Antimicrobial Consumption in Latin American Countries: First Steps of a Long Road Ahead

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Abstract

Background: Irrational antimicrobial consumption (AMC) became one of the main global health problems in recent decades. **Objective:** In order to understand AMC in Latin-American Region, we performed the present research in 6 countries. **Methods:** Antimicrobial consumption (J01, A07A, P01AB groups) was registered in Argentina, Chile, Colombia, Costa Rica, Paraguay, and Peru. Source of information, AMC type, DDD (Defined Daily Doses), DID (DDD/1000 inhabitants/day), population were variables explored. Data was analyzed using the Global Antimicrobial Resistance and Use Surveillance System (GLASS) tool. **Results:** Source of information included data from global, public, and private sectors. Total AMC was highly variable (range 1.91-36.26 DID). Penicillin was the most consumed group in all countries except in Paraguay, while macrolides and lincosamides were ranked second. In terms of type of AMC according to the WHO-AWaRe classification, it was found that for certain groups like "Reserve," there are similarities among all countries. **Conclusion and Relevance:** This paper shows the progress that 6 Latin-American countries made toward AMC surveillance. The study provides a standardized approach for building a national surveillance system for AMC data analysis. These steps will contribute to the inclusion of Latin-America among the regions of the world that have periodic, regular, and quality data of AMC.

Keywords

antimicrobial, consumption, data source, information, GLASS, Latin America

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Background

Antimicrobials are key elements for substantially increasing life expectancy of human beings.[1] Self-medication; the systematic use of antibiotics in food producing animals; or the indiscriminate prescription of antimicrobials for non-infectious diseases have contributed to their inappropriate use.[2]

Studies of antimicrobial use showed over-prescription of antimicrobials related to irrational or unnecessary use where the indication does not correlate with the disease,[3] the clinical diagnosis does not require any medication, or when diagnostic tests have discordant results.[4]

Antimicrobial misuse is the main driver for antimicrobial resistance (AMR), which has became a major global health problem,[5] especially in developing countries.[6] No Latin American countries' regularly measure their antimicrobial consumption and only a few of them occasionally review the overall consumption of antibiotics in their territory.[7] Factors affecting antibiotic consumption in developing countries include to inappropriate prescription practices, inadequate patient education, limited diagnostic facilities, unauthorized sale of antimicrobials, and lack of appropriate functioning drug regulatory mechanisms,[8,9] Surveillance and monitoring systems for antimicrobial consumption

(AMC)[10,11] are essential elements for assessing and controlling global trends in both AMC and microorganisms' susceptibility patterns in different countries.[12,13] AMC provides information about the types and quantities of consumed antimicrobial medicines. AMC data are collected on an aggregated level from pre-existing administrative databases (eg, for import, sales, and reimbursement). AMC data is not patient-level data and does not provide information on why the antimicrobials were used. Thus, it is a proxy for actual use of antimicrobial, for which data collection is more laborious.

The strategy of the World Health Organization (WHO) for measuring AMC proposes 3 levels for surveillance: national, regional,[14] and global strategies, such as the "Global Action Plan" (GAP)[15] or the "One Health" approach.[16] For this reason, WHO promoted international projects to understand and evaluate AMC processes like the new European One Health Action Plan[17] or the Central Asian and Eastern European Surveillance of AMR network (CAESAR).[18] However, in order to compare consumption among countries and inside each territory, it is necessary to use a unique way of measuring. That is why, to standardize AMC data collection and national reporting, WHO developed a common method, which applies the same metrics and tools. This method incorporated to AMC module into WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS-AMC) and it is now available to be applied by any country.[19]

Even though this monitoring methodology (as proposed in WHO-GAP strategy), enables each country to evaluate and track its own AMC national data[17] it has not been implemented worldwide, so it is still not possible to perform a global AMC comparison. Unfortunately, Latin America is one of those regions in which details of AMC remains unknown.[7,20-24] It is for this reason that research perform in to the reality of the AMC in each country is necessary.

The objective of this work is to evaluate countries' estimation of their national consumption of antimicrobials according to the WHO methodology.

Methods

2.1. *Study Design*: This research is a descriptive study of national antimicrobial consumption in Latin American countries.

2.2. *Participants*: The countries enrolled in the study were Argentina, Chile, Colombia, Costa Rica, Paraguay, and Peru.

