

Original Article

A cross-sectional study of antibiotic misuse among Chinese children in developed and less developed provincesYannan Xu¹, Jingjing Lu¹, Chenhui Sun¹, Xiaomin Wang¹, Yanhong Jessika Hu², Xudong Zhou¹¹ *The Institute of Social and Family Medicine, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China*² *Murdoch Children's Research Institute, University of Melbourne. Royal Children's Hospital, Parkville, Australia***Abstract**

Introduction: Antimicrobial resistance is a global health crisis and primarily caused by antibiotic misuse. Antibiotic misuse among children is particularly concerning, and its prevalence may vary from region to region in China with different development levels.

Methodology: Zhejiang and Shaanxi were selected to represent developed and less developed provinces in China, respectively. Data of 2924 parents in Zhejiang and 3355 parents in Shaanxi whose children were 0-13 years old were collected through multi-stage stratified cluster random sampling and a self-administrated questionnaire. Chi-square tests and logistic regression models were used for statistical analysis.

Results: Compared to parents in Zhejiang, those in Shaanxi were more likely to keep antibiotics for children at home, to engage in self-medication with antibiotics for children, and to make their children take antibiotics prophylactically. While there were no significant provincial differences between parents' requests for antibiotics during pediatric consultations, parents in Shaanxi province were more likely to receive prescribed antibiotics.

Conclusions: Children in less developed provinces face higher risks of antibiotic misuse at home as well as when attending medical practitioners. Comprehensive educational interventions are required to improve antibiotic use for children all over China but particularly in less developed provinces such as Shaanxi. Furthermore, non-prescription sales and over-prescribing of antibiotics should be reduced by targeted strategies.

Key words: antibiotic use; children; regional disparity.

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Introduction

Antimicrobial resistance (AMR) is recognized as a grave global health threat [1,2]. AMR has already lengthened the course of infectious diseases and increased the mortality rates as well as treatment costs [3]. The rapid development of AMR is primarily caused by widespread misuse of antibiotics [4-6] which accelerates the natural process of genetic selection thereby making organisms increasingly resistant to antibiotic treatments [7,8]. Antibiotic misuse among children is particularly concerning, because children fall ill frequently and are therefore more likely to be exposed to unnecessary antibiotics. Children are also more vulnerable to the consequences of AMR than adults [9]. Furthermore, children are grouped together in nurseries and schools, catalyzing the spread of drug-resistant bacteria [6]. Antibiotics are commonly used for children with viral upper respiratory tract infections, despite the fact that these diseases are self-limiting and do not respond to antibiotic therapy [10,11]. Antibiotic misuse and AMR are most prevalent in low and middle

income countries due to these countries' greater burden of infectious diseases and weaker public health systems [12].

Previous research has revealed that Chinese children are becoming less likely to benefit from antibiotics specifically as a result of AMR [13]. It has also been warned that antibiotic misuse remains rampant among Chinese children, and that both the supply and demand sides are to blame [14]. On the supply side, antibiotics are frequently prescribed to children during pediatric consultations [15-17] and non-prescription antibiotics are widely available at community pharmacies [18] despite prohibitory regulations [14,19]. On the demand side, many parents and caregivers admit to keeping antibiotics at home [10-12] and giving children antibiotics without seeing a doctor, which is a form of self-medication with antibiotics (SMA) [11,12,20,21]. SMA can be wasteful and harmful, and home-stored antibiotics provide a reservoir for it [22]. Moreover, some parents expect

antibiotics to be prescribed thereby influencing doctors' diagnostic and prescribing processes [23].

Antibiotic use and habits vary across China. There are appreciable socioeconomic and public health disparities between different regions which, in turn, affect the degree to which antibiotics are available and used by Chinese population [15,24]. Recent research has also proven that socioeconomic status of a population has profound impact on its antibiotic consumption and prevalence of AMR [25]. Generally, eastern coastal provinces are more prosperous than other parts of China. One study mentioned that the location of a child's residence in China might influence the rate of antibiotic misuse by his/her caregiver [20]. In accordance with that, another research in urban China found that children from an eastern city were much less likely to receive non-prescription antibiotics from caregivers than their counterparts from a western city [11]. It was also reported that regional economic statuses in China have corresponding rates of antibiotics sales in hospitals [26]. So far, little is known about the potential behavioral discrepancies on antibiotic use among different regions in China with unequal development levels especially for children's cases, which may imply intervention priorities in the future.

