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Research Paper

Prevalence of Antibiotics Consumption in Children in Central Iran: 2019-2020

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ABSTRACT

Background: One of the challenges in medicine has been the exaggerated use of antibiotics. The purpose of this study was to investigate the prevalence of antibiotic usage in children in Arak, Iran (2019-2020) to determine the factors related to antibiotic prescription and consumption in children.

Methods: This was a population based, cross-sectional study conducted in Arak, the capital city of Markazi Province, Iran. Stratified random sampling was applied to recruit children who were up to five years old, and registered in the healthcare system between Jan. 2019 and Jan. 2020. A response rate of 85% was obtained from the subjects' parents. Face-to-face interviews were used to collect the data from the children's mothers. Univariate and adjusted linear regression analyses were applied to assess the determinants of antibiotic consumption in these children.

Results: A total of 1483 children were enrolled in the study; most of them were boys with the mean age of 2.1±1.5 years old. The annual prevalence of antibiotic consumption in Arak was found to be 62.4% for at least one antibiotic. The most consumed antibiotic was azithromycin (24.2%). Among antibiotic groups, the most consumed group was macrolides (26.9%). Upon multiple logistic regression analyses, a lower consumption rate was observed among the younger children with older mothers, and children whose fathers had permanent jobs than other children groups. A higher consumption rate was observed among families with higher parity.

Conclusion: The annual prevalence of antibiotic consumption in this study was very high, with the most consumed drug being azithromycin. We recommend that the use of antibiotics be reconsidered by drawing future healthcare policies, aiming at reducing the heavy antibiotics consumption in children.

Keywords: Antibiotics Consumption; Children; Drugs; Iranian Children; Parity; Population

Introduction

One of the challenges in the medical field has been the over-rational use of antibiotics with improvement in this regard being one of the main policies in all countries. According to the World Health Organization (WHO) guidelines, in order to achieve rational drug consumption, it is necessary to use appropriate drugs that can relieve the clinical needs of patients in a geographical areas with minimal complications and reasonable costs (1, 2).

On average, antibiotics make up 30-50% of prescription drugs. Although antibiotics are necessary to treat most bacterial infections while non-prescription can be life-threatening in some cases. Studies have shown that antibiotics have been prescribed incorrectly in at least 30% and inappropriately in 60% of cases by either physicians or due to self-medication (3-6). Children are more susceptible to infections, especially viral and bacterial ones (7).

Consequently, antibiotics are prescribed more for the age group 2.1 ± 1.5 years old by physicians. So, the misuse of antibiotics for viral infections is significant in children (8). Moreover, antibiotics use without a physician order has been observed in many cases. There is always a concern that new strains of microbes cannot be treated with existing antibiotics because of antibiotic resistance. The highest incidence of resistance to antibiotics has occurred in countries with the highest proportion of antibiotics use (9, 10). Thus, it is essential to

implement new and effective policies to control the overuse of antibiotics.

In 1990, antibiotics accounted for 12% of all drug sales worldwide; this rate was 19% in the developing countries while the rate reached 34% in 2000. Economically, the cost of antibiotic treatment in 2000 was estimated at 40 billion dollars. Thus, despite remarkable efforts made, the price growth of antibiotics, especially in developing countries, has continued (11). Despite various studies on the use of antibiotics in various countries at different levels of the societies, few studies have been conducted in this regard in Iran (12-14).

Aim of the Study: This study aimed to investigate the prevalence of antibiotics consumption in children aged five years old or younger in Arak, Iran, between 2019 and 2020, and to determine the major factors associated with the use antibiotics in that population.

Methods

Study Design and Setting: This cross-sectional study was conducted in Arak, the capital city of Markazi Province in Iran. A stratified random sampling method was applied to recruit the study population between January 2019 and January 2020. The study sample consisted of children aged up to five years old who were registered in the Arak Healthcare System. It was estimated that more than 70% of the households in Arak were enrolled in a national registry system (SIB). Health Centers in Arak are public agencies that provide free healthcare to the population, especially in the care of mothers and children. We used strata based on 50 Health Centers that provide healthcare services to all residents in Arak, and each stratum covers a portion of the population of the study setting. The sampling was determined based on each stratum randomly from the household codes recorded in the health centers. Therefore, 1754 children were invited to participate in the study. Finally, 1483 children were approved for the study, with a response rate of 85%. This study was approved by the Ethics Committee at Arak university of medical sciences (Registration Code: IR.ARAKMU.REC.1398.217).