2.3. *Period of the study*: The data correspondings to the period from 01/01/2019 to 12/31/2019 was collected, consolidated, and evaluated between August 2020 and March 2021.

2.4. *Variables considered in the study*: The following variables were assessed: name of the country, source of information, type of antimicrobial from groups J01, A07A, and P01AB; active principles according to the ATC classification system, number of packages, pharmaceutical formulation, concentration of antimicrobial in the pharmaceutical presentation, total amount of active ingredient (expressed in mg), AWaRe group,[25] DDD (Defined Daily Doses), DID (DDD/1000 inhabitants/day), and population under study.

2.5. *Antimicrobials studied*: Antimicrobials included in the study corresponded to subgroups: J01, A07A, and P01AB of the WHO Anatomical Therapeutic Chemical (ATC) classification system,[26] where J01 constitutes "antibacterial for systemic use," A07A "intestinal anti-infectives," and P01AB "nitro-imidazole derivatives for diseases caused by protozoa." Sub-groups included in this research are described in Table 1.

2.6. *AMC measurement method*: Data was evaluated using the WHO methodology for a global program on surveillance of AMC,[14] using the ATC classification and the DDD as a standard unit of measurement to express the average maintenance dose per day for a drug used for its main indication in adults.[26] DDDs were then transformed in DDDs per 1000 inhabitants per Day (referred as DID).

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Table 1. Antimicrobials Evaluated According to the WHO Anatomical Therapeutical Chemical (ATC) Classification[a].

Subgroup	Antimicrobial
J01A	Tetracyclines
J01B	Amphenicols
J01C	Beta-lactams, penicillins
J01D	Other beta-lactams
J01E	Sulfamides and trimethoprim
J01F	Macrolides, lincosamines
J01G	Aminoglycosides
J01M	Quinolones
J01X	Other antibacterials
A07A	Neomicine, nistantine, rifamixine, vancomicine
P01AB	Metronidazole, ornidazole, tinidazole

[a]WHO Anatomical Therapeutical Chemical (ATC) Classification.

Antimicrobials consumed were also classified according to the WHO Access-Watch-Reserve (AWaRe) classification.[25] This tool categorizes antibiotics into 3 stewardship groups: Access, Watch, and Reserve, to emphasize the importance of their optimal uses and potential for antimicrobial resistance. Access includes antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups. Watch group includes antibiotics that have higher resistance potential with relatively high risk of selection of bacterial resistance. Reserve group includes antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multi-drug-resistant organisms. Antibiotics in Reserve group should be treated as "last resort" options.

2.7. *Source of Information*: AMC information was obtained from sources available in each country in agreement with the local authorities. Each country selected the source that would allow it to include at least 80% of its population, thus ensuring that the extracted data would be meaningful. Sources included: data from local antimicrobial production/imports from pharmaceutical laboratories, distribution chain, and sales in pharmacies and/or hospital dispensing. Commercial sources of data such as IQVIA were included in 2 countries (Argentina and Chile), in order to estimate pharmacies' consumption. Each country provided their data through their Ministry of Health, the National Regulatory Authority, or the Pharmacovigilance Departments.

Argentina

Argentina measured their antimicrobial consumptions in 3 ways (Globally, Public Sector, and Private sector)

- Total/Global antimicrobials produced at the national level, plus antimicrobials imported by pharmaceutical laboratories: this data was provided directly from laboratories (sales + purchase) to the National Administration of Drugs, Food and Medical Technology (ANMAT). Therefore, these data represented the global consumption at country level, without distinction by hospital or community sector, public or private.
- "Remediar" Program: a program from the Ministry of Health that supplies free medicines from a list of essential drugs, which are delivered to the Primary Health Care Institutions in the public sector.
- IQVIA: commercial source, corresponding to private pharmacy sales.

Chile

- Central Supply of the National Health Services System (CENABAST), which is a part of the Ministry of Health: these are comprehensive data (outpatient and hospital inpatient consumption) that represents the public sector.
- IQVIA: representing private pharmacy sales.

Colombia

- "Medicines Information System" (SISMED), from the Ministry of Health, which registers all sales from medicines provided by manufacturers and importers. The source considered all AMC data (public and private sector; inpatients or outpatients).

