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Antimicrobial Resistance in Water in Latin America and the Caribbean: Available Research and Gaps

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Introduction: Antimicrobial resistance (AMR) is a public health concern that has gained increasing global awareness, and it is estimated that there will be 10 million deaths annually by 2050. The importance of the role of the environment in disseminating clinically relevant AMR is a concern. Although research on AMR in Latin America and the Caribbean (LAC) has been conducted, these data have not been analyzed together to better understand which areas in AMR have been more studied, and which require more attention.

Objective: Determine the state of knowledge and identify the information gaps for AMR in water in LAC through an exploratory review that identifies the scientific articles that have addressed the topic.

Method: The process of selecting scientific articles from databases consisted of the four phases of an exploratory review focusing on eight themes of interest.

Results: The selection process identified 289 studies that were published between 1973 and October 2017, and these studies were included in the analysis. Most of the research was performed from 2008 to 2017. Brazil was the main contributor to the study of AMR in the region while no research was identified in AMR in water in eight of 18 of LAC countries. The most researched topics in water are phenotypic detection of AMR (theme VIII), detection of antimicrobial resistance genes (ARG) (theme V), and degradation of AMR (theme III). Limited research was identified on insects, agricultural products, aquatic organisms, livestock, and wastewater other than hospital wastewater. Research on emerging pests and diseases with a potential impact on the production of AMR (theme VII), impact of the use of antimicrobials on agricultural production (theme IV), and negative effects of AMR on wildlife (theme II) was scarce.

Conclusions: We suggest to focus research efforts and resources to study themes I, II, IV, VI, and VII, for which there is little research in LAC, without hindering the valuable research conducted on themes III, V, and VIII. The AMR environmental situation is mainly driven by a few countries that are not representative of the LAC region, and therefore, research is needed in other LAC countries besides Brazil.

Keywords: agriculture, antibiotics, health effect, heavy metal, livestock, environment, co-selection, antibiotic resistance genes

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INTRODUCTION

Antibiotics are crucial therapeutic tools to treat infectious diseases in human and veterinary medicine. Since the introduction of antibiotics, millions of human lives have been saved, highlighting the impact of these drugs for humanity (1). In agriculture, antibiotics have played a crucial role for the modernization of food production, which has supported global food security and accessibility of food (2). However, the overuse of antibiotics has led to a major threat for human and animal health, which is the global emergence of antimicrobial resistance (AMR) (2). Antibiotics are largely used in food-producing animals as therapeutic, metaphylactic (to treat healthy animals in the same flock), or prophylactic treatments; to eradicate disease; or to promote growth (2). It is well-recognized that antibiotic exposure is a selective pressure for AMR, in which pathogenic and commensal or native environmental bacteria could acquire AMR (3). A susceptible bacterium can become multidrug resistant in one conjugation event through the transfer of plasmids carrying clusters of antibiotic resistance genes (4). Currently, AMR is one of the most important public health problems, and it is estimated that there will be 10 million deaths annually by 2050; there is also an estimated economic impact of 100 trillion USD if no new interventions are developed and available to combat AMR (5, 6).

Currently, there is worldwide recognition of the role of the environment as an important source and dissemination route of antibiotic resistance (3). The use of antibiotics in food production (e.g., to treat sick animals or plants) and in human activities (e.g., discharge from pharmaceuticals) releases AMR into the environment (7). However, current evidence raises a debate on the major contributor to AMR in the environment and the risk to human health from environmental AMR. An improved understanding of this is extremely relevant in terms of the implementation of mitigation strategies to control AMR dissemination in the environment. Major sources of these contaminants can originate from agricultural, livestock, and human activities, such as application of fertilizer with an animal origin, use of treated wastewater for irrigation, and direct excretion of animal, household, or hospital waste into the environment (8). Sources such as sewage, wastewater treatment plants, and water bodies are recognized as important vectors of AMR, and they play a role in bacterial transmission between hosts (humans, food animals, and wildlife). However, the human health impact that is attributed to the dissemination of environmental AMR is not fully understood and even less understood is the ecological impact of AMR dissemination in the environment (3).

Worldwide, most of the studies have investigated AMR in zoonotic and foodborne pathogens, such as *Salmonella* spp. and *Campylobacter* spp. Studies that have evaluated the links between the use of antimicrobials in animal husbandry and the health impact to humans have been reported in several countries (7). Recently, studies have diversified to integrate the abundance and diversity of AMR in soil and water and their association with spatial and temporal changes (9, 10). The current ability to use cutting-edge technologies, such as high-throughput qPCR or whole genome sequencing to determine the environmental resistome, is starting to advance our current knowledge in this area (9). The human risk of the environmental resistome depends on multiple factors, which varies according to the microorganism, resistance mechanism, location within the genome of the resistance genes (e.g., plasmid-encoded), and environmental factors (e.g., presence of heavy metals) (7).

For AMR in water, most studies have investigated water source categories such as aquatic environment dedicated to aquaculture (fish, shrimp), effluents from wastewater treatment plants, and surface and irrigation water (11–14). However, currently, the role of the aquatic environments with fresh or marine water contamination by AMR is poorly understood. In addition, the main sources of AMR in water are not clear. A review reported the following bias in current studies (8): little data are available to assess the magnitude of the effects of environmental antibiotics and antimicrobial-resistant bacteria and genes. Therefore, although plausible mechanisms for these effects exist, the level of exposure of humans, wildlife, agricultural systems, and natural ecosystems to antimicrobial resistant bacteria and genes in the environment and its consequences has not been elucidated. Consequently, intervention strategies to combat environmental dissemination of AMR are difficult to design and implement (3). Only a few countries have publicly accessible AMR surveillance systems or are active in AMR research in Latin America and the Caribbean (LAC). Although research on AMR in water in LAC has been conducted, most identified research corresponded to individual studies that focused on the description of resistant isolates or resistant genes, mainly in human pathogens, but there has been no analysis that has combined these individual studies. The main objective of the present scoping review is to analyze peer review studies to examine the available information and identify research and/or information gaps regarding eight themes of interest for AMR in water in LAC. The knowledge resulting from this scoping review will provide information to focus research efforts and funding in areas with no or little research in the LAC region.

