Inappropriate Use of Antibiotics among Children Under Five in Rural and Urban Communities of Cambodia

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Abstract

Background: Inappropriate use of antibiotics is a major treat especially in low- and middle-income countries with antibiotic resistant. Cambodia with high prevalence of infectious diseases among children under five, antibiotics use in urban and rural setting has not been clearly identified. Therefore, this study aimed to investigate the situation of inappropriate antibiotic use among children under five in urban and rural communities of Cambodia.

Methods: An analytical cross-sectional study was carried out in both urban and rural communities in Cambodia from September to November 2020 by structured questionnaire interviewed among 512 Cambodian caregivers on antibiotic use for the under 5 children.

Results: Among 512 children, majority were males both in urban (55.6 %) and rural (50.3%) settings, with the median age of 29.5 (3:59) months in urban and 30.0 (3:59) months in rural. The prevalence of inappropriate use of antibiotics among children under five was 79.3% (95% CI = 75.55 to 82.60), of which it was 26.0 % in urban and 53.3% in rural. Most of the rural respondents (82.1%) use antibiotics for bacterial infection diagnosed by doctors. However, it was only 52.6% in rural areas. Similar proportion of 58.6 % in urban and 61.1 % rural used antibiotics for fewer days than prescription.

Conclusions: Inappropriate use of antibiotics were found in more than 3 quarters of children under five, of which the proportion in rural areas were much higher than urban. The further investigation on factors contributing to inappropriate use of antibiotics should be conducted.

Keywords: *Antibiotics, antibiotic resistance, caregivers, children under five, and inappropriate use of antibiotics*

Introduction

Infectious disease is one among the major reasons driven to great morbidity as well as mortality ([1]). Consequently, this made consumption of antibiotics rose remarkably from 21.1 to 34.8 billion daily dose (DDDs) from 2000 to 2015 ([2]). However, antibiotics were not always prescribed, dispended or used in a rational way ([3, 4]). This inappropriate use of antibiotic contributing to the escalation of global antibiotics resistance as well as antimicrobial resistance ([4-6]). Antibiotic resistance could impact on many aspects such as the augmentation of adverse drug

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reaction (ADR), re-consultations, complications of disease, and increase in healthcare cost ([7]), delay in hospitalizations, the increase in the length of recovery time and death rate in severe infection ([8-11]). Centers for Disease Control and Prevention (CDC) reported that the serious form of antibiotic resistance was developed in more than 2 million people annually, which led to 23,000 deaths with the cost of health care around $20 billion globally ([12]). It has been considered as a global threat.

In most countries about 20 percent of antibiotics were used in healthcare facilities, and 80 percent were used in the community ([13]) of which about 30 % is used inappropriately ([14]) because community colonizes with freely antibiotic selling, widespread of self-medication of antibiotics and other improper forms of antibiotic use. Many findings highlighted the association between outgrowth of antimicrobial resistance with the improper use of antimicrobials in the community setting ([15]).

Importantly, inappropriate use of antibiotics seemed exceptionally grave among the pediatric group of population in the developing countries ([16]). In the similar context, Cambodian children population younger than 5 years old which accounted for 1.8 million ([17]) living in one of the developing countries, was considered as in the risk situation ([18]). In many countries there were significant different of inappropriate use of antibiotics between rural and urban settings. Meanwhile, the extent of inappropriate use of antibiotics in children under five in the urban and rural communities has not yet been studied in Cambodia.

Therefore, this study aimed to investigate the situation of inappropriate antibiotic use among children under five in urban and rural communities in Cambodia.

Materials and Methods

Study design

This analytic cross-sectional study was carried out in Cambodia from September to November 2020. Data collection was carried out in four urban and eight rural communities covering one capital city and two provinces (Phnom Penh capital city, Kampong Chhnang and Prey Veng Province) in Cambodia. The participants were caregivers of children under five.

Study variables

Dependent variable (outcome) was appropriateness / inappropriate use of antibiotics.

Independent variables consisted of gender of caregivers, age of caregivers, marital status of caregivers, education level of caregivers, occupation of caregivers, sex of children, age of children, family size of children, average monthly income of children's family, financial status of children's family, and relationship between caregivers and children.

Sample size determination and sampling technique

A sample size was calculated by proportion formula with reference from a previous study done in Northwest Ethiopia (19).

5 percent of participants (24) were added original sample size (488) because we spared 5 percent in case of error or incomplete information in some questionnaire. The final sample size was 512 (488 +24).

