

Antibiotic use without prescription in Ecuadorian children according to their families' socioeconomic characteristics

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ABSTRACT

Background: among the many processes responsible for antimicrobial resistance, inappropriate antibiotic use and self-medication are major public health concerns. To tackle antibiotic resistance and its widespread misuse, is important to identify the social, cultural, and economic differences associated with the problem. **Objective:** to determine the percentage of antibiotics used without medical prescription in children under five years old with symptoms of upper respiratory tract infection according to their families' socioeconomic characteristics in Ecuador. **Materials and Methods:** a cross-sectional design was set, using a structured questionnaire to assess mothers who attended urban and rural primary health care units with their children under five years old and belonged to the middle or lower social strata. A sample of 947 individuals was obtained from February to April 2011. Informed consent was acquired from those willing and eligible participants. The descriptive analysis used frequencies, percentages, means, standard deviation and chi-square. Quantitative information was processed using SPSS version 17. **Results:** those from lower socioeconomic strata used antibiotics to treat symptoms of upper respiratory infections of their children without medical prescription in a higher percentage (35.57%) than middle socioeconomic strata (27.7%, $p < 0.01$). Mothers who had university level education had more knowledge about measures to prevent antibiotic resistance (57.14%) than those with only a primary school education (13.59% $p < 0.05$). **Conclusion:** antibiotic use in children under five years old with symptoms of upper respiratory infection is high, mainly among those study participants corresponding to lower socioeconomic strata who mostly live in the rural area. **MÉD.UIS. 2017;30(2):21-7.**

Keywords: Drug Resistance, Microbial. Self medication. Social Class. Social Determinants of health.

Uso de antibióticos sin prescripción en niños ecuatorianos según las características socioeconómicas de sus familias

RESUMEN

Introducción: entre los múltiples procesos responsables de la resistencia antimicrobiana, el uso inadecuado de los antibióticos y la automedicación son problemas alarmantes en salud pública. Para la contención de la resistencia a los antibióticos y la ampliación del mal uso, es importante identificar las diferencias sociales, culturales y económicas asociadas al problema. **Objetivo:** determinar el porcentaje de uso de antibióticos sin prescripción médica en niños menores de cinco años, con síntomas de infección del tracto respiratorio superior de acuerdo las características socioeconómicas de sus familias en Ecuador. **Materiales y métodos:** se realizó un diseño transversal utilizando

un cuestionario estructurado para evaluar a madres pertenecientes a estratos sociales medio y bajo, quienes asistieron con sus hijos menores de cinco años a unidades urbanas y rurales de atención primaria de salud. Se obtuvo desde febrero a abril de 2011, una muestra de 947 individuos que dieron su consentimiento informado. Se hizo un análisis descriptivo mediante el uso de frecuencias, porcentajes, medias, desviación estándar y chi cuadrado. Para el procesamiento de la información cuantitativa se utilizó SPSS versión 17. **Resultados:** los estratos socioeconómicos más bajos usaron antibióticos sin prescripción médica para tratar síntomas de infecciones respiratorias del tracto respiratorio superior de sus hijos en un mayor porcentaje (35,57%), comparado con los del estrato económico medio (27,7%, $p < 0.01$). Las madres con educación universitaria tuvieron más conocimiento sobre medidas para la prevención de la resistencia bacteriana (57,14%) que aquellas con solamente educación primaria (13,59% $p < 0,05$). **Conclusiones:** el uso de antibióticos en niños menores de 5 años con síntomas de infección respiratoria alta es elevado, principalmente en aquellos participantes pertenecientes al estrato socioeconómico bajo, quienes viven en su mayoría en el área rural. **MÉD.UIS. 2017;30(2):21-7.**

Palabras clave: Farmacorresistencia Microbiana. Automedicación. Clase Social. Determinantes sociales de la salud.

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INTRODUCTION

Antibiotics have been successfully used to reduce and prevent death from infections and have helped to transform many previously deadly diseases into manageable health problems especially in developed countries. Worldwide, according to the World Health Organization the leading causes of death in children under five years old are pneumonia 13%, diarrhea 9% and malaria 7%¹ and about 37% of all child mortality is caused by infectious diseases, highlighting the importance of studying antibiotic use and emergence of resistance at the community level². In Ecuador, despite the fact that child mortality has decreased steadily since 1990 at a 3.9 annual rate reduction, infectious diseases still have a significant percentage^{1,3}.