METHODS

The methods used in this scoping review are consistent with the JBI Reviewer's Manual 2017 guidelines (15). The framework for conducting a scoping review is described in Levac et al. (16) and Khalil et al. (17) and consists of the following processes: (i) identify the research question; (ii) identify relevant studies; (iii) select the studies; (iv) present the data by charting results in a tabular and narrative format; (v) collate the results to identify the implications of the study findings for policy, practice, or research; and (vi) consult with stakeholders (optional). Steps 1 through 3 were specified and documented in advance in a protocol (18). Only relevant information regarding steps 1 through 5 and modifications of the Moreno-Switt et al. protocol (18) will be presented in this section to allow a more fluent and clearer reading of this study. Refer to the Moreno-Switt et al. protocol (18) for further and specific details regarding the process for conducting this scoping review.

Literature Search Strategy and Selection of Studies

A search for published AMR studies in LAC was based on the following eight themes of interest regarding AMR in water: (I) Livestock and aquatic production systems as sources of antibiotic resistance in environmental water; (II) Negative or unexpected effects of AMR and antibiotics on terrestrial and aquatic wildlife living organisms; (III) Degradation of AMR in the environment; (IV) Impact of the use of antimicrobials in agricultural production; (V) Transmission of AMR genes from both humans and animals through water and detection of microorganisms harboring resistant genes; (VI) Crossed AMR between antibiotics and heavy metals; (VII) Emerging pests and diseases with potential impact in the production of AMR; and (VIII) Detection of microorganisms with phenotypic evaluation of AMR in water. Refer to the Moreno Switt et al. protocol (18) for further details on the rationale and description of each theme.

A search for articles published on any of the themes of interest was performed using the electronic databases PubMed, Scopus, and Web of Science from July to October 2017. The process is summarized in **Figure 1**, and it consisted of four phases of a scoping review (15): (i) *Identification*: detection of articles with search criteria consisting of a combination of keywords; (ii) *Screening*: examination of the titles and abstract of articles to determine whether these continue in the selection process or were excluded; (iii) *Eligibility*: revision of the full text to assess suitability; and (iv) *Inclusion*: data extraction and final classification of the selected articles in at least one theme of interest.

The search for articles was based on specific search criteria. The articles that were identified using these search algorithms were subject to a further selection process where the articles were classified into each of the target themes based on specific inclusion criteria or removed if the article met any of the exclusion criteria (18).

Data Extraction

Data on the following variables were extracted and recorded from each article as described in the Moreno-Switt et al. protocol (18): (i) Title; (ii) First author; (iii) Publication year; (iv) Country where samples were collected or the research was executed; (v) Identification number of the paper (Pubmed ID, Doi, or Web of Science accession number); (vi) Matrix of interest from which samples were taken and analyzed; (vii) Antibiotic, biocide, heavy metal or resistant gene evaluated in the study; (viii) Objectives of the study; (ix) Main findings or conclusions; and (x) Gaps identified. The data for each variable was extracted from the selected articles and recorded in an excel spreadsheet. When an article referred to more than one theme or country, the variable was counted and considered as an article. The counts were recorded and analyzed as described in **Figure 2**.

The number of articles identified in this scoping review were classified by decades and countries to identify the variation on

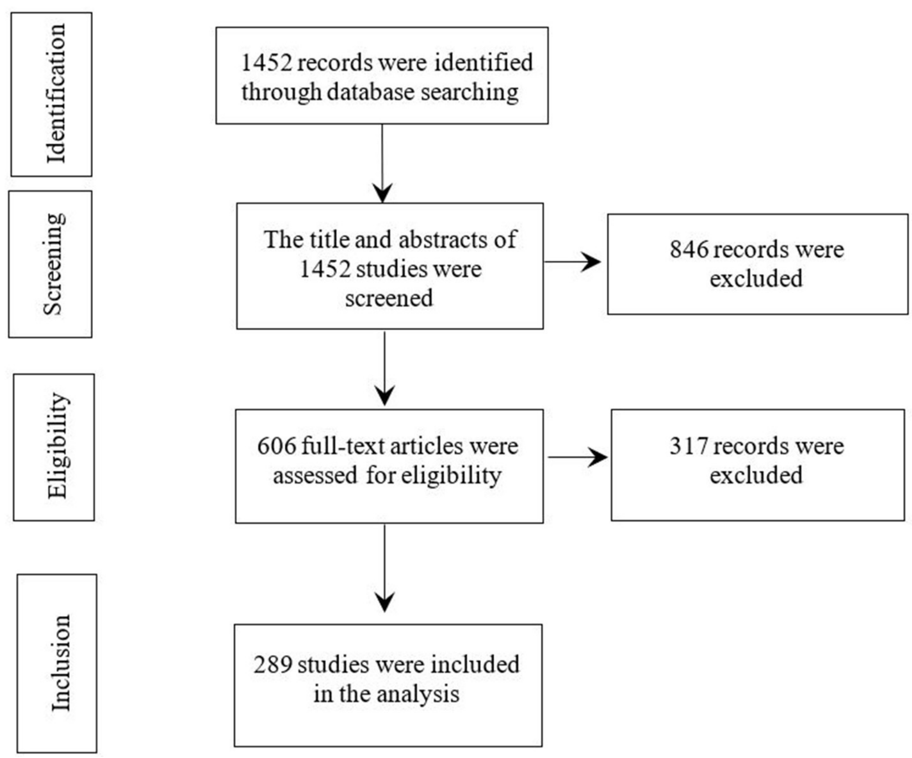

FIGURE 1 | Flow of information through the different phases of a scoping review regarding AMR in water in Latin America and the Caribbean.

