BMJ Open Non-prescription antibiotic use for cough among Chinese children under 5 years of age: a community-based cross-sectional study

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ABSTRACT

Objective This study aimed to investigate the non-prescription use of antibiotics for cough among children under 5 years in China.

Design A community-based cross-sectional survey.

Setting A face-to-face interview based on a standard questionnaire in the community from October to December 2019.

Participants A total of 3102 children under 5 years of age were enrolled with probability proportionate to size sampling method. The children's caregivers provided the responses as their agents.

Outcome measures Cough in the past month, non-prescription use of antibiotics after cough.

Results 1211 of 3102 children were reported to have a cough in the past month. Of these, 40.2% (487/1211) were medicated with antibiotics, and 18.7% (91/487) of these were not prescribed. Cephalosporins were the most frequently used antibiotic (52.8%), and community pharmacies were the main source (53.7%). Children who coughed for 1–2 weeks (OR 1.73, 95% CI 1.03 to 2.90) or 3–4 weeks (OR 2.39, 95% CI 1.08 to 4.97), with runny nose (OR 1.86, 95% CI 1.13 to 3.19) or those whose family annual income between ¥50 000 and ¥100 000 (OR 4.44, 95% CI 1.52 to 18.95) had a higher risk of non-prescription use of antibiotics than those coughing for <1 week, without runny nose or with family annual income <¥50 000.

Conclusions Our findings indicated that a high proportion of infants and young children had been treated with antibiotics for cough, and nearly one in five of them were used without prescription. More public health campaigns and further education on the appropriate use of antibiotics are needed to ensure the rational treatment of cough in children.

INTRODUCTION

Cough is a common symptom in childhood¹ and one of the most frequent reasons for consultation in daily paediatric practice.² It has been reported that over 50% of patients with acute cough/lower respiratory tract infection are prescribed antibiotics in primary healthcare.³ However, cough can be triggered

Strengths and limitations of this study

- This is the first community-based study to investigate the prevalence, source, type, and associated factors of non-prescription antibiotic use for cough among children under 5 years in China.
- Adoption of probability proportionate to size sampling method enables higher representation of the participants.
- Well-trained interviewers fluent in the local dialect conducted a face-to-face interview.
- Potential recall and report bias may exist as we relied on caregivers' retrospective descriptions.
- Absence information about clinical diagnosis of cough constrained further investigation.

by a variety of causes, in which uncomplicated viral acute respiratory tract infections account for the majority and antibiotics are ineffective for the symptomatic relief in such cases.^{2–5} In contrast with prescribed antibiotics, those used without prescriptions have more potential hazards as they are often consumed without prior disease knowledge and, therefore, contribute to more antimicrobial resistance, adverse drug reactions and masking of underlying disease processes.^{6,7} Additionally, infants and young children are more vulnerable to the risks of non-prescription antibiotic use due to their immature physiology and special organic feature.⁸

Children under 5 years are probably more frequent users of antibiotics because of their greater burden of infectious diseases and associated mortality risks compared with older children and adults.⁹ A systematic analysis showed that antibiotic use for treating cough with fast or difficult breathing symptoms among children under 5 years of age was at 61.0% (95% CI 29.1% to 84.1%) in upper-middle-income countries and 49.6% (95% CI 14.3% to 84.5%) in lower-middle-income

countries.⁹ China has the largest consumption of antibiotics in the world and has a high prevalence of non-prescription use with 36% frequency.^{6 10 11} Although the purchase of antibiotics from retail pharmacies without a prescription has been forbidden by China's Food and Drug Administration regulations since 2004, several studies using the simulated client method (SCM) demonstrated that customers can still easily obtain antibiotics from retail shops or private pharmacies.^{12–14} Given the commonness and possible dangers of coughing, we put forward the hypothesis that there is a certain proportion of non-prescription antibiotics use after coughing in children under 5 years. Addressing the frequency and the corresponding factors of non-prescription use of antibiotics after the onset of cough in children is important for antibiotic abuse prevention and control. Therefore, the aim of this study was to investigate the prevalence and associated factors of non-prescription use of antibiotics in children under 5 years after cough.

