66.9 (64.7–69.1)	1098 (93.4)	1655 (1.4)	15	Cefoperazone and enzyme inhibitor Cefixime Azithromycin

Hospital PC=primary children hospital, Hospital SC=second children hospital, Hospital SG=second general hospital, Hospital TC=tertiary children hospital, Hospital TG=tertiary general hospital.

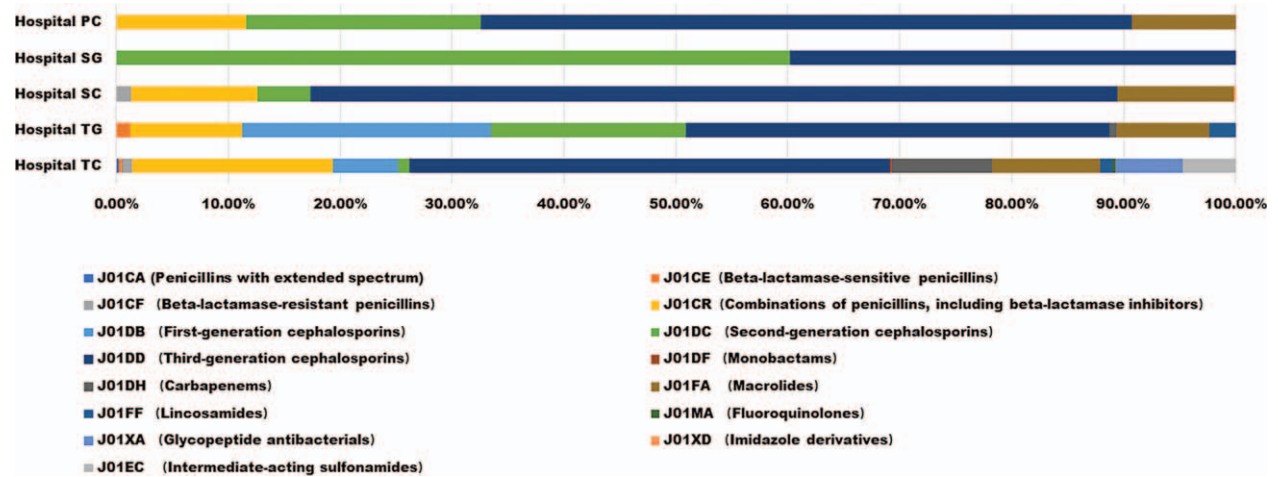


Figure 1. Antibiotic use of hospitalized children in difference hospitals.

categories, of which 14 categories were used in TC. *Cephalosporins* were the most antibiotic, especially *third-generation Cephalosporins*. Furthermore, *Macrolides* was the second common category except for hospital SG, in which prescriptions only consisted of *second-generation Cephalosporins* and *third-generation Cephalosporins*.

Different antibiotic categories were used largely due to different diseases and the bacterial resistance in hospitalized children among hospitals. The reasons of antibiotic prescriptions were shown in Table 2. The spectrum of disease was more diverse in hospital TC than that in other type hospitals. The conditions of Cardiovascular infections, prophylaxis and infection with malignancy individually occurred in hospital TC. As a whole, 56.8% and 22.2% of antibiotic prescriptions in pediatric inpatients were consumed in LRTIs and URTIs. There was statistical difference in the ratio of antibiotic on URTIs ($P < .001$). Compared with Hospital TC, higher rates were shown in other hospitals even up to 49% in Hospital SG.

LRTIs was the leading reason for antibiotic consumption in all pediatric wards of different type hospitals. The 678 children with LRTIs were prescribed with 969 antibiotic prescriptions. 84.6% of LRTIs children was young than 5 years. The composition of

prescriptions was presented in Figure 2. *Third-generation Cephalosporins* (60.3%) and *Macrolides* (12.3%) was the most antibiotic category.

4. Discussion

In this study, a comparative data of antibiotic prescriptions in pediatric wards among different types hospitals were collected. The results revealed that 66.9% of hospitalized children were prescribed with antibiotics, which was higher than the percent of other studies have reported. Some point prevalence surveys reported 40.9% of pediatric inpatients were on antibiotic in UK,^[8] 37% in Riga and 26.3% in Vilnius.^[9] The data in those studies as mentioned above were collected on one selected day during hospitalization. In our study, however, all inpatients antibiotics information was extracted throughout the hospitalization. A cross sectional study in Ethiopia with a method similar to us shown that almost 74% of hospitalized children received antibiotic therapy,^[10] which is higher than the proportion of this study. There are Geographical difference in antibiotic use of pediatric inpatients though they should be evaluated in the same way. The fact that higher rate of antibiotic use in Asia in children

Table 2

The reasons of antibiotic prescription among hospitals.