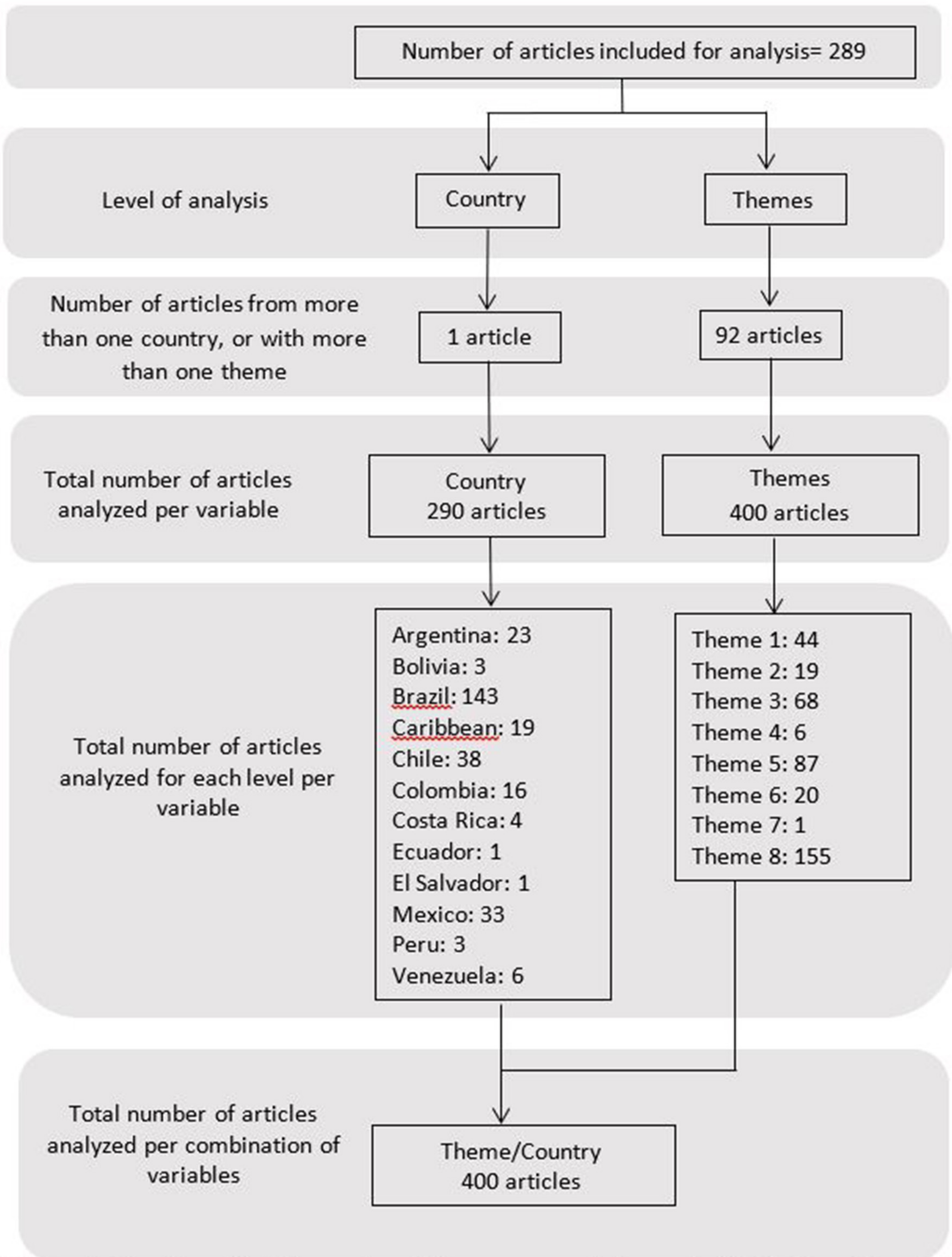

FIGURE 2 | Number of articles analyzed by country and theme, individually and combined.

the number of published studies in any of the themes of interest based on year of publication and country were the samples were collected or the study was conducted. Furthermore, an analysis based on the gross domestic expenditure on research and development (GERD) as a percentage of the gross domestic product (GDP) of each country was conducted. The original database was downloaded from the UNESCO website (19). Modification of the original database consisted in including only those LAC counties that had GERD data reported in at least 1 year between 2010 and 2015, a mean value for these 6 years was calculated and presented as **Figure 3**.

Initially, attempts were made to contact authors for clarification, but because of the lack of responses, this approach was not implemented throughout the entire study. Analyses of the articles were included in the present scoping review for LAC and the gaps were identified in each of the themes. The quality of each included article was not evaluated because the aim of this scoping review was to identify the available research on AMR in the region's water regardless of the quality of the research.

RESULTS

Available Research on AMR in Water in LAC

Literature Search Strategy and Selection of Studies

The initial search identified 1,452 potentially relevant studies (**Figure 1**). After reviewing the titles and abstracts, 606 studies were considered for further screening because they met the inclusion criteria and none of the exclusion criteria (18), of which 317 were not eligible because at least one of the exclusion criteria was met after revising the full text. After examination of the title, abstract and full text, 1,163 studies were removed, and 289 studies were included for further analysis. The studies identified and included in this scoping review were published between 1973 and October 2017. **Supplemental Table 1** provides a summary of the data that were extracted by publication year, country, and theme, with their respective references.