METHODS

Study design and participants

We performed a cross-sectional survey in Yiwu, a county-level city of about 2 000 000 people situated in the central Zhejiang Province of China. The survey was conducted from October to December 2019 and targeted children under 5 years of age.

We estimated a sample size of approximately 2305 for a conservatively assumed prevalence of non-prescription use of antibiotics after cough of 25%, a permissible error of 2.5%, a 5% level of significance (α) and a design effect of 2.

The subjects were enrolled from all 14 townships in Yiwu using a two-stage stratified sampling procedure. First, probability proportionate to size sampling (PPS) method was used to adopt 50 clusters (villages or communities) from 14 townships (see online supplemental appendix 1). Then, a quota sampling method based on age and sex was used to select a fixed number of participants from each cluster for the questionnaire survey (see online supplemental appendix 2). Considering the potential problems of non-response, we targeted 60 individuals in each of the 50 clusters to accommodate nonparticipation.

During this study, well-trained interviewers fluent in the local dialect conducted face-to-face interviews using a standardised questionnaire. The children's parents, grandparents or other caregivers who made routine decisions on children's medication responded as their agents. Data were entered into the panel computer. We selected only one child as a participant from every household, without replacement. Impermanent residents from the sampled village (residential community) who lived in Yiwu for less than 6 months were excluded. In China, the permanent population refers to the residents living in survey place for more than 6 months. Children who had a cough in the month prior to the study were included in the final analysis of non-prescription use of antibiotics.

Patient and public involvement

No patient or member of the general public was involved in the design or planning of the study, the selection of outcome measures or the conduct of data collection.

Study questionnaire

We used a 30-item questionnaire to access the cough status and non-prescription antibiotics use behaviour of the participants (see Supplemental online supplemental appendix 3). The questionnaire was further revised after discussion and revision by the project team experts and on-site preinvestigation before it was officially used. Furthermore, logical verification was carried out in the design to avoid filling errors and missing information. The questionnaire consisted of three parts. The first part collected basic information including age, sex, ethnic group of children, occupation, educational level and annual family income of parents (caregivers). The second part covered the history of cough, including the time of onset (during the past month), the cough duration, cough characteristics, accompanying symptoms, and health-seeking behaviours. Health-seeking behaviours included whether they went to a doctor because of the last cough, which health facilities they chose for treatment, and whether the antibiotics were administered to the children after the onset of the cough. If respondents reported antibiotic administration, the source and type would be asked in detail with multiple responses. The third part included the knowledge of antibiotics, measured by nine questions related to their rational use. Each question was answered with a 5-point Likert-type scale (strongly disagree, disagree, uncertain, agree and strongly agree).

Definitions of variables

Cough

In the current study, cough was assessed by asking the respondents 'Has your child had a cough during the past month?' The duration of cough was categorised into less than 1 week, 1–2 weeks, 3–4 weeks and >4 weeks. Accompanying symptoms included expectoration, runny nose, fever, sore throat, dyspnoea, headache and lethargy.

Non-prescription use of antibiotics

Non-prescription use of antibiotics was defined as intermittent or continuous use of antimicrobial agents to treat self-diagnosed diseases or symptoms without medical guidance. It was assessed by asking participants the source of antibiotics (if they used any). The respondents would be regarded as using antibiotics without prescription if they reported any of the following approaches for antibiotics: self-purchase from pharmacies in the community, remainder from a previous course of treatment, storage at home or use of medicine given by friends.

Other covariates

Demographic and socioeconomic characteristics included age, sex, residential area (rural or urban) of the children, education level (primary school or below, middle/high

school, college or above) and annual family income (<¥50 000, ¥50 000~¥99999, ¥100 000~¥199999, ¥200 000~¥499999 and ≥¥500 000) of the children's caregivers.