Nowadays throughout the world, Antimicrobial Resistance (AMR) is increasing and compromising pharmacologic treatment of the most common infectious diseases. The processes responsible are varied and complex, including physiological and biochemical mechanisms. It is worth mentioning that the use of antibiotics, apart from being one of the most commonly prescribed and used drugs in human medicine, is the single most important factor leading to antibiotic resistance around the world. However, up to 50% of the time antibiotics are not optimally prescribed, often when not needed or ordered with incorrect dosing or duration of treatment⁴. Paradoxically, despite the growing problem of AMR, there has been an alarming decrease in research and development of new antibiotics. As there are virtually no new classes in the research and development in pipeline, clinicians are now facing a scenario where the probabilities of empirical treatments'

success are significantly reduced and where multi resistant bacterial infections are becoming more common^{5,6}. Infections caused by resistant bacteria and their associated morbimortality cause, prolong hospitalization stays and expensive treatment regimens, affecting the health system as a whole⁷.

It is estimated that 80-90% of antimicrobial use occurs in the community, therefore containment strategies should be targeted to minimizing any unnecessary and inadequate use⁸. A large percentage of these are used to treat Upper Respiratory Infections (URI) from viral etiologies that do not require antimicrobial treatment⁹. This occurs in part due to inappropriate health personnel prescription but also to self-medication and insufficient or inaccurate knowledge by the population in general, as well as limited access to health services because of geographic, economic and cultural reasons^{10,11}.

The main aim of this study was to determine to what extent antibiotics are used without medical prescription in children under five years old presenting symptoms of URI, who were served by primary healthcare clinics in accordance with their socioeconomic characteristics of their families in Ecuador. Additionally, to investigate if knowledge about antibiotic use and resistance is associated with the rate of usage without prescription to treat those symptoms.

MATERIALS AND METHODS

STUDY DESIGN AND STUDY POPULATION

A cross-sectional design was used to query mothers of children younger than five years old with signs and

symptoms of URI from different social strata. URI was diagnosed by the community physicians from each health unity, using Integrated Management for Childhood Illness criteria, IMCI (WHO, UNICEF). The data was collected through interviews, using a structured questionnaire with 49 questions that was validated in a previous pilot study¹² and applied by the health unit physicians. Mothers were asked about the name of the drugs used, then the physicians defined if it was an antibiotic.

Five primary health care units were included in the study; these were selected taking into consideration their geographic location, population coverage, demographic, economic and social characteristics. Two outpatient clinics of primary level public hospitals in Naranjal, located in the Coastal region of Ecuador and Sigsig in the Highlands; as well as three primary health care centers in Azuay province were selected.

We worked with the following sample restrictions: population of 28 162 children under five years old, living in the geographic area of study according to the National Institute of Statistics and Censuses of Ecuador (INEC 2011)¹³, a reported prevalence of 59.9% in children under age five with acute respiratory infection¹⁴, a minimum sample of 365 individuals for the total study population with 95% CI and 5% error estimated by applying the statistical program Epidat 3.1; inclusion criteria were mothers who wanted to participate whose children were under five years old and presented acute URI at the outpatient department of the participating health units. Mothers from upper social strata (those who ran their own company, factory, mine, agricultural unit with > 10 workers) were excluded since we found very few families belonging to this social strata and the sample would not have been representative. It was proposed to work with a total of 1000 participants of the five sites established and a sample for convenience of 947 mothers was obtained in a period of three months from February to April 2011.

The study participants were grouped into middle and lower social strata, based on the employment patterns of the head of the household. The middle strata was formed by independent professionals, traders, small agricultural producers (farm owners) and master craftsmen, while the majority of the lower strata population included laborers, agricultural workers, street vendors and craftsmen,

peasants who were employed but didn't own a production unit; we also took into account the family's patterns of consumption and access to basic needs: clean water, sanitation, health access, education, recreation, food and housing conditions of overcrowding defined as ≥ 3 people per room, according to Breilh's classification¹⁵.