Available Research Information by Country

In this section, 289 articles were included for all the LAC countries when analyzing the information regardless of the theme studied. However, as one study was conducted in Peru and El Salvador (20), the number of articles analyzed for the various countries increased to 290 (**Figure 2**). As shown in **Figure 4**, Brazil has the most articles included in this scoping review with 143 of 290 articles (49.3%), followed by Chile with 38 articles (13.1%), Mexico with 33 articles (11.3%), Argentina with 23 articles (7.9%), Caribbean countries with 19 (6.6%), Colombia with 16 articles (5.5%), Venezuela with six articles (2.1%), Costa Rica with four articles (1.4%), Bolivia and Peru with three articles (1%) each, and El Salvador and Ecuador with one article (0.3%) each.

Available Research Information by Decade and Theme of Interest

The time frame for studies conducted in LAC that were included for any of the themes of interest was 44 years, from 1973 to October 2017 (**Figure 5A**). During that time frame, 400 studies were identified that analyzed various themes. The difference in the article count between variables is detailed in **Figure 2**, and it was caused because some articles referred to more than one theme. For example, Cordano and Virgilio studied themes IV, V, VI, and VIII, contributing five articles to the total count for the various themes (21). Since 1973, the number of selected studies that were conducted in LAC and that related to at least one of the themes of interest has significantly increased over time (**Figure 5A**). In the 1970s and 1980s, seven of 400 studies (1.75%) were published; in the 1990s, 31/400 (7.75%) were published; in the 2000s, 93/400 (23.2%) were published; and between 2010 and October 2017, 270/400 (67.5%) were published.

When analyzing the information by theme (**Figure 5B**), themes VIII (155/400 articles; 38.8%), V (88/400 articles; 22%), III (68/400 articles; 17%), and I (45/400 articles; 11.25%) were identified as the most studied, while themes II (19/400; 4.7%), VI (20/400; 5%), IV (6/400; 1.5%), and VII (1/400; 0.25%) were the least studied (in descending order based on the number of studies that were identified in this scoping review). **Figure 5C** shows the number of articles included by theme of interest and by publication decade. Themes that show a consistent increase in the number of articles published over time were themes I, II, III, V, and VIII, while themes IV and VI maintained a similarly low number of published articles. Theme VIII was the most studied theme in LAC (155 of 400 articles; 38.8%).

Gaps Identified in the Selected Articles

The gaps that were most frequently reported in the identified articles focused on conducting more research in the following areas: (1) resistance transfer; (2) AMR surveillance; (3) evaluating the health impact of AMR; and (4) improving water treatment for AMR removal. Further analysis of these four gaps is presented in the discussion section.

DISCUSSION

The main objective of this scoping review was to examine the available information to identify research and/or information gaps regarding eight themes of interest for AMR in water in LAC.

Available Research Information by Country, Decade, and/or Theme

There were considerable differences in the number of articles identified by LAC countries, with Brazil having noticeably more articles published that were related to the themes of interest than other LAC countries. One of the many explanations for this difference is the gross domestic expenditure on research and development (GERD) as a percentage of the gross domestic product (GDP) of each country (19). Brazil was shown to have the highest GERD as a percentage of GDP in LAC counties (**Figure 3**). Chile is in the sixth position regarding GERD, and it is the second country in LAC to conduct research on any of the themes of interest, indicating that AMR is of interest to researchers in that country. In addition, Ecuador and Uruguay have a similar GERD compared to Chile, but there was little or no research on any of the AMR themes of interest identified in Ecuador and Uruguay, while Chile was the second country in LAC with more articles related to the themes of interest published. Little to no research was identified for Panama, Nicaragua, Paraguay, Peru, El Salvador, and Guatemala, which could be because of the low level of GERD and/or other country priorities.

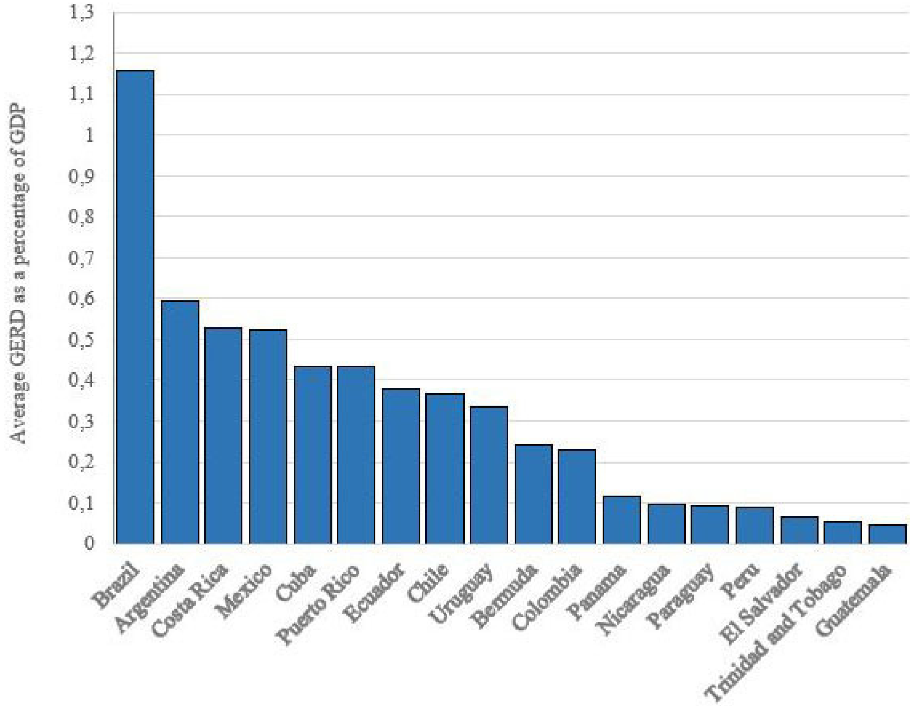

FIGURE 3 | Average of the gross domestic expenditure on research and development (GERD) as a percentage of the gross domestic product (GDP) for 2010–2015. Data were extracted from UNESCO (2018), and data for countries that are not shown in the figure were not reported.