Statistical analysis

The participants' characteristics were described as frequencies and percentage for categorical variables. The source and type of antibiotics used were evaluated based on multiple response questions, and all responses were calculated as multiple response frequencies (percentages). The 5-point Likert-type scale responses to the nine questions related to the rational use of antibiotics were reclassified into three levels and depicted in the bar chart, among which 'strongly disagree' and 'disagree' were combined to 'disagree', 'strongly agree' and 'agree' were combined to 'agree', and another response was uncertain. We calculated the correct response rate for each question separately. Among these nine questions, the correct response to question3 was 'agree', and the others were 'disagree'. We used both univariate and multivariate logistic regressions to estimate the associations of demographic characteristics and features of cough with non-prescription use of antibiotics. All analyses were conducted using the R software V.3.5.1. A two-sided $p < 0.05$ was considered statistically significant.

RESULTS

A total of 3123 caregivers of under-5-year-old children participated in the interviews. After eliminating invalid questionnaires from 21 caregivers, data from 3102 respondents were analysed (figure 1). Of the 3102 respondents, 1211 reported that their children had experienced cough during the past month. These participants were included in the final analysis of non-prescription use of antibiotics. The majority of the respondents were children's mothers

Figure 1 Flow of participants through the study.

Table 1 Characteristics of the total population and individuals with cough in the past month

Characteristics	Total population n=3102	Individuals with cough in the past month n=1211
Child's sex		
Male	1740 (56.09%)	690 (56.98%)
Female	1362 (43.91%)	521 (43.02%)
Child's age, months		
0–11	756 (24.37%)	183 (15.11%)
12–23	623 (20.08%)	197 (16.27%)
24–35	613 (19.76%)	236 (19.49%)
36–47	558 (17.99%)	307 (25.35%)
48–59	552 (17.79%)	288 (23.78%)
Child's residence		
Urban	1870 (60.28%)	714 (58.96%)
Rural	1232 (39.72%)	497 (41.04%)
Child's cough duration, weeks		
<1		732 (60.44%)
1–2		347 (28.65%)
3–4		99 (8.17%)
>4		33 (2.73%)
Caregiver's relationship with children		
Mother	1975 (63.67%)	794 (65.57%)
Father	552 (17.79%)	221 (18.25%)
Grandparents	560 (18.05%)	188 (15.52%)
Else	15 (0.48%)	8 (0.66%)
Caregiver's education level		
Primary school and lower	446 (14.38%)	154 (12.72%)
Middle school	1053 (33.95%)	356 (29.40%)
High school	680 (21.92%)	289 (23.86%)
College and higher	923 (29.75%)	412 (34.02%)
Family annual income (RMB)		
<¥50 000	356 (11.48%)	127 (10.48%)
¥50 000~¥99 999	890 (28.69%)	339 (27.99%)
¥100 000~¥199 999	1222 (39.39%)	476 (39.31%)
¥200 000~¥499 999	488 (15.73%)	212 (17.51%)
≥¥500 000	120 (3.87%)	48 (3.96%)
Unknown	26 (0.84%)	9 (0.74%)

(65.6%), followed by their fathers (18.2%) and grandparents (15.5%). The characteristics of the total participants and children who had cough in the last month are shown in table 1.

Figure 2 Types of antibiotics prescribed by doctors and those used without prescription. (A) The types of antibiotics used without a prescription. (B) The types of antibiotics prescribed by doctors. *Penicillins include amoxicillin, ampicillin, amoxicillin and clavulanate potassium. Cephalosporins include cephalexin, cefuroxime, cefminox, cefepime and other cephalosporins. Macrolides include azithromycin, erythromycin, roxithromycin and clarithromycin.

Non-prescription use of antibiotics

Among the 1211 children who had a cough in the last month, 487 (40.2%) received antibiotics and 91/487 (18.7%) received them without prescription. The most common source of the non-prescription antibiotics was community pharmacies (53.7%), followed by storage at home (30.5%) and leftover from a previous course of treatment (15.7%).