Interviews: Face-to-face interviews were held to collect the study data from the children's mothers. To gather valid self-reported data, the interviews were conducted by pre-trained interviewers. The data collection form was installed as an "*Android app*" on the interviewers' cell phones, and it took approximately 10 to 15 minutes to collect the data from each mother.

Study Variables: The included study variables were child age (years) and gender, parent's education level and occupation, parity, and socioeconomic status. We provided the mothers with a list of antibiotic drugs, consisting of azithromycin, amoxicillin, erythromycin, penicillin V, injected gentamycin, injectable ceftriaxone, cefixime, ciprofloxacin, co-amoxiclav, co-trimoxazole, metronidazole, and cephalexin.

Statistical Analyses: Descriptive statistics were used to describe the basic features of the study data, including frequency, mean, and standard deviation (SD). The socioeconomic status (SES) was estimated based on asset indices and principal component analysis (15). Chi-square and Mann-Whitney U tests were used to compare the mean or median values. Univariate and multiple logistic regression models were applied to assess the determinants of antibiotic consumption. Those variables that had a *P*-value > 0.2 in the univariate model were excluded. A *P*-value < 0.05 was considered as being statistically significant. All analyses were performed on SPSS version 16.0 and STATA version 12.0 softwares.

Results

Descriptive Analysis: In this study, 1483 mothers with their children who were five years old or younger participated. Most children were boys (n = 772; 52.1%). The mean age of children was 2.1±1.5 years old. Among the participants, 6.9% (n = 102) were not covered by any insurance. The education level of the majority of parents was high school diploma (38%, mothers Vs 37.8%, fathers). Most mothers were housewives (88.2%) with the fathers having permanent jobs (61%). The mean parity was 1.66 (SD: 0.72), and the mean birth weight of the children was 3.17 Kg (Table 1). On univariate analyses by Chi-square or Mann-Whitney U tests, there were significant differences among such variables as annual antibiotic consumption, mother's education (p = 0.033), father's occupation (*P* = 0.008), and income levels as defined by economic experts (*P* = 0.001) and the socioeconomic status (*P* = 0.032) (Table 1).

Prevalence of Antibiotics Consumption: The annual prevalence of antibiotics consumption among families in Arak (n = 925) was 62.4% for at least one of the drugs. The most consumed antibiotic was azithromycin (24.2%; n = 359) (Table 2). Among the drug groups, the most consumed drug was macrolides (26.9%; n = 399) (Table 3).

Predictive Factors of Antibiotics Consumption: Upon univariate logistic regression analyses, there were significant associations between self-reported antibiotics consumption and children's age (*P*=0.001), mothers' education (*P*=0.012), fathers' education (*P*=0.007), fathers' job (*P*=0.003), and parity (*P*=0.001). Upon multiple logistic regression analysis, there were lower antibiotics consumption among girls than boys (*P*=0.070), and children whose fathers had permanent jobs than those with temporary jobs or being unemployed (*P*=0.027). Moreover, increasing the age of mothers were significantly associated with decreasing the antibiotic consumption (*P*=0.001). Further, there

were statistically significant associations between increases in parity and/or children's age with antibiotics consumption (Table 4).

Table 1. Demographic Characteristics of the Health Literacy among Mother of Children under 6 Years, (2018-2019).