Therefore, this research aims to assess antibiotic use in Chinese children in two different regions in the hope of exposing regional disparities. The purpose of this study is to compare the following behaviors of parents in developed and less developed Chinese provinces: 1) requesting as well as receiving prescribed antibiotics during pediatric consultations, 2) SMA for children's illnesses, 3) keeping antibiotics at home for children, and 4) making children take antibiotics prophylactically.

Methodology

Data collection

The data from this study were collected between June, 2017 and April, 2018 as a part of a larger cross-sectional research project targeting Chinese parents with children under 13 years old. Based on their location and latest provincial GDP per capita [27], eastern Zhejiang province and western Shaanxi province were selected to represent developed and less developed regions of China respectively. A multi-stage stratified cluster random sampling method was adopted as this method provides adequate representation in a socioeconomically diverse population. We anticipated a study population of approximately 3000 parents per province as a sufficient sample size for subgroup

analyses. In each province, a prefecture-level city was randomly selected. Within that city, an urban and a rural district were randomly chosen as sampling sites. At each site, a complete roster of kindergartens, primary schools, and vaccination clinics (in the latter, over 90% of children under 3 received basic immunizations [28]) was obtained. A certain number of them were randomly selected as clusters depending on their scales or daily flows to meet the anticipated sample size. All parents of children aged 4 to 6 years in selected kindergartens, 7 to 13 years in primary schools, and under 3 years old in vaccination clinics were sampled.

We used a self-administered questionnaire (see Supplementary File 1) on Wen Juan Xing (<https://www.wjx.cn/>), the largest online survey platform in China. Informative leaflets with a unique QR code linked to the questionnaire were issued to parents so that they could access and complete the questionnaire on their smartphones. In kindergartens and primary schools, class teachers helped distribute these leaflets and consent forms to students, which would be presented to their parents after school. Parents who were willing to participate signed the consent form and completed the questionnaire online. Consent forms were brought back to class the following day and collected by teachers.

At vaccination clinics, our research assistants presented the parent(s) with informative leaflets and explained about the survey while they waited for the child's vaccination. After receiving consent, parents completed the questionnaire in the observation area once the child had been vaccinated. In both the school and clinic-based contexts, participants were explicitly informed that: 1) the survey was voluntary and participants could withdraw any time they wanted; 2) anonymity and confidentiality were guaranteed; 3) if the participant had more than one child, the child in question referred to the one receiving vaccination or attending the kindergarten/primary school; 4) the questionnaire should be completed by the parent who acted as the main caregiver of the child.

Measurements

The survey contained four sections: 1) Socio-demographic characteristics, including the parent's gender, whether the parent and his/her spouse lived in a rural or urban area, their monthly household income, their level of education, whether they had ever studied medicine or embarked on a medical career, and finally the gender and age of the child in question. 2) The child's recent medical history: whether the child suffered from any illness in the past month including

but not limited to a cold, fever, sore throat, diarrhea, and/or otitis media; whether the parent only self-medicated the child, took the child to a doctor after self-medication failed, or directly sought medical advice (including all levels of health facilities). 3) Antibiotic use: whether the parent gave antibiotics to the child during self-medication; when seeking medical advice directly or after self-medication failed, whether the parent requested antibiotics during consultation and whether the parent received a prescription of antibiotics. 4) Other behaviors, including whether the parent kept antibiotics at home for children and whether the parent made the child take antibiotics for prophylaxis in the past year. ‘Prophylaxis’ here refers to giving a child antibiotics who is not sick with the intention of preventing common infections (e.g. a cold or flu). This questionnaire was drafted and tailored to the Chinese context based on literature review [10,12,29,30] and through interviews with stakeholders and experts, and finalized after a pilot test on validity and reliability with 315 respondents.

Statistical analysis

Data analyses were performed with IBM Statistics 24.0 and a *p*-value less than 0.05 was considered statistically significant. Chi-square tests and t-tests were used to compare socio-demographic characteristics and behaviors between parents in Zhejiang and Shaanxi provinces. Logistic regression

models were applied to further explore regional disparities in antibiotic-related behaviors by controlling for social-demographic variables.