Costa Rica

- Accounting and Supplies Computer System (SICS) of the Costa Rican Social Security Fund (CCSS), which provides high-quality information from social security and the public sector. CCSS covers almost the entire population (91%). However, the 9% of the population who are not insured remains uncovered within the present evaluation.

Paraguay

- The public sector considered dispensing of out patients and inpatients in hospitals and institutions depending of the Ministry of Public Health and

Table 2. Sources of information selected by each country.

Country	Data source sector	Sector			Covered population	% covered population of total country inhabitants[a]
		Total	Hospital	Community		
Argentina	Laboratories	x			44 938 712	100
	Remediar			x	16 000 000	35.6
	IQVIA			x	44 938 712	100
Chile	CENABAST	x			14 903 628	78
	IQVIA			x	15 842 072	82.91
Colombia	SISMED	x			49 395 678	100
Costa Rica	CCSS	x			4 608 402	91.08
Paraguay	SICIAP		x		5 082 767	71.9
	Private institutions		x		586 745	8.3
Peru	SISMED + EsSalud	x			25 062 492	78

[a]The percentage of the population reached by each data source was extracted from the total number of beneficiaries that the source declared in each country, data subsequently confirmed by the focal points in every case.

Social Welfare (MSPBS) through its "Automated Inventory Control and Information System of Paraguay" (SICIAP).

– A separate assessment with data provided by a group of major private hospitals in the country was used to estimate private consumption. It was not possible to assess the consumption of most private pharmacies.

Peru

– Public and social security sector data were extracted from the "Medicines Supply System" (SISMED) from the Ministry of Health (MINSA) though the General Directorate of Medicines, Supplies and Drugs (DIGEMID).

– The Social Security subsector (Es-Salud) also provided their data. For Peru, both sources were consolidated in order to reflect data from around 80% of the national population.

The information sources used by each country to obtain the AMC data, as well as the health sector involved, the level of coverage, the covered population and the percentage of the total national population that represent each source are shown in Table 2. As mentioned, sources in Argentina and Colombia allowed evaluating a global consumption at the national level. For the rest of the countries, according to the source selected, the percentage of coverage was variable. Different populations were considered for estimating consumption for each source of information.

2.8. Data Collection: Once the sources were selected, data collection was carried out by the following procedure:
   a. Nomination of an official referent in each country.
   b. Training referents in data enrollment though PAHO "Training on the WHO methodology for the surveillance of AMC (2020)" course. c. Data Registration using AMC data collection instrument described in the Global AMR and Use Surveillance System (GLASS) manual for the management of AMC data.[27] d. Quality control process of data recording. This procedure was performed as an external audit carried out by the University Center of Pharmacology (CUFAR), National University of La Plata, Argentina (WHO-PAHO Collaborating Center). This control included detection and recovery of missing data. e. Validation of data collected. After the quality control process, each country in collaboration with CUFAR, validated the consumption data registered for each antimicrobial, using the WHO tool.[27]

Results

The overall results corresponding to each country are shown in Table 1. Total AMC, expressed in DID (DDD/1000 inhabitants/day), was highly variable: from 1.91 DID in private institutions in Paraguay to 36.26 DID in Argentina (Table 3).

The relative consumption of antimicrobials analyzed according to the ATC classification, is shown in Table 4.

Penicillins and their derivatives (J01C) were the most consumed group in all subgroups of population studied, except in Paraguay (private and public sectors). Macrolides and lincosamides (J01F) were ranked second in Argentina (IQVIA), Chile (CENABAST and IQVIA), Colombia (SISMED), and Peru (SISMED + EsSalud).

In Argentina, penicillins and their derivatives exceeded 50% of the total AMC, both in the laboratory (production + import) base, and in the IQVIA base (51.63% and 51.57%, respectively). This percentage reached 90.77% for the Remediar Program.

Table 3. Total Consumption in DID for Each Country.