FIGURE 4 | Map of the distribution of published articles included in this scoping review (number of articles included for the country [percentage of included articles at LAC level]). Map created using MAP tool in Microsoft Excel, Powered by Bing ©DSAT for MSFT, GeoNames, Microsoft, Navteq.

When analyzing the data by decade, although the number of studies conducted in LAC that were related to any of the themes of interest has considerably increased since 1973, the selected articles could be underrepresented because LAC researchers often publish in journals that are not indexed in major citation databases and they might not be identified in this scoping review (22). Furthermore, the results for the 2010s could also be underestimated because this period only included papers that

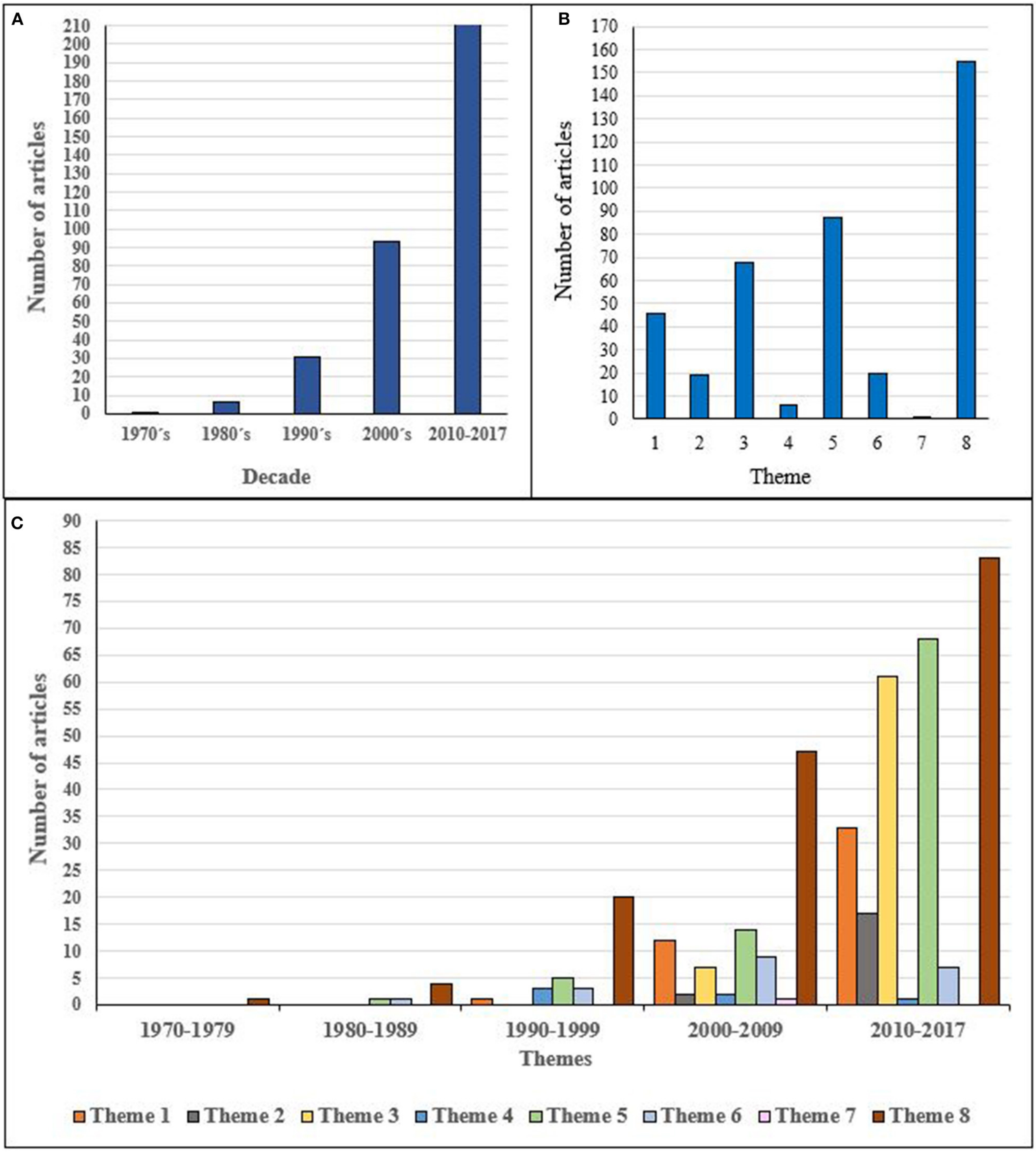

FIGURE 5 | (A) Number of articles for all themes published per decade; **(B)** Number of articles for each theme identified in the selected articles; **(C)** Themes published per decade. Themes: (1) Livestock and aquatic production systems as sources of antibiotic resistance in environmental water; (2) Negative or unexpected effects of AMR and antibiotics on terrestrial and aquatic wildlife living organisms; (3) Degradation of AMR in the environment; (4) Impact of the use of antimicrobials in agricultural production; (5) Transmission of antimicrobial resistance genes from both humans and animals through water and detection of microorganisms harboring detection genes; (6) Crossed antimicrobial resistance between antibiotics and heavy metals; (7) Emerging pests and diseases with potential impact in the production of AMR; (8) Detection of microorganisms with phenotypic evaluation of AMR in water.

were published up to October 2017. However, these data show that there were as many articles published from 2010 to 2017 as there were in previous decades (1980–2009), indicating a notable advancement in AMR research in water in the region. The results presented here follow a similar increasing trend compared to the publication records in Latin America that were reported by Van Noorden (22). The increase in the quantity of research that was identified in the last two decades could be because of the expanding economies in South America (22).