Variables	N (%)	Self-Reported Consumed Antibiotic		
		Yes (%)	No (%)	P-Value
Child Gender				0.097[a]
Boys	772 (52.1)	497 (64.4)	275 (35.6)	
Girls	711 (47.9)	428 (60.2)	283 (39.8)	
Mother's education				0.033[a]
Illiterate and preliminary	99(6.7)	61(61.6)	38(38.4)	
Guidance school	183(12.3)	125(68.3)	58(31.7)	
High school	60(4.0)	45(75)	15(25)	
Diploma	564(38.0)	362(64.2)	202(35.8)	
Higher diploma	115(7.8)	65(56.5)	50(43.5)	
Undergraduate	396(26.7)	227(57.3)	169(42.7)	
Postgraduate	66(4.5)	40(60.6)	26(39.4)	
Father's education				0.081[a]
Illiterate and preliminary	102(6.9)	70(68.6)	32(31.4)	
Guidance school	188(12.7)	129(68.6)	59(31.4)	
High school	66(4.5)	36(54.5)	30(45.5)	
Diploma	560(37.8)	358(63.9)	202(36.1)	
Higher diploma	149(10.0)	91(61.1)	58(38.9)	
Undergraduate	302(20.4)	175(57.9)	127(42.1)	
Postgraduate	116(7.8)	66(56.9)	50(43.1)	
Mother's job				0.619[a]
Unemployment	6(0.4)	3(50)	3(50)	
Housekeeper	1308(88.2)	820(62.7)	488(37.3)	
Temporary job	45(3.0)	30(66.7)	15(33.3)	
Permanent job	124(8.4)	72(58.1)	52(41.9)	
Father's job				0.008[a]
Unemployment	15(1.0)	12(80.0)	3(20.0)	
Temporary job	563(38.0)	375(66.6)	188(33.4)	
Permanent job	905(61.0)	538(59.4)	367(40.6)	
Parity		1.7(0.7)	1.5(0.7)	0.001[b]
1	692(46.7)			
2	631(42.5)			
3	138(9.3)			
4	19(1.3)			
5	3(0.2)			
Birth weight				
Mean ± SD	3174 ± 466.7	3168 ± 473	3183 ± 455.1	0.820[b]
Socio-economic status (SES)				0.032[a]
1st quintile	297(20)	179(60.3)	118(39.7)	
2nd quintile	297(20)	190(64.0)	107(36.0)	
3rd quintile	296(20)	197(66.6)	99(33.4)	
4th quintile	297(20)	195(65.7)	102(34.3)	
5th quintile	296(20)	164(55.4)	132(44.6)	

a = Chi square test; b = Mann-Whitney U test

Table 2. Descriptive analysis of mothers self-reported drugs in children at 0-5 years old in Arak, Iran (N = 1483).

Self-reported Drugs	N (%)
Azithromycin	359 (24.2)
Erythromycin	42 (2.8)
Amoxicillin	228 (15.4)
Penicillin V	3 (0.2)
Injected Gentamycin	2 (0.1)
Injected Ceftriaxone	3 (0.2)
Cefixime	315 (21.2)
Ciprofloxacin	3 (0.2)
Co amoxiclav	99 (6.7)
Cotrimoxazole	6 (0.4)
Metronidazole	8 (0.5)
Cefalexin	82 (5.5)
Total	1150 (100)

Table 3. Descriptive analysis of self-reported drugs group by mothers among children with 0-5 years old in Arak, Iran (N = 1248)

Self-Reported drug Group*	N (%)
Macrolide	399 (26.9)
Cephalosporine	389 (26.2)
Penicillin	320 (21.6)
Others	19 (1.3)

*Macrolide include: Azithromycin or Erythromycin, Cephalosporine including: Cefalexin or Injected Ceftriaxone or Cefixime, Penicillin including: Co-amoxiclav, Amoxicillin or Penicillin V, others including: Injection Gentamycin or Ciprofloxacin or Cotrimoxazole or Metronidazole.

Table 4. Association between self-reported consumed antibiotics and independent variables in univariate and adjusted analysis among mothers of children under 5 years old (2018-2019).

Variable	Univariate Analysis		Adjusted Analysis*	
	OR (95%CI)**	P-Value	OR (95%CI)**	P-Value
Child's gender	0.83(0.67, 1.03)	0.087	0.82 (0.66, 1.02)	0.070
Age of child	1.16(1.08, 1.25)	0.001	1.20(1.11, 1.29)	0.001
Age of mother	0.98(0.97, 1.01)	0.117	0.96(0.94, 0.98)	0.001
Mother's education	0.92(0.86, 0.98)	0.012	-	-
Father's education	0.92(0.86, 0.98)	0.007	-	-
Mother's job	0.93(0.78, 1.12)	0.445	-	-
Father's job	0.72(0.59, 0.89)	0.003	0.78(0.63, 0.97)	0.027
Parity	1.46(1.25, 1.70)	0.001	1.60(1.34, 1.90)	0.001
Birth weight	1.00(0.99, 1.01)	0.619	-	-
Socio-economic status	0.97(0.90, 1.04)	0.388	-	-

*Excluding the variables with $P>0.2$ values; **OR: Odds ratio; CI: Confidence intervals.