Country	Source	Denominator	Total DDDs	DID
Argentina	Laboratories	44 938 712	594 705 051	36.26
	Remediar	16 000 000	95 344 246	16.33
	IQVIA	44 938 712	180 439 478	11.00
Chile	CENABAST	14 903 628	34 854 715	6.41
	IQVIA	15 842 072	68 253 807	11.80
Colombia	SISMED	49 395 678	323 337 682	17.93
Costa Rica	CCSS	4 608 402	21 456 885	12.76
Paraguay	SICIAP	5 082 767	685 438	3.38
	Private institutions	586 745	216 417	1.91
Peru	SISMED + EsSalud	25 062 492	114 324 644	12.50

Abbreviations: DDD, defined daily dose; DID, defined daily dose per 1000 inhabitants per day.

In the case of data extracted from laboratory (production + imports) source, the second most used group was nitroimidazole derivatives (P01AB), with 13.60%, and in third place, macrolides and lincosamides, with 13.34%. However, in the IQVIA database, the second most used group was macrolides, with 18.88% and the third was quinolones (J01M) (12.30%).

In Chile, in both databases, CENABAST and IQVIA, penicillins and their derivatives group were also the most consumed antimicrobials (44.78% and 44.60%, respectively), followed by macrolides/lincosamides (23.46% and 24.57%) and quinolones (9.07% and 13.79%).

The same pattern (penicillins first, macrolides/lincosamides second, and quinolones in third place), was also repeated in Colombia (35.34%, 17.06%, and 12.82%, respectively).

In the case of Costa Rica, first place was penicillins and their derivatives (25.95%), followed by cephalosporins and carbapenems (J01D) (16.61%), then by tetracyclines (J01A) (14.78%) and lastly by sulfonamides/trimethoprim (J01E) (14.77%).

In Paraguay, the public sector data showed that the group of antimicrobials most consumed was macrolides (28.9%), followed by penicillins and their derivatives (28.49%) and quinolones (17.97%). In the private sector, it was observed that the group of cephalosporins and carbapenems was the most consumed (41.66%), followed by quinolones (31.97%), and in third place, macrolides (14.20%).

In Peru data demonstrated that penicillins and their derivatives were in first place (35.91%), followed by macrolides (16.01%) and quinolones (14%).

Table 5 shows the relative consumption calculated by source of information and involved population according to the WHO AWaRe Classification.

In all populations studied except in Paraguay, the "Access" group exceeds 60% of total consumption, with variations ranging from 60.05% for Chile (IQVIA), to 95.25% for the Remediar Program in Argentina.

An inversely proportional AMC from the "Watch" group was observed in all countries, with the data varying from 4.75% for the Remediar Program in Argentina to 39.89% in Chile (IQVIA).

Paraguay had a prevalent consumption of the Watch group versus the Access group in both the private (58.02% and 38.26%, respectively) and the public (59.76% and 19.46%, respectively) sectors.

The "Reserve" group represents less than 0.8% of consumption in all countries.

Discussion

The WHO methodology for AMC monitoring allows for data to be collected on an aggregated level and does not rely on person-level data, which is largely unavailable in many countries. The flexibility in the choice of data sources for AMC enables countries with limited resources to use pre-existing data sources to build up sustainable systems for AMC surveillance. This approach builds up on the long-term practice developed by the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) of the European Centre for Disease Prevention and Control (ECDC) to monitor national trends in AMC over time.[28] Where available, countries are encouraged to link AMC data with clinical and microbiological data to learn about the indications for antimicrobial use and improve practices.

Results from this study showed wide variations in the quantity and types of antimicrobials consumed. This variation likely reflects actual differences in AMC but might also be partially attributed to differences in data coverage. Countries enrolled in this research used different sources of information to determine AMC, which is directly tied to the population enrolled in terms of percentage of inhabitants considered in the analysis.

In the case of Argentina, information was obtained from the public sector through the largest national program for the provision of drugs to the outpatient population without

Table 4. Relative AMC in Each Country, According to ATC Classification, Different Sources of Information and Involved Population; Expressed in DID (DDD/1000 inhab./day) and as a Percentage (%) of the Total Consumption.