While this is a noticeable increase in the publication of articles regardless of the theme of interest that was studied, there are variations in the publications when the theme is considered. Research related to theme VIII was identified as the most studied theme between 1990 and 2017, and it was the earliest theme with published research. These studies relate to the phenotypic evaluation of AMR in water, focusing mostly on cultivable microorganisms that were pathogenic (e.g., *Vibrio cholerae*, *Shigella*), zoonotic (e.g., *Salmonella*, *Campylobacter*), commensal (e.g., *Escherichia coli*, *Enterococcus*), and environmental (e.g., *Aeromonas*, *Pseudomonas*, *Bacillus*). Furthermore, these studies characterized the antibiotic resistance profile using Kirby Bauer or minimum inhibitory concentration (MIC) upon isolation of microorganisms. While this is relevant information, most of the non-culturable bacteria are not included in these studies and might harbor antimicrobial resistance that has not been evaluated (23). This was the only theme in which a specific search algorithm was not applied (18). Caution is advised when interpreting the data for this theme, because the selection of articles for theme VIII was based on the search criteria that were used in all the other themes. Therefore, the data collected for theme VIII might be underestimated.

Theme V was the second most studied theme and it included articles that aimed to detect an antibiotic or heavy metal-resistant gene in bacterial microorganisms, or that evaluated the dissemination of these genes through plasmids, integrases, transposons, or other mobile genetic elements. The rapid development and current ability to use molecular cutting-edge technologies, such as high-throughput qPCR or whole genome sequencing (9), can explain the increase in publications on this theme. We expect that the number of studies that evaluate this topic will increase in the near future because genomics and metagenomics are methodologies that are becoming more accessible and inexpensive (24), providing relevant information that will cover many of the research gaps that were identified in this scoping review.

Theme III is related to reduction of AMR in water, and it was identified as the third most evaluated theme. Although the interest in theme III had a slow and late start, the number of articles published has been increasing since the year 2000, with the greatest increase in the 2010s. This can be explained by the global awareness that AMR in the environment is an actual concern, and therefore, methods to remove contaminants that are related to AMR (antibiotics, resistance genes, and resistant bacteria) in water are more frequently evaluated because it is crucial to reduce the AMR load in the environment. This theme is also interesting because when analyzing the data in detail, most of the selected studies corresponded to reduction of antimicrobials (antibiotics, antimicrobials, and/or anti-tuberculosis drugs). Few studies focused on reducing heavy metals and resistant bacteria harboring resistant genes or bacteria that were phenotypically identified as resistant to heavy metals or antibiotics. The number of studies that evaluated the reduction in antimicrobials, anti-tuberculosis drugs, and heavy metals could be underestimated because the search algorithms focused only on antibiotics. Only one of the selected studies evaluated the reduction of antimicrobial genes that were released by killing bacteria using the evaluated methods (25). Therefore, there is an urgent need to evaluate the reduction of heavy metals, resistant bacteria, and resistant genes in environmental water because all of them are associated with the AMR overall problem as the main sources of contamination (26).

Theme I relates to livestock and aquatic production systems as sources of antibiotic resistance in environmental water. The studies identified for this theme focused on terrestrial productive animals including cattle, dairy buffaloes, poultry, and swine, and on aquatic organisms such as fish, prawns, bivalves, algae, and aquatic amphibians. These studies evaluated the presence of antibiotic-resistant bacteria using phenotypic and genetic analysis. In most cases, bacterial studies correspond to the matrix evaluated. For example, in studies conducted on poultry, the target bacteria were mainly *Salmonella* or *Campylobacter*, and in those conducted on aquatic organisms, the target bacteria were mainly *Vibrio*, *Aeromonas*, and *Pseudomonas*. For this theme, none of the papers studied the link between the use of antimicrobials in animal production and generation of AMR in the environment, specifically in water. Instead, the papers focused on research that evaluated the presence of resistant microorganisms in feces of productive animals or the environment. In this scoping review, articles related to the evaluation of AMR in feces or productive animal premises were included under the assumption that the AMR detected in feces and premises could be disseminated at some point into environmental water. Articles that evaluated AMR in animal tissues were excluded because it was assumed that the presence of AMR microorganisms or genes from those tissues were not linked directly to environmental water. This agrees with global trends in which most of the studies investigated a link between animal production and human health, and mostly focused on foodborne and zoonotic pathogens, but without looking at the impact on the environment (7).

Theme II narrates the negative or unexpected effects of AMR and antibiotics on terrestrial and aquatic wildlife living organisms. Studies included in this category evaluated the impact of antibiotics or resistant bacteria on the health of only aquatic organisms (shellfish larvae, fish, shrimp, bivalves, crustaceans, amphibians, and algae), insects (Diptera), and the microbial community from the sediment in a water source. Studies related to terrestrial animals that consisted of evaluating the presence of AMR in feces or tissue without reporting negative health effects, were excluded. The health effects reported in the articles that were included for this theme could be categorized into the following two types of studies: (i) those that evaluated the health effects of antibiotics using *in vivo* models with outcomes such as survival rates, growth, cellular, and metabolic changes, among others;

and (ii) those that assessed the health effects of antimicrobial resistant bacteria and its relationship with outcomes such as disease, mortality, lesions, and outbreaks. These findings suggest that further research is needed to understand the health impact of AMR, especially on wildlife and terrestrial animals, which is currently lacking.

The number of published articles in themes I and II have also increased over time, although not as dramatically as for themes III, V, and VIII. From a global perspective, the link between the use of antimicrobials in production animals and the impact of AMR on the environment is controversial, and the problem caused by the existing link between antimicrobial drug use on farms and human health risks associated with antimicrobial resistant infections must be solved (7). Thus, more research regarding these topics should be conducted in the near future.