A multistage sampling method was used to select samples based on the 2014 National Census retrieved from the Ministry of Planning in Cambodia for observing the distribution of children under five. The study area consisted of both urban and rural settings which were stratified into 3 levels of city/ province, district, and commune (community). The study population was caregivers aged from 18 years old and older, lived in the selected study areas, caring, and clearly aware of their children administered of antibiotics at least once in the previous six-month counting from the date of interview backward. Caregivers who critically ill or had communication

problems were excluded from this study.

Data collection tool

A face-to-face structured questionnaire interview was conducted among the participants by three well-trained pharmacy students. The questionnaire was pretested by 3 experts for content validity and tested in the actual context of the population on suitable for data collection. The structured questionnaire consisted of three parts as the following (supporting file 1):

Part 1: Demographic and socioeconomic characteristics of caregivers and children with 12 items

Part 2: Practice in antibiotic use with 10 items to measure the outcome. The novel tool was developed by following the definition of inappropriate use of antibiotic of World Health Organization (20).

Operational definition

Inappropriate use of antibiotics

According to WHO, the inappropriate use of antibiotics is defined as using in the incorrect purpose/ indication, inappropriate dosage, inappropriate timing, incorrect duration, over-prescription, omission of prescription/self-medication, incorrect selection, incorrect route of administration, requesting antibiotic from health care providers and unnecessary expense (20).

Data quality management

Content validity index (CVI) of questionnaire was assessed by 3 experts in pharmacy, medical, health literacy and statistics field. Pretest was tried out in 30 participants outside the study area in order to check the reliability of the tool. Some modifications were made after CVI assessment and pretest. Data collectors were given training and supervised daily by principal investigator to collect quality data. Double data entry validate check and exploratory data analysis were done to check the completeness of data. For the rest of minimal missing data was solved by using listwise data deletion, mean substitution, hot deck imputation, expectation maximization approach and raw maximum likelihood methods or multiple imputation.

Data analysis procedure

All analyses were performed by using the Stata program version 10.0. The baseline characteristics and other variables were analyzed and presented as frequency and proportions for categorical data and mean, standard deviation, median, maximum, minimum for continuous data. To estimate the prevalence of inappropriate use of antibiotics, it was calculated with frequency having value as percentage and confidence interval at 95%.

Ethical considerations

This study was conducted after receiving permission from the office of the Khon Kaen University Ethics Committee in Thailand for human research for endorsement of ethical approval of this research with approval reference number HE632210 and ethic approval from National Ethics Committee for Health Research in Cambodia with the approval reference number 196 NECHR.

Result

Demographic and Socioeconomic Characteristics of Caregivers

Out of 512 households, 350 were in rural. Majority of caregivers were female, 96.9 % in urban and 94.6 % in rural. Their median age was 32.5 (20:66) years old in urban and 33.0 (18:75) in rural. More than three quarter of both urban (85.8%) and rural (88.8%) were married/ living with a partner. About half of caregivers (43.8) % in urban and only 1.7% in rural completed bachelor's degree, whereas only 6.8 % urban and 12.0% rural caregivers were illiterate. Around 40.7% of caregivers in urban, and 20% in rural were employee while only 0.1% but nearly 40% of participants in urban and rural were farmer, respectively.

Demographic and Socioeconomic Characteristics of Children Under Five

Among children under five, the proportion of male and female gender both in urban and rural was comparable. Their mean age was 30.8 (±15.8 S.D) years old in urban and 30.7 (±15.7S.D) in rural. Children from both urban (58.6%) and rural (57.5%) areas were mostly from 4 to 5 members-family while the median family sizes were 5, both in urban and rural. The median monthly family income was 750 (22.5:10,000) for urban, whereas it was only 150 (15:1,000) US$ in rural. As regarding to financial status, 38.9% urban and only 4.6% rural children's family had enough money with saving while the proportion of those which having not enough money with debt was higher in rural (42.9%) than in urban (16.7%). Caregivers of children under five both in urban and rural areas were mostly mother/father with a similar proportion of (79.6% vs 78.3% respectively).