ATC code	ATC group	Argentina (laboratories: production + imports)	Argentina (Remediar Program)	Argentina (IQVIA)	Chile (CENABAST)	Chile (IQVIA)	Colombia (SISMED)	Costa Rica (CCSS)	Paraguay (Public sector)	Paraguay (Private sector)	Peru (SISMED + EsSalud)
A07A	Intestinal anti-infectives	0.249 (0.69%)	—	—	0.039 (0.61%)	0.079 (0.67%)	0.139 (0.78%)	—	—	0.001 (0.05%)	—
J01A	Tetracyclines	1.589 (4.38%)	—	0.600 (5.45%)	0.0007 (0.01%)	0.198 (1.68%)	1.796 (10.01%)	1.885 (14.78%)	1.23E-04 (0.004%)	0.005 (0.26%)	0.980 (7.84%)
J01B	Amphenicols	—	—	—	—	—	—	—	—	—	0.035 (0.28%)
J01C	Beta-lactams, penicillin	18.719 (51.63%)	14.819 (90.77%)	5.673 (51.57%)	2.869 (44.78%)	5.265 (44.60%)	6.338 (35.34%)	3.31 (25.95%)	0.962 (28.49%)	0.136 (7.13%)	4.488 (35.91%)
J01D	Other beta-lactams	2.144 (5.91%)	0.517 (3.17%)	0.872 (7.93%)	0.527 (8.23%)	0.505 (4.28%)	1.967 (10.97%)	2.119 (16.61%)	0.594 (17.59%)	0.795 (41.66%)	1.313 (10.50%)
J01E	Sulfonamides and trimethoprim	0.657 (1.81%)	0.214 (1.31%)	0.419 (3.81%)	0.198 (3.09%)	0.211 (1.79%)	0.986 (5.50%)	1.884 (14.77%)	0.023 (0.68%)	0.032 (1.68%)	0.761 (6.09%)
J01F	Macrolides and lincosamides	4.836 (13.34%)	0.598 (3.66%)	2.077 (18.88%)	1.503 (23.46%)	2.901 (24.57%)	3.059 (17.06%)	1.671 (13.10%)	0.976 (28.90%)	0.271 (14.20%)	2.000 (16.01%)
J01G	Aminoglycosides	0.060 (0.17%)	—	0.005 (0.05%)	0.031 (0.49%)	6.44E-04 (0.005%)	0.332 (1.85%)	0.104 (0.82%)	0.087 (2.58%)	0.015 (0.79%)	0.271 (2.17%)
J01M	Quinolones	2.510 (6.92%)	0.178 (1.09%)	1.353 (12.30%)	0.581 (9.07%)	1.628 (13.79%)	2.30 (12.82%)	0.285 (2.23%)	0.607 (17.97%)	0.610 (31.97%)	1.749 (14%)
J01XA	Glycopeptides	0.058 (0.16%)	—	0.0004 (0.004%)	0.018 (0.27%)	0.000001 (0.00001%)	0.009 (0.05%)	0.068 (0.53%)	0.100 (2.96%)	0.024 (1.26%)	0.041 (0.32%)
J01XB	Polymyxins	0.016 (0.04%)	—	0.0001 (0.001%)	0.002 (0.03%)	—	0.002 (0.01%)	1.82E-04 (0.001%)	0.027 (0.80%)	4.23E-04 (0.02%)	0.003 (0.02%)
J01XD	Imidazole derivatives	0.048 (0.13%)	—	—	0.075 (1.17%)	0.000006 (0.00006%)	0.107 (0.60%)	0.047 (0.37%)	—	0.016 (0.84%)	0.052 (0.42%)
J01XE	Nitrofuran derivatives	0.428 (1.18%)	—	—	0.390 (6.09%)	0.858 (7.27%)	0.447 (2.50%)	1.056 (8.28%)	—	—	0.302 (2.42%)
J01XX	Other anti-bacterial	0.013 (0.04%)	—	0.001 (0.009%)	0.003 (0.04%)	0.00005 (0.0005%)	0.023 (0.13%)	0.005 (0.04%)	—	3.57E-04 (0.02%)	0.009 (0.08%)
P01AB	Nitroimidazole derivatives	4.931 (13.60%)	—	—	0.170 (2.66%)	0.158 (1.34%)	0.428 (2.39%)	0.323 (2.53%)	—	0.002 (0.1%)	0.493 (3.94%)
	Total	36.257 (100%)	16.326 (100%)	11.000 (100%)	6.407 (100%)	11.804 (100%)	17.934 (100%)	12.756 (100%)	3.377 (100%)	1.908 (100%)	12.497 (100%)

Abbreviations: ATC, Anatomical Therapeutic Chemical (ATC) Classification System; DDD, defined daily dose; DID, DDD per 1000 inhabitants per day.