Ethics approval

This study was approved by the Institutional Review Board of School of Public Health, Zhejiang University (reference number: ZGL201706-2).

Results

Socio-demographic characteristics

A total of 2,924 questionnaires from Zhejiang and 3,355 from Shaanxi were completed and collected. Table 1 presents the socio-demographic characteristics of the children and parents. No significant differences were reported between respondents in the two provinces regarding their children’s gender and age, or the parents’ medical background as well as residential location (*p* > 0.05). Compared to parents in Zhejiang province, those in Shaanxi reported significantly lower levels of education and monthly household incomes (*p* < 0.001).

Parents’ responses to children’s illness and behaviors on antibiotic use

As Table 2 shows, more children in Shaanxi suffered from illnesses in the past month than those in Zhejiang. Among those sick children, the most commonly reported illnesses were a cold or sore throat

Table 1 Socio-demographic characteristics of children and parents in Zhejiang and Shaanxi provinces.

	Zhejiang (N = 2924) N(%)	Shaanxi (N = 3355) N(%)	χ ² /t	p
Gender of the child				
Male	1511 (51.68)	1683 (50.16)	1.429	0.232
Female	1413 (48.32)	1672 (49.84)		
Age of the child, mean (SD)	6.19 (3.63)	5.62 (3.53)	6.270	0.236
Gender of the parent				
Male	668 (22.85)	676 (20.15)	6.752	0.009
Female	2256 (77.15)	2679 (79.85)		
Parents’ highest level of education				
Middle school or below	430 (14.71)	914 (27.24)	423.5	< 0.001
High school	615 (21.03)	1156 (34.46)		
College or above	1879 (64.26)	1285 (38.30)		
Parents’ medical background				
No	2579 (88.20)	2919 (87.00)	2.054	0.152
Yes	345 (11.80)	436 (13.00)		
Monthly household income				
≤ 5000RMB (645EUR)	642 (21.96)	2047 (61.01)	1345	< 0.001
5001-10000RMB (645-1290EUR)	1033 (35.33)	1040 (31.00)		
> 10000RMB (1290EUR)	1249 (42.72)	268 (7.99)		
Residential location				
Urban	1715 (58.65)	1940 (57.82)	0.441	0.507
Rural	1209 (41.35)	1415 (42.18)		

Table 2 Parents’ responses to children’s illness and behaviors on antibiotic use in Zhejiang and Shaanxi provinces.

	Zhejiang N (%)	Shaanxi N (%)	χ^2	<i>p</i>
Children suffered from illnesses in the past month	1021 (34.92)	1294 (38.57)	8.949	0.003
Ever engaged in self-medication	559 (54.75)	696 (53.79)	0.213	0.644
Self-medication with antibiotics	105 (18.78)	297 (42.67)	81.26	< 0.001
Ever sought medical advice	716 (70.13)	899 (69.47)	0.115	0.734
Requested antibiotics during consultation	56 (7.82)	61 (6.79)	0.636	0.425
Received prescribed antibiotics	351 (49.02)	509 (56.62)	9.238	0.002
Kept antibiotics at home	1333 (45.59)	1950 (58.12)	98.38	< 0.001
Used antibiotics prophylactically in the past year	489 (16.72)	924 (27.54)	104.8	< 0.001

in both Shaanxi and Zhejiang (88.95% vs. 86.68%, *p* > 0.05). To manage the illnesses, about half of the parents in both provinces engaged in self-medication (*p* > 0.05). Significantly more parents in Shaanxi reported using antibiotics when they self-medicated their children than those in Zhejiang province (42.67% vs. 18.78%, *p* < 0.001). Around 70% of the parents in both provinces reported ever seeking medical advice for their children with or without self-medication (*p* > 0.05). There was no significant provincial difference between the proportions of the parents who requested antibiotics during consultations and those who did not (*p* > 0.05),

but more parents received prescribed antibiotics in Shaanxi than in Zhejiang (56.62% vs. 49.02%, *p* < 0.01). Besides, significantly more parents in Shaanxi reported having in-home antibiotics at the time of the survey (58.12% vs. 45.59%, *p* < 0.001) and administering prophylactic antibiotics to their children over the previous year (27.54% vs. 16.72%, *p* < 0.001).