OUTCOMES

The variables analyzed included demographic and socioeconomic characteristics of the child and family, mother's formal education level, and questions regarding knowledge of antibiotic use and resistance. The main outcome measures included: antibiotic use to treat the last URI episode of the child, whether the antibiotics were prescribed or not by a healthcare professional; knowledge of mothers regarding any risks associated with antibiotic use and resistance or about measures to prevent AMR by formal education level, and finally we studied if higher knowledge of the risks associated with antibiotic use and resistance were associated with use of antibiotics without prescription.

STATISTICAL ANALYSIS

Quantitative data was processed and analyzed using SPSS version 17, Excel 2010 and Epidata 3.1 software. The analysis used frequencies, percentages, and measures of central tendency such as means, standard deviation, and chi-square for statistical significance was used with levels of significance set to $p \leq 0.05$.

RESULTS

The non-response rate was 5.2%; these were mainly mothers living in remote areas. Reasons given by mothers for not participating were concerns about the amount of time spent at the health service and time needed to return home. The mean maternal age of the middle and low social strata participants in the study was 30(SD10) and 27(SD9) years respectively. The mean size of core family was 5(SD2) members, similar for both social strata, and mean family income was higher for the middle strata (\$560) compared with those from the lower strata (\$263).

Participants of the middle strata in this study sample lived mostly in urban areas; had low rates of overcrowding and a higher adequate basic services and formal education level compared to those from

the lower strata. Mothers from the lower social strata mostly resided in the rural area with significant levels of overcrowding, lack of basic services in a high percentage and managed signs and symptoms of URI using antibiotics without prescription before seeking medical consultation in a significantly higher percentage than those in the middle strata (35.57% versus 27.7% respectively, $p < 0.01$). Antibiotics without prescription were obtained at a pharmacy in most cases, 26.16% and 18.58% in middle and lower strata respectively, to a lesser extent, but no less importantly; antibacterials were obtained from other sources such as food stores, friends, the market and others (See Table 1).

Table 1. Basic Socioeconomic Characteristics of the Study Population in the last episode of URI by social strata

Characteristics	Social strata		
	Middle n=409(100%)	Low n=538(100%)	P
Urban residence	261(63.81)	193(35.87)	<0.05
Rural residence	148(36.19)	345(64.13)	<0.05
Overcrowding	33(8.14)	167(31.09)	<0.05
Adequate basic services	386(94.38)	426(79.18)	<0.05
Secondary-University level education	319(78)	258(47.96)	<0.05
Acquired antibiotics without prescription in the last episode of URI	113(27.7)	191(35.5)	<0.01
Acquired antibiotics in a pharmacy	107(26.16)	160(18.58)	<0.25

Source: Authors

Among both groups only a small percentage of mothers were aware of the risks of antibiotic use, resistance and measures for its containment, although a higher percentage from middle strata stated they were better informed about this (See Table 2). We also found that mothers both with and without knowledge about antibiotic use and resistance, had used them in similar percentages, 30.71% versus 38.46%, respectively (See Table 3).

Additionally, the level of schooling was related with knowledge on antibiotic resistance and preventive measures for its containment. Mothers with university studies were aware in a higher percentages than those with primary school and high school (See Table 4).

Table 2. Knowledge of mothers about risks of antibiotic use and antibiotic resistance by social strata

	Social Strata		
	Middle	Low	p
Total responders	n=409(100%)	n=538(100%)	
Yes, I have heard about the risks of antibiotic use	142 (34.72%)	89 (16.54)	<0.05
Yes, I have heard about what antibiotic resistance is	133 (32.52)	109 (20.26)	<0.05
Yes, I have heard about how to prevent antibiotic resistance	120 (29.34)	71 (13.2)	<0.05

Source: Authors

Table 3. Antibiotic use without prescription by knowledge of mothers about risks of antibiotic use and antibiotic resistance

Antibiotic use without prescription	Without knowledge n=687(100%)	With Knowledge n=260(100%)	P
Yes	211 (30,71%)	93 (38,46 %)	<0,152
No	476 (69,28%)	167 (64,23 %)	<0,152