Table 5. Relative AMC According to AWaRe Classification, in Each Country, According to the Different Sources of Information Expressed in DID (DDD/1000 inhab/day) and as a Percentage (%) of the Total Consumption.

AWaRe classification	Argentina (Laboratories: production + imports)	Argentina (Remediar Program)	Argentina (IQVIA)	Chile (CENABAST)	Chile (IQVIA)	Colombia (SISMED)	Costa Rica (CCSS)	Paraguay (Public sector)	Paraguay (Private sector)	Peru (SISMED + EsSalud)
Access	28.263 (77.95%)	15.550 (95.25%)	7.250 (65.90%)	3.996 (62.37%)	7.088 (60.05%)	12.560 (70.03%)	10.554 (82.73%)	0.657 (19.46%)	0.730 (38.26%)	8.327 (66.63%)
Watch	7.716 (21.28%)	0.776 (4.75%)	3.687 (33.51%)	2.401 (37.47%)	4.709 (39.89%)	5.173 (28.84%)	2.166 (16.98%)	2.018 (59.76%)	1.107 (58.02%)	4.158 (33.27%)
Reserve	0.031 (0.09%)	—	0.0006 (0.005%)	0.005 (0.08%)	0.00005 (0.0005%)	0.021 (0.12%)	0.005 (0.04%)	0.027 (0.80%)	0.002 (0.16%)	0.013 (0.1%)
Without classification	0.247 (0.68%)	—	0.063 (0.57%)	0.005 (0.09%)	0.007 (0.06%)	0.179 (1%)	0.031 (0.24%)	0.676 (20.01%)	0.069 (3.61%)	—
Total	36.257 (100%)	16.326 (100%)	11.000 (100%)	6.407 (100%)	11.804 (100%)	17.934 (100%)	12.756 (100%)	3.377 (100%)	1.908 (100%)	12.497 (100%)

Abbreviations: DDD, defined daily dose; DID, DDD per 1000 inhabitants per day.
AWaRe Classification System according to 2019 WHO AWaRe classification of antibiotics for evaluation and monitoring of use. Geneva: World Health Organization; 2019. (WHO/EMP/IAU/2019.11).

specific insurance called "Remediar"; but also, information was obtained from a private consulting organization (IQVIA) which registers sales performed in all pharmacies in the country to outpatients. Both of these sources provide information only about ambulatory AMC. That is the reason why Argentina chose a third source of information, which consisted of information provided directly by the laboratories that produce and import antimicrobials. This Global Data includes both outpatient data information about the use of antimicrobials in hospital settings either in public and in private sector, which is the 100% of the country's population. Although, data for this research could be obtained just from this Global Data source; the 3 sources were shown in the analysis (Table 3), since it is interesting to demonstrate the great differences that exists among these data sources. This discrepancy might be explained by the type of population that each one of the sources considered. While "Remediar" program only includes public sector, mostly socially vulnerable inhabitants that has no other health insurance; the IQVIA data only includes the population that obtains their ambulatory medicines from pharmacies; and Laboratories source includes all antimicrobials that were dispensed in the country (either ambulatory or inpatients; public, social security, or private sector). That is why, it is considered that this last source reflects the situation that is closest to reality, and might be an important tool for future research.

Chile, Colombia, and Costa Rica each had a unique national source of information provided by health authorities that contained consumption data from the public sector or from the health insurance sector.

In Chile, this source is called the CENABAST data base, which consolidates information from the public sector and the health insurance sector encompassing both ambulatory and hospital antimicrobial consumption. Hence, the source includes the great majority of the population in the country with the exception of the private ambulatory consumption data, which was obtained from the IQVIA data base (an international advisor group) which allowed the inclusion of the private sub-sector data from people who paid for their antimicrobials using cash in private pharmacies.

In Colombia, the national data base (SISMED) includes either public, insurance, or private sectors which constitute 100% of the population.

In Costa Rica, the source was the Health Insurance System (CCSS). Although, not all the population is included in this system, it was considered an excellent source of information since more than 91% of the inhabitants in the country have this coverage.

Paraguay included AMC data from public health institutions (information extracted from antimicrobial purchase and distribution by the Ministry of Health). The private sector was represented by the main private health institution. Between both databases the majority of the population was represented in the study, however, for further studies the social security sector called IPS should be enrolled (then 100% of the population will be included in the analysis).