The regional disparity in behaviors on antibiotic use

Table 3 presents the logistic regression analyses of the regional disparity in parents’ behaviors on antibiotic use. After adjusting for socio-demographic factors,

Table 3 Logistic regression analyses of the regional disparity in parents’ behaviors on antibiotic use.

	Self-medication with antibiotics N = 1255 aOR (95% CI)	Requested antibiotics N = 1615 aOR (95% CI)	Received prescribed antibiotics N = 1615 aOR (95% CI)	Kept antibiotics at home N = 6279 aOR (95% CI)	Used antibiotics prophylactically N = 6279 aOR (95% CI)
Province					
Zhejiang	1.00	1.00	1.00	1.00	1.00
Shaanxi	2.82 (2.06,3.86)***	0.75 (0.49,1.17)	1.46 (1.16,1.84)**	1.93 (1.72,2.17)***	1.82 (1.58,2.10)***
Gender of the child					
Male	1.00	1.00	1.00	1.00	1.00
Female	0.94 (0.73,1.20)	0.94 (0.64,1.37)	0.90 (0.74,1.10)	1.02 (0.92,1.13)	1.11 (0.98,1.25)
Age of the child	1.00 (0.96,1.04)	1.08 (1.02,1.14)**	1.02 (0.99,1.05)	1.05 (1.03,1.06)***	1.02 (1.01,1.04)*
Gender of the parent					
Male	1.00	1.00	1.00	1.00	1.00
Female	1.19 (0.84,1.68)	0.73 (0.47,1.16)	1.21 (0.94,1.56)	1.22 (1.08,1.39)**	0.88 (0.76,1.01)
Parents’ highest level of education					
Middle school or below	1.00	1.00	1.00	1.00	1.00
High school	0.85 (0.58,1.25)	0.50 (0.29,0.86)*	1.20 (0.90,1.61)	1.38 (1.19,1.60)***	1.09 (0.93,1.29)
College or above	0.77 (0.53,1.14)	0.46 (0.27,0.78)**	1.25 (0.93,1.67)	1.55 (1.33,1.81)***	0.94 (0.79,1.13)
Parents’ medical background					
No	1.00	1.00	1.00	1.00	1.00
Yes	1.00 (0.70,1.42)	1.33 (0.73,2.42)	0.94 (0.68,1.30)	1.60 (1.37,1.88)***	0.62 (0.50,0.77)***
Monthly household income					
≤ 5000RMB (645EUR)	1.00	1.00	1.00	1.00	1.00
5001-10000RMB (645-1290EUR)	0.76 (0.57,1.03)	1.14 (0.71,1.83)	0.97 (0.76,1.24)	1.03 (0.91,1.17)	0.98 (0.85,1.13)
> 10000RMB (1290EUR)	0.81 (0.54,1.21)	0.91 (0.49,1.70)	1.07 (0.78,1.47)	1.16 (0.99,1.36)	0.90 (0.74,1.10)
Residential location					
Urban	1.00	1.00	1.00	1.00	1.00
Rural	0.79 (0.60,1.03)	0.69 (0.45,1.05)	0.67 (0.54,0.82)***	0.88 (0.78,0.98)*	1.07 (0.94,1.21)

p* < 0.05, *p* < 0.01, ****p* < 0.001.

parents in Shaanxi were more likely to engage in SMA for children than those in Zhejiang (aOR = 2.82; 95% CI 2.06-3.86). While no significant regional disparity was found on the likelihood of requesting antibiotics during pediatric consultations, parents in Shaanxi were more likely to receive prescribed antibiotics than their counterparts in Zhejiang (aOR = 1.46; 95% CI 1.16-1.84). In addition, parents in Shaanxi were more likely to keep antibiotics at home for children (OR = 1.93; 95% CI 1.72-2.17) and to administer prophylactic antibiotics to their children (OR = 1.82; 95% CI 1.58-2.10).