Themes with a similarly low number of published articles are themes IV and VI. The number of articles identified for theme IV was low and the publication rate has slowly decreased by decade since the 1990s, suggesting that this topic is not a priority for LAC countries. Theme IV corresponds to the impact of using antimicrobials in agricultural production. Each of the included studies investigated different produce (tomatoes, carrots, lettuce, and legumes). Moreover, these articles focused on the following three main groups of microorganisms: (i) foodborne pathogens (*Salmonella* and *E. coli*); (ii) phytopathogen (*Erwinia carotovora*); and (iii) soil associated bacteria (*Rhizobia* stains). The most frequent methodology was based on phenotypic evaluation of antibiotic resistance, and only one study focused on detection of bacteria harboring resistance genes for antibiotics. None of these studies focused on heavy metal resistance or on evaluating antimicrobial use in agriculture and the presence of antimicrobial resistant bacteria, focusing instead on detection of AMR in produce. Although the LAC region is considered to be an important agricultural producer for both local and international consumption, few studies were identified for this theme (27). A similar trend was identified for theme VI, which corresponded to evaluating cross-resistance between antibiotics and heavy metals. The articles selected for this theme consisted mostly of studies that detected microorganisms that were resistant to both antibiotics and heavy metals, but there was no specific research to identify and find an association between them. There was a reduction in the number of articles published in the 2010s. There are 2 years left before the beginning of the 2020 decade, and therefore, the number of papers for themes IV and VI could reach the same level as in the 2000s.

Theme VII, which is related to emerging pests and diseases with a potential impact on the production of AMR, was the least studied, with only one study identified (28). In this study, both pathogenic and environmental resistant bacteria were isolated from Mexican fruit flies, providing evidence that insects could play a role in disseminating AMR (28). More research on this theme must be conducted in LAC to provide information about the role insects play in disseminating AMR in the environment.

The trends identified in this scoping review could be explained by the worldwide relevance of the AMR problem and by the development of research infrastructure (laboratories and equipment), knowledge (universities, training courses, post graduate research, and training), and regional interest in the development and innovation (I+D) of research (e.g., creation of national commissions for scientific and technological Research in LAC) (22). Furthermore, the development and improvement of detection methods (cutting-edge technologies) such as whole genome sequencing (WGS) allow for more advanced research on AMR such as elucidation of the genetic mechanisms that underlie resistance in different multi-drug-resistant organisms and to characterize the relationship between antibiotic resistance determinants that are found in different human and environmental reservoirs (29). The FDA is using WGS to monitor pathogen occurrence and persistence in the environment and the food industry and to monitor for potentially emerging pathogens or development of antibiotic resistance (30, 31). Thus, an increase in research in theme V is expected.

Gaps Identified in the Selected Articles

Resistance Transfer

Several of the included studies agreed that more research should be conducted to evaluate resistance transfer, and two of these studies referred to the transmission among and between animals (32), especially those related to *Campylobacter jejuni* and animals besides broiler chickens and humans (33). The findings of this scoping review are consistent with this gap because most of the studies identified in theme I were conducted on poultry. Other studies referred to the need for research related to the resistance transfer into the environment. Research on AMR transfer in wastewater (34), hospitals, hospital effluents, natural environments (35–37), and irrigation canal sediments and vegetable surfaces (38) was reported as essential. Many of the articles included in this scoping review were conducted in wastewater, especially hospital sewage, and within the themes that were related to AMR transfer (themes V and VI). Few studies conducted on AMR in produce were identified and included, which is consistent with the knowledge gap reported by Roe et al. (38). Several articles reported that there is a need to study the mechanisms and molecular basis of AMR transfer and spread to and among microorganisms (39, 40), especially to those of clinical relevance for animals and/or humans (41–43). Because research on theme V has been increasing significantly in the last decade, in addition to molecular methods becoming more accessible and affordable, more research is expected to be conducted to fill this gap.

AMR Surveillance

Several of the selected articles in this scoping review frequently reported the need for more AMR surveillance and monitoring to evaluate undesirable consequences on the surrounding environments (44), the local biota, and population health (45, 46). In addition, it was reported that surveillance to better understand the emergence and spread of AMR in microbiota in hatcheries and salmon farms is also needed (44, 47). This agrees with the small number of articles that were identified for theme II in this scoping review. Several studies suggested the needed for continuous surveillance and monitoring for the emergence and spread of AMR (48, 49). Among the studies conducted on aquiculture, Miranda et al. (50) indicated that a surveillance program is necessary to monitor the continuing evolution of distribution of tetracycline genes in fish farm environment outside Japan, Europe, and North America. This gap and the few articles that were identified in the themes of interest in this scoping review emphasize the need for more research in this area in LAC. The same author indicated that surveillance to document the spread of antibacterial resistance in microbiota associated with scallop larvae and rearing hatcheries in Chile is also required (44), especially for florfenicol resistance (47). Aizawa et al. (51) pointed out the need to evaluate the changes in the epidemiology and frequency of extended spectrum beta-lactamases (ESBLs) in different ecosystems and animal hosts. This is in agreement with Palhares et al. (52), who stressed the need for detection of antibiotic resistance in microorganisms in basins that are characterized by intensive animal production. The few articles conducted in superficial water and related to themes I and VIII that were identified in this scoping review focused on aquiculture water rather than water in proximity to terrestrial animal production, which also highlights the need for more research on this topic. Based on the information provided by some of the selected studies, continuous surveillance and monitoring using molecular techniques are critical to better understand of the emergence and spread of AMR in aquatic and terrestrial environment and their microbiota.