Source: Authors

Table 4. Knowledge of mothers about antibiotic resistance and means of prevention and acquisition of antibiotics by formal education level

	Formal Education level			P
	Primary School	Secondary School	University	
Total responders	n=368(100%)	n=468(100%)	n=105(100%)	
Yes, I have heard about antibiotic resistance	63 (17.75)	106 (22.6)	62 (60.95)	<0.05
Yes, I have heard about prevention of antibiotic resistance	49 (13.59)	83 (17.3)	59 (57.14)	<0.05

Source: Authors

DISCUSSION

In our study, we found that antibiotics are often used to treat symptoms of URI in children under five years old in Ecuador and that frequency of use and self-

medication patterns differ according to the children families' socioeconomic strata with higher use in the lower one, in which most lived in the rural area.

We found that antibiotics were primarily bought from a pharmacy without the need of a prescription, followed by grocery stores and obtained from friends. These findings were similar to those described in the city of Barranquilla, Colombia in a study conducted in a low social strata neighborhood¹⁶, and is comparable with other studies in Spain¹⁷, Mexico¹⁸ and Georgia¹⁹. Furthermore, symptoms that encourage self-medication are similar, and their knowledge regarding undesirable or adverse events concerning antibiotic use, as well as their therapeutic effects was found to be similar. However, a notable difference between these researchers' studies and the present study is that we included social strata as a variable to explore if significant differences existed when comparing mothers receiving care in the same health unit and who lived in the same geographic area but belonged to different social strata.

Despite the fact that antibiotics are not considered over the counter medications in Ecuador, in the practice the country lacks tight control for drug marketing and distribution, which makes antibiotic availability without prescription simple as evidenced in the study, a situation that contributes to higher rates of adverse events, drug interaction and the possibility of a delay in diagnosis and mistreatment of potentially lethal infections as well as the emergence of AMR²⁰.

Antibiotic use without prescription is also associated with inappropriately shorter periods of use, dosing and inadequate drug election according to a study conducted by Okeke *et al.* and several other studies in communities where antibiotic use was frequent²¹⁻²³. If we take into consideration that population from lower social strata tend to have less access to information and often may not recognize some medications as antibiotics, the true proportion of patients who frequently use antibiotics is possibly much higher.

It should be noted that antibiotics have been perceived as low-risk drugs. However, they are the second leading cause of adverse drug effects in the United States and its use without prescription has been associated with severe adverse effects. Specific

solutions are needed to improve or change the use of antibiotics without prescription^{24,25}.

Although improvement has been made, many people in our country have restricted access to health care services, and in a lot of cases do not possess basic information regarding appropriate use of medicines and therefore are more likely to consult untrained drug sellers underestimating the potential risks associated with these medications²⁶. In our study, only a small percentage of mothers have received information about the risks of antibiotic use, resistance and measures for its containment from health care professionals. We know that children of mothers belonging to the lower social strata are highly vulnerable to infectious diseases due to their life conditions and malnutrition and are more likely to receive antibiotic treatment and other medications without prescription as other studies have described²⁷.

Maternal schooling was associated with the use of antibiotics without prescription. Those with a high level of schooling presented low percentages of antibiotic use without prescription. We believe mothers from low social strata have developed what can be interpreted as a survival strategy. They are more likely to access informal health care due to restricted access to formal state health care system and they have shown capacity to do so in our study. This situation presents a social, scientific and communicational challenge for the formulation of public policy to prevent antibiotic resistance.

Our study also suggests that knowledge of adverse effects and risks of antibiotic use did not decrease its use without prescription among the study population, even though this result did not reach statistical significance. This raises the necessity for further studies to achieve understanding of the content and the quality of the knowledge that the population manages regarding antibiotic use and resistance. It also arouse a challenge for decision-makers responsible for enabling regulation and safety, availability and access to antibiotics.

Among the limitations of our study, we report that antibiotic use was self-reported by the participants, which could introduce ascertainment or recall biases. Another limitation was the constitution of the sample. Due to feasibility we selected study sites by convenience, trying to represent the different geographical areas of the country.