Figure 2A shows the types of antibiotics used without a prescription for cough treatment. Cephalosporins were most frequently used (52.8%), followed by penicillins (amoxicillin, ampicillin, amoxicillin-clavulanate potassium) (30.3%) and macrolides (16.8%). Figure 2B shows the types of antibiotics prescribed by doctors. There was no significant difference in the types of antibiotics between those prescribed by doctors and those used without prescription by the caregivers ($\chi^2=0.934$, $p=0.627$).

Cognition of rational use of antibiotics

Figure 3 shows the respondents' knowledge and attitudes toward the use of antibiotics. In total, the correct response rate to these ten questions ranged from 31.6% to 80.1%. Of the respondents, 16.5% believed that antibiotics should be used as soon as possible for coughs.

Figure 3 Knowledge of caregivers on the use of antibiotics. *Except for Q3 to which the correct answer was 'agree', the correct answers to all questions were 'disagree'.

More than 60% of respondents failed to distinguish between antibiotics and anti-inflammatory drugs. Moreover, 12.5% of respondents believed that patients have the right to decide on antibiotic use and that the patients can request the doctor to prescribe antibiotics. Further, 12.9% of them believed that the more expensive the antibiotics, the better the effect. Additionally, 11.7% agreed that intravenous antibiotics are more effective than oral antibiotics. However, 80.1% of respondents agreed that antibiotics are a prescribed drug and should be used with prescription only.

Factors associated with non-prescription use of antibiotics

The association of sociodemographic and cough-related characteristics with non-prescription use of antibiotics after the onset of cough is presented in table 2. In univariate analyses, the caregiver's relationship with the children and annual family income were associated with non-prescription use of antibiotics. In multivariate analyses, cough duration, accompanying runny nose and family annual income were associated with non-prescription use of antibiotics. Compared with children who coughed for less than 1 week, those who coughed for 1–2 weeks (OR 1.73, 95% CI 1.03 to 2.90) and 2–3 weeks (OR 2.39, 95% CI 1.08 to 4.97) had a higher risk of non-prescription use of antibiotics. However, there was no significant difference between those who coughed more than 4 weeks and those who coughed for less than 1 week. As for accompanying symptoms, runny nose was associated with a higher risk of non-prescription use of antibiotics (OR 1.86, 95% CI 1.13 to 3.19), while expectoration and fever were not. Further, children whose annual family income was between ¥50 000 and ¥100 000 (OR 4.44, 95% CI 1.52 to 18.95) had a higher risk of non-prescription use of antibiotics than those whose family annual income was less than ¥50 000.

DISCUSSION

To the best of our knowledge, this is the first community-based study to investigate the prevalence, source, type, and associated factors of non-prescription antibiotic

Table 2 Univariable and multivariable analyses of the influencing factors of non-prescription use of antibiotics for cough