Discussion

To the best of our knowledge, this is the first study investigating parental behaviors on antibiotic use for children to encompass both household and medical settings in developed and less developed Chinese provinces. Our main finding is that children in less developed provinces like Shaanxi are more likely to engage in antibiotic misuse than those in developed provinces like Zhejiang. Our study reveals that parents' reactions to children's illnesses were similar between regions at different development levels without taking antibiotics into account. However, living in a less developed province increased the likelihood of both parents and doctors misusing or unnecessarily prescribing antibiotics to treat children's illnesses. Parents in Shaanxi were also more likely to keep in-home antibiotics and administer prophylactic antibiotics to their children.

Self-medication is commonly practiced worldwide. People in both developed and developing areas self-medicate as a supplement to, or replacement for formal medical consultations [21]. When parents temporarily feel their children's illness too minor for seeing a doctor, they may attempt to self-medicate their children at first, and turn to hospitals if their children do not get better as they expected [31]. Despite equal proportions of parents in Zhejiang and Shaanxi choosing self-medication or going to a doctor, results were significantly different on the subject of antibiotic use. Consistent with previous research [11], our study found that parents in the less developed Shaanxi province were more likely to keep antibiotics at home and to give their children antibiotics as SMA or prophylaxis. These findings mirror a study in Europe, which showed storing in-home antibiotics and self-medicating with antimicrobial drugs were more prevalent in less developed countries [32]. The common trend can be attributed to cultural and socioeconomic factors that

influence public perceptions of children and antibiotics as well as access to non-prescription antibiotics.

In China, preserving children's health is a strong priority in most Chinese families as a result of the previous national one-child policy. When children fall ill, parents strive for the best medicine available [21,33]. In less developed regions, antibiotics are often loosely regulated and erroneously seen as panaceas [34,35]. Perceived experiences of recovery after taking antibiotics for symptoms of viral infections, a phenomenon described as a self-fulfilling prophecy by some clinicians [36], make parents develop their preferences when choosing drugs [33]. More worrying is that parents tend to impose their own use of antibiotics on children [37]. In China, previous studies have found regional disparities in parental understandings of and attitudes towards antibiotic use. Fewer caregivers in the less developed city of Xi'an recognized antibiotics as prescription drugs, while many more agreed that they could self-medicate their children with antibiotics for minor illnesses compared to their counterparts in the more developed city of Shanghai [11]. Also, it has been reported in Jiangxi, a less developed province in central China, that nearly 80% of parents believed antibiotics could cure viral infections, and about 50% thought antibiotics would help shorten the duration of upper respiratory tract infections [12]. More importantly, many Chinese people used to simply regard symptoms of common infections as inflammation, and there is a widespread belief that antibiotics are the same as anti-inflammatories [38]. Significantly more parents in Xi'an than in Shanghai agreed on this belief [11]. Above all, these misunderstandings potentially explain why parents in less developed provinces like Shaanxi had a greater preference for storing antibiotics at home and self-medicating children with antibiotics.

Easy access to non-prescription antibiotics in pharmacies is another contributing factor to antibiotic misuse in children [39]. Due to the lack of licensed pharmacists in China, salespeople at retail pharmacies can abet antibiotic misuse to make more profits [40]. Loose regulations on the sale of antibiotics indemnify their actions in less developed regions. In a Lebanese study, 69.2% of pharmacists in lower socioeconomic areas reported dispensing antibiotics to children compared to 27.1% in higher socioeconomic areas [41]. In China, significant regional disparities in non-prescription sales of antibiotics for the case of pediatric diarrhea were discovered, with a rate of 57.7% in Nanjing (a more developed Chinese city) versus 73.7% in Xi'an [18]. It was also found that when considering

the source of non-prescription antibiotics used in SMA for children, more came from community pharmacies in Xi'an than in Shanghai, which might be attributable to better implementation of existing prohibitory regulations and better public awareness of appropriate antibiotic use in Shanghai [11]. Since Zhejiang province is also located in the Yangtze River Delta Economic Region, like Shanghai and Nanjing, it seemed reasonable to presume that parents in Zhejiang were less likely to use non-prescription antibiotics for children.

The regional disparities in receiving antibiotic prescriptions during pediatric consultations were also highlighted by our study. In contrast with a previous study which found a positive correlation between regional economic statuses and sales of antibiotics in hospitals [26], our study found a negative association between regional development levels and antibiotic prescription rates. We believe our results differ from theirs because eastern developed provinces in China have more adequate medical resources, including better availability of antibiotics than other underdeveloped sub-regions. Our study focused on the rate at which antibiotics were prescribed for children's common illnesses in outpatient settings, whereas theirs considered the aggregate antibiotic consumption of all patients. The different inclusion criteria as well as computing methods might have led to the differing results. Additionally, their findings were based on secondary data cited from earlier studies which had been conducted at different times rather than contemporaneous field research.