CONCLUSIONS

Mothers belonging to the low social strata in the study population acquired antibiotics for their children without medical prescription in higher percentage than those in the middle strata to treat upper respiratory infection symptoms. Also, level of schooling was correlated with acquisition of antibiotics without prescription and associated with previous knowledge about antibiotic resistance and preventive measures for infection control at the community level.

Public health plans and strategies for health promotion and education for self-care should take into consideration and enhance the social, cultural and economic characteristics that are associated with antibiotic use, treatment adherence and increased antibiotic resistance. Interventions tackling antimicrobial resistance must be developed with direct participation of the communities in the process of health education. It is important to work with families from low socioeconomic strata who have been historically excluded from specific strategies to promote their rights and improve the accessibility to the health system.

There is an urgent need for a multilateral national policy involving health professionals and members of the community that considers cultural background and social vulnerability of different socioeconomic levels, and that evaluates long-term effectiveness of interventions constructed with the communities themselves. We recommend conducting and funding studies at a national or regional level to deepen knowledge of the underlying causes of antimicrobial resistance taking into consideration social determinants. In the absence of rigorous studies, the scope of interventions to reduce self-medication of antibiotics is very limited.

CONFLICT OF INTERESTS

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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ETHICAL CONSIDERATIONS

The Bioethics Committee of the Faculty of Medical Sciences of the University of Cuenca approved the research study. Additionally, in the health units where surveying was conducted, the physicians approved of and were involved in the study, and the results were shared with the health centers. The research objectives were explained verbally to each participant and informed consent was obtained from mothers of children under five years who were eligible and willing to participate in the study.

REFERENCES

1. WHO: World Health Organization web site. [Internet]. Washington D.C.: 2013 [citado 30 dic 2015]. Global Health Observatory (GHO) data. [about 1 screen.]. Disponible en: http://www.who.int/gho/child_health/mortality/causes/en/
2. WHO: World Health Organization web site. [Internet]. Washington D.C.: 2015 [citado 30 dic 2015]. Child mortality rates plunge by more than half since 1990 but global MDG target missed by wide margin. [about 2 screens.]. Disponible en: <http://www.who.int/mediacentre/news/releases/2015/child-mortality-report/en/>
3. UNICEF. Levels and Trends in child mortality. Official Report 2015. [Internet]. New York: UNICEF. September 2015 [citado 30 dic 2015]. Disponible en: http://www.childmortality.org/files_v20/download/igme%20report%202015%20child%20mortality%20final.pdf
4. CDC: Centers for Disease Control and Prevention web site. [Internet]. Druid Hill-Georgia: 2015 [citado 30 dic 2015]. Disponible en: <http://www.cdc.gov/drugresistance/about.html>
5. Nordberg P, Monet D, Cars O. Antibacterial Drug Resistance. Project: Priority Medicines for Europe and the World "A Public Health Approach to Innovation". [Internet]. Geneva: World Health Organization: 2005 [citado 30 dic 2015]. Disponible en: <http://apps.who.int/medicinedocs/documents/s20244en/s20244en.pdf>
6. Black R, Cousens S, Johnson H, Lawn J, Rudan I, Bassani D, et al. Global, regional and national causes of Child mortality in 2008: a systematic analysis. *Lancet*. 2010;375(9370):1969–87.
7. Laxminarayan R, Duse A, Wattal C, Zaidi, Wertheim H, Sumpradit N, et al. Antibiotic resistance -the need for global solutions. *Lancet Infect Dis*. 2013;13:1057-98.
8. Hughes D, Anderson D. Evolutionary consequences of drug