Reasons of antibiotics n (%)	Hospital TC	Hospital TG	Hospital SC	Hospital SG	Hospital PC	Total
URTI	33 (8.1)	105 (36.7)	62 (18.6)	49 (45.4)	12 (27.9)	261 (22.2)
LRTI	207 (51.0)	138 (48.4)	249 (74.6)	52 (48.1)	22 (51.2)	678 (56.8)
CNS infection	21 (5.2)	8 (2.8)				29 (2.5)
Gastrointestinal tract infection	16 (3.9)	5 (1.8)	12 (3.6)	2 (1.9)	5 (11.6)	39 (3.3)
Urinary tract infections	9 (2.2)	3 (1.1)	3 (0.9)		1 (2.3)	16 (1.4)
Cardiovascular infection	2 (0.5)					2 (0.2)
Skin/ soft tissue infection	4 (1.0)		3 (0.9)			7 (0.6)
Sepsis	22 (5.4)			2 (1.9)		24 (2.0)
Unexplained fever	3 (0.7)	13 (4.6)	2 (0.6)		1 (2.3)	19 (1.6)
Other	15 (3.7)	13 (4.6)	3 (0.9)	3 (2.7)	2 (3.7)	36 (3.1)
Prophylaxis	22 (5.4)					22 (1.9)
Infections with malignancy	52 (12.8)					52 (4.4)
Total	406	285	334	108	43	1176

CNS = central nervous system, Hospital PC = primary children hospital, Hospital SC = second children hospital, Hospital SG = second general hospital, Hospital TC = tertiary children hospital, Hospital TG = tertiary general hospital, LRTI = lower respiratory tract infection, URTI = upper respiratory tract infection.

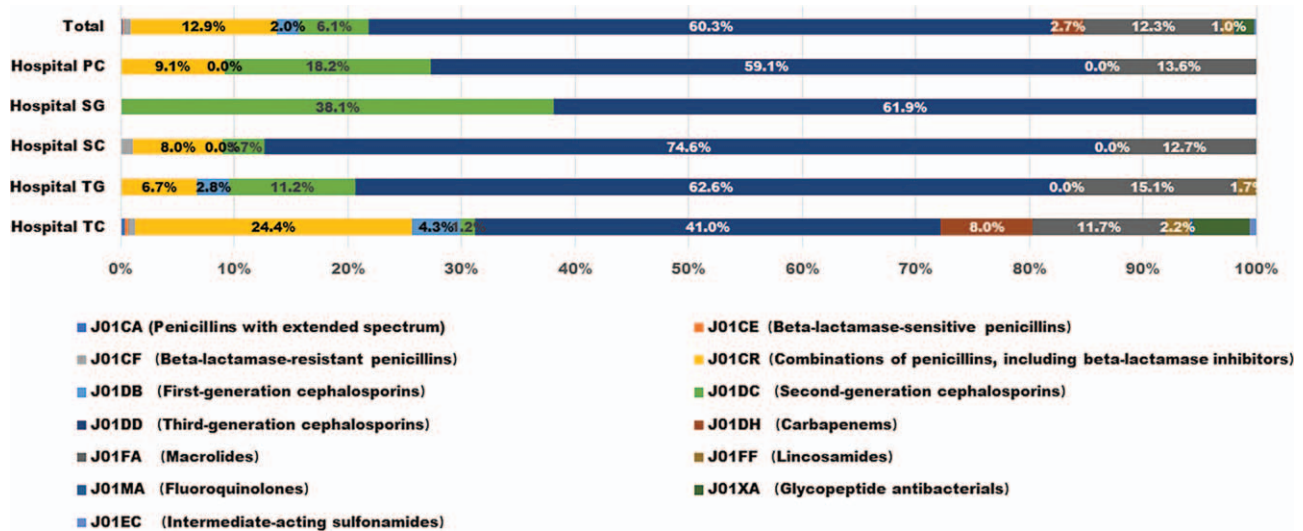


Figure 2. Antibiotic use of hospitalized children with LRTI in difference hospitals.

than that in Europe and North America is recognized.^[11–12] In this study, the percent of antibiotic use in Hospital TC (46.1%), meet the Chinese national management strategy, in which the proportion of antibiotic prescription in hospitalized children does not exceed 60%.^[13] But in other four hospitals including general hospitals or non-tertiary children hospitals almost 90% proportion prescribed antibiotic were far beyond the rule, which indicated overprescribing and irrational antibiotic utilization were obvious. This may be caused by poorer and suboptimal knowledge on antibiotic use of doctors and pediatric-specific resources, which has also been put forward in other reports.^[7,14] Ongoing education programs on pediatric antibiotic manage for secondary, primary children care setting and general hospitals should be carried out for further improvement.