	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Child's characteristic				
Female sex (vs male)	0.95 (0.61 to 1.45)	0.360	0.93 (0.59 to 1.46)	0.756
Age (every 1-year increase)	1.02 (0.87 to 1.19)	0.815	0.97 (0.83 to 1.15)	0.753
Rural residence	0.80 (0.51 to 1.25)	0.336	0.81 (0.51 to 1.28)	0.375
Cough duration, weeks				
<1	1.00 (ref)		1.00 (ref)	
1–2	1.57 (0.98 to 2.49)	0.059	1.73 (1.03 to 2.90)	0.037
3–4	1.86 (0.89 to 3.61)	0.079	2.39 (1.08 to 4.97)	0.024
>4	0.47 (0.03 to 2.25)	0.457	0.54 (0.03 to 2.85)	0.559
Accompanying symptoms(vs not)				
Expectoration	1.23 (0.79 to 1.89)	0.355	1.22 (0.76 to 1.94)	0.400
Fever	0.62 (0.32 to 1.12)	0.140	0.75 (0.37 to 1.41)	0.397
Runny nose	1.60 (0.99 to 2.68)	0.064	1.86 (1.13 to 3.19)	0.018
Hospital visit	0.41 (0.26 to 0.62)	<0.01	0.29 (0.18 to 0.47)	<0.01
Caregiver's characteristic				
Relationship				
Mother	1.00 (ref)		1.00 (ref)	
Father	0.53 (0.26 to 0.96)	0.049	0.59 (0.29 to 1.11)	0.125
Others	0.43 (0.19 to 0.85)	0.026	0.64 (0.26 to 1.40)	0.295
Education level				
Primary school and lower	1.00 (ref)		1.00 (ref)	
Middle school	2.11 (0.86 to 5.19)	0.106	1.62 (0.65 to 4.64)	0.327
High school	2.03 (0.81 to 5.12)	0.133	1.58 (0.59 to 4.79)	0.379
College and higher	2.29 (0.94 to 5.55)	0.067	2.00 (0.75 to 5.97)	0.183
Annual income, RMB				
<¥50 000	1.00 (ref)		1.00 (ref)	
¥50 000~¥99 999	2.69 (1.43 to 5.62)	0.004	4.44 (1.52 to 18.95)	0.017
¥100 000~¥199 999	2.31 (1.24 to 4.79)	0.015	2.52 (0.84 to 10.92)	0.145
¥200 000~¥499 999	2.19 (1.09 to 4.79)	0.036	1.56 (0.44 to 7.32)	0.633
≥¥500 000	1.51 (0.46 to 4.34)	0.461	1.31 (0.16 to 8.66)	0.861
Unknown	1.39 (0.07 to 7.69)	0.759	3.27 (0.15 to 31.99)	0.437

use for cough among children under 5 years in China. Overall, 40.2% of the children who had a cough in the past month had been medicated with antibiotics, and 18.7% (91/487) were non-prescription use. Cephalosporins were the most frequent type of antibiotics, and community pharmacies were the main source. Children coughing for 1–4 weeks, with accompanying runny nose, or those whose annual family income between ¥50 000 and ¥100 000 had a higher risk of non prescription use of antibiotics than those coughing for <1 week, without runny nose, or with an annual family income <¥50 000.

A national study conducted in 15 provinces in China reported that 2-week prevalence of cough was 9.39% in children aged 0–6 years old.¹⁵ In the present study, 30.9% (1211/3102) of children had experienced a cough in the month prior to the study, and 40.2% of them had

been medicated with antibiotics, which indicated a high frequency of cough and a high proportion of antibiotic use among children under 5 years. Actually, cough is a defensive physiological reflex arising from a wide range of etiologies, of which uncomplicated viral respiratory tract infections account for the majority¹⁶ and antibiotics are ineffective for etiologic or symptomatic relief in most cases.^{17 18} The diagnostic and treatment guidelines for cough recommend that antibiotics should not be prioritised and only given after adequate assessment.^{5 19 20} Parental self-medication of children with antibiotics for cough may be even more dangerous and harmful. In our study, the prevalence of non-prescription antibiotic use was 7.5% (about one-fifth of antibiotic users for cough). This was relatively lower than that reported in previous studies conducted in children^{14 21–24} and could

be explained by the difference in populations, specific scenarios, and time interval as our study focused on children under 5 years and restricted the condition to cough within the month before the study. However, despite the lower proportion, non-prescription antibiotic use was still concerning because most caregivers lacked knowledge on rational antibiotic use. For example, more than 60% of respondents failed to distinguish between antibiotics and anti-inflammatory drugs in the present study. This indicates the need for further public health campaigns and education on the rational use of antibiotics.