Discussion

Nowadays, the overuse of antibiotics is an important health issue in various countries from the developed to developing countries. The antibiotics side effects can affect people's health in several ways. In addition, their excessive consumption can lead to microbial resistance. Before conducting this study, the authors were concerned about the inappropriate consumption of antibiotics in many households in Arak. Based on the WHO reports issued in 2015, the daily antibiotics dosage consumed in Iran has been 38.78 per 1000 people, with macrolides' dosage being 19% and that of quinolones being 11%. The results of the present study demonstrate that the use of antibiotics in Arak is higher than that of the national average, and compared to those reported by WHO for antibiotics consumption in Iran (10).

In a cross-sectional review conducted by Ilam Youngster, *et al*. in 2017 (10), seven cohort studies conducted between 2008 and 2012 were analyzed on the use of antibiotics in children in six countries. It was found that the results varied substantially among the six nations. The highest antibiotic use belonged to South Korea, which were about 3.41 treatment courses per child-year. The lowest usage belonged to Norway with 0.5 courses per child-year. They also reported that Italy, Spain, the United States, and Germany had the highest to the lowest antibiotics consumption rates, respectively. Considering the information presented by that study,

it appears that it is necessary to draw policies to rationalize the use of antibiotics, not only in the six countries but also globally. At the same time, it is imperative for each nation to conduct independent investigations on its antibiotics consumption, and to draw plans to achieve safe and effective usage of antibiotics (10).

Similar to other drugs, the antibiotics side effects can cause health problems for consumers when there is no need for their usage. The excessive use of antibiotics can lead to microbial resistance in the users. This is also an important cause for concerns, as new mutations have been found in microorganisms that have become resistant to existing antibiotics. In addition, interactions of other drugs with antibiotics can cause irreversible side effects in the consumers. In a study by Hosseini-zadeh, *et al*. in 2012 (11), the patterns of resistance to antibiotics including Vancomycin-resistant *Enterococci* were examined. In this study, antibiotics resistance was investigated on erythromycin, teicoplanin, vancomycin, ciprofloxacin, tetracycline, gentamicin, cotrimoxazole, and linosol, after isolating and detecting 150 strains of *Enterococci* from clinical specimens.

Also, the minimal inhibitory concentration (MIC) test was performed on vancomycin-resistant specimens with vancomycin and teicoplanin by broth microdilution method (11). This test showed that 14.6% of the samples were resistant to vancomycin, and 5.3% to teicoplanin. It was also found that the samples resistance to the antibiotics were as follows: erythromycin (64%), cotrimoxazole (40%), ciprofloxacin (38.6%), tetracycline (6.6%), linosol (0.0%), and gentamicin (38.7%). Fourteen samples were highly resistant to vancomycin, all of which had large MIC values (256 µg/ml). Based on these findings, it is highly likely that vancomycin resistance to *Enterococci* strains is present in Arak, as it is the case in many parts of the world (11). Thus, it is imperative to choose appropriate treatment for *enterococcal* infections in Arak and the region.

In 2010, a study was conducted by Rafiei and Ashrafzadeh (12) on the prescription of antibiotics in surgical and pediatric wards, comparing the results with the standard dosages. It was found that the indications for the use of prescription drugs were consistent with the standards. However, the least effort has been made on the dosage and duration of treatment (12). This clearly shows that even in patients admitted to hospitals, there are fundamental problems with respect to the use of drugs and treatment methods, despite the fact that patients are treated by highly specialized medical teams.