Evaluation of the Health Impact of AMR

Gaps related to evaluation of the AMR health impact in aquatic organisms were reported most frequently. Expanding knowledge about the consequences of sub-lethal effects and chronic exposure to antimicrobials and their metabolites in aquatic invertebrates, fish, other aquatic species, and aquatic environment was identified as an important necessity (53, 54). Peltzer et al. (55) pointed out the need for additional risk assessments to show bioaccumulation of antibiotics in tissue and organs of amphibian larvae and consequently ecological impairments in water and aquatic system sediments. Several authors pointed out the need for toxicological studies to evaluate and better understand the health risk that these bacteria may present (54, 56, 57). However, toxicological evaluation was not included in this scoping review because the focus was on AMR in the water. In addition, the aquatic organisms that were mainly studied corresponded to articles related to theme II, especially fish and aquatic invertebrates. Therefore, gaps related to aquatic organisms were expected. Controversially to the reports on fish, no studies conducted on wildlife or terrestrial productive species, including outbreaks occurring on terrestrial animals related to AMR, were identified in this review. Therefore, more studies are needed to expand the knowledge about the effect of AMR in these animal species.

Water Treatment

The theme that has the greatest increase over time has been the removal of AMR (theme III) and antibiotics from water. However, numerous gaps related to this area were identified in the selected studies, highlighting the necessity for more research to design more efficient ways of treating different wastewater (58) and aquiculture systems (59) to ensure the removal of AMR. More effective sewage treatment to remove pathogens (60, 61), suitable wastewater purification procedures before their discharge into receiving waters (62), and approaches that reduce environmental microbial contamination by hospitals (63) in developing countries (64) were identified as important measures that require implementation. To achieve efficient AMR removal from the water, re-evaluation of the criteria, laws, and regulations used to analyze the microbial quality of drinking water (65) and sewage treatment beyond hospitals (66) is required. Based on our knowledge, there are no water treatment regulations or laws that consider the removal of AMR from water. To create adequate policies, the environments that are potential sources of resistance traits that pose a threat to human populations need to be determined (67). In addition, greater use of massively paralleled deep sequencing approaches for community analysis to identify novel genes and indicators to assess water quality are also required (68). In summary, removal of AMR from water requires education and training, molecular methods to easily detect AMR in water, and adequate regulations and laws about AMR in water treatment plants especially in wastewater, aquiculture farms, and hospitals.

Recommendations Related to AMR in Water

Among the selected studies, several pointed out that to reduce the AMR problem, responsible prescription and use of antibiotics on productive animals, aquiculture farming, and humans is required (33, 69–71). Surveillance to establish accurate measures that eventually safeguard the effectiveness of last-resort antibiotics is also crucial to control AMR (72). This might be more important in developing countries because environmental risk associated with the use and emission of pharmaceuticals into the environment in developing countries might be higher than in developed countries, although more research in needed to test the validity of this hypothesis (73). Education and training for professionals about adequate drug prescribing is essential (52, 74) as well as education for farmers and the general public on the harm done by improperly using antimicrobials (52) are also control measures that could be implemented to reduce the AMR problem. In addition, regulations could be implemented on the sale of aquatic invertebrates (such as scallops) when antibiotics (such as florfenicol) has been used (75). Improving water treatment to address the AMR phenomenon, especially water associated with aquaculture systems and wastewater treatments, was another control measure that was reported to be required (59, 76, 77). These suggestions are in agreement with the WHO Global action plan on antimicrobial resistance, and therefore, are measures that urgently require implementation.

CONCLUSIONS AND KEY MESSAGES

Most of the research conducted in LAC that was identified in this scoping review was conducted in the present decade with Brazil as the main contributor to the study of AMR in the region, followed by Chile, Mexico, and Argentina. Although at least one scientific publication was identified for most of the LAC countries many countries (eight of 18 LAC countries evaluated) have not conducted research regarding AMR in water. This is a growing concern because the studies on the environmental situation for AMR is mainly driven by Brazil, Chile, Mexico, and Argentina, which represent almost 75% of the total area of the LAC region.

Overall, the most investigated themes were themes VIII (phenotypical selection of AMR in water) and V (molecular detection of resistance genes and plasmids in water). However, there is a rapid increase in research on theme III (degradation of AMR in water).

For theme III, most of the studies that were identified in this systematic review evaluated methods to remove either resistant microorganism or antibiotics. However, none of these studies evaluated the environmental impact of reducing resistant genes, microorganisms harboring resistant genes, or antibiotics or their residues from water. This means that no study was conducted to establish a threshold level of AMR in the environment to reach a significant beneficial impact in both humans and animal health. More studies should be conducted in these areas.

Although research on all the themes of interest was identified in at least one LAC country, there has been little research on themes I, II, IV, VI, and VII that was identified in this systematic review. For example, the only study that isolated resistant microorganisms from an insect was conducted in Mexico. Therefore, we suggest that research efforts and resources should be focused on studying these themes, without hindering the valuable research conducted on themes III, V, and VIII.

More research is needed in other LAC countries besides Brazil because studies from this country might be influencing the AMR reality of the entire LAC region. There is an urgent need for research from countries such as Uruguay, Paraguay, Guatemala, Honduras, Nicaragua, and Panama because no published articles were identified in these countries for any of the themes of interest. In addition, more research should be conducted on those countries with few publications identified such as Ecuador, El Salvador, Bolivia, Venezuela, and the Caribbean.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the article/**Supplementary Material**.

AUTHOR CONTRIBUTIONS

AM-S, DR, MC, DN, and AA contributed to the conception and design of the study, analyzed the results, contributed to the manuscript revision, and read and approved the submitted version. AM-S, DR, and AA followed the steps for a scoping review and collected the data for each one of the themes analyzed in this study. AA wrote the first draft of the manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2020.00546/full#supplementary-material

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