The main source of non-prescribed antibiotics in this study was community pharmacies, in parallel with previous studies.⁶ A survey of 2423 community pharmacies from 221 districts or counties across China reported that non-prescription antibiotic dispensing (NPAD) was observed during 70.1% of adult upper respiratory tract infection (URTI) interactions.¹² Another multicentre cross-sectional study conducted in three provinces reported that 73.3% of the SCM interactions generated NPAD.¹³ Therefore, more strict supervision should be implemented to regulate antibiotic sales. Our finding of cephalosporins as the most frequent type of self-medicated antibiotics was consistent with a cross-sectional study using the standardised client method in Shenyang, northeastern China. Li *et al*¹⁴ found that cephalosporins were dispensed most frequently in simulated scenarios of paediatric acute cough in community pharmacies, which indicated cephalosporins were more accessible or more likely to be provided by pharmacy staff for children and could explain our results.¹⁴ Interestingly, we found there was no significant difference in the types of antibiotics between those used without prescription by the caregivers and those prescribed by doctors in the present study. A study evaluating antibiotic use for acute URIs in paediatric outpatient also reported that cephalosporins were used more frequently, followed by macrolides.²⁵ It should be noted that this did not mean the caregivers' behaviours were appropriate because misuse of antibiotics was also serious in paediatric outpatient.^{25 26}

In the present study, the duration of cough and accompanying runny nose were associated with non-prescription antibiotic use in the multivariable analysis. Children who coughed for 1 to <4 weeks had a higher risk of non-prescription use of antibiotics than those who coughed for less than 1 week, while those who coughed for more than 4 weeks did not. In paediatrics, cough is generally classified into three categories depending on its duration—acute cough (lasting less than 2 weeks), protracted acute (also called subacute) cough (2–4 weeks) and chronic cough (more than 4 weeks).¹⁹ Our results indicated that a subacute cough was a potential risk for non-prescription antibiotic use. The most common cause of subacute cough is postinfectious cough, followed by upper airway cough syndrome and cough variant asthma.²⁷ Identification of any preceding respiratory infection and empirical treatment for postinfectious cough are important for the management of subacute cough.

Meanwhile, the OR of runny nose for non-prescription use of antibiotics approached two, which suggested runny nose could increase caregivers' anxiety and more health education merits to be enhanced. A runny nose with clear secretions is a clinical manifestation of the common cold, usually with no need for antibiotics.²⁷

We also found that mothers were more likely to self-administrate antibiotics to their children in the univariate analysis, which is in parallel with studies conducted in Mudanjiang.²⁸ This may be explained by the fact that women are more sensitive to their children's physical signs. However, the association became insignificantly after adjusting for multiple factors, which indicated more studies are needed to confirm this impact. As expected, hospital visit was a protective factor for non-prescription antibiotics, since doctors' administration or explanation could alleviate caregivers' anxiety and confusion. In addition, we also found that the income bracket of ¥50 000–¥1 000 000 was associated with a higher risk of non-prescription antibiotic use. The possible explanation for this phenomenon could be that caregivers, whose annual income was below this level, struggle financially and were reluctant to spend money on medicine, while those at a higher income level tended to visit a doctor for professional consultation.^{29 30} Moreover, a previous study of 1596 children aged 2–18 years showed that non-prescription antibiotic use increased with children's age.²¹ However, we did not observe a similar association, which might be because of the narrow age range in our study.

Our study has several strengths, including the community-based population and the adoption of the PPS method for representative samples. However, our findings should be interpreted in the context of the following limitations. First, this cross-sectional study cannot exclude potential recall and report bias, even though we enquired information within the past month to reduce such biases. Second, a certain proportion of the respondents (18.5%) were the children's grandparents, who were less educated and may have affected our results. Third, we were unable to access the diagnosis of cough in this study, which could be an unmeasured confounding variable. Fourth, no patient or member of the general public were involved in the design, conduct or reporting of this study. However, we conducted an on-site pre-investigation and optimised the questionnaire to make it more understandable before it was officially used. Finally, the subjects in our study were enrolled from permanent population in only one district, and thus the generalisability of our findings to other Chinese populations may be limited. Therefore, multicentre studies with larger sample size are warranted to make a firm complement to the current study.

CONCLUSIONS

A high proportion of infants and young children had been treated with antibiotics for cough in China, and nearly one in five of these antibiotics were used without prescription. The cough duration, accompanying runny nose and

annual family income were the influencing factors. More public health campaigns and further education on the appropriate use of antibiotics should be implemented to ensure the rational treatment of cough in children.

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Competing interests None declared.

Patient consent for publication Not applicable.

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