Situation of antibiotic use in children under five years of age

Table 1 Situation of antibiotic use in children (n= 512)

Antibiotic use	Urban (n=162)		Rural (n=350)	
	Number	%	Number	%
Source of antibiotics for children				
Doctor's clinic	81	50.0	182	52.0
Health center	20	12.4	74	21.2
Hospital	41	25.3	46	13.1
Pharmacy shop	20	12.3	43	12.3
Shop	0	0.0	5	1.4
Purpose of using antibiotics for children				
Fever	120	74.1	256	73.1
Bacterial infection diagnosed by doctors	133	82.1	184	52.6
Common cold/running nose	85	52.5	196	56.0
Cough	83	51.2	114	32.6
Sore throat	107	66.1	75	21.4
Diarrhea	17	10.5	47	13.4

Cont... **Table 1 Situation of antibiotic use in children (n= 512)**

Antibiotic use	Urban (n=162)		Rural (n=350)	
	Number	**%**	**Number**	**%**
Wound with pus	4	2.5	17	4.9
Swelling, red wound or other types of injuries	2	1.2	19	5.4
All types of infections (bacterial, viral, parasite or other microorganisms)	5	3.1	2	0.6
Route of antibiotic administration				
Different from recommendation by physician or instruction in the prescription	20	3.9	34	6.6
As recommendation by physician or instruction in the prescription	142	87.7	316	90.3
Dosage of antibiotics				
Less than dosage prescribed by doctor	28	17.3	41	11.7
Same as dosage prescribed by doctor	134	82.7	301	86.0
Higher than dosage prescribed by doctor	0	0.0	8	2.3
Number of times per day of antibiotics				
Less frequent than the instruction by doctor	44	27.2	51	14.6
Same as the instruction by doctors	116	71.6	295	84.3
More frequent than the instruction by doctor	2	1.2	4	1.1
Number of days of using antibiotics				
Shorter than the instruction by doctor	95	58.6	214	61.1
Same as the instruction by doctor	64	39.5	130	37.2
Longer than the instruction by doctor	3	1.9	6	1.7

Cont... **Table 1 Situation of antibiotic use in children (n= 512)**

Antibiotic use	Urban (n=162)		Rural (n=350)	
	Number	%	Number	%
Over-prescription of antibiotics				
Not use for any other purpose than prescribed by doctor	130	80.3	308	88.0
Used for any other purpose than prescribed by doctors	32	19.7	42	12.0
Using the leftover antibiotics (for children antibiotics when they had a similar sign to the previous illness take antibiotics from family members/friends when children had a similar sign to those relatives/ friends without having to see a medical doctor):				
No	120	74.1	272	77.7
Yes	42	25.9	78	22.3
Using non-prescribed antibiotics/self-medication for children				
Never	145	89.5	296	84.6
Rarely	2	1.2	18	5.1
Sometimes	3	1.8	16	4.6
Often	9	5.6	15	4.3
Always	3	1.8	5	1.4
Requesting antibiotics from physicians/doctors or other healthcare providers even children had mild disease that you were not sure whether it was caused by bacteria or not.				
No	153	94.4	306	87.4
Yes	9	5.6	44	12.6

Most of caregivers both in urban and rural setting received antibiotics for their children under five from health care facilities such as health center, hospital, doctor's clinic rather than pharmacy or general shops. Those caregivers mostly brought their children to see doctor before getting antibiotics, which was a appropriate practice. However, the most common reasons antibiotics used for children were fever (74.1% in urban and 73.1% in rural), bacterial infection (82.1% in urban and 52.6% in rural) and common cold/running nose (52.5% in urban and 52.6%). Almost all children both in urban (87.7%) and rural (90.35) were given antibiotics as its correct pharmaceutical form. Most of their caregivers both in urban (82.7%) and rural (86.0%) gave them the antibiotics in the amount as prescription. Noticeably, the percentage of caregivers in urban who were likely to give antibiotics less frequent than the

instruction was double, compared to those in rural. Approximately 80 per cent of caregivers in urban and rural administered antibiotics to their children with the same frequency times as physician prescribed. In concern with number of days using antibiotics, the proportion of the right period of course of treatment was only 39.5% in urban and 37.2 %, which was the most concerning issue. Caregivers in urban (19.7%) prone to use antibiotics for any other purpose than prescribed by doctor, compared with those in rural (12.0%). Approximately, one third of caregivers in Cambodia were more likely to practice wrongly in using leftover antibiotics to their children, 25.9% in urban and 22.3 % in rural, see Table 1.