- resistance: shared principles across diverse targets and mechanisms. *Nat Rev Genet.* 2015;16(8):459-71.
9. Zaidi A, Huskins W, Thaver D, Bhutta Z, Abbas Z, Goldmann D. Hospital acquired neonatal infections in developing countries. *Lancet.* 2005;365(9465):1175-88.
 10. Huynh B, Padget M, Garin B, Herindrainy P, Kermovant-Duchemin E, Watier L, et al. Burden of bacterial resistance among neonatal infections in low income countries: how convincing is the epidemiological evidence?. *BMC Infect Dis.* 2015;15:127.
 11. Spyridis N, Syridou G, Goossens H, Versporten A, Kopsidas J, Kourlaba G, et al. Variation in paediatric hospital guidelines in Europe. *Arch Dis Child.* 2016;101(1):72-6.
 12. Quizhpe A, Encalada L, Andrade D, Alessio S, Barten F. Schoolchildren's perceptions and practices on the causes, gravity and treatment of acute respiratory infections, Azuay, Ecuador, 2012. *Rev. Fac. Cienc. Méd. Univ. Cuenca.* 2013; 31(3):18-25.
 13. INEC. Población por grupos de edad, según provincia, cantón, parroquia y área de empadronamiento. [Internet]. 2011; [Citado Junio de 2013]. Disponible en: <http://190.152.152.74/informacion-censal-cantonal/>
 14. Reyes A, Beltrán P, Astudillo J. Prevalencia de Infecciones Respiratorias Agudas en Pacientes Menores de 5 años y su Asociación con Desnutrición. *Jadán.* Enero-Diciembre 2014. *Rev Med HJCA.* 2015;7(2):100-105.
 15. Breilh J. *Medicins du Monde.* [Online].; 2008 [cited 2015 Octubre 5]. Available from: <http://www.medecinsdumonde.org/content/download/1864/14305/file>.
 16. Panuela M, De la Espriella A, Escobar E, Velasquez M, Sánchez J, Arango A, et al. Factores Socioeconómicos y culturales asociados a la autoformulación en expendios de medicamentos en la ciudad de Barranquilla. *Salud Uninorte.* 2002;12:30-8.
 17. Tejedor N, Zafra E, Sánchez del Vizo Y, López A, Vidal C, López de Castro F. Trastornos comunes en salud: Autocuidado y Automedicación. *Aten Primaria.* 2005;16(1):13-17.
 18. Angeles P, Medina M, Molina J. Automedicación en población urbana en Cuernavaca, Morelos. *Salud Publica de Mex.* 1992;34(5):554-61.
 19. Kandelaki K, Lundborg C, Marrone G. Antibiotic use and resistance: a cross-sectional study exploring knowledge and attitudes among school and institution personnel in Tbilisi, Republic of Georgia. *BMC Research Notes.* 2015;8:2-8.
 20. Muñoz G, Mota L, Bowie W, Quizhpe A, Orrego E, Spiegel J, et al. Ecosystem approach to promoting appropriate antibiotic use for children in indigenous communities in Ecuador. *Rev Panam Salud Publica.* 2011;30(6):566-73.
 21. Okeke I, Laxminarayan R, Bhutta Z, Duse A, Jenkins P, O'Brien T, et al. Antimicrobial resistance in developing countries. Part I: recent trends and current status. *Lancet Infect Dis.* 2005;5(8):481-93.
 22. Lodato M, Kaplan W. Antibacterial drug resistance. En: WHO. *Priority Medicines for Europe and the World: 2013 Updated Background Paper.* Boston: WHO; 2013. p. 68-74.
 23. Marmot M, Allen J, Bell R, Bloomer E, Goldblatt P. WHO European review of social determinants of health and the health divide. *Lancet.* 2012;380(9846):1011-29.
 24. Food and Drug Administration. Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals. [Internet]. Maryland: US Department of Health and Human Services; 2015 [Citado 15 Nov 2015].; [about 1 screen.]. Disponible en: <https://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM534243.pdf>
 25. Gu Q, Dillon C, Burt V. Prescription Drug Use Continues to increase: US Prescription Drug Data for 2007-2008. *NCHS Data Brief.* 2010;(42):1-8.
 26. Okeke I, Laxminarayan R, Bhutta Z, Duse A, Jenkins P, O'Brien T, et al. Antimicrobial resistance in developing countries. Part II: strategies for containment. *Lancet Infect Dis.* 2005;5(9):568-580.
 27. Morgan DJ, Okeke IN, Laxminarayn R, Perencevich EN, Weisenberg S. Non-prescription antimicrobial use worldwide: a Systematic review. *Lancet Infect Dis.* 2011;11(9):692-701.