In the current study, it was found that the prevalence of at least one antibiotic use per year in Arak was 62.4%. In a study conducted in Tehran in 1998 on the frequency of antibiotics use in patients, it was observed that 43% of the prescribed drugs were antibiotics (13). Similarly, in another study focusing on the pattern of antibiotic use at Taleghani Hospital in Tehran, the results showed that about 57% of the patients had received antibiotics (14). The results of the latter study are closer to those of the current study. The differences may be due to the fact that previous studies were performed on outpatient referrals to pharmacies or on inpatients. However, our study focused on a public population, where random samplings were made to survey the antibiotics consumption at both hospitals and outpatient health centers. Based on our study findings, it may be concluded that the most common antibiotic used in children (0-5 years old) in Arak was azithromycin (24.2%), which belong to antibiotic group of macrolides (26.9%).

In a study carried out in 2010-2011 by Khoshdel, *et al*., the pattern of antibiotics use was investigated in 265 children at Hajar Hospital, Shahrekord, Iran. These children received antibiotics during their hospitalization in the first seven days of each month throughout a year. The authors found that about 37% of antibiotics used were incorrect, with the most common one being ceftriaxone (83%). Moreover, this study reported that antibiotics were administered experimentally in 90% of cases despite ordering cultures for the patients. This means that the results of cultures had no effects on the choice of antibiotics given to the children (15).

Likewise, in another study on the use of antibiotics in pediatric wards at Italian hospitals, it was revealed that the use of penicillin and beta-lactamase inhibitors had significantly increased during the years in some wards, such as surgery (P=0.038) (16). The differences in the results reported by different studies are because most research on the use of antibiotics had been conducted at hospitals. In contrast, in the current study, the community-based use of antibiotics was examined on randomly-selected participants and compared the results to the prescription information recorded by their insurance companies.

In a study by Zolaly, *et al*. who investigated the factors affecting antibiotics administration among 776 patients, it was reported that 48.1% of patients were prescribed antibiotics. However, the results of the current study revealed a significant relationship between antibiotics use and other factors such as father's job, parity, and age of both the mother and the child. Thus, there were lower antibiotics consumption in younger children with fathers' having permanent jobs than those with temporary jobs or being unemployed. The findings of this study demonstrated that the level of education of the majority of mothers and fathers was having a high school diploma (~38%). Besides, most of the mothers were housewives (88.2%) and the fathers

had permanent jobs (61%), with the mean parity being 1.66.

The antibiotics usage in children is a critical issue, hence being the main focus of this study. Despite the small share it has in human lifespan, the first few years of life make a significant contribution to his/her health during adulthood (17). Children are prone to a variety of diseases due to their under-developed immune systems (18). This implies that the use of antibiotics in children deserves greater attention in future studies. In this context, improving the community's knowledge and attitude has a fundamental impact on the antibiotics usage in children. Therefore, it is essential to focus on the health literacy of the community members as a basic strategy to reduce the arbitrary consumption of drugs, especially antibiotics. Health literacy is a collection of cognitive and social skills, insight, and knowledge that determines the motivation and ability of individuals to access, and use information to maintain and promote their own health and that of their families (19, 20).

Limitations of the Study: We may consider the self-reported questionnaires to collect data as a limitation. This method may be susceptible to underestimating the measures under study and may lead to bias and misunderstanding by the participants (9, 21).

Recommendation for Future Studies: It is recommended that greater efforts should be made in future research to address the above mentioned limitation by including a bias analysis in the study protocol (22). Further, although the face-to-face interviews could have some degrees of bias; however, surveys are not always the best method for collecting data in studies with a focus on drug consumption (23-25).

Conclusions

Based on this study's analyzed data, the annual prevalence of antibiotics consumption in Arak was very high, with azithromycin being the most consumed drug. The findings of this study also revealed that there were less antibiotics consumption among younger children with older mothers and children whose fathers had permanent jobs than in other groups. Higher antibiotics consumption was also found among children in households of higher parity than in those with low parity.

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Ethical Considerations

The study protocol was reviewed and approved by the Ethics Committee of Arak University of Medical Sciences, Arak, Iran (Ethics code: IR.ARAKMU.REC.1398.217).

Conflict of Interests

The authors declare no conflict of interests with any internal or external entities in conducting this study.

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