Prevalence of inappropriate use of antibiotics (IUA) by urban vs rural and overall prevalence of IUA (n=512)

Table 2 Prevalence of inappropriate use of antibiotics (IUA) by area (n=512)

Antibiotic Use	Number	%	95% Confidence Interval
Urban (n=162)			
Appropriateness (10 scores)	29	5.7	3.96 to 8.04
Inappropriateness (<10 scores)	133	26.0	22.35 to 29.96
Rural (n=350)			
Appropriateness (10 scores)	77	15.0	12.19 to 18.41
Inappropriateness (<10 scores)	273	53.3	48.97 to 57.62
Overall prevalence			
Appropriateness (10 scores)	106	20.7	17.40 to 24.45
Inappropriateness (<10 scores)	406	79.3	75.55 to 82.60

Overall, almost 80% of those children (95% CI: 75.55 to 82.60) faced problem of inappropriate use of antibiotics, of which children residing in rural tended to face almost two-folds of inappropriate use of antibiotics (53.3%: 48.97 to 57.62) when comparing with those in urban settings (26.0%: 22.35 to 29.96) see table 2.

Discussion

Inappropriate use of antibiotics (IUA) among under five children in Cambodia was extremely high (79.30%).This rate was higher than a study among Chinese children (35.12%) ([21]) and another study among adult of Northwest Ethiopia (30.9%) ([19]). However, it was similar with a study carried out among children in Saudi (41-92%) ([22]). This inconsistent in prevalence of inappropriate use of antibiotics might be due to variation on level of awareness, education level, belief, cultural preference, accessibility to health facilities, and other socio-economic characteristics of participants in the studies.

Interestingly, prevalence of IUA tended to be high among children who residing in rural areas (53.3%), compared to those in urban settings (26.0%). The possible reasons might relate to limited accessibility to antibiotics and information on antibiotic use, which might be in those with low family income, inconvenience in traveling to health facility, few health facilities and licensed healthcare providers as well as low level of education. These factors seemed to be better in urban settings. In contrast, a study in Northwest Ethiopia did not prove any great controversial regarding the proportion of IUA between urban (33.1%) and rural (29.2%). The reason to explain this situation by researcher was that those communities were in the close proximity leading to exchange of information ([19]). The disparity in these findings might be due to different context of study areas and population. Similar finding was reported in a study in China showing that respondents in less developed areas tended to use of antibiotics inappropriately ([23]). The reason might be associated with socio-demographics characteristics.

The high prevalence of inappropriate use of antibiotics in this study might related to caregiver factors. The situation of antibiotic use was improper in all criteria. Many Cambodians had wrong perceptions concerning antibiotics. For instance, antibiotics were believed to be effective for treating common cold, fever, general pain, malaria, and inflammation. In addition, left-over antibiotics could be used. Mostly, inappropriate use of antibiotic is related to unrestricted accessibility of antibiotics. People could easily get them from pharmacies, shops, nurses as suppliers and unlicensed medical providers in villages ([24]), which increased of self-medication practices. However, laws and regulations to control non-prescription antibiotics seemed to remain ineffective ([25]). Remarkably concerning the period of treatment, about two third of them did not completed the full course of antibiotics recommended. This was the most common inappropriate use of antibiotics found in this study. Low level of awareness about the significance of correct indication and dosage of purchasers and dispensers and limited affordability on medication expense fostered the practice of buying a few doses of antibiotics ([26]), as well as self-medication in developing countries ([27]). Other issues involving sources of antibiotics, routes of administration, dosage, number of times, and over-prescriptions did not show any seriously wrong practices among Cambodian caregivers. However, it could be noticed that rural participants were more likely to have inappropriate practices than urban ones. The underlying reasons might be due to level of education of caregivers in rural was still lower than those in urban as evidenced in findings on the characteristics of caregivers in this study. Level of education was more likely to relate with knowledge on antibiotic use. Appropriately, 94.4 % of urban and 87.4 % of rural participants did not request antibiotics from physician for their children without diagnosis, of which they might not know about medication that good for the children illness.

Conclusion

Inappropriate use of antibiotics among Cambodian children under five was very high and was much higher in rural than urban communities. Only about half of the rural respondents used antibiotics for bacterial infection. Both urban and rural tended to use antibiotics only for a few days. The situation could increase antibiotic resistance and leading to not only increase health expenditure but also shortage of effective antibiotics in curing bacterial infections in the future**.** The finding from this was emphasize the prominence in conducting further studies to discover determinants of inappropriate use of antibiotics and more possible and efficient approaches that antibiotic resistance can be combated in communities both in urban and rural Cambodia.

Limitation

This study used information reported by the participants which could be subjected to recall bias. However, the potential of recall bias was minimized as much as possible by decreasing time frame of

retrieving information dated back to six-month before data collection.

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