In the case of Peru, the data was obtained from the public sector. Although it accounts for a large percentage of the population (>78%), there is still a non-negligible percentage of the inhabitants that was not considered in the analysis. In order to include 100% of the Peruvian population, it would be necessary to include the private sector and to develop a unique data base to register all antimicrobial commercialization the future AMC analysis of the country.

An issue that is directly related to the source of information and which is also just as important, is identifying the population to whom these antimicrobials are administered/dispensed (potential consumers). This will become the "denominator" of the consumption formula. For a national estimation of consumption, there is no doubt that the appropriate population is the total population of the country (all age and gender groups combined). This is the case of Argentina and Colombia. However, in countries like Chile, Costa Rica, Peru, and Paraguay, only the population that reflects the real coverage provided by each source was considered, in order to avoid the overlap of data sources. For this reason, for each country enrolled in this study, all sources and population were submitted to a careful analysis process in order to validate them.

About the type of antimicrobial consumed, the majority of antimicrobials consumed in all countries, except for Paraguay, belonged to the "Access" group which is the expected situation in a global analysis. Noteworthy, in Paraguay, both private and public health sectors, antimicrobials from the "Watch" group were the most consumed. In the public sector of this country, it was also found that a high percentage of AMC (20.01%) could not be classified within the AWaRe groups, which corresponds to amoxicillin-sulbactam and cefoperazone-sulbactam, both fixed-dose combinations, considered by the WHO to be antimicrobials not recommended for daily clinical practice, due to the lack of evidence-based indications for use or recommendations in high-quality international guidelines. Another fact to highlight about Paraguay is that, in the private sector, the use of macrolides doubles the use of beta-lactams, a situation contrary to that observed in all other countries analyzed. Antimicrobial consumption (classified as Access, Watch, and Reserve groups) is an important information mainly for each country`s health authorities, since, each administration will be able not only to compare future data to the baseline, but also to monitor the impact of health policies guiding[29] toward the rational use of these medicines.

Concerning the number of antimicrobials consumed in terms of DID, the study shows a wide diversification of results where Argentina had the highest total AMC

measured in DID and Paraguay the lowest. These situations might be based on population access to antimicrobials, and local AMC policies.

The limitations of the study and the potential problems in obtaining regular AMC information from countries are related to the absence of a global health information system[30,31]; the fluctuation of governments' engagement; the lack of resources, the lack of rules and regulations, and the limited staff assigned to this topic.[31,32] The evaluation of AMC is not yet a well-developed and standardized process in countries of the Americas, and additional efforts should be made in the future to fully validate sources of information, ensure the coverage and avoiding potential overlapping among sources. The present work set a path for standardization and systematization of a methodology for this purpose.

Government plays a major role in collaboration with national and international stakeholders in setting health policy rules and regulations like antibiotic use.[33,34] Periodic estimation and analysis of AMC data, as developed in this study, may help to establish trends at the national level and comparisons with other countries or regions' data by enrollment into GLASS-AMC, evaluating potential achievements of local health policies toward the rational use of these medicines.[34] Studies like this one will encourage the authorities of other countries in the region to begin periodically registering the consumption of antimicrobials in their territory, which turn will allow them to make the right decisions not only with regards to improving the use of these medicines, but also avoiding resistance to antibiotics.

Conclusions

This paper presents for the first time AMC data from six Latin American countries employing the same WHO standardized methodology for the analysis. Each country identified its own source of information which guaranteed independent valid data about amount and type of antimicrobials consumed during the year 2019.

A great heterogeneity among the countries was seen in terms of total antimicrobial consumption measured in Defined Daily Doses/1000 inhabitants/day (range from 1.91 to 36.26). The majority of antimicrobials consumed in almost all countries belonged to the "Access" group which correlates with a rational AMC scenario.

This study can help in future research to monitor trends, correct errors, improve procedures and create a sustainable and periodic evaluation of national consumption, as a powerful tool for decision-making in health. The commitment of each national authority to this type of project is essential for the improvement of data recording system in order to know which and how antimicrobials are used in different health sectors. These steps will contribute to making Latin America one of the regions of the world that have periodic, regular, and quality data of AMC.

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