Parenteral route was widely administrated in this study and some antibiotics like *Amoxicillin and enzyme inhibitor*, *Azithromycin*, *Cefuroxime* were administrated intravenously in Hospital TG, Hospital SC, Hospital SG, Hospital PG even if they can be taken orally. Studies on antibiotic route shown that rate of exclusively oral antibiotics varied widely, ranging from 0 to almost 80% with the average 21.5% in hospitalized children across hospitals.^[15] The parenteral route proportion (93.4%) of this study was amazing and inappropriate. Parenteral administration may indeed be preferable in certain situations, such as chosen antibiotics with limited oral bioavailability, complicated infections or central nervous system infection and children who cannot take oral medication. The route of administration depends on the type and severity of diseases, meanwhile the route also be affected by irrational social acceptance in hospitalized patients that intravenous drugs are more “effective” compared with oral antibiotics. Several randomized trials revealed that oral amoxicillin is equivalent in safety and effectiveness to parenteral penicillin for pediatric patients with community acquired pneumonia,^[16–18] which is a most common infection in children. In addition, oral administration has potential to avert suffering of children, minimize the risk of hospital infection, reduce nursing burdens, shorten hospital stay and decrease medical expenses for many hospitalized children with common pediatric infections.^[19] Early switch from

parenteral to oral has been proposed to be a quality indicator for improving antibiotic prescribing on pediatric inpatients worldwide.^[12] This study provides a strong evidence that multiple efforts should be made on overuse of parenteral route in Chinese hospitalized children.

This study found that a high proportion of antibiotic were prescribed for URTIs in pediatric inpatients, especially in general hospitals, in which the percentages were more than 30% suggests overprescribing. Actually, a majority of URTIs are caused by virus and do not require antibiotics.^[20] Overuse of antibiotics is common in children with URTI including in china,^[21–23] which might be affected by difficult distinguishing bacterial infections form viral URIS and insufficient knowledge of pediatrician and parents on antibiotic use for URTIs.^[24–25] American Academy of Pediatric proposed that judicious antibiotic prescribing for URTIs in pediatrics should follow 3 principles:

- (1) determine the likelihood of bacterial infections according to clinical symptoms,
- (2) weigh benefits and harms of antibiotics on strict bacterial diagnosis,
- (3) choose advisable strategies based on the severity of diseases.^[26]

Reducing unnecessary antibiotic use in pediatric URTIs may be another aspect we need pay attention for controlling inappropriate use of antibiotic in China.

Pneumonia is a major cause of childhood morbidity and mortality,^[27] Empirical medications are always given to reduce serious complications before determining accurate pathogen. Results shown that LRTI was the leading reason for antibiotic consumption up to 56.8% and Cephalosporins were the most prescriptions, especially third-generation Cephalosporins (60.3%). According to the management of WHO that oral amoxicillin and parenteral ampicillin and gentamicin were recommended as first-line treatment for severe pneumonia,^[28] the misuse of antibiotic was found in this study. In china, the common bacterial etiology of community-acquire pneumonia (CAP) among children under 5 years were *Klebsiella pneumonia*, *Streptococcus pneumonia*(SP), *Escherichia coli*, *Staphylococcus*

aureus(SA), *Haemophilus influenzae* (Hi),^[29] and SP and Hi are the most common for hospitalized children.^[30] At present, SP and Hi are high sensitive to penicillin, amoxicillin and Clavulanate separately according to the latest consensus in China.^[31] Antibiotic de-escalation may be necessary according to bacteriological cultures and resistance in LRTI. Furthermore, the introduction of *pneumococcal* vaccines and Hi conjugate vaccines can effectively decrease the incidence of global pneumonia,^[32–33] but only 25.2% of children received the vaccines in *ShangHai*, a developed city of China.^[34] Therefore, increase vaccination may be another way to reduce the inappropriate use of antibiotics in LRTI.

Limitation: This is a short-term cross-sectional survey and data are only collected from April 2018 to June 2018, which may lead to the seasonal bias. However, to some extent it does reveal the general situation of current antibiotics use. Comprehensive investigation can be done and help us to understand the seasonal characteristics. Otherwise further attention can also be pay to other aspects of inappropriate antibiotic use like the dose and combined medication of antibiotics.

5. Conclusion

This study shown the inappropriate use of antibiotic in Chinese hospitalized children including overuse of antibiotic prescriptions, misuse of parenteral administration, overprescribing of antibiotic on URTI and the de-escalation requirement of third-generation Cephalosporins in pediatric inpatients with LRTI. The irrational use was more serious in general hospitals and non-tertiary children hospitals. Management strategy should be implemented on quality improvement of antibiotic use.

Author contributions

Conceptualization: Chaomin Wan, Yu Zhu.

Data curation: Ruixue Miao, Yun Zhao.

Formal analysis: Ruixue Miao, Zhiling Wang.

Funding acquisition: Ruixue Miao, Chaomin Wan.

Investigation: Ruixue Miao, Jialing Xia.

Methodology: Ruixue Miao, Chaomin Wan, Yu Zhu.

Project administration: Chaomin Wan.

Resources: Yun Zhao, Liling Zhang, Juan Liu, Jing Qin, Jialing Xia, Huiqiong Yan.

Software: Yu Zhu.

Supervision: Ruixue Miao, Chaomin Wan, Zhiling Wang, Yu Zhu.

Validation: Ruixue Miao, Yu Zhu, Yun Zhao, Liling Zhang, Juan Liu, Jing Qin, Huiqiong Yan.

Writing – original draft: Ruixue Miao.

Writing – review & editing: Chaomin Wan, Zhiling Wang.

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