The Chinese government issued a National Essential Medicine List in 2009 including certain antibiotics and all governmental health institutions are required to sell the drugs in the List at cost only, which is also called 'zero markup drug policy' [42]. However, prescribing options can still be affected by personal relations with sales offers and pharmaceutical companies who may provide discounts to amenable doctors [41,43]. As a result, the antibiotic prescription rate could be influenced by doctors' financial incentives, especially in less developed regions [44]. Previous research has claimed that primary care doctors' salaries in western underdeveloped provinces are too low to live on since these doctors are usually self-employed and part-time, and they receive no government subsidies which are reserved as a bonus for medical practice [45]. Consequently, they have no choice but to rely on prescription profits to make ends meet, sometimes even prescribing multiple antibiotics for self-limited infections. Village doctors may even

prescribe as a function of their patients' capacity to pay, that is, as many drugs as a patient can afford [33].

It has been asserted that parental requests for antibiotics encourage doctors to prescribe them [46]. In some less developed regions of China, doctors act as influential community members and have the freedom to tailor treatments to individual needs [33]. Our study found relatively low rates of parents requesting antibiotics in Zhejiang and Shaanxi. However, there were still high antibiotic prescribing rates in both provinces. This was particularly true in Shaanxi, where parents received many more antibiotic prescriptions than their counterparts in Zhejiang. Our research team previously conducted a survey to compare antibiotic misuse among university students in Zhejiang and the less developed province of Guizhou. We found a significantly higher proportion of students in Guizhou who reported asking for antibiotics and who received prescribed antibiotics when seeing a doctor in the past month [44].

Our results differ from the above study of university students. A possible explanation is that when parents decide to take their young children to a doctor, they may already have doubts as to the reliability of their self-diagnosis and the safety of antibiotics, and may feel more reliant upon professional advice than university students who went to see the doctor for themselves. This kind of special concern for children appears to be universal. A study in Hong Kong showed that Chinese parents became more cautious when giving their children antibiotics because they had major concerns about children's tolerance to side effects [47]. Another study in the UK also found that mothers were more likely to accept non-antibiotic treatments for their children than for themselves [36]. As noted earlier, antibiotics are useless at treating most of the conditions reported in this study [6], thus, the prescribers of antibiotics may bear most of the responsibility for antibiotic misuse in medical contexts. A study in western China found that nearly half of prescriptions from village clinics contained antibiotics [48]. Some practitioners, especially the still practicing so-called "barefoot doctors" who were preliminarily trained to serve huge populations in less developed regions of China, might not be aware of guidelines regarding appropriate antibiotic use issued over the last few decades [49]. When antibiotic misuse is repeatedly advised by health practitioners, the practice spreads among the general public and becomes a social norm [3].

Our findings reveal the need for region-specific education programs for parents to correct their

misconceptions about antibiotics and inform them of appropriate treatment strategies for children's common illnesses. New stronger regulations as well as more stringent enforcement of existing regulations are needed to eliminate non-prescription sales of antibiotics at community pharmacies. Training professional pharmacists and supervisors is particularly urgent in less developed areas. In addition, unnecessary antibiotic prescriptions should be restricted by standard guidelines and regulatory institutions. To that end, programs to train doctors on appropriate prescribing practices would be tremendously useful. Doctors could then participate in public campaigns to change social norms regarding antibiotic misuse. To decrease doctors' financial incentives, public investments in primary health care - specifically aiming to increase practitioner incomes in less developed areas - are required. If the link between doctors' and hospitals' incomes can be severed from drug sales, this will begin an unadulterated flow of prescriptions from hospitals to retail pharmacies, which may help reduce both over-prescribing and non-prescription sales of antibiotics [39].

There are several limitations in this study. First, inpatient use (e.g. inpatient intravenous antibiotics) which requires no patient input was not included because our respondents were parents. Secondly, our findings were based on self-reported data, which may be distorted by report bias. We are nonetheless generally confident in our data given the short recall period of one month for questions related to children's illnesses. Finally, even though the sample sizes were large, our study only examined two Chinese provinces. More provinces at different levels of development must be investigated to further concretize the conclusions of this study.

Conclusion

There are regional disparities in antibiotic misuse among Chinese children. Children in less developed provinces face higher risks of antibiotic misuse both at home and when attending medical practitioners. To solve the problem, large-scale educational programs on appropriate antibiotic use will be required as well as more stringent enforcement of prohibitory regulations on non-prescription sales of antibiotics. Doctors and hospitals should be liberated from drug profits from unnecessary antibiotic prescriptions, and lead to change social norms of antibiotic misuse. Only when antibiotic misuse among children is addressed by considering the underlying impact of local environments and the

interests of stakeholders, can the problem be effectively handled.

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Authors' contributions

YX analyzed the data and drafted the manuscript. XZ is the PI of the study and participated in the coordination of data collection and critical review of the manuscript. XZ and XW led the study design. YX, JL, CS and XW participated in data collection. JL, CS, XW and YH revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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Annex – Supplementary Items

Following from next page: Questionnaire of Parents' Knowledge, Attitudes and Practice of Children Antibiotic Use in China.

Questionnaire of Parents' Knowledge, Attitudes and Practice of Children Antibiotic Use in China

Part 1: The General Information

If you have more than one child, the child in this questionnaire refers to the one who is currently taking the vaccine at the vaccination site or the one who is attending the sample kindergarten or primary school.

1. Gender of your child: Male Female
2. The child's date of birth: _____
3. Number of children:
 - 3.1 How many children do you have? _____;
 - 3.2 Which one is the child involved in this survey? _____
4. You are the child's: Father Mother
5. Who is the main child caregiver at home?
Father Mother Grandfather Grandmother Others
6. Your education level:
Primary school or below Middle school High school/Technical secondary school
College/Junior college Postgraduate or above
7. Your spouse's education level:
Primary school or below Middle school High school/Technical secondary school
College/Junior college Postgraduate or above
8. Your location of residence? Rural Urban
9. Do you have any medical education background? Yes No
10. Does your spouse have any medical education background? Yes No
11. Are grandparents at home involved in treatment decisions when your child is ill?
Never Sometimes Often Always
12. Your average household income per month (RMB)?
<3,000 3,001-5,000 5,001-10,000 10,001-20,000 >20,000

Part 2: Antibiotics Related Knowledge

13. Antibiotics are effective for viral infections.
Yes No Don't know

14. Antibiotics are anti-inflammatory drugs.
 Yes No Don't know
15. The more frequently people use antibiotics, the harder it is to cure the bacterial infections.
 Yes No Don't know
16. Excessive use of antibiotics can lead to bacterial antibiotic resistance.
 Yes No Don't know
17. Expensive antibiotics are more effective than cheap ones.
 Yes No Don't know
18. Excessive use of antibiotics is a serious problem in China.
 Yes No Don't know
19. Bacterial antibiotic resistance in China will become a serious problem.
 Yes No Don't know
20. New antibiotics are more effective than old ones.
 Yes No Don't know
21. Excessive use of antibiotics can produce superbugs.
 Yes No Don't know
22. Do you think the following drugs are antibiotics (or not)?
- Penicillin (amoxicillin, etc.) Yes No Don't know
 - Cephalosporin (cefaclor, ceftriaxone sodium, etc.) Yes No Don't know
 - Non-steroidal anti-inflammatory drugs (ibuprofen, aspirin, etc.) Yes No Don't know
 - Steroids (dexamethasone, prednisone, etc.) Yes No Don't know
 - Quinolones (norfloxacin, ofloxacin, etc.) Yes No Don't know
 - Macrolides (azithromycin, roxithromycin, etc.) Yes No Don't know
23. Do you think antibiotics are appropriate when your child has the following conditions (diseases)?
- Sore throat Yes No Don't know
 - Common cold (cough, runny nose) Yes No Don't know
 - Diarrhea Yes No Don't know
 - Fever Yes No Don't know
 - Otitis media Yes No Don't know

24. Using antibiotics can speed up your child's cold recovery.
Yes No Don't know
25. Using antibiotics can alleviate your child's cold symptoms.
Yes No Don't know
26. If your child needs antibiotics, it is better to be administered by infusion.
Yes No Don't know
27. Once your child's symptoms are relieved, antibiotic use should be stopped immediately.
Yes No Don't know
28. There will be fewer and fewer effective antibiotics in the future if we don't use antibiotics properly.
Yes no Don't know
29. Antibiotics are effective for child's viral infections.
Yes No Don't know

Part 3: Antibiotic Use Behaviors (can't go back to Part 1 or Part 2)

Dear parent, before you start answering the following questions, please read the following messages about antibiotic knowledge:

1. Antibiotics are different from anti-inflammatory drugs; antibiotics can kill bacteria but are not effective for viral infections.
2. Common-used antibiotics include:
 - Penicillin (amoxicillin, etc.)
 - Cephalosporin (cefaclor, ceftriaxone sodium, etc.)
 - Quinolones (norfloxacin, ofloxacin, etc.)
 - Macrolides (azithromycin and roxithromycin etc.)
 - Sulfa

You may find that some of your answers to the questions in the second part of this survey are wrong, but it doesn't matter because what we need is to know your genuine antibiotic knowledge level. Please don't be uneasy about the answers.

30. Did your child get sick in the last month?

Yes No (skip to No.42)

31. If yes, which condition or disease did your child get?

31.1 Common cold (cough, runny nose): Yes No

31.1.1 If yes, the cold lasted for ___ days.

31.2 Fever: Yes No

31.2.1 If yes, the fever was up to ____ °C;

31.2.2 If yes, the fever lasted for ____ days.

31.3 Sore throat: Yes No

31.3.1 If yes, the sore throat lasted for _____ days.

31.4 Diarrhea: Yes No

31.4.1 If yes, the diarrhea lasted for _____ days.

31.5 Otitis media: Yes No

31.5.1 If yes, the otitis media lasted for _____ days.

31.6 Others: Yes No

32. Did your child get treated? Yes No (skip to No. 42)

33. If yes, what treatment did your child get?

Pure self-treatment (skip to No. 33.1)

Self-treated first, then sought formal health care if not getting better (skip to No. 33.2)

Sought formal health care (skip to No. 36)

33.1 Did you use antibiotics for your child during self-treatment?

Yes (skip to No. 34) No (skip to No. 42)

33.2 Did you use antibiotics for your child during self-treatment?

Yes (skip to No. 34) No (skip to No. 42)

34. If yes, please tell us the name of the antibiotic(s): _____.

35. Where did you get the antibiotic(s)?

Household storage

Purchased over the counter at the pharmacies

Brought by others

Others

36. Which health facility did you go to?

● Private clinic/Village clinics No Yes

● Community health centers/Township hospital No Yes

● Secondary/County hospital No Yes

● Tertiary hospital No Yes

37. When visiting the doctor at the health facility, did he/she prescribe any antibiotics for your child?

Yes No (skip to No. 42)

37.1 If yes, please tell us the name of the antibiotic(s): _____.

38. If the doctor prescribed antibiotics, were they used by oral administration or infusion?

Oral administration Infusion Both

39. Did you immediately stop using antibiotics (either oral administration or infusion) when your child's symptoms were relieved?

Yes No

40. When visiting the doctor, did you request antibiotics from the doctor (either oral administration or infusion)?

Yes, I requested for infusion.

Yes, I requested for oral antibiotic prescriptions.

No (skip to No. 42)

41. Did the doctor agree to your request for antibiotic prescription (either oral administration or infusion)?

Yes No

42. Do you keep antibiotics at home for your child (not for current use) at the time of the survey?

Yes No

43. If yes, where did you get the antibiotics?

Leftover prescriptions

Purchased over the counter at the pharmacies before

Brought by others

Others

44. In the past year, did you give your child antibiotics to prevent diseases (e.g. when your child's classmates got a cold or flu)?

Yes No

45. As a parent, what are the main information sources for you to get knowledge about dealing with child's common cold, fever, diarrhea and other diseases?

- Medical advice No Yes
- Family advice/experience No Yes
- TV No Yes
- Internet No Yes
- Radio No Yes
- Newspapers/magazines/books No Yes
- Weibo, Wechat or QQ No Yes
